



Special Report

The International Consensus Classification of Mature Lymphoid Neoplasms: a report from the Clinical Advisory Committee

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REVIEW ARTICLE





LYMPHOMA

The 5th edition of the World Health Organization Classification of Haematolymphoid Tumours: Lymphoid Neoplasms

Rto Aleggio C. Catalina Areador C. Ioannis Aragnostogoules C. Ayuma D. Attygolic C. Ioannis Service de Oliveiro Araqio Centro Scotia Baget C. Annia Maria Sorges C. Daniel Boyer C. Marianta Catalina C. Anny Chadburn C. John K. C. Chan C. Whith Checke C. Wee Foo Ching C. John K. Choo C. Shin Sorge Chaining C. Sarah E. Coupland C. Magdalina Casder C. Sandope S. Daning C. Danina de Jang C. Ming-Ding Du C. Sandope S. Casar C. Coupland C. Magdalina Casder C. Sandope S. Daning C. Daniel de Jang C. Ming-Ding Du C. Sandope S. Casar C. Coupland C. Marian Hamis C. Marian Checker C. Marian Cardon C. Marian Hamis C. Marian Charles Hamis C. Marian Charles Charles C. Marian Cardon C. Marian Cardon C. Marian Charles C. Marian Cardon C. Marian Charles C. Marian Charles C. Marian Cardon C. Marian Charles C. Marian Cardon C. Marian Charles C. Marian Cardon C. Marian Charles C. Marian Charles C. Marian Cardon C. Marian Charles C. Marian Cardon C. Marian C. Mari

⇒ The Author's) 2022

We have present an avenum of the upsarroing 5° addition of the World health Disparlection Coverfication of Hadmentymphoid Turnous focusing on lymphoid neoplasms. We do and introcycline oplasms will be presented in a separate accompanying article. Builder litting the setting of the classification, we highlight and explain though from the revised 4° addition. These include reorganization of emitted by a higherthical system as is allogified throughout the 5° edition of the WHO dissolution of surround of all engar-species, madification of numericalities for some certains, revolute of disgressic entries or excitation of certain entities, and immediation of new emittees as ricks on of turnous like lessing measurements (select to lymph node and adding and germine precipations) syndroms associated with the lymphoid recordance.

(mintee (2022) 35:1720-1740; https://doi.org/10.1036/s41375-022-01529-2

INTRODUCTION

Estitement-based classification of disease is fundamental for the teatment of individual parimets, monitoring of global disease incidence, and investigating all aspects of disease cascation, presention and therapy. The World Health Organization (WHO) classification of lymphoid tumours has provided a global reference for the diagnosts of lymphoid resolvents stack in 3° edition in 300 [1] which was based on the REAL Classification developed by the International Lymphomo Study Group (ILSG) in the carry 1990s [2]. The definitions laid down in the successive WHO classifications [3, 4] have not only been adopted for use by parthologists, clinicians, and basis and translational research significant. Classification of Diseases ICDI codes, and thereby serve as a global seference for epidemiological manifoling across

national and international health policy organizations. In this article, we provide the conceptual framework and evapor dynamin in lymphoid neoplaints in the spotaving 5th collision of the WHO Classification of Harmatslymphoid Tumous (MHO HAEMS) scheduled to be published in 2022. An overview of myeloid neoplasms will be published separately.

The international Agency for Research on Contor (MRC) instance the process sulminating in WHO-HARMS in 2018 by laying out the generative rules and classification principles for the critic all Edition series of the WHO classification of tumours, comprising 14 waternes, each declarated to neoplasts of specific organ systems and/or deficial contexts (Preclaric Tumours and Genetic Tumour Syndromes), in 2021, expert members of the editional board and suptions wavelimited to contribute to WHO-HARMS based on their records of dispressor and/or scientific expertise, explorat

Received 3 May 2022 Box Seed 17 May 2022 Scorped, 26 May 2022 Published soline: 22 June 2022

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Cutaneous lymphomas

WHO 5ed

Mycosis fungoides & variants

Sézary syndrome

Adult T-cell leukemia/lymphoma

Cutaneous CD30+ lymphopr. disorders

Cutaneous anaplastic large cell lymphoma

Lymphomatoid papulosis

Subcutaneous panniculitis-like T-cell lymphoma

Cut. extranodal NK/T-lymphoma, nasal-type

Cutaneous γ/δ T-cell lymphoma

Aggressive epidermotropic CD8+ CTCL

SMPCD4+T-cell lymphoprolif. disorder

Acral CD8+ T-cell lymphoproliferative disorder

Systemic chronic active EBV disease

Peripheral T-cell lymphoma, NOS

Cutaneous marginal zone lymphoma

Cutaneous follicle center lymphoma

Diffuse large B-cell lymphoma, leg-type

Intravascular large B-cell lymphoma

EBV+ mucocutaneous ulcer

International Consensus Classification 2022

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Acral CD8+ T-cell lymphoproliferative disorder

Chronic active EBV infection

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Cutaneous marginal zone lymphopr. disorder

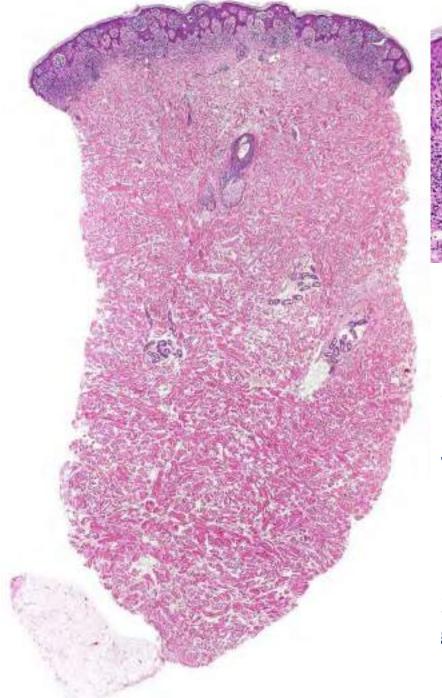
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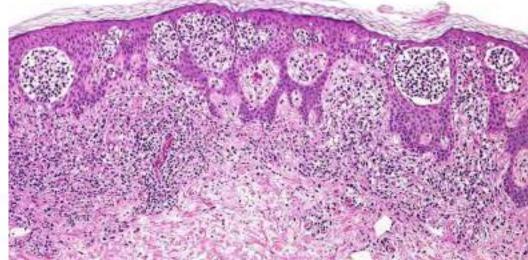
Diffuse large B-cell lymphoma, leg-type

Intravascular large B-cell lymphoma

EBV+ mucocutaneous ulcer

Lympheul Neoplesies: a report from the Clinical

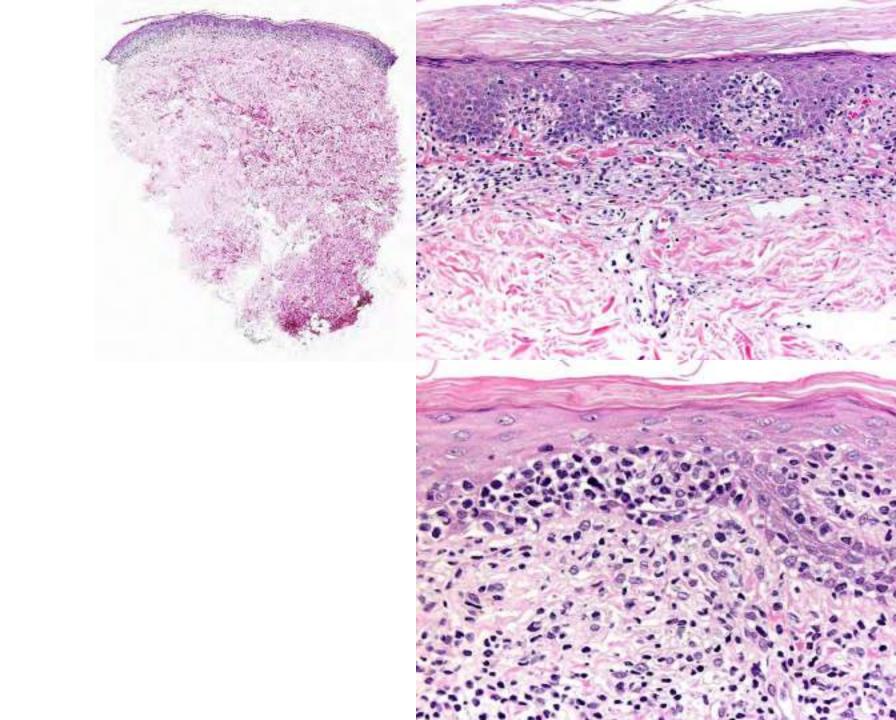


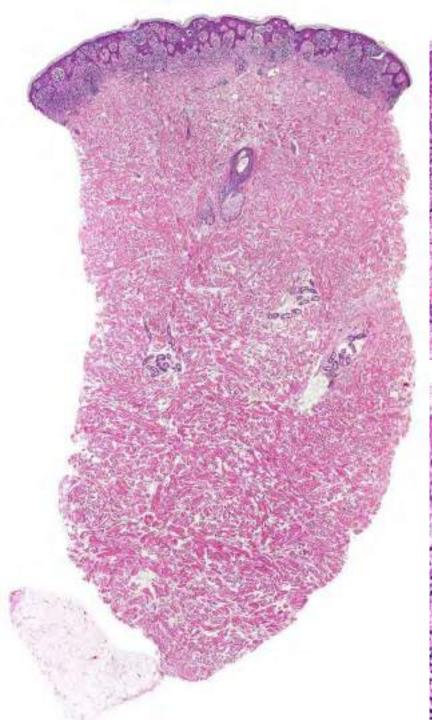


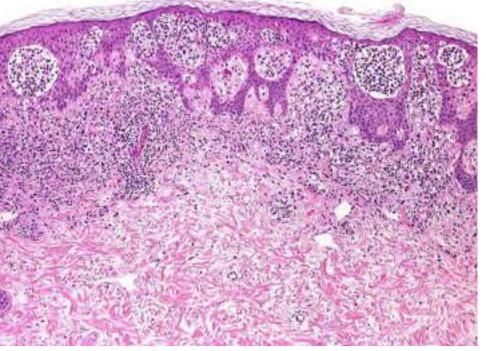
Mycosis fungoides

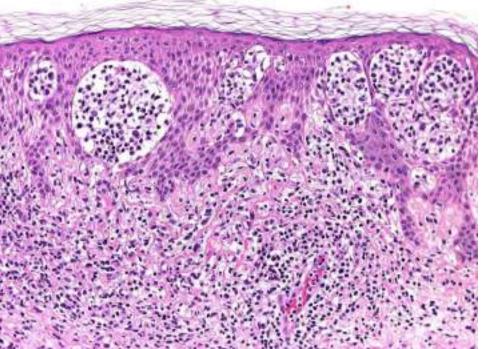
Represents the most common cutaneous T-cell lymphoma and is characterized by a chronic, indolent course. Histology shows in early stages band-like, epidermotropic infiltrates, sometimes with formation of intraepidermal collections of lymphocytes (Darier nests). The phenotype is mostly CD4+ T-helper (may by CD8+ or γ/δ +). In later stages formation of tumors.

Four main clinicopathological variants: 1) "classic"; 2) adnexotropic; 3) pagetoid reticulosis; 4) granulomatous slack skin.









Histopathologic Features of Early (Patch) Lesions of Mycosis Fungoides

A Morphologic Study on 745 Biopsy Specimens From 427 Patients

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PATIENTS AND METHODS

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Cutaneous Eruption Limited to Skin Covered by a Swimming Suit

Renato Grilli, MD; Luísa Soriano, MD; Carmen Fariña, MD; Lucia Martin, MD; Luis Requena, MD; Fundación Jiménez Diaz, Madrid, Spain

REPORT OF A CASE

A 72-year-old white woman with a history of hypertension that had been treated in the past with nifedipine presented with an asymptomatic cutaneous eruption that was limited to the skin covered by her swimming suit. The eruption had first appeared 3 years earlier, and she attributed its origin to a new swimming suit that she had worn during the summer when the rash first appeared. The next 2 summers she had worn the same swimming suit, without noting any change in the cutaneous lesions. Her primary care physician attributed the eruption to nifedipine use and changed her medication to verapamil, but the cutaneous lesions remained unchanged. The patient did not use any underwear that covered the same areas as her swimming suit.

Physical examination revealed a cutaneous eruption that was limited to the areas of the skin that had been covered by the swimming suit. The eruption consisted of erythema, scaling, and telangiectases (Figure 1 and



Figure 2.

Figure 2), Skin folds under the breasts and redundant abdominal wall were less affected. The rest of the physical findings were within normal limits.

The results of patch testing with standard textile resins and dye trays were negative.

A cutaneous biopsy specimen was obtained from the lesions on the abdominal wall (Figure 3 and Figure 4). What is your diagnosis?

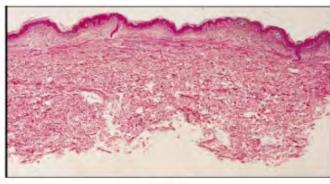


Figure 3.

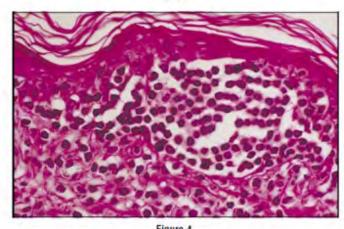
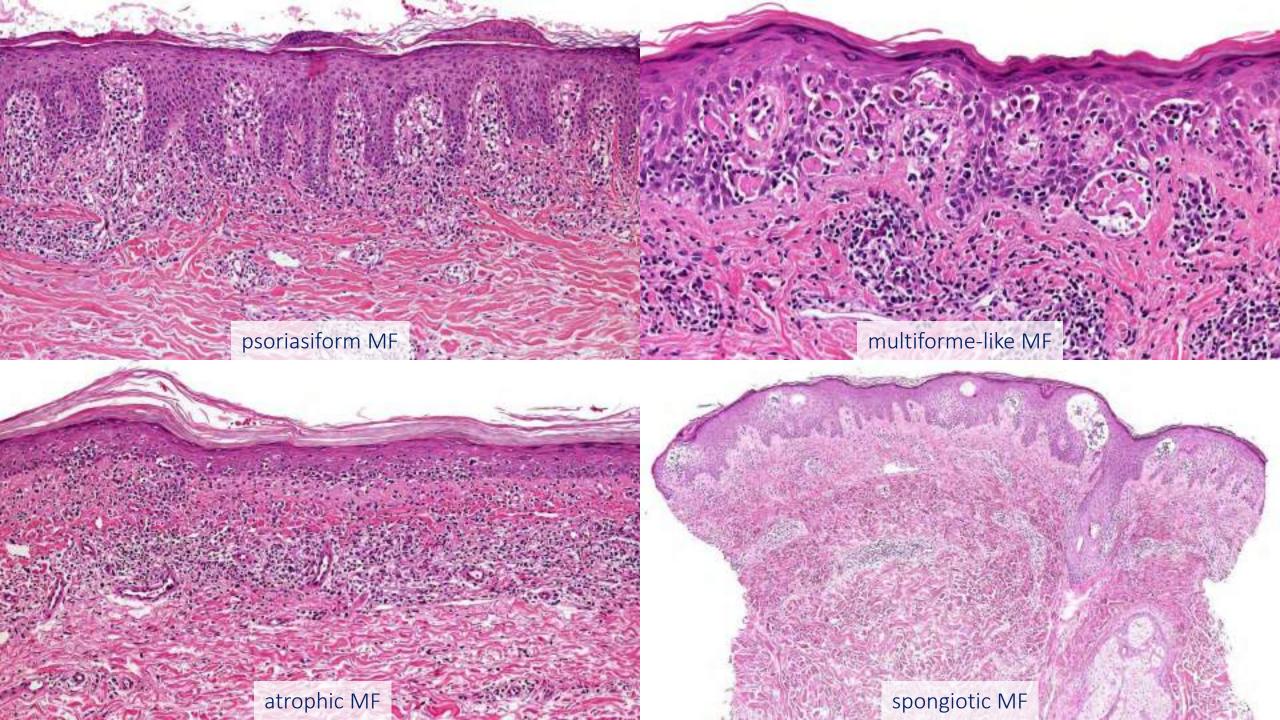




Figure 1.



Histopathologic Features of Early (Patch) Lesions of Mycosis Fungoides

A Morphologic Study on 745 Biopsy Specimens From 427 Patients

Centre Massing, MD, of Kazno Kodimu, MD, of Helmin Keel, MD, and Lorenza Cestoni, MD+

Alletract: The kinologic diagnosis of ourly pycosis fauguitles (MF) is our of the most vehicle problems in demantipatiology. We ornicwool the histopethologic features of 745 biogry specimena from 427 patients (mile femile 277, 158); medianage, 12 years mage, 3 95 years with such (petch) brimes of MO collected from the beginness distance of the Department of Demokskip of the Moderal University of Circa (Austria). In all potents, the diagnosis was established by elizicopathologic correlation. The most reasons histopothologic yieldon consisted of a buist-like or patche lichenoid. indiffure admisss with count bundles of colleger in the superficial demois. Egidemiorisphinism from placy in was observed to man cases in one or more farms (single famely/size mideral/torsion, 22%; burfar lymphacytes. 25% Pleatier's pricontinuous. 19%: "baked" Newhorster, 47%: disproportional: expectable, 17%; pagetoid quite: metropian. Phi) in 4% of cases, qual-metropian was completely moving. Applied hymphocytes used present only in \$5% of cases. Features of inharines domaittie was absented at 50% of cases. Office mount findings was the presence of mondo haratesayus. (21%). melanginess (PG), sed entragantul architectus (Phi). In 29 parameter, more or many his generalist on or the paper divide different body sites showed different testamalishings suggests, engleshing the process. formers of MF even as a displic patient at a given time. Our study expends previous observations on histographologic finances of early holong of MF Although sporetrum the kinnentiologic riprints stona diagrassic, they should be unsidered consisters with MF and the rate rate out the disgression.

Key Words: myses finguists, parasons Deck frephone, early dispusse, hosepathologic factores

Lin J. Surg Haled 2005;29:550-5001

The histologic diagnosis of early (pendit bettern of mycons) flurgoides (AIP) is often difficult because the histoprihologic features may straighte a curiery of influrmatory skin disorders, indeed before the delization of procise criteria by Kerl and Kreabsch²⁸ and Sanchez and Ackermann¹⁸ in 1976, the branchtologic fathers of those lessons were considered in the monspecific. * **Orbital**** "and participate mode the diagnosis of MF only in cases therefore the projection maked by hyperchaomatic, cerebrikem hymphocytes in the spidenmis forming the so-called Parasich inknownesses. **Orbital the years, several audious mempinal to refine the interparticipate criteria for diagnosis of carly lexions of MS (**SSS******). For the diagnosis and differential diagnosis of these lesions are still considered one of the most voting problems in derivationaries.

We on several the histopothologic florance of 146 biopsy, specimens from 427 patients with early (putch) become of MF to define the aspects that may be beinful the histologic diagnosis of early become of the disease.

PATIENTS AND METHODS

Buts from 463 patients with early lesions of MF mess retrieved from the lightplurms debibour of the Department of Decreasingly, Medical University of Great (Austra). Thirty-cit. ensus were excluded because bionsy apenimens were technically tradequate or because of link of exact classed informations. A total of 745 hiopsy specimens from 427 perfores made famale utio = 1.8%; mean age, 57.2 years, median age, 52 years; age range, 3-95 years) with early spatch; leaves of MF were available for the study. The diagraphs of MF was continued in all case by constituin with the clinical features leaber observing. personally the parient in the outpresson service for cutureouslymphones of the Department of Demandagy, Medical University of Genz. Genz. Austria, or reviewing the potient's struct and elisinal granuous. Tropolox some taken as rown of disease or from recovery powher. Biopsies obtained under empoting treatment were not included.

Cases of Secury syndrome or epidermotropic natureness. T-cell lymphomas other than MF were excluded. We also accluded patients with so-celled "social plaques purapounters" because of the controverses concerning classification of these cases, and patients with MF associated with following magnetics.

Histology

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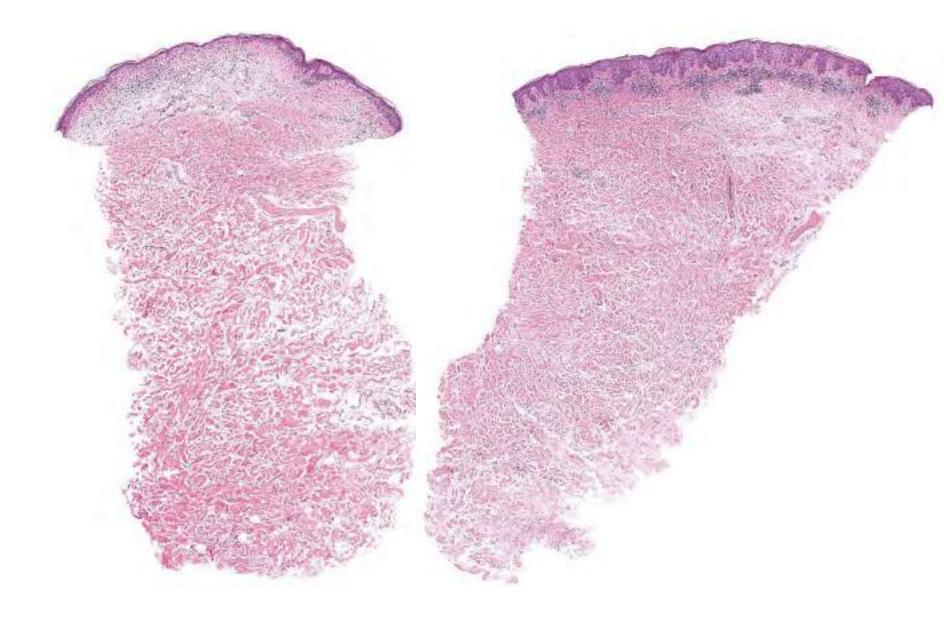
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TABLE 1. Histologic Features of Early (Patch) Lesions of MF Observed in 745 Biopsy Specimens

Feature	No. (%)	
Normal epidermis	356 (48)	
Psoriasiform hyperplasia	258 (35)	
Irregular hyperplasia	34 (4)	
Flat and/or atrophic epidermis	97 (13)	
Marked spongiosis	28 (4)	
Necrotic keratinocytes	172 (23)	
Changes at the dermoepidermal junction		
Focal interface dermatitis	438 (59)	
Widespread interface dermatitis	30 (4)	
Epidermotropism*		
Single lymphocyte epidermotropism	161 (22)	
Basilar lymphocytes	170 (23)	
Pautrier's microabscesses	140 (19)	
"Haloed" lymphocytes	298 (40)	
Disproportion exocytosis	124 (17)	
Pagetoid epidermotropism	17 (3)	
Absence of epidermotropism	32 (4)	
Atypical lymphocytes		
Only in the epidermis	27 (4)	
Both in epidermis and dermis	38 (5)	
Only in the dermis	2 (0.3)	
Dermal lymphocytic infiltrate		
Band-like	227 (30)	
Patchy-lichenoid	492 (66)	
Superficial perivascular	26 (3)	
Dermal changes		
Papillary dermal fibrosis/coarse collagen bundles	725 (97)	
Melanophages	56 (8)	
Purpura	32 (4)	
Edema of the papillary dermis	0	

^{*}More than one feature was observed in some cases.



2 biopsies taken on the same day

LORENZO CERRONI

SKIN LYMPHOMA

THE ILLUSTRATED GUIDE

FIFTH EDITION







WILEY Blackwell

CHAPTER 3 Mycosis fungoides

Alycests languides in the most cummon type of cataneous. lumphomic representing almost 50% of all lymphomic arriving. grimorily in the skir [1-4]. It is defined as a tamor composed of small/medium-stood epidermotropic T-beiper lymphocytes. (but I cytotoxic variants are not unconsenue, and neoplastic cells may be medium/large in advanced stages).

Mycosic fungetees is the sidest entity in the field of cutaneous Imphomas, having been described more than two centuries ago, in 1806, by the French dermanologist Allinest Traditionally it is divided into these clinical phases; parch, plaque, and remorstage. The clinical course can be protracted over years or becades. In the 2018 appear of the Gossification of cinasposis lymphomas by the European Organization for Research and Treatment of Career (EOKTC)/World Health Organization: (WHO) [1] and in the WHO Chargeaven of Inneses of Harricanistic and Loophold Tisses, the term 'my mais fongardes" to restricted to the classic type of the disease (so-called Affinery-Battin), characterized by the typical slow evolution and with early mycosia languides unither progress to tumor stage nor show extracutationis munifestations of the disease [5, 6]. Philipping and general studies alsowed that entities described. of the root in "rapidly progressive" invoises fangoides (e.g., securit. Sungrides a traverse directive, generalized pagetoté. mount of aggressive continents cytotoxic natural killer (NKET-Ill is repharmay (see Chapter 7).

- "cases III'c with many regional variations and with a regular victorie in regent devades (7, 8). A stabilization of the incidence two been nated in the Emiled States in the period 1998-2009 [9]. there is a frigher medicine in black parients (10), and the marage use of anion seems to be younger for black than for white pacients () U.

In operator decades of research, the encourge of exposus tangennew company automics. A genute-predisposition may play a role. or same com. A tignifial suggested of the above has been reported in a time resummer including disease most in identical from 112-161, but a large scale on Danich patrions showed that thems of patients affected by anyonest largeades or Sezary

productie did not develop the disease after a median period at observation of 20 years image: 3-40 years) (15). A study conducted among livarily lewish patients showed a significantly greater alicle frequency of HLA DQBI'03, suggesting that genertic factors may play a role in the etiology of the disease, at least in selected groups of patients [36]. On the other hand, reversia languides has been rarely abserved in unrelated married individuals, pointing to the custence of erroremental factors [17], for this context, a study on learnin veteriris confirmed to have exposure to suffer mustard during the tray-from our of the 1980s. showed as increased incidence of mycesis fungoides compared with the frances, general pupilistion (18). Association with longterm exposure to various allergers and association with chronic skin disorders have also been suggested as possible etiologic betom, but no epidensologic study confirmed these hypotheses beyond doubt. In this context, it has been suggested that bacterul triggers may be involved in disease unset and progression. and staphylococcal enversation A elimitates STAT3 activation. protected cores (1, 3). It is estimated that over 90% of patients and IL 17 experience 1(9, 20). STATS is implied in neoplastic cell survival in revcests fungoides [22]. In fact, antibiotic treatment induces a reduction of the tumor liquiden in advanced stages (see section on thermy below in this chapter). A relationthip with floratia harplorfor infection, human T-lymphoropic virus I (HTLV-I), cytomegalovinus (CMV), human herpesvirus *Hardman - Keirme-Goodman) are better classified among the HHIV 6. Method cell polynometrus (MCPyV), and Epitein-Barr (irus (EBV) his ofm been investigated, but se far a link is infectious agents could not be demonstrated [22, 23]. The incidence of the disease confidence is probably around. Interestingly, reversity fungaides has been observed rarely in patients who received solid organ transplicatation, suggesting that immune suppression may contribute to the development of the disease [24, 25]. In one exceptional case, mycosis furgoides has been acquired as a donor-derived muligrancy following influed-inensity hematopoietic stem cell transplantation from a matched untriated donor [26]. In short, genetic background, environmental factors, chooses: artigenic stimulation, and exposure to carcarogenic agents seem to play a role in myoneis. fingoides (as in many other human cancers), but the frame keeping all of these factors together is still choose.

> Correctio alternations have been identified marrily in late stages of the disease, and their appartunce for disease mitiation is

Table 3.4 Clinicopathologic and phenotypic variants of myceus fungoides

Clinical variants with "conventional" histopathological features

Acurthous regricers-like mycoss fungoides.

Atopic demartis-like nycess fungades'

Enythrodermic mycosis fungoides

Hypopigniented mycosis fungoides

Elithyoulorm mycosis fungostes

Falmoplantar mycosis fungoides.

Fapular mycoss fungocies

Expulserythroderms of Offuji (subset of cases)

Paragisonasis Clarge patch") (for a discussion on small and large patch) paraponiusis, see Chapter 23

Perioral dermatris-like mycosis fungordes

Phynaia Ichenoides-like mycola fungoides (clinical variant)

Promodern mycous fungodes

Universional (scritting) mycosa fungoines

Zimberform invoces fungoides

Clinical variants with peculiar histopethological features

Authenotropic mycesh lungoides, including printropic flohiculobapia. miscoss fungaides (with as without folloular miscossis), mycosis fungodes with eruptive infundabiliar gists and corredones, and syntholic mycasis fungoras:

Anertodermic mycosia fungodes (myrosus fungardes weft secondary anespecimic (secondary anetoderma may be observed also in generalized foliative musinosal

Bullings (versulabulinus) myspen fungasass

Dyshidrotic microsis fungacies

Loidermai mucinous in mystosis fungades.

Granulorisdous sweet skin.

Hyperpiginented mycosis fungoides

"invisible" mysasis fungoides

Pageloid eticslose (Wormger-Kolopp type)

Polkrode/matous mycosis fungoides

Funputic mycosis fungoides

Further mycosis fungaides

Verrupous/typersenatosic medess fungoides

Histopathological variants

Ahrudar Etheroid dermastis of youth-like mycosia fungoides

Cramatomatous mycosis fungardes -

Intersatium recognification and a fundamental

Large cet transformation.

Physicus Icheroscies-Hormscore hangoides distopathelogical variants

Schroung mycosis lungoides (lichen adelowa-like)

Phenotypic variants'

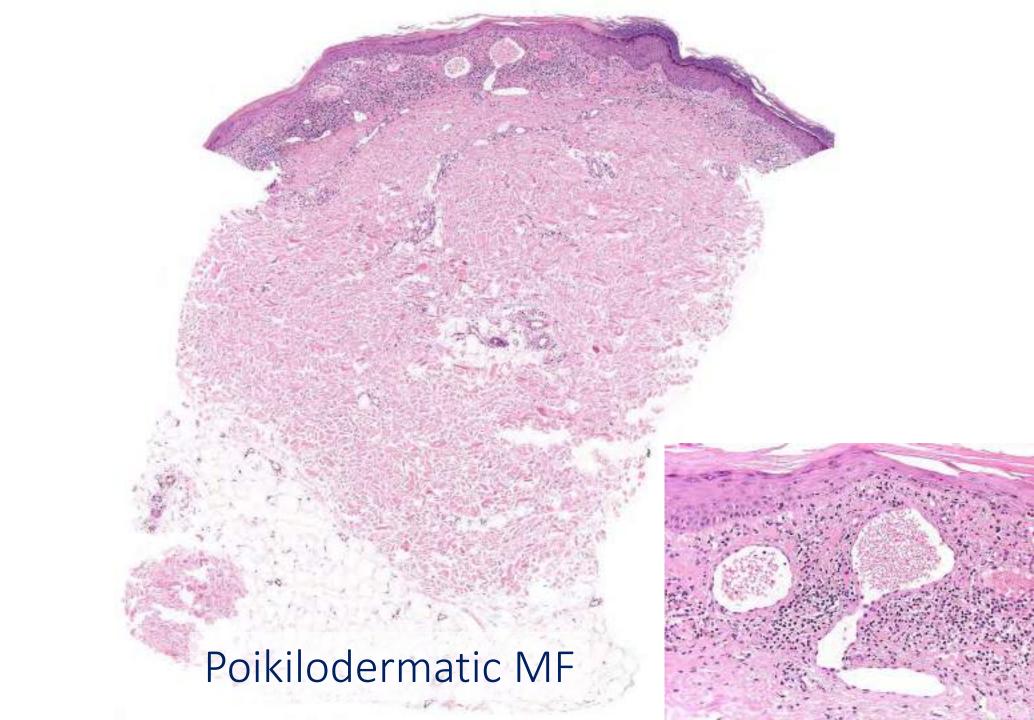
Extratoxic myrosis tungoides ICDP undior yW: sawly CD4" with expression of sytotoxic proteins)

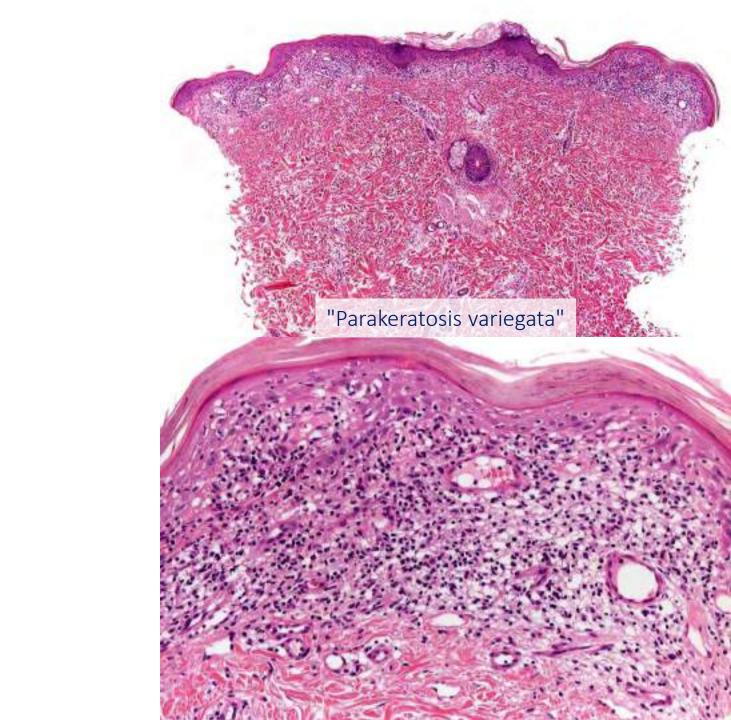
Mycoss fungados with T fallicular helper (T_m) phenotype Mycomic fungoides with T-regulatory (Trag) phanotype

 Histogramologically characterized often by variable spongratic changes.

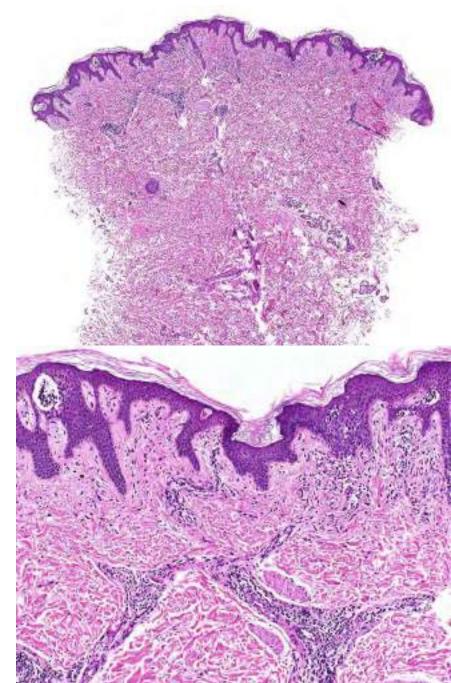
Notiopic mycous fungoids; and syringstropic mycost fungoids may be observed independently from one another, but in many instances of sympotropic mycoss fungation the hair follows are involved as well. Thus the term advesorropic mycosis lungaries better reflects the direcognitiological leatures of the variant of the disease. *A phanotypic switch may occur in sequential biopixes, and sometimes different phenotypic features are present in different biopses taken on tifve server day.

the boyease. To disposed to advice the common Corner.





Hypopigmented MF



Papular MF

Papular Mycosis Fungoides Is a Distinctive Variant of Early-stage Mycosis Fungoides

Extended Retrospective Study With Long-term Follow-up

Andrea Saggint, MD,* † Regina Fink-Puches, MD,* Carlo Cena, MD,‡ Viriana Eora, MD,‡ Heide Potzingen, MD,* Cesare Massone, MD,§ and Lorenzo Cerroni, MD*

Abstract: Partiler reveous fungantes (PMF) is a rate various of inyonsis flugioldes (MF). The exact rounlings and prognosis of PMF are still and/or. We reproportisely identified cases of PMF then the tiles of the Department of Departmetagy of the Medical University of Graz. Austria, said checked the following data. The polients composed 13 men and 5 women (median age: 51.5 c. mays. 13 to 77 %. In 4 potents, an initial distempelationals diagmajo of appear posturals lichenoides was made, these cases were tablequently polassified as PMI due to the open of conventional patches of MF during follow-up: Follow-up data of our cases showed that 2 patients died of disease progression 50 unit-199 months after the flow presentation, respectively. Two potents our alive with projectors observe after 215 and 500 months, reapactively. For parameter are alive with stable disease (creditor: 70) met. Four potients were in complete remission at but follow-upviii) (median: 215 me; 3 of them died of arrelated causes). Our data confirm that PMF represents a dividopetrologic variant of early MP with prognosic signiliar to conventional precentations of the disease. Familianty with PMF and statement from other oufunction pupilier brophoid profilerations is necessary for a precise disgnotic and evangement of these patients.

Kry Words: repcons despoides, popular repcons despoides, bymphomacoid populosis, physicis lichenoides, cuomeson T-cell bymphoma

(An J Suy Polist 2004/3/1129-1134)

Mycosis Paugoides (MF) is the most vommon type of primary cutomous T-cell lymphoma. In early stages, it is characterized clinically by the presence of irregular erythemators gatches iso-called patch-stage of MF1.1 In 2005, our group described a clinical variant of MF characterized at ones by the presence of small popular other than patches (papular MF—PMF).2 Following our initial study, a few tree reports of PMF with limited following data have been published.1-11 Soute authors treve questimed whether PMF exists suggesting that most cures may be resented as a seatom of hypothematoral graphicals (LAP) type R 22.0.

We present the long-term follow-up of the 6 cases first reported in 2005 describing in addition 12 novel cases of PSEF

METHODS

A total of 18 cases of patanta with PMF were rerieved from the files of the Research Unit Dermatopathology, Department of Dermatology, Medical University of Graz, Austria, Six of these cases were included in the original publication. Clinical data were avoidable for off patients. The histopothologic diagnosis of MF was made according to the criteria listed in the World Health Orgasization (WHO), classification of numers of huntatopoietic and lymphoid tissues published in 2017 (fourth revised actions.) The study has been approved by the othical committee of the Medical University of Graz.

RESULTS

Classial and follow-up data of all patients are summargred in Table 1. The patients comprised 15 men and 5 momen. Age at first diagnosis remond from 13 to 77 years fraedim: 57.5 s). Clinically, all patients showed, at first presentation, small erythernatous, partly scaly popules in the altience of patches.or playtes (Figs. 1, 2). The issions store located on the trunk (industing traffactor & patients), trunk and examilies ()] reatents), or lower extremities (1 reating). A drag graption could be encluded in all cases by the abunca of portitent history. In all cases, the diagnosis of PMF was confirmed by one or more biotoses with histopathologic features of MA: large cell transformation was observed to subsequent biopsies. in I cases. No involvement of hor fallicles or corine glands was present. Intromobiotochemistry proceded a conventional phenotype (CD4"/CD8") in 14 cases, while 4 cases displayed a critatoric elemetype (2 being CD4/XCD8), and 2 double positive for CD4 and CD5 as well as for the sytotoxic protein. TIA-1). Staining for CD90 was negative in the first diagnostic. history in all of our cases. Moissian unabots of the Total

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18 patients (M:F = 13:5); Median age: 57,5 (range: 13-77)

M, 57 ((1-JAAD)	D- (239)	(bronchial carcinoma)
F, 58 ((2-JAAD)	A+ (215)	(progressive disease)
F, 57 ((3-JAAD)	D- (194)	(ovarian carcinoma)
M, 41 ((4-JAAD)	A+ (300)	(progressive disease)
M, 59 ((5-JAAD)	D+ (50)	(death of disease progression)
M, 61 ((6-JAAD)	A- (236)	(remission at last follow-up)
M, 77		A- (88)	(remission at last follow-up)
M, 49		D+ (199)	(death of disease progression)
M, 64		A+ (62)	(stable disease)
M, 55		A+ (107)	(stable disease)
F, 67		A+ (6)	(stable disease)
M, 68		A+ (113)	(stable disease)
M, 70		A+ (304)	(stable disease)
M, 76		A- (17)	(remission at last follow-up)
M, 13		A+ (20)	(stable disease)
M, 15		A+ (66)	(stable disease)
F, 43		A+ (46)	(stable disease)
F, 17		A+ (74)	(stable disease)
I .			

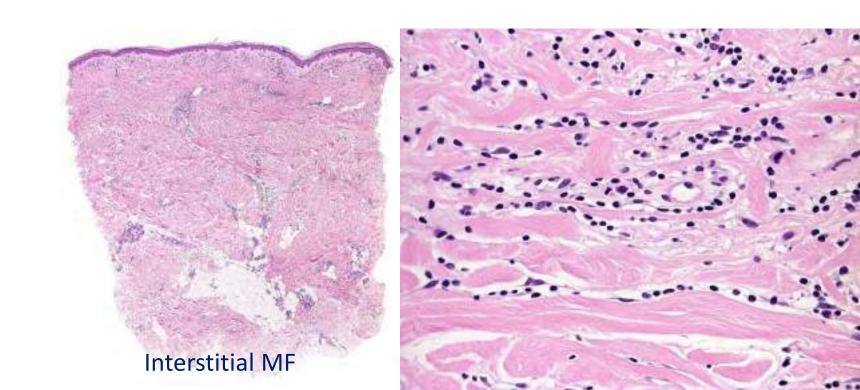
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Conflicts of interest and beaute of freeding. The outliers have disclosed from they have no significant catalogs days with, or francial interest to, any contractals compared parenting to this relate.

Correspondence Liverno Correal, MD. Deputation of Demokalogy Modern University of Grag. Asserbragging Str. 8, Grag. A 909. Austra. Journal (Compts arrest) Proceedings on 81.

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Are / Surg Pochal * Volume 43, Number 8, August 2019



Interstitial Mycosis Fungoides A Clinicopathologic Study of 21 Patients

Camillà Reggiani, MD,*† Cesare Massone, MD,*; Regina Fink-Puches, MD,* Carlo Cora; MD,‡
and Lorenzo Cerroni, MD*

Abstract Investigat myrosis fregordes (IMF) is a rure tistogorhologic vorting of reveals fraguldes (MF) that may mining other inflammatory democoses, mainly intentival granulous amuttee dillumentery member, and interstical monthsstatons dermititis. Ordy greatl turnes and sporadic case reports of IMF have been described in the literature. We reviewed 27 specimens from 21 parlants with IMF (M:F = 11:19), modiss aga-60) to better characterize clinical, histopathologic, and imuntuchistochemical features of this discuss. Most postents prosected clinically with purches and/or players. Consentional MF was documented before, componitant with, or other BMF in 12 potingly, Oherens only in 2 parameted illinear bropsics showed exchange features of IMF over a period of 4 and 191 months. respectively. Histology reveded in all cases surisbly long, Inner agarentes of demail Numbervies soleving the collision fibers. invelving predominants the superfictal and mid-dentric (6 cases) or the entire demos (21 cases). Immunohistodicusted statings resealed a systetonic phanetype in 9/18 seems mass. Variable amounts of histiocytesisnacrophages were found interminable in all tested biogsags but never represented a population threer fram that of T lymphres tay Our energy shows that IMF is a puralize variant of MF with frequent extensive phenotype. This incopechologic version to most cases regresses a translest nation in otherwise conventional MF. Accuracy dimergrathologic corretotion and girenotypic strates of atypical demail intervibal tymphohistocytic satisfrans allow to make a corner diagnosis.

Key Words: myoute fungendes interacted myouse languistics, outsieven Veeli lymphosis, Verteronic lymphosites

Lin. J.Say Femiral 2016 (20.1380-1387)

Pean the "Remarch Unit Demantsporterings: Department of Demantalogy, Medical Charcesis of Groz, Graz, Austra, (Department of Demantology, Convessity of Medican and Regges Gualia, Medican (Department of Demantology, Galliera Licenter, and Education of Demantology, Galliera Demantological Entirety, British Intel.

Cardiott of Interest and Source of Fourling. The authors have distorted that they have use significant artificiated by with, or thousand narrows in, any consumeral companies permissing to the artificial

Coreap-outring Lemons Corona, MD, Rasunch Coat of Operandoperticles; Department of Dismuncleay, Missing Transactive of Gen. Associatiographics 8, Gran 2016. Associat pressil. Intercentageous in producing act 51.

Coyenghi C 28th Waters Kleiner Hadds, Inc. All rights reserved.

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M yeoses (ampoides (MF) is the most common type of cutuments (surphema. 12 Several clinicapathologic carious have been described (reviewed in Cornos?). Interstitial myonesis limpoides (IMF) is a rare varient of MF municidag histopathologically inflammatory demanous, especially interstitial granuluma annulum, inflammatory morphes, and interstitial granulumations demantic (IGfb). Only small series and acoradic case reports of IMF have been published to date. We reviewed 21 cases of IMF to better characterize this rare histopathologic variant of MF.

MATERIALS AND METHODS

Cases of IMF were remeited from the files of the Research Unit of Derminopathology, Department of Demaslobogy, Medical University of Graz (Australi, The study has been approved by the ethical committee of the Merical University of Graz.

Clinical appearance of the lesions and history of biopsies of conventional MF (before, concomitant with, or after the biops; classified as IMF) were evaluated in each case.

Skin biopsies were fixed in 4% buffered formaling and embedded in paraffin. Histofogic examination was performed on sections stained with humstoaylis and coosis, ascessing the following features: architecture of the infiltrate, epithebitropism, depth of the infiltrate, and cell morphology. Immunolistochemical analyses were performed with a standard immunopercoidase method using the following panel of antibodies: CD2, CD3, CD4, CD5, CD367 (Novocastra Leier Mikrosysteme, Vienna, Austra), and TIA-1 (Immunotech-Heckman Coulter, Vienna, Austra).

RESULTS

A total of 27 biopses from 21 patients, were included in the study (M.F. 11:10; median age, 60 y; mean age, 57.5 y) (Table 1). A clinical diagnosis of MF was made in all patients, Biopsical lesions were located on the runk (n = 15), upper limbs (n = 5), lower limbs (n = 5), or buttocks (n = 2). According to the staging system proposed by the International Society for Cutaneous Lymphomas and the European Cepanization for Research and Presentation for Research and Presentation for in stage 1 (1A. 5 cases, 18: 10 cases), and 3 were in stage 1 (1A. 5 cases, 18: 10 cases), and 3 were in stage 1 (1B.

An J Song PothW + Volume 40, Number 10, October 2016

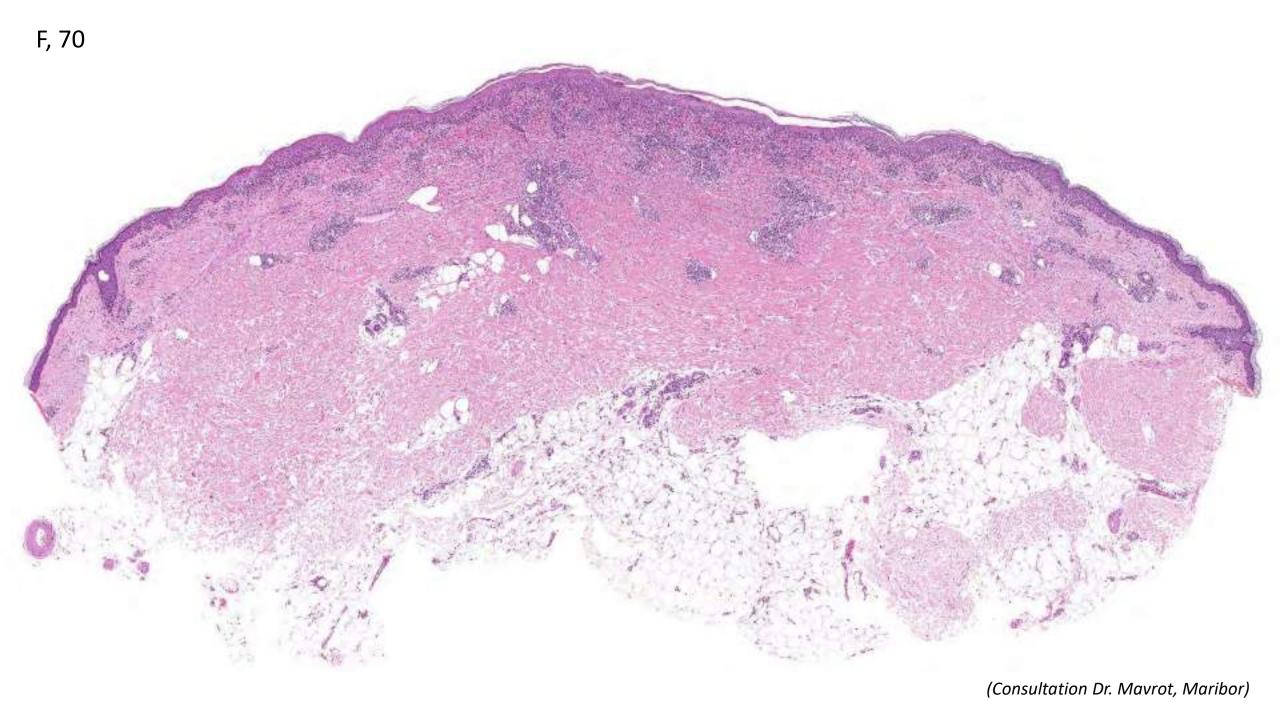
TABLE 1. Clinical, Histopathologic, and Phenotypic Features

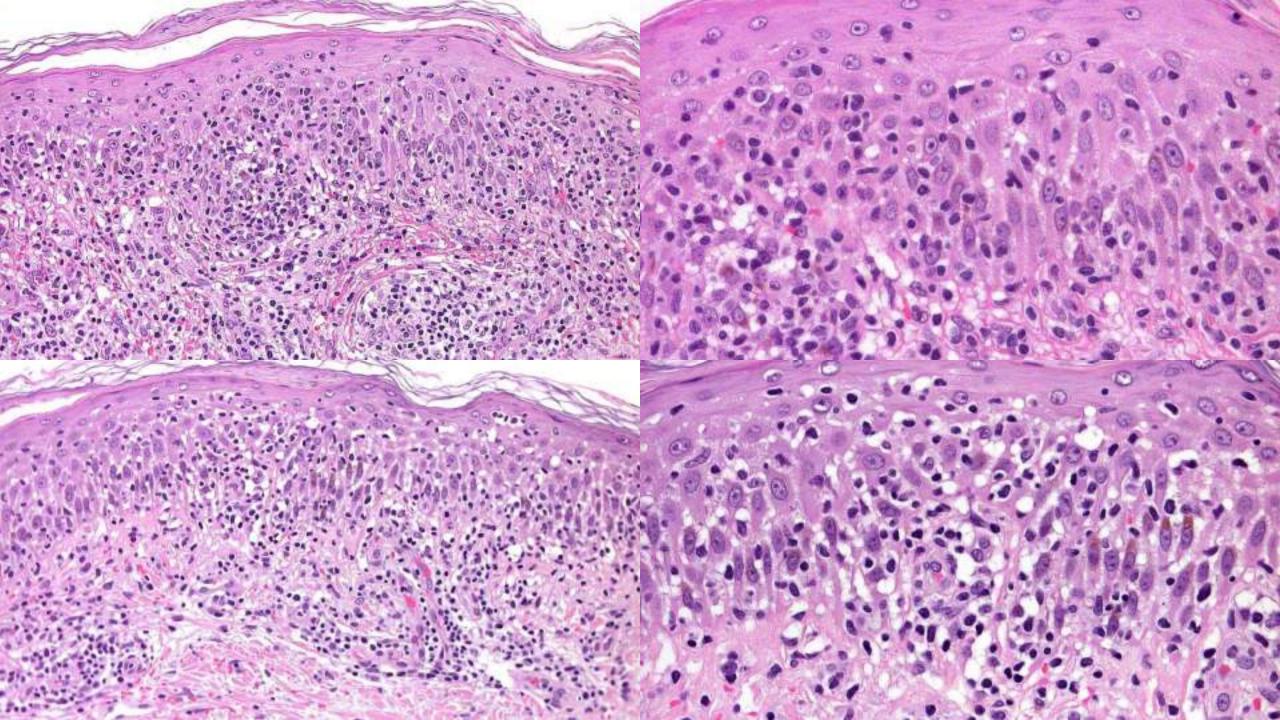
Patient #	Age (y)	Sex	Conventional MF Before (mo) or Concomitant (C) to IMF	Stage at Time of Diagnosis of IMF	Conventional MF After IMF	Follow- up (mo)	Biopsy Site	Clinical Morphology of Biopsied Lesion
1	78	M	Yes (C)	IA		NA	Right arm	Plaque
2	63	F	Yes (19)	IA		NA	Right leg	Patch
3	55	\mathbf{M}		IA		A + (3)	Trunk	Plaque
4	44	M		IB		A+ (2)	Trunk Trunk	Plaque Plaque
5	28	\mathbf{M}	Yes (257)	ПВ	Yes	DoD (42)	Trunk	Flat tumor
6	41	M	Yes (2)	IB	Yes	A + (125)	Trunk	Patch
7	59	M	75.75	IA		A + (1)	Right leg	Patch
8	68	F	Yes (26)	IB	Yes	A+ (9)	Trunk Trunk	Patch Patch
9	39	F		IA		NA	Trunk	Plaque
10	58	F		IA		NA	Trunk	Patch
11	67	F		IB		NA	Trunk	Plaque
12	74	M	Yes (C)	IB		A+ (12)	Trunk	Plaque
13	60	F	(-)	IB		A+ (191)	Left arm	Patch
	-					SEC VILLE	Left arm	Patch
1.4	CO		3/ (C)	TA		NIA	Right arm	Patch
1 4 15	69 51	F M	Yes (C)	IA IB	37	NA A L (FA)	Right leg	Plaque
	42	M	V (77)		Yes	A + (54)	Trunk	Patch
16	42	IVI	Yes (77)	шв	Yes	DoD (40)	Trunk Buttock	Plaque Plaque
17	70	F		IB		NA	Trunk	Patch
18	62	F		IB		A + (4)	Right arm	Patch
						8.8	Left leg	Patch
19	73	F	Yes (3)	IB	Yes	A + (110)	Trunk	Patch
20	45	\mathbf{M}	Yes (36)	пв		NA	Left leg	Flat tumor
21	62	M	Yes (C)	IA		A + (85)	Buttock	Patch

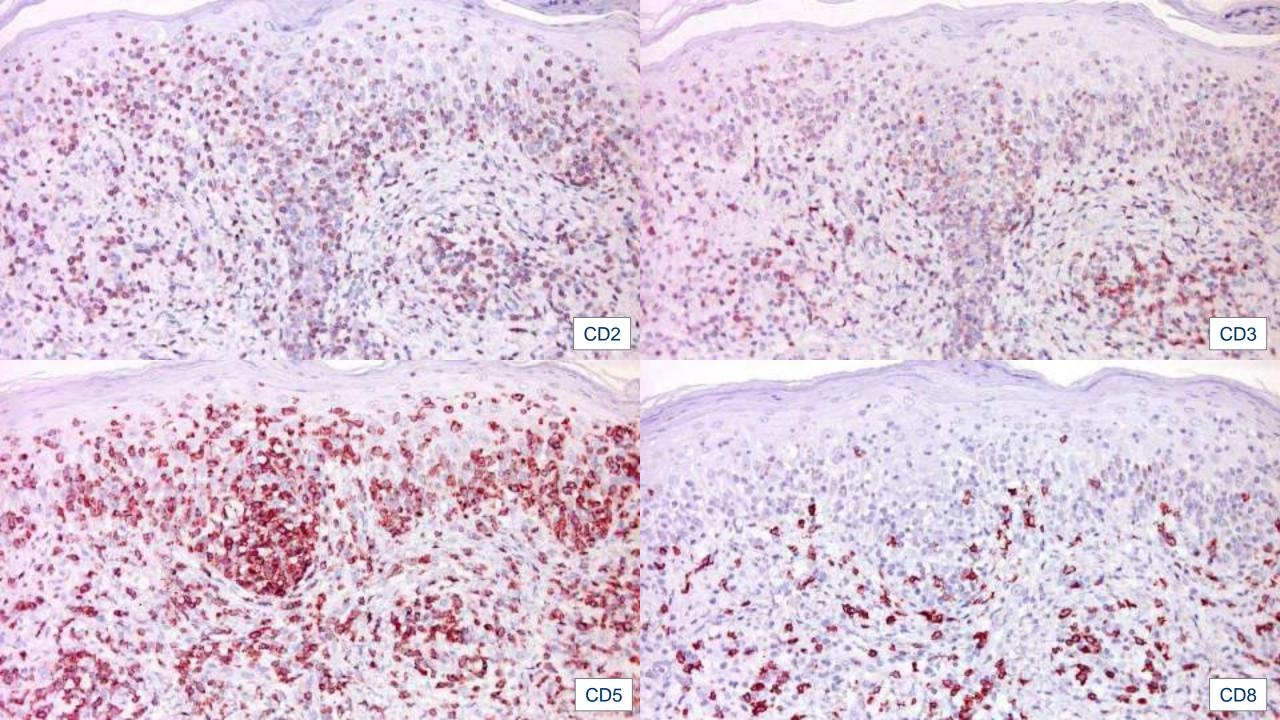
^{*}See text for explanation.

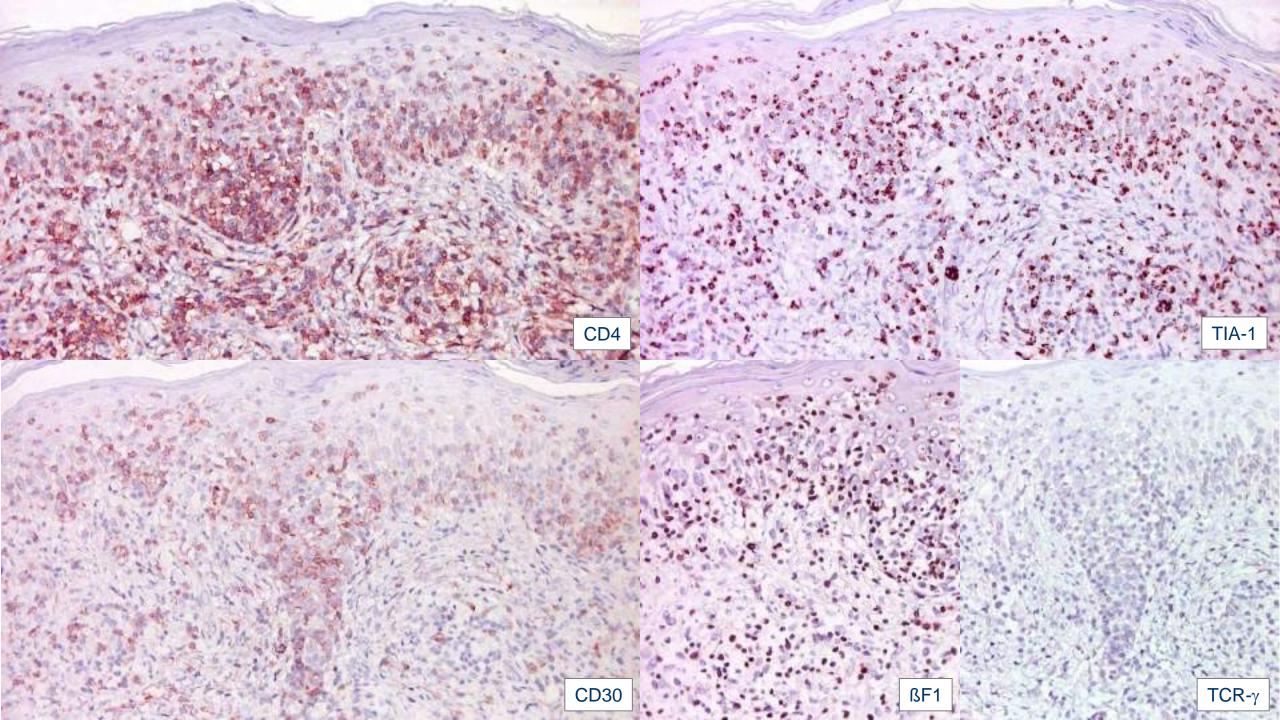
A+ indicates alive with skin disease; DoD, death of disease; F, female; M, male; NA, not available; ND, not done; SD, superficial and deep dermis; SM, superficial and mid-dermis.

Beware the crucial importance of clinicopathological correlation



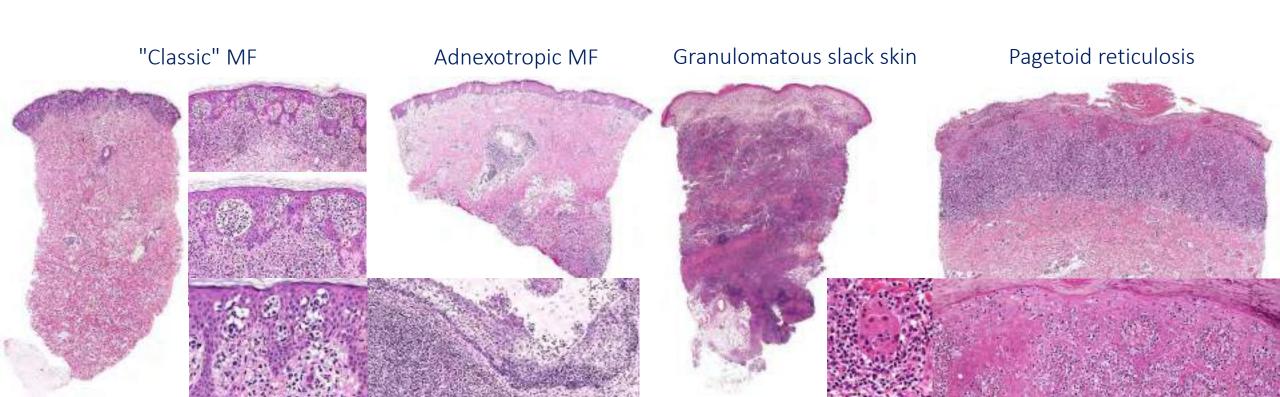


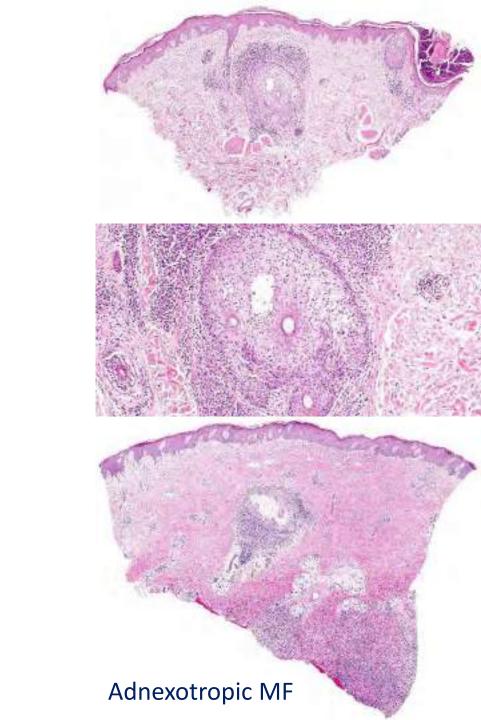




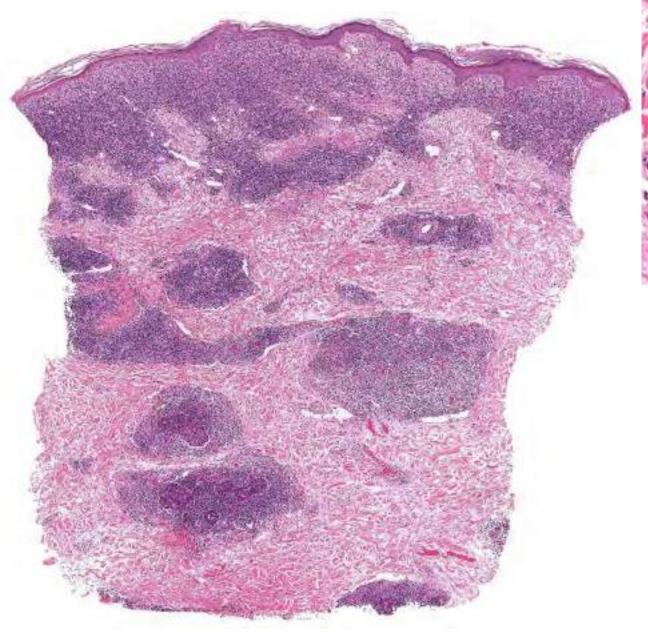
Lymphomatoid papulosis, type B

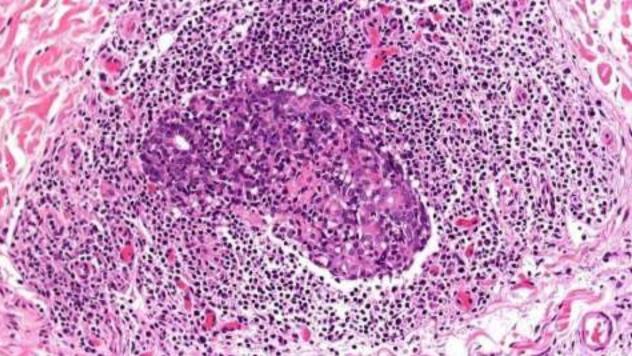
- Epidermotropic variant of lymphomatoid papulosis mimicking the histopathological features of MF
- Phenotype: CD4+ (distinct from type D, also epidermotropic but CD8+); it may express cytotoxic proteins
- In old reports described as "CD30⁻ variant": it is always positive with antigen retrieval methods (but the positivity may be weak); repeat staining in case of doubt; a diagnosis of "CD30⁻ LyP" should be judged critically





Adnexotropic MF (syringotropic)





Syringotropic Mycosis Fungoides: A Rare Variant of the Disease With Peculiar Clinicopathologic Features

Aleisandro Pdevi, MD,*? Fabio Facchetti, MD,* Arno Rütten, MD,\$ Ginseppe Zumiani, MD,\$ Schastiana Boi, MD,* Regina Fink-Puches, MD,* and Lorenzo Cerroni, MD*

Abstract: A rare variant of revenois fungoides (MF) character real by prominent involvement of the ecenine glands with swingometaphoia has been reported in the post as "swingobripliced hyperplasia with alopecia," "syringotropic cutomoun-I-cell himphoms," "adsevotopic T-cell hypphoms," or "iversuptropic MF." The eliminopathologic features of this variant are not well understood, and only a few case reports or small series have been published to date. We reviewed that dinicopathologic features of 14 patients with syringotropic MF iniale female 1874; median age, 59 years; mean age, 57.8; age range, 32 to 93-y). Six patients had variably large, softery. positive or plaques, located on the thigh in -35, arm, trunk, or cyclrow () each). The other 5 gaments had multiple, mostly generalized lesions. A firstory of MII was known in 4 of these 5. raticuts. With the execution of 1 biosey specimes that was too. superficial and did include the extrine sections code but not the recrine about, all cross showed prominent approximent of the ecerine glands. Variable degrees of syringometaplasia ranging from small to large epithelial complexes more present in all speciment. The econic glands and syningmentalistic structures were narrounded by done hymphole influence with provincenepitheliotropins. Concerniture involvement of the epithemia and of the hear follicles was observed in 15 and 8 biopsies. respectively. This is the largest series of syringstropic MF. showing that this is a rare variant of the disease with peculiar dinicopathologic features. Dermatologists and dermatopathologests should be aware of the care various of MF to award felased diagnosis and treatment.

Key Worde: mycrois fungosidos, syringutropic mycrois fungosidos, attansous. T-adl Ipraphorus, myingolymphosid hyperplasia with alopecia, pilotropic mycosis fungosidos, folliculomopic mycosis fungosidos.

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(Am J. Surg. Paylot 2011;35:300-109).

M yeosis furgoides (MF) is the most common type of cutaneous lymphosms, accounting for approximately 50% of all cases of primary cutaneous lymphoma. *** In the World Health Organization classification of hematological muligraneous and in the World Health Organization-European Organization for Research and Treatment of Cinter classification of cutaneous lymphomas, besides the conventional type of MF iso-milled Alibert-Buam type), 3 variants of the disease are explicitly mentioned, namely, solitary pageteid reticulosis (Woringer-Kolopp), followlotropic MF, and granulomatous slack skin. *** Besides these presentations, many other clinical and/or histopathologic variants of the disease have been described.**

A rise variant of MF characterized by prominent involvement of the extrine glands with "synagometa-plasia," has been reported in the past as "synagolymphoid hyperplasia with alopeoin, "LSG023223050" syringotropic cutantons. T-cell hymphoma, "LSG02323050" syringotropic cutantons. T-cell hymphoma, "LSG02323050 "syringotropic Cutantons. T-cell hymphoma, "LSG02323050 ME." "31 The clinicopathologic features of this variant and not well understood, and only a few case reports or small series have been published to date.

Herein, we report 14 patients with syrings/tropic MF with emphasisy on the efficient and histopathologic features of this rare variant of the disease.

MATERIALS AND METHODS

We reviewed the lymphone directors of the Research Unit Dermate/path/dogs. Department of Dermate/legs. Medical University of Graz for cases of MF that showed prominent involvement of the scenne dands idefined as dense, nodular lymphoid infiltrates around hyperplastic occini structures—with syringstropismi. Cases of MF showing lymphoid infiltrates surrounding the occinic coils or gloods, but without epithekal hyperplasia and/or syringstopism were not included tour aso Fig. 10. All diagnoses were confirmed by histopathologic examination and combation with the chincal picture and/or detailed choical data. Thirteen cases matching the inclusion criteria were found. We also included 1 additional case that showed prominent involvement of the occurre coils. The biopsy of this cross was too superficial and did not include the occurre.

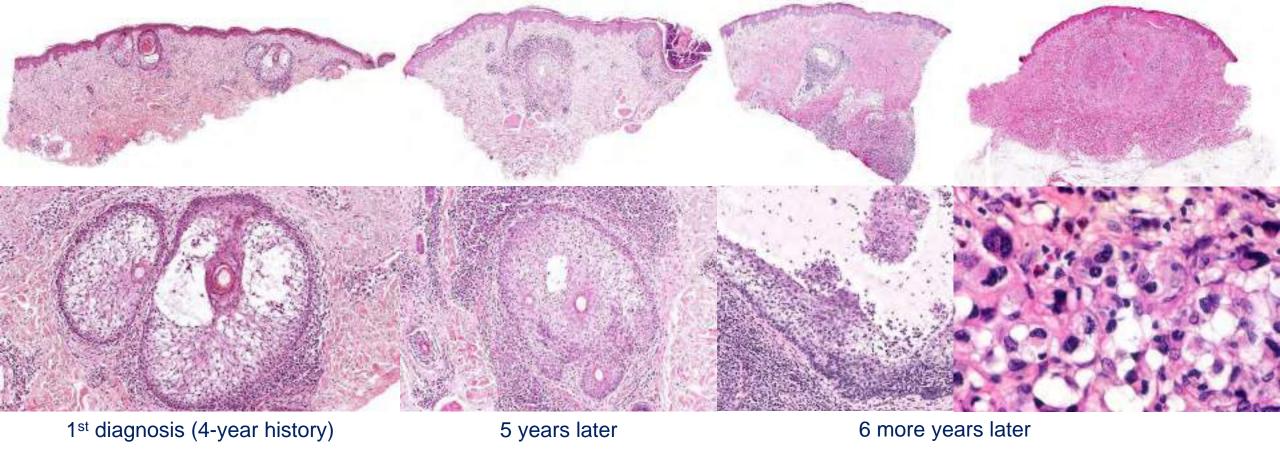
 Clinico-pathologic variant of mycosis fungoides; sometimes solitary lesions

- Clinical manifestations oft different from "conventional" MF
- Prominent involvement of the eccrine glands; syringometaplasia
- Oft concomitant involvement of the hair follicles (syringotropic-pilotropic MF; "syringolymphoid hyperplasia with alopecia")

From the "Broanth Talk of Bermanopularings Department of Dematology, Medical University of Ginz, Austria: "Department of Informs Medicine, Genomes and Sephotogy, Drivess of Bermanology, Lavorsky of Belogas; [Department of Pathology, University Special Cedi of Bessen; Departments of Demanology, "Barmalogus/Delays, Praisiles Opendadon's Chiara, Trans. Italy, and (Demanopularing) proceedings of Chiara, Trans.

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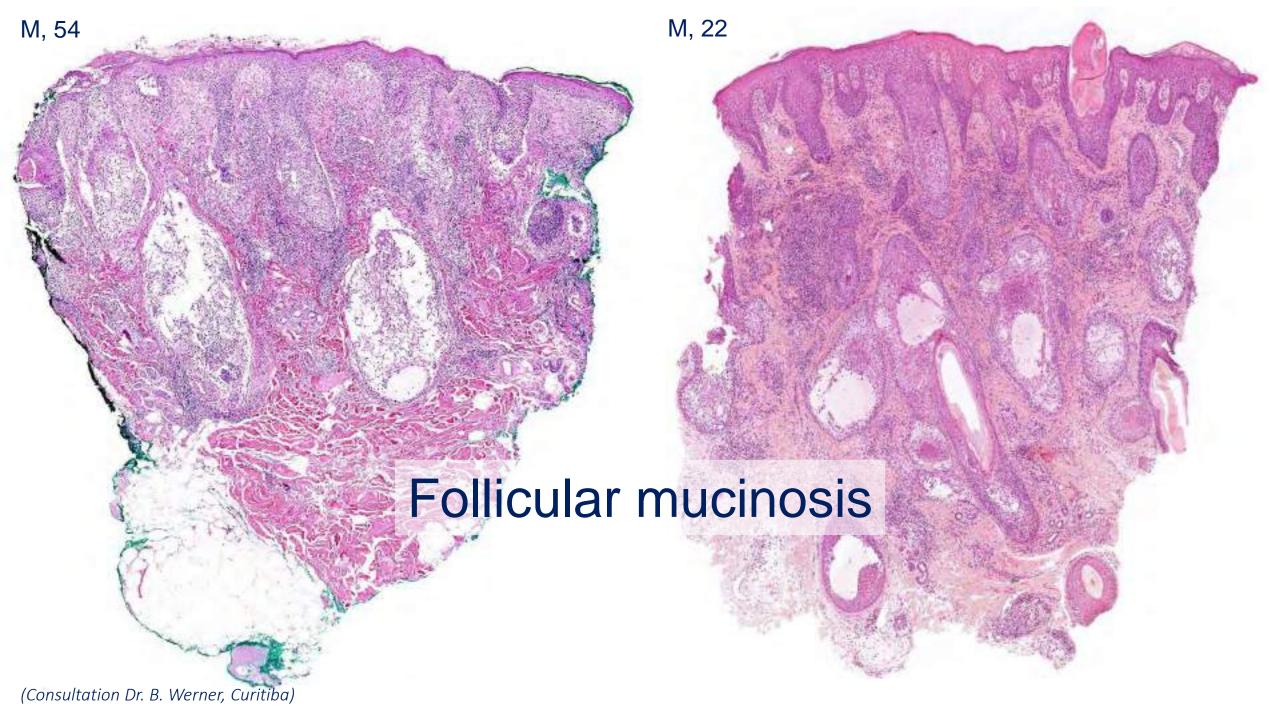
Correspondence: Leonary Centrus, MD. Rosarch Unit Dermaropathology. Department of Demandings, Medical University of Gran. Assubroggerplat. 8, A 8006-Grat, Austra to-mail teorate servora introdumenta. 41.

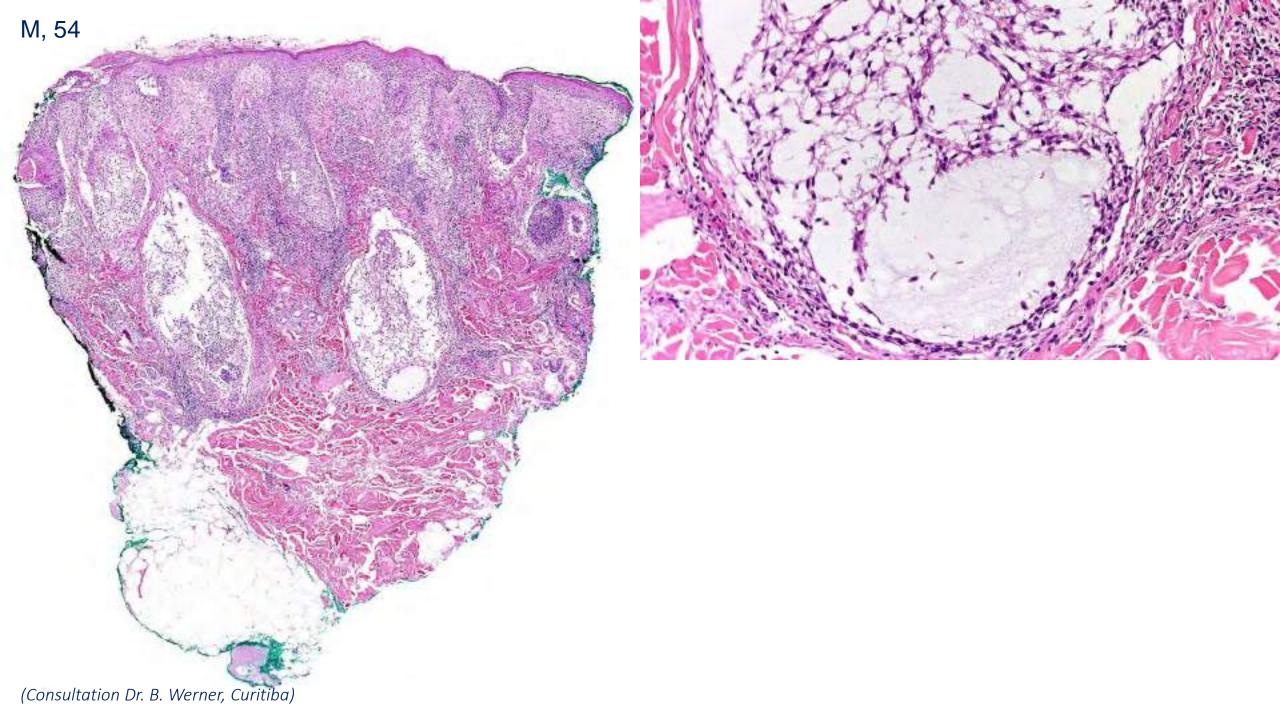


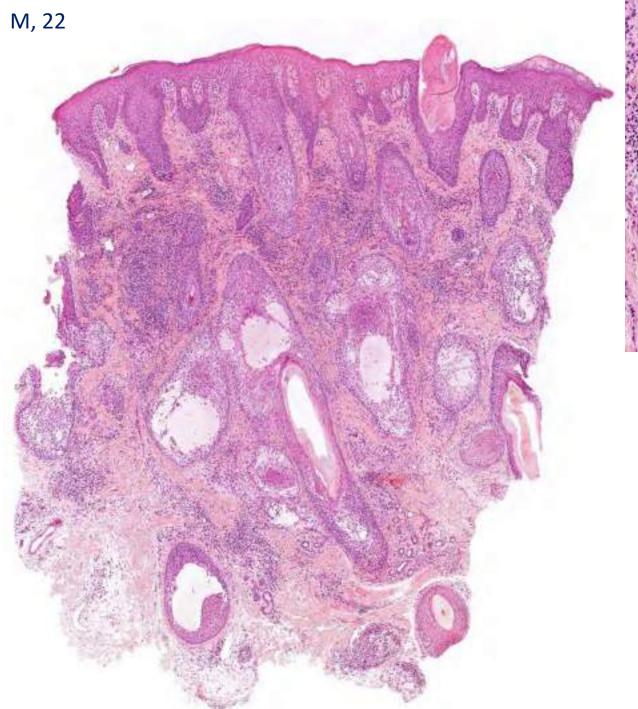
Died of progressive MF, November 1989 (12 years after 1st diagnosis, 16 after onset of disease)

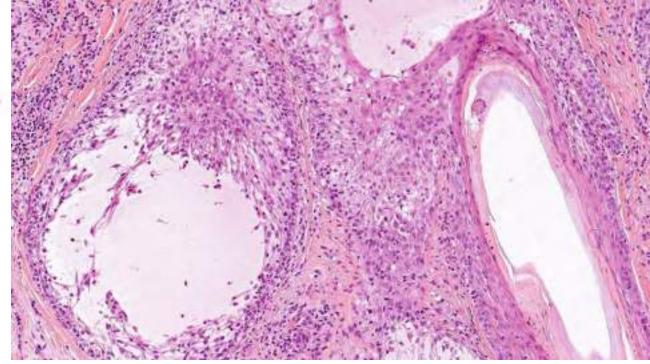
"Idiopathic" generalized follicular mucinosis

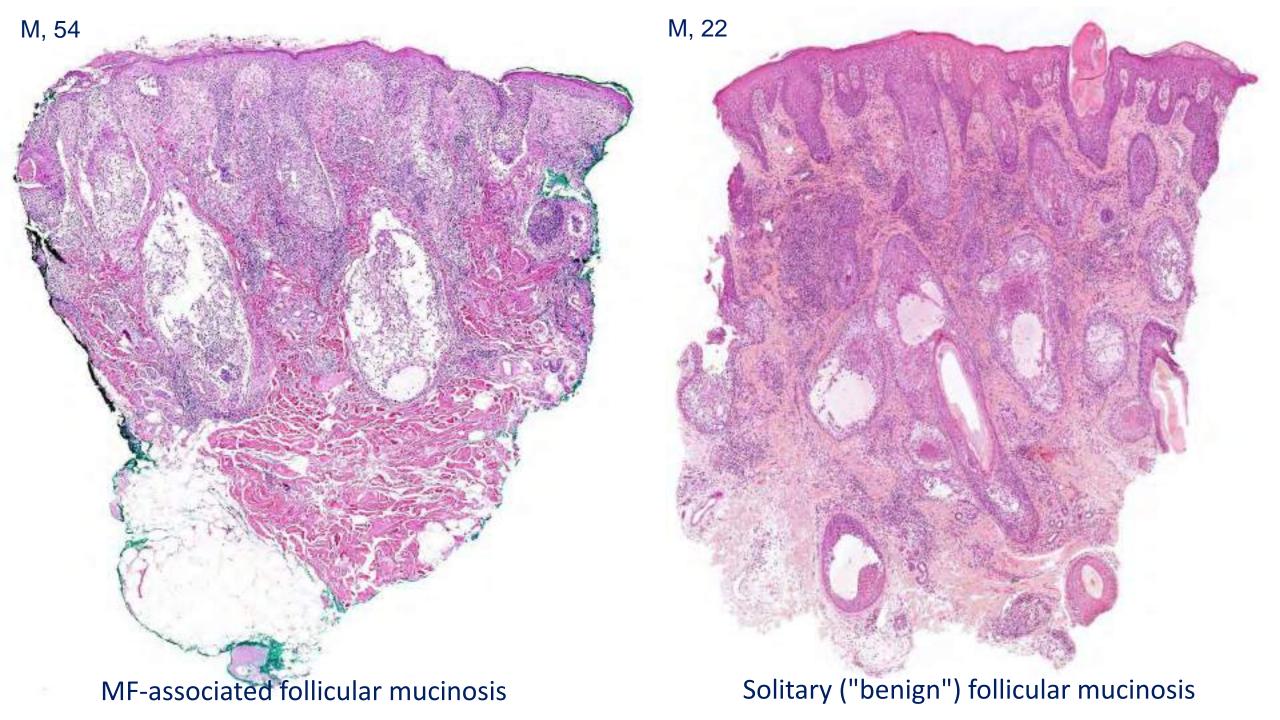
- "Idiopathic" generalized follicular mucinosis is a form of early pilotropic MF
- Course and prognosis similar to early "conventional" MF, but response to skin-directed treatment may be less pronounced and/or more delayed
- Avoid aggressive treatment; manage as other cases of early MF, eventually with the association of systemic retinoids to other standard options





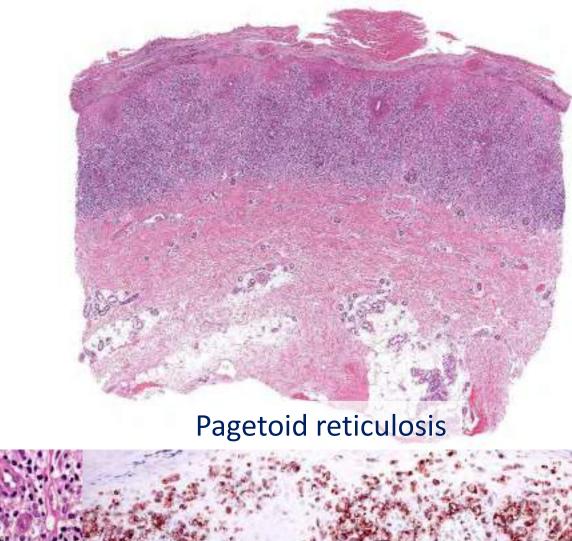


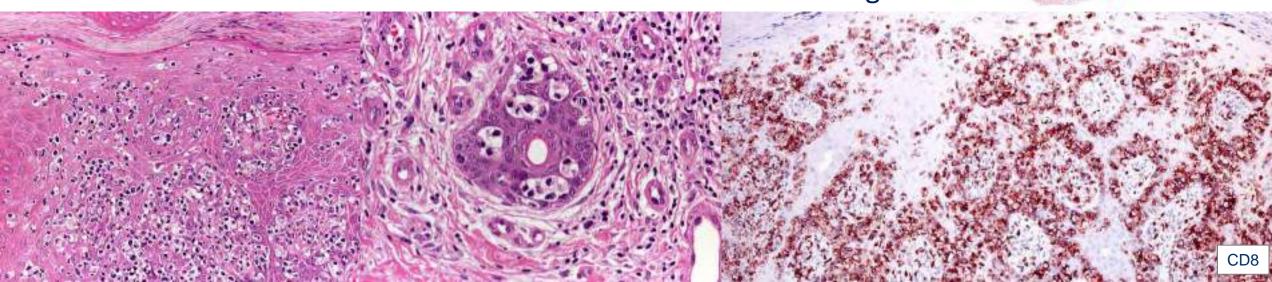




Pilotropic & adnexotropic mycosis fungoides

- A variant observed in all ages including children; pilotropic & syringotropic patterns may be present in the same lesion
- Several clinicopathologic presentations; some variants similar to those observed in MF (e.g., hypopigmented follicular mucinosis)
- Classification of "benign alopecia mucinosa" yet unclear
- Morphological, phenotypic and molecular features don't allow to separate MF-associated cases from "benign" ones
- Conservative approach; avoid aggressive treatment (but local radiotherapy may be an option)
- Non-malignant follicular mucinosis may be observed histologically on the background of several inflammatory and neoplastic conditions





Pagetoid Reticulosis

- Pagetoid reticulosis is considered as a localized (often solitary) variant of MF (Woringer-Kolopp disease)
- Mostly on acral skin; may mimic viral warts or inflammatory dermatoses – clinically deceptive ("non-responsive eczema"), histologically clear-cut
- Prognosis usually favourable
- Similar histopathological features may be observed also in clinically "conventional" MF

Case Reports

Br. J. Derm. (1970), 82, 397.

Department of Dermitology, Harvard Medical School.

GRANULOMATGUS MYCOSIS FUNGGIDES

A. BERNARD ACKERMAN AND B. ALLEN FLAXMAN*

SUMMARY,—An unusual form of mycosis fungoides was characterized clinically by the spontaneous resolution of ulcerated nodular lesions into poikilo-derma and histologically by a granufomatous malignant lymphoma.

As extraordinary form of asycosis fungoides was characterized clinically by extensive observed modules, many of which healed spontaneously leaving atrophic scars and patches of policiloderms. Granulomatons malignant lymphoma was found on histological examination.

CASE REPORT

For 18 years, a white factory worker aged 46 had a skin disease consisting of polynorphous lesions. It becam as scaling on the thighe and abeliance and one diagnosed as pacciasis. Those lesions increased in number and offer 13 years involved most of the body. Five years before his admission to the Massachusetts General Hospital, some of the lesions became mobilar and observed. These uncertain nodules showed a pronounced tendency to heal spontaneously, but now lesions continued to appear. The patient did not seek derivated opening help because he thought that "psermais" was not travelle. Despite the extensive involvement of the skin, he felt well and continued to work.

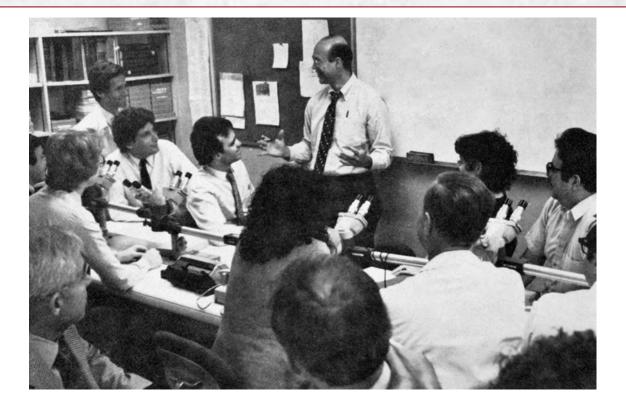
Physical convination.—The entangents become were generalized (Fig. 1). There were redshib-purple noclules, many of which were ulterated and covered with purplent material, on the scalp, buttocks and tunds (Fig. 2). Violacrous, indurated scaling plaques with irragular bookies, some absented, were distributed over the entire body. There were numerous areas of atrophy at sites of previous broises. Some of those residual lesions had features of possible derma with atrophy, by po- and hyperpagniculation, and telargicietasis (Fig. 3). There was scarring alspecia of the scalp (Fig. 4) and partial loss of the right cyclerow. The pulme and soles were not involved. Except for minimally enlarged inguital lymph under, the remainder of the physical examination was accurate

Histopathology.—Multiple loopsies from nodular fesions showed parakeratoris and sloopation of the rete sides with preservation of the rete papillae pathern. The interface between the epidermis and dermis was partially obstaired by an infiltrate compresed of fromy historytes, lymphocytes, essemphile, and large monomories cells with atypical phococyphic nuclei, some of which wave in mitusis (Fig. 5). These atypical monomorbur cells were scattered throughout the epidermis and some formed small collections in the region of the granular wave. Large dense aggregates of this polynorphous infiltrate were present throughout the dermis. Within the infiltrates were longe giant

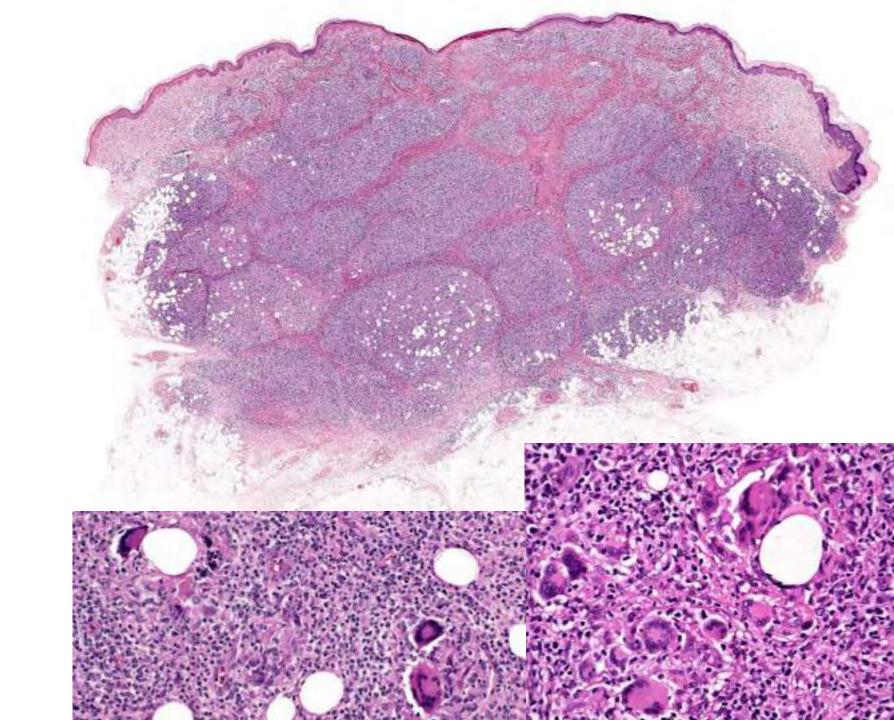
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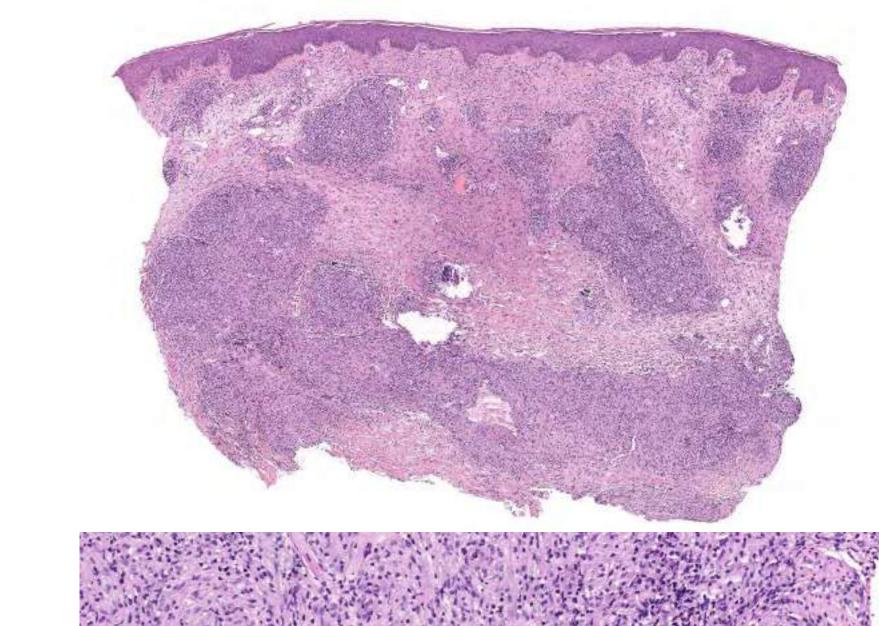
* Follow of the Medical Foundation, Inc., Boston, Manachusetta

iros characteris de cliqueally by the spontaneous resolution of iderated hodulated lessons into pointalogically by sprandomatous malignes to bymphoma.



Bequests for reprints should be abbreved to Dr Asharona, Department of Bernantslogy, University of Mapar School of Madaras, P.O. Box 875, Name, Physica 31132.





Progressive, Atrophying, Chronic Granulomatous Dermohypodermitis

Autoimmune Disease?

Jacinio Convil, MD; Francisco Kerdel, MD; Mauricio Geologia, MD; hatanio J. Roselon, MD; Jone M. Sato, MD, Carvega, Venezuela

A chronic, progressive dematosis is described, characterized by papular lesions forming plaques in various parts of the body, with secondary phonomena of acquired cutis laxa. Histologically, the lesions were typified by a granuloma formed by hisliccytes, apitheliod cells and grant cells, lymphocytes, plasmocytes, and lipophagia abenomena.

The disease started after the successive injection of Mitsuda antigen and of BCG vaccine. One of the initial lesions appeared at the site where the Missoda antigen had been injected. The disease evolved during a period of more than 20 years.

Oral treatment with corticosteroid produced partial regression. When treatment with this drug was discontinued the clinical manifestations became worse, with fever and arthralgia.

In face of such a special clinical picture we thought of the possibility that it might be an autoimmune disease. When azathioprine was administered, there was regression of the lesions.

The patient died after a period of intense diahrrea. He also had a generalized inflammation of lymph nodes. The postmortem study of one of his lymph nodes rendered a diagnosis of Hogdkie's disease.

Accepted for publication April 4, 1972.

From the Institute Nacional de Dermatelogia,
Caracas, Venezuela.

Reprint requests to Institute Nacional de Decembrologie, Apertudo Postal 4043, Carmon 101, Venezuola (Dr. Carrott). Unusual diseases may represent
"experiments of nature." Reporting their occurrence may help in
understanding mechanisms of general interest—or at least in creating
awareness of possible ways in which
the body may react.

We now describe a case that has been followed up for more than 20 years. The illness started after the injection of BCG vaccine and lepromin. Clinical features were highly unusual, and did not fit into any previously described entity known to us. The condition improved when conticosteroids or other immunosuppresive agents were given, but finally, the patient died in a rather precipiious final course. Postmortem studies showed Hodgkin's disease.

We feel that a detailed report of the evolution of this case may be of interest, because of its unusual clinical and histopathological features, and of the likelihood of a connection between lymphoid tissue malignancy and manifestations of autoimmune disease.^{1,3}

Report of a Case

The patient was 37 years old and darkskinzed. When 15 years old, he consulted a skin specialist about two srythematous, popular plaques, one of which was located on the anterior side of his right forearm and the other in the left delteid region. Those plaques measured about 5 cm in diameter. He had been under control as a contact since his mother suffered from lepcontaines leprosy. The lepromin reaction
on his right firearm was negative after
three weeks. He was consequently given
two introduction BCC varianticos, both
on his back, 0.1 ml of a suspension that
contained I milligram of bacilli per millibtor. He was tested again with 0.1 ml of
standard Mitsuda (160×10° acid-fret hestillus/ml) and showed a positive reaction.

He indicated that the plaque on his right forearm appeared at the exact site where he had been given the Mitsuda test, a few weeks after he had been racconsted with BCG.

The dermatologist whom he consulted took a skin specimen for hispsy from the plaque on his right forearm and disgressed the case as tuberculoid leprosy on the basic of the histological fladings, the clinical supect of the lesion, and epidemiological reasons.

When he later developed several "tamerations" in his left armpit, they were diagcused as "supparative hidrosdenitis" and were treated with penicillin.

We first saw the patient in 1960 when he was 26 years old. He showed crythematous infiltrated plaques on his chin, left delicid region, anterior area of both forecame, and on the back of his right hand. The plaque on the left delicid region had an atrophic coater with a noticeable depression, around which the infiltrated horder appeared as a ruised ring (Pig 1). On the left armptt, the skin formed a large hanging hag-like fold (Pig 2).

The patient had been receiving dapsone treatment (DDS) since he first saw a der-



The contraction of the contract of the contrac

Fig 4.- Great hanging bag-like fold on left armost, lifteen years evolution.



To all present and self-self-street free parties from

Fig. 5.- Sneet hanging bug-like fold on left

ampit, fifteen years' evolution, under treat-



Fig. 5.— Lautes street proper beneau a more, by Esternia helt. Hen paper audicities.



Fig 6. - Lation or left arrepit with important

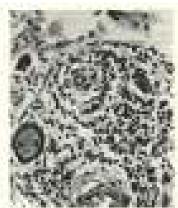




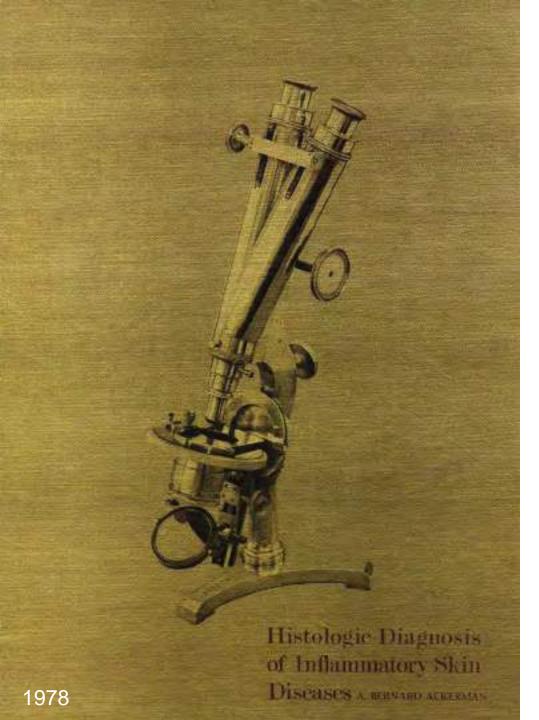
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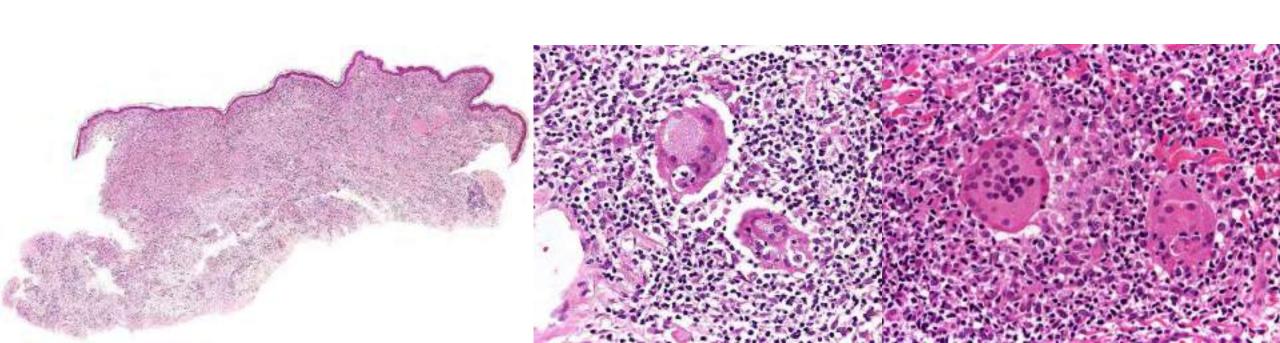
White states to be a first to



- Histiocytes, many multinucleated, scattered throughout the entire dermis and subcutis
- Epithelioid tubercles associated with numerous lymphocytes, plasma cells, and eosinophils throughout the dermis and subcutis
- Calcified bodies of various sizes and shapes within histiocytic giant cells and in a fibrotic stroma; some matter polarizable
- Fibrotic stroma replacing the normal dermis and the subcutaneous fat
- -Fibrotic collagen mostly aligned parallel to the skin surface
- Bandlike mixed inflammatory-cell infiltrate in the upper part of the dermis and a few mononuclear cells within the epidermis



This rare condition seems to have a predilection for young adult men who, over several years, progressively develop pendulous skin that droops on the arms near the axillae and on the flanks. The skin is not only slack like that of cutis laxa, but it has surface features of parapsoriasis en plaques. Whether this distinctive condition of granulomatous slack skin inevitably eventuates in malignant lymphoma has yet to be determined.



OBSERVATION

Granulomatous Mycosis Fungoides and Granulomatous Slack Skin

A Multicenter Study of the Cutaneous Lymphoma Histopathology Task Force Group of the European Organization for Research and Treatment of Cancer (EORTC)

Werner Kennef, MD: Senje Culceren-Michaelis, MD: Marco Paulli, MD: Marco Lucioni, MD: Jorine Wochsler, MD: Beiler Andring, MD: Cons. j. L. M. Metter, MD: Beiler Andring, MD: Cons. j. L. M. Metter, MD: Emilio Bent, MD: Laming Current, MD: Marco Sustain, MD: Christian Indiaments, MD: March Berneteng, MD: Senje Citionest, MD: Advant Research, MMRS: Marco Metebalis, MD: District V. Kazaloni, MD: PhD: Inter Petrolla, MD: Splee Francia, MD: Agent Gerletti, MD: Philippe Controlla, MD: MD: Bullett Laming, MD: Robbins (MD: Robbins MD: Robbins MD:

Backgrounds Grandemizour organisms T-cell lyrighmmas (CTCLs) are not and represent a diagnostic challenge. Only firsted chain in the difficient/follogical and prognostic leatons of genulamation CTCLs are available. We studied 19 potents with grandemation CTCLs in further characterist the classicapathological, therapeatic, and prognosic features.

Observations: The group included 1.5 parisms with granulomators narcosts languistes (GMF) and 4 with granulomators stack sizh (GSS) defined according to the World Health Cognitistion-Enotypeon Organization for Research and Treatment of Canon crossification for Councius lymphomats. Patients with CMU and GSS displayed overlapping listoring between and differed only detected by the According to the CSS. Histologically, epidennomogism of lymphocyus was not a primition of the CSS.

Stable or progressive disease was observed in most paticus despite various metaneat modelities. Extra maneous spend occurred in 5 of LP patients (25%), secural lymphod neophosms developed in ± of 19 patients (21%), and find 19 patients (32%) died influen disease. Disease-specific 5-year minyiral rate in GMF non-66%.

Gondosisma: Chara use flatical differences between GM1 and GSS, but they shaw overlapping findulage fundings and therefore cannot be discriminated by histologic exweight on alone. Development of hanging skin folds a restricted to the intertrigitious body regions. Gonsilatrations CTCL schows a facture resentant, slowly progress are course. The prognosis of GMF appears were than that of classic mongranding motions envisable trapping.

4KADaniatri, 2008;144(12):1009-1617

ne UCCURRENCE OF SAMcold-like grantforms in a we'll-known phonoments in malignan' lymphoms and is most commande observed in policies with Hodgkin disease. ¹² In contrast, grantformstoss features nocarely found in primary consecouslymphonus (CLs), with approximately 25-of al CLs, displaying grantformstous Features. ¹³

Granderna formation was reported in a broad sainty of primary Cia, "such as Seriety by primary conference until property of the property of th

toon reported in the literature. The flut. World Health Organization-Function Organization for Research and Treatment of Cascer (W-NC-17)FTC) clossification for commons templatents, closs a considered a distinct subtype of NLF with classification of climated and bisologic features.

These have been only a limited timbles of studies on granulmination of TCLs, particularly growth maxima. ATCLs are studied by granulminations of the course of granulminations CTCLs are still possely characteristical. The granulmination combined on the very cateristic, so that the histologic diagnosis of lymphome may be delived, and the fluidings are often initially mustingnessed as granulminational transition. Them is continued by a granulmination of the constates with a bench progressia. "If They a mediate restain was conducted to washese the clinical histological liminosopienoscopic, and granulmination."

wurter 4 Mateurs am fesstlie die end of dazweilde. "There are clinical differences between GMF and GSS, but they show overlapping histologic findings and therefore cannot be discriminated by histologic examination alone."

Patient No.	Greath Pattern	Epidermotropism	Cell Size	Grantona	Giant Cells	Lass	Elastophagocytosis	Cas.	Plants	Ingio	Phonolype	Genetice
						-7-T-M	Finguides*	-	-	-		-
1	Othor	14	S Mides		1	1	,		0		003+, 4+, 8+, 30+, 164-1+	7031+
2	diffuso		S-Mphie	114	40	464	NA				GD1', 4"	NA.
3	Periodecular	+5- Linksgrap	8		+ (Feet	NA.	14%	-	-	100	0001, 41	1031+
4	Perivancinal	1777 A. T. T. C. W. Car.	\$1		+ (feu)	MA	NV				MA	TOH+
3	Pethosocular peradrecal		S-Mpleo	+ (Feb)	+	Ŧ		.#			000°, 4°, 8°, 207°, 30-3°/	TON-
é	Partfoliosiar/ persettessal	- 14	6	- 1	4	1	8		=	=.	GD3+, 4+, 8-, 50 ; TM-1	JCR)
7	Perfivercular/ nedular		S-M-L piec	-		+		+ (('90')	+		001,4; 41,381; 18,117	101+
1	Neouser	7	S-Mples	-	1	+	-	7			GD3*, 4", 30°, TW-3*	ICH+
2	Nedular	++	\$	9	-	+		0		3)	0001, 41, 81, 501, TAL-11	TGH+
10	Workday		5.			+					CDJ: 4, 8:	2035
11	Siffering		8	3	+	+	9	1	8	3	(203*, d*, R. 30*, TIA-1	109+
12.	Hillian	1	S-Mplee	-11	=	+	8	7	-	#	0001, 41, 81, 001; TIA-1	3031+
10	bithuse	100	8	7		+		1			GD0*, 4*, 8	TOH+
14	Northan	d*	8	1		+		26	1	3	GDS*, 4*, 8-, 50°, T8A-1	TOU
ţā.	Pittuse		8	-7	*	+		=	=	13	0001, 41, 81, 301, 784-1	JOH+
-701				Gra	mionale	en Sie	ok Slon	III V I PAUS	170		NAME OF TAXABLE PARTY.	Mark 1
博	tittus		8	= 200	+	+		+ (Fear)	+	+	GB3", 4", 8",	TCH+
17	Pillane		8	7	Ŧ	+	+	+ (Fwar)	*		GD3*, 4; 8*, 39*; 194, 4; stanzine B*	708+
10	Sittuse:	15	S-Muleo	1.2	+	+	+	+	-	4	CB3+ 4+ 8:	JOI+
250	Diffuse	14	S-Mpton		4	4	125	12	+	4	CD3*,4*,8	TGH+

Abbreviations: Angio, angiocentric growth; if I ass, loss of elastic Rivers on elastics steining it os, exemptritic gramtocytes; I, large; M, medium state! NA, not available; Plasm, plasma catts; pico, picomorphic; S, smalt TA-1. T-call interaction antigen it. TCR. T-call receptor management (+, monoconsc, -, polyconal); + present/positive; -, absent/positive; -, +, very lew cells positive (<5%); +/-, lew positive cells (10%, 20%).

"All corespt patient 3 had multiple besions. Patient 6 had folicate traject decase.

The changes Large dat Separat Belongs Synap (2003) (2003) (2003)

\$1700. Laurent Williams & Williams Tex. Photographer.

Cutaneous Lymphomas With Prominent Granulomatous Reaction

A Potential Pitfall in the Histopathologic Diagnosis of Cutaneous T- and B-Cell Lymphomas

Alessandra Scarabello, M.D., Bernd Leinweber, W.D., Marco Andisci, W.D., Arno Rutten, M.D., Alfred C. Feller, M.D., Helmut Kerl, M.D., and Lorenzo Cerroni, M.D.

The presence of a graphic motors pourtion in lessons of dataaccess lyasphoness has been described in the pool in several. mass. Benedally in inscious feagrides, a "prarefrontions" various of the disease has been well dismotorized. We studied file divisorpathologie Seatness of custnesses (ymptomas with prominers grandomerous nowthen, hadeding both conserve-T-cell lymplemus and H-cell lymplemus (primary connectolymphoms 22 secondary colours is lymphoms into). Biopiers of 23 potierts with histopathologic features of catalonies T-cell brighous or entracous B-cell lymphous with prominent gransformious ocaction were included in fine study. A promiami gotal organic motion was defined as the proctor of a printilenators component exceeding 25% of the dermit inflihote. Those wore 14 years of myonin forgoides, two of salesatoneous purniculius-like T-cell lymphome, four of smill medium phomorphic T-cell lymphonia, one of follote. secure will lymphous, one of longe B-will lymphous, and one of secondary conneces periptarial T-cell hyrphoma. Altagother, a prominent granulousature resoline seedd for observed. in 18% of all patients with counteres lymphoma (primary or secondary) regionated in the filter of the Dispartment of Demandogy of the limmonthy of God (Grag, Austria), deteonstraing that there is a distinct, albeit small, proportion of neco wrealing the profile staction patient. It seem coas a misdegnosis of gratoformators demethis preceded the correct Singstonin for a period of 1-216 months, suggesting that seprental biopsics and emplote phenetonic and molecular asienc asayses should be coroed out to pases of "orange" entakmatess demaktis

Key Words: Grantountoes lymphome-Chapters: T-odl. lymptome - Caspone 5-ccli lymptome

Am J Surg Probed 3tt (ft): 1259-1268, 2002

of the skin with a prominent granulomatous reaction.40

We stufied the clinical, histologic, and molecular Scatures of exteneous lymphoness with prominent granalimitous reaction, including both citanoous T-ex'l. lymphomas (CTCLs) and commeons B-red lymphomas

MATERIALS AND METHODS

Patients

Biopsies of 23 patients with histopathologic features of CTCL or CBCL with promisent granulematous seaction were included in this study. Hupsies of seven other patients were not included because of tack of sufficient clinical information. Primary cutargous lymphoma was defined as absence of systemic involvament for a period

The prosence of a granal mustous reaction in leasons of cutamente lymphomax has been described in the port in several cases. Especialty in mycosis fungrides (MF), a "granufornatous" variant of the disease has been well shandlerweil. 124/12 Another well-lewism, albeitrare, entity of granulomatous cubaneous lymphonia is reprosented by granulogratous stack skin (CSS), which can be associated with either MF or Hodgkin's disease (HD): 735 In the literature, however, there is no sessimute study on "granulomotous" eutanenus lymphomas, i.e., lymphomas

(CBCLs).

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TABLE 1. Clinicopathologic features of patients with cutaneous granulomatous lymphoma

Patient no.	Sex age (y)	Lesions	Bite	Granulomatous reaction	Misdisgnosis of granulomatous demnetitis (mo)	TCR	1gH	Follow-up
Mycosis fi	ungoides					985.5		727 (100)
1	M/82	G	6	++		ND		A+ (29)
2	M/39	G	6	++		Monodonal		A++ (225
2 3 4 5 6 7 8 9 10	M/75	G M	2.4			Smear		A+ (12)
4	M/51	S	4	+		Monodonal		A- (16)
5	M/53	G	6	++		Monodonal		A++ (451
6	M/73	G	666666664	+		Monodonal		A = (18)
7	F/56	G	. 5	+		Monodonal		A+ (8)
8	M/75	9999	5	++		Monoclonal		A+ (2)
19	M/57	G	6	44		ND		D+ (192)
10	M/53	G	5	++	Yes (60)	Monodonal		A+ (215)
11	M/80	M	24	++	1,00 (00)	Monoclonal		At (11)
12	F/60	M	2	+++	Yes (216)	Monocional		A- (240)
Mycosis fi	ungoides-sas	ociated gran	utomatous	stack ston				
13	M/29	M	2	Control Control		Monodonal		A+ (21)
14	M/52	66	2, 3, 4			Monodonal		A+ (130)
Suboutan	eous Trool ly	mohoma						
15	F/60	M	4	++	Yes (1)	ND		A+ (105)
16	F/50	M	3.4	**	Yes (12)	Menodonal		A+ (60)
Small/mar	dkim pleomor	minic T-cell I	veneboma					
17	M/80	8	2	4		Monodonal		A- (13)
18	M/49	S	3	*		Smear		A+ (8)
19	F/84	M	2			Smear		A+ (12)
20	F/61	S	4	***	Yes (20)	Monodonal		A- (80)
Periohera	T-cell lymph	noma						
21	M/73	M	1.2	4+	Yes (1)	Menodonal		$A \leftrightarrow (4)$
Folicle ce	enter cell tyme	ohoma:						
22	M/56	M	2	+			Smear	D- (60)
Large B-c	sell lymphoms							
23	M/75	60	2 3 4	+++	Yes (1)		Menedonal	A+ (8)

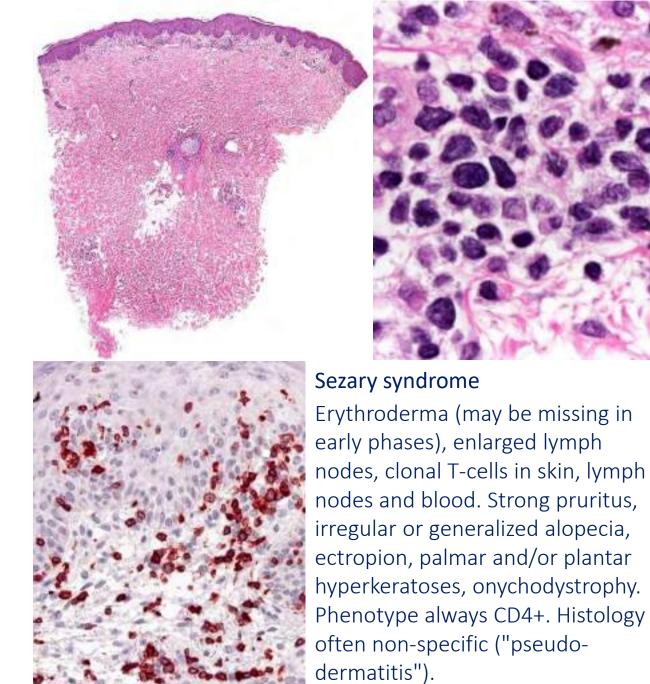
S, solitary lesion; M, multiple lesions; G, generalized; 1, head and neck; 2, trunk; 3, upper extremities; 4, lower extremities; 5, generalized: A+, alive with skin disease. A++, alive with skin and systemic disease; A-, alive in complete remission. D-, dead of unrelated causes: D+, dead of disease; ND, not done

Powertte Department of Demontology (A.S., &L., M.A., M.K., L.C.). Delvaralty of Gray, Scar, Austria, Barmacopetiologischie. Demoinschaltshar (A.R.), Frieddeledusies, and the Department of Pathology (A-CF), University of Libeck, Lateck, Germany.

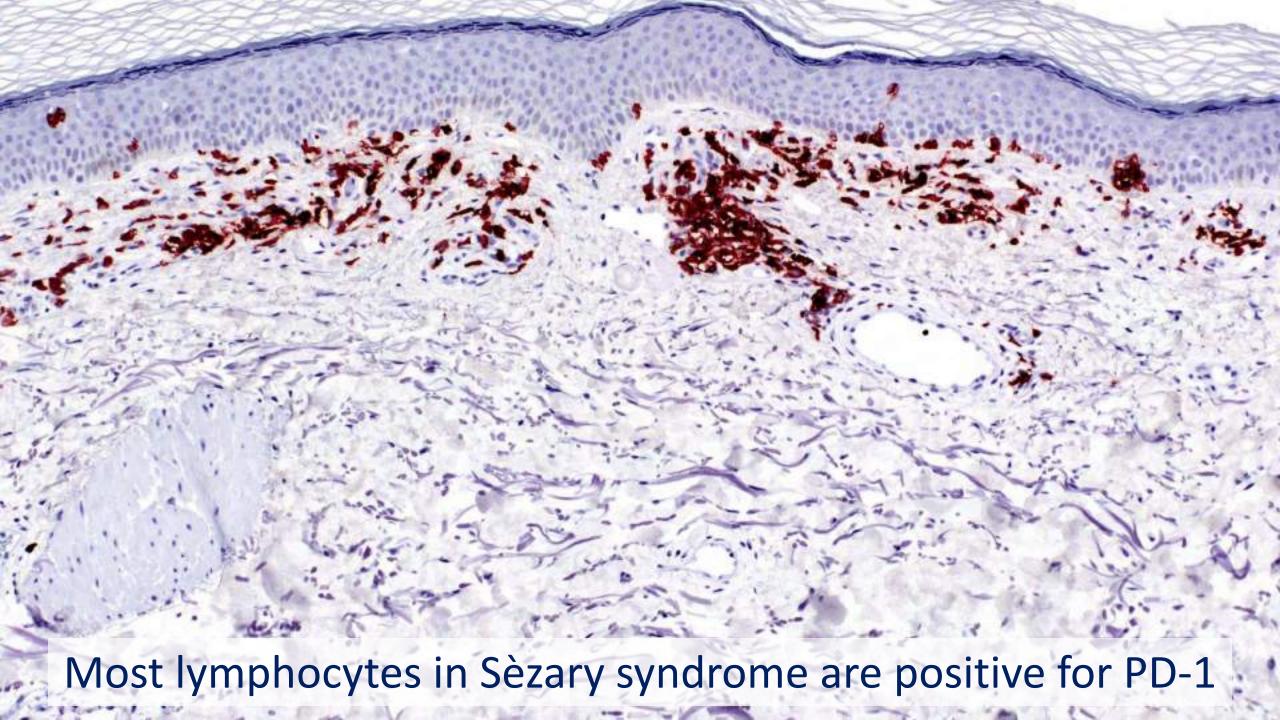
Dr. frombello was a vising fellow from the Department of Dismitology, University of Molena, Moleca, Buly The Antiget word a conting fellow from the Department of Hersteinings.

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CD3





Genetic and epigenetic insights into cutaneous T-cell lymphoma

Comule P Tersor, Korn D. Quint and Mainur H. Verneur

Department of Demotropy, Leider University Merical Dester, Leiden, The Nedwidands

Primary cutaceous T-cell lymphomas (CTCLs) constitute a heterogeneous group of non-Hodgkin T-cell lymphomas that present in the skin. In recent years, significant progress has been made in the understanding of the pathogenesis of CTCLs. Progress in CTCL classifications combined with technical advances, in particular next generation sequencing, enabled a more detailed analysis of the genetic and opigenetic landscape and transcriptional changes in classly defined diagnostic entities. These studies not only demonstrated extensive heterogeneity between different CTCL subtypes but also identified recurrent elterations that are highly characteristic for diagnostic subgroups of CTCLs. The identified attentions, in particular, involve epigenetic remodeling, cell cycle regulation, and the constitutive activation of targetable

oncogenic pathways. In this respect, observant IAK STAT signaling is a recurrent theme; however, it is not universal for all CTCLs and has seemingly different underlaying sauces in different emistion. A number of the material genes identified are potentially actionable targets for the development of novel therapeutic strategies. Moreover, there studies have produced an enormous amount of information that will be critically important for the further development of improved diagnostic and prognostic ble-markers that can assist in the chical management of patients with CTCL. In the present review, the main findings of these studies in relation to their functional impact on the malignant transformation process are discussed for different subtypes of CTCLs.

Introduction

Princey intersects Triall lymphones (TTCIs) constitute a has engineering group of non-findager. Triall lymphones that makes in the soft. Obserpatibilings studies comprised with large term followed, were insteady important to deliving different types of CTCIs with highly discrete microstrand friends of the control highly discrete microstrand friends on the control highly discrete microstrand from the control of the control

As a most of these codes, primary CTCs were included as detract in disclosure (hypotheras days facilities. The fine cleans, codes indeclosed to extensions (whicherines was the World Hooth Organisation-European Organization for Research and Teatment of Carties (WHO EDERTC) concernas cleans/based published in 2005 mile was subjequently independently the 2006 WHO desistation and its 2018 revision. These advances in Aproportion desired in the CTCs. One Trible 1 for goodness desired in CTCs.

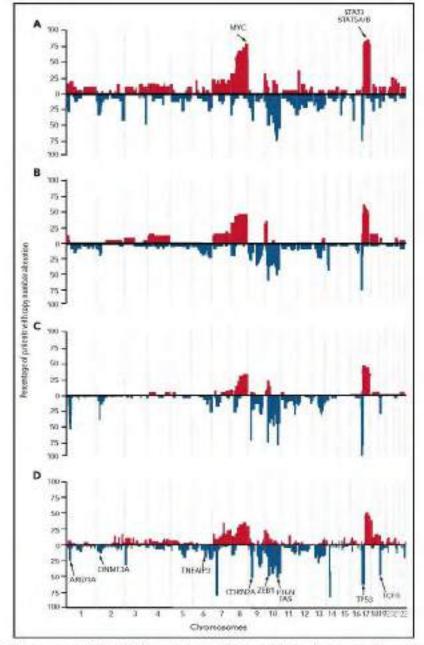
I knesser, until recently, remotivative of encountries the properties. For end progression of different CTCL subspace removed to get in virtues. Early opinions as a time interconnect webspread in the contribution of webspread.

generals instability and complex long objects, but recurrent remainstations or other recurrent general attentions were not found. The testing energy in the recurrent objects of specified with the locked appropriate recurrent educant law jet number of information of their sections of information of their sections.

Recent sechnical arbanical industry array based economics yenometry(mission pCGI) and, in particular, not operation any energy (NGS) embled a miss of called analysis of genetic, entigenesis, and immediational changes in CTCL lutter only. These statios continued the extension hexatogeneity assessor and within CTCL subgross but also identified requirem trokes by abortions affecting incogenic conveys in different types of CTCLs. In the present review, the main findings of these studies for different subgross of CTCL are presented.

Genetic alterations in Sézary syndrome copy number alterations

Early studies on gariest attractions in Serary synthomic (Set readly using a sign and categoriested attently identified extension gares is industry with conclusive beyong the 2⁻¹ A series of generate scatters using sCEII or single-scatterable polymorphism arrays therefore considerational regions a factor to arrays therefore considerations.



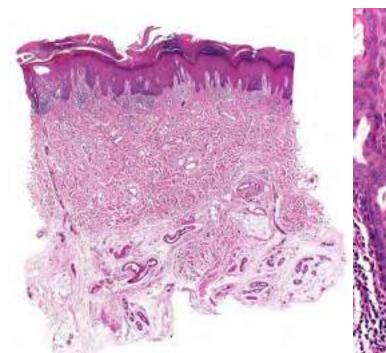
Extensive genetic instability with complex karyotypes.

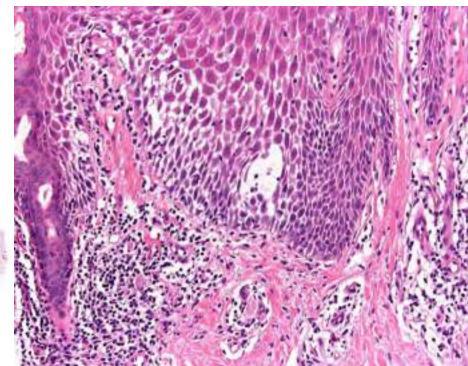
Significant gains in regions with known oncogenes like MYC; common STAT3/5B amplifications and P53 deletions.

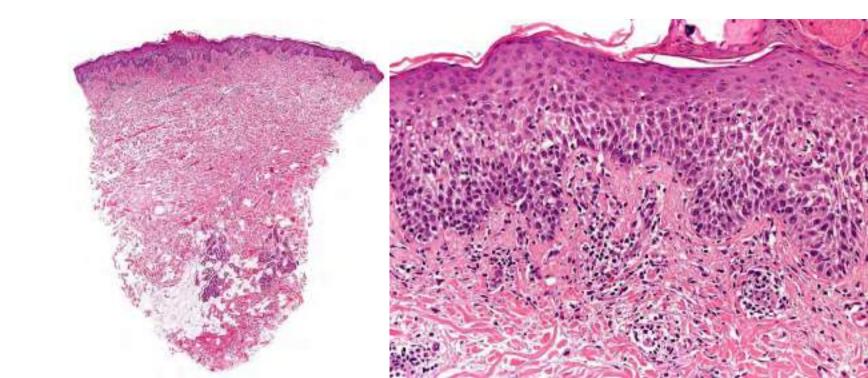
Aberrant JAK-STAT signaling is a hallmark of T-cell lymphoma and appears to be of critical importance in Sèzary syndrome.

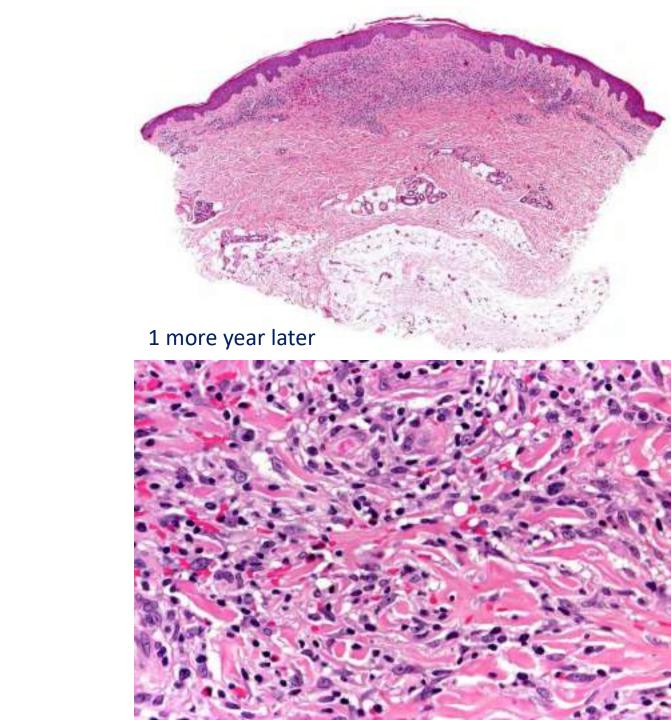
Figure 1. Schematic representation of CNAs in DNA of tumor cells of periodic with Scillatorated for independent calculat sating different platforms. Compared to independent calculate sating different platforms and compared to the compared

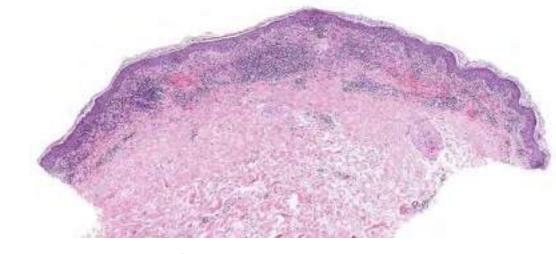
M, 51
According to the patient itchy,
"eczematous" lesions for the last 3 years.



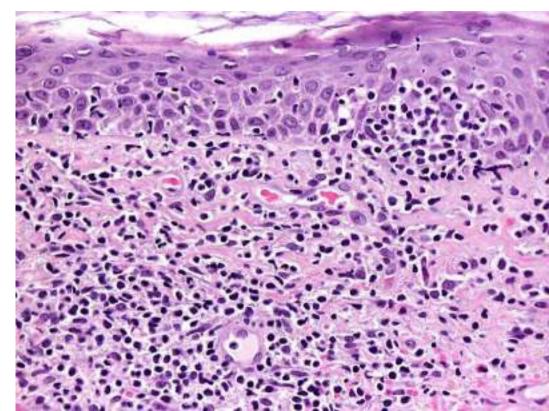






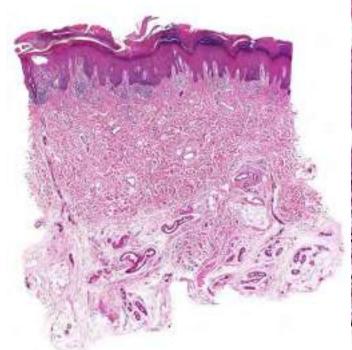


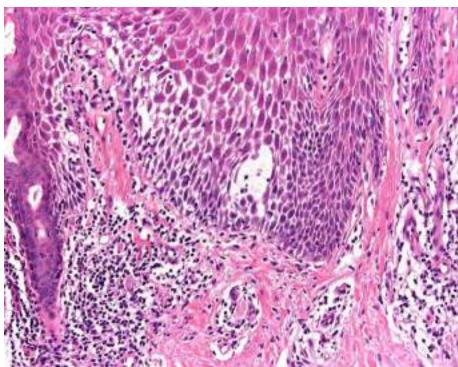
3 more years later (5 years after first presentation); DoD (8y survival)



Prodromic phases of Sézary syndrome may mimic clinically an inflammatory disease, particularly an eczematous / pruriginous dermatosis ("red man syndrome").

Histopathological features of overt Sézary syndrome may be non-specific as well, simulating a spongiotic dermatitis ("pseudo-dermatitis"); neoplastic cells may "colonize" an eczematous dermatitis in prodromic, subclinical phases of the disease ("koebnerization").





LORENZO CERRONI

SKIN LYMPHOMA

THE ILLUSTRATED GUIDE

FIFTH EDITION







WILEY Blackwell

Table 28.1. Classification of extension precipity methors including "mulignatif" precipity militaria

Cleicopathologic entity	Serulated mulignant lymphoms				
Chonic adminic dermatins lockinic initiation() (prophorential dermatins lockinic initiation) (prophorential dermatins lockinic initiation muchoss and other beings alternopic inhibitions (inheritation dermatins) (inheritat	Mycmic flungardes/Sécrity syndrome:				
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"Acrailmendolymphomotous angicilisatura in chabrer (WACHE)," "T-uid-inth angichiacoid polypoid poeudolymphome," "(Herdina lymphoplamharpic plaquaria (Inhabian "1"774-cell angichiadoid paeudolymphome"). Nebuluir poeudolymphomotous cultaneoius intribates in congeneral instrume deficienties. Peludolymphomas in lettoic Chall-insh rostulia verse (I).	Cucarecia COH sinalimedium Ficali junghopaliferative uscadar oi marginia zone lymphoma				
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It was the cases recognists, cells of a myelood leaderno are present within the intercale of the acquired Soviet sundcome.

REVIEW



Cutaneous pseudolymphoma—A review on the spectrum and a proposal for a new classification

Christina Mitteldorf

Werner Kempf^{2,3}

Department of Certainstage Version orage and Alkoyolmay, University Medical Curtor, Gettingen, Detroory

Resident (faits Histologie) & Dispressite. Zimb Sameoni

Digital residual Consultation (Information Hospital Dielek, Tirturk, Sweppeland.

Cornerwines

Clinicaling Witnessor, M.D. Department of Damotology, Venezuology and Atturpology. Jahren TV Medic / Gertan, Rosert-Kactholin. 10, UTCPS Cathinger, Germani, Emplit charleting natical confluence, and gesttingerufe.

Abstract

Cutaneous preudolymphoinas IPSLO belong to a group of lymphocytic inflitrates that histopathologically and/or clinically simulate lymphomas. Different causative agents ing. Bornfo sp., injected avantames, lattoo, arthropod bitel have been described. fals in many case no cause can be identified hence the error bloomink PSI. Clinical pathological correlation is important to make the dismosts. Four main groups of cutamenta PSL can be distinguished bywed on hintopathologic and/or clinical presentation: (a) portion PSL; (b) pseudo regonis fungcides (pseudo MF) and simulators of other CTCLs, (c) other PSL degresenting distinct clinical entities), and (d) Intravascular PSL, This article gives an overview of the histopathologic and official characteristics of outaneous PSLs and proposes a new classification.

KEYWORDS

B-cel lymphonia, Borrelies's cionality, cutaleous pseudokrophonia infection, T-cell lymphonia, lythur

INTRODUCTION

11 Definition

Caseous peuddisruhoru PSJ is described in the Rendard and rescthe Implemational output his histopical grady and/or circuity interesuserose implicess." Blood on this wide difficient 8 is clear that many progresses Safflithe criteria of PSL. Not supersingly, the terre PSL. defined in the way source as have been eversorabled in the fourture. Many infectious and sem infectious diseases are characterized by atypicallymphocras, hillwates, which can be easily maintegreted as cubiecies fyrmytorm based on histographics, features where. To limit the usage of the term outerwork PSL, we suggest a surrower definition in ambigy to cutareous longificials, chapatinformation is expediate write ing at the ologorous. By inintepediatogy alone, the diagnosis of cutamosus proudolymphows parcin many cases, only lic suspented. Additional clinicut information and further diagnostic work up are necessary to confirm the suspected alignosis. Therefore, the term cutaneous PSI, should be empirited to cursor that himspatroke/celly simulate outsineous lympinsnoishness technic value wivergob eates wis need till ton ob law-and Figure 1. Wurtrates this approach.

12 Etology

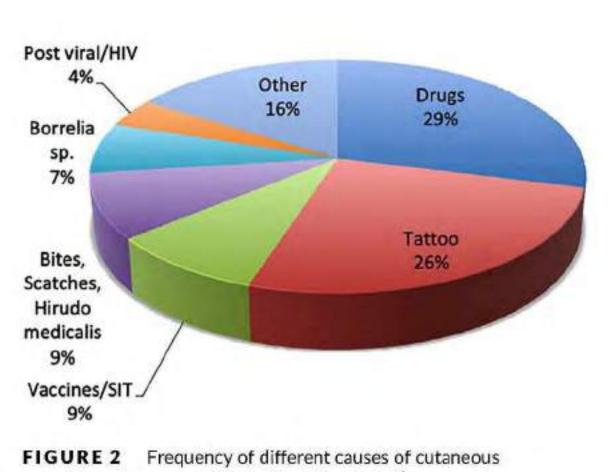
The filmbure dicurrence is wide range of causes of PSL himsely. divided into infections, drugs, and foreign agents (Table 1). Miguel et of surmorized the frequency of different, values of PSL (Figure 2). Displits the wide range of agards, for every PSL concerns trigger over be-Found mathicases are denigrated as eliquethic PSL.

1.3 Classification.

The flucture describes many approaches to clearly cusperous PSL. These include a seguitation according to the presioninging immuniphenotype (Trock Broft or visind), the hisopathologic growel) persons, two orlinopy, or distinct obvious frequency (reviewed to Rofu. 1,2,5]. Morar of flame approaches allows accommission of your traping features. Moreover, the phenotype and ethilogy are not evidera at first phone: further dispressio work-up to emental. The composition of the infiltrate is variotic, being influenced by generic and immune togical flattors of the how, as extented in the observation that inertical agents degs, Barrello soil can Viduce elitter B-PSL or T-PSL

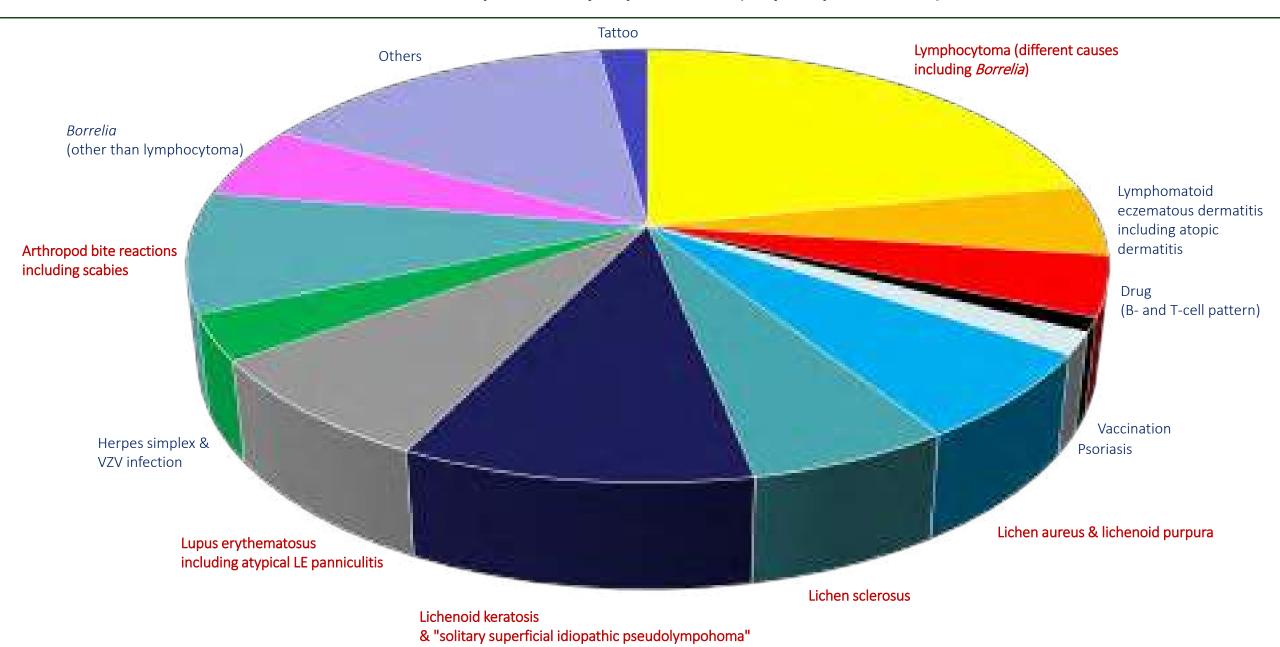
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1 Climp Patrol. 2020/11/10-97. why reins then y consymmetrics



pseudolymphomas, modified after Miguel et al4

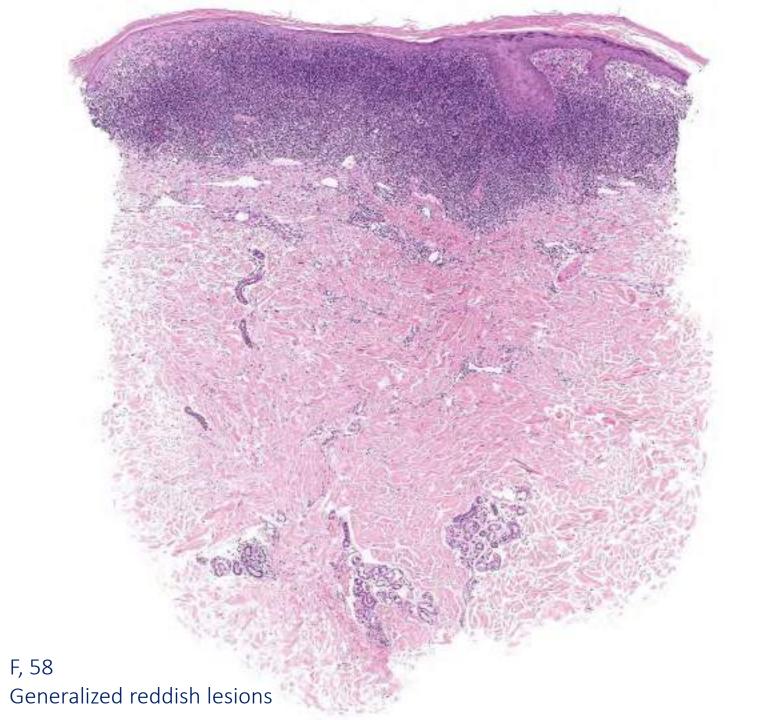
Cutaneous pseudolymphomas (my experience)

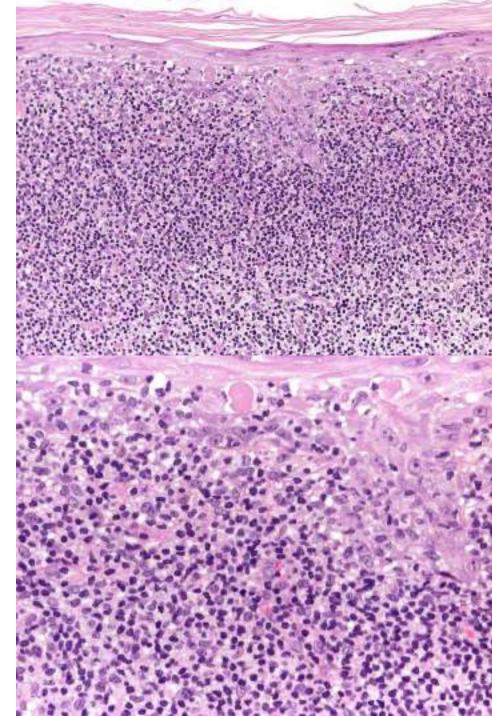


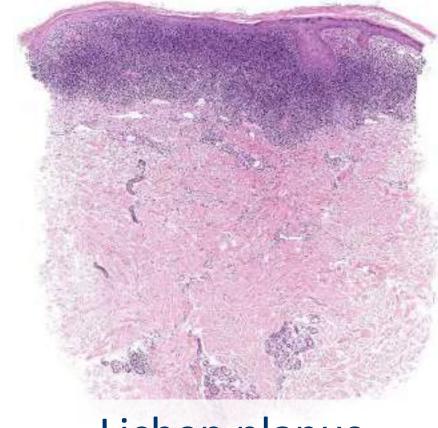
Cutaneous Pseudolymphomas

General Histopathologic Remarks

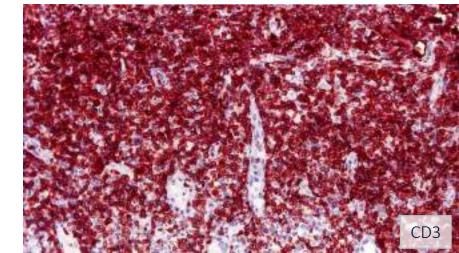
- A band-like T-cell infiltrate with intraepithelial lymphocytes is not restricted to MF or other CTCLs, and is not uncommon in several inflammatory disorders (e.g., lichenoid dermatoses)
- Low-grade malignant cutaneous B-cell lymphomas are usually characterized by a prominent population of reactive lymphocytes that may be the predominant one
- Identification of the neoplastic population crucial for proper diagnosis and classification (phenotype, proliferation pattern)
- kappa/lambda ratio for detection of monoclonality: 10:1; lambda/kappa: 4:1

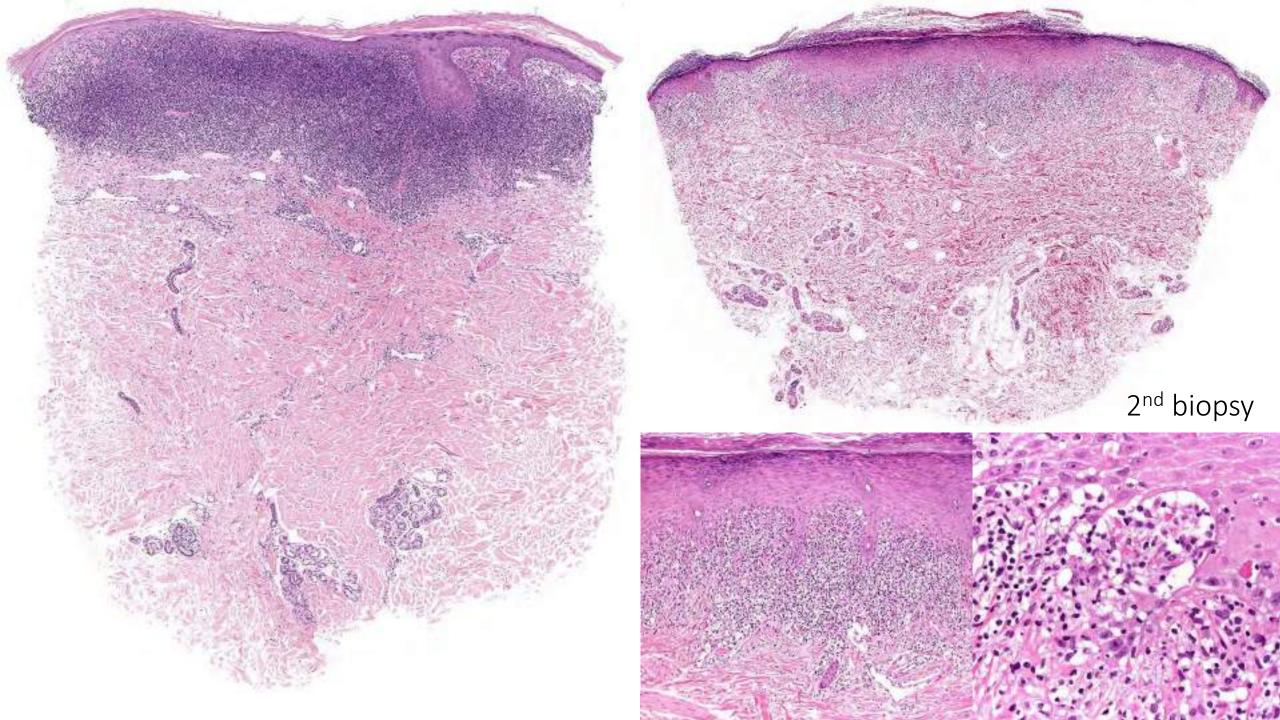


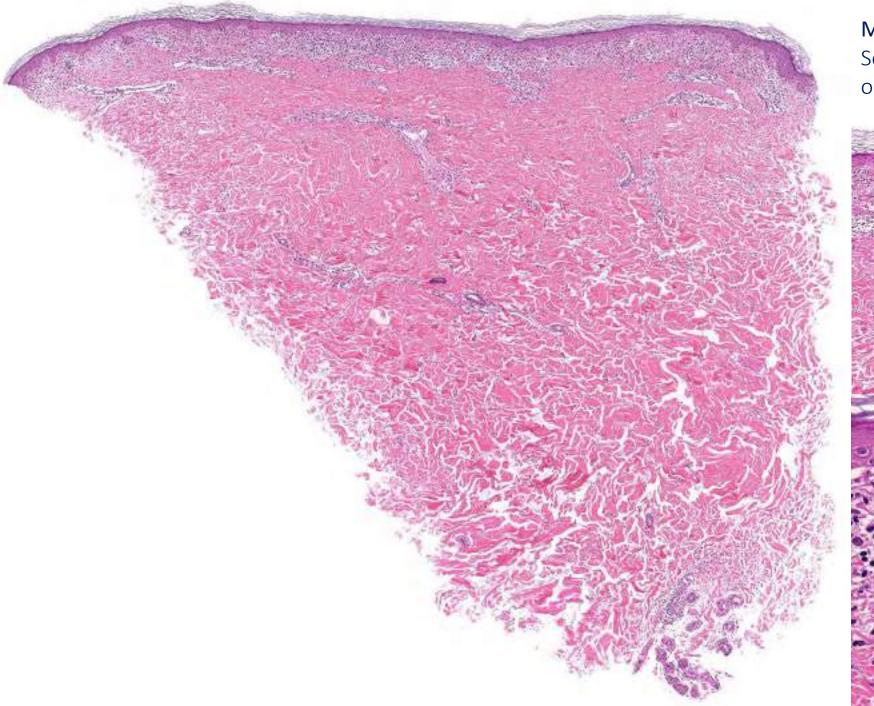




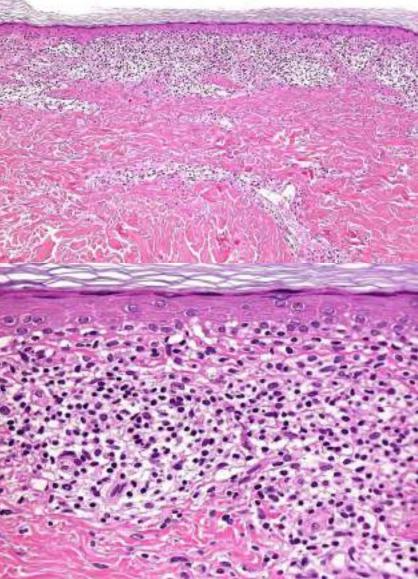
Lichen planus

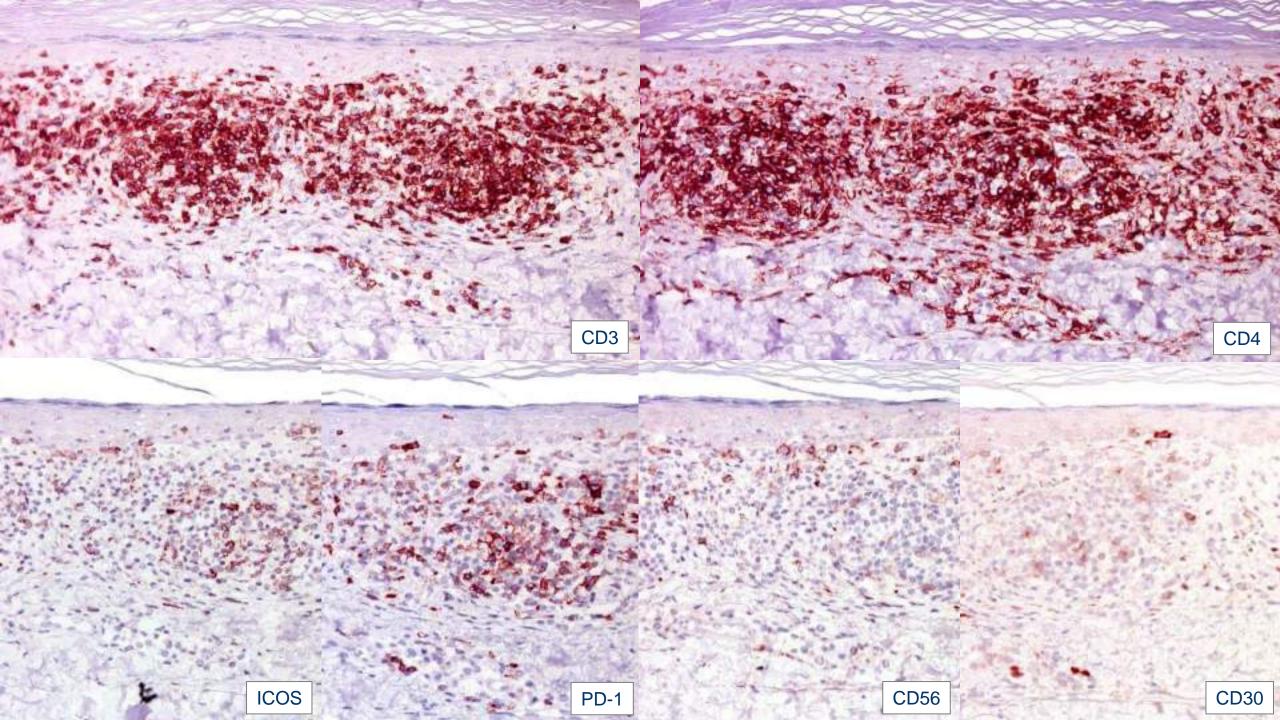


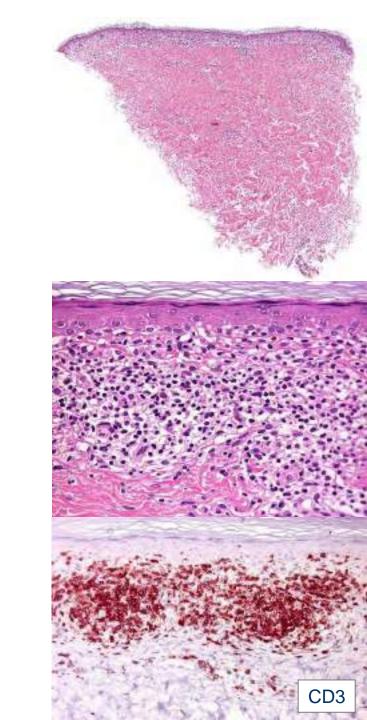




M, 50.
Several, partly hyperpigmented macules on the trunk and flexural regions.







Pseudolymphomatous lichen planus

- The lichenoid infiltrate of lichen planus is easily distinguished from band-like infiltrates of MF in the vast majority of cases
- In some cases lack of other typical histopathological features of lichen planus (e.g., epithelial hyperplasia, hypergranulosis) and presence of epidermotropic lymphocytes may be the reason for concern
- Phenotypic features of these cases do not provide differential diagnostic criteria; correlation with the clinical picture and/or repeat biopsies allow a precise diagnosis

OSKETS In Hills O' See ATT Plumper by Time Prize of See July

ournal of Cutaneous Pathology



Evaluation of follicular T-helper cells in primary cutaneous CD4+ small/medium pleomorphic T-cell lymphoma and dermatitis

Background: CD4+ small/mailium-sized phomocphic T-cell houphoma (SMPTCL) is a contrince sid primary cutamous lymphoma, in which the candidate neoplastic cells express a follicular T-helperphenotype. We describe 16 cases of SMPTCL and compare expression. sCPD-1, CXCL-13 and ICOS in these rumors with 40 derimatin cases Methods: Histopathologic examination and immunocytochemistry. were performed for 16 namers and 40 assorted demanitis cases. Results: All but one parient presented with solitary lexions. Each biopsy revealed a dense nodular new epitheliotropic infiltrate of anypical T-cells. Neoplastic rells were CDS+/CD4+/CD8(-/CD50+). Cutamous recurrence occurred in one patient over a median follow up of 8 months (range 3 - 36). All turnors widely expressed PD-1 and ICOS to a lesser extent. CXCL-D strined much fewer cells. Of the deemating cases. PD-1 imost purperous and KXOS hizeled lymphoid cells in allcases, albeit fewer than in the tumors, and CXCL-13 was negative in 52. A cosette pattern of PD-1 expression was identified in all the SMPTCL cases but not in demnation

Conclusions: There remains uncertainty about the appropriate. nosological status of SMPTCL, which name authors omsider to be a perudolymphoma. However, this study suggests a significant difference is the prevalence and patient of follicular T-helper cell markets between this tumor and lymphoid problerations known to be mactive,

Teyoroti: cuamoosa lymphoma, folicular T-helper cell, PD-1. perudolymphorus, smal/medium plecusophic T-cell lymphorus

Ally MS, Prasad Hustasebally RY, Rodriguez-Justo M, Martin B, Verdolini R. Amard N. Child F. Anygalle A. Whittaker S. Morris S. Robsem A. Foodustion of lifficular T-helpey refly is primary cutaneous CD4+ snal/medium pleomorphic T-cell lymphoma and dermaticis-J Cutan Patriol 2013; 40: 1006 - 1013. © 2013 John Wiley & Som A/S. Published by John Wiley & Sons Ltd.

Mina S. Ally*, Ranganna Y. Prasad Husasehelly², Manuel Redriguez-Justo³, Blanca Martin1, Roberto Verdolini4 Natalie Attard1, Fiona Child1, Ayoma Attygalie⁵, Sean Whittaker¹, Stephen Morris⁶ and Alistair Robson^t

"St John's limit tute of Dertriabilities: London

²Princes of Wales Hospital, Bridgent, UK This wently College Hospital, London, UK. Princess Alexandre Hospital, Harriso, UK. Raval Marston Hispital London, UK, and

"Si Thomas' Hospitat, Landon, UK.

Dr Albinsk Rebson, FRCFylls Dig RCPsh. SEJORNS ENDINGE OF BEITHROODS, SETTIONNEY Horaital, Wedstandar Bridgs Rast, Lordon SET

Tel: 144 207 1847 186 Fee: +44307188090 s-mail: attitus repromūtiniae uk-

Apopted for suplication July 9, 2019

Primary cutaments CD++ small/medium-sized pleomorphic T-cell hyphoma (SMPTGL) is a provisional entity in the WHO-LORTC else/ification of cutaneous houphoreas. It represents

approximately P5 of all primary cutations lymplemus. Clinically, SMPTCL is characterized by a solitary plaque or numor on the head, neck or extremines. Less frequently it can present

SMPTCL: 16 (15 solitary)

Fczema: 11

Drug reaction: 10

Lupus erythematosus: 5

Psoriasis: 2

Hidradenitis suppurativa: 2

Lichen aureus: 2

Erythema nodosum: 1

Folliculitis: 1

Erythema annulare centrifugum: 1

Viral exanthema: 1

Lichen sclerosus: 1

Lichen planus: 1

Urticaria: 1

AHWE (epithelioid hemangioma): 1

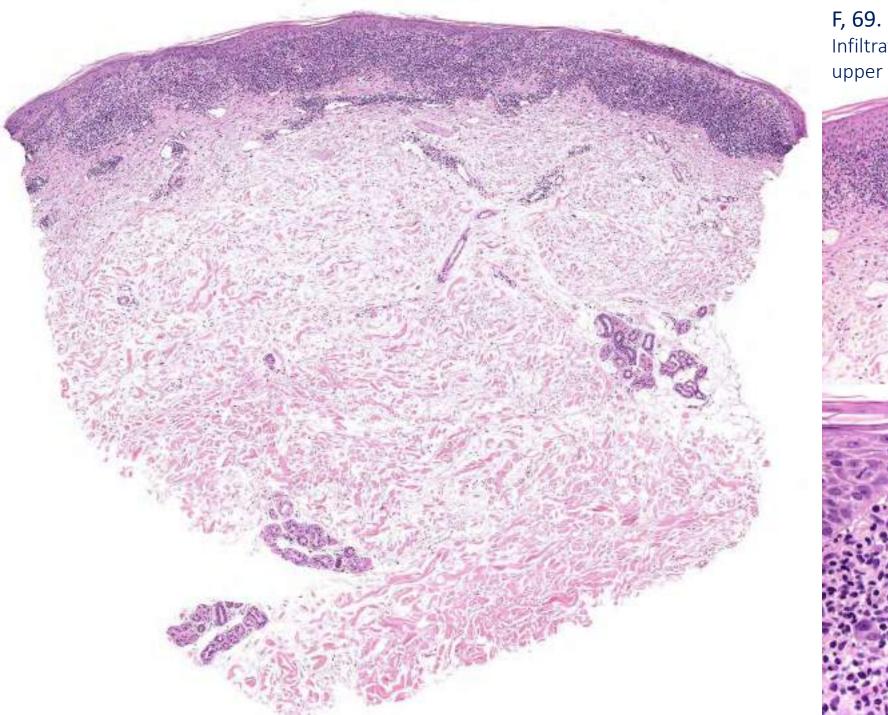
SMPTCL: all cases positive for PD-1 and

ICOS (ICOS: lower # of cells); CXCL13

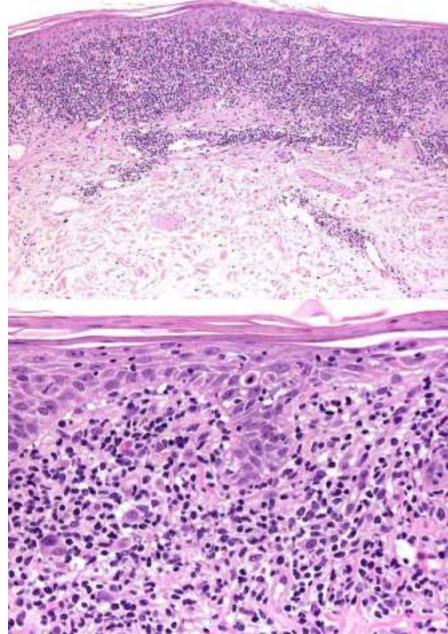
stained "much fewer cells"

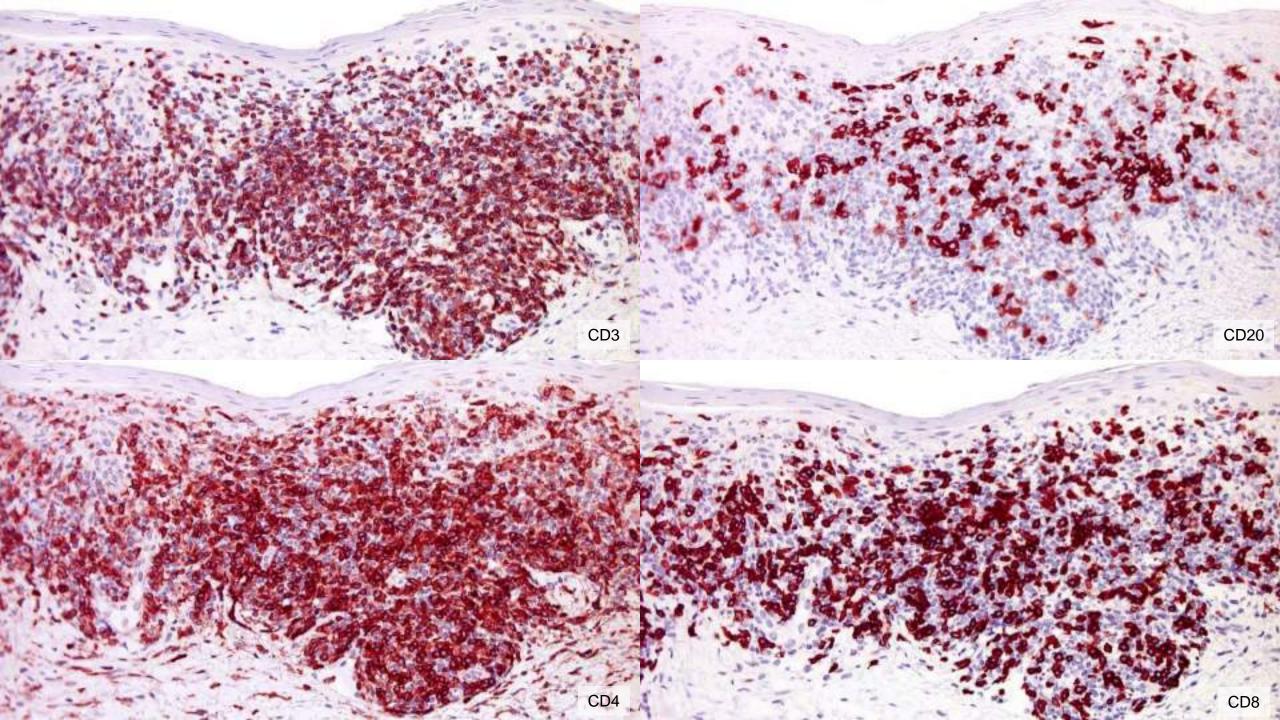
Controls: all cases positive for PD-1 and

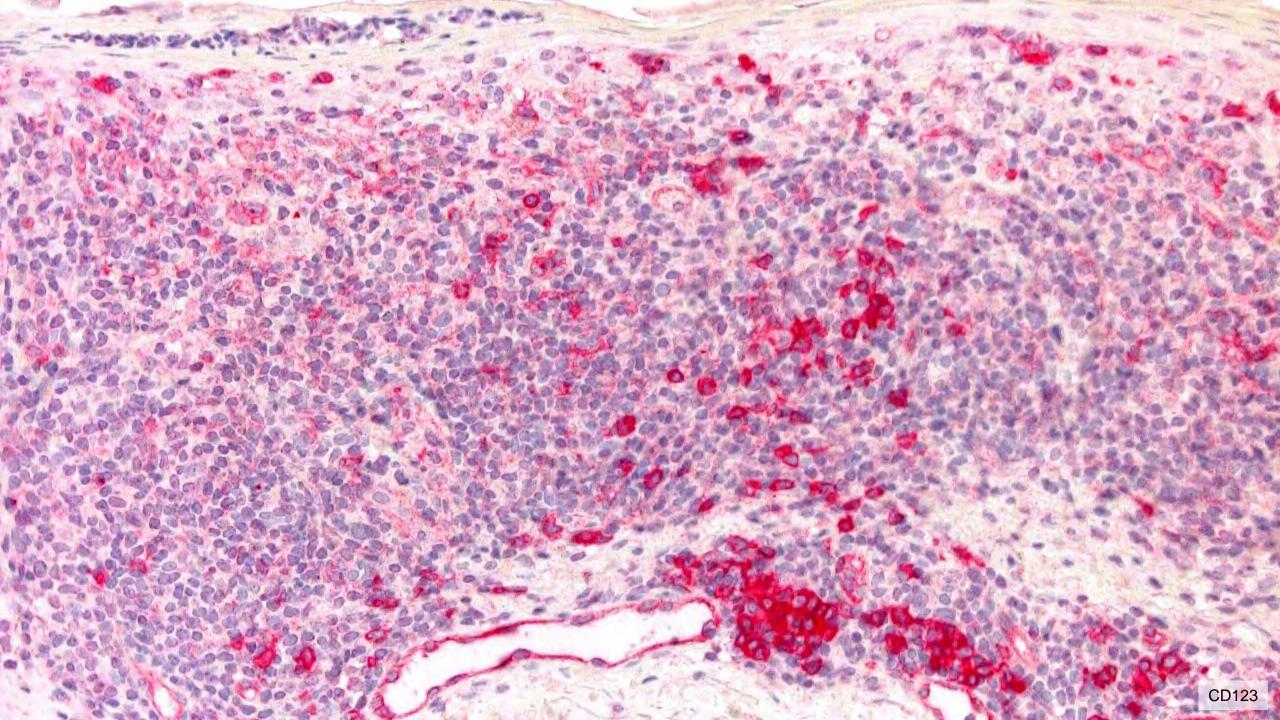
ICOS (ICOS: lower # of cells); CXCL13-

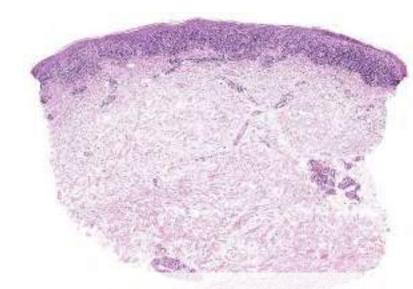


F, 69.
Infiltrated, reddish papules and plaques on the upper trunk.









"Pseudolymphomatous" LE

ANA 1:1280

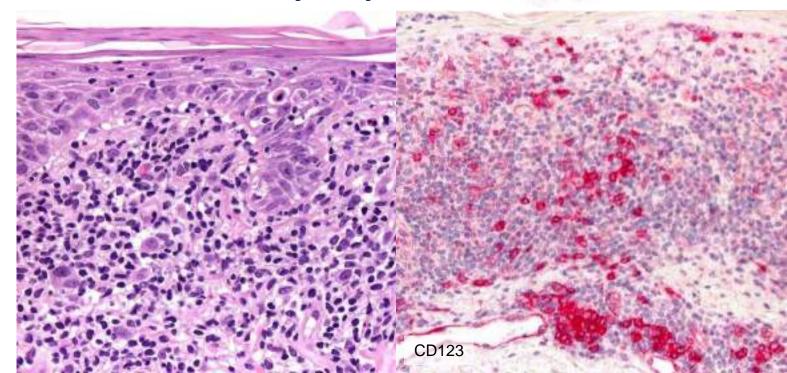
ENA > 32.0 U/ml (0-1)

Ro-Abs > 240.0 U/ml (0-10)

Ro 52-Abs > 240.0 U/ml (0-10)

Ro 60-Abs > 282.0 U/ml (0-10)

La-Abs 19.0 U/ml (0-10)



ORIGINAL STUDY

The Histopathological Spectrum of Pseudolymphomatous Infiltrates in Cutaneous Lupus Erythematosus

Amunda Persira, MD.*† Gerarda Ferrara, MD.*‡ Panla Calamaro, MD.*§ Carla Cata, MD.\$ Cesare Massone, MD.*|| Francisca Boggio, MD.*** Lucia Printa-Torrez, MD.*†† and Lorenzo Cerruni, MD*

Abstract: The manners of profiburgheeston militate in catheren layor emberiation (LT) is described match in layer. parairaists and hope transfer-braphocytic infiltropies of the skip Cleaner Knieff. We collected 15 sales of pseudobrechamous of 1 other from topes prantimitis and lopus turnibs (Mil) 411; sign mage: 15-79 years; most age: 585 years; moffan age: 57 years), OF the 15 cases, 9 (60%) were characterized by dasse nodular infillrates. Time nees (20%) showed an unsuemitic preem with symbolical atgrits of Tyanplacel wells: T cases (13.7%) aboved a break-like intilitials. unimisting sycosis finguiles, and I have lad mixed features of the hard-like and augmentain patterns. Class to the histographylogical disposis of elli way pessent si interfact dematts, choten si plantacytoid destrice orbi, and demail terms deposition. Dur study shows but the spectrum of pseudohorphomocous presentatives of all its in broader time previously described, including build-like cases that may be missimum as myemis (maniles, and apprendic cases that may be minimized at an appearing lymphome Bangolius. of each open is provide only on contributing and belong correlative. not a wolle of notingue located of histopathological suspection to allow a corneet diagnosis and the proper transgement of the particula-

Key Words: enturent lapor tryffermionis, enturent postdoljusphorus, tateffine demarkis, plasmeryteid deadric cells, busé-like nellven, sugacentric infiltute.

Clin J Diminispedial 2018;44:241 2251

INTRODUCTION

Catoreous logur exphenatosus (cLD) is a chronic automatuse disease of the skin which may be associated

Faux En "Research USS Demandrosoftsings, Department of Demandrings, Street Harrisoft of Gran, Gwa, Austria, "Androine Politicipy Cert. Harrisoft Demandros Professor Burnaria University of Phylosoft Land of Sin Ellings University Federal of Single Greater. Proceedings Foods of Androine Publishing Cert. Monerate this special Soliton and Employer Engineering Chronical Proceedings of Single and Employer Engineering Chronical Proceedings (Certain, Bullet Sin Children Phromatogra Selfuna, Boyana Greate, Barrie, Buly, Beynnings) Selfuna, Boyana Greate, Barrie Children Charlesoft Demandring of Branching Control Proceedings (Selfuna, Boyana Greate, Barrie Olderston, Climanny of Billian, Demandring Bernard Control Proceedings (Selfuna Bellin, Sentantino) of September 10 (2014) Billian, Sentantino, Sentan.

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Conseign C 2017 Wolton Kirner Holds, Inc. Altriche mornel

Am (Demosopothol + Volume 40, Number 4, April 2018

wife systemic acvolvement.4 Histopothologically several posents can be observed, depending on the type of cl.3) and the akin structure (sa involved. The most typical features are the presence of interface demantity with vacuolar changes of the firest kerminocytes and necrosic kerminocytes, mucht deposition, and variably dense lymphoid cell infiltrates.2 The latter sensily do not pose differential diagnostic problems with cutaneous lymphonous, with 2 exceptions, namely (1) lopes pronocultis, which may mimic subcommence panniculari-like V-cell lymphoma*; and (2) lanus turnishas/lymphocytic infiltration of the skin (Jessen-Kumf), which may be mistime-pened complisingseally as a comnous lymphoproliferative deserter. 14 In dire, only associated reports have focused on the occurrence. of oseudolymphomatous infiltrates in cases of cLE other then lipus permiculitic and lupus turtidus/lymphocycle infiltration of the skin. 55 However, because of the common obsence of systemic symptoms and/or immunological abcompalities, and the possible negative direct immunofloprojected test even in involved slette2 a cl.E with atymed lympheid siffitures cuty be ministerposted as a carations lymphopmiferative disorder, particularly in cases is which a careful etimicopathologie carrelation is not possible.

We describe the homosphalogical findings in 15 mans of cl.1: characterised by pseudo)uplomatous utilitzaes, with maphasis on the different patterns minimizing various cataneous lymphopolitenesse conditions.

PATIENTS AND METHODS

The cases were received from the files of the Research. Unit Demonstrately, Department of Demonstrately, Medical University of Grae, Austra. The study has been approved by the ethical committee of the Medical University of Grae. Come of layer principalities and layer transition by appropriate infiltration of the skin were excluded because they were already described as potential dragment practic. It is all cases, the final dimensis of pseudolymphonomous cliff. Was based on the synthesis of classical additionarchylogophological data.

All slades were reviewed for mehiteerinal and sytological features of the infiltrate, and for the presence absence of to superintegred features consistent with cf. it. in all cases, as appropriate panel of artibothes had been autially applied because of the histoprehological suggestion of a commons hypophymoletrative disorder.

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Conseptation © 2018 Western Klassor Health, for, Unionlines and reproductions of this arrests to probabilist.

15 cases

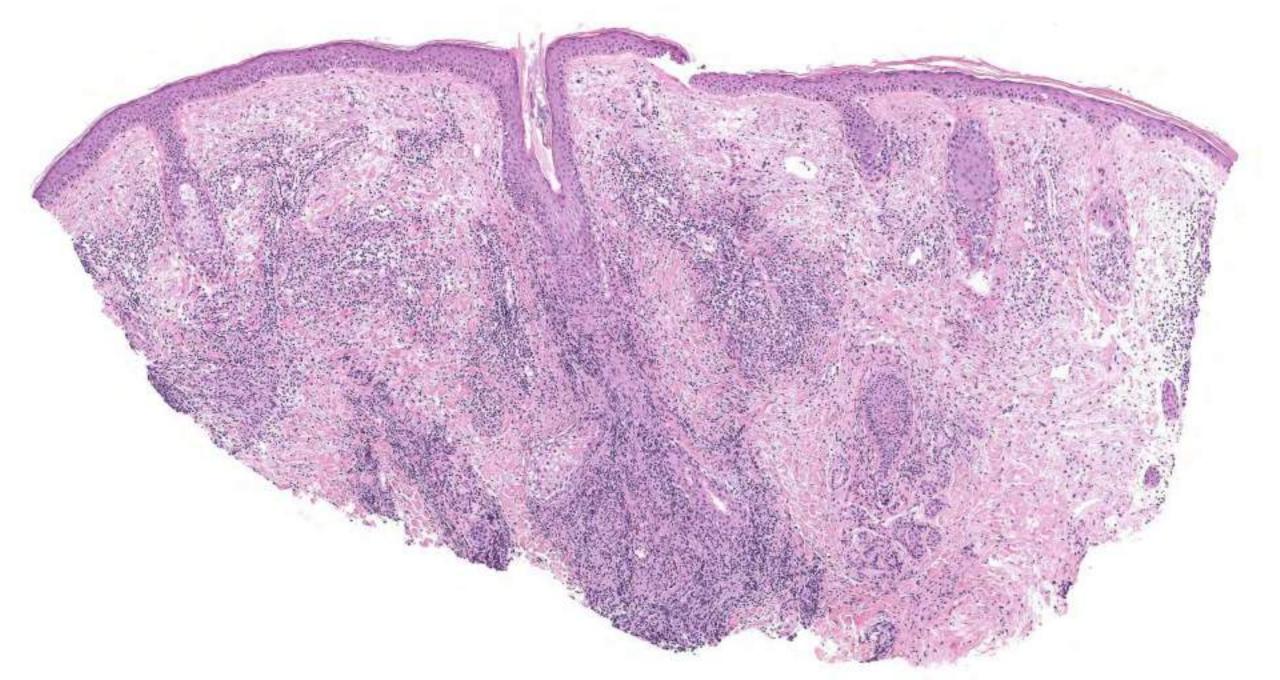
9 cases: dense nodular infiltrates

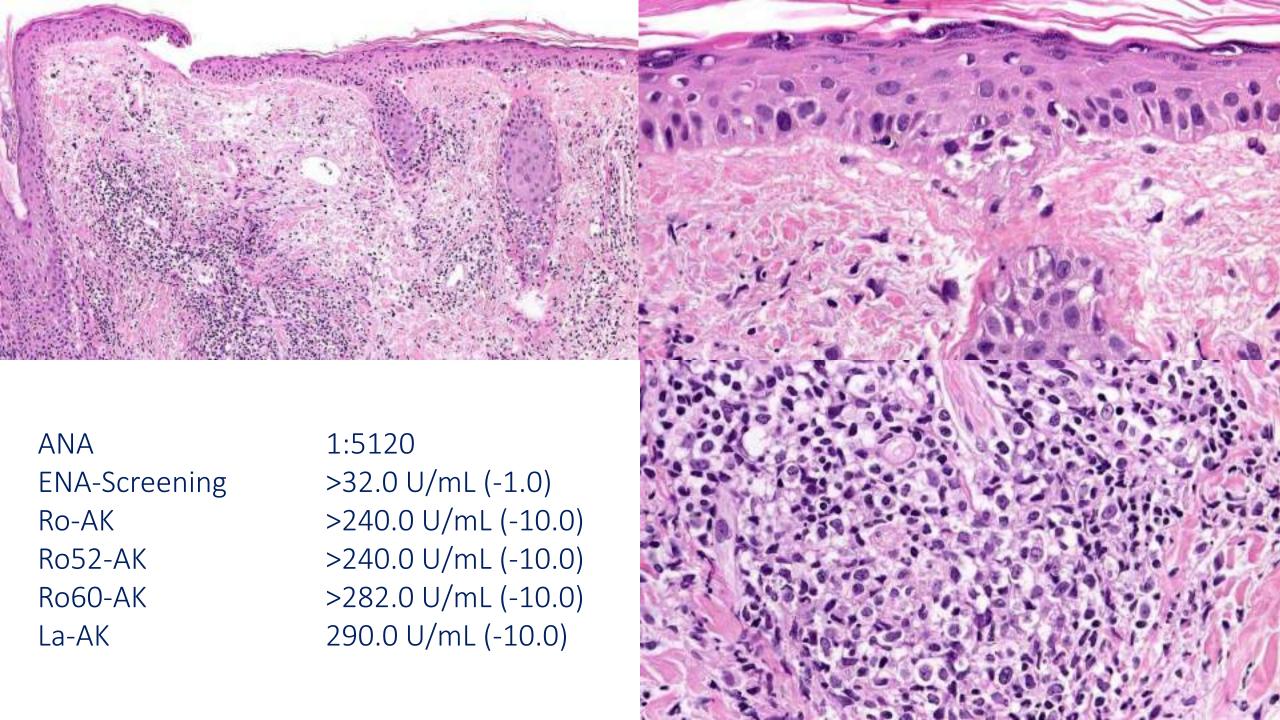
3 cases: angiocentric pattern

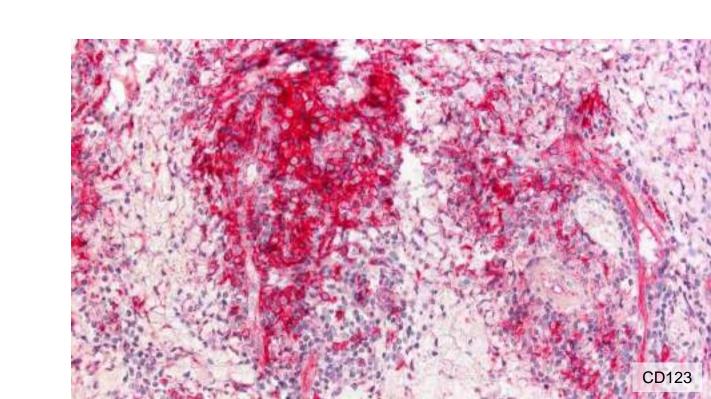
2 cases: band-like pattern

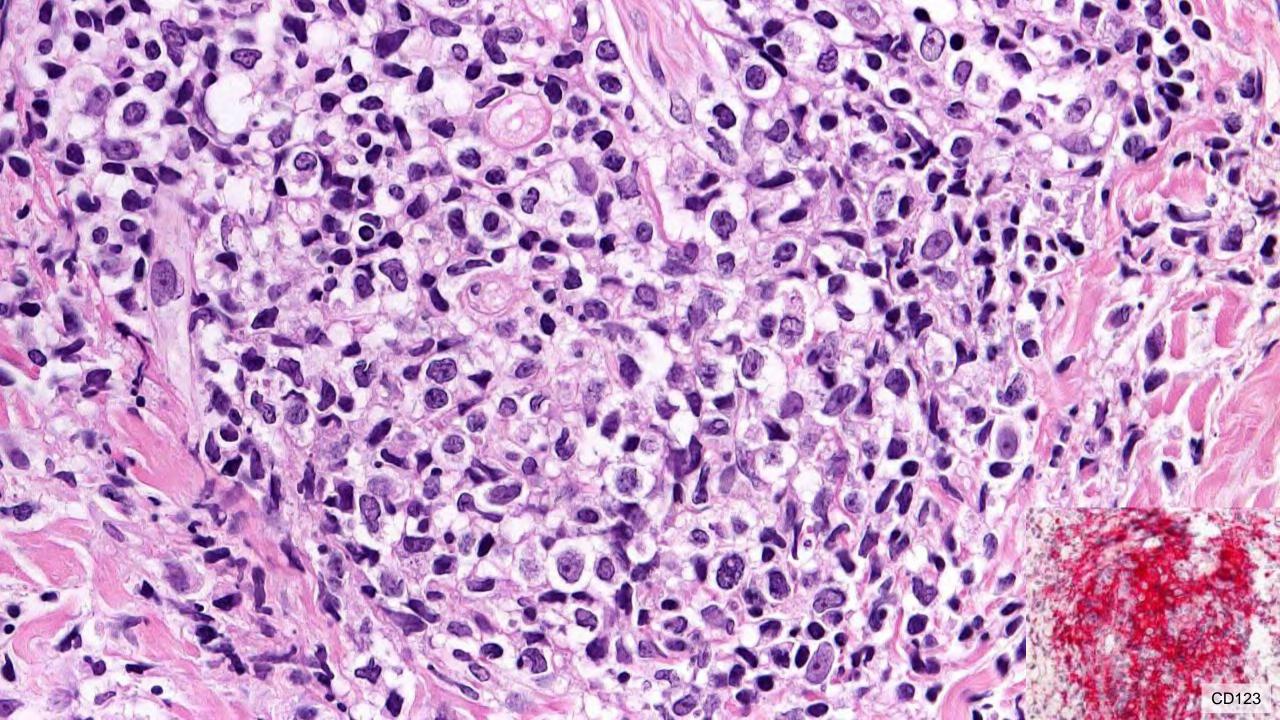
1 case: band-like + angiocentric pattern

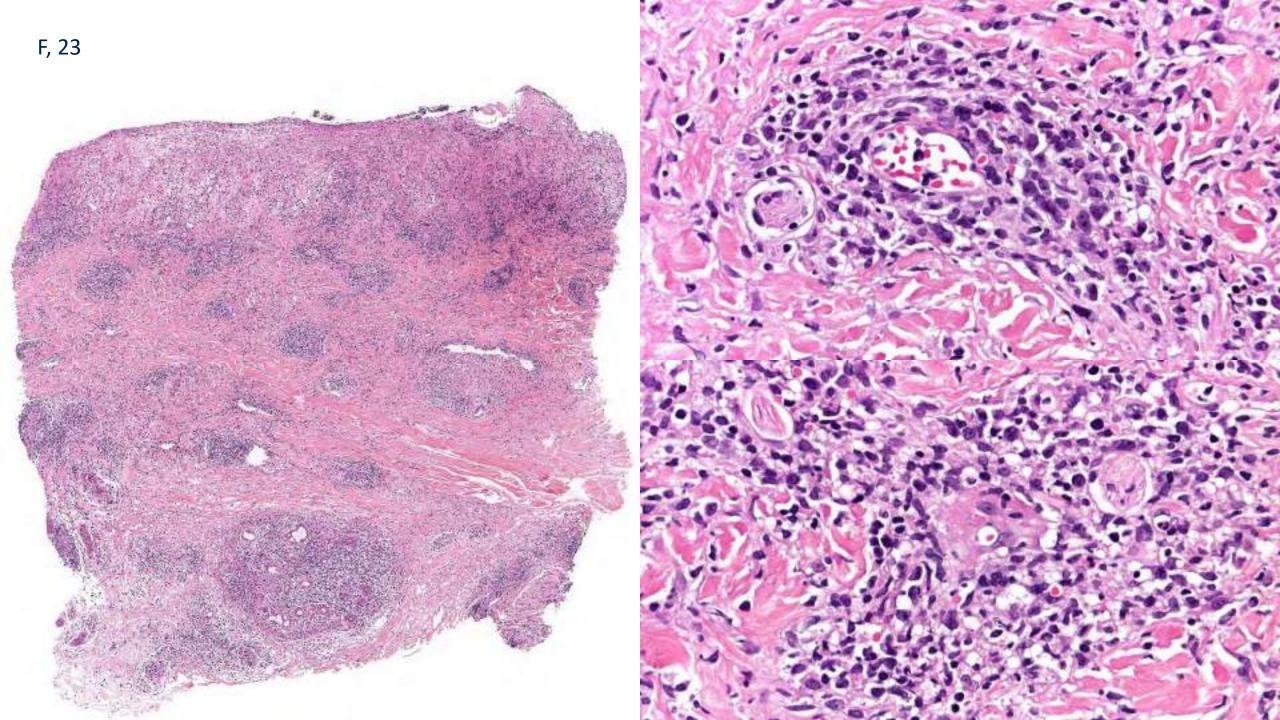
F, 35, pregnant.







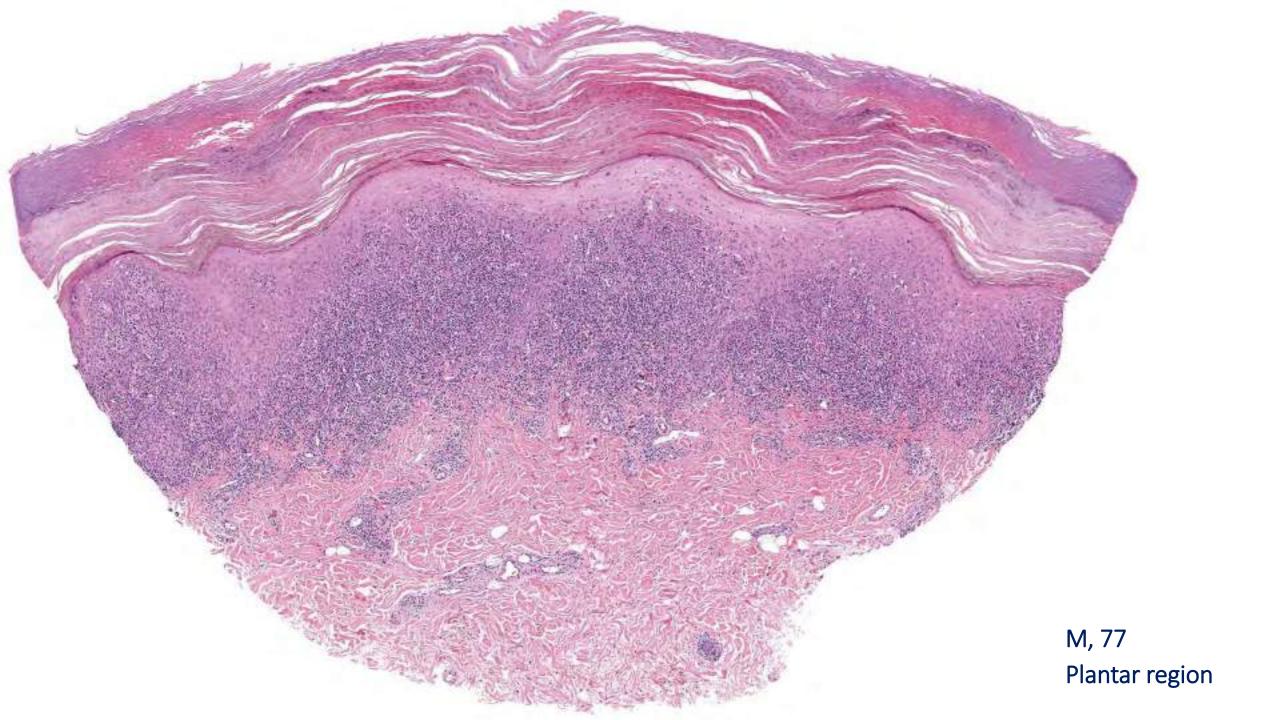




Variants of lupus erythematosus

- LE tumidus / Jessner-Kanof
- LE profundus (LE panniculitis)
- Neonatal LE
- Chilblain LE
- Multiforme-like LE Rowell syndrome / Toxic epidermal necrolysis-like eruption of ACLE (acute syndrome of apoptotic panepidermolysis - ASAP)
- Bullous LE
- Drug-induced LE
- Paraneoplastic LE
- Linear LE
- Urticarial neutrophilic dermatitis in LE
- Verrucous LE
- Follicular LE

- Acrosyringeal LE
- Alopecia in LE (cicatricial and non-cicatricial)
- Mucosal involvement in LE
- Interstitial granulomatous dermatitis in LE
- Papulonodular LE with diffuse mucin deposition
- SLE / scleroderma overlap syndrome
- LE / lichen planus overlap syndrome
- Pseudolymphomatous LE (several variants)
- Reticular erythematous mucinosis
- ? Degos disease (malignant atrophic papulosis)

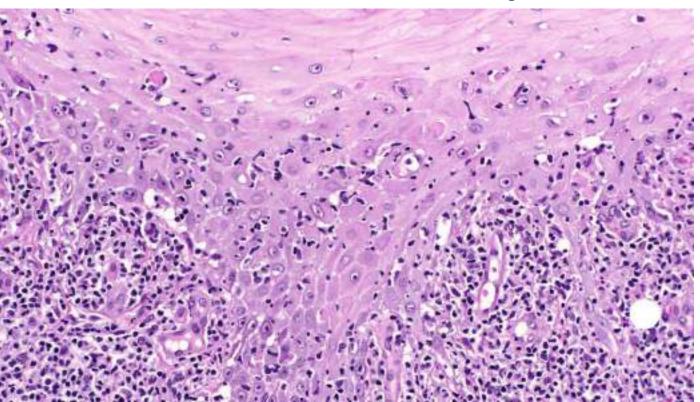


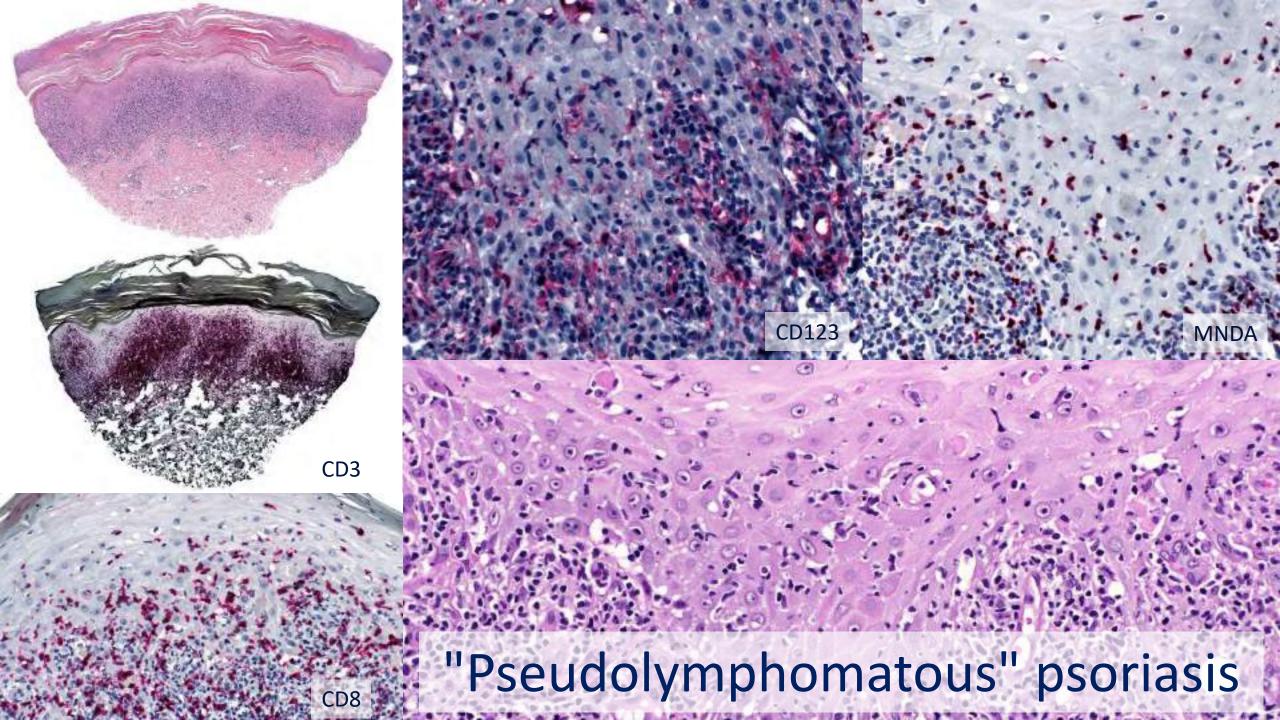


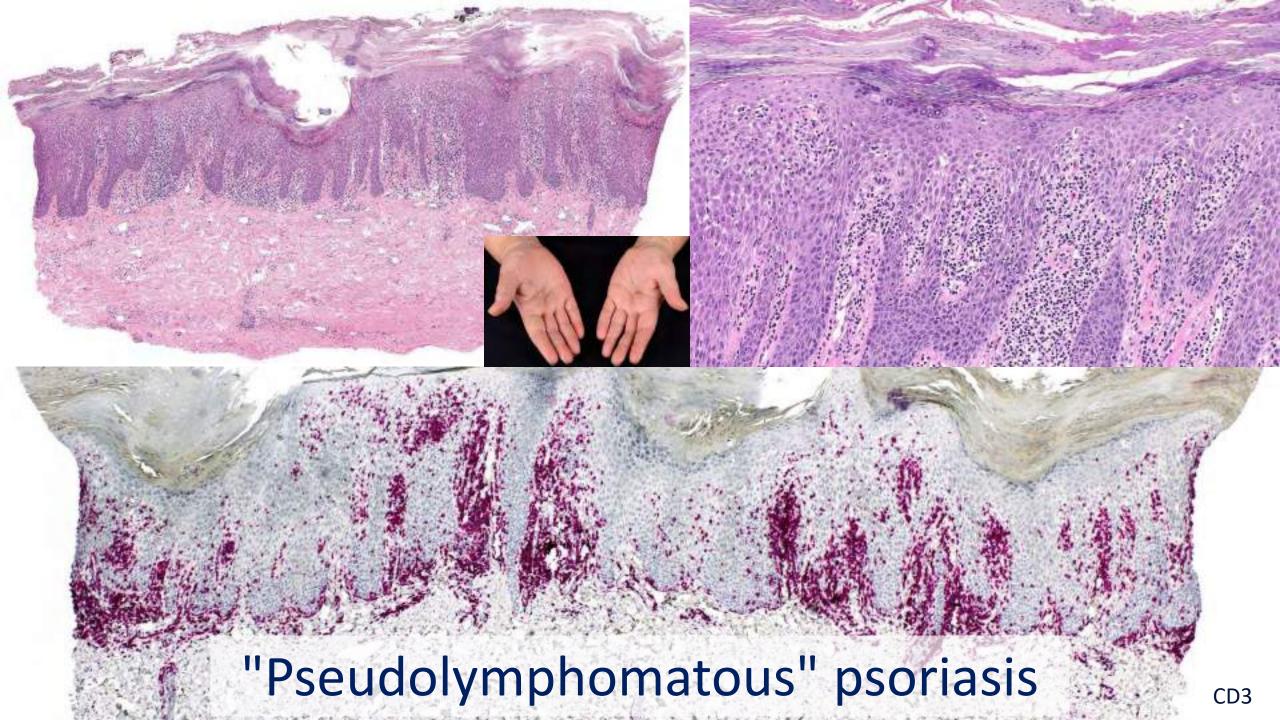
According to the patient lesions on the soles for approximately 3 years. Mostly asymptomatic, sometimes mild pruritus.

M, 77

Last sexual intercourse 12 years previously. Screening for syphilis negative.







Thomas Susko, Striot, MC, USAF, Dari E. Vander Pineg, M.D. and Richard L. De Villez, M.D. Kan Annonio, TX

The case of a 45-year-old Latin American man, who presented to the Damustatogy Clinic with a 6-month history of byperkenstate legions. continent to the points and the pathoar espects of the digits of both master, in digitassid: thiopsy of these festors revealed the classic hintologic tradings of myousis forgoides. The obvious and histologic suffwantial diagnosis of mycosis fungoides is considered. (I Am AGAD DERMOTHE 7:192-196, 1982.)

The clinical diagnosis of myestis funguities may arrienes be difficult because of the variability of its clinical presentation and course. The histologic diagnosis car also, at times, be difficult. and several entities have been described which cannot be separated tastologically from myousis fungoidas. 1-9 The hintogic behavior of the lesions. in any given patient is the altimate confirmation of the correct diagnosis. We present a patient with amount effected and histologic indiags and discase the difficulty of prospective analysis of a petient with premycotic stage myerals langeides.

CASE REPORT

A 45-year-old Mexican American man presented to the Demandagy Clinic at Audio Murphy Versions Hurpital with a 8-month history of hyperkeratotic lesizes coalised to the paints and the painter tapects of the digits of both lands. The patient has previously been tresped for several months with various tentical ateroids without improvement. The nations devied any history of

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extensive expenses to promule minds, frequent correct with invitants, meany bustory of contact offerey. Medications at the Sear of presentation lockuled NPSI issuing. 10 anits such morning, for adult-count diabetes meliture present since 1915; annual trolling, 200 mg four times a day, and manaprosenes of suffice inhalar, 1.3 mg from times a day, for almosic asthma and electric obstructive gui rurmary clisique; rad chi rediaparos ide à viroch inside. (Librium) for a long-standing againty removis-

The insiem consisted of small hyperlements pits and small hyperkennestic planters. These hadren were productionardy located on the pulpter sepert of the digits. Clinically the lesions assumbted a head ecomo-

A biopsy was taken which revealed a pseciasiform enidence with a darso Tcheroid infritate of moreoveclear cells (Fig. 2). Closer examination showed the infiltrate to cursu in predominantly lymphocytes, many with large, atypical machi. Ne apongowie of the opdensis was observed. Large, atypical monuncieur cults could be seen within the opidentsis, singly unt in gracuis. In some press, small, norspongious rescersesfilled with stypical transveriese cells could be seen

Singe the parison front guits a rileyeste from San-Autonia, on interval of approximately 7 months alapsed before his sent visit. Owing this period, the nations was treated with kerpentytics and high-pouncy topical surrook. On nours his lesions had very med slightly.

A biopsy was again obtained. Histotogie hadlargs were identical to these of the previous sample. A specimes was also primited for election oteroscopy.

Volenni 7 Number 6 Docember, 1982





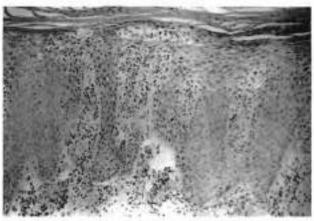


Fig. 2. Proriestform epidermis with dorse tichmoid Infiltrate of monomicleur cells. (Hematoxytin-assin stain; original magnification, × 100.)

This examination revealed in the dermis the presence of lymphocras with large hyperconnulated nactor

Complete physical examination at this time was unremarkable except for the lesions on the hands. In particular, there was no palpoble adenorative and no palpublic increase in liver at spicen site. Fatch testing was performed with the standard troy of the North American Patch Test Kit, with negative results. A blind axillary note triops; was performed, and no namor was found

psoriasis by the density and bandlike characteristics of the lymphohistiocytic infiltrate and the lack of polymorphonuclear cells in the dermal papillae. The cells seen in the epidermis and in the abscesses are atypical mononuclear cells rather than polymorphonuclear cells."

"Our case may be distinguished from

Sopies rounds in Many Tropped Statio, University of Lyap Hosts Science Center of Six Associate 7All Flood Carl Dr., Six

^{*}The opinions or unsertious creasined head a secrete private stone of To affirm and se so to be somered in tilbule or as effecting Be view of the Department of the Air Fancy or the Department of

Clinicopathologic features and T-cell receptor gene rearrangement findings of mycosis fungoides palmaris et plantaris

Sang-Tao Kim, MD.* Yuang-Soung Jeon, MD.* Hyong-Jun Sim, MD.* Sung-Hoo Kim, MD.* Yun-Keew Kim, MD.* Kee-Sock Sult, MD.* Jeong-Boon Fuck, 5tD.* and Sung-Wook Park, 5tD.* Burnn, 2002/2 Norse.

Biologround: https://doi.org/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/10.1009/1

Objective Oer purpose was to evidean the clinicopathologic features. T-off excepts: (TCR) goes incompanies findings, and progressis of MPPP.

Patients and methods: This reprospective endry has been reviewed in the clinicopathologic, TCE yigme rearrangement findings and follow-up study of 12 patients with MERIC.

Results: The dustion of duesies ranged from 9 months to 25 years with a mean duration of 5.3 years. Chairarthy hyperhorance pacture and plaques were observed main cases, with 6 cases thorough on the patine and soles and 6 cases on the gatine only. In TNM characterises, the cases were confined to TNASM cases, with a cases were confined to TNASM cases, by sharing an early stage of improve targetes ONF. Histoparticlegat findings remained hyperkerations, participations with plasma, applicancement, controlled hyperhologies, findings remained brophocytus, done infillings of transparence in all 12 cases (100%, Parapers interestances in 9 cases (15%), a very bundle of indigger in 11 cases (91.7% and busin applicancemption in 3 cases (25%). TOR by give returnated was performed except for the case and manuschinality was detected in 60 of 11 cases. In the comparison giving with juriances infilmmunory dominates, it cases a systemic actions and moduscrates. Most patients shared a good responder, in the following study of 9 cases for a main period of 47% months, only one posterior skip beginns were exceeded to the trook and lace, but the other patients laid to sign of entangalances, any executive and laid.

Limitations: These usuals were obtained from patients with MIPP in Korea. A cooperator study with lefter ethnic groups will be helpful.

Conclusions: If a patient has conditions polynoplanes derivated, MEPP should be suspected and languallylogic scales with TCB gene comprehensive should be above for early diagnosis of MEPP.

(1) Am Acad Dermand 2005;54:466-31.)

From the Department of Parmetology, Read University CoRego of Madician's and Sutan Pall Foundation Heopital, and Taja University Medical College."

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Conflicts of interest: None identified.

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Reprint requests: For Earlt Sult, MD, Department of Destruitings; Notile University Callege of Medicine, 31 forthcombons, Sockar Reser, 662-750, South Roles, Eymel Independent and CON. (1964-9622532.0)

© 2006 by the Parenton Readersy of Demistology, Inc. doi:10.016/j.jaed.2005.11.1851 M scosts/improdest/MP is the most common type of outerpools T-cell Imphorate, which has 3 clinical stages of patch, plaque, and tensor Histopothologic findings of cert). All three quite similar to other customers influentately demaitsees, utilitie the plaque and turnor stage of MF, making the diagrams difficult. T-cell receptor (TOM) y generotrangement analysis on leakenal along polymerate chain reaction (PCR) may be helpful as an adjanct to the litisopathologic features of cady MF. TOR generous management analysis has breen performed using Southern blot rechnique or PCR.

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Fig 1. Case I. Relatively well-demarcated, erythematous to brownish, hyperkeratotic plaques on the foot.

and face. However, to date, the remaining cases showed no further development of the skin lesions and no extracutaneous involvement (Table 1).

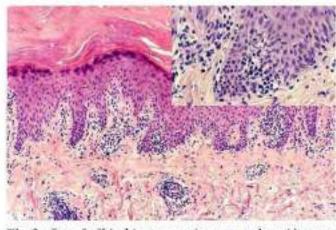
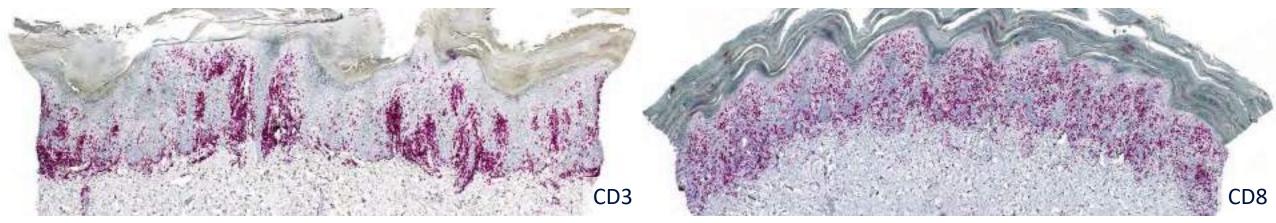
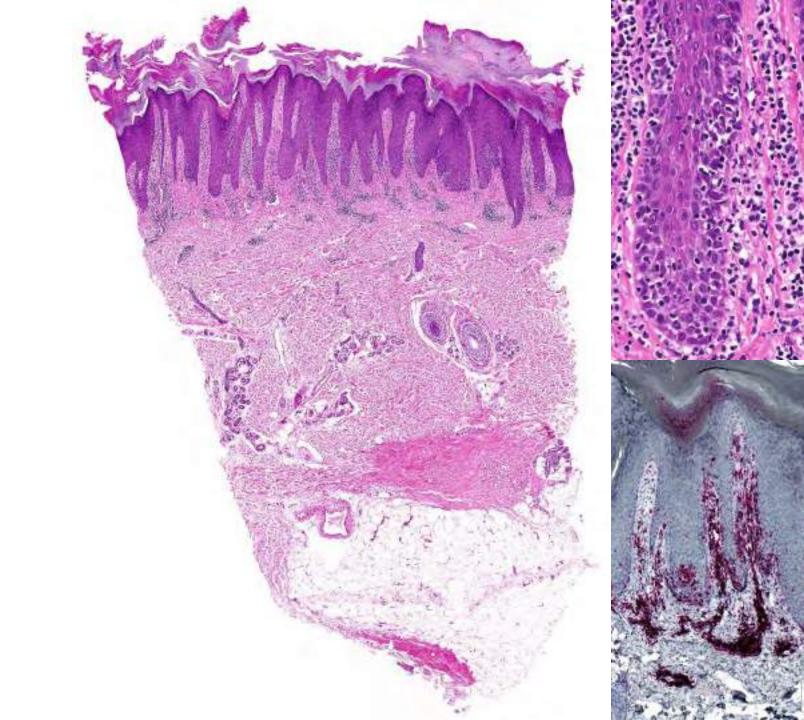


Fig 2. Case 2. Skin biopsy specimen reveals epidermotropism and coarse papillary dermal collagen. Epidermotropism composed of atypical hyperchromatic lymphocytes are seen (inset). (Hematoxylin-eosin stain; original magnification: ×100; inset, ×400.)



Mycosis fungoides may involve the palms and soles, in exceptional cases without lesions at other sites of the body; these cases usually clinically atypical and histopathologically showing infiltrates that involve also the reticular dermis. At least some of the published cases probably do not represent genuine MF. Palmoplantar psoriasis may present with band-like lymphocytic rather than neutrophil-rich infiltrates; a diagnosis of MF in a patient with lesions confined to the palms and/or soles should be made only when features are compelling; positivity of some of the mononuclear cells for MNDA may represent a clue.

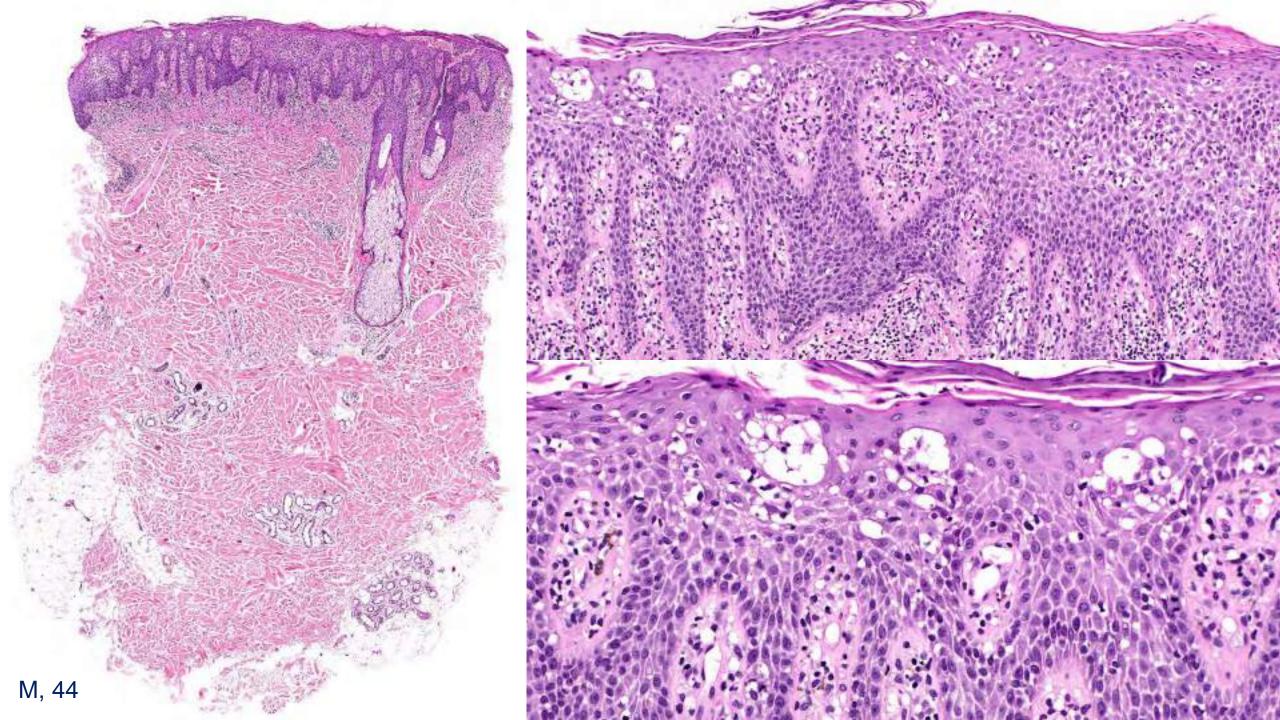


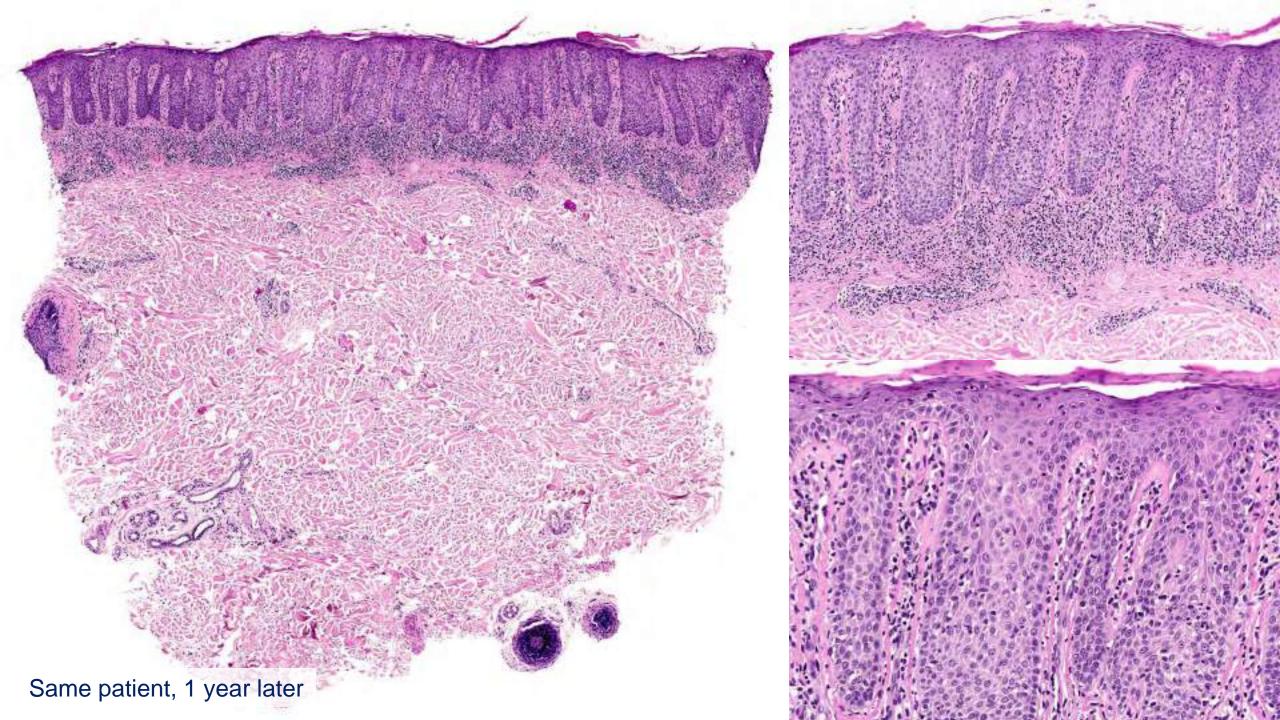
CD5

Psoriasis mimicking mycosis fungoides

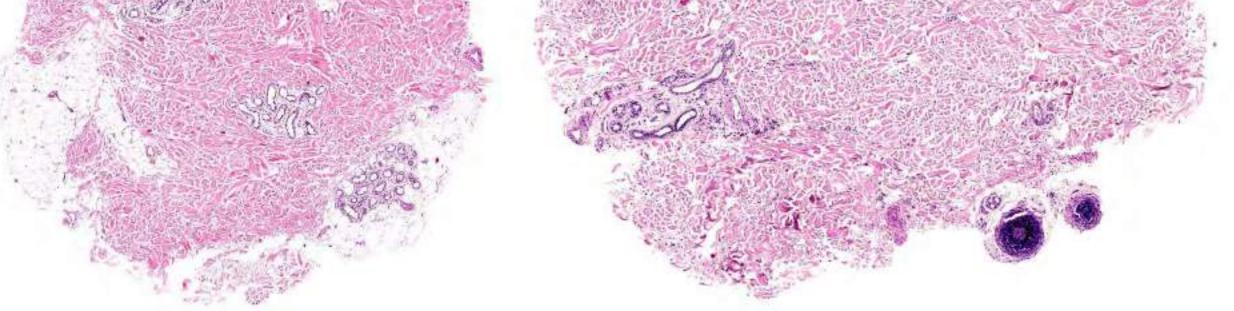
- A variant of mycosis fungoides restricted to the palms and soles has been described in the literature as "mycosis fungoides palmaris et plantaris"; in my opinion this variant does not exist, and these cases are examples of psoriasis with a band-like infiltrate of lymphocytes and many epidermotropic cells
- Variable numbers of intraepidermal lymphocytes may be observed also in psoriasis at sites other than palms and soles (usually CD8+); these cells are admixed with MNDA+ histiocytoid cells (most likely neutrophilic precursors)

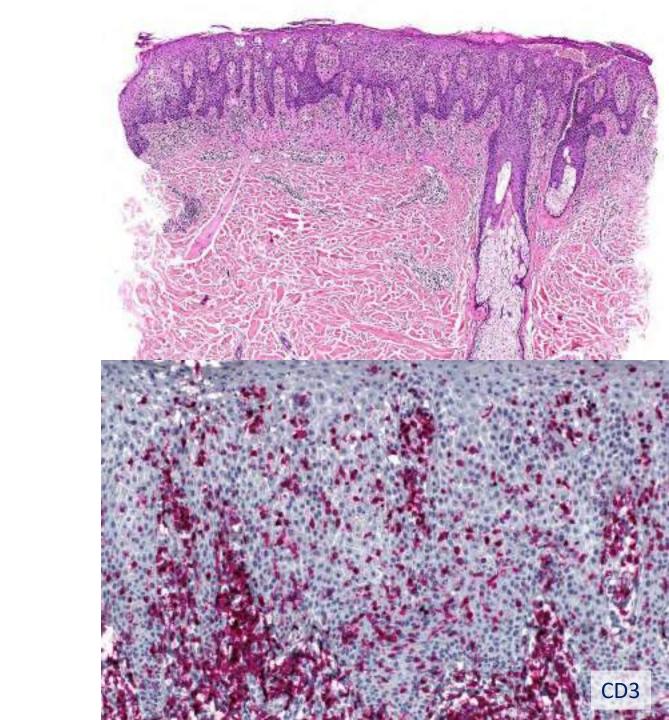


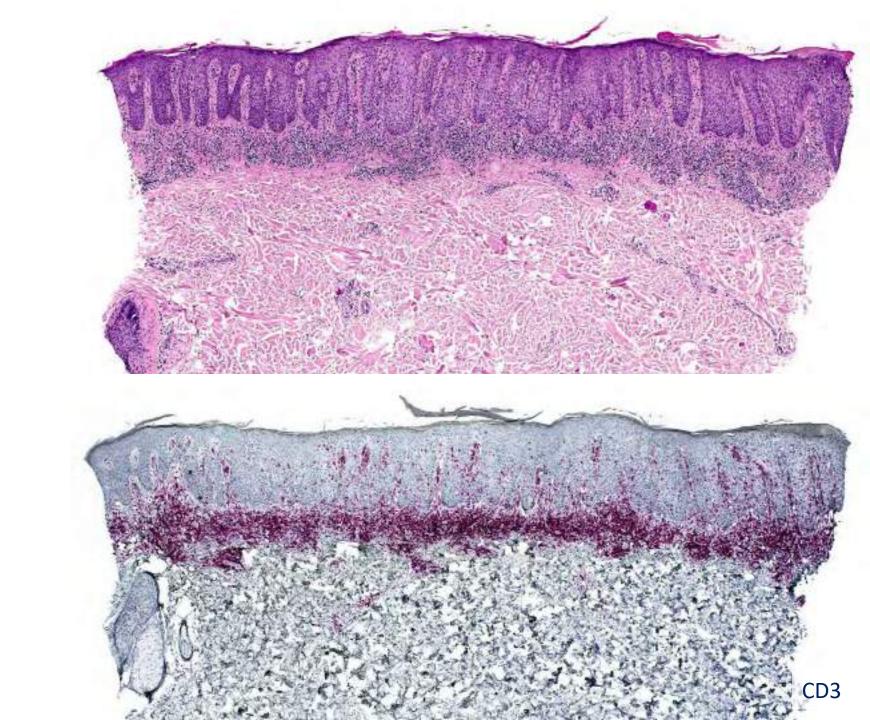


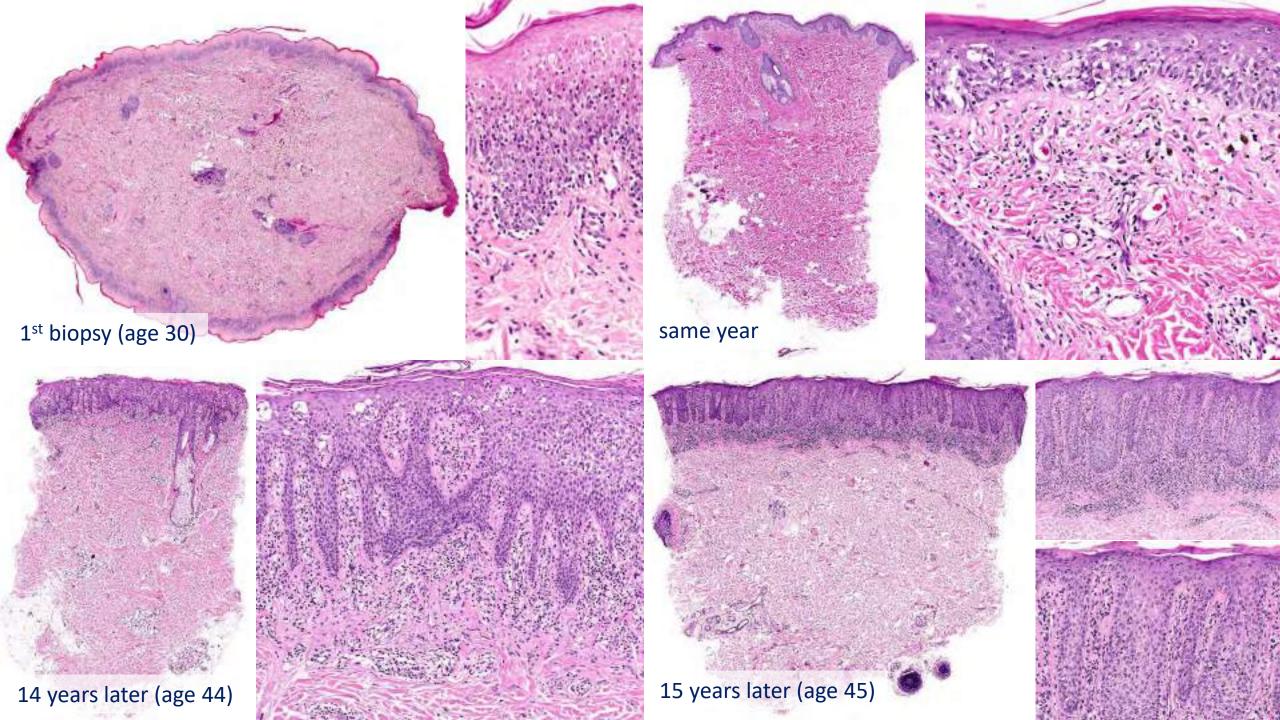


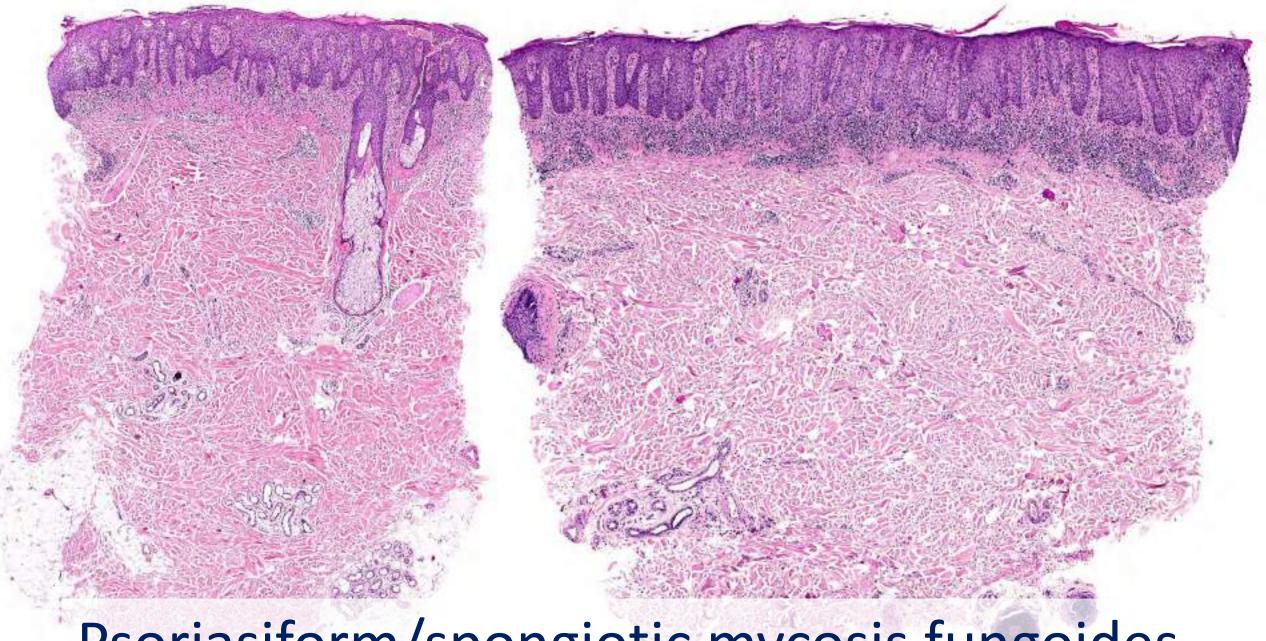












Psoriasiform/spongiotic mycosis fungoides

Histopathologic Features of Early (Patch) Lesions of Mycosis Fungoides

A Morphologic Study on 745 Biopsy Specimens From 427 Patients

Cesare Massone, MD, *7 Kazuo Kodama, MD, *1 Helmut Kerl, MD, * and Lorenzo Cerroni, MD*

Abstract: The histologic diagnosis of early mycosis fungoides (MF) is one of the most vexing problems in dermatopathology. We reviewed the histopathologic features of 745 biopsy specimens from 427 patients (male:female = 277:150; median age, 52 years; range, 3-95 years) with early (patch) lexions of MF collected from the lymphoma database of the Department of Dermatology of the Medical University of Graz (Austria). In all potients, the diagnosis was established by clinicopathologic correlation. The most common histopathologic pattern consisted of a band-like or patchy lichenoid infiltrate admixed with coarse bundles of collagen in the superficial demnis. Epidemnotropism of lymphocytes was observed in most cases in one or more forms (single lymphocyte epidermotropism, 22%; basilar lymphocytes, 23%; Pautrier's microabscesses, 19%; "haloed" lymphocytes, 40%; disproportionate exocytosis, 17%; pagetoid epidermotropism, 3%). In 4% of cases, epidenmotropism was completely missing. Atypical lymphocytes were present only in 9% of cases. Features of interface dermatitis were observed in 59% of cases. Other unusual findings were the presence of necrotic keratinocytes (23%), melanophages (8%), and extravasated crythrocytes (4%). In 28 patients, two or more biopsies taken on the same day at different body sites showed different histopathologic aspects, underlying the protean scutures of MF even in a single patient at a given time. Our study expands previous observations on historiathologic features of earlylesions of MF. Although sometimes the histopathologic features are not diagnostic, they should be considered consistent with MF and do not rule out the diagnosis.

Key Words: mycosis fungoides, cutaneous T-cell lymphoma, early diagnosis, histopathologic features

(Am J Surg Pathol 2005;29:550-560)

Kerl and Kresbach²⁸ and Sanchez and Ackermann¹³ in 1979, the histopathologic features of these lesions were considered to be nonspecific, 8-10,17-24,30,34,31,42,37 and pathologists made the diagnosis of MF only in cases characterized by the presence of markedly hyperchromatic, cerebriform lymphocytes in the epidermis forming the so-called Pautrier's microabscesses. ^{13,43} In the last years, several authors attempted to refine the histopathologic criteria for diagnosis of early lesions of MF, ^{25,29,37,40,48} but the diagnosis and differential diagnosis of these lesions are still considered one of the most vexing problems in dermatopathology.

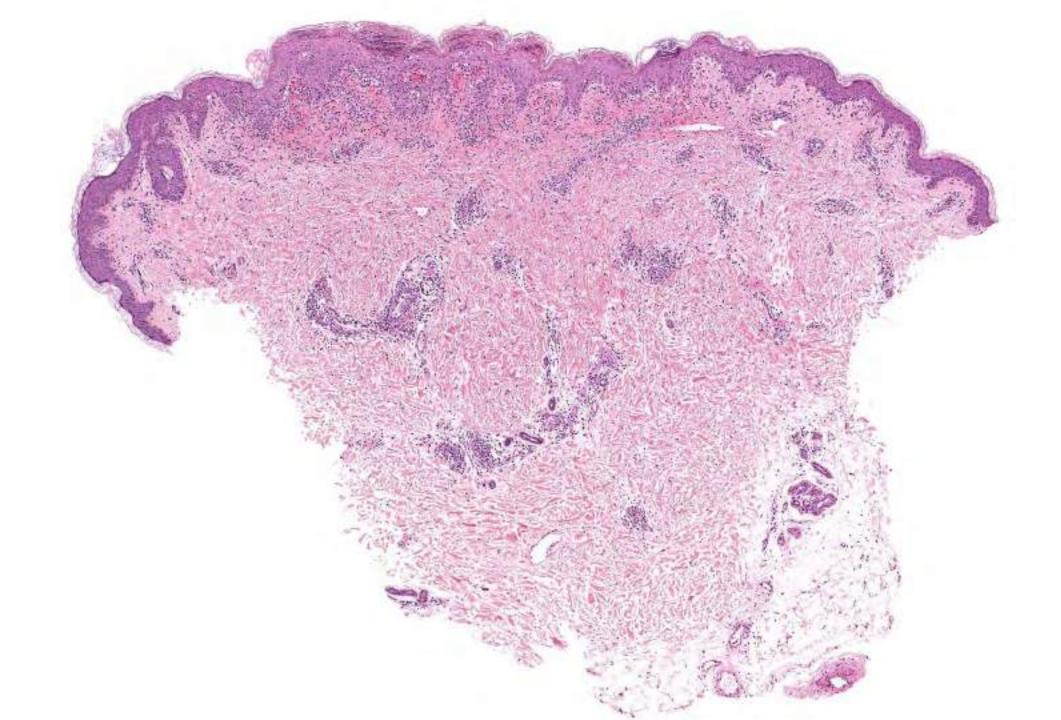
We reviewed the histopathologic features of 745 biopsy specimens from 427 patients with early (patch) lesions of MF to delineate the aspects that may be helpful for histologic diagnosis of early lesions of the disease.

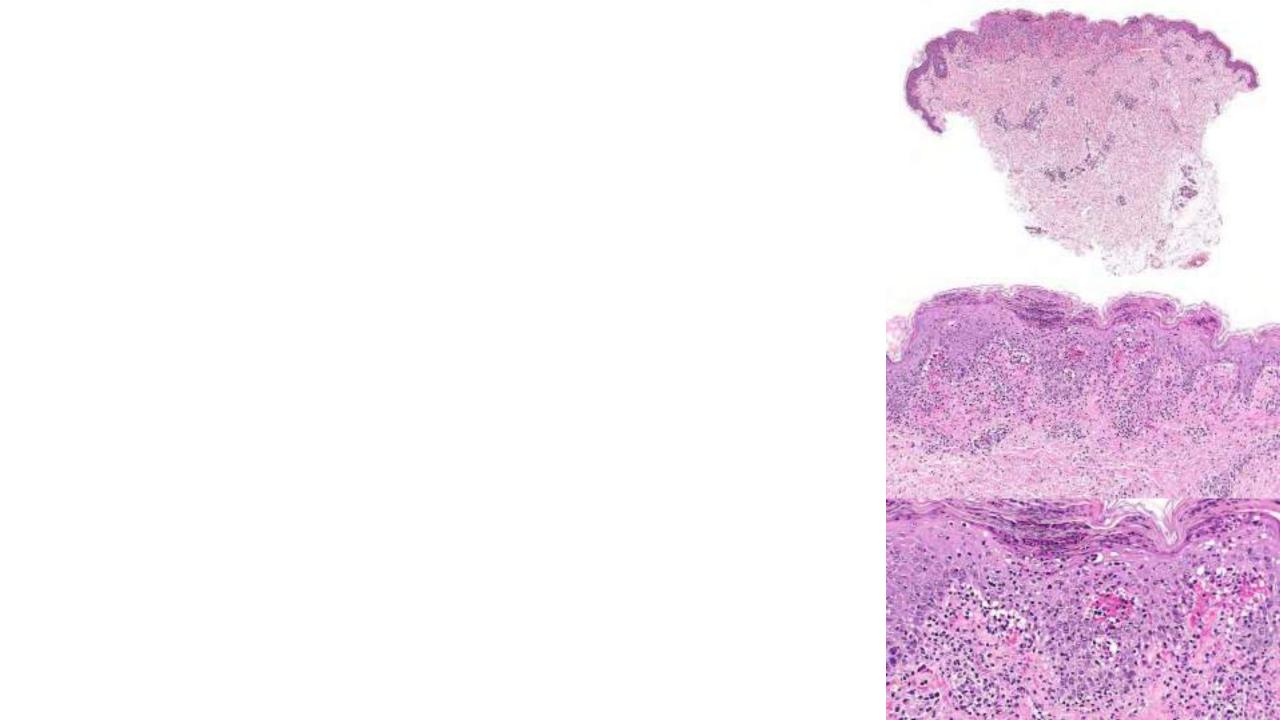
PATIENTS AND METHODS

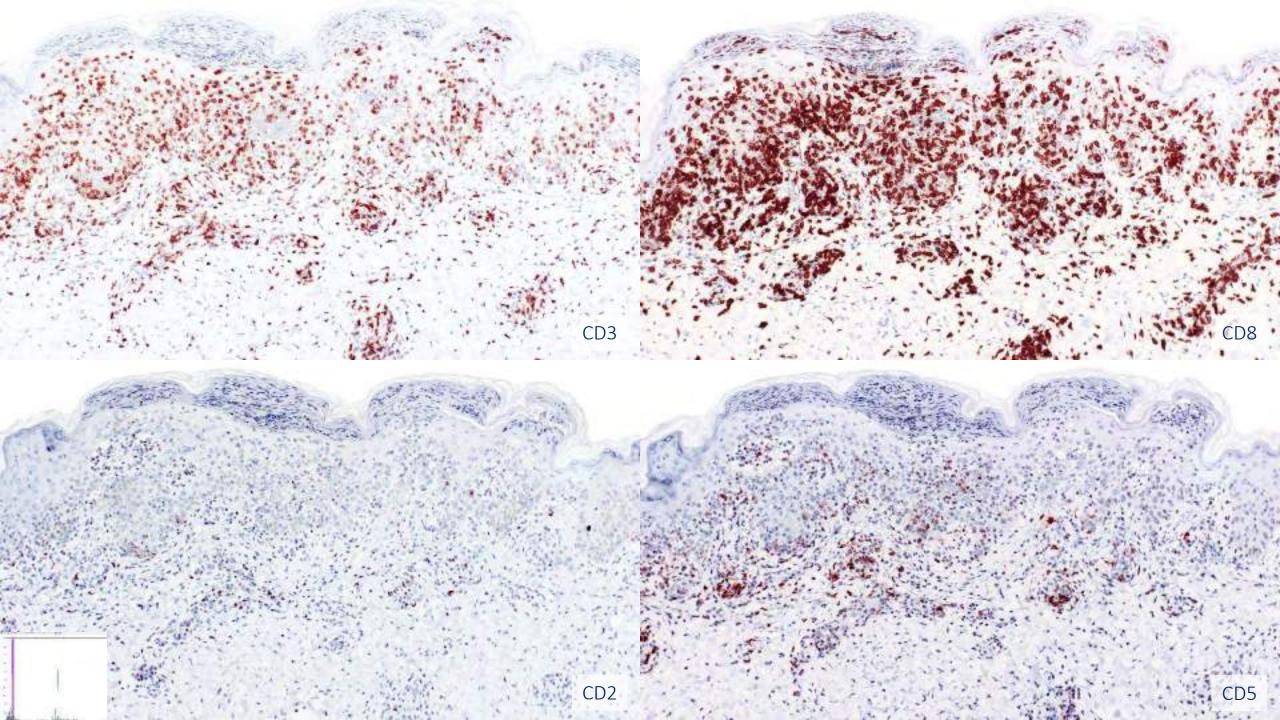
Data from 463 patients with early lesions of MF were retrieved from the lymphoma database of the Department of Dermatology, Medical University of Graz (Austria). Thirty-six cases were excluded because biopsy specimens were technically inadequate or because of lack of exact clinical informations. A total of 745 biopsy specimens from 427 patients (male:female ratio = 1.8:1; mean age, 57.2 years; median age, 52 years; age range, 3-95 years) with early (patch) lesions of MF were available for the study. The diagnosis of MF was confirmed in all cases by correlation with the clinical features (either observing personally the patient in the outpatient service for cutaneous lymphomas of the Department of Dermatology, Medical University of Graz, Graz, Austria, or reviewing the patient's chart and clinical pictures). Biopsies were taken at onset of

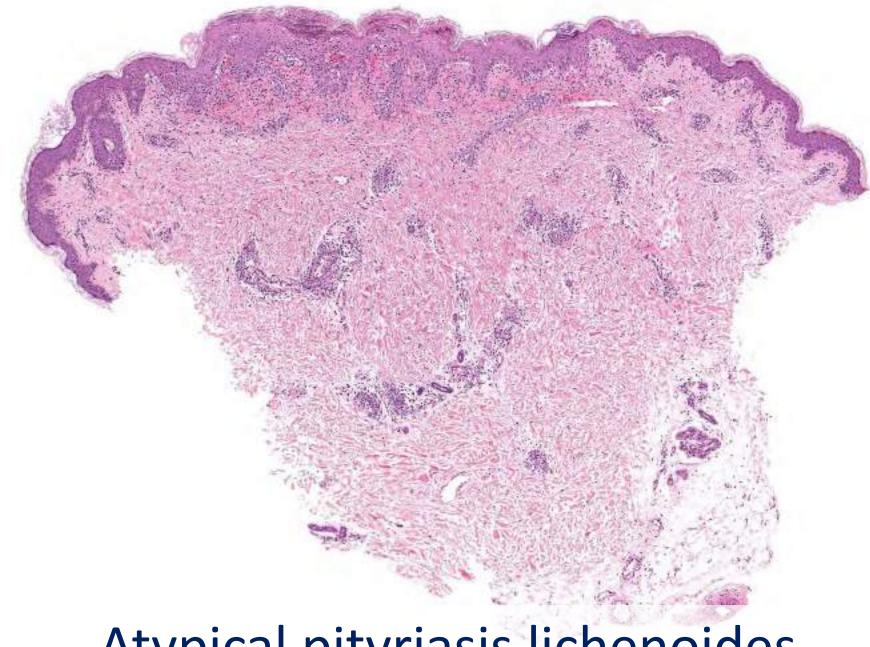
TABLE 1.	Histologic Features of Early (Patch) Lesions of	of MF
	in 745 Biopsy Specimens	

Feature	No. (%)	
Normal epidermis	356 (48)	
Psoriasiform hyperplasia	258 (35)	
Irregular hyperplasia	34 (4)	
Flat and/or atrophic epidermis	97 (13)	
Marked spongiosis	28 (4)	
Necrotic keratinocytes	172 (23)	
Changes at the dermoepidermal junction		
Focal interface dermatitis	438 (59)	
Widespread interface dermatitis	30 (4)	
Epidermotropism*		
Single lymphocyte epidermotropism	161 (22)	
Basilar lymphocytes	170 (23)	
Pautrier's microabscesses	140 (19)	
"Haloed" lymphocytes	298 (40)	
Disproportion exocytosis	124 (17)	
Pagetoid epidennotropism	17 (3)	
Absence of epidermotropism	32 (4)	
Atypical lymphocytes		
Only in the epidermis	27 (4)	
Both in epidermis and dermis	38 (5)	
Only in the dermis	2 (0.3	
Dermal lymphocytic infiltrate		
Band-like	227 (30)	
Patchy-lichenoid	492 (66)	
Superficial perivascular	26 (3)	
Dermal changes		
Papillary dermal fibrosis/coarse collagen bundles	725 (97)	
Melanophages	56 (8)	
Purpura	32 (4)	
Edema of the papillary dermis	0	

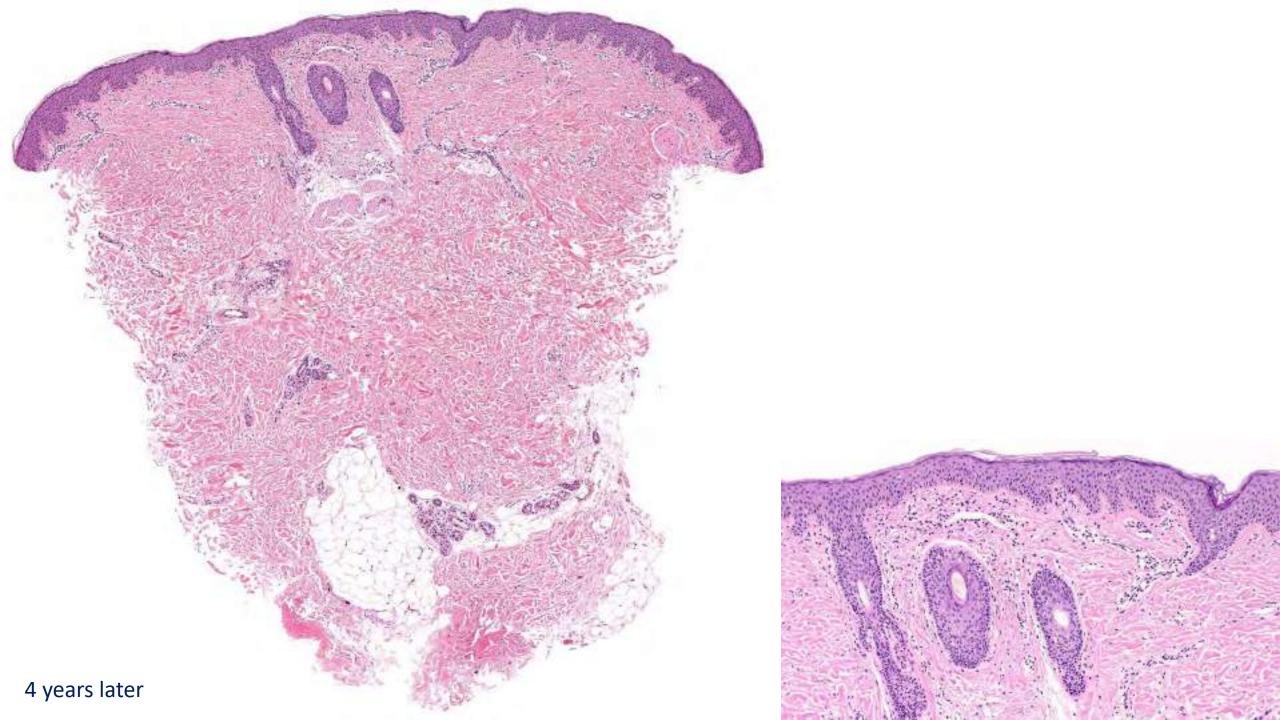








Atypical pityriasis lichenoides



Report.

Adult phyriasia lichenoides-like mycosia fungoldes: a clinical variant of mycosis fungoides

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4 patients (M:F=2:2); Age: 35-70

Pityriasis Lichenoides, Atypical Pityriasis Lichenoides, and Related Conditions

A Study of 66 Cases

Tiziana Borra, MD,*† Ana Custrin, MD,*† Andrea Saggiat, MD,*† Regina Fink-Puchez, MD,* Curio Cour, MD, William Fermt, MD,† Fubio Furchest, MD,† and Lorenzo Certoni, MD*

Abstract Pinniage Econoridas (PLo Jean oppermon dist disease of address enclose. In yours ways, an empiral limit of PL has Peers (Secretaris, showing coverlapping Statutes with processis filesgoign (MF) and Imphoratoid papakais. We statiod 68 patients with an initial histographologic diagnosis of PL (MH=3431). median age, 15x; narge, T to 85x5. According to desiral and phenotypic feature, cases were dissided july 4 categories (III Contentional Pt. elementotic claims former of H. without phecoppic aberrations) (i.e.20; M:Pic/RII: rendus and 37 to range, 9 to 74xy: (2) Atypical form of PL scharecteristic diction Ranges of PL was phenotype operations in =25: M.F.=16.5. maken ago. It ye sange, T to 72 (). Four of those persons areseparativ developed MF: (3) Lampisonatout populous towars and woming lesson and positive for 17000 m=10; M.F=44. median age, 41 to mage, 16 to 65 to 46 MF televial features typical of MP1 (x v 11; Mt.F v 8.5; notion out, 17 v; may, 6 to 57 vi. Midaralar madroes of doublis of the leafterin did not several rolevant differences among those 4 growns. Our study suggests that partients with an install histopatisskipte diagnosis of PL stars belong. to different groups, showing that classicalist-opic correlation and complete glassotypic unalyses are guranomit in order to addiese proper classification. Although the substandin between FL and MF or yet a uniter of debate; at the present state of innodesign. potients with a cheacognithologic procupation consistes with PL. her with obeyont phonorspic districts should be programed to orthat to sintest a possible evolution into Mir.

Key Wurde phytuma lateranides, phytuma fichelación el veriolifación acusa, provoso flaspodes, bruphosistoid populosis, impliad phytimus fichesoldes, calamaco T-cell hypphysis.

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skin discare of miknowa choicers, quality classified into un acute (piteriais lichmoides at variolifornis acuta [PLEVA] and a chronic (pilpriasis lichenoules chronica) variant.12 A considerable overlap exists between these 2 variants, in terms of both clinical and histopathologic presentation. 44 In record years, in any pioul form of physicials Schenolden (APL) (usually referred to an atypical PLEVA) has been described, characterized unitally by phenotypic aborations in otherwise convertional PLEVA. The exammostleup of PL, including the atypical form, is set a matter. of discussion, and some inthors consider it as a type of cutamous Imphopoliferative disorder showing overlapping features with mysosis frequides (MF) and lymphomateid papulosis (LAP)." In fact, cases of PLEVA growing line MF have been reported in the part,7 th Inaddition, some internatiologic features of PLEVA; such as presence of interface demantitis and of necrotic keratinocrites are not infrequent in MP, IV and a histogramologic variant of MF similar to PLEVA has been described, than further complicating the classification of those cases. 11.15 Finally, a small series and a few case reports described a C'D30+ various of PLEVA, and PL and LyP are sunsidered as being part of a spectrum by some authors. (3-1) We evaluated to purients with an aritial histopatho-

D tyriaga icheroides (PL) is an incommon inflammatory

PATIENTS, MATERIALS, AND METHODS

logic diagnosis ait PLEVA, accordaing the historichologic

features with clinical data, immunohideschemical invo-

tigations, analysis of the T-coll recopers (TCR) games re-

netragement, and followers.

Data of 66 patients with an initial isosopathologic diagnosis of PLEVA were retireved from the files of the Research Cair Decreatopathology, Department of Dermatology, Medical University of Gent, Austria, Gulyrasse with complete dialosi information at presentation at well as sufficient phenotypic analyses in all kest I happy have been included forms of the coses had been sent for second capter opinion to 1 of us (L-C). The analy harbeen approved by the efficial committee of the Medical University of Graz.

A lotal of 106 hispaire from the 66 patients was available for mady. Open corrotation with clinical and phenotopic features, the costs have been classified into Lof

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TABLE 1. Clinical Features of the Cases					
Case #	Sex/Age (y)	Classification	Follow-up (mo		
1	F/12	PL	A+ (1)		
2	M/10	PL	A- (96)		
3	F/48	PL	A- (103)		
4	F/44	PL	A- (68)		
5 6	M/55 F/23	PL PL	A- (4)		
7	M/13	PL	A= (74) A= (60)		
8	M/9	PL	A+ (3)		
9	F/45	PL	A- (182)		
10	M/25	PL	NA NA		
11	F/32	PL	A- (264)		
12	F/17	PL	A- (240)		
13	F/60	PL	A- (186)		
14	M/31	PL	A- (23)		
15	M/63	PL	A- (117)		
16	F/54	PL	A- (99)		
17	F/42	PL	A- (171)		
18	M/74	PL	A- (2)		
19	F/45	PL	NA		
20	F/10	PL	NA (25)		
21 22	M/11	APL	A- (25)		
23	M/15 M/24	APL APL	A+ (58)		
24	F/21	APL	A- (8) A+ (3)		
25	M/7	APL	A- (181)		
26	M/9	APL	A- (170)		
27	M/12	APL	A+ (65)		
28	F/53	APL	A- (49)		
29	M/49	APL	A- (108)		
30	M/28	APL	A- (56)		
31	M/25	APL	A- (240)		
32	F/72	APL	A-(42)		
33	M/12	APL	A- (77)		
34	F/7	APL	A+ (28)		
35	F/43	APL	A+ (46)		
36	M/11	APL	NA		
37	M/13	APL	A+ (20)		
38	F/17	APL	A+ (74)		
39 40	M/15	APL APL	A- (89)		
41	F/28 M/7	APL	A- (99) NA		
42	F/25	APL	A- (80)		
43	M/22	APL	A+ (1)		
44	M/31	APL	NA		
45	F/24	APL	NA		
46	F/41	LyP	A+ (35)		
47	M/30	LyP	A-(22)		
48	M/57	LyP	A= (54)		
49	M/23	LyP	NA		
50	F/83	LyP	A- (76)		
51	F/16	LyP	A- (94)		
52	F/41	LyP	A+ (74)		
53	F/51	LyP	A+ (73)		
54 55	M/50	LyP	A+ (3)		
56	F/18 F/27	LyP MF	A+ (86) A+ (114)		
57	F/85	MF	NA NA		
58	M/82	MF	A+ (3)		
59	M/8	MF	NA NA		
60	M/9	MF	NA		
61	M/11	MF	A+ (2)		
62	M/17	MF	A+ (8)		
63	F/14	MF	NA		
64	F/8	MF	A+ (120)		
65	F/27	MF	NA		
66	M/56	MF	NA		

A- indicates alive without disease, A+, alive with disease; F, female; M, male; NA, not available.

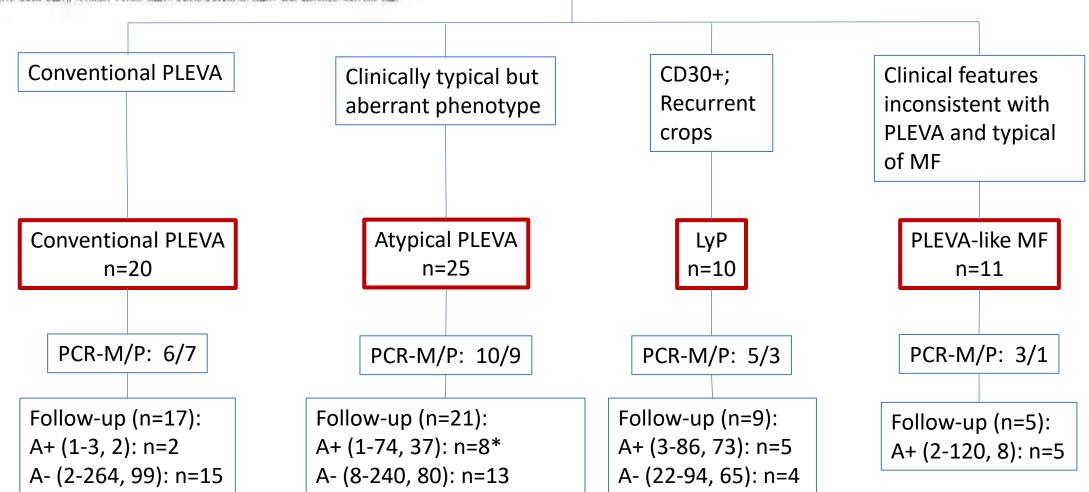
Pityriasis Lichenoides, Atypical Pityriasis Lichenoides, and Related Conditions

A Study of 66 Cases

Tittana Borra, MD*f. Ana Custrin, MD*f. Androa Sageon, MD,*§ Regina Fink-Puches, MD* Carlo Casa, MD. || William Vermi, MD. + Fabio, Facebetti, MD. + and Larence Cerroni, MD. +

66 cases Initial histopathological diagnosis of PLEVA

Phenotype, Clinical presentation, Follow-up

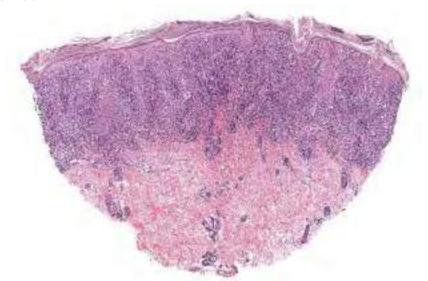


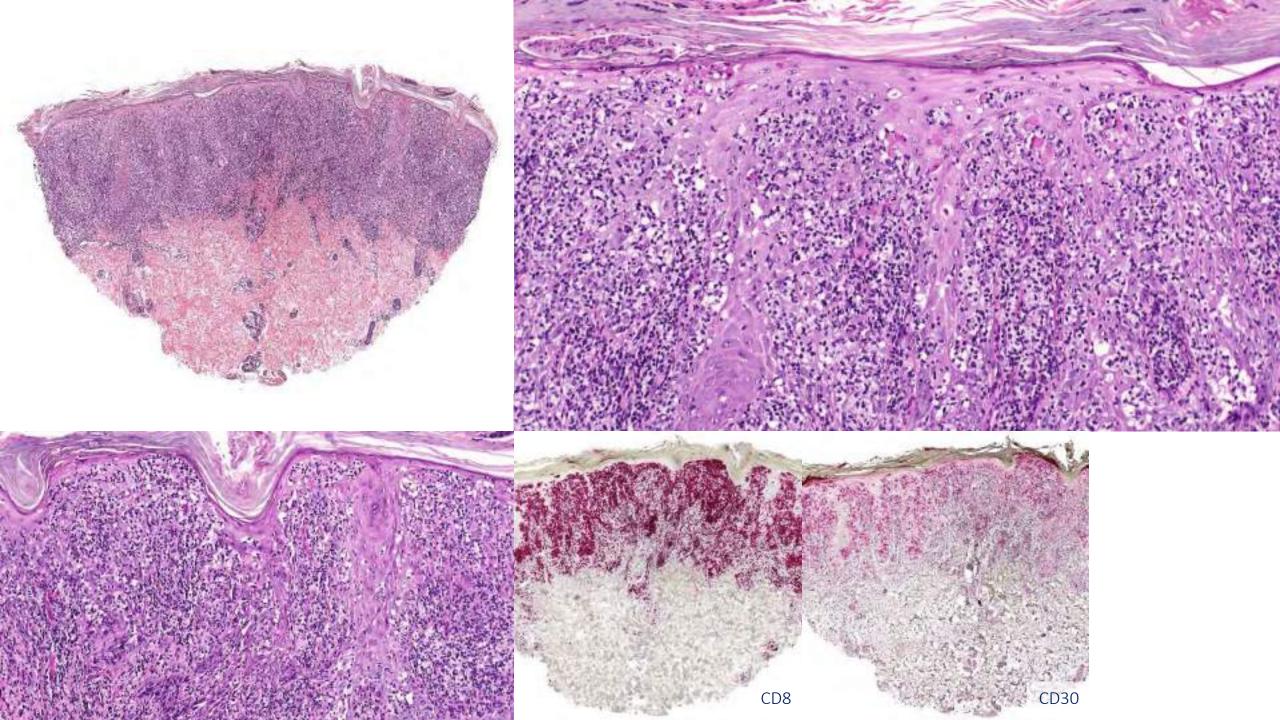
*"Progression" to MF: n=4

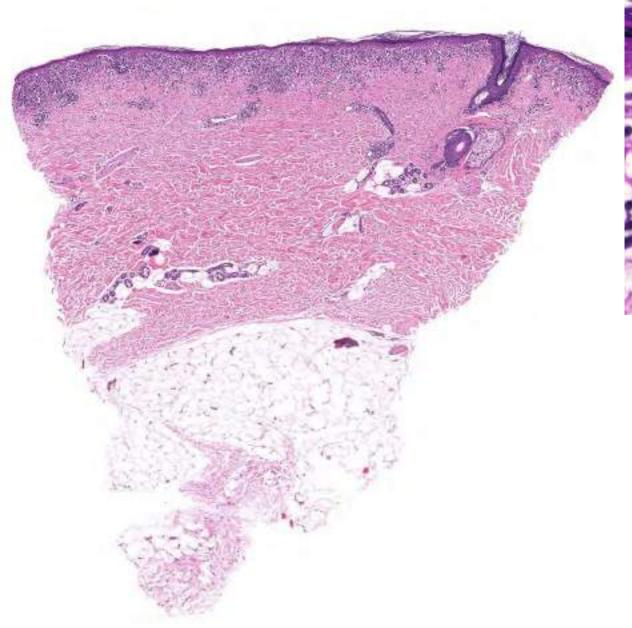
F, 44 Lower arm

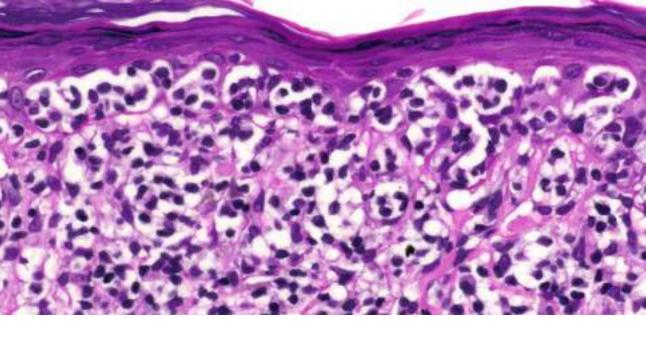
F, 44

According to the patient asymptomatic skin lesion on the left lower arm for approximately 9 months (picture taken after a punch biopsy).

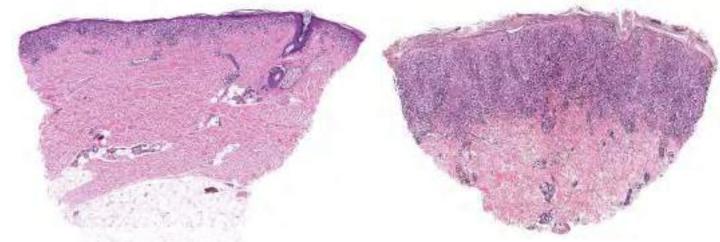






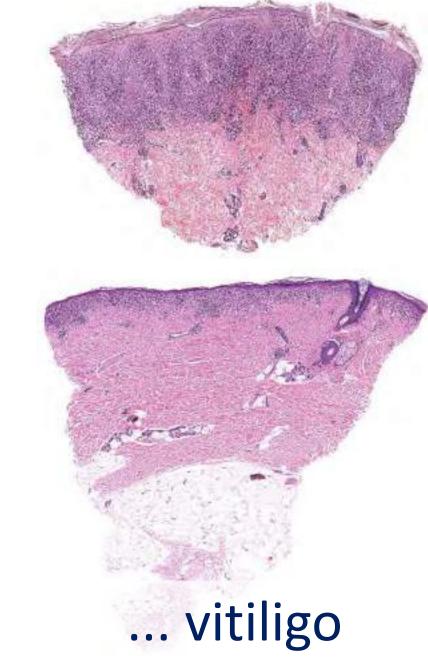


Two further lesions on the lower leg and left arm (biopsy from the arm).



Reported as mycosis fungoides...

(pagetoid reticulosis-like)



(pagetoid reticulosis-like)

Baby Wet Wipes: An Unusual Culprit of Lymphomatoid Contact Dermatitis Mimicking Mycosis Fungoides

Entily Coleman, MD and Jag Bhawan, MD

Abstract: Lyunkousself contact demailies (LCD) is a rais. briggs pseudobangilosus with chricopribelogic resture of both ellergie contact dermatria and automous T-cell lengthous (CTEL). In this intinfe, we report a fiscentiate case of LCD secondary to chronic tails wer wise use with clinical features of ellergic context demarks and Videouthelage charge of myrous languids, a contrapts of CTCL. We upper that ECO should be added to the list of ministers of invoces diagoides, a subrype of CTCL.

Key Words: hyphensied centart demotios, myraus fungrides, consecus T cell lengthorus, allerais portact derraidtis, claviconstiologic nowfeste-

(doi:10 Demonsperiol 2012;44:265-206)

BACKGROUND

Exemphoremoid contact derroritis (LCD) is a rure, benigo pseudotymptores with overlipping clinical and pathologic features of allergic contact demonth's and cutantour T-cell implants (CTCL) that often represents a diagnostic challenge. Chiccopathologic correlation is essentrol in the diagnosus of LCD. At this article, we report is cash of buby wet wipes use as the cultest of LCD shawing typical histograthologic changes of mycosts funguides (MF), LCD should be added to the list of numerical of MI-20.

REPORT OF A CASE

An African American woman at her 5% with wellcontrolled hypervassion presented with a history of discoloration of the inguinal and interplated areas, fishally she was seen by a gynecologist who performed a biopsy that was reported as nondinguousis. Two years later, she passented to demotology for evaluation of the personner lessons. Molications and firmly harmy were nurcommitmory. Clinical examination revealed hypopyments, minimally scaly petches with focal ensure and environs overvine the supropulsic, interplates), and bilateral togains! wear (Fig. 1). Two 3-min punch biopsies revealed abundant lymphocytic endernotopism with occasional Pattrier incombinesses. (Fig. 2A), an intential proliferation of lymphocytes, and populary deciral fibrosis (Fig. 28). There was a

Free the Department of Demandage, House, University School of Mediates.

The neithern declare an conflicts of interest.

Unwespecial profit Coleman, Adly, Department of Demographen, Byster Distance School of Manufac, Alli Albary Street Rooms, MA, 201111 (2-mail: Emily) and Columbiological comp.

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prepontenace of CDR and CDA lymphocytes in the epidermis (Fig. 3A) and dermis (Fig. 3B), respectively. A mild decrease in epidennal melatiscistes was mored sin MART-1 staining. T-cell receptor (VCR) gene retarminament polymouse claim reaction studies demonstrated a clause T-cell population, supporting a diagnosis of hypopiguanted MF. However, given a lack of chincopathologic correlation for MF, additional proleing revented frequent channing with haby wer wises. Topical contisosameds and consistion of latin wer wipes led to complete resolution of the lesions without RECEPTORICS.

DISCUSSION

Although humbleic and polymerase chain reaction mongs were consisters with MF, the lack of choiced existence of MF led to the conclusion that this case represented LCD. Furthenume, given resolution of the lesions with occasion of buby was wipes, we concluded that faces were the etsologic agent of LCD. In addition, we would not expect to see clinical resolution of Mr with observiors of hoby wer wiser, which further imports the dispussion of LCD.

First connect in 1976 offer 4 perients with CTCL had positive patch tests for proophorus scuqueulfide accendany to machbox use, LCD is a oscudolymphona with clinicopathologic famous of both allergic contact demuttin and CTCL.4 The distribution of knowns of LCD mong the buttocks, polying and opper less more closely mirrors the so-called "tothing minic" distribution of the lesions MF, which often clouds diagnosis.1 In addition to the tuttist report of phosphotous susquisuffice.4 other consulve allergem identified include directly) furname, ethylerediamine ditydendriorde, amdises, gold sodium throughter, orbit reghtherete, nickel suifate, N-isopropyl-N-plintyl-p-plenylenediamine, p-phenylemedianine, Tecrorus gravalos, peru-rectyl-butyl phonol. methylchlossisothismlusme/methylisothisms/innise and parabens, henzdamine bridrochleride, and mathylchlomisothigso-Broome guardenamen-15.7 Similar to our case, caoud wignes were the empative ment of LCD on the battock, sepitals, or interglurial cleft in 2 reported cases, with multy chlorosofticrolitting as a compact underlying allergen identified by parity costing in both cases.1.5 Although we did not conduct much testing, this agent may have been the illergen in our ease as

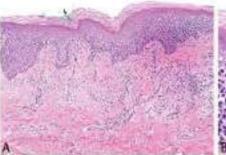
Although LCD may have features of Mb, 14 none of the previously reported coses had the event and intensity of epidemotropism as som in our case. Our case is unique in that the histopethological festures were indistinguishable from All: Funtamions, LCD rarely shows TCP pose

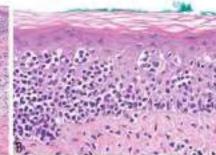
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FIGURE 1. A. The inguinal and genital regions demonstrated a hypopigmented, minimally scaly plague with a mildly erosive plague posteriorly. B, The intergluteal cleft was notable for a hypopigmented patch with a cluster of 0.1-0.3 mm erythematous macules coalescing into a patch centrally.



FIGURE 2. A, Hemotoxylin and eosin revealed abundant lymphocytic epidermotropism with occasional Pautrier microabscesses, an interstitial proliferation of lymphocytes, and papillary dermal fibrosis ×10. B, Epidermotropism with Pautrier microabscesses are easily seen in higher magnification ×40.



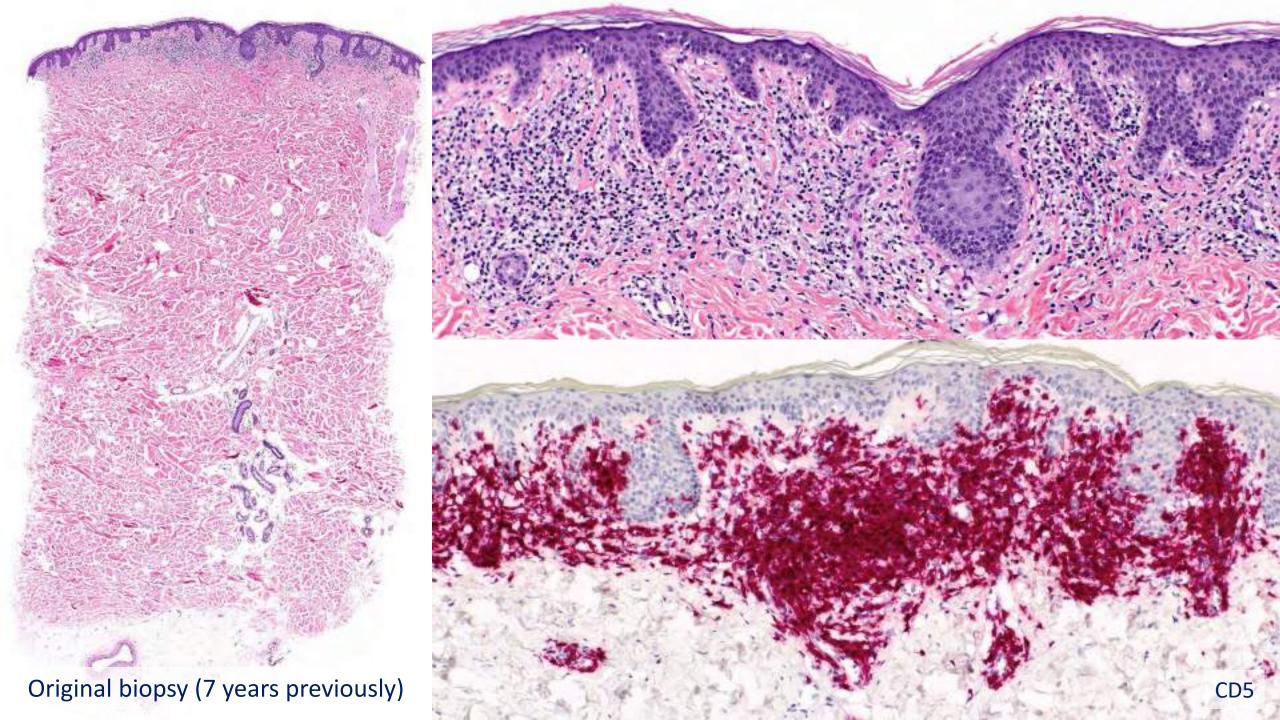


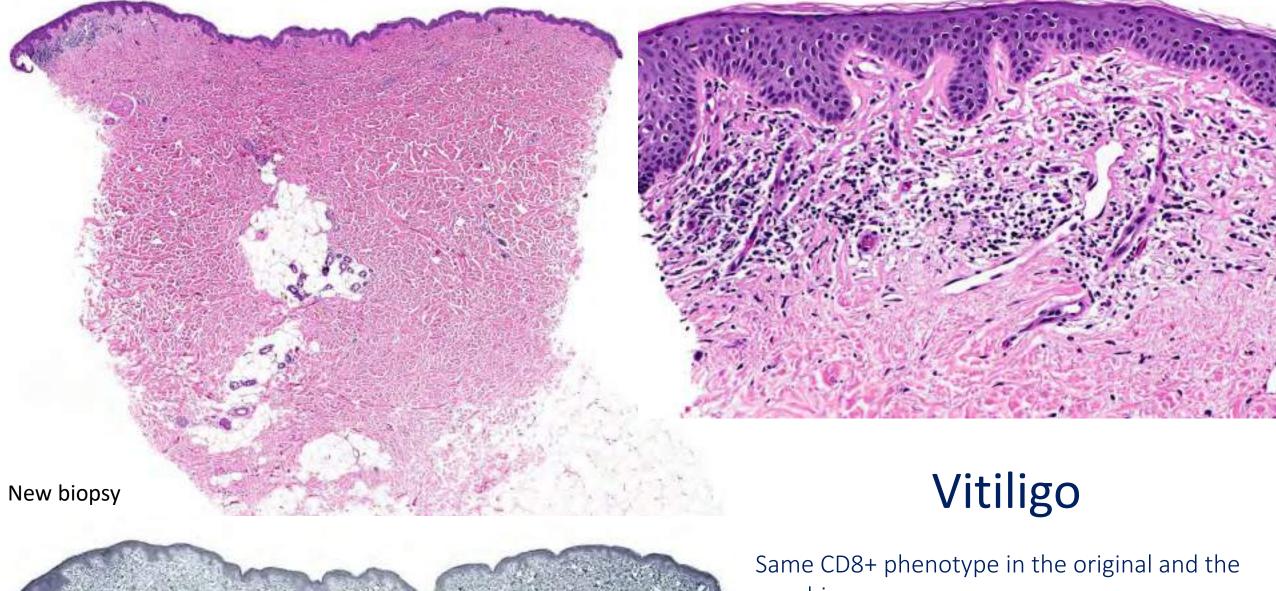
M, 71

History of cytotoxic MF diagnosed histopathologically 7 years before presentation.

Managed as hypopigmented MF since diagnosis.

Comes for a planned control; a new biopsy is taken (including both the hypopigmented area and the erythematous rim).

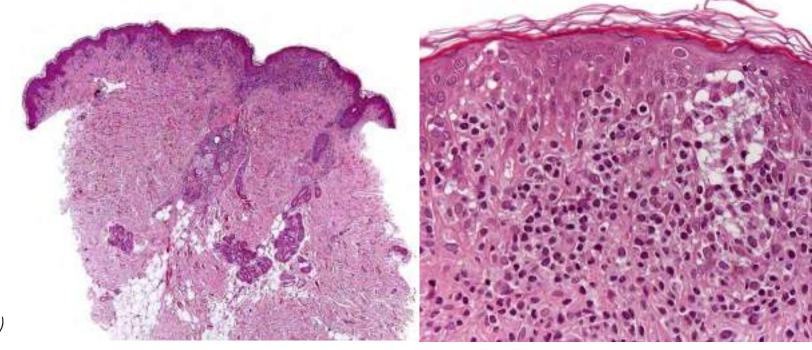






new biopsy.

Absence of melanocytes in the hypopigmented area.



(consultation Dr. Riccioni, Cesena)

Vitiligo – Inflammatory stage

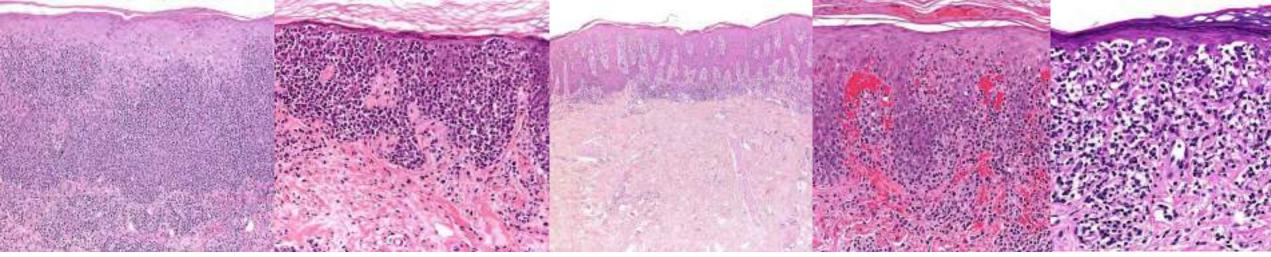
- Erythematous patches with evolving central depigmentation; borders not as sharply demarcated as in later stages; "inflammatory" borders may persist around central depigmentation
- Band-like infiltrate of lymphocytes; several epidermotropic lymphocytes
- Cytotoxic lymphocytes (CD8+) predominate (similar to cases of hypopigmented MF)
- A source of dermatopathological mistakes (my humble experience: 3 out of 3 (100%) "MF-like" cases missed...)

Prominent ("pagetoid") epidermotropism

Aggressive T-cell lymphomas

Indolent T-cell lymphomas

Pseudolymphomas



Aggressive epidermotr. CD8+ cytotoxic T-cell ly Generalized, partly ulcerated plaques and tumors. CD8+ by definition; CD30 usually negative (Ddx from LyP type D); TCR β + / TCR γ δ -.

Cutaneous γ/δ T-cell lymphoma
Generalized, partly ulcerated plaques and tumors. TCRγ/δ cytotoxic phenotype prerequisite for diagnosis; TCRß may be coexpressed. Angiocentricity, concomitant subcutaneous involvement; Haemophagocytosis.

Conventional clinical presentation or features of solitary pagetoid reticulosis. Pagetoid epidermotropism mostly in cases with cytotoxic phenotype.

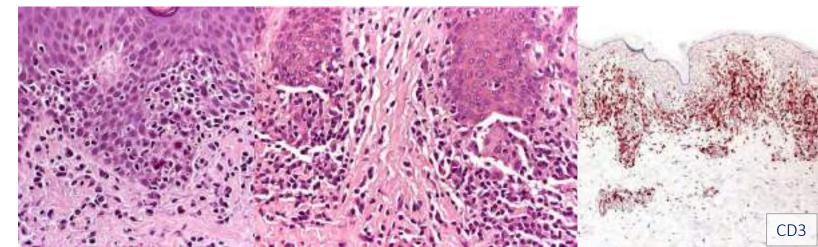
Mycosis fungoides

Lymphomatoid papulosis, type B or D Waxing and waining papules and small nodules. Positivity for CD30 and CD4 (type B) or CD8 (type D) are a prerequisite for the diagnosis; may be positive for TCR γ/δ .

Exceedingly rare
Vitiligo.
Lymphomatoid contact dermatitis.
Lichen sclerosus.
Usually predominance of CD8+ T
lymphocytes.



Annular lichenoid dermatitis of youth



Annular lichenoid dermatitis of youth

Giorgio Annessi, MD, Mauro Paradisi, MD, Corrado Angelo, MD, Marie Perez, PhD, Pietro Puddu, MD, and Giampiero Girolomoni, MD Rome, Italy

Background: Lichenoid dermatoses are composed of a wide spectrum of disorders with a common histopathologic interface pattern but diverse causes and pathophysiology.

Objective: We describe a series of young patients with a peculiar annular lichenoid dermatitis, the clinical appearance of which initially suggested diagnoses of morphea, mycosis fungoides, or annular erythema.

Results: The study involved 23 patients (median age 10 years; age range 5-22 years). Lesions consisted of persistent asymptomatic erythematous macules and round annular patches with a red-brownish border and central hypopigmentation, mostly distributed on the groin and flanks. Histology revealed a peculiar lichenoid dermatitis with massive necrosis/apoptosis of the keratinocytes limited to the tips of rete ridges, in the absence of dermal sclerosis and epidermotropism of atypical lymphocytes. The infiltrate was composed mainly of memory CD4⁺ CD30⁻ T cells with few B cells and macrophages. Analysis of T-cell receptor-γ-chain gene rearrangement in skin biopsy specimens revealed polyclonality in all the 15 cases studied. Topical and systemic corticosteroids or phototherapy were effective in most patients with relapse after treatment withdrawal.

Conclusions: We suggest that this is a distinctive inflammatory condition, and we propose to term it "annular lichenoid dermatitis of youth." (J Am Acad Dermatol 2003;49:1029-36.)

ichenoid dermatoses are composed of a wide spectrum of disorders characterized histologically by vacuolar alteration and necrotic/apoptotic keratinocytes in the basal layer of the epidermis together with a bandlike lymphohistiocytic infiltrate obscuring the dermoepidermal junction. These histologic changes are associated with disparate clinical lesions, including erythematous macules, flat-topped violaceous papules, papulovesicles, and plaques that can be arranged in linear or, more rarely, annular pattern.¹

During the last 6 years we have observed a series of young patients with peculiar skin changes consisting of persistent erythematous macules and annular patches mostly localized on the groin and flanks. In all cases the clinical picture was suggestive of inflammatory morphea, patch-/plaque-stage my-

From the Istituto Dermopatico dell'Immacolata, IRCCS. Supported by the Italian Ministry of Health. Conflicts of interest: None.

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cosis fungoides, or annular erythema. However, all 3 of these diagnoses were excluded histologically with a distinctive superficial lichenoid dermatitis with massive necrosis/apoptosis of the keratinocytes situated at the tips of rete ridges.

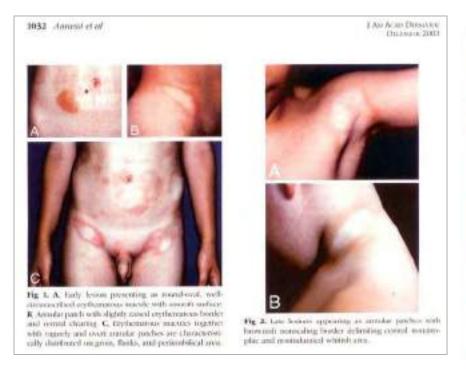
In this study we describe the clinical, histologic, immunohistochemical, and molecular characteristics of this condition, which we have termed "annular lichenoid dermatitis of youth" (ALDY), and discuss the differential diagnosis with morphea, patch/plaque-stage mycosis fungoides, and annular erythemas.

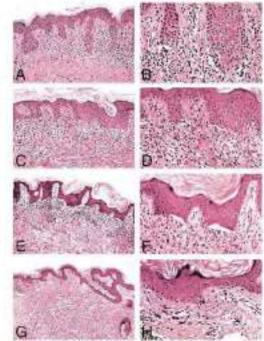
PATIENTS AND METHODS Patient selection

We reviewed the history, clinical photographs, and histologic slides of 23 cases of ALDY, which have been seen during the last 6 years at our institution.

Histology and immunohistochemistry

From 23 patients, 32 biopsy specimens were collected for histologic study. In each case 2 hematoxylin and eosin sections were prepared. In all, 2 biopsy specimens from lesions at different stages of evolution were acquired from 6 patients; in another 3 patients, skin samples were obtained from both initial lesions and lesions recurring after 6 to 12





- Characteristic clinical presentation resembling morphea or MF
- Histopathologic features mimic MF; necrosis of keratinocytes at tip of rete ridges ("squaring" of rete ridges) typical of ALDY
- Polyclonal pattern of TCR genes rearrangement
- Benign behaviour (yet few cases described, relatively short follow-up)
- Long-term follow-up advisable

Annular Lichenoid Denmatitis of Youth ... and Beyond: A Series of 6 Cases

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Two young girls Four adult males

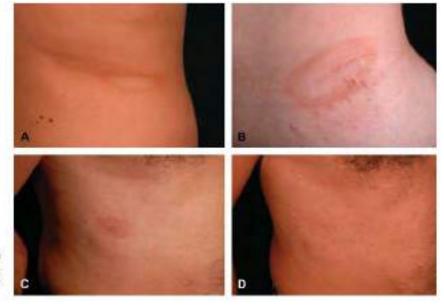


FIGURE 1. Clinical presentation in case 6 (A), case 1 (B), and case 5 (C). D, Complete resolution in patient 5 at the 24-month follow-up.

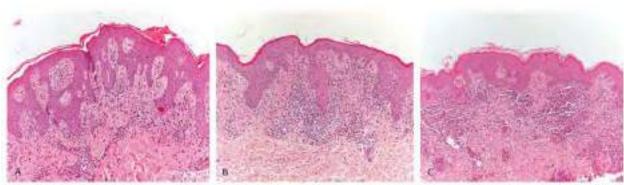
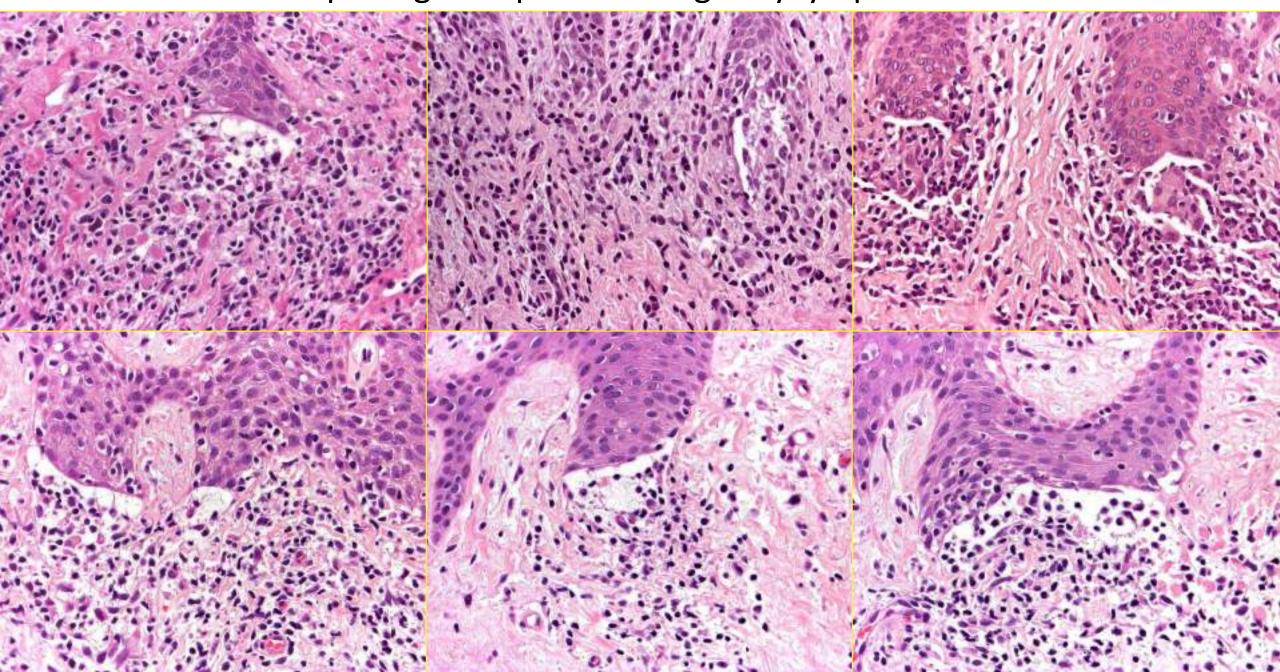


FIGURE 2. Lichenoid lymphocytic infiltrate with basal vacuolization in case 3 (A), case 5 (B), and case 1 (C) (hematoxylin and eosin, ×100).

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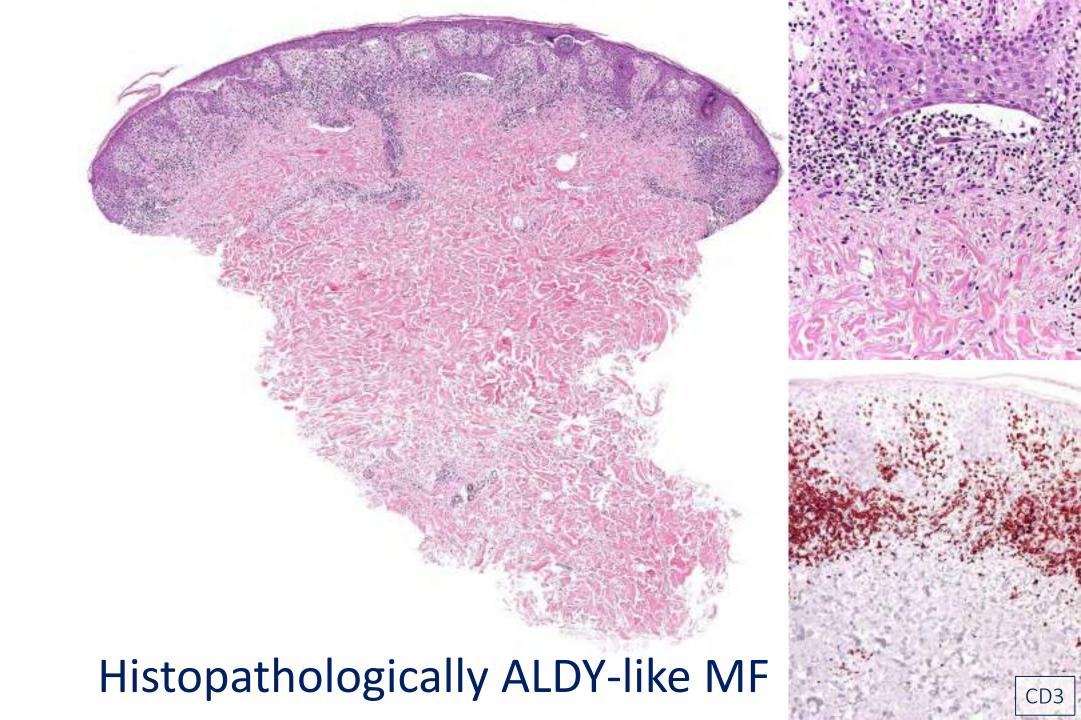
Clue: "squaring" of tip of rete ridges by lymphoid infiltrate

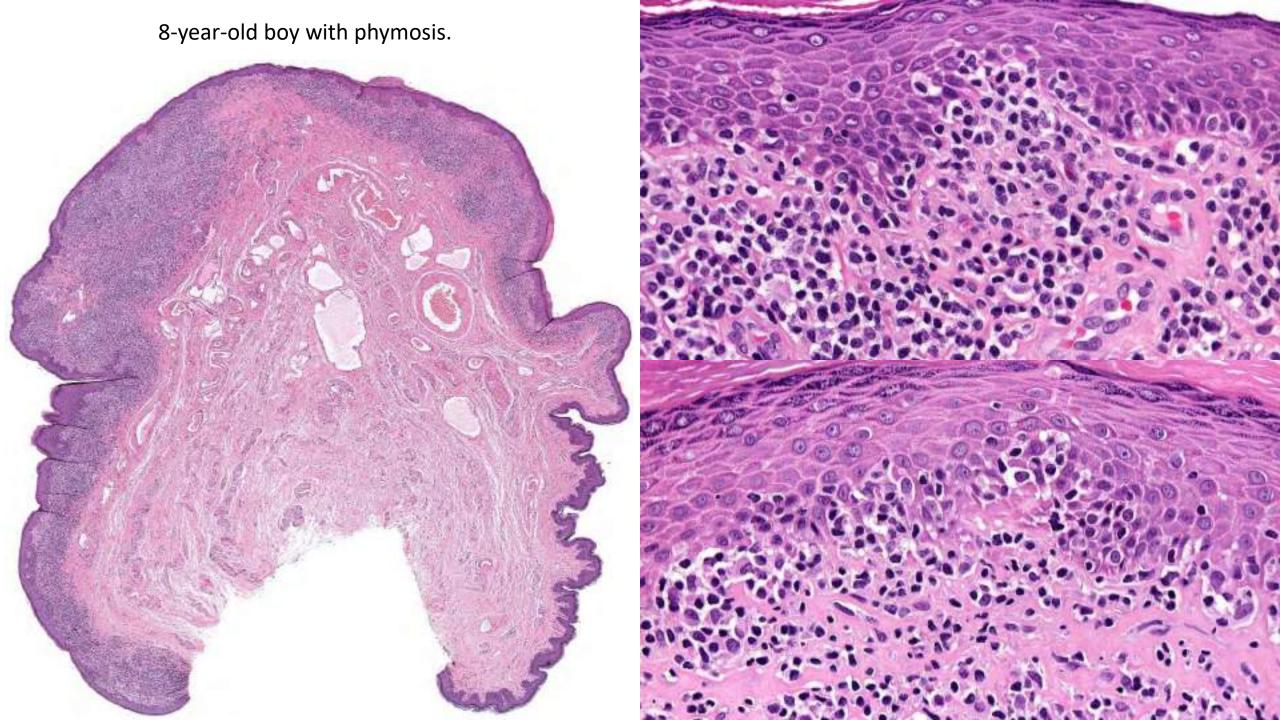


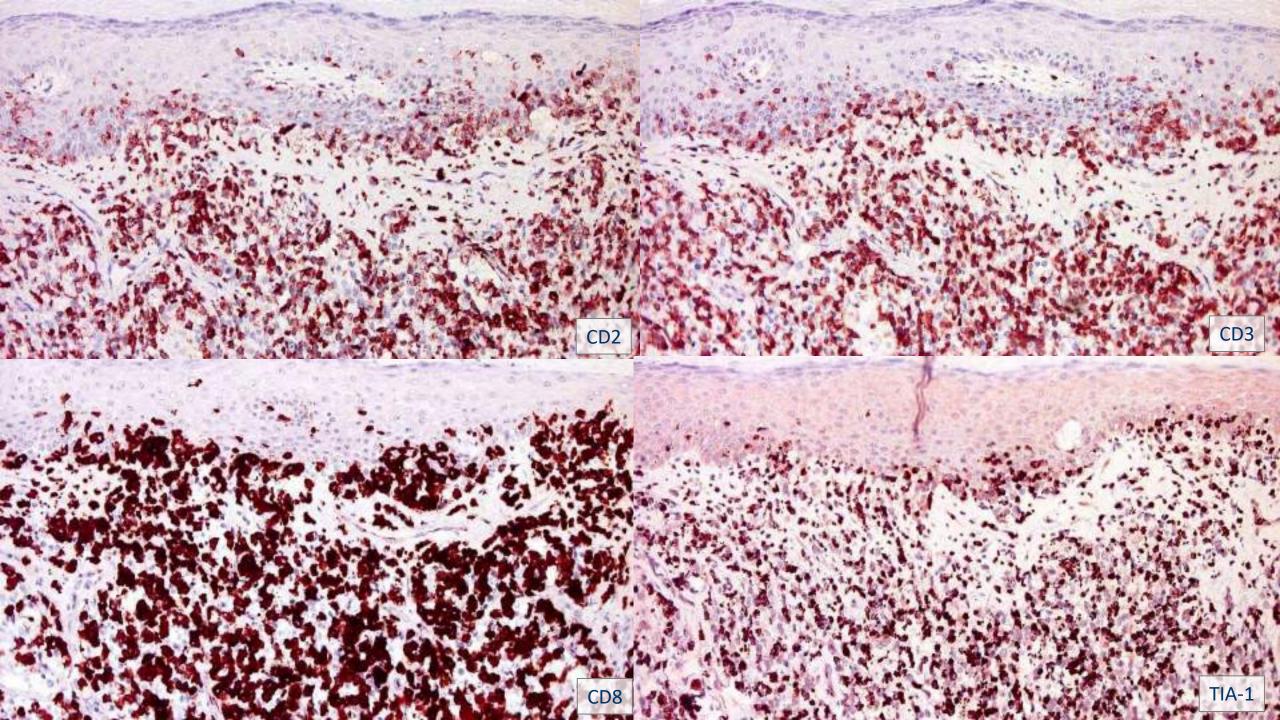


Clinically ALDY-like hypopigmented MF









Lichen sclerosus, inflammatory stage

- Pseudolymphomatous features are observed almost exclusively in genital LSA
- Most frequent presentation is phymosis in male children
- Band-like infiltrate of T-lymphocytes with variable numbers of epidermotropic 'haloed' cells; CD8+
- Conventional histopathological features of LSA are often missing or present only focally; clinicopathologic correlation crucial

Extrem Scienosus with Histopathologic Features Simulating Early Mycelli Fungoides

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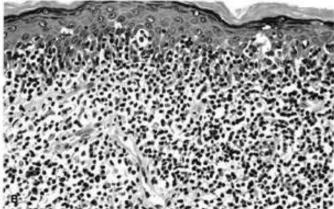
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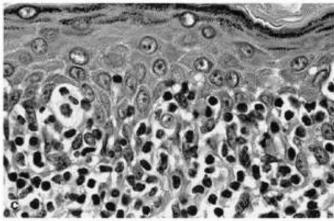


FIGURE 1. A, Dense band-like infiltrate in the superficial dermis. B, The infiltrate obscures the dermo-epidermal junction and involves the epidermis. C, Note intraepidermal lymphocytes with "haloed" nuclei resembling epidermotropic lymphocytes in MF.

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Lichen Sclerosus et Atrophicus With Histopathologic Features Mimicking Mycosis Fungoides

A Large Series of Cases Comparing Genital With Extragenital Lichen Sclerosus

Eleanora Leont, MIX* Werner Kempt, MD,77 and Lorenzo Cerront, MD§

Abstract: Lichen scienosas et atmeticas (LSA) is a chronic in-Hammatory deemstoric of unknown stockery layorking the penitil and/or et/magnitul and allowing histogeneologically a characteristic homogenolatrion and admosts of the superficial colleges with variably done temphoid infiltrate. Intraspidental fyrophocytes may be observed, and in some pages may pose diffferential disgnostic problems with auronal fungoises (MF). We studied the histopathologic features of 121 cases of USA with deese hurphoid infiltrater (period) 94: rislefessale: 93:1, age sange: 2 to 67 y; motion age: 11 y; estrogenical: 27 molesfonale. U.E.E. age times. 11 to 19 s; motion age: 59 s), to better dureacterize the intereprisental horpsoid infiltrate and to compare pacitol with enterpresid cases. Epidenootropic lymphocytes manicking the instepathologic features of MF were present to 93.6% of the genital specimens but none of the extragerital cases: homostingly, typical features of ESA were moving at 30.4% of pential LSA, and it a further 25.5% were present only forally. Immunoholachemical analysis showed a predominance of CDS. 1 Jyuphneytes within the epidemia. Molecular studies of the T-ord succeptor genes precaled a connectional population of T isymphocytes in much half of the mass. Our study shows that MF-The histograficality features are intremely common in perittal LSA but are never incountered in extragenital cases. A diagnosis of MIP in the senital tees should be made only upon crompelling features, lengting in morel the frequent pseudolymphometons aspects of LSA.

Key Words licher selevore, raycosa fragosido, certament J-cell puradelymphoras, cutureous T-adl byrophoras, entrascora poradelymphoras, communical fiduci selevoras

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Conflictual Interest and Source of Hundrag: The authors have districted from they have no agrificant catalogs deposition of from with the fact they constructed companies perceiving to this set it.

Correspondence: Lorento Cerroni, M.D. Department of Destandons Madical Cristonity of Gray, Austraggaptata 8, Gray A 2016 Alastra (crisis) (control correspondences):

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Lichen selections of attrophicus (LSA) is a chronic inflammatury demantists of turknova etiology involving the gential mucesa or the extragerital skin. The typical histograthologic lindings are characterised by attoghic epidetmis with orthologicities overlying a papillary domic showing homogranized, scientife collagen, and a suniably dense lymphocytic inflirate. In replical cises, the histograthologic diagnosis of LSA is not problematic; some cases, however, may belt typical features being characterized instead by a dense lymphocytic inflirate with prominent exocytosis of lymphocytes within the epidemis, thus ministring mycross furginales (MF). ¹⁻³

We studied the clinicopathologic features of LSA with particular emphasis on histopathologic features mimicking MF, and with comparison of genital with extragenital cases.

PATIENTS AND METHODS

One hundred twenty-one patients (male female = 3.81) age range 2 to 17 y; mean age 30.6 y; median age; 15 y) possenting with L5A have been included in our study. Ninety-line cases were from the amoremial area (male female = 93.1) age range; 2 to 87 y; median age; 11 y), and 27 frest the entraganital area includential==0.1 it age range; 11 to 74 y, median age; 59 y). The cases were collected at the Department of Demandlegs of the Medical University of Graz and at the Kempt und Pfaler. Histologische Diagnostik, Zmich, Switzerland, Vansbly dense lymphoid infiltrates were excluded). Partial data cas 9 cases had been published previously. The study has been appeared by the efficial committee of the Medical University of Graz.

A foral of 123 formalin-fixed, paraltin-embedded biopsy spacinaris were available for histopathologic analysis. Following histopathologic fearures were evaluated; presence of typical aspects of LSA, possence of epidermotoupic lymphocytes (pseudo-wascular aspects); presence of pronounced hernorthage (pseudo-wascular aspects); presence of associated morphos; presence of granulomatous philibitic, presence of germinal centers; pro-ence of perincurs) inflammation; infiliaties.

In 69 cases Q7 from the estingental, 42 from the gentral areas, immunohistochemical analyses were performed with a standard immunoperovaluse cachinque using

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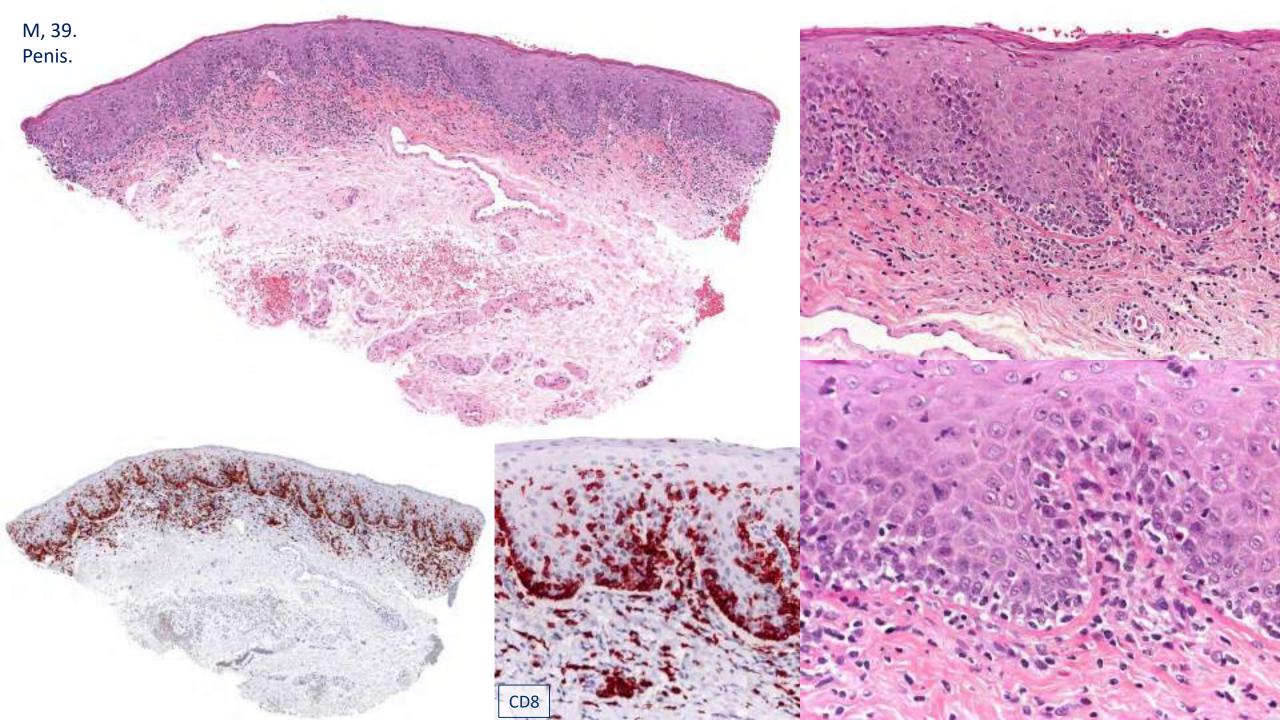
Am./ Surg Postrul = Volume 00, Number 00, ■ ■ 2021

121 cases of LSA with dense lymphoid infiltrates (genital: 94; M:F: 93:1; age range: 2-87; median age: 11; extragenital: 27; M:F: 0.1:1; age range: 11-79; median age: 59).

Epidermotropic lymphocytes mimicking the histopathological features of MF were present in 93.6% of the genital specimens but none of the extragenital cases.

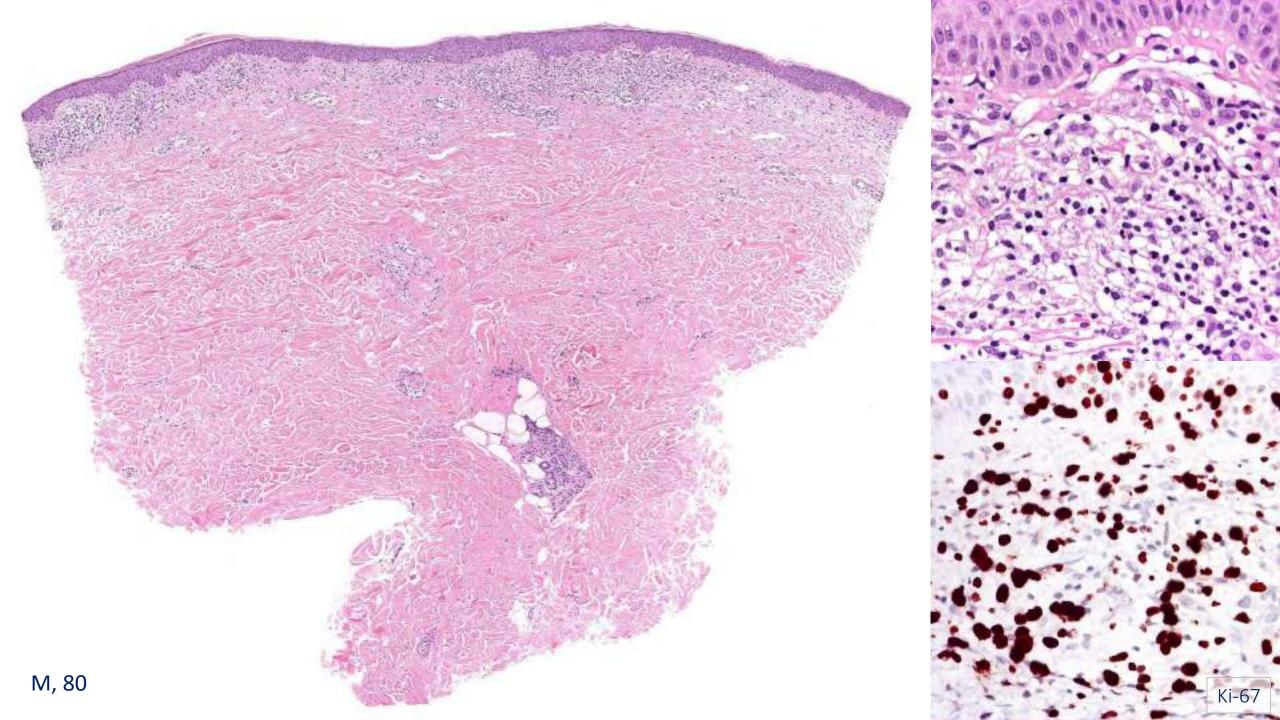
Interestingly, typical features of LSA were missing in 39.4% of genital LSA, and in a further 25.5% were present only focally.

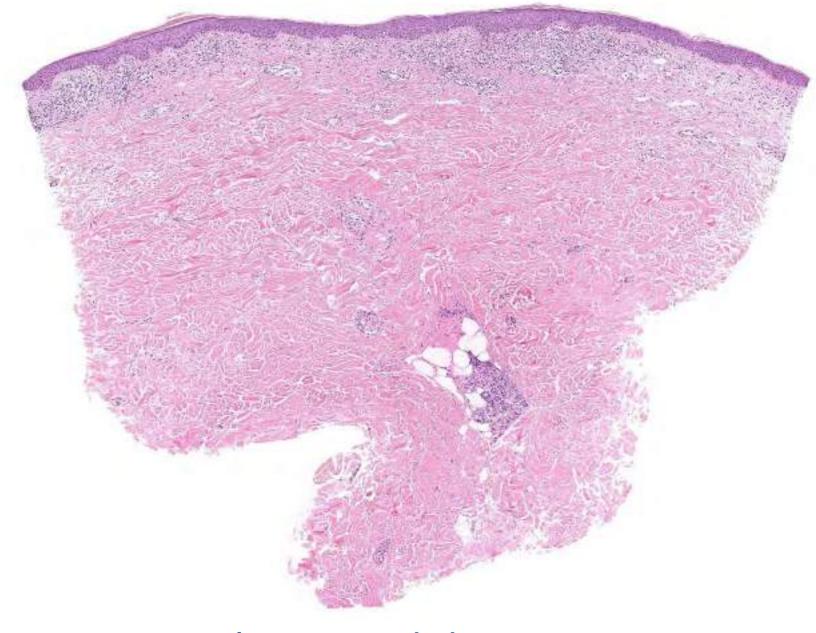
In genital "pseudo-MF" cases, immunohistochemical analyses showed a predominance of CD8+ T lymphocytes within the epidermis. Molecular studies of the T-cell receptor genes revealed a monoclonal population of T lymphocytes in nearly half of the cases.



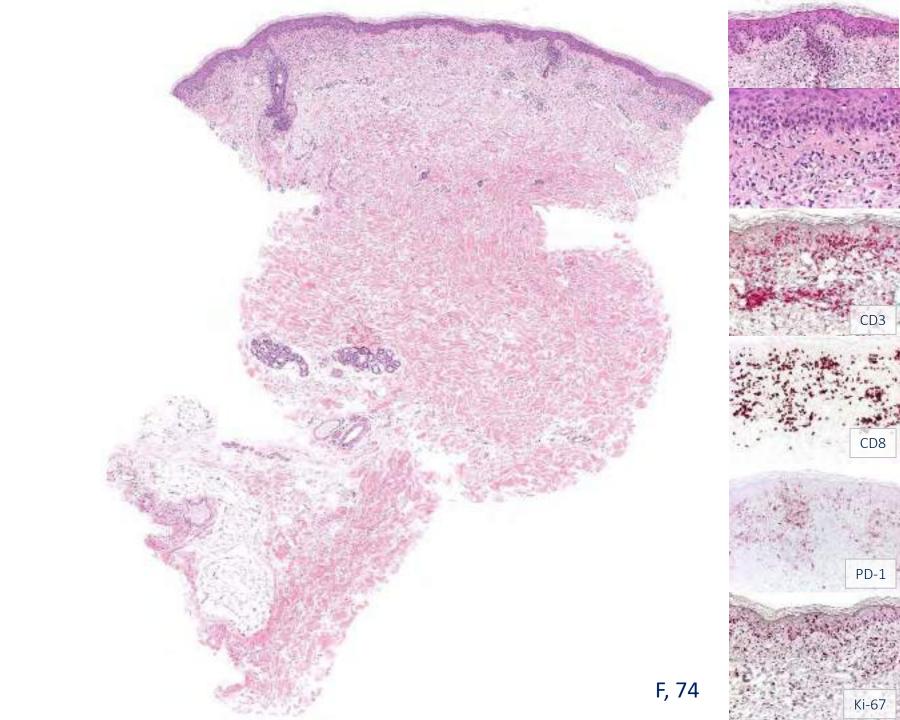
Pseudo-MF features on genital skin

- MF-like histopathological features are very common in genital lichen sclerosus and may be observed rarely also in balanitis / balanoposthitis / vulvitis
- In all such conditions presence of intraepidermal (epidermotropic) lymphocytes, usually with cytotoxic phenotype (CD8+)
- The genital area may be a special site for MF-like cytotoxic
 T-cell infiltrates
- A diagnosis of MF on genital skin should be made only upon compelling evidence





Lymphomatoid drug eruption



Lymphomatoid drug eruption (T-cell pattern)

- Drug eruptions may occasionally mimic histopathologically a cutaneous T-cell lymphoma (MF-like or lymphomatoid papulosislike)
- Sudden onset, generalized distribution; Resolution upon discontinuation of the offending drug
- Cases with T-cell pattern show band-like lymphoid infilrates with several activated cells and often with high proliferation (>90%);
 Epidermotropism usually minimal but atypia may be striking
- Cases with CD30+ activated lymphocytes usually characterized by mostly perivascular rather than interstitial CD30+ cells

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Besiew article

Drug induced pseudolymphoma

Cyathia M. Magro", Brianne H. Danieli, A. Neil Crowson

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ABSTRACT

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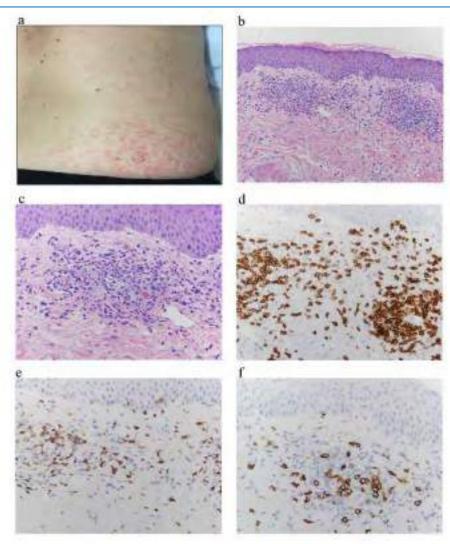


Fig. 6. a: The patient presented with a 1 week histony of an light much composed of 1-3 mrs marains. and popules on the trusts, fare and entrenities which spared the remous rientranes and palms and soles. is The peach biopsy shows a striking inflarymentry process comprised of a lymphabilitiestic inflicate closely opposed to the capillaries and venules of the superflaini ball of the dressis with sed cell estasvacation, c. The lymphacytra are small to intramediate in size with some degree of matinic contour. inegativity at well as transferred immunoblastic. elements doedy opposed to the venuels, il: The lymphocytic infilirate to highlighted by a CDS imministain is The CB7 preputation highlights the symptomystic inflirence but in significantly distributed compared to CDS: f. A mapher of large transformed cells are politive for CD30 within the lymphomatoid. perivascular infiltrate.

^{*} Regional abilities Extension, 4142 Total Margo Floor, Trans, OK 24140-2010, Transi Shane

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Drug-Induced Immune Dysregulation As a Cause of Atypical Cutaneous Lymphoid Infiltrates:

A Hypothesis

CYNTHIA M. MAGRO, MD. AND A. NEIL CROWSON, MD.

The pations encommend iff patients in when a skie impethread attained Inseptional Enganglishs and in whom a references those bistory abouted impedicas of one or more agrees before festional esset, for 13 perious, the Hapey had been performed to rule out a diagnosis of malignose lymphosis, whereas in the other eine the clinical improvious was that of a drug emption. Among the name frequently prescribed agents were arking channel bindown, augic-Standard converting company (ACSC) inhibit new annihilation contracts, annihilation mines. & blockers, been disrepiese and food-levering apove, all of which are althor become to partiall frequencies describe or have been implicated as a cause of pseudolymphometa. Toolive of the patients were on two at more of these drugs. The office of drug medication on the clinical coarse was excessed. The clinical presentatives were as one or more erythemismus plaques or or hiple infiltrative papules. or as suitage codules. The patients had been on one or more of the alacterisationed draw from 2 weeks to 2 years before developing the bisiness Depolation of the emptions occurred in 17 partents within I to 52 weeks (name, 7 works) of discontinuing the excitation. Five additional patients half complete experies of softary legions softwer recoverage, A history of atopt, autoingrame disease, or previous carriesome non-elected to the patients. All hisper specimens showed stypical boughold intitrates, which assumed one or more of the following patterns: pecusis fungaides (MF)-like, a hosphomorald vaccular re-

Getancours pseudolymphomata are benign infiltrates that mimic malignant lymphous and encompass a spectrum of entities including lictions renewald, Eikucha's disease, Romi-Dorfman disease, Jessner's bymphocytic infiltrate of skin, lymphomogoid populosis (LMP), pseudolymphomonous angiokycatoms of thildren," and hypersensitivity reactions to artigens such as viruses," Bernita toughteyers," unlargedes," contacrants,4 or drugs.1.2 An aberrant inumine regionse to microbial or other antigens may reflect a state of systerrite immune dysregulation as is proposed for eosinophilic pustake folicular rescions, diphenyllychmion (Dilantin) associated pseudolymphoma," and pseudo-Imphoroma developing in the setting of leukemin." The distinction between pseudolymphoms and maligmust lymphoma may be problemente, because a pseudo-Imphoma can mimic both cirraneous T-cell and B-cell Iyaqohuana.20 Furthermore, a pseudolemplomea may progress so malignant lymphoma."

active, hyphocytems colle, and fullicular mucinosis. Based on the hittepathelogy of the brogoled lesions and the climat source being one of being resulation after consistent of sing through or architect of a noticery laden without subsequent recurrence, a diagnosis of dragosoveleted himphometric hyperservicinity was contributed in all. spectroses. A diagnosis of drap-associated pseudolocaliseau should he evaluated before a diagnosis of estamous lymphoma is rendered, and streak be considered if the patient is on a deag known to alter brogiveryte function, particularly in the sorting of systemic immune. derrogalistics or positioling therapy when agents may not conceptable cally or canadiation as after brophoid function. The archors pentslife that the drug eary promote an abertout immune corporar to an retigon that may be the fong tact! or some other almaka, A side. bingsy may be pictivakely helpful, on the lesions of drug associated. pseudolymphona have a receptology distincted from realizant lyanghoma. Here Perture. 27:125-182, Conseright to 1995 by W.S.

Bay words desprisely and hospital dependant, because dyanga-

Abtornations ACE, angioverals exercing current MF, receive fragolism LVF, implemental papalests: LyVR, implemented vercular traction. AEL, engineering politicative feedure: IIII-6, delayed type impresentativity.

The authors describe 22 patients who devaluped drug-associated atypical cutaneous hymphoid influence consistent with possibility included the fact an acrossopic light microscopic features existed the distinction of these influences from malignant lymphoms. A role for drug-induced immunic description is proposed at the mathogenetic basis for the evolution of these learners.

MATERIALS AND METHODS

The one-through in impropries from 59 patients were oriented from 70,000 spectroers accrossred over a 10-much period. or the deceasespeabology laboratories of Pathology Services. har: (Confinting), MAC and Control Medical Laboratories (Whinter, Carata), and commed by conventional light raicroscopy. In 10.00 the spacement, the elimeten questioned a drug empition, and in two respectfic drug was mentioned. In all specimens, a complete drug history was absolved by the sulture before finalizing the bispo report, rowaling dragingestion before lesional owers, in all speciments, although int. attricted lymphoid infiltree was observed, the authors rendered a final diagnosis of probable drug assertions houghtsmuteid hypersemutates hased on specific histological entertacodined laws. In 12 specimens, stalignass kurphoma was the second bisological differential disquote Counties of drug through non-recognized by the authors, and in 20 of 12 speciment, this prices was actual to by the effection. The effect cal courses of all pastenus some inflessed for up to 1.3 years. after consumo of drug themps:

Pattern		
MF-like	69,6%	(n= 16)
Angiocentric	39,1%	(n= 9, 8 with MF-like features)
Folliculotropic	8,7%	(n=2)
Lymphocytoma	17,4%	(n=4)

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Histopathologic Characterization of Mogamulizumab-associated Rash

Jennifer T. Wong, MD*† Kelsey E. Hirotsu, MD* Tatiana M. Neal, BA*
Shyam S. Ragiuran, MD, f. Bernice Y. Kwong, MD* Michael S. Khododonet, MD, PhD*§
Ryame A. Brewn, MD, MBA*† Roberto A. Novoa, MD*† Your H. Kim, MD*§
and Kerri E. Rieger, MD, PhD*†

Abstract Right to use of the most approximately exceeds observed with megantalization, an serio-C-C chemoking receptor 4 monoclocul anticedy approved for previously treated moves a fragistic (ME) and Server syndrome (SS). Given the memperific clinical presentations of the rash, histopishologic distinction from MFSS as united for informing distinal measurement, we performed a

comprehensive dismoterization of the histoparticities. moganulicusal-secouled rash (MAR) with the in high finoughput semencing of T cell receptor (TCR) two blopsy specimens from 19 pritents were evel spectively. These major histologic reaction patterns us opongioscopsurizations dominitis (\$1/57), interfac-(11/52), and grandomstons demailie (8/51). Almos speciment (1950) showed at least 2 of these read consumantly. (Neural everyopids ware not a count being present in only half (27/52) of spectrons and only 3: Postures minicking MDSS, including fymph tosis, Junellar Resoptissa, and adretal implyened month seen but touled to be focal and suits. In 286 with unitable immunchioschemists, intragridamol denominated a CDACDS ratio \$1:1. Low backers the potinit's previously identified MF(SS-associated T no were depresentated in 2046 speciment makes throughput expansive of TCR. We couclede that demonstrate diverse instalogic fortuna. Findings ti tinguist MAR from MESS metale the levered of CEACES ratio within intragridental hosphocytes stration of about or nondeceipout lends of Gues TCR agreezes. Combition with the chinesi finds munoristochemical and malecular chroscorrection of

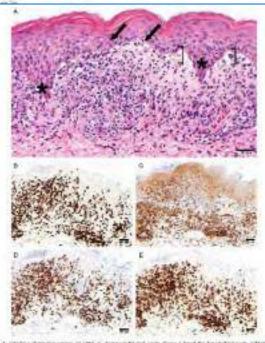
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Correspondence Kirro E. Rieger, M.D. PED, Department of Strategic University School of Machiner, 450 Bookway S. E. Hoor S. Riedercol City, CA 91481 Serial Scringer's Corporate of 2021 Wolston Klauve Holder, Inc. All-egate MFSS before magamakraroth, when possible, may fashinte recognision of MAR.

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Am J Surg Pathol + Valume 44, Number 12, December 2028

Mogamulizumab efficacy is underscored by its associated rash that mimics cutaneous T-cell lymphoma: a retrospective single-centre case series*

N.A. Trum (a, 1) J. Zain, J. X.U. Martisez (b, 1) V. Pareldt, M. Afchami, F. Abdulla, M.R. Carson, S.T. Rosen, S.C. Bonnott' 28 and C. Querfeld (a) 1-4

Summary

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Conflicts of Interest.

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Entgrant Magamatrament is a numerical antitody against chemicals, received type 4. If was recently approved by the 188 read and Brug Administration for traped or refractory repeats foregodes (MF) and Sinary syndrome (SS). The most commonly responded absent event in the phase III According trial was thought respond (28%), new terrord magamatraments-associated sale (MAR). Climial recommendations are in MAR and to treatment differ between the current package inters and postappined chagois reported from two angle-scarce scalins that focused on its characterization, but less so an outcomes and characterization from concerning trial lymphomes (CTCL).

Discuss To describe our experience in the diagnosis of MAR and troitment of patients with CTCL with magazinization.

Methods This is a single-control terrospective case series study.

Builds We livered a signer transferace of MAR as patients with CTCL (1.7 of 24, 68%) than previously reported. MAR development is associated with complete (11 of 17) or portial (four of 17) respectes, with an overall expense too of 88%, compared with 18% (two of several to patients without MAR. Diagnosis of MAR may be obserted by its ability to minote key CTCL features but a clinically and histologically, but an absence of T or, receptor elevating and relatively decreased CD4. CD8 onto compared with baseline beautiful services MAR case, returned disease.

Gerham MAI has the potentia to desire a significant management problem lice potents on magazialismush. Misidemissions of MAI as returned CTCS may detrimentally result in the premature discontinuation of magazinizmush in particular viscos through the interest of most instrumentally had to too. Through this coparational towards and of new kilous during restricts with magazinizmush is required to inform ideal resonant decisions and achieve better nationals.

What is already known about this topic?

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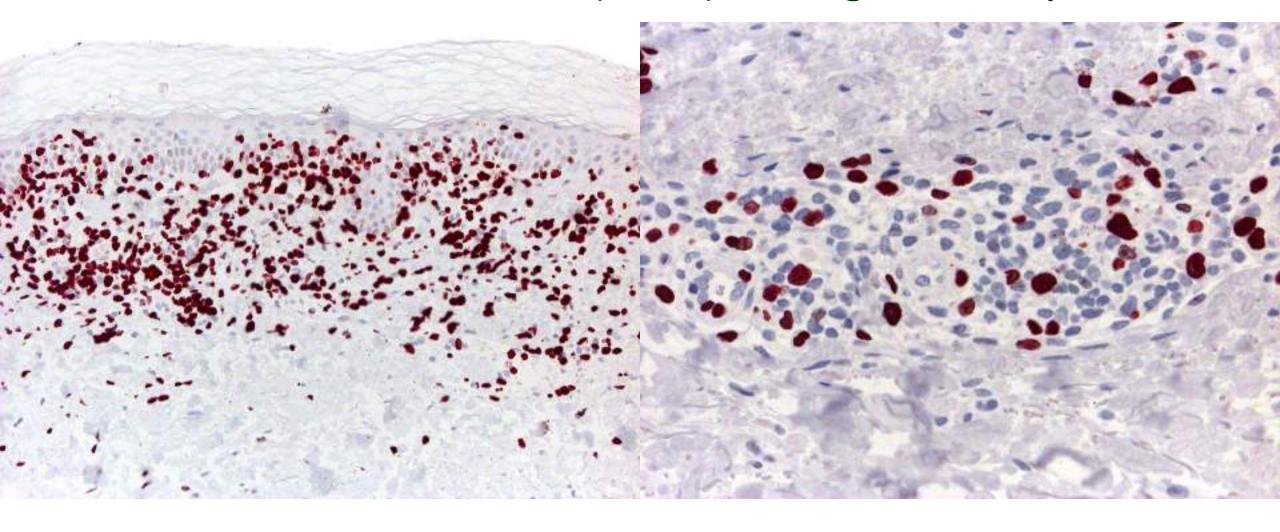
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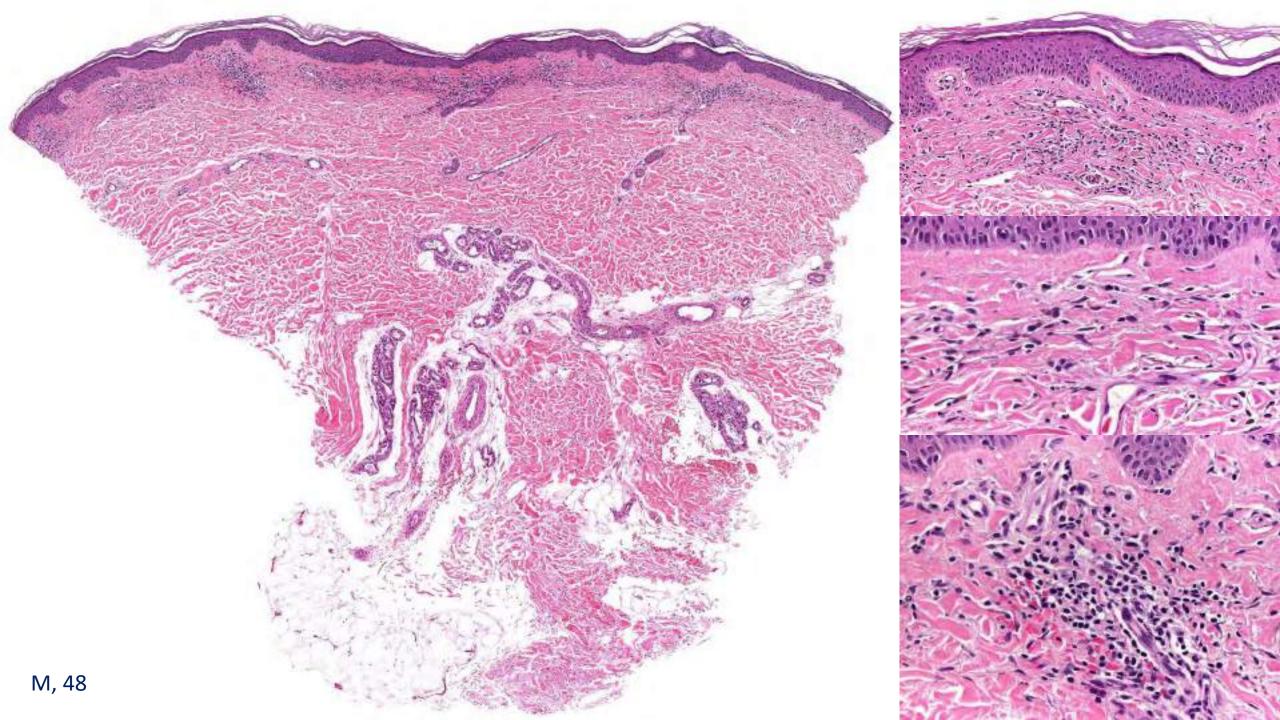
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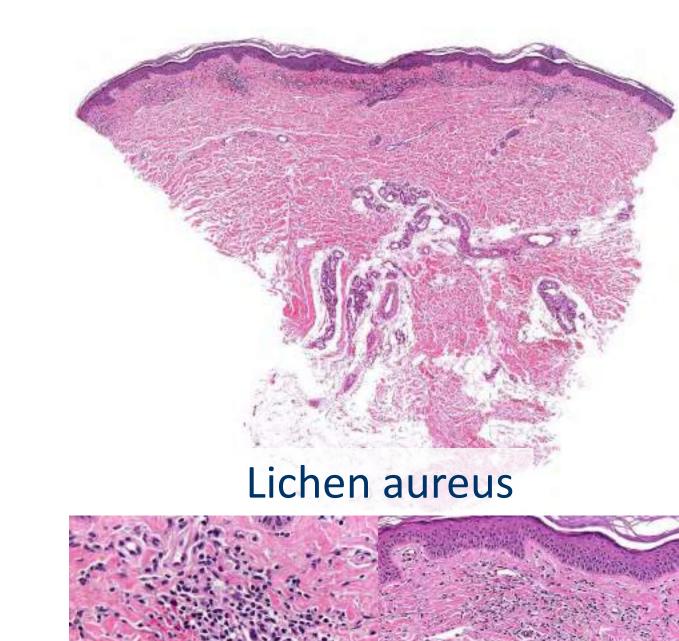
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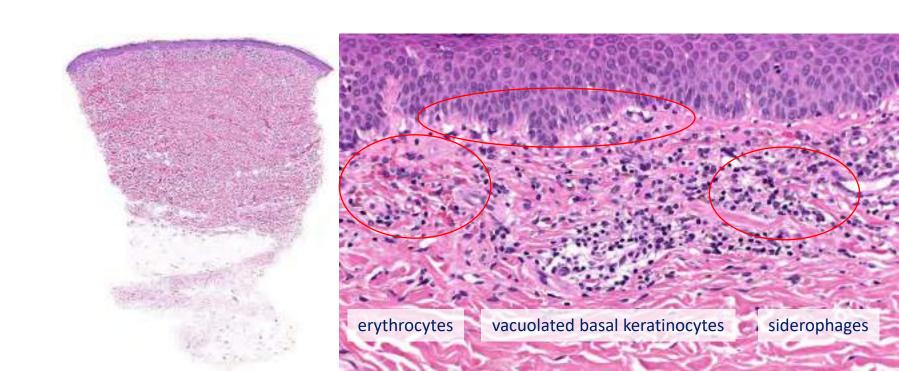
[&]quot;College of Phoesiacy, University of South Caroline, Colombia, SC, USA

Clue: Proliferation rate (Ki-67) too high for early MF









Lichen Aureus

- Persistent, localized form of "pigmented purpuric dermatitis"
- Spontaneous resolution observed in >50% of cases; in some cases lesions persist unchanged for years
- T-cell monoclonality in ~50% of cases
- No relationship between treatment / clonality and outcome
- Probably represents one of so-called "clonal dermatoses" follow-up advisable

Persistent Pigmented Purpuric Dermatitis and Mycosis Fungoides: Simulant, Precursor, or Both?

A Study by Light Microscopy and Molecular Methods

Jorge R. Toro, м.D., Christian A. Sander, м.D., and Philip E. LeBoit, м.D.

Myonix fungcides (MF) can present with purpure lusions, and rare patients who seemed to have persistent pigmented purpuric dermatitis (PPPD) have developed MF. We recently excountered two patients referred to our cutaneous lymphoma clinic who had PPPD rather than MF and two others who appeared to have both conditions, leading as to explore the histologic similarities of these diseases. We axiamined specimens from 56 patients with PPPD to determine the frequency of MF-like histologic configurations. namely, the pseriasiform lichenoid, pseriasiform spongietic lichenoid, and atrophic lichenoid patterns. We also noted the degree of spongiosis, epidermotropism, papillary decmal fibronis, lymphocytic stypia, and epidermai hyperplasia, the number of extravasated erythrocytes and siderophages, and the distribution of lymphocytic infiltrate within the opidermis. In 29 of 56 patients, there were natherns typically seen in MF. PPPD can feature lymphocytes aligned along the epidermal side of the dermoepidermal junction, with few accretic keratinocytes, as can MF. Pspillary dermal edema occurred frequently in PPPD but not in MF, while lymphocytos in MF but not PPPD had markedly atypical muclei and had ascended into the upper apisous layer. Given these similarities, we tested for cloudity of the T-cell population using a polymerase chain reaction assay for y-chain rearrangements. Clonal populations were present in three of three and one of two specimens from patients with both PPPD and MP, but also is 8 of 12 specimeas typical of lichenoid patterns of PPPD. These findings

raise the possibility that the tichenoid variants of PPPO are biologically related to MF.

Key Worth: Mycosis hargoides—Persistent pigmented purparic dermatitis—T-cell gene rearrangements—Lichemoid purpara—Schamberg's disease—Cirianeous Tcell implication.

The many clinical and histological features of mycusis fungoides (MF) are more than curiosities because MF is one of the most common non-Hodgkin's lymphomas. The profusion of variants may be due to the admixture of non-neoplastic inflammatory cells in many lesions of MF and the skin's large repertoire of reaction patterns (1). Among the variants of MF is one in which purpuric areas develop within lesional skin (2-4).

Several considerations lad us to examine the relutionship between MF and the group of conditions known as persistent pigmented purporic dermaticis (PPPD). Purpuric lesions can occur in MF. The first patient reported in the American literature as having lichen aureus (5) later proved to have MF (6). The diagnosis of several patients referred to our cutantous lymphoma clinic was changed from MF to PPPD following review of sections from their akin biopsies. Last, we have seen two patients with both conditions: in one, PPPD preceded MF. We therefore examined sections from a large group of cases of PPPD to determine how often MF-like patterns of lymphocytic infiltration were present and ascertained the degree to which other features characteristic of MF, such as papillary dermal fibrosis and lymphocytes aligned along the epidermal side of the democepidermal junction, were present. Upon determining that MF-like histopathologic leatures were common in PPPD, we used the polymerase chain reaction (PCR) to test for clonal rearrangement of the T-cell receptor ychain yene.

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Dr. Toro was a follow in the Department of Demandogy at the University of California, San Prantisco, California, U.S.A., at the time this coally was performed. He is currently a resident in the Division of Demandogy at Southern Blaces State University School of Medicine in Springfield, Illinois, U.S.A.

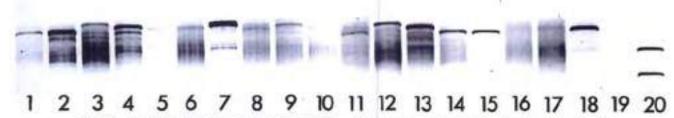
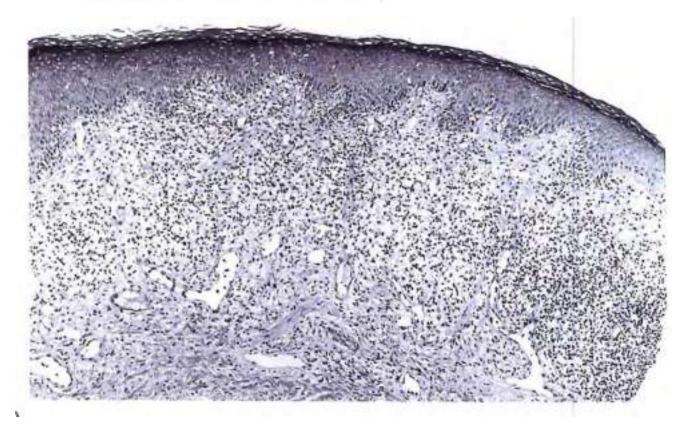


FIG. 6. Results of PCR reaction for T-cell γ-chain gene rearrangement using the V_γ10 probe. Positive control is in lane 18, negative control lane 19, and molecular standards lane 20. Bands signifying rearrangements are present in lanes 1,2,4,7, and 12–15. Smears or faint bands are present in the remaining lanes.



OBSERVATION.

Lichen Aureus

Clinicopathologic Features, Natural History, and Relationship to Mycosis Fungoides

Rogina Fixts-Pucker, MD; Peter Welf, MD; Helson Rox, MD; Lorenzo Cerron, MD;

Background: A pressive association between helen aureus (J.A) and miscous lungesdes (MF) has been suggested in the post, We evaluated the clusto-parhologic features of LA and its arlationship to MF. Data from 20 patients with a clinicopschologic diagnosts of LA were reviewed.

Observations: Lesions were asymmetrically localized in Larca of the body (mostly Lexionnip) and were characterized hisologically by dense, buildlike lymphocylic infiltrates. A minoclonal T-cell population was detected in helf of the cases. After a mean follow-up of 192.1.

months. 14 patients had no sign of shin disease. 7 patizets had originalitized skin lesions, and 2 other patients with monorified skin lesions had died of smallood and diffuse. Descript modalitizes out and other the outtoms. These was no relationship between the presence or absence of morocolamality and patient status at fellow-up assessments.

Conclusion: Furents with classic lesinns of LA da not show progression to ME.

Architemans, 2008;14(0);07(0):1173



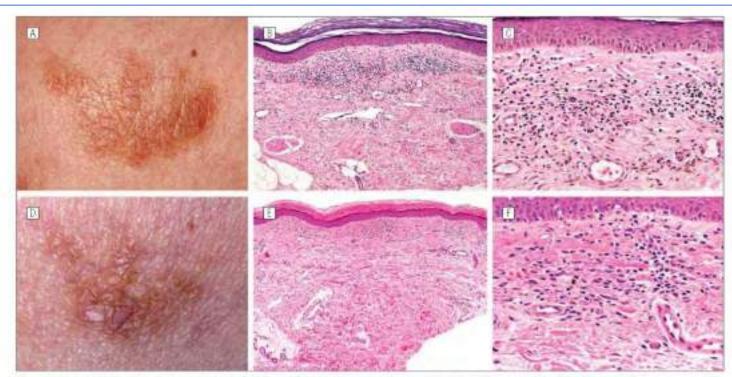
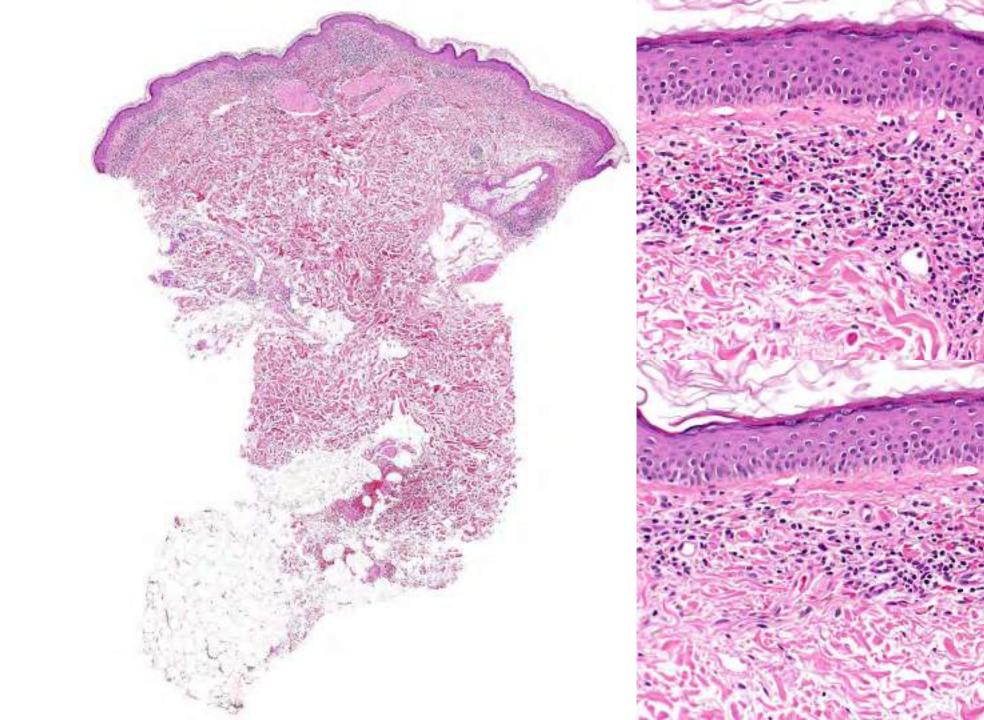
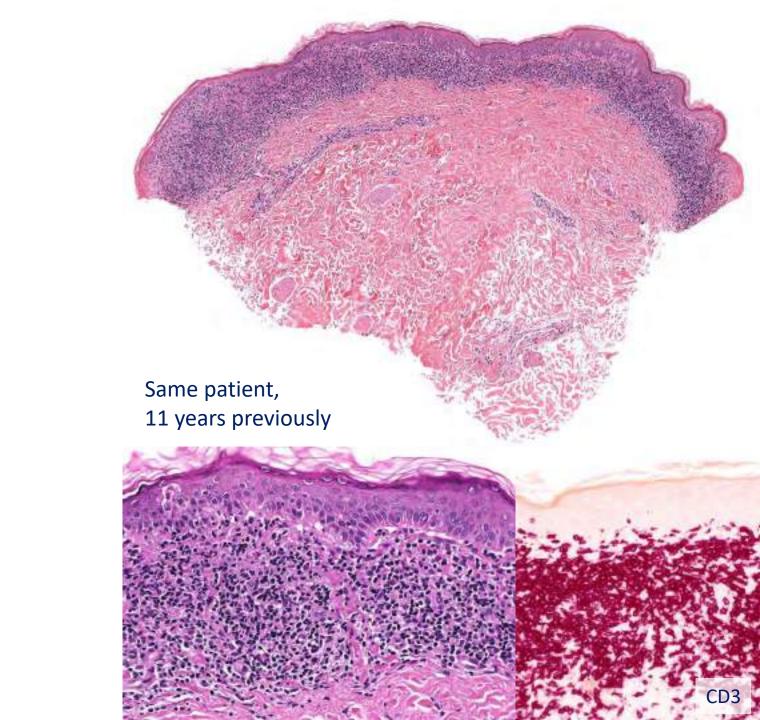


Figure 3. Patient 3 in the Table A, Appearance of skin lesion in 1990. B, A biopsy specimen obtained in 1990 showed a bandlike infiltrate. C. Note sparse hemorrhage and coarse bundles of collagen in the papillary demis. D, Appearance of the lesion in 2007. E, A biopsy specimen obtained in 2007 revealed persistence of the lymphocytic infiltrate. F, Note features similar to those of the biopsy specimen obtained in 1990. Hematoxylin-eosin, original magnification ×10 (B), ×20 (C and F), and ×4 (E).





OBSERVATION

Lichen Aureus

Clinicopathologic Features, Natural History, and Relationship to Mycosis Fungoides

Region Fink-Picker, AD; Piter Wolf, MD; Heinar Kerl, MD; Lounzo Commi, AD

Buckground: A possible association between lichen onsens (LA) and mycosia languisles (AIF) has been suggested to the past. We evaluated the clinic opatiologic features of LA and its originathing to MJ. Data from 23 patients with a clinic opathologic diagnosis of LA wenwelconed.

Observational Lesions were assume trically localized on Lowenfithe body unusuly 1 expensivy and some diagnostical distribution for the hardlike lymphocytic infiltrans. A commissional T-cell population was desired in half of the cases. After a meant follow-up of 102.1

rounts. 14 paients had no sign of shin disease, 7 paients had unasselfied shis lessons, and 2 other patents with unacothed with lessons had shed of amounts conditions. Incomment modalities did not affect the concease. There were no relationship between the presence or absence of essencionality and gattern status at follow-up assessments.

Conduction Parison with closer listers of LA darant show progression to MP.

Arch Demutri, 2008;184(5);11(0-1173)

DOUGH AURIUS (LA) IS A cheunic persistent pigmental purporte demantis (PPPD) characterized closedly by withward lecolled golden brown totons and histopathologically by a lichenoid lymphoevic intiferne. The lesions are stable, are usually symptomicss, and mor persist for years. Alabaugh all body regions may be affected, LA occurs mently on the legic Histopathologically, 1A differs from other PRPDwin the density of the Juhenood tiesure reaction and the marked accumulathen all harmonderns containing macrophages,1 in some owes, because of the themse transfiller inflatration, the histogration logic differential diagnosis relative to mycusia liengestales (M1) may be difficult on impossible. In fact, perpune lesions insembling LA histopathologically base been described in 50%. Co

An association between FPPD and MF has been reported in the context of cases of PPPD progressing to MF* or the precute of propose in lexions of MF.* in a study of many cases of FPPD. To counter, workers* suggest that this condition may be related in MF.

The general our study was to available the class opaths dopte factors and natural listacy of LA in a sample of patterns. We also must to define us relationship if are, to MF.

METHORS

PATIENTS

Data from 13 patients from the bler of the Department of Dermatchery, Medical Dimensors of Guer, were included in this study is each case, the original histographic partitions were entirewed by one of set (i.e.). Leftern assess was diagnosed according to clinicopathologic correlation by reviewing clinical photographs when involvable urby reviewing redical records. Clinical data analyzed included age, set, data of kint diagnose, distance of behaviour, and stress of disease at the last follow up assessment.

HISTOLOGIC, IMMUNORISTOLOGIC, AND MOLECULAR REOLOGIC EVALUATION

sections with a mechanism thickness of 4 pm and arabased with bettintoxylin comin, oursing and periodic acid schol's were unit after first amount of the first model of the many acid in which a pacifier black model be intowed, mady in of the T-cell morphic was performed using polymenus claric treatment (PCR) exchanges and primers as published previously. The acid acid morphism based by the T-cell morphism of th

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Patient No./		T-Cell	Fol
Ser/Age v	Site	Regrangement	

Table, Clinical Data of Patients

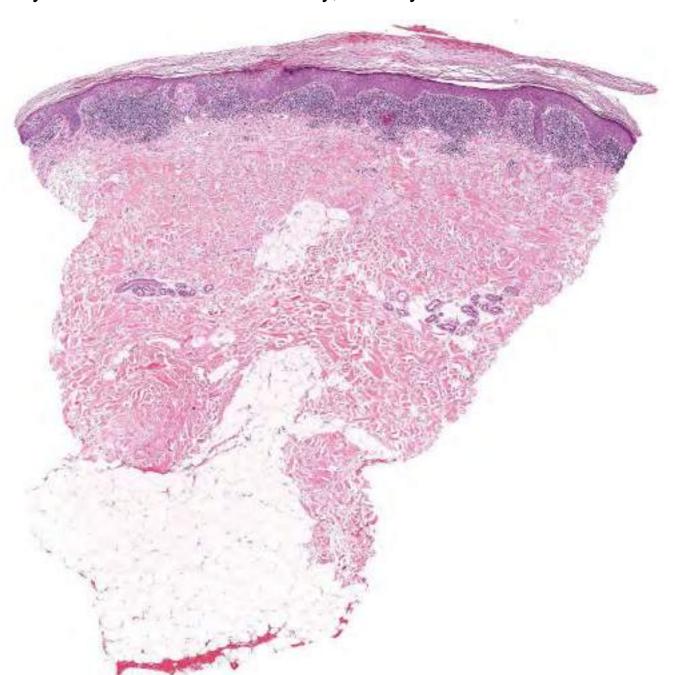
Patient No./ Sex/Age, y	Sile	T-Cell Rearrangement	Follow-up, mo	Status
1M/37	Hed	Polyclonal	- ti	A-
24/60	Thigh	Polyclonal	154	A-
3.F/53	Krive	Monoclonal	204	A+
4F/51	Buttocks	Monoclonal	89	A-
SMV77	Thigh	Menoclonal	.51	Av
6F/13	Lowerleg	Monocional	76	A+
7/M/47	Forearm	Monocional	30	D+
8M/75	Opperami	Polyclonal	30 25	B+
SM/61	Popilisal	Polyclonal	20	A+.
10/F/51	Lowerleg	Menocional	20 37	Α-
11/M/36	Lowerleg	Monoclonal	64	A+
12/M/65	Foot	Polyclonal	41	A±
13/F/44	Lowerley	ND	89	A-
14/1-725	Back	Polyclonal	281	A-
15/1/35	Knee	Monectonal	144	A- A- A-
1674630	Thigh	Polyclosat	67	A-
17/M/50	Lowerleg	ND	30	A+
18/F/49	Lowerleg	Polycloral	103	A+
19/M/7	Shoulder	ND	104	
20/F/24	Breast	ND	168	A-
21/5/37	Lowerleg	ND	72	A
22/1/1	Forearm	ND	168	A- A- A- A-
23/M/33	Right frunk	ND	382	A-

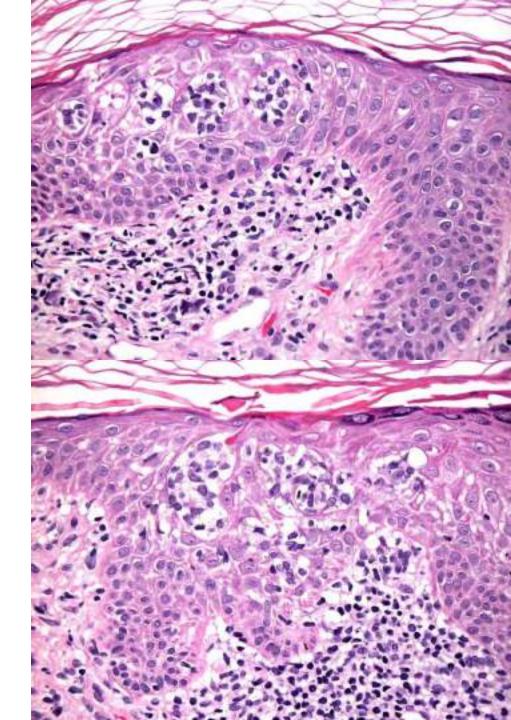
Abbreviations: A-, alive without skin disease; A+, alive with skin disease; D+, dead of unretated conditions with persistent skin disease; ND, not done.

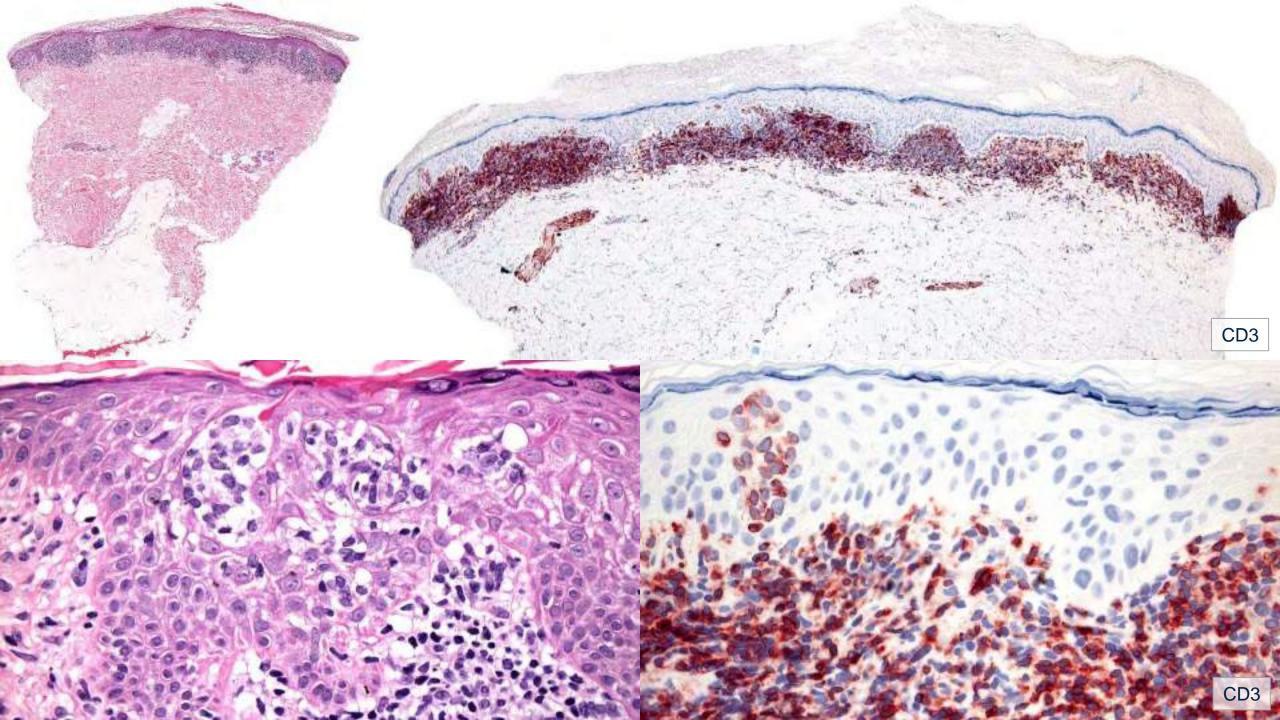
Monoclonal: 8 (50%)

Persistent disease: 9 (39,1%) (20-204)

70-year-old woman with a scaly, solitary lesion on the breast.







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Lichenoid (lymphomatoid) keratosis

- Dense, band-like infiltrate with sharp lateral circumscription (not visible on partial biopsies!)
- Epithelial hyperplasia (variable); sometimes remnants of an epithelial tumor (e.g., lentigo actinica, seborrheic keratosis)
- Mixed infiltrate of T-cells (predominant) and B-cells
- Lack or minimal fibrosis of papillary dermis
- Variable numbers of intraepithelial ("epidermotropic")
 lymphocytes; may be larger than normal
- In the past reported often (and published) as "solitary" MF (also by me...)

Solitary Skin Lesions With Histopathologic Features of Early Mycosis Fungoides

Lorenzo Cerroni, M.D., Regina Fink-Puches, M.D., Laila El-Shabrawi-Caelen, M.D., H. Peter Soyer, M.D., Philip E. LeBoit, M.D., and Helmut Kerl, M.D.

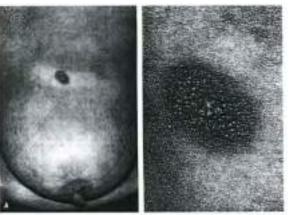
Myomis firegoides (MF), is a crumous T-cell by usually tegins with cutmenus putches that evolve and tumors. A few recent reports describe a solita MF distinct from localized pagetoid reticulosis, which solitary verrecots letters occur on acral skin lesions with some of the histopathologic fr. rarriy occur during treatment with several thru annicommon or unthisturines. We malyzed to ologic features of 20 patients with solitary skin ha histopathologic features of patch: or early play Eight men and 12 women (mean age 50.6, range Z 40) had relisary, small stythessaurus patches to pl. on the trunk (16 cases, 6 of them on the breast), as ties (3-cases), and inguina) region (1-cases. Teatreated with one or more drugs; only two of the antidopressures or antibistanines. Histopathologic revealed in all owen a hand-like infiltrate in the s frequently with epidermotropium of solitary ! Applical lymphocytes were present in a minumy munotimology showed a predominance of CD3 cytis, is most cases admixed with clusters of CI Only a small proportion of the infiltrate was CDS analysis of the rearrangement of the T-cell recept performed in 16 owen ming the polymerase of (PCR) technique and revealed a reconcional band After surgical excision, 2/14 patients had a recurr surgical scar. In 15 patients with complete follow evidence of "classic" MF postd be observed after tow-up at 31.9 months. Solitory skin lesions w pathologic features of MF can be considered as a icopathologic entry, probably representing a notic mycosis fungoides

Key Words: Schary myonis fungoids—Cau lymphona—Cutaneous T-cell pseadolymphos lymphonatous drug etaptions.

TABLE 1. Clinical data, drug history, and results of PCR analysis of TCR genes

Patient no.	Sex	Age	Location	Drugs	PCR analysis of TCR genea	Treatment	Follow-up (months)	
1	ŧ	59	back	no	P	TE	A&W (45)	A&W (8
2	F	53	breast	10.00	M	TE	A&W (50)	A&W (1
23456789	F	45	breast	Developed new lesions	P	TE	A&W (26)	A&W (1
4	F	23	breast	no	M	TE	A&W (76)	A&W (2
5	F	44	inguinal	unknown	ng	TE	LFU	LFU
- 6	M	63	breast	no	P	TE	A&W (7)	A&W (2
7	M	71	flank	no	nd	TE	A&W (38)	A&W (1
В	M	47	arm	unknown	P	TE	LFU	D- (30)
9	M	47	back	no	M	TE	ASW (75)	A&W (2
10	M	75	flank	Isosorbide 5-mononitrat	M	TE	A&W (48)	A&W (48
11	м	36	back	Clofibrate; Atendiali, Allapurinal	М	local steroids	A&D (15)	A&W (3
12	F	51	breast	Developed new lesions & LyP	P	local	A&D (6)	A&W (1
13		58	back	Hydrochlorothiazide Sucraltate: Ramitidine; Famotidine	P	steroids local steroids	A&D (11)	A&W (1
14	F	56	breast	Levothyroxine	M	local steroids	A&D (57)	A&W (1
15	F	29	abdomen	Levothyroxine	P	TE	A8W (23)	A&W (1
ié	F	70	a/m	Levothyroxine; Isradipine; Allopurinol; Bisoprolot, Terbutaline; Chlordiazepoxide;	P	TE	A6W (22)	A&W (2)
1000	2.0	2.6	pack	Amitriptyline; Ketotifene		TE		
17	F	34	Dack	no	M	TE	recumence	
							(36)	
18	F	43	back	Fluoretine	M	local steroids	A&D (18)	
	M	24	back	no	P	local	A&D (8)	
20	М	82	am	San Francisco Naproxen, Acelyl Sallcylic acki, Acetaminophen	O P	steroids TE	recurrence (12)	

PCR, polymerase chain reaction; TCR, T-cell receptor; nd, not done; TE, total excision; recurrence, recurrence within surgical scar, PB, punch bigpsy; M, monoclonal band; P, polyclonal smear; A&W, alive and well; A&D, alive with persistent disease; LFU, lost to follow-up.





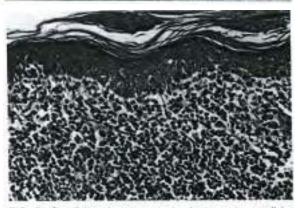
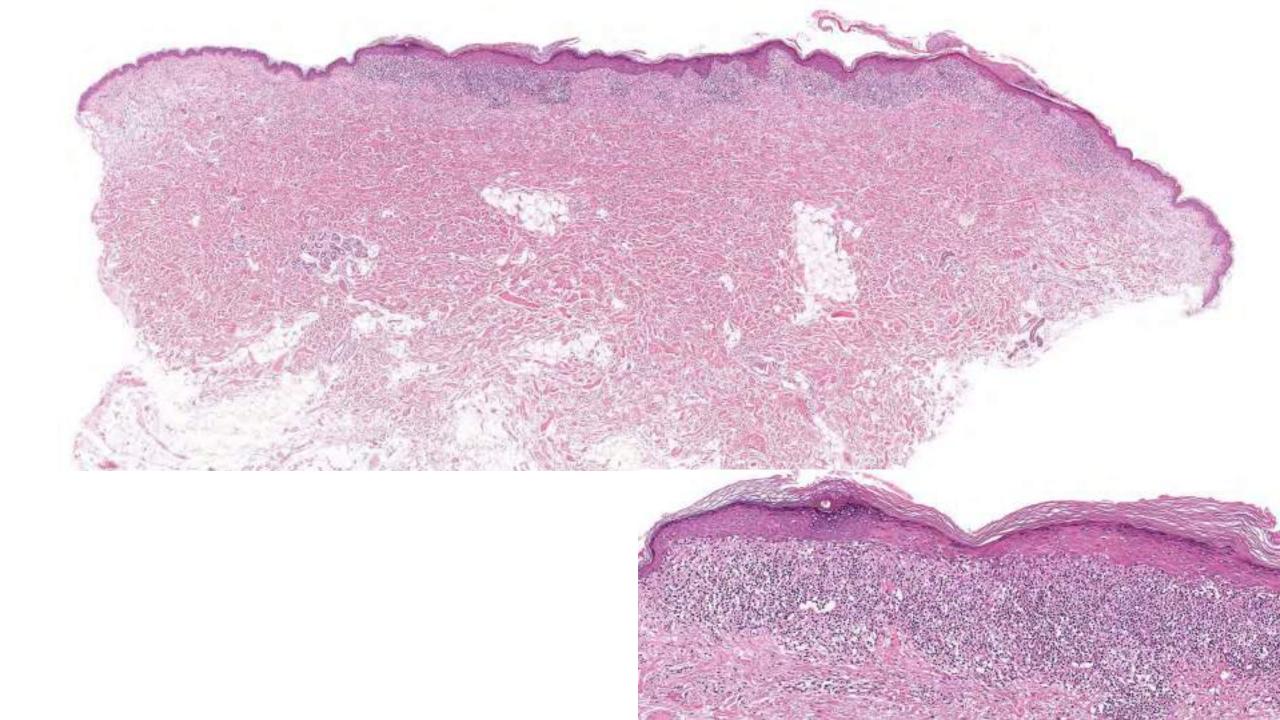


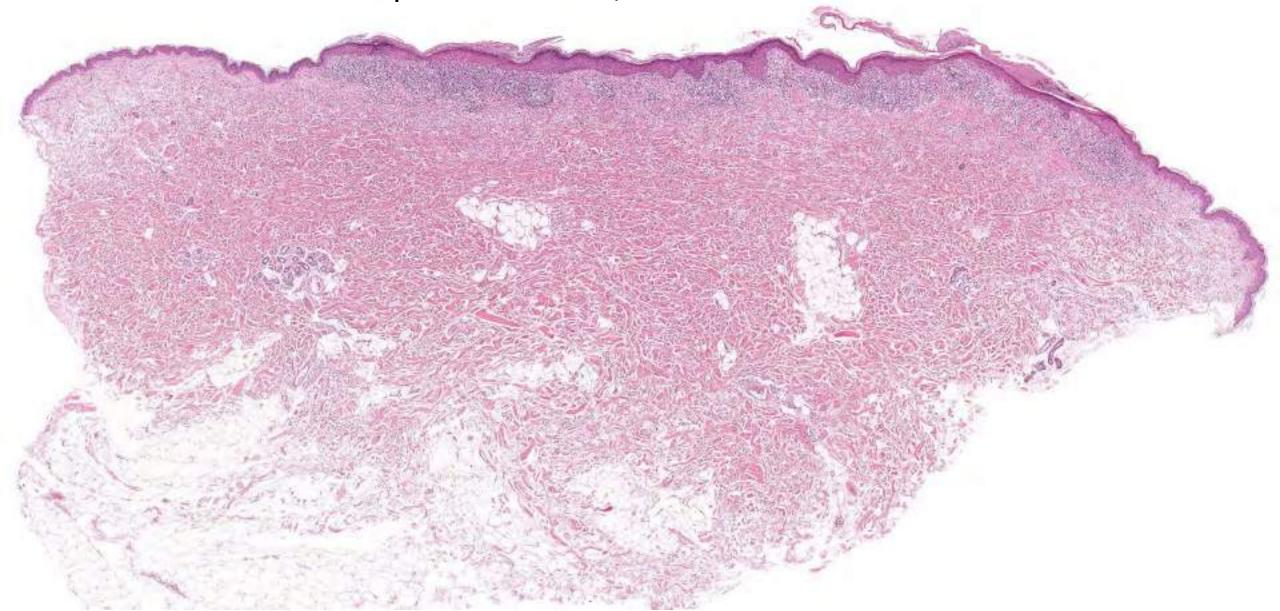
FIG. 5. Small lymphocytes predominate; note small intraepidermal collection of lymphocytes.

From the Department of Demandagy (L.C., R.P. ILP.S., U.K.), University of Graz. Austria, and Demandtion (F.EL.), Department of Demandagy and Polish of California, Sea Francisco, U.S.A.

Address correspondence to Lourno Corone, M.D., Dermaniogy, University of Gear. Auestrage-plate. 8 Auetra, E-mail: Institutorymosilikiosiatez at at

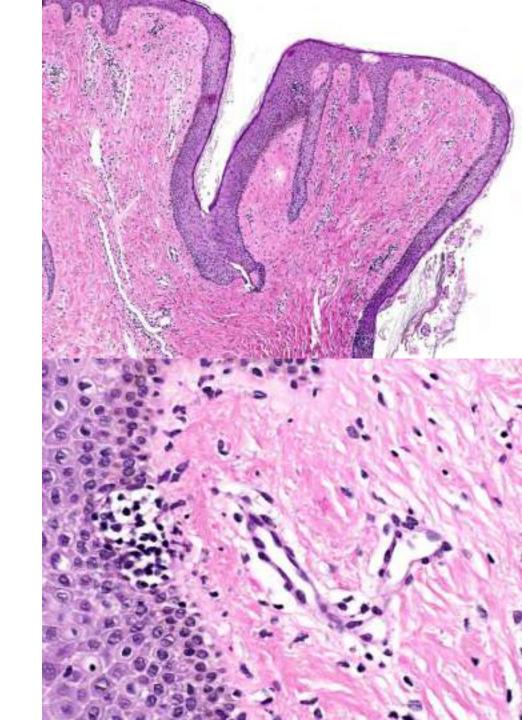


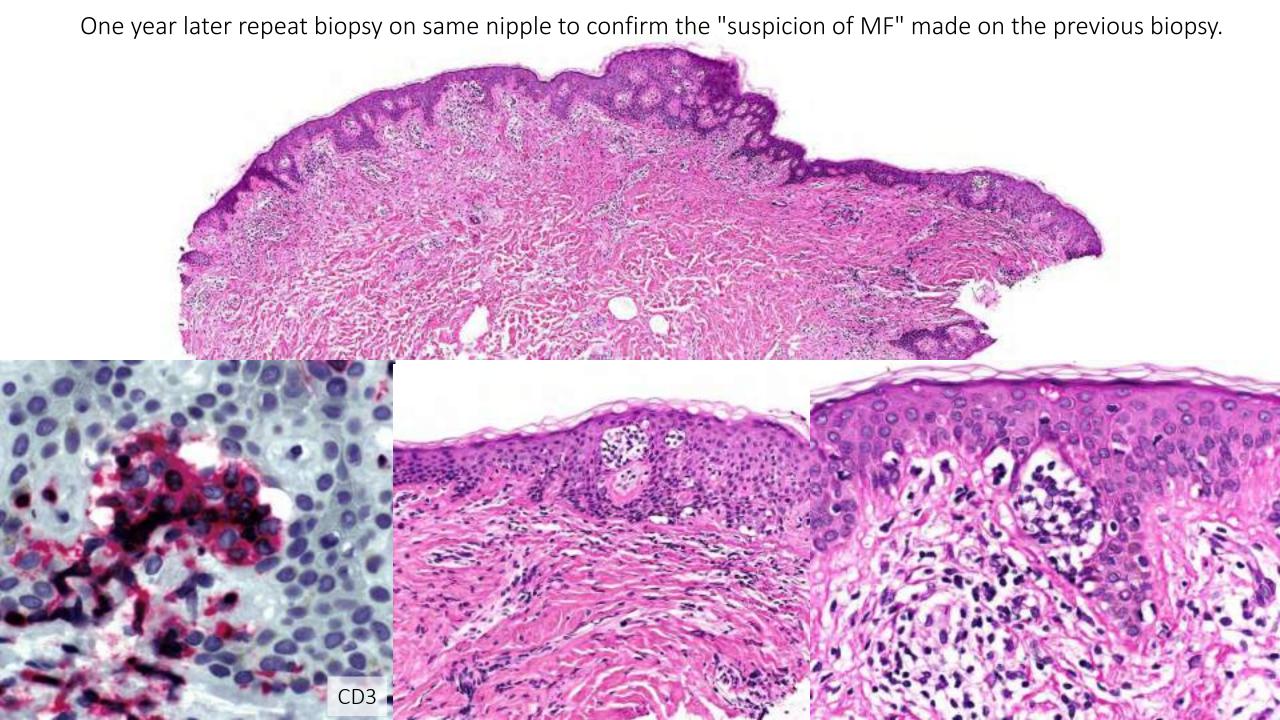
Clue: sharp circumscribed, dense infiltrate; mixed T- and B-lymphocytes; in many cases focal rests of an epithelial tumor, often seborrheic keratosis

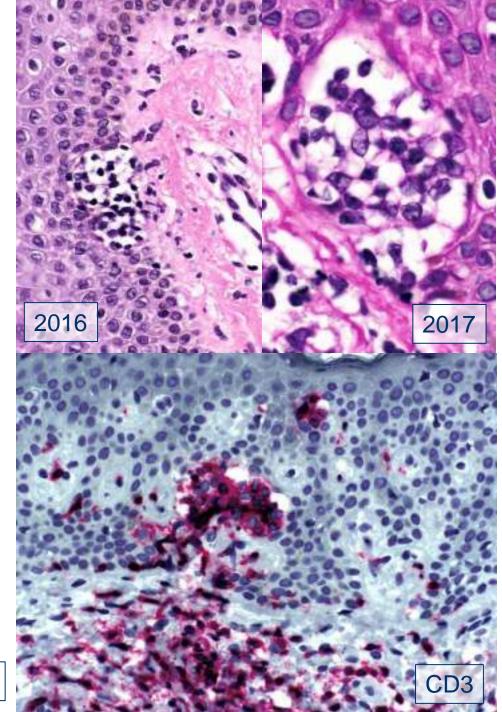




Reported as "suspicion of MF"







Clinical correlation (available only 2 years after the second biopsy, 3 years after the first one).

Nevoid hyperkeratosis of the nipple

Nevoid hyperkeratosis of the areola misinterpreted as mycosis fungoides

Neword hyperkenators of the niggle and areola is a benign unradition: with fewer than 70 cases reported in the fittature. We report a case of unaliteral devoid hyperkeratoris of the areola with intraspidermal. lymphocytes that resembled Pautrier's microabacesses on histological examination. This is the third report of mycosis fungoides-like changes in nessed bypeckeratosis of the nipple and areals. In addition, this is the line case to present immumulistochemical and T-cell gene marrangement studies of the immeridential lymphocytes. This case highlights a potential histopathological pittld. In the diagnosis of nevoid In perfectations of the mipule and areola-

Kraywsk: roycosis flangoides, urvoid hyperkeransis, pitfall, simulant

Rossum IS, Uepzer DM, Lind AG, Anadka MJ, Nevoid hyperherations of the arcela minimum averal as myconic finguides, J Comm Pathol 2012; 39: 516 - 548: @ 2012 John Wiley & Som A/8.

Hana S. Rosman¹⁺ Conna M. Hepper24 Anne C. Line2 and Millan J. Anadkat³

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Nevoid hyperkenassis of the nipple and areidais a rare benign condition with fewer than 70 cases reported in the literature. Nexcel hyperkeratosis presents as asymptomatic verruonus plaques on the nipples and/or areabse and is characterized histopathologically by hyperkeratosis, aranthosis, papillomorosis and beratin plugging or hyperteramsis.

We report a case of undateral newed hyperkerarcsis of the arcola with menerackerral lymphocytes that reasolided Pastrier's collections on nouroscopicexamination. To our knowledge, this is the third report of neycont languades like changes in nevoid hyperfernations of the nipple and accola, In addition, this case is the first to present immunohistochemical. andies of the introepidential lymphocytes and the results of T-ord grac massing-ment analysis.

Case report

A 43-year-old Caucasian worsen with no agrificant medical himney presented with a 4-year himney of thickening of the right arcohe like bad so history of freatment with oral contracepuves or other bornous agents. These years given, the area hadbeen biguist and diagnosed as myorair languides by dermatograthulogists at an outside haticurese. The ballor had tomalined stable over the aubsequent yours. with only octanional pruriers. Interestient treatment with a regical conficuencial was employed without benefit. She presented to our clinic for a second gracion prior in indergoing finites recomesa for mycosis firmoides.

On physical examination, as irregular verticens phagoe tracprovent on the right arcela with extension. of a velocity tan plaque beyond the nurgin of the arcola (fig. 1). There was no lymphoderopathy, and no other untimeous losions were ovident.

Two 4-mru punch biopines of the right meets were perkarried during her visit to our montetion. The findings from both showed similar features, including hyperkeratosis, popullarrasceis and acanthosis Fig. 7. There were occasional small aggregates of monomuckor cells within the epidermis, and the superficial derrors was schrede with gellare-uppearing fibroblasts (Figs. 3 and 4: A CD) immunohistochemical stain highlighted the rusuomutlear cells, including the endermal aggregates.

Demangathology 2015 2 61-66

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Case Studies

The Dilemma of Coexisting Nevoid Hyperkeratosis of the Nipple and Areola in Mycosis Fungoides: A Report of Three Cases

Algun Polat Bönci* Suie Ozturk Sari* Nesimi Buyukhabani* Can Baykal*

Departments of *Dermatology and Venerology and *Perhology, latential Medical faculty Istanbul University, Istanbul, Turkey

Key Words

Nevoid hyperkeratosis of the nipple and the areola - Mycosis fungoides.

Abstract

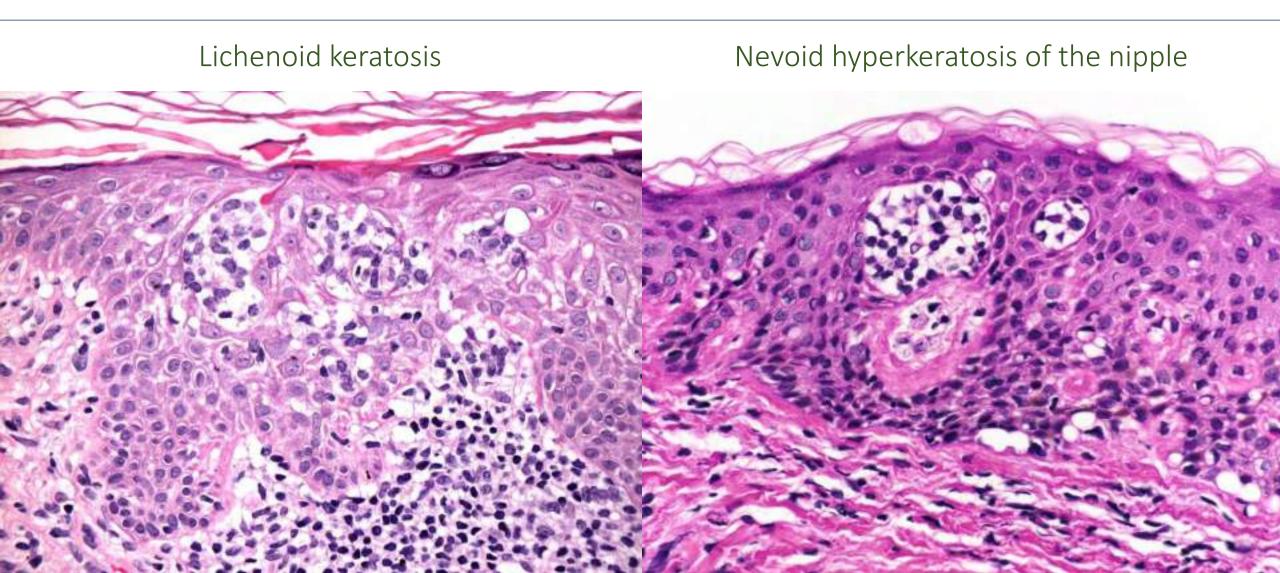
Nevoid hyperkeratosis of the nipple and areola (NHNA) is a rare clinicopathological entity. showing persistent and strictly localized hyperkeratotic lesions of the nipple, areala or both with unknown etiopathogenesis. A similar directal appearance may also be seen in different diseases with specific histopathological features. There are a few enecdotal reports on the association of NHNA with mycosis fungoides (MF), but they de not describe a uniform condition. In this report, we present 3 patients with hyperkeratotic lesions of the nipple and areola associated with MF but showing different histopathological features. We also review similar cases in the literature and discuss possibilities concerning this association. Two of our cases represent the association between MF and NHNA without histopathological features of MF on the nipple-ereola complex. The other case represents hyperkeratosis of the nipple and areals with specific histological and immunohistochemical features of MF. Hence, we would like to hypothesize that MF may implie the nipple and areola and have an appearance similar to NHNA. Intriguingly, however, NHNA may occasionally also be seen in association with MF. However, this peculiar association requires further explanation.

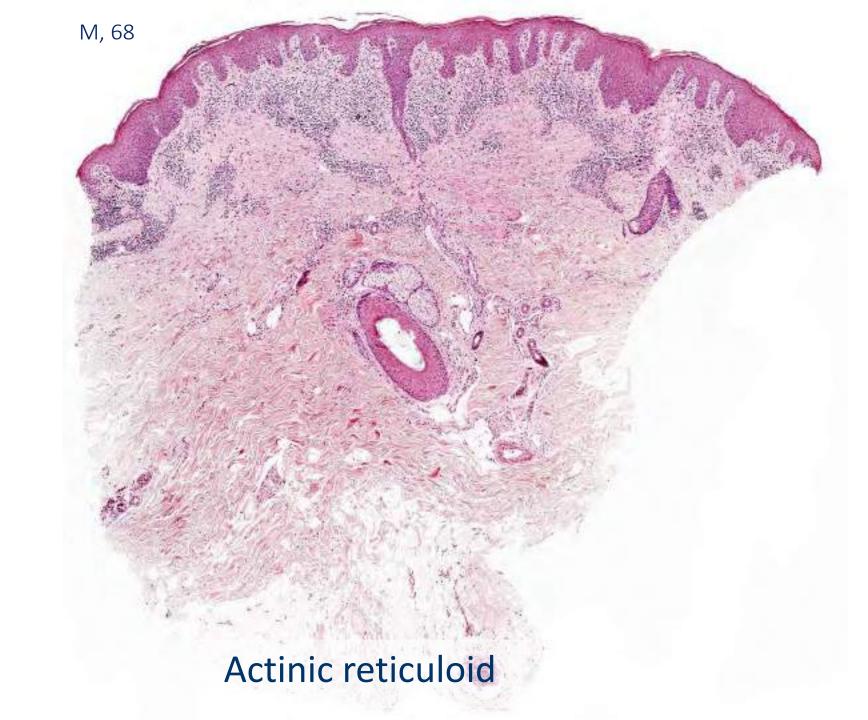
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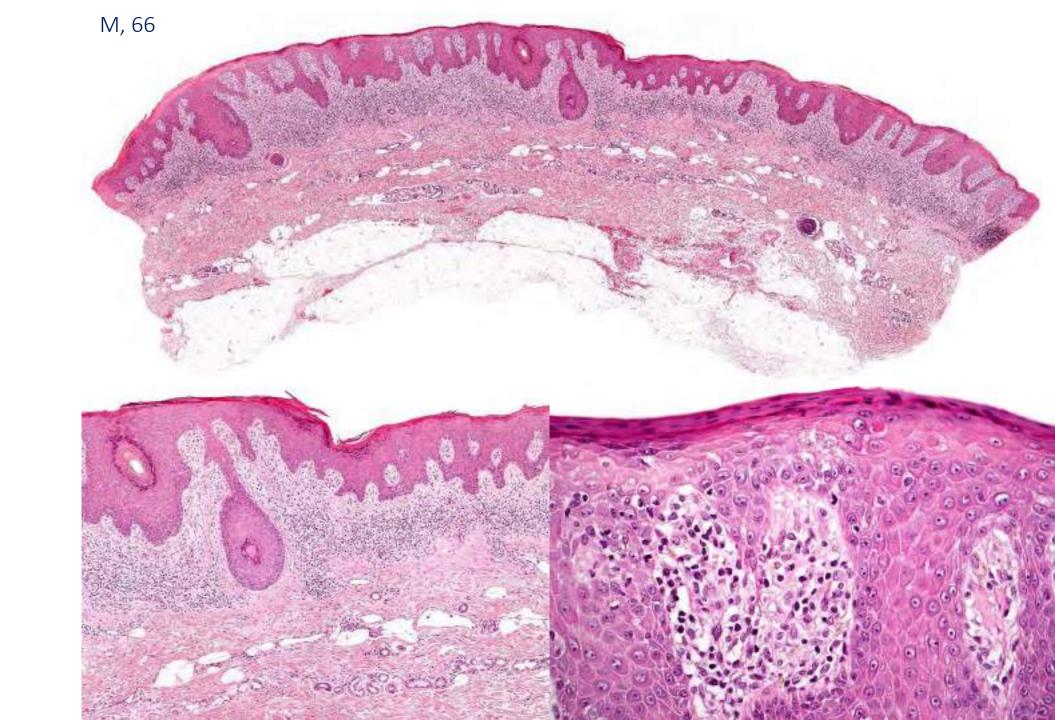
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Benign intraepidermal collections of lymphocytes ("pseudo"-Darier nests / Pautrier microabscesses)







Differentiation between actinic reticuloid and cutaneous T cell lymphoma by T cell receptor 7 gene rearrangement analysis and immunophenotyping

V. Bakoli, J.W. von Occaveer, A. H. Preesman, C.J.L. M. Meijer, R. Willeman

Abus-Differentiation between actinic reticulaid and cutaneous T cell lymphoma clinical picture is characterised by an occurrycan be extremely difficult. Demonstration of cloud T cell receptor (TCR) gene rearrungements has been suggested as a lexions spread to covered areas, leading to potential diagnostic orbanies, but the orytheodorna. This synhodomic version of results obtained than for have been one- action reticuled can resemble Steam sysflieding. This study investigated whether drone, a type of curascens T cell (purphorns TCRy gone rearrangement analysis, using Apart from crythrodorms, prunton, lymphadbination with decesturing gradient gal electrophorosis (DGGE) and immunohibtochemistry, can serve as a diagnostic cel-

Alwhode-PCRDGGE was performed on skin, peripheral blood monanuclear cells. and/or lymph nodes of seven patients with notinic reticuloid. 11 partients with Souncy syndrome, and 15 patients with a benign

Actual reticules dis a sewere, chronic phosesiensitivity disorder, that described by Ive." The tons, gratitic eraption, predominantly present on light exposed areas of slan. Frequently, polymerase chain reaction (PCR) in com- supports, and the presence of atypical hymphocens in the peripheral blood, patients with the enythrodormic form of activic neticuloid and putients with Sinary syndroms may also have alopecia, palmoplantar hyperkeratosis, or onychodystrophy.

Histologically, extract reticuleid is characterised by the presence of extensive derival infiltrants of readism soud lymphoid cells with conduitorm or convoluted audit. These cells form of erythrodorms. The results of they epidemetropism and sometimes even PCR/DGGE and Southern blot analysis of form Pannier-like microabcesses. There cel-TCR\$ gene rearrangements were com- lules and histological follows are also characpared. In addition, CD4:CD8 ratios in skin peristic for reposits fungoides, the most com-

Immunophenotypic analysis demonstrated increased proportions of CD8+ T cells in the skin in seven of seven cases of patients with actinic reticuloid.

Convenies Barpins CTLM Meter

Department of University Hospital. 1004 CX Usechi, Netherlandi A. H. Dieterrate

Consponental Dr Wilkston

Accepted the publication

analysis, in combination with immunohistochemistry, may be an important adjunct in differentiating between actinic reticaloid and cutaneous T cell lymphoms, in patients suspected of having notion reticulaid, application of both techniques is recommended.

CF Che Rule 1998,31.154-158.

Represents activic resentends T cell recovers grow reamangement; catacours T sell lymphonis: polymerase chain maccionidicantering gradiers gel-

Therefore, we investigated the presence of cionai T cell populations in skin, lymph noste and/or paripheral blood samples of patients with actinic reticuloid. Sexery syndrome, or a bengo form of erythroderms, by moins of polymense thain reaction (PCR) amplification. of the TCRy gene in combination with denumeing gradient get electrophoresu (DGGE). In addition, immunophenotypic analysis was performed on skin and peripheral blood samples to saints the proportions of CD4" and CD8" T cells.

Chronic Actinic Dermatitis/Actinic Reticuloid: A Clinicopathologic and Immunohistochemical Analysis of 37 Cases

Michael Ballropoulos, MD, MSc.* Janvana Deunicia, MD,* M. Extels Martines-Escala, MD,* Pedrom Gerami, MD,*† and Joan Guitari, MD*†

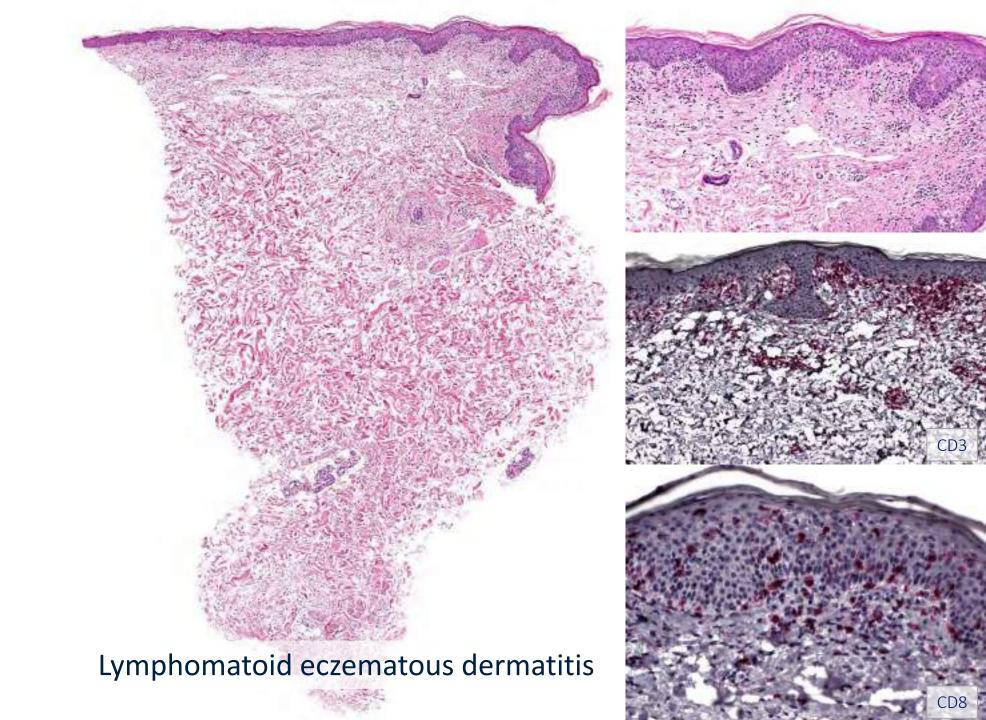
Characteristic	Total Sample (%)
Acanthosis	37/37 (100)
Spongiosis	37/37 (100)
Dermal lymphocytic infiltrate	37/37 (100)
Papillary dermal fibroplasias	37/37 (100)
Melanin-laden macrophages	37/37 (100)
Prominent stellate dermal dendrocytes	37/37 (100)
Multinucleated dendritic cells	35/37 (95)
Plasma cells	33/37 (89)
Eosinophils	33/37 (89)
Parakeratosis	31/37 (84)
Medium-large reactive lymphocytes	25/37 (68)
Follicular infundibulum spongiosis and exocytosis	18/27 (67)
Exocytosis	23/37 (62)
Solar elastosis	23/37 (62)
Superficial serous exudate	18/37 (49)
Pautrier-like microabscesses	13/37 (35)
Epidermal infiltrate	
CD8 ⁺	20/25 (80)
$CD4^+$	5/25 (20)
CD4:CD8 ratio	
<1:1	9/25 (36)
1:1	11/25 (44)
>1:1	5/25 (20)

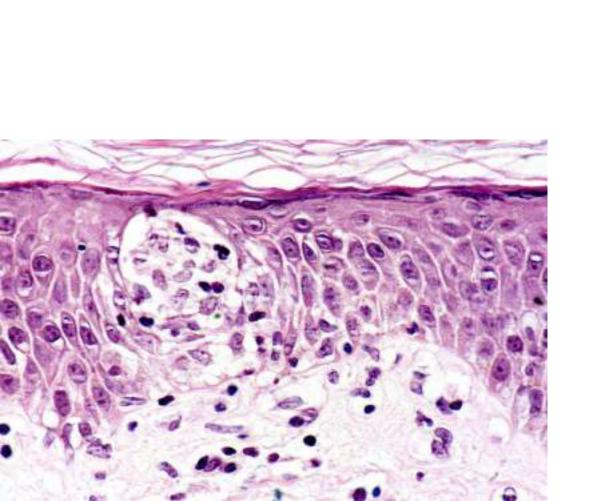
Am (Cennosopotivi + Valume 36; Number 11, November 2014

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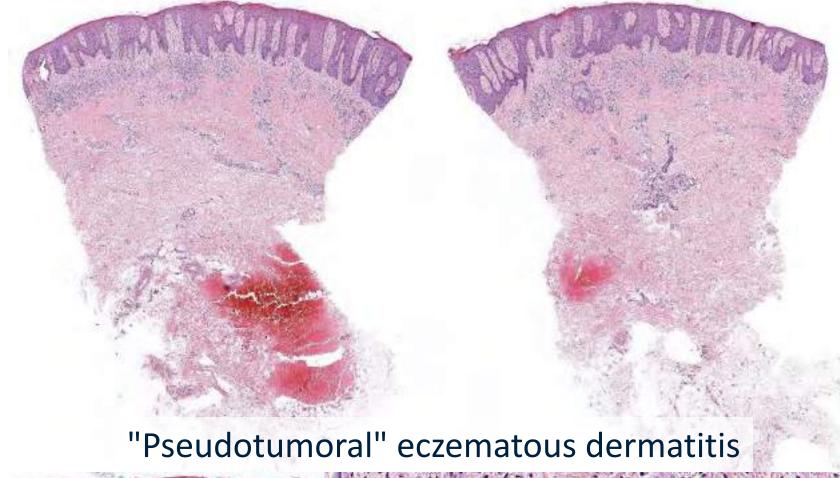
Actinic reticuloid

- Considered as a "prototypic" T-cell pseudolymphoma, yet most cases do not resemble histopathologically mycosis fungoides or other CTCLs (it may be indistinguishable from a chronic eczematous dermatitis)
- Clinically may become erythrodermic
- Hyperplastic epidermis with variable spongiosis, similar to lichen simplex chronicus
- "Bizarre" fibroblasts in the superficial dermis
- UV test necessary to confirm the diagnosis









M, 51 (Consultation Dr. T. Wiesner, Vienna)

Lymphomatoid contact dermatitis

A syndrome produced by epicutaneous hypersensitivity with clinical features and a histopathologic picture similar to that of mycosis fungoides

J. GÓMEZ ORBANEJA, L. IGLESIAS DIEZ, J. L. SÁNCHEZ LOZANO AND L. CONDE SALAZAR Hospital Clinico de San Carlos, Facultad de Medicina, Madrid 3, Spain

Four cases have been studied which were clinically suggestive of mycosis fungoides because of their infiltrated plaque-like lesions, but in which the suspicion of a topical hypersensitivity arose when a positive patch test was obtained with the striker part of a box of matches.

Key words: contact dermatitis - mycosis fungoides.

Received for publication October 30, 1975

We have had occasion to observe several cases which could be interpreted clinically, from the morphological character and persistence of the lesions, as a form of xanthoerythrodermia perstans or parapsoriasisen-plaques; with their complaint of intense pruritus they were reminiscent of mycosis fungoides. Several cases were histologically diagnosed as such. We consider it important to report these cases because they are caused by a hypersensitivity reaction.

Case histories

Case 1. A 54-year-old male had noticed a dry, pruritic erythematous plaque about the size of the palm of his hand on his right thigh about four months earlier. The plaque grew progressively in area and in depth. Some time later, a similar lesion appeared on his left thigh. The first lesion appeared in August 1973. During the ensuing months, there arose multiple erythematous, oedematous, ill-defined lesions all over the face,

retroauricular areas and the sides of the neck. Their course was one of remissions and exacerbations. Topical treatment with corticosteroids did not produce any improvement. Later, he developed another lesion on the left pectoral area. Examination showed on both thighs two plaque-like lesions, about 10 cm wide, which were erythematous, scaly, intensely infiltrated and with well-defined borders. Violaceous erythematous, scaly infiltrated plaques were also found on the face, behind the ears and on the neck. There was another plaque, the size of the palm of a hand, on the left pectoral region; it had the same features as the others. Multiple biopsies were obtained which showed a dense infiltrate, band-like with histiocytes, lymphocytes and some eosinophils. There was lymphocytic exocytosis, sometimes forming nests and in some areas, limited spongiosis. The histologic picture and its clinical counterpart were like that of infiltrated mycosis fungoides.



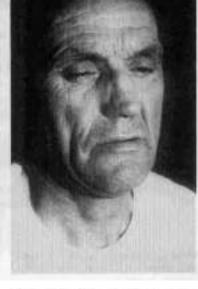


Fig. L. A and B. Thigh and face lesions

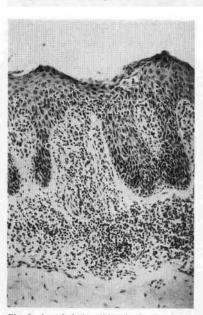


Fig. 2. Acantholytic epidermis. In the dermis there is a dense infiltrate in the form of a superficial band.

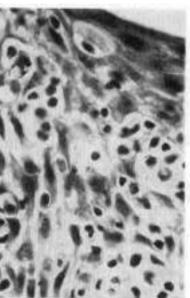


Fig. 3. Lymphocytic exocytonic sometimes forming nests, and limited spongiesis.

In my experience not restricted to contact dermatitis; may be observed in any "eczematous" dermatitis, including atopic dermatitis, xerosis cutis, and lichen simplex chronicus among others.

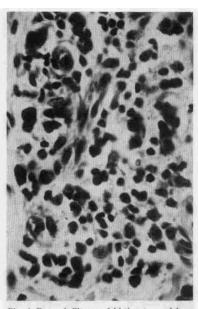
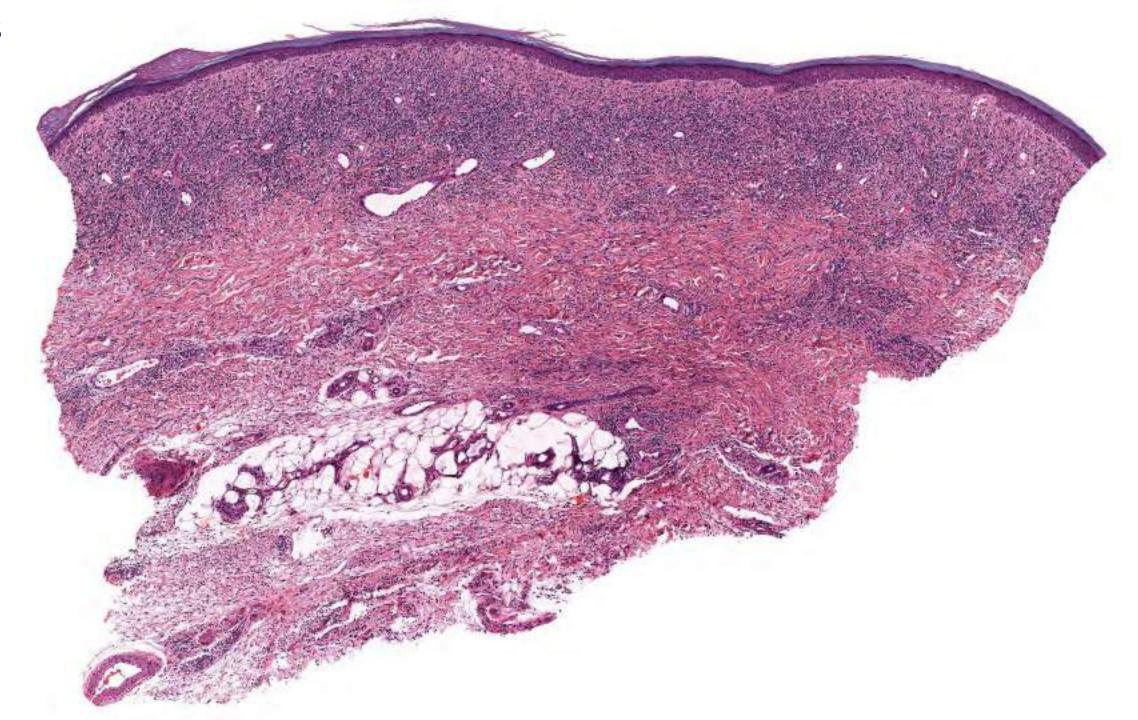


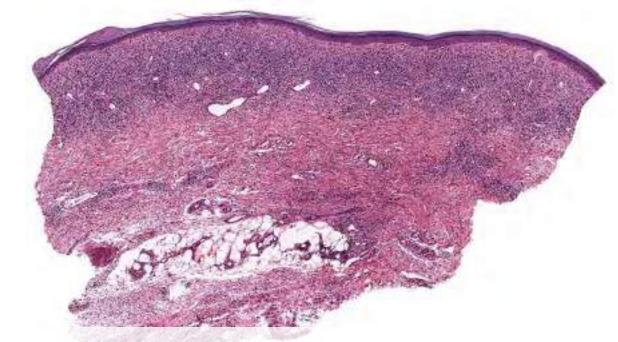
Fig. 4. Dense infiltrate of histiocytes and lymphocytes, some of which are hyperchromatic.

Lymphomatoid eczematous dermatitis

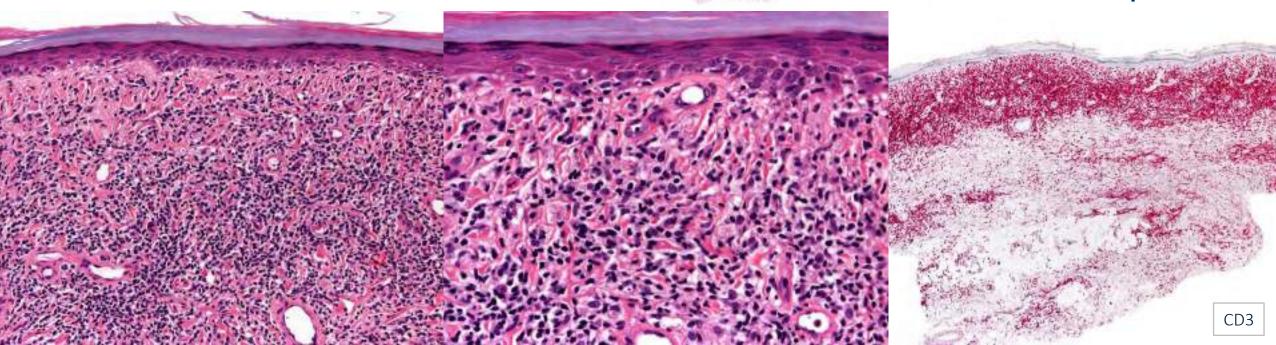
- Not restricted to contact dermatitis; can be observed in different types of "eczema" including atopic dermatitis
- Band-like lymphoid infiltrates with some epidermotropic lymphocytes
- Spongiosis variable (minimal in chronic eczematous dermatitis)
- Clinically may present with "pseudotumoral" lesions
- Correlation with the clinical picture allows to classify cases correctly in the vast majority of cases

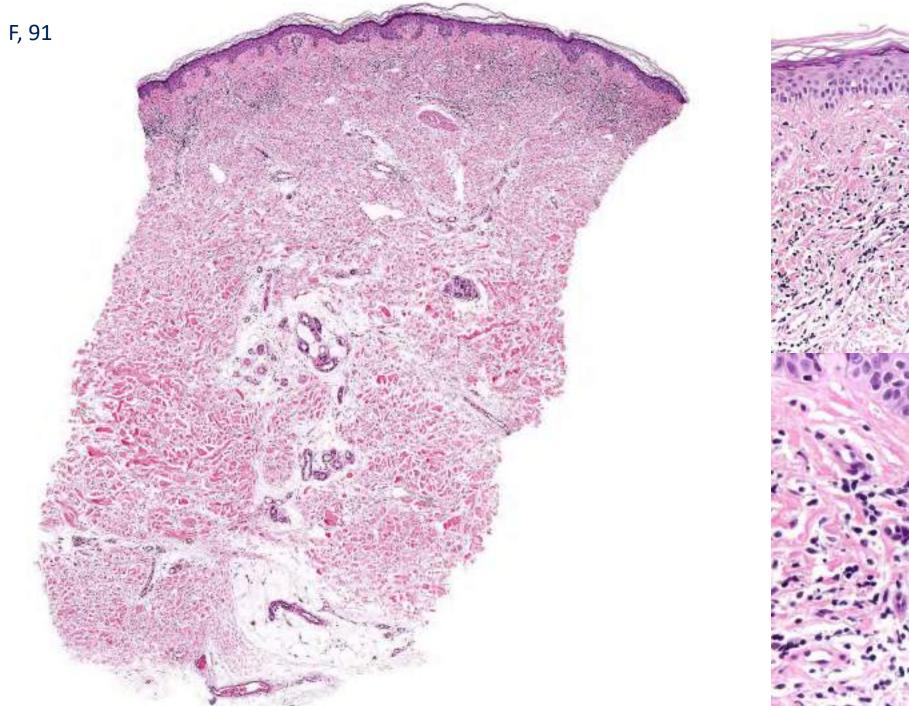
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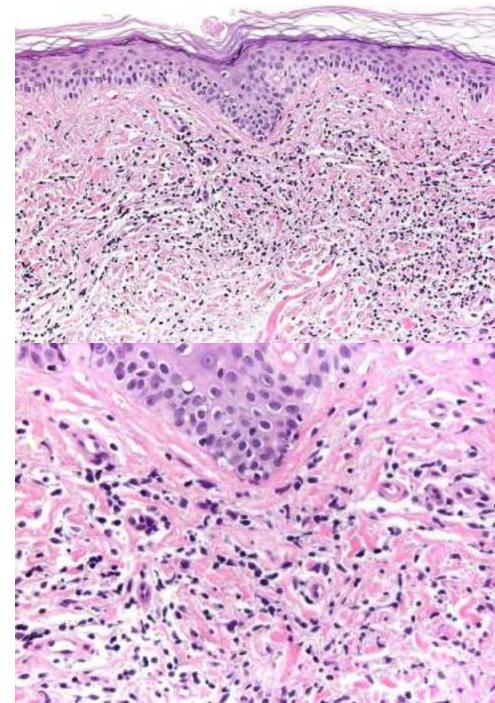


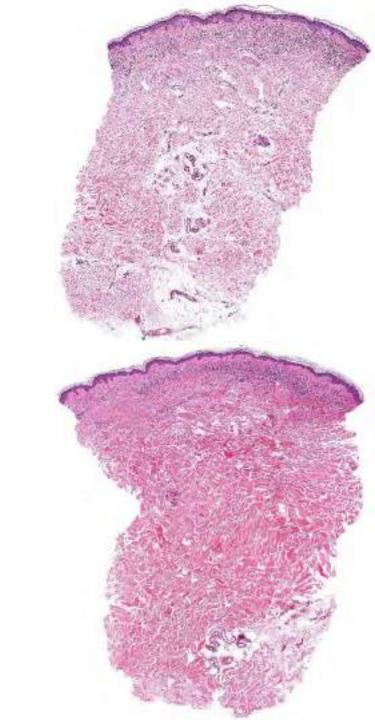


Acrodermatitis chronica atrophicans









Acrodermatitis chronica atrophicans

Pseudolymphomatous ACA

- Acral sites (particularly leg, foot); usually asymmetrical distribution; may simulate histopathologically either MF or MZL
- Dense inflammatory infiltrates; frequent band-like arrangement
- T lymphocytes predominate in some cases; plasma cells reveal a polyclonal pattern
- Positive Borrelia serology; PCR positive for Borrelia
- Resolution with antibiotic treatment

ORIGINAL STUDY

Acrodermatitis Chronica Atrophicans With Pseudolymphomatous Infiltrates

Shang-law Tee, MRCP, ** Marrola Martinez-Eucanamé, MD, * Daniel Zuriel, MD, ** Isahella Fried, MD, * Ingrid Wolf, MD.* Cesave Massave, MD.* and Lorenzo Cerroni, MD*

Abstract: In this study, we describe the Unicopulating a retimes of pseudohorphorostom infiltrates. Avail within lesions of nenefermatits classics strophoess (ACA). We studied 11 posterio (10 femdes, 1 units, age major (0. 85 years). The diagraphy of ACAs. in all cases was cardioned by divisoral to logic correlation and postive seedings for flowerie. Histopathickops exentination seveded prominent possibly applymentous inflammatory cell infligence in all uses, with 2 district patterns. Highland 11 uses showed a hand-like lymphocytic militrate, encourage of lymphacrine and a filtural papillary demis, similar to fintures seen in mycons financides. The other 3 mass showed dense, socials -diffuse demail infiltrates with many plants cells and witness germant covers. The phones cells expressed both supported basishs compossibilities high chains with is polyclosul pattern in all 5 cases. In conclusion, ACA trass present with pseudok rephorestons infiltrates absorbing both a #-cell and, how forwards, a th-cell prises. These leakes post to be disregulated Tokic a crimacous hosphoina. In the context of the importedge of Recyflassociated patenness lymphomes. followers seems odvisolde in these ones.

Key Words: saidcrastiff chronics thoplocus, perudolympiorus, Borrella.

LAY J. Germanyorkel 2017;25:118-542)

INTRODUCTION

Acrodementals chronic atmobients (ACA) is a late cutaneous runifestation of infection by Noverla aftern.' It rypically affects elderly resence, assurily involving the dorsal surfaces of acral sites. After an initial inflamentatory phase characterized by edemenus swelling and blash-red discolorstion, tie den becomes strephic, dry, and wrinkled with prominent telengictissus, domal sciencis, and lose of appendigged structures. The dispressic evaluation of surpected cases commonly includes a himogethological commotion. Characteristic histopothologic abstracts of ACA melade. (T) a superficial and deep, perivoscular, and investigat decand

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inflammatory willtrate composed of lymphocytes, histocytes and plasms crits. (2) strophic drems with reduction in size and number of rangual structures. On thinning of the epiderturn with flattered sets ridges, (4) variable dermal aderga-

Rarely, preminent demial tymphoid infiltross may be present within lesious of ACA, which may minute a cursoeous emphoria. In this study, we present the eliminopathologic features of 11 cause of ACA with pseudolymphometric addresses.

PATIENTS AND METHODS

Patients

We proposed the disablese of the Research Unit Demotorathology, Department of Demotology, Medical University of Graz for cases of ACA containing dense simpleste infiltrates to all cases, the dequasts of ACA was conferred climeally and by postave serology for Borvela. We excluded cases in which hotopathological specimens were inodegone, or in which complete chimal influention was apprailable.

Histopathology

All apsenters were fixed in 4% buffered formalin, municity processed and ambuilded in paraffin. Sections were subsequently stained with bemorehylm and occan for restrict histoporthologic trialesis.

Immunohistology

Immusohistidogy was performed to 4 cases on retufirsts fixed, paraffin-embedded visige sections amorting to a previously described 3-step immunoperoxiduse technique." The pore) of monoclosed are bodies included the following marken: CDS (Newseastra, clone PS), althoug 1:100), CD4 (Novecasire, close 3F6, climion 1:30), CD8 (Dako, Dakopatts, close C8/144b, difution 1/25), CDM (Dako, Dukopatts, clone 1.2% dilution 1:500), kappo and lambda light chains thosh Diko, Dukoperis, clones R10/2-13 and N10/2, respectively, diluter 1 deep in 500 at 1. Hopey specimens of torsid tosas were used as positive controls. Negative controls were obtained by smitting the primary anabody or updating it with populai bungo serum. Hen-indoced antiper unrieval was perforward for all the untibudies.

Molecular Biology

In I cases, analysis of Boyellis DNA was performed by polymensus whate marries (ICR) with stooded methods.

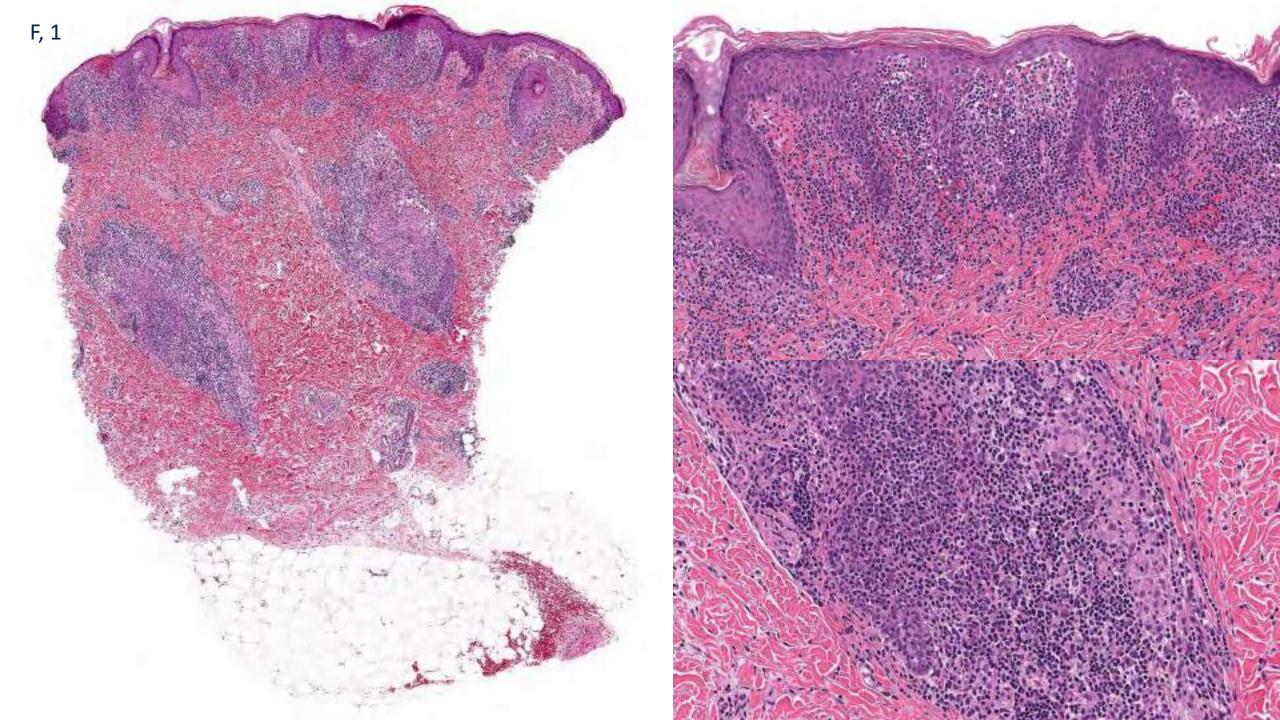
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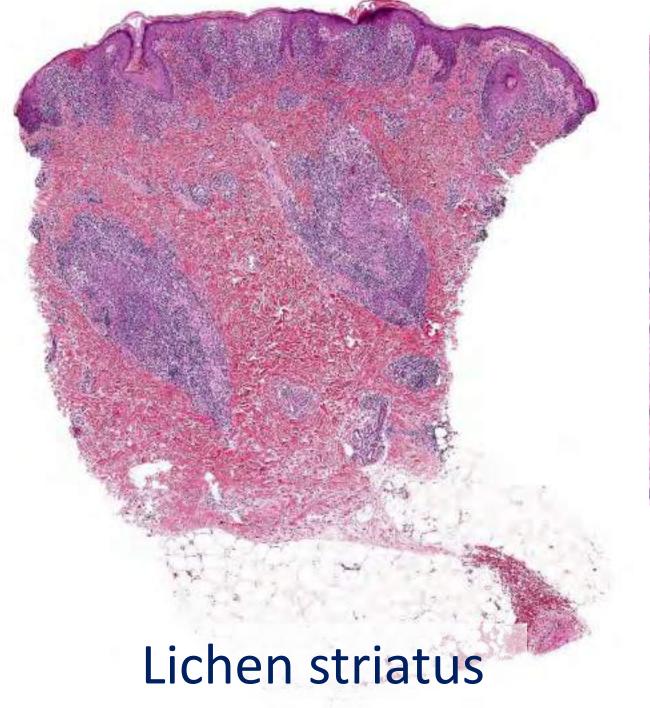
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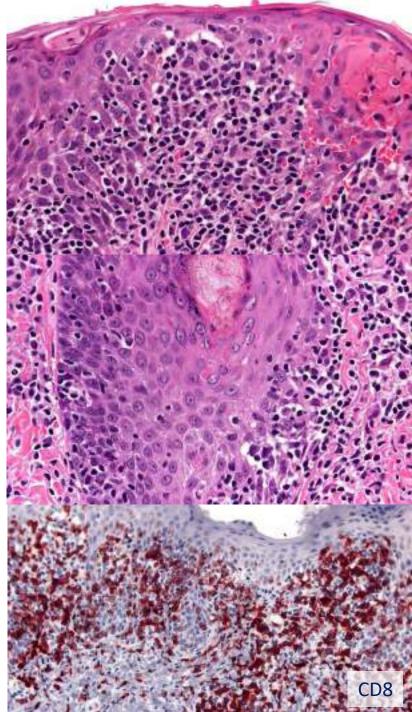
TABLE 1. Clinical Data of the Patients and Histopathologic Pattern

No	Sex, Age (yrs)	Location	Histological Pattern	Borrelia PCR	Borrelia Serology	Follow-up (Time)
1	F, 70	Foot	Band-like	ND	IgG and IgM	NA
2	F, 68	Foot	Band-like	Positive	IgG and IgM	CR (2 mos)
3	F, 64	Foot	Band-like	ND	IgG and IgM	CR (13 yrs)
4	F, 68	Leg	Band-like	ND	IgG and IgM	CR (8 mos)
5	F, 77	Leg	Superficial and deep, diffuse with plasma cells	Positive	IgG and IgM	CR (8 yrs)
6	F, 60	Leg	Band-like	ND	IgG and IgM	CR (8 yrs)
7	M, 88	Hand	Band-like	ND	IgG and IgM	NA
8	F, 60	Hand	Superficial and deep, diffuse with plasma cells	ND	IgG and IgM	CR (22 yrs)
9	F, 77	Leg	Band-like	Positive	IgG	Almost CR (16 mos
10	F, 61	Leg	Band-like	ND	IgG and IgM	CR (2 mos)
11	F , 74	Leg	Superficial and deep, diffuse with plasma cells	ND	IgG and IgM	CR (2 mos)

CR, complete remission; F, female; M, male; NA, not available; ND, not done; PR, partial remission.







Correspondence Clincal Letter

Correspondence

Lichen striatus mit histopathologischer Imitation einer Mycosis fungoides

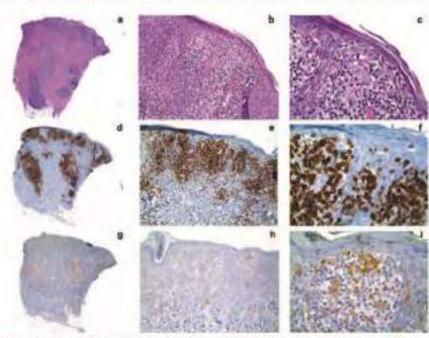
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Abbridung : Die Bropse zeigt ein bandfürmiges lymphocytikes infiltrat in der oberen Dermis und ein dichtes perifolikuläres. hymphorystères infiltrat in der mittlieren und tiefen Bermei (HBC), as ab (a) werdickte Epidermis mit deutlicher lymphorystères Except use und Vesikelbildung geloppett mit einem bandförmigen lymphosytären Inflit at in der papillären Dermit 846 E. Houk (B); deaths by Tymphocytare Exceptore and Minne Westerl (MicE, 2007) (C) terminal around the CD3 weight due Ober weigen von TZellen (CDs, as codif), trandiferringes subepolerondes infritrativa, aux T-Zellen (CDs, aso si es), destriche Exprytose von T Zellen (CD₂, 200 x) (f); incounfilrbung für CD is anglening Langerban). Zellen (g. CD is, 15 x; h. CD is, 100 x) (g. h); ninige Langerhars-Zeffen in epidermaler Veskelt (CD1a, 100.i) (i).



Approchang a traphogen Marchen mit er othernstöven Papela an Inewer Ausbreitung (a); Detail arcicht der Efflores aurgem (b).

CDB7 segative Zellen auf. Die vorlaufige Diagnose einer Automor lyarphage all heats wer. Extransioner, our Verdaulis and Mescus fungoldai (MF) woode savaills, and die Histwirdigheit einer engen Konnelation mit der Anarmees und dem klimarkin Rischmungstald der Linionen warde im histolognoben liefendbenehr betont.

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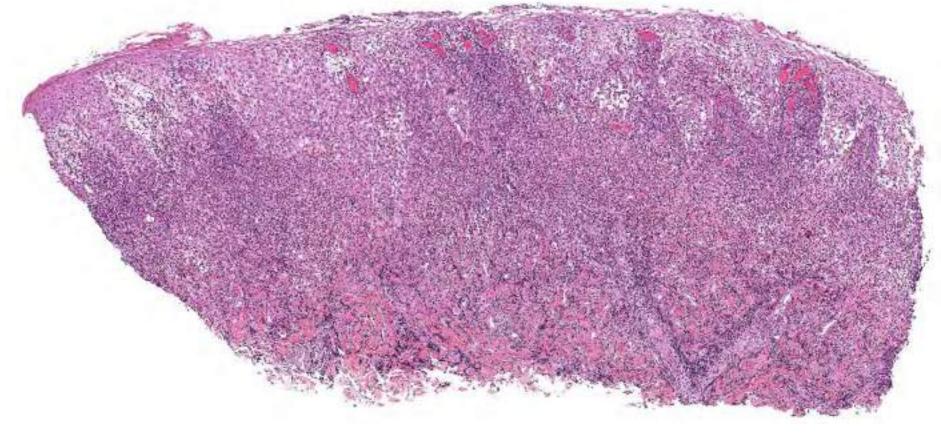
Diskussion

Li at one reftere reflationirerede entradido Enco-Yong vorwiegend der Arme, Beine und Schaltern, die vorallen hei Kindern auftrich [L. 2]. Ublicherweise zeigen nich multiple ment asymptomatische Papele, die lineur entlang. der Blanchko Linten angewichet und [3]. Die ereinen Falleheden raconn innerhalt weater Minute, einige Palle mit Johns, beyor an abholes [4].

gen, die den Blaschko-Linies folgen, wie Procings, Ispor erytherasocies and Mosphes, unterstander laters with, Beraht die Diagnose in der Regel auf dem Edunchen Februd [5]. Trocaten kare, in unblaven faller size Harrimone etforteilth sen. Der hittelogarike Befund ist normalerweise eacht georgekrafts; und neigt handformige entrandliche lympion and krimograine infilmate to der papillates Deresti mit sudermaler Alexathese, Baraker atons and lymphorytaust Broarwinge III. Day Infilities of order University lend dicht and um the skiennen Driven und Gefode berum veronit. Kleine intraspidernale Vesikel, die Lymphoryten und Lanserbara Zellen enthalten, konnen verhanden sein. Gelegenthich unsthapper the hotopathologochen Estoads not denen bei Lichen nitidun, Lichen plannt, Lichen aufern, führenolden Armennmelexurthenes oder ME. Bei Kindens neut die ME hijafiger hygopigmestierte oder hitymann lichmoides-ahnlithe Laurence, kinn ther selen auth alt inester Exarthen auftrette [6-8]. MF ist histograthologisch durch ein insolformiges Belifica in dat papillates Decres gelomatechast. welcker san moromorphes, brougholder Zeiler, ammorbiedliden Atenappalas bestalt. Oftende demineras en Iraber MF kleine Lyaqdooyum, and anyonder Zellen treton releas auf 161. Ein Egetennotropamus der Lymphopster kann in verschiederen Formen auftreten, auch mit ertlang der Busalmembreu aufgereiten Lemphiczsten und der Eildung von Danmar Mikrothepenen [8], Die neoplastischen Lympkour ten ber MF beigen normaler weise amen CD3+, CD4+, CD6prolongierre: Aktivitätigkate perintieren für zwei bir den Päänntyp [6]. Ein Verlast der pan-T-Zell-Market-Skyprettion Fami manchmal probaction worden, in his fraiser 1837 (edoch-Obvohí die Eskumbrug sick klimock sherbick von li- och; sehra (6), Bestuden un Kindesshie kommer jedoch assem Nan ode chromoth-entanglisher Hosteti makur- karfig CD4+ protomache TZellen vor (s. 2). Ba uniene

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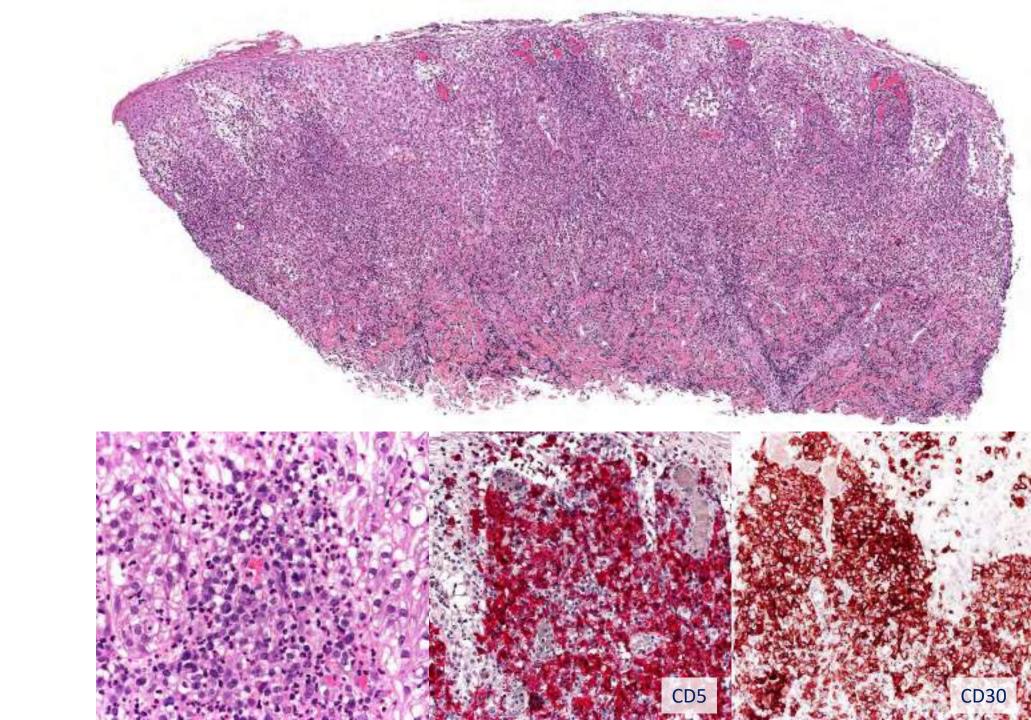
- A prototypic example of the "linear dermatoses"
- Psoriasiform epidermal hyperplasia and variably dense lichenoid infiltrate, involving the deep dermis growing along the adnexal structures
- Epitheliotropism may be prominent
- Phenotype not studied in detail; some cases are positive for CD8



Cutaneous anaplastic large cell lymphoma

Solitary lesions (rarely grouped), mostly ulcerated. Spontaneous regression (mostly partial) common. A clinical presentation with extensive involvement of one lower extremity has a worse prognosis (extensive limb disease)

Mixed infiltrate with predominance of CD30+ T-lymphocytes (>70% of the infiltrate). Common intralymphatic complexes of neoplastic cells. Phenotypic aberrations common. Rearrangement of the *DUSP22* locus at 6p25.3 occurs in 20-25% of C-ALCL. The t(2;5) chromosomal translocation is absent in most cutaneous cases. Indolent behavior, excellent prognosis.



Chromosomal Rearrangements of 6p25,3 Define a New Subtype of Lymphomatoid Papulosis

Lords J. Kone, MSP 5 Mordelf E. Barles, 2002 Day A. Day 3000 Appea C. Strovett, 4002 Short F. Roscolini, MYS. Joint A. Zantion SS, Carp. States L. Faldman, MSW

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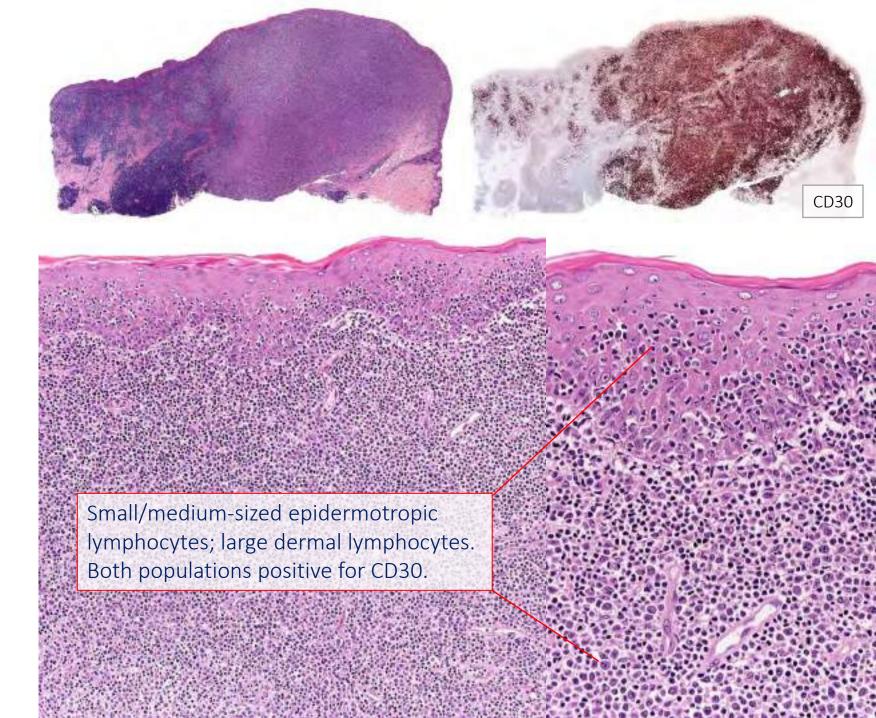
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11 patients (M:F = 9:2; age: 67 to 88 y)

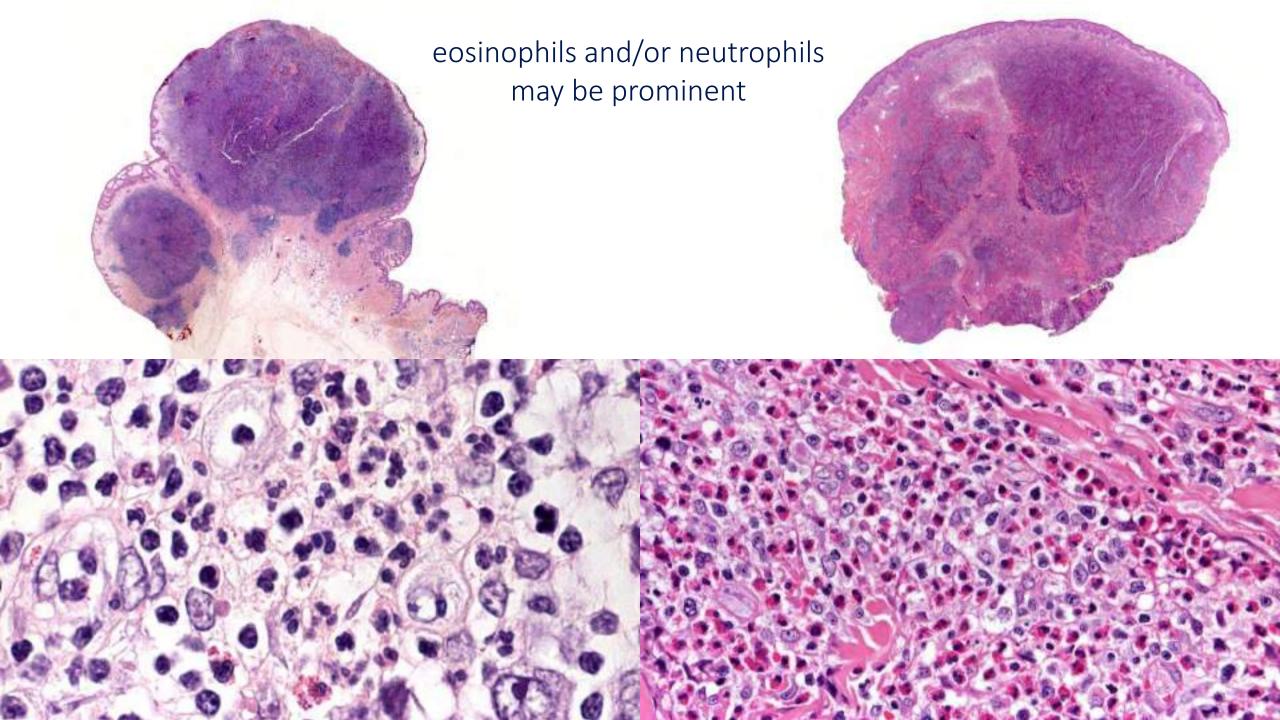
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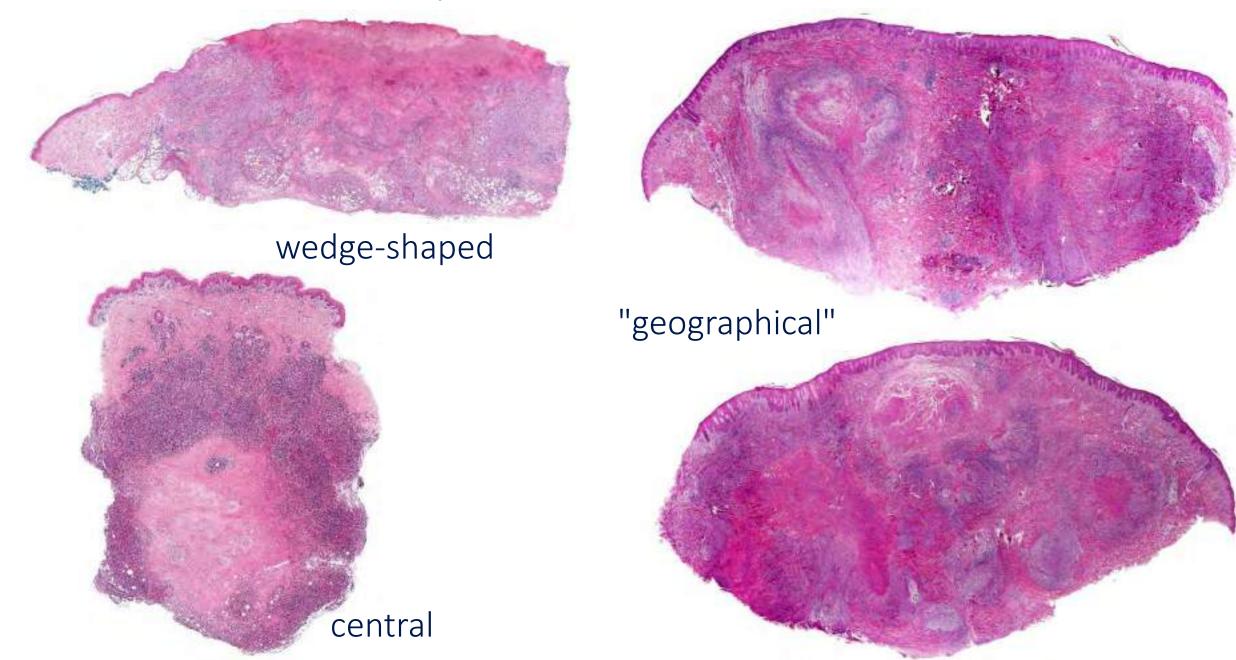
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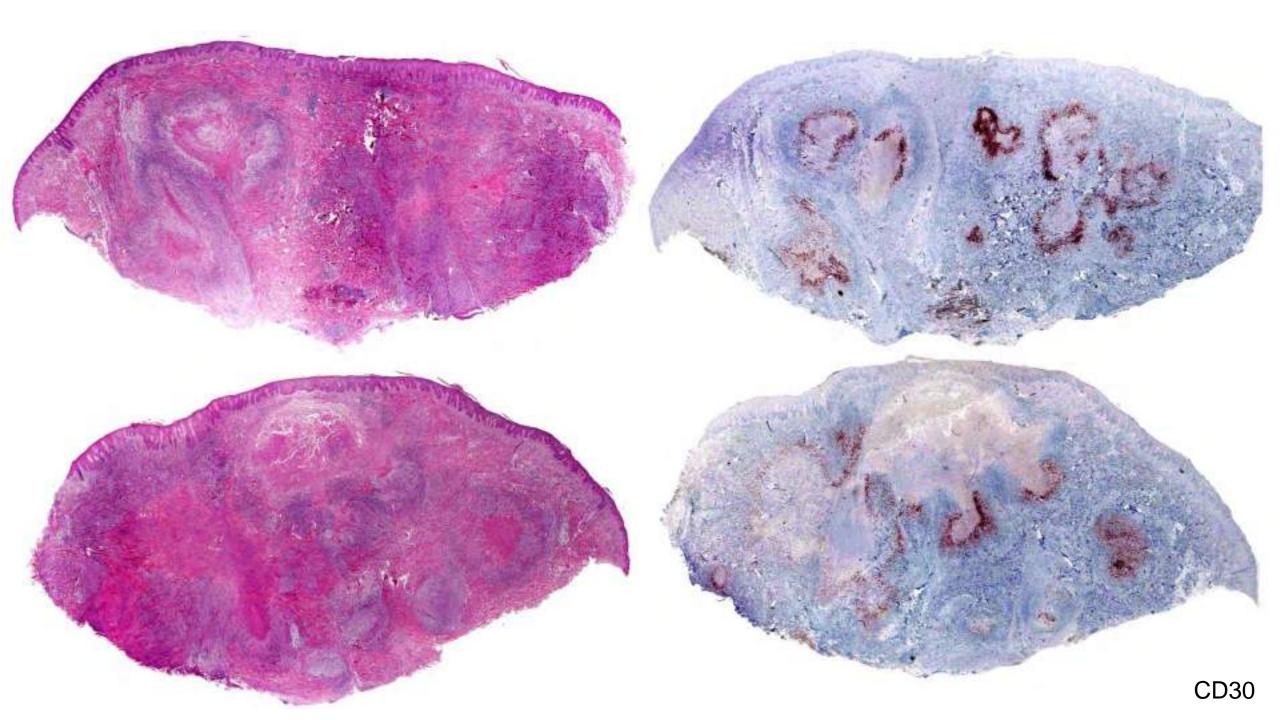


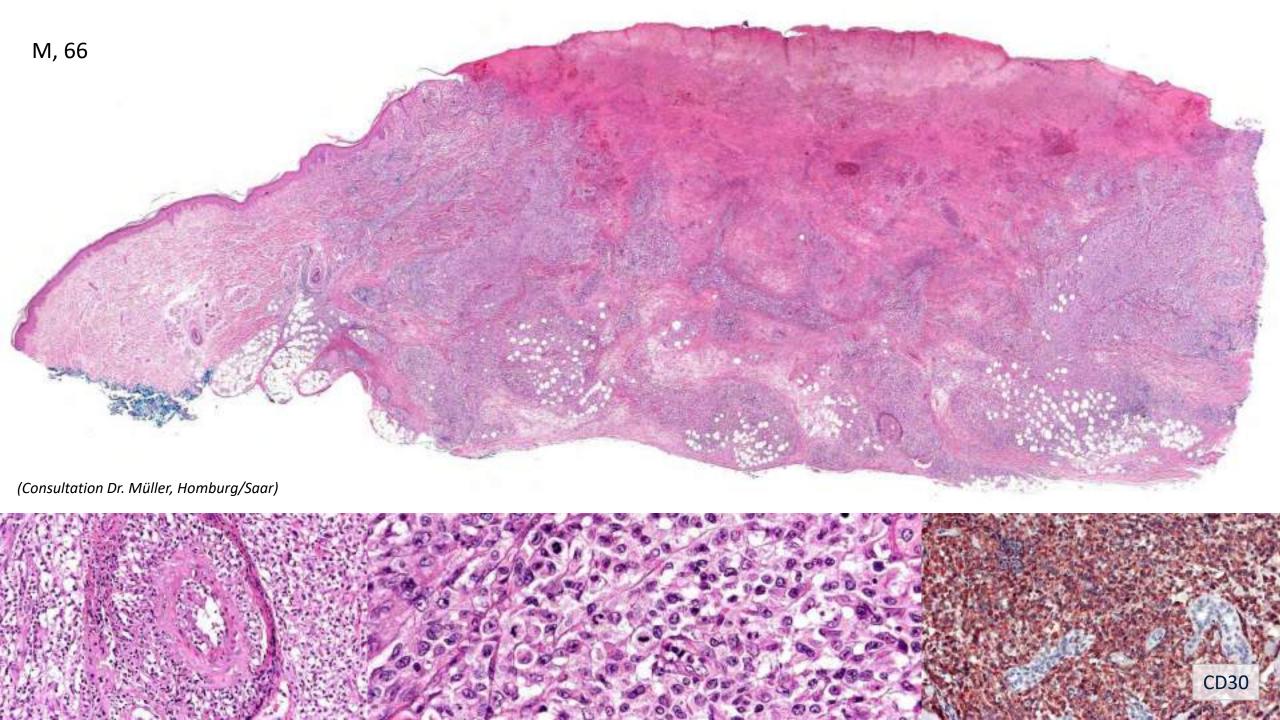
Histological pattern of rearrangement of the *DUSP22* locus at 6p25.3



Different patterns of necrosis in cALCL







The morphologic spectrum of primary cutaneous anaplastic large T-cell lymphoma: a histopathologic study on 66 biopsy specimens from 47 patients with report of rare variants

Background: Primary cutmeous anaplastic large T-tell lymphoma PCALCL is a well-defined entity with prognostic differences from the notal counterpart fineful anaplastic large cell lymphoma (NALCL). Several hisological variants of NALCL, have been characterized sommon, lymphohistocytic and small cell). However, audies on morphological variants of PCALCLs are lacking.

Methods: We analyzed retrospectively the elisticopathologic features of 66 biopsies from 47 patients (M.; F = 27: 20; median age: 53 years; mean age: 51.8 years; range: 14: 02) with PCALCL, in order to better characterize the spectrum of this unusual neoplasm.

Results: The 'common variant' was the most frequent (40.4%). In contrast to NALCL, in PCALCL, marked reactive infiltrates are more commonly present. In fact, 25 cases were classified as 'inflammatory type' (15 cases) and 'tempholistic-cytic' (13 cases). Concerning the predominant cell morphology, large anaplastic cells (33%) were almost as frequent as large phomorphic (36%) and small to medium-sized cells (26%). We reported for the first time in the skin 2 rare cases with the predominance of large cells with a 'tigner-ring-like appearance. Epidemnotropism and presence of cosmophils were found in a proportion of cases in all PCALCL variants.

Conclusions: PCALCL is characterized by variable histopathological presentations and a broad cytomorphologic spectrum.

Masone C, El-Shahrawi-Cuelen L, Kert H, Cerroni L, The morphologic spectrum of primary cutaneous anaplastic large T-rell lymphoma: a hisospathologic study on 66 biopsy specimens from 17 patients with report of rare variation.

Cotan Pathol 2008; 35: 46-53. © Blackwell Muniogrand 2007.

Cesare Massone, Laila El-Shabrawi-Caelen, Helaut Kerl and Lorenzo Cerroni

Department of Dornstology, Research Unit of Demotopathology, Medical University of Snat. Grat. Austria

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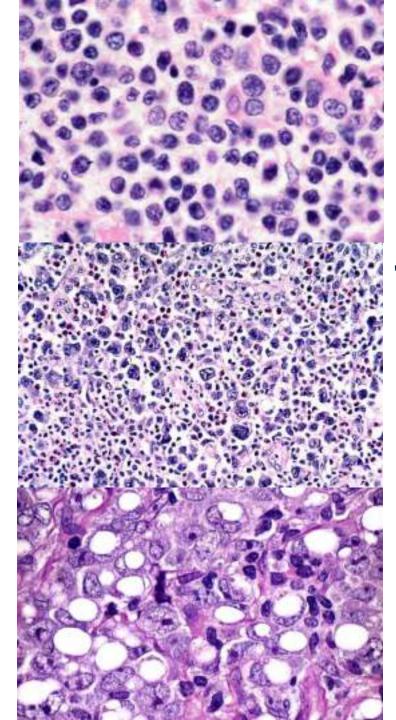
Tel: +40-016-360-0403 Fax: +40-616-360-0468

HIRE TOYOU, ONTO YORK PROJECT

Accepted for publication Mech 7, 2007

Primary curaneous anaplastic large T-cell lymphona PCALCL₂ is a well-defined entity with prognostic and foological differences from the modal counterpart.^{1,2} In fact, cases arising in the lymph nodes and the skin are classified into separate groups

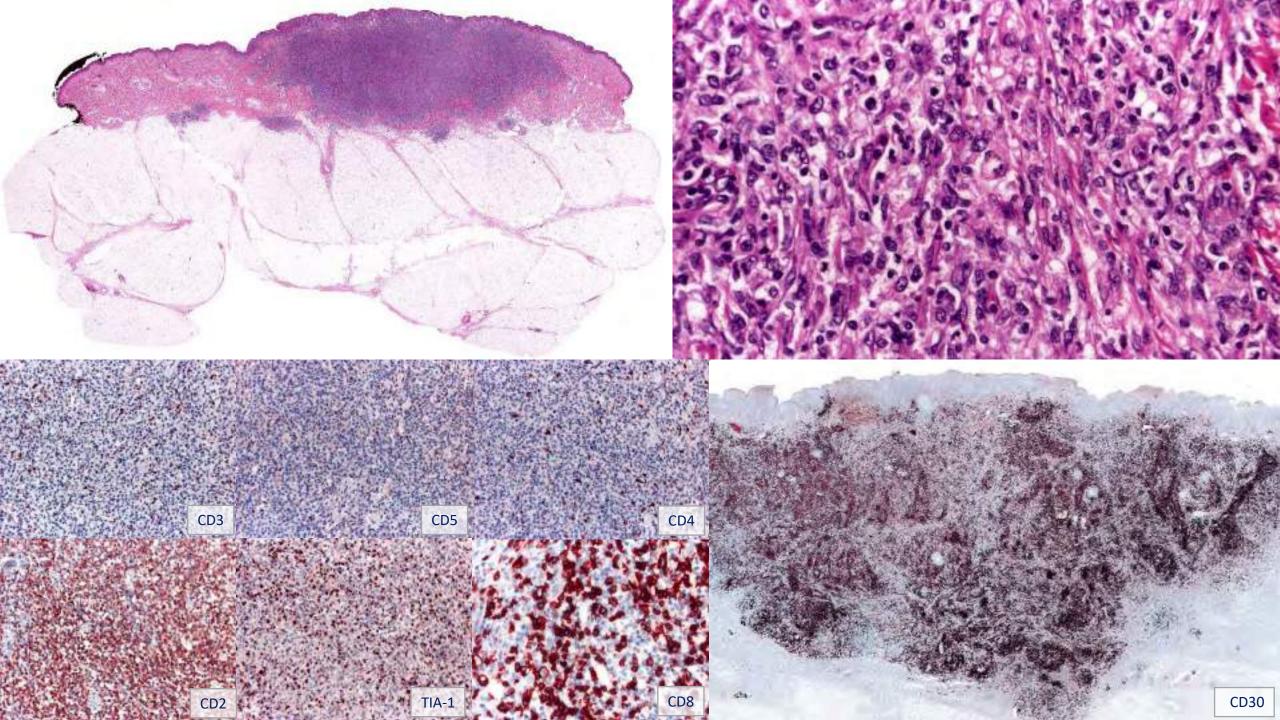
in the World Health Organization (WHO) classifiration for hematopoietic neophams.² In spite of prognostic differences, PCALGL and nodal anaplastic large cell temphorus (NALGL) are morphologically identical and cannot be distinguished based on



small cell type

"inflammatory" type

signet ring cell type



Phenotypic Variability in Primary Cutaneous Anaplastic Large T-cell Lymphoma: A Study on 35 Patients

Cerare Massone, MD and Lorenzo Cerroni, MD

Abstract: Princey concerns amplicis: bage T-cell lynghous (pcALCL) is a well-defined entry characterized by reoplastic cells expressing CD90, CD2, CD3, CD4, and CD9. Cases with different phenotype have been reported, including variable loss of CD2, CD3, and CDS, and expression of cyrotoxic phenotype (CDF) and/or of cylotoxic proteins. Aburunt phenotypes represent a stagnostic pitfall and may be the cause of misdiagnoses. We seviewed 35 cases of pcALCL (MF = 19:16; musn age, 50.8 stars; range, 14-92 years). to better classification the intrinsipples otypic spectrum of the docuse. Twelve cases (34%) had a T-helper phenotype (CD4+CD8+), and TIA-T was preciou in 5 of 8 stained cases. Six macs (18%) hall is T-eylotoxic phenotype (CD4" CD0') and were also prointed by TIA-1. Positivity for both CD4 and CD8 was observed in 7 ceses (20%), 4 of which were stained for TIA-1 and found to be positive. wherea both CB4 and CB8 were regative in 9 cases (26%, only 15% tested cases being TIA-1 positives CDZ was positive in 21 of 27 toxid. cases (1976), CDH in 21 of 34 cases (62%), and CDD in 13 of 31 cases 648%. Interestingly, 11 cases (31%) showed a perfoundly aberrunphenotype lacking virtalitationally arrigoil T-cell starkers. Our data allow a better characterization of pcALCL with abertant phenotypes, showing the remarkable variability in expression of different

Key Words: primary estateous ampliante large T-cell lymphoma. CD00' sutmour imphorolikutive dissolute autoreus Tselllymphoma, immunophimotype

Gin J Dermanyiohol 2014;36:153-1571

INTRODUCTION

Primary cataneous amplastic large T-cell lymphoma (peALCL) is a well-defined entity with prognostic and biological differences from the nodal counterpart. It is murally characterized by large cells with anaplastic, pleomorphic, or immunoblastic morphology, but several histopathologic variants have been described." Neutrophils ("inflammatory-type" patient), lymphocytes ("lymphohistiocytic" pattern), or even eosinophils can predominate in the infiltrate, and cases with small- to medium-sized rells ("small-cell" patient) or signetring cell morphology have also been reported. 45

Am / Domutopathol + Volume 36, Number 2, February 2014

Reprints Loomus Corner, 20D. Department of Demantings, Medical

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Neoplastic cells in conventional cases of peALCL express CD30 and CD2, CD3, CD4, and CD5 (T-helper phenotype), and are negative for CD8, CD56, and extotoxic proteins." Cases with different phototype have been reported, including variable liss of the T-cell markers CD2, CD3, and CD5, and expression of extotoxic phenotype (CD8') and/or of cytotoxic proteins (gransyme H, TIA-1, perform), 1-10-11 Abernut phenotypes represent a diagnostic pitfall and may be the cause of misdagnoses. Although pcALCL is traditionally considered us a lymphoma of T-helper lymphocytes, the exact proportion of cases with ahemost plenotype is unknown. In this study, we analyzed the clinicopathologic and immunophenotypic features of 35 patients with pcALCL, to better chametenze the immanophenotypic spectrum of this cutaneous lymphonsa.

MATERIALS AND METHODS

From a total of 114 cases of peALCL documented in the lymphoma database of the Research Unit of Dermstopathology, Department of Dermatology, Medical University of Graz-(Graz. Austria), 35 cases were selected for the study. The other 79 eases were excluded because of lack of complete data or of available material for further stainings. Patients with history of mocosis finguides (MF) or lymphomatoid papulosis (L+P) and "huderline cases" of CD36" catazeous lymphoproliferative disorder trases in which a definitive distinction between pcALCL and LyP could not be made; and cases of entimeous Hedgion disease have been excluded from the study. Diagnosis of pcALCL has been made according to the WHO classification of lymphomas.12 Primary skin involvement was defined as the presence of cataneous lymphoma without nodal and/or visceral involvement after complete stating procedures.12 Details of some of the cases have been published previously."

Biopey specimens were fixed in 10% buffered formalin and subsequently embedded in paraffer. Sections were stained with hematoxylin-cosist for routing histopathologic evaluation. All cases and stamings have been reviewed independutily by body the unifors.

Immunohistology

Detailed immusophenetypic analyses were performed on routinely fixed paraffin-embedded tissue sections according to a previously described 3-step immunoperoxidate method. Memorary enhancement was used for all the antibodies. Second and third antibodies were obtained from Dako (Dakopatts: Glostnia, Detmark). The first artifody were from

CD2- 6/27 (22%)

Common loss of pan-T-cell antigens:

CD3- 13/34 (38%)

CD5- 16/31 (52%)

4/35 cases (11%) lacked all pan-T cell markers

Often cytotoxic phenotype:

CD4+/CD8- in 12 (35%) (TIA-1+ in 62,5%)

CD4-/CD8+ in 6 (18%) (all TIA-1+)

CD4+/CD8+ in 7 (21%) (all TIA-1+)

CD4-/CD8- in 9 (26%) (TIA-1+ in 12%)

TIA-1+ in 16/26 cases (62%)

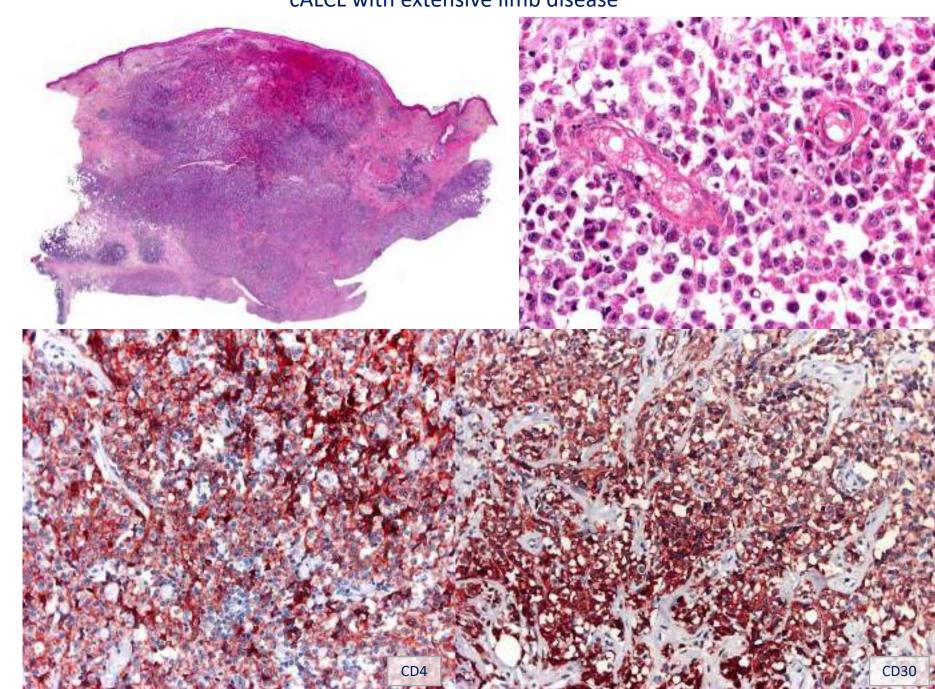
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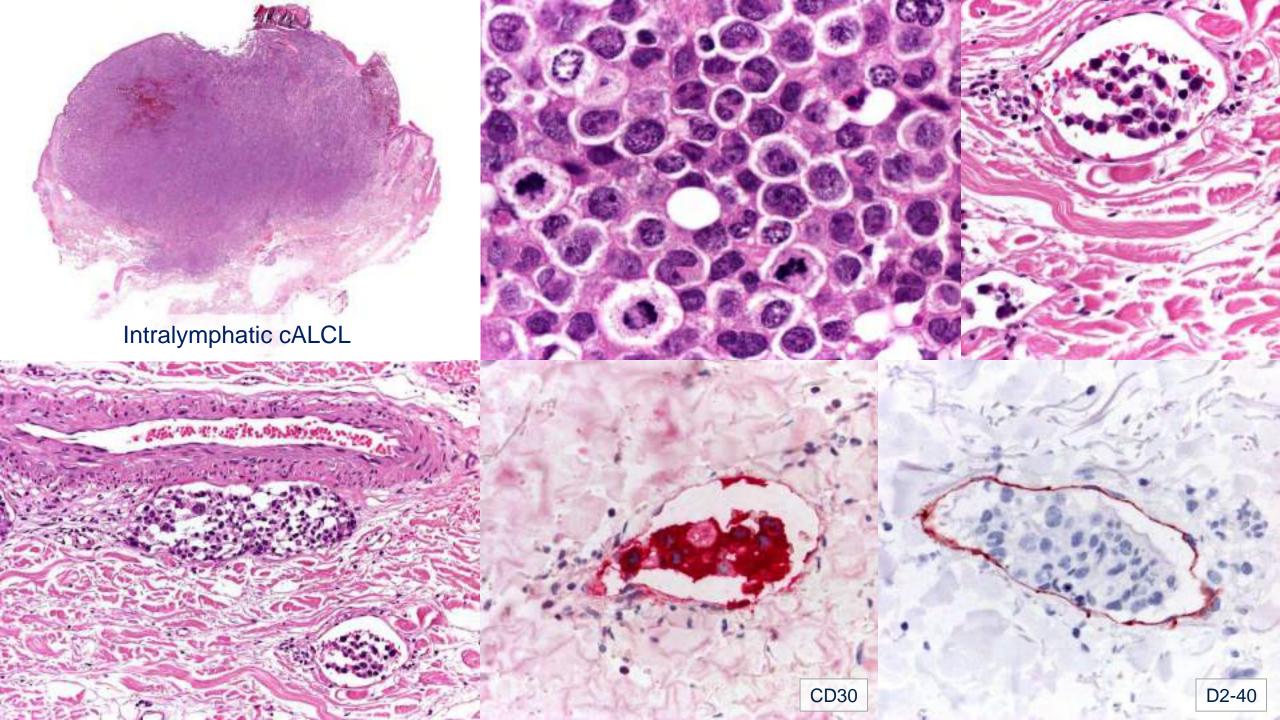
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cALCL with extensive limb disease





ORIGINAL ARTICLE

Intralymphatic Cutaneous Anaplastic Large Cell Lymphoma/Lymphomatoid Papulosis

Expanding the Spectrum of CD30-positive Lymphoproliferative Disorders

Mark A. Samols, MD.* Albert Su. MD.† Seving Ra. MD.†2 Mark A. Cappel, MD.§ Abner Louissant, Jr., MD. | Rvan A. Knudson, CG/ASCP/CM, S. Rhett P. Ketterling, MD. S. Jonathan Said, MD.† Scott Binder, MD,† Nancy Lee Harris, MD.) Andrew L. Feldman, MD.* Jinah Kim, MD, PhD.* Youn H, Kim, MD.it and Dita Gratzinger, MD, PhD.

Abstract: Intravescular large B-cell (symphotias and EBV 1 NK. T-off lymphorus autmonly follow an aggressive clinical. course. We recently reported an entirely intravascular anaphytic long cell tymphomo (ALCL) in the skin with a surprisingly indolent clinical course; interestingly, this lymphoma involved the lymphatic rather than the blood vasculating. We hypothesteed that intravescular skin-limited ALCL is distinct from aggreeing systemic intravascular hymphomas in its intralverphytic localization and clinical counc. We now describe 18 cases of eutaneous intransector large cell lymphografilerations from 4 institutions, All 12 intravascular large T-cell lesions were intralymphatic: the majority (9) were CD30.1 T-cell lymphoproliferative disorders (TLPDs), 5 further dissolled as intravascular ALK ALCL One ALX ALCL and 2 bengn microscopic attravecular Tradi profiferations were also intralymphatic. A sinde gase of otherwise typical outmoons fulfide center lymphema contained intralouphatic centroblass. The clinical and perhalogic characteristics of the CD50" TLPDs were similar to those of their extravoscular counterports, including extra-Symphatic derival involvement in a subset, DUSP22-IRFV transfocations in half of tested ALK. ALCLs, and associated myrous fungeides in 1; nost were skin-limited at baseline and remained so at relapse. All 5 cases of intravioleular lorge B-cell. lymplama involved the blood vasculature and behaved in a clinically aggressive manner; the ALK ALCL, although intrafemphatic, was systemic and clinically aggressive. We propose that outaneous ALK - ALCL and related CD301 - AEK TLPDs involving the lymphatics are part of an expanding spectrum of CD'0" TLPDs. The identification of intralymphatic as distinct from bland suscular localization may provide entical prognostic and therapeutic information.

5 ALK- ALCL

1 ALK+ ALCL

lymphoid blasts

2 benign intralymphatic proliferations of T-cell

3 "LyP-like"

Key Works: anaplastic large cell lymphoma, intravascular, CD301 commons hanglusproliferative disorder, lemelusic

Care J Steet Porker 2014;38:1203-1211)

Anaplastic large cell lymphoma (ALCL) comprises 3 morphologically and immunophenotypically similar but dinically discinct entities 2 systemic lymphomas-ALK ALCL and ALK ALCL and primary cutaneous ALCL.3 Primary cutaneous ALCL is distinguished by its generally indolent clinical course with a propensity to cutaneous but not systemic relapse.4 Primary cutaneous ALCL can be histologically indistinguishable from hymphomatoid populosis, particularly type C, whereas the clinical presentation differs (a solitary alcenting nodule in ALCL vs. multiple popules that negress spontaneously or was and want in lymphomatoid papaloss). For this reason, skin biopsies may be diagnosed more generically as CD30 T-cell lymphoproliferative disorders (TLPDs) pending further clinical follow-up.5 Recently, there have been several case reports of cutaneous intravascular prosentation of CD30. TLPDs, including ALCL⁶⁻¹⁰ and lymphomatoid papulosis type C.13 These patients typically presented with localized cutaneous disease and an indolent clinical course. Interestingly, the reported cases of intravascular ALCL presenting in the skin appeared to involve lymphatic channels rather than blood vessels,

intravascular large B-cell houphousa (IVLBCL), 2 which presents with extranodal involvement of small vessels.

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- Mayor Clinic, Brichester, MN

The only lymphoma classified by the World Health Organization according to its intravescular location is

Am J Surg Pathol • Volume 36, Number 9, September 2014

From the Departments of Pathology: #Becautology, Scanford Unisensity School of Medicar, Stanford: PUCLA Medical Center, Low-Angeles, (San Diego Pathologists Medical Group, San Diego, CA.) (Department of Demattslogs, Majo Clinic, Jacksonville, FL: (Departners of Parketogy, Massachosette General Hospital, Boston, MA; and *Department of Laborators Molicine and Pathology,

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Intralymphatic Spread Is a Common Finding in Cutaneous CD30" Lymphoproliferative Disorders

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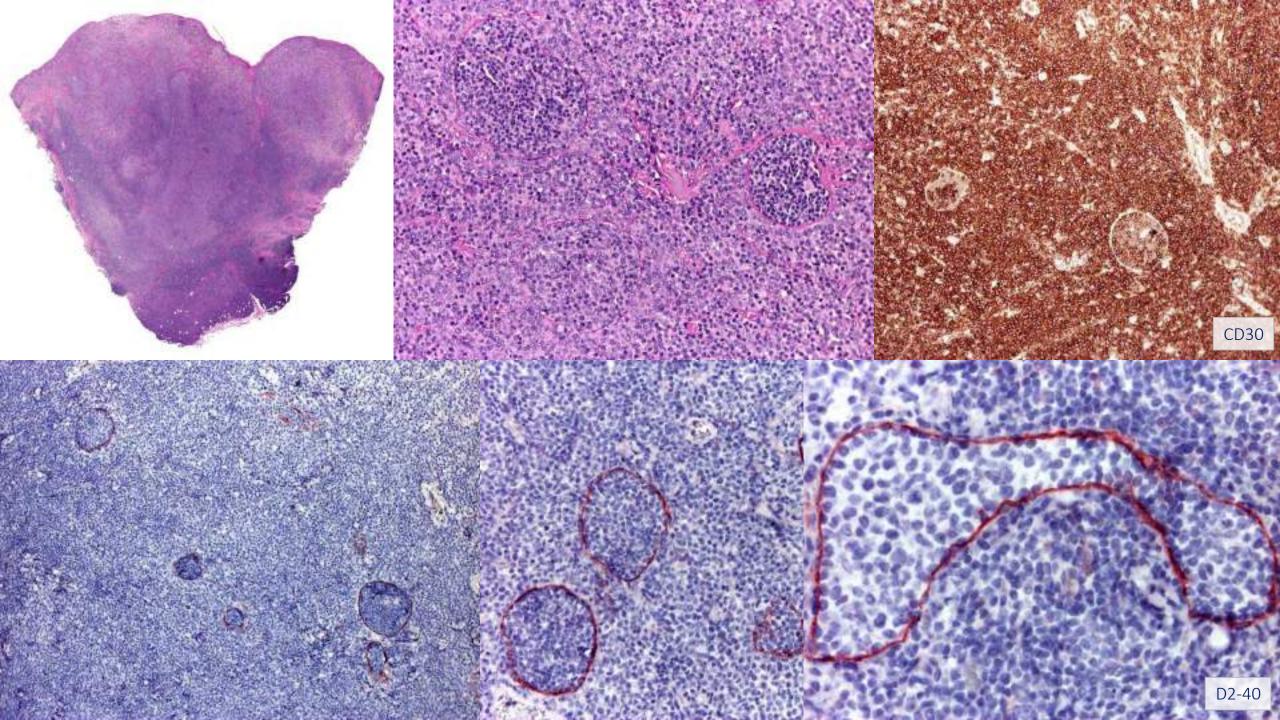
Lymphatic vessel involvement was found in 36/60 cases (60%) of ALCL (primary

cutaneous: 24; concomitant: 3; secondary

cutaneous: 4; staging unknown: 5), and in

6 cases (37.5%) of LyP.

Follow-up data, available in 28 patients with ALCL and 11 with LyP, suggested that lymphatic vessel involvement had no negative prognostic implication.





Case Reports



Lymphomatoid Papulosis

A Continuing Self-Healing Eruption, Clinically Benign—Histologically Malignant

Warren L. Macaulay, MD, Fargo, ND

A 41-year-old woman has an asymptomatic eruption of three years' duration. The clinical course is benign and is characterized by a continuing, random, coming and going of papules, some of which undergo necrosis, and all of which involute spontaneously within three to four weeks. Results of repeated physical examinations and laboratory studies are normal. Yet, biopsies of the skin lesions show an alarming infiltrate of anaplastic cells of disputatious origin, suggesting to most reviewers a diagnosis of malignant lymphoma. A number of comparable cases are reviewed, their similarity implying an uncommon entity.

HERE IS A paradox: a 41-year-old woman has a skin eruption of three years' duration which is best described as clinically resembling acute parapsoriasis (pityriasis lichenoides et varioliformis acuta. Mucha-Habermann's disease). Lesions are continually developing and regressing at random. The patient's health is good, results of physical examination and laboratory studies are normal. Yet, repeated biopsies of her skin lesions (an average of four biopsies a year since coming under my observation in August 1964) consistently reveal an alarming infiltrate of large pleomorphic hyperchromatic cells which expert histopathologists and hematologists have variously classified as highest grade malignant lymphoma (a

Clinic, Fargo, ND.

Reprint requests to Department of Dermatology,
Fargo Clinic, Fargo, ND 58102 (Dr. Macaulay).

majority opinion), malignant reticulosis, metastatic carcinoma, malignant melanoma, undifferentiated malignant tumor. The details of this case are herewith reported, a number of similar cases noted, and this curious phenomenon discussed.

Report of a Case

The patient is a 41-year-old woman. She had acute appendicitis and appendectomy in 1950. In 1963, she experienced an episode diagnosed by her local physician as subacute glomerulonephritis. This was associated with a transient elevation of blood pressure and edema of the hands and feet. Erythrocytes and polymorphonuclear leukocytes were present in the urine with only a slight trace of albumin. This ailment cleared uneventfully and without apparent residua. Aside from these two illnesses, the patient has enjoyed good health. Married for 19 years, she has never been pregnant although she has not practiced contraception.

The patient has worked in the business office of a dairy for 22 years. For years, both the office and the contiguous dairy have been routinely sprayed every three months with organic phosphate and/or chlorinated hydrocarbon insecticides. This practice has now been discontinued in the office section.

The patient takes aspirin for headache about once a week. Otherwise, there is no drug history.

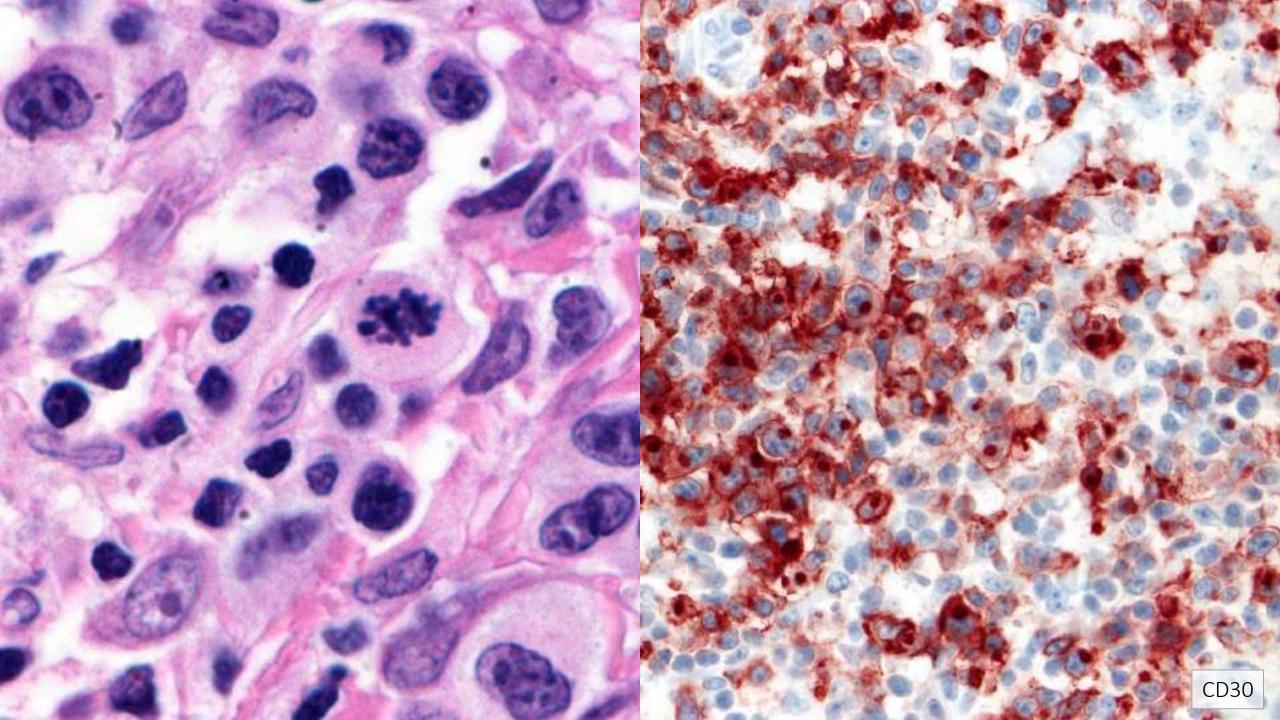
The Eruption

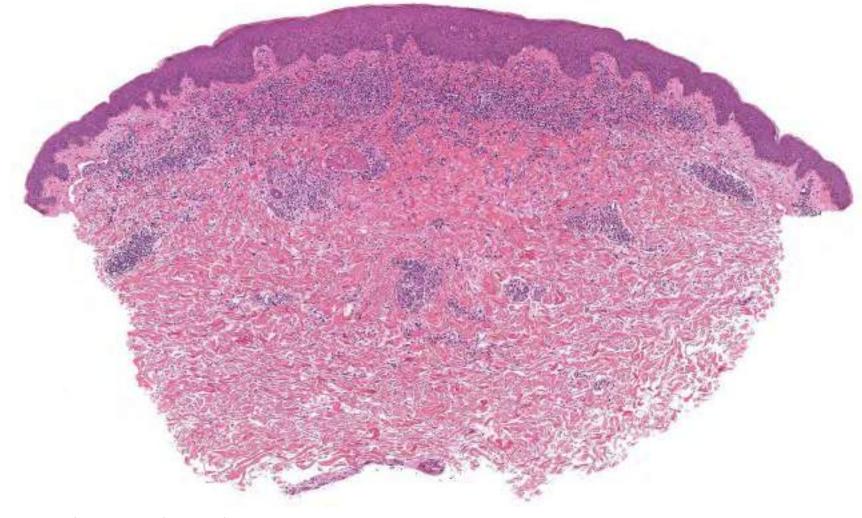
In the spring of 1964, an eruption first appeared on the buttocks and soon lesions

"Here is a paradox:..."

HERE IS A paradox: a 41-year-old woman has a skin eruption of three years' duration which is best described as clinically resembling acute parapsoriasis (pityriasis lichenoides et varioliformis acuta, Mucha-Habermann's disease). Lesions are continually developing and regressing at random. The patient's health is good, results of physical examination and laboratory studies are normal. Yet, repeated biopsies of her skin lesions (an average of four biopsies a year since coming under my observation in August 1964) consistently reveal an alarming infiltrate of large pleomorphic hyperchromatic cells which expert histopathologists and hematologists have variously classified as highest grade malignant lymphoma (a majority opinion), malignant reticulosis, metastatic carcinoma, malignant melanoma, undifferentiated malignant tumor. The details of this case are herewith reported, a number of similar cases noted, and this curious phenomenon discussed.

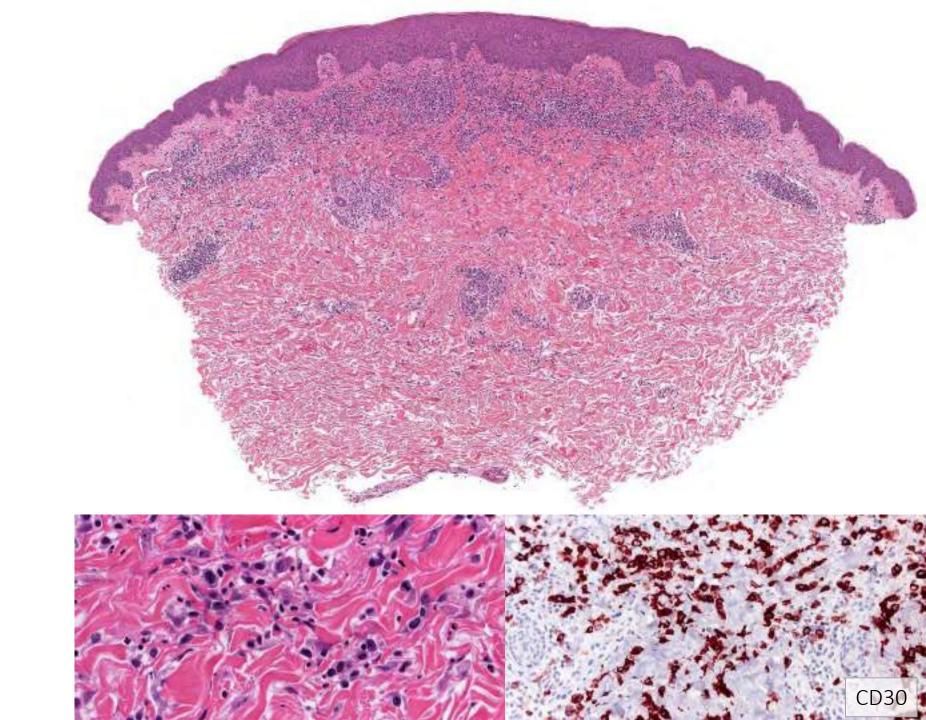
Accepted for publication June 28, 1967. From the Department of Dermatology, Fargo

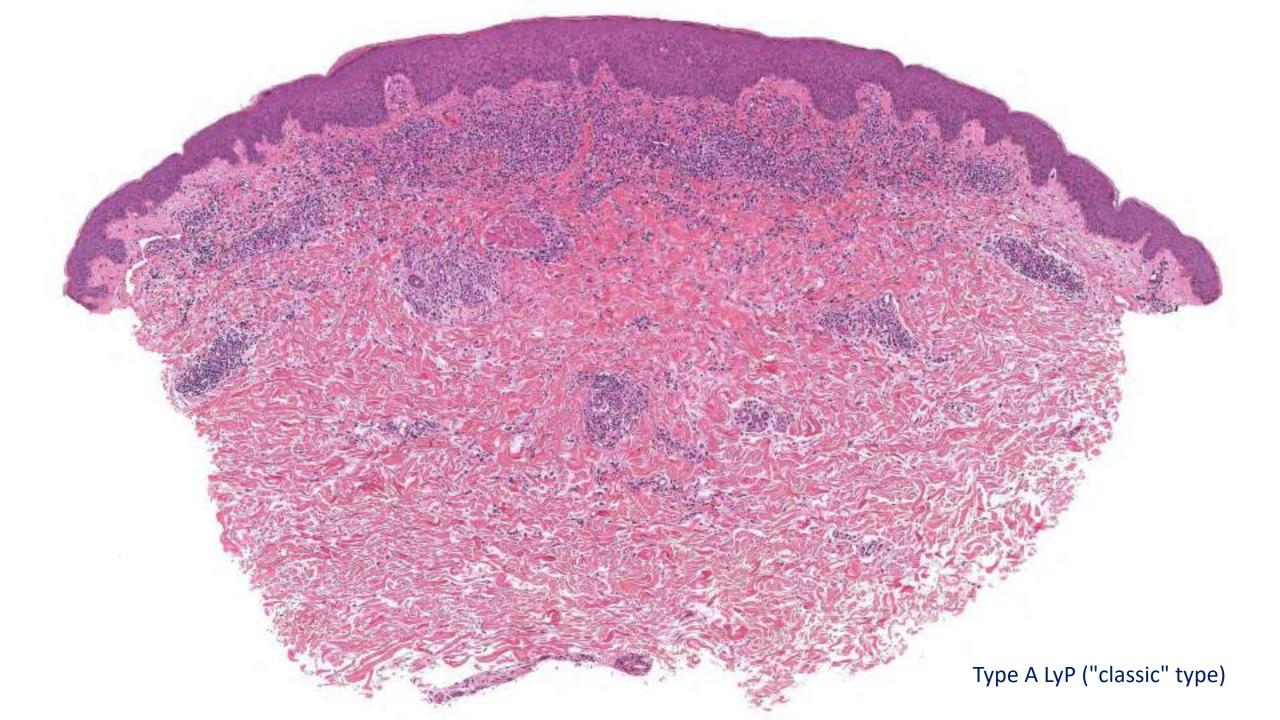


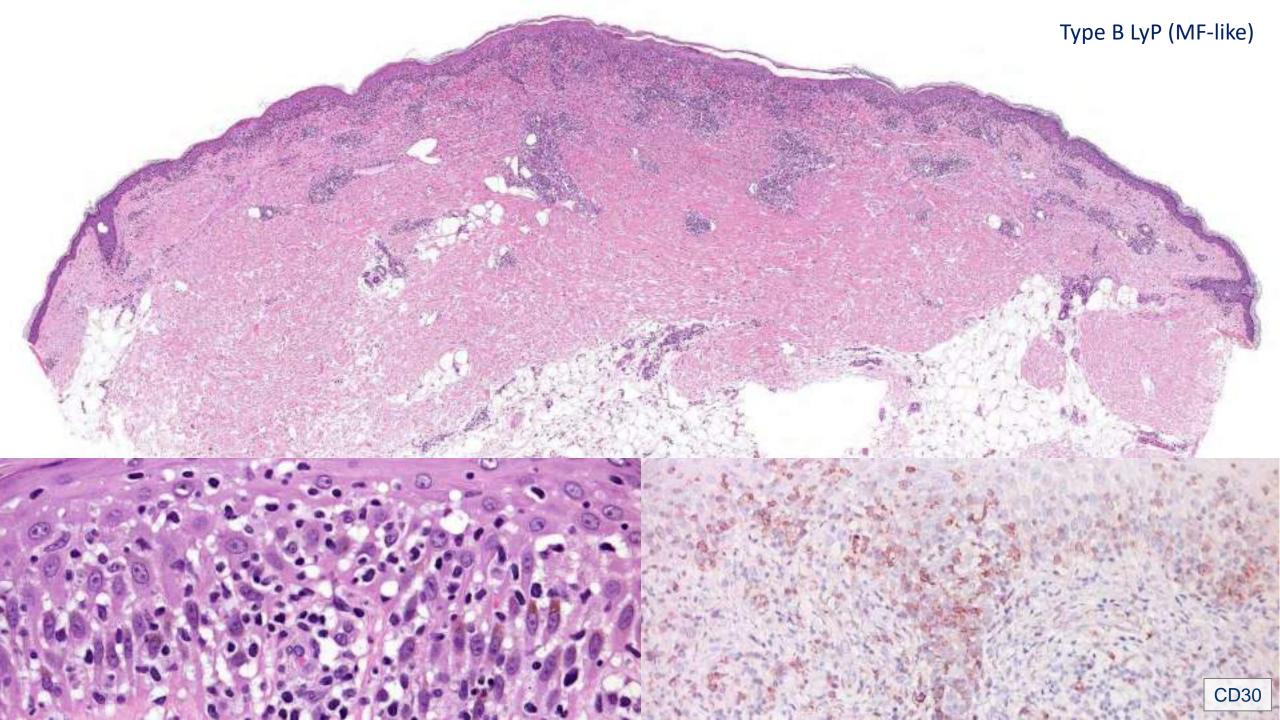


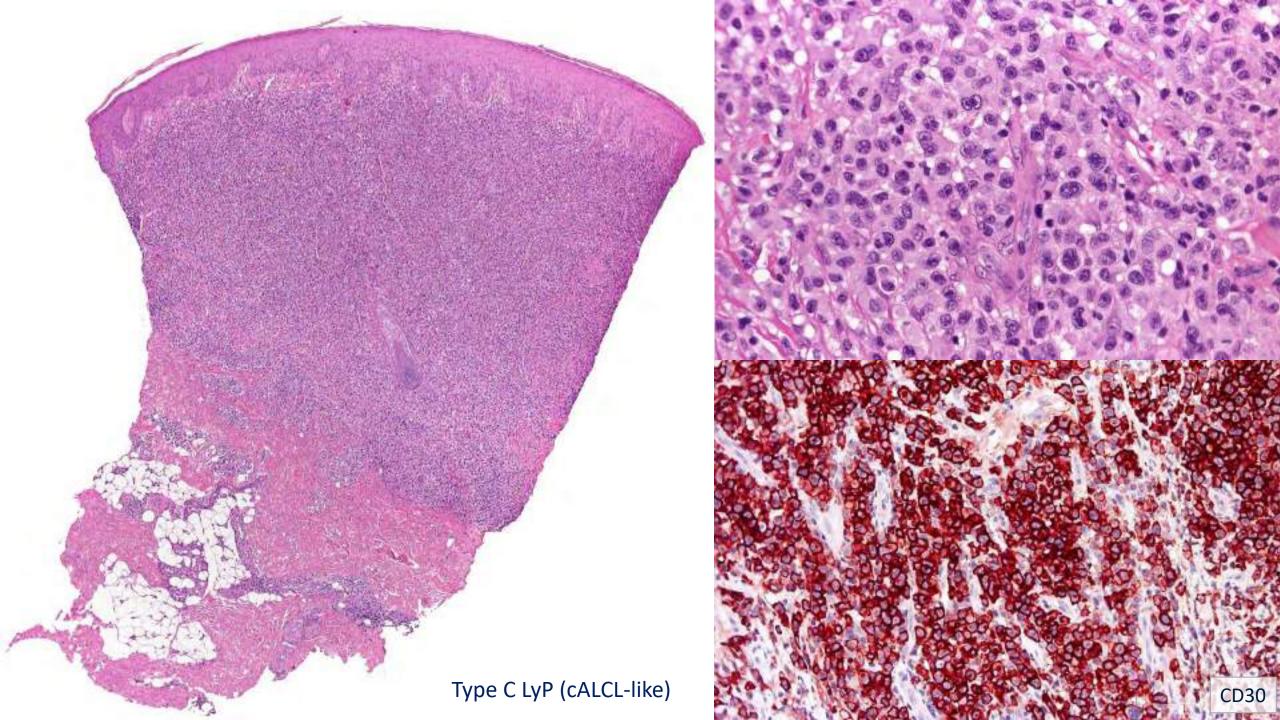
Lymphomatoid papulosis

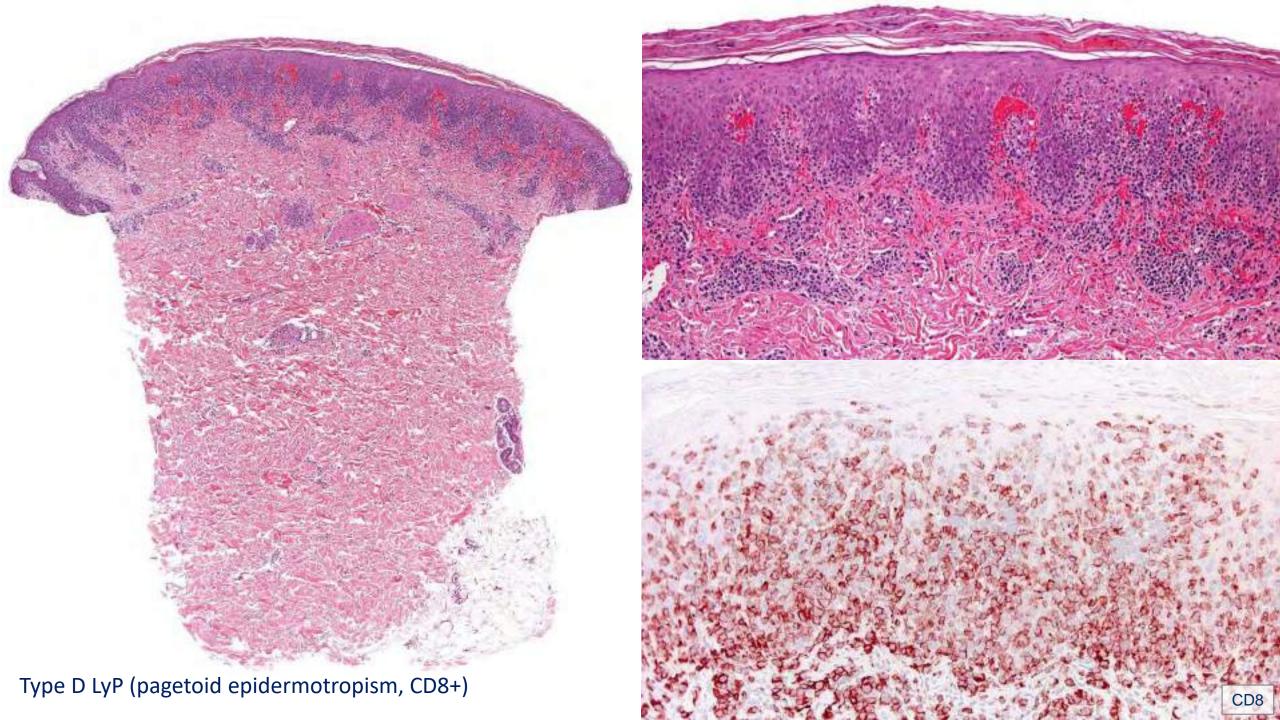
Recurrent, waxing and waning eruption of papules and small nodules that tend to ulcerate and may resolve with scars. Number of lesions variable from a few to >100. Number of crops variable as well (in some patients continuous presence of lesions, in other only occasional crops). Several types according to clinic-pathological presentation. Benign, but may be associated with other cutaneous lymphomas.











A Variant of Lymphomatoid Papulosis Simulating Primary Cutaneous Aggressive Epidermotropic CD8+ Cytotoxic T-cell Lymphoma. Description of 9 Cases

Andrea Saggini, MD.*† Andrea Gulia, MD.*‡ Zvolt Argenvi, MD.\$ Regina Fink-Puches,*
Amelia Lissia, MD.\$ Mario Magaila, MD.* Luis Requesa, MD.#
Ingvid Simunitsch, MD.** and Lorenzo Cerroni, MD*

Abstract: Lymphometeid papulosis (LyP) is a recurrent, selfhealing emption belonging to the spectrum of cutaneous CD30 - hatphoproliferative disorders. Three main histologic subtypes of LsP are recognized: type A distrocytic), type B imposis finguides-(MF)-likei, and type C (interlastic large cell lymphoms-like). We reviewed 26 biopsies from 9 patients (M.F. = 6.3, median age: 29; mean age 27.2; age range 40 to 38) who presented with clinical features typical of LyP but with hinopathologic uspecs that resembled privary cutaneous aggressive epidemiotropic CDX+rytonnia Tsell lynghoma. In all but I case avenical brainhood cells showed eureesian of CD30, and in 3 of 9 cases a T-cell extotoxic phenotype could be observed (BFT+, CD)+, CD4+, CD4+). Expression of at least 1 cytotoxic marker (HA-L grutzyme B) was observed in all cases. Polymerase chain reaction analysis of the T-cell receptor genes revealed a moscolonal reconsparent in 2 of 5 cases tested. Follow-up data available for 8 patients uncunfollow-up time 84mo median: 32.5mo; range: 1 to 305mo) regulal that some of their developed systemic involvement or signs of other cutaneous lymphomas. This extotoxic variant of ExP way be histographologically indistinguishable from primary cutaneous aggresorse apidermotropic CD6= synotoxic T-cell lymphoma, and may be the source of pitfalls in the dagnesis. and classification. We propose the term LyP type D for this unusual suriant of the disease. Accurate dinicoparbologic correlation is required in this setting, with crucial implications exactling prognosis and monagement of potients.

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Consupradore: Louizzo Corrini, MD, Department of Democrologi, Medical University of Graz, Austheragorphics 8, A-8656 Graz, Austria to mall: berous/coronals/moleuspracest. Corporals 8: 2008 by Esponanti Williams & Wilkim Key Words: Ignificantinal populesis, printary cutassous aggressive quidemnatorie CD8+cytotoxic T-cell lymphoma, mycosis fargoides, cytotoxic lymphoma, cutamerus T-cell hamphoma.

Lifes J. Novg. Parisol 2010;34:1168-11751

emphoriatoid papalosis (LyP) is defined as a chronic. -recorrent, self-healing eruption of papules and small nodales, characterized by a waxing and waning course and by histoguthologic features of a cutaneous T-cell lymphomic 24. LyP is currently classified within the spectrum of the primary cutaneous CD30 - lymphoproliferative disorders in both the 2005 WHO-EORTC classification of cutaneous lymphomas and the 2008 WHO elastification of tumors of humatopoietic and lymphoid tissues.21.31 Historathologically, 3 subtypes are recognized, namely, type A fluishocytics, type B (mycoss fungeides -(MF)-like), and type C (maplastic large cell lymphoma-(ALCL)-like).10-32 All 3 types may be seen in 1 and the same patient. Type B LyP, the least common and the most controversial variant, is considered as a histopathologic simulator of MF, 10,15

We describe 9 gatients who presented with typical aspects of LyP clinically but with unusual histopathologic features resembling pagetoid reticulosis, simulating primary cutaneous aggressive epidermotropic CD8+cytotoxic T-cell lymphoma. This lymphoma is characterized by an aggressive course with very poor prognosis, 2-17 thus differentiation from LyP is cracial for proper management of the patients.

PATIENTS AND METHODS

In the last few months one of as (LC) reveived 5 cases in consultation characterized by histopathologic features resembling those of pagetard reticulosis, but clinical aspects typical of LyP. On the basis of this experience, we reviewed all specimens of LyP type B registered in the database of the Research Unit Dermatoputhology, Medical University of Graz and found additional 4 cases with similar clinicopathologic features. Two further similar cases (one sent in consultation and

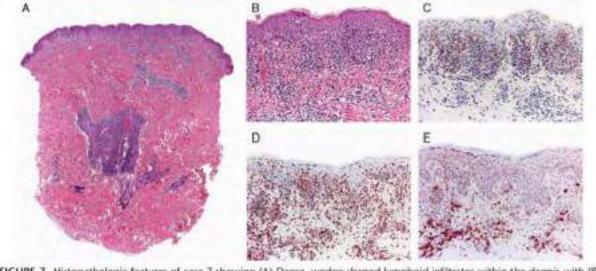
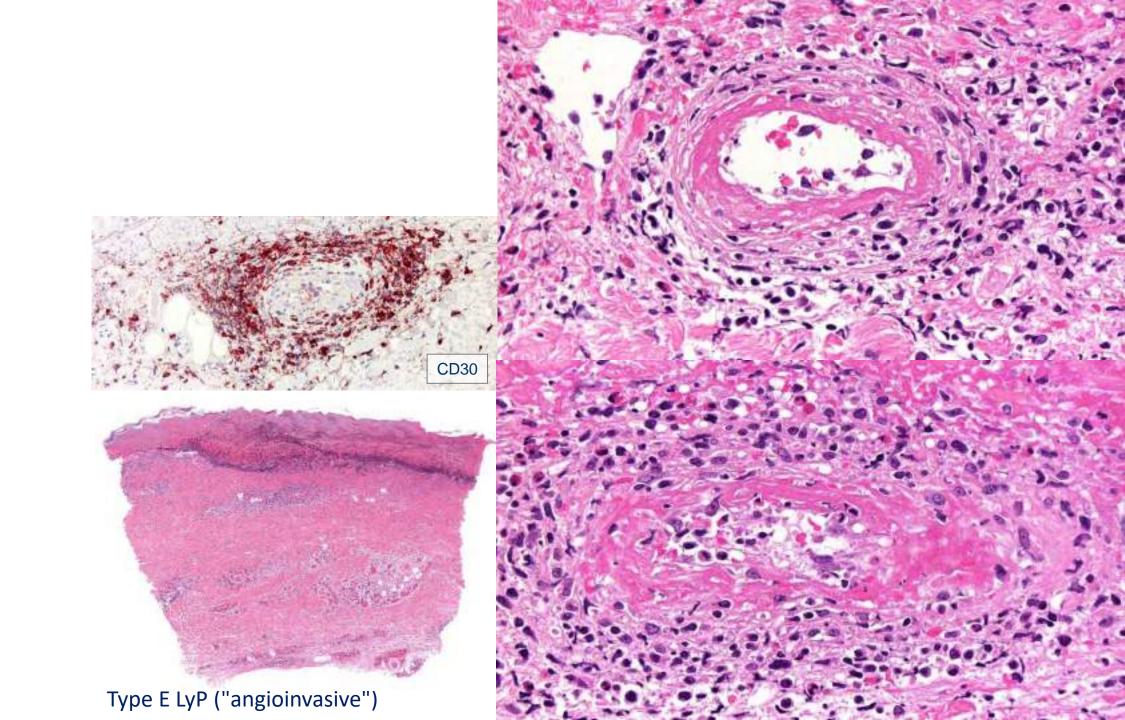


FIGURE 7. Histopathologic features of case 7 showing (A) Dense, wedge-shaped lymphoid infiltrates within the dermis with (B) prominent epidermotropism; (C) positive staining for CD56 and for (D) CD3 but (E) loss of CD5 expression.

"This cytotoxic variant of LyP may be histopathologically indistinguishable from primary cutaneous aggressive epidermotropic CD8+ cytotoxic T-cell lymphoma, and may be the source of pitfalls in the diagnosis and classification. We propose the term LyP type D for this unusual variant of the disease. Accurate clinicopathologic correlation is required in this setting, with crucial implications regarding prognosis and management of patients."



Angioinvasive Lymphomatoid Papulosis A New Variant Simulating Aggressive Lymphomas

Werner Kempf, MD,*† Dinitry V. Kazakov, MD, PhD,‡ Leo Schärer, MD,§ Acno Rästen, MD,§ Thomas Mentzel, MD,§ Bruno E. Paredes, MD,§ Gabriele Palmedo, PhD,§ Renato G. Panizzon, MD, | and Heinz Kutzner, MD,§

Abstract: Lympliomatoid populosis (LyP) belongs to the spectrum of primary cutaneous CD50-positive lymphoproHignative disorders. Clinically, LyP is characterized by a variable number of adf-heating populo-nodular lesions, with the typical waxing and warring course. Histologically, 4 types (A. B. C. and D) have been shiftmented. Augiorious was growth and large ulcors are now findings. in LyP and simulate aggressive lymphoma. We retrospectively analyzed the clinicopathologic and molecular features of angrounding LyP in a series of the patients. This new form of LyP is characterized by oficolesional popules that rapidly utcente and evolve into kirgs necrotic exchar-like lesions with a diameter of \$\footnote{t}\$ to 4 on and an angiocoura and audiodestructive infiltrate of small-sized to mechan-sized atypical lamphocytes expressing CD30 and frequently CD8. As in other forms of LyP, the leaons underwent spontaneous regression after a few weeks. Recurrences were common, but the prognosis was excellent with no extraditaneous spread or disease-related deaths. Complete remission: occurred in 9 of 16 partients (56%). This LyP systems should be distinguished from aggressive forms of angiocentric and angiodestructive and cytosoxic T-cell lymphomas. We propose the term LyP type E for this climically and hisodogically unusual variont.

Ker Words (symptoms, skin, CDR, CDR), lymphomatoid papulosis, extotextic (symphoma, angiotropic

Lifer J Story Probed 2013;37:1-13)

Lymphomatoid papulosis (LgP) belongs to the specfrum of primary cutaneous CD30-positive lymphoproliferative disorders (CD30⁺ LPDt ^{1,2} Histologically, 4

From the "Kerupf and Pfatz, Hinteligencer Diagnostik, "Department of Dematology, University Boostat, Zirish, "Dematology, Cargo Booglaber Universitate Vand, Lessanta, Switzerland, Diputations of Pathology, Faculty of Medicine in Place, Charles University in Prague, Coxeb Resolute, and (Dematoquithologie Friedrichshafm, German).

Case I was presented by I of the author (W.K.) at the Self Assessment Course of the XXRH annual receiving of the International Society of Demanding/thelogy (ISDP), 2002, in Stress, Italy.

Conflicts of Interest and Source of Funding: The authors have doctored, that they have no significant relationships with, or insocial interest in, was commercial companies perturing to this arricle.

Corragandow, Werner Korepf, MD, Korepf and Pddie Hstologische Diagnostik, Surinarstrasse 1, CH-1002 Zeitek, Switzerland w-millwerner korepf@accost.ork.chx.

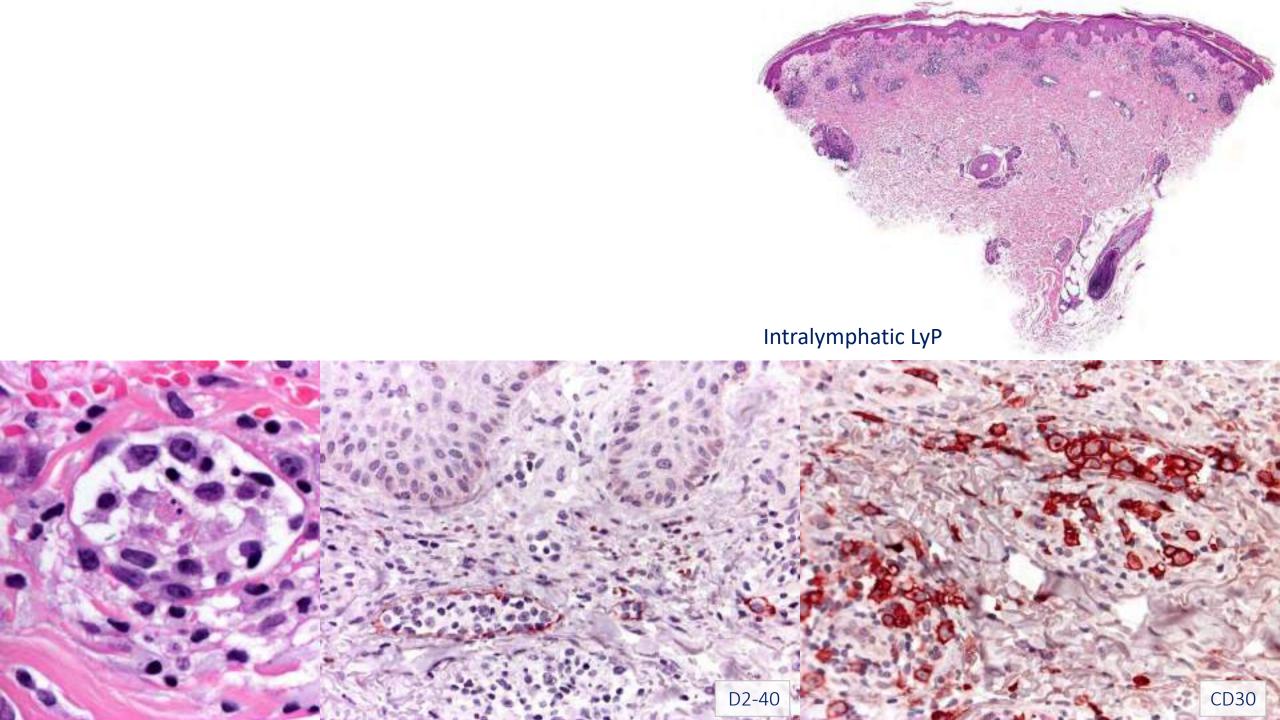
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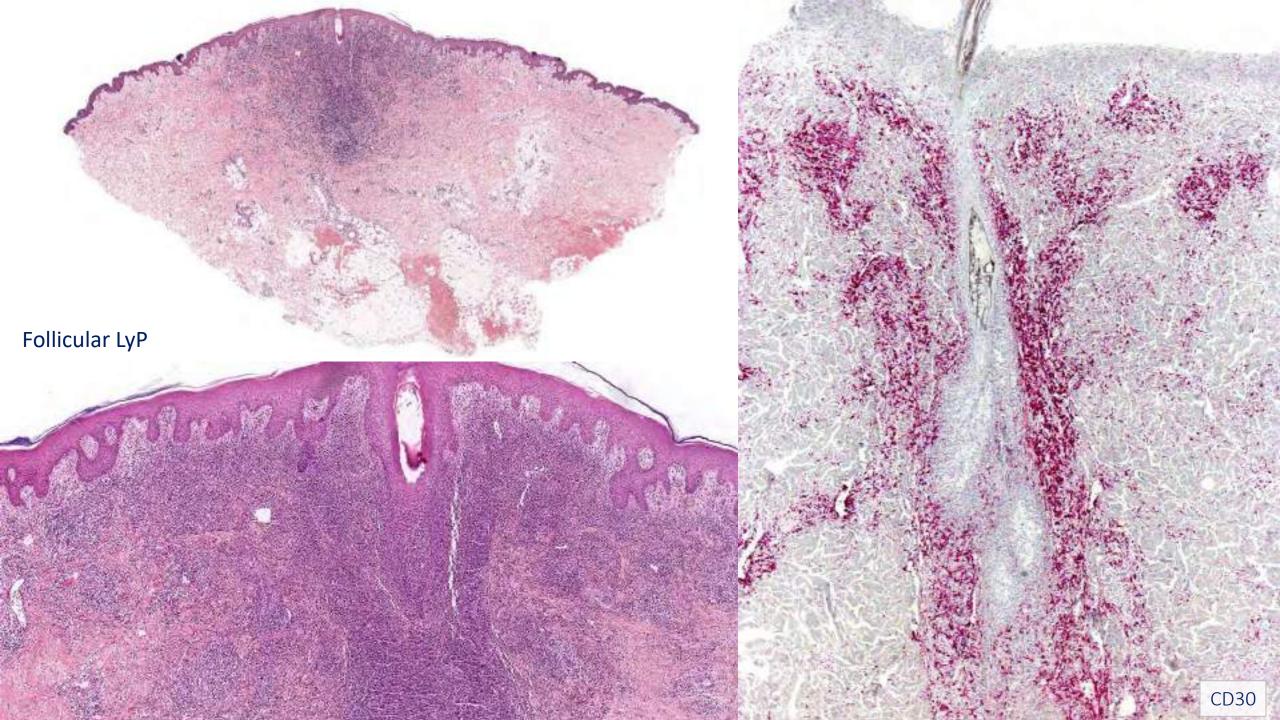
LyP types (A. B. C. and D) have been identified. Type A is characterized by the presence of large pleomorphic or anapiastic CD30 T cells scattered or in small clusters within the background of eosinophilic and neutrophilic granulocytes, histiocytes, and small lymphocytes. Type B shows epidermotropic infiltrates of small-sized to mediam-sized hyphoid edls, with variable extent of CD90 expression. In type C, a nodular dense infiltrate of cohesive sheets of pleomorphic or anaplastic CD00+ cells is present, and it usually contains only a few eosmophilic or neutrophilic granulocytes.37 Recently, type D has been described, which displays an epidermotropic infiltrate of CD8' and CD30' small-sized to medium-sized lymphoid cells.3 Within the same patient, different lesions may show different histologic types, either synchronously or metachronously.9 The CD30 symphoid cells may express CD4, CD8, or CD56, with CD4 immunoreactivity being the most common phenotype. 8311 Independent of its histologic pattern and the immunophenotype, Loft is clinically characterized by a variable number of selfhealing papulo-nodular lesions, with the typical wasing and waning course. The individual lesions undergospontaneous regression within a few weeks, sometimes accompanied by ulceration on top of the lesions and occasionally leaving behind varietiform sears. Despite the presence of medium-sized to large-sized pleomorphic or anaplastic cells suggesting a highly malignant course. LvP exhibits a favorable prognosis and requires no aggressive

We report a series of 16 patients with LyP who presented with a clinically and histologically rennual manifestation simulating highly aggressive amnocentric and angiodestructive T-cell lymphoma. These patients developed recurrent papular lesions that rapidly turned into hemorrhagic recrotic ulcers (eschar like) with a diameter of > cm and spontaneous regression, often leaving behind a sear. The typical features were rather large size of ulceration exceeding the size of the preexisting popule nodule and presentation with only a few lesions at a given time. Histologically, predominantly angiocentric and insnodestructive infiltrates of CD30 and mostly CD8" lymphoid cells as well as necrotic areas were the hallmark. Remarkably, the skin lesions resolved spontaneously, and none of the patients manifested progressive disease with extracutaneous involvement or died

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"We retrospectively analyzed the clinicopathologic and molecular features of angioinvasive LyP in a series of 16 patients. This new form of LyP is characterized by oligolesional papules that rapidly ulcerate and evolve into large necrotic eschar-like lesions with a diameter of 1 to 4 cm and an angiocentric and angiodestructive infiltrate of small-sized to medium-sized atypical lymphocytes expressing CD30 and frequently CD8. (...) We propose the term LyP type E for this clinically and histologically unusual variant."





DERMATOPATHOLOGY

Follicular lymphomatoid papulosis revisited: A study of 11 cases, with new histopathological findings

Werner Kempf, MD, Drittey V. Razakov, MD, PhD, Hans-Peter Baumgarines, MD, and Heinz Kutzner, MD. Zärich and Zug, Sunzerland. Pitten and Prague, Greek Republic, and Productional Commun.

Brokgrowel: Follouter lymphometric gapulosis (LyP) describes a variant of LyP with perthilicular trifficates and come degree of trifficationoppers of LUSE* applical tymphocytes, be for, only a few cases of folloutar LyP it are been described.

Objective Our goal was to study the chacepointologic features of foliatilar type in a series of 11 cases (9 moto. 2 female, age range 5-78 years, mean age 50 years).

Methods in all, 113 cases of typ were reviewed to select cases allowing folicital involvement. Histology was considered with the clinical data to exclude cases of CR30" maphastic large-sell lymphoma or folicylogopic mycose fungovies.

Resolver Six cases were classified as type C and if as type A, whereas the consisting one manifested epidementorpoint of small purpheases to a background of a typical type A lesion form-inpense type A 100. Perilablicator utilizates of CD30° atypical typicals of the services in all 11 cases with influence of the same recognised with a channel glands in 2 cases in addition to bair folicle influence, appeal with some recognised within schemens glands in 2 cases. How feedings were presented in more contribution in restricting in 2 patients, who chirally had positive in addition to papeles. Other bacquitological features excurred archided periconne influence in a (n - 3), and (n - 3)

Linuxations: The war a manageouse study.

Conclusions: Foliated by the a current of LyF with involvement of his foliates, mostly in the form of perillulation inditions with combine degree of belle obscription. Other charges including hyperplace of the foliate, and foliates minimals are less common. Knelly, intra-foliated promples can be seen to the foliates epithelium, such indicate quarter characteristics. (I Am Anal Demand 2013;68809-16.)

Key words: CD30; folicular muchoeis; lymphoma: lymphomacus pagulous; slain.

Several clinicoprishological variants of lymphounited papalesis (LyP) have been deliticated, acoustines exclaining in the same individual. The commences indepenhological variants are LyP type A and C, which are characterized by wedgechaped or neckdar infiltrates of large plecomorphic or anaplastic. CD90° hymphoid cells arranged as scattered atypical cells in the background of seamophils and matrophile thype A) or in crobestrethesis/trainles with core-than 50% of atypical cells. Dype C) intenting CD9tf* anaplastic large-cell fenplants. Less observes forms see LyP type II and the executly described type D both aboving an epidernymoric infiliate of analog lamphocytes will

Pyon the Kernyl und Pfeltz, filtraloptiche Dagmostik, Zurch'; Department in Pathology, Family of Medicine in Churc, Churles University in Practice, Family of Medicine in Churc, Churles Decreases Indiagrams between the September 1984 and Decreases States. Series.

Conflicts of interest: Nover declared. Accepted for publication December 3, 2012. Report requires: Women Kompt, MD, Sampf and Philitz, Histologisthe Diagnostik, Sonivarrance: 1, OH-8082 Züseh, Seltzetund, Ernalt usepilihimopf-staltzich. Published onfere tribinary 4, 2013.

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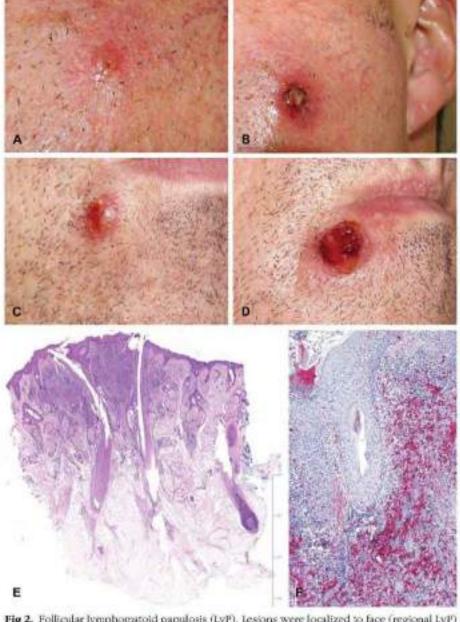
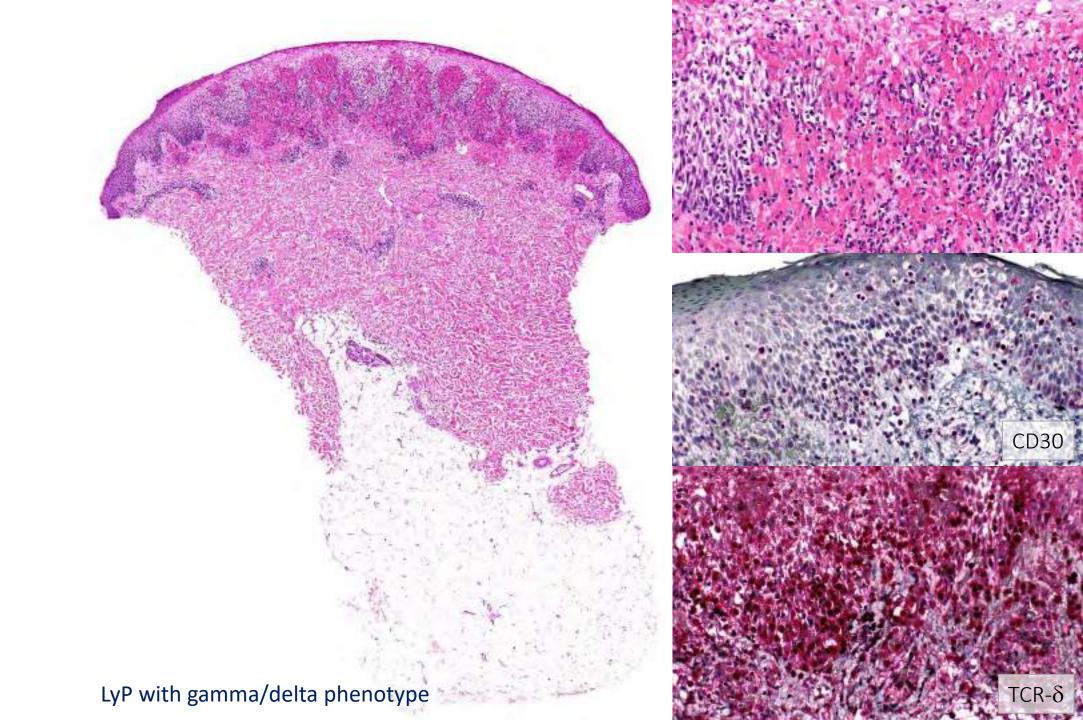
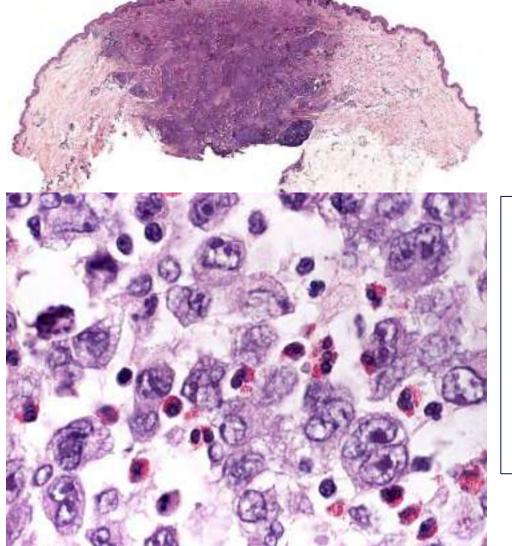


Fig 2. Follieular lymphomatoid papulosis (LyP). Lesions were localized to face (regional LyP) (A to D). Pustules are present (A and C). Histopathologically, there is perifollicular infiltrate composed of CD30* large cells along with numerous neutrophils and debris in comified layer atop infundibulum of hair follicle (E and F) (case 9).





Primary Cutaneous Hodgkin's Disease

Unique Clinical, Morphologic, and Immunophenotypic Findings

Nicholas Sioutos, M.D., Helmut Kerl, M.D., Sharon B. Murphy, M.D., and Marshall E. Kadin, M.D.

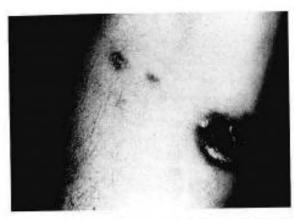
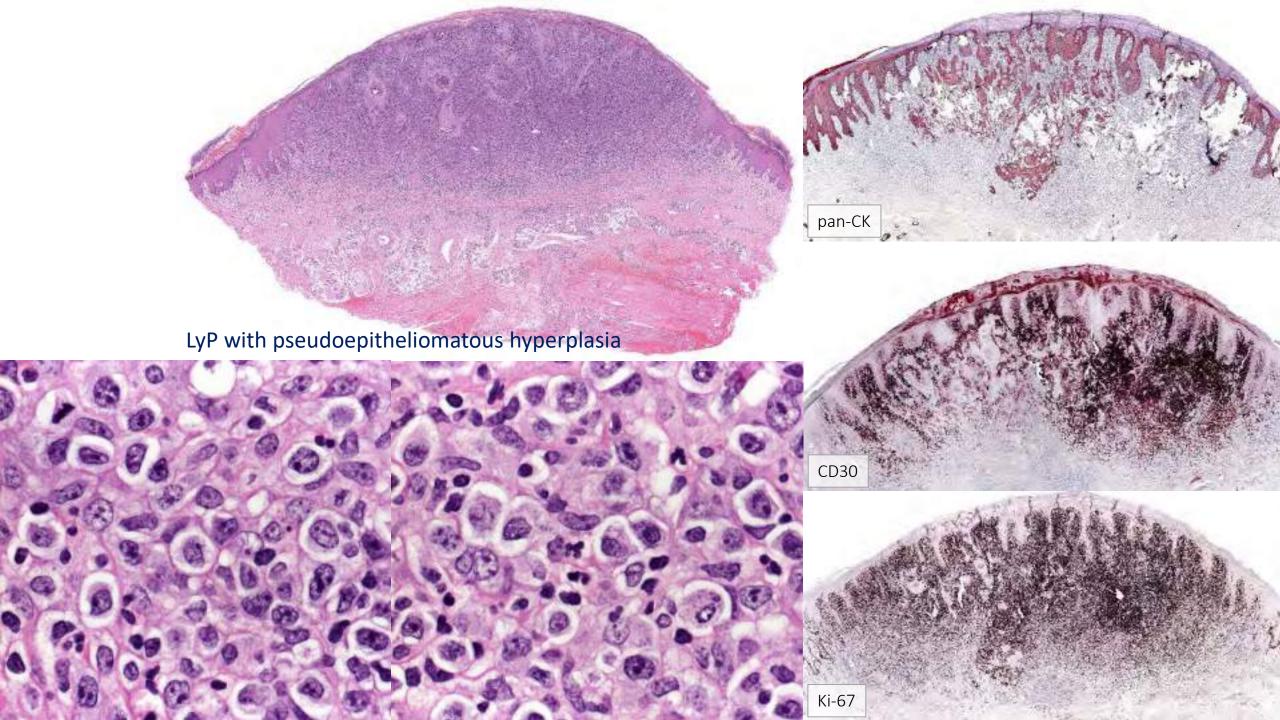
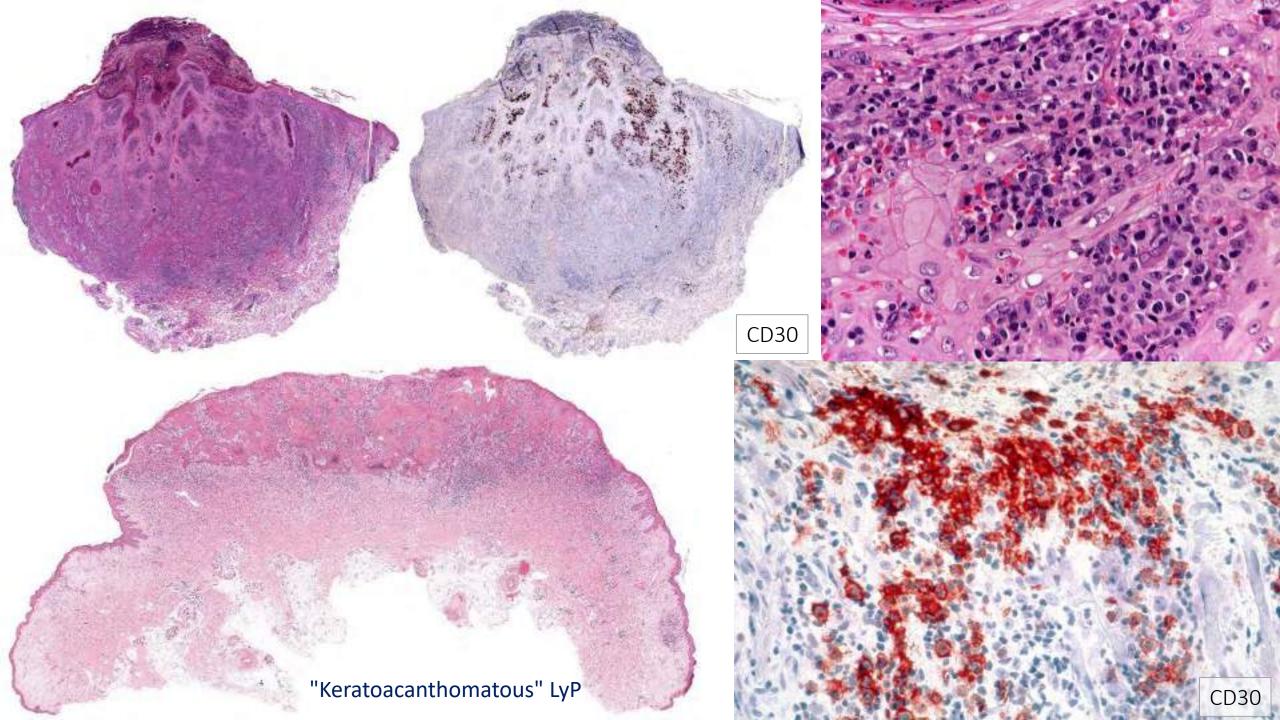


FIG. 1. Case 2: large tumor nodule and nearby papules on the right forearm.

Hodgkin-lymphoma-like LyP

The patient subsequently developed several new papules and nodules on the same arm over a period of >20 years, always with similar histopathologic features and without systemic involvement ("regional" lymphomatoid papulosis).





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Journal of Cutaneous Pathology

Lymphomatoid papulosis with pseudocarcinomatous hyperplasia in a 7-year-old girl: a case report

Lymphomatost papulosis (LyP) belongs to the group of cutmicous CD30+ lymphoproliferative disorders. Pseudocarcinomatous hyperplasia has rarely been reported in patients with LyP. In this report, we describe a case of LyP presenting as pseudocarcinomatous hyperplania. The patient was a 7-year-old girl who presented with a recturrent papulonodular ecuption on her face and truck for 2 months. Histograthologic examination revealed an irregidar growth of hyperkeratotic epidermis into the whole dermal layer with marked nests of squirmons cells in the background of diffuse atypical lymphoid. cells, cosmophils and neutrophils. The large arepical cells were possive for CDS0 and CD5, but negative for CD4, CD5, CD8, CD20 and CD56. A TCRy clone was identified by polymerase chain reaction (PCR). The correct diagnosis in cases of LyF with overlying pseudocurcusomarous spithelial hyperplania run be very difficult both clinically and histopathologically. Clinical and intropathologic characteristics should be integrated to avoid an erroneous diagnous of squamous cell carcinoma or keratoacanthoena.

Keyconte curancour CD50+ lymphopeolificrative dicorders. kermoacarchoesa, lymphoma papulosis, pseudocarcinomatous hyperplasia, squamous cell caccinoma

Kiong J. Ma V. Chen H. Xu X. Sen J. Lymphomatric papulosis with pseudocarcinomatous hyperplasia in a 7-year-old garl: a case report.

J Čutas Pathol 2016; 48: 480–483. © 2015 John Wiley & Sons A/S Published by John Wiley & Sons Ltd Jingshu Xiong, Yiping Ma, Hao Chen, Xiulian Xu and Jianlang Suu

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Acceptation palicies dos may 1,2015.

Lymphoemicid papulosis (Ly#) belongs to the group of cutaneous CD2044 freephoproliferative disorders that includes primary cutaneous anoplastic large cell lymphomic and benderline CD2044 lesions. Pseudocarrimomanous hyperplasta has rarely been reported in patients with LyP. Rendering the contect diagnosis in cases of LyP with overlying pseudocarrimonatous epithelial hyperplasia can be very difficult both clinically and histopachologically. In particular, the epithelium in such cases can reseauble agrammus.

cell corrisonat or kerzonacombosca and, in some cases, the angical hymphocytes are sparse or obstured by a deuse infiltrate of cosmophils and neotrophils. We describe a case of LyP with pseudocarcinomatous hyperphisia that simulated an epithelial inmor.

Report of a patient

A Fyear-old girl presented with a recurrent papulentedular eruption on her face and treat-

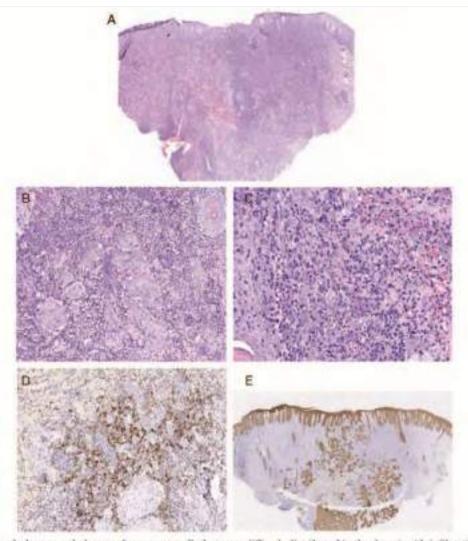
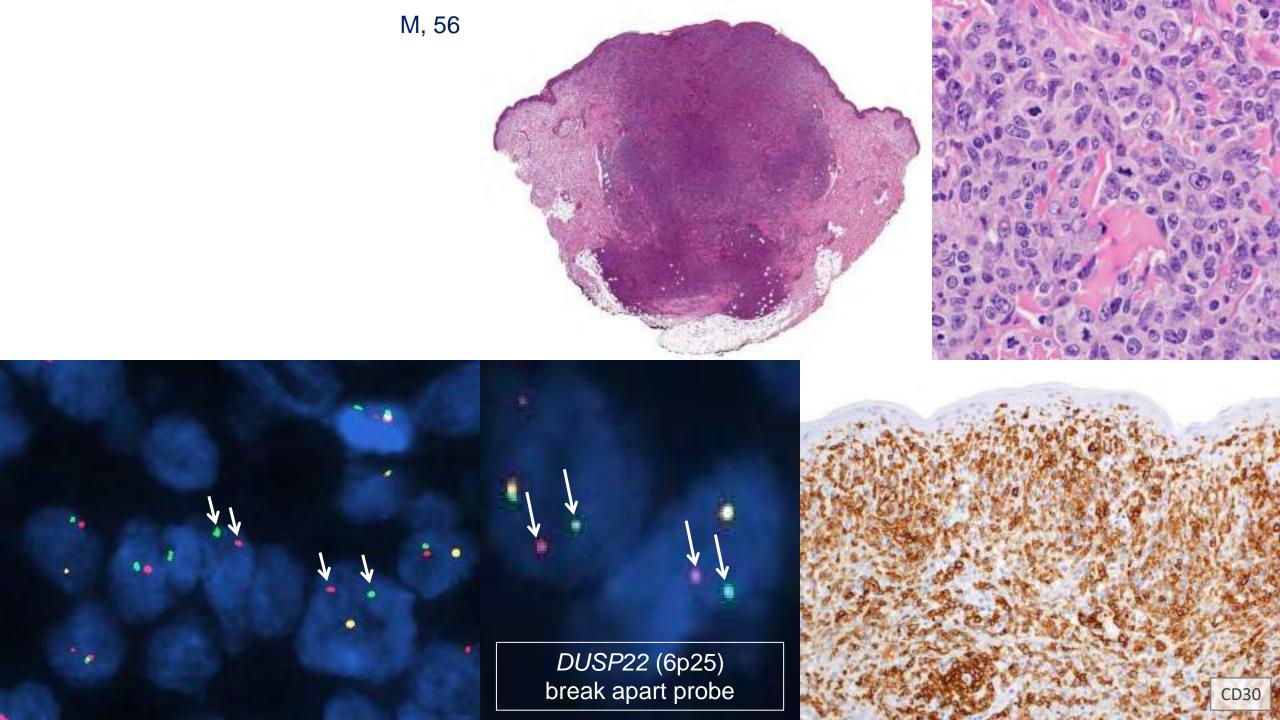
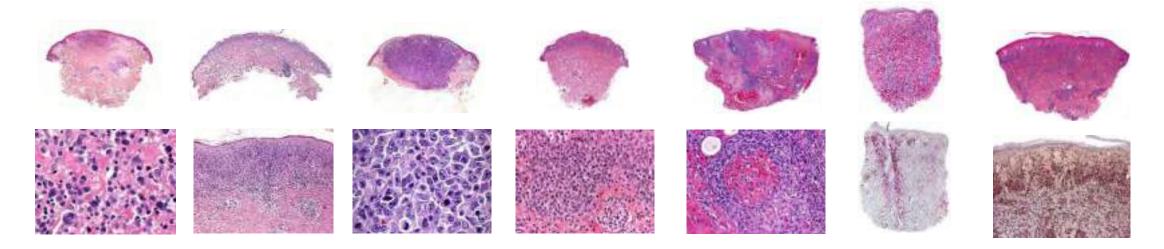


Fig. 2. A) Histopathology revealed nests of squamous cells that were diffusely distributed in the dermis with infiltrations of abundant lymphocytes, eosinophils and neutrophils [hematoxylin and eosin (H&E), ×10]. B) Nests of squamous cells in the dermis (H&E, ×40). C) Some lymphoid cells were obviously atypical with large and hyperchromatic nuclei (H&E, ×100). D) Immunohistochemical staining showed CD30+ large atypical cells (×100). E) Immunohistochemical staining: the cells were positive for CK (×10).





Subtypes of lymphomatoid papulosis are not a classification:

Just a caveat (particularly for dermatopathologists)

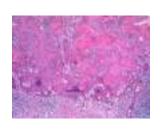
in order to avoid misdiagnoses!



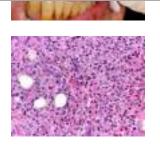
Type H Hodgkin-like



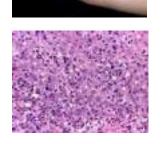
Type I
Intralymphatic



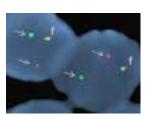
Type K



Type M Mucosal



Type R Regional



Type 6
6p25.3
DUSP22-IRF4

Variants of lymphomatoid papulosis

- Many clinical or histopathological "types" of lymphomatoid papulosis have been described after the original report by Macaulay
- Clinically and prognostically no differences between the various types of lymphomatoid papulosis
- Some variants may be a chance finding (e.g., follicular LyP)
- The identification of different histopathological types of LyP is important exclusively for the diagnosis (i.e., rule out other cutaneous lymphomas)
- Not necessarily part of the histological report !!!

Journal of Cutaneous Pathology

Large CD30-positive cells in benign, atypical lymphoid infiltrates of the skin

Background: Connecess infections and inflammatory diseases may contain a significant number of CD90-positive cells, thus mimicking lymphomatoid papulosis (LyP) or anaplastic large cell lymphoma. Methods: We reviewed our cases of non-neuplastic skin conditions with large, CD90-positive cells and searched the literature for similar cases.

Results: A total of 28 cases were included in the study: Milker's nodule (n = 0). Herpes simplex virus infection (n = 7), lymphomatoid drug reaction (n = 3), mollowant comagiosum (n = 3), nodular walnes (n = 2), krishmaniasis (n = 1), sophilis (n = 1), pernio (n = 1). ruptured infundibular cyst (n = 1) and pseudohmphoma in a sear (n = 1). CD50-positive cells were often arranged in clusters and provaded both Golgi and membrane positivity, similar to what was observed in LvP and CD30+ anaplastic large T-cell lymphoma. Conclusions: Analysis of our data and of those published in the literature shows that viruses and drugs are the most common cause for occurrence of large CD30-positive cells in rutaneous pseudolymphomatous infiltrates. Arrangement of these large, CD30positive cells in small clusters is not imigae to cutaneous CD30-positive lymphonas, and in many cases a precise diagnosis can be made only upon accurate clinicopathological correlation or using ancillary mediads such as polymerase chain reaction analysis for viral DNA.

Werner B, Massone C, Kerl H, Cerroni L. Large GD30-positive cells in benign, atypical lymphoid infiltrates of the skin. J Cattan Parliel 2008; 35: 1100-1107. © Blackwell Munkagaard 2008.

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"Hoppial in Clitical Department of pathology, Universidate Federal do Parana, Quinto, Section of Department of Department of Demackogy, Medical University of Sec, Grac, Austria

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e-mail: lummys.comoxi@maduro-gruzal

Expression of the CD30 antigen is the ballmark of a group of primary entancess. T-cell truphomas including the spectrum ranging from hymphomatoid pupulosis (L₂P) to primary entancous anaplastic large T-cell lymphomas (cALCL). ¹² CD30-positivity on neoplastic cells of cutaneous malignant lymphomas, however, is not a feature exclusive is LyP and cALCL, as it can be observed in cases of Hodgkin's lymphoma amoléog secondarily the skin' as well as in several Tcell ¹³ and B-cell hymphomas. ⁵⁻⁸ natural-killer cell lymphomas or even in granulocytic succome, ¹³ Furthermore, in the past years, CD30-positive cells have been disected in several reactive lymphocytic inflitrates of the skin ¹²⁻³² and oral nuccosa.

We reviewed our eases of mon-peoplastic (inflammators or infections) skin conditions in which large CD30-positive cells were detected among the infiltrating lymphocytes, analyzing the pattern of cell positivity and discussing the significance of the finding of CD30-positive lymphocytes in curaneouslymphoid infiltrates.

Material and methods

Files from the Research Unit of Dermatopathology, Department of Dermatology, Modical University of Graz, Austria, and cases sent in romalitation to one of its L. G.) were scarched for pseudolymphomas practive benign inflammatory or infectious conditions) showing presence of large CD30-positive cells within the inflatate, Bopps specimens obtained in Graz were fixed as 10% buffered formalin and

Table 1. Reactive cutaneous infiltrates containing large CD30-positive lymphocytes included in our study

Condition	Number of cases
Milker's nodule	8
Herpes simplex virus or Varicella-Zoster virus infection	7
Lymphomatoid drug reaction	3
Molluscum contagiosum	3
Nodular scabies	2
Cutaneous leishmaniasis (oriental sore)	1
Syphilis (stage I)	1
Pernio	1
Re-excision scar of basal cell carcinoma	1
Ruptured infundibular cyst	1
Total	28



A review of CD30 expression in cutaneous neoplasms

Franziska Kampa

Christina Mitteldorf

Disperiment of Durantenary, Veransiday, and Aktrology University Media (Contr.) Charges, Granges, German

Correspondence

Derestation, Venerotopy and Alexanius University Wealtest Cortic Göttingen Roberts Kirth-Strass 4D S7075 Gridinger, Deballey, Eyem rivados reto-bay Eyesolore Dotteronule

Abstract

Background: The surface protein CD30 is a therapeutic target of monoclarar antibody bierapy. Knownedge of the frequency of CD30 expression and its programtic relevance is therefore inseresting, not only in lyen-houroititerative disorders IEED birt. also in solid turnors of the skin.

Methods: A review was completed in PubMed for all published reports of CD30 expression in cutaneous Amphomas, mastecytosis, epithelial tumors and rarcomas from 1982 to April 2019. Only accessible setticles in English and Germanwere convidered Entities with an expected CEXO expression, such as CEXE-positive GPD, were net evolution.

Results: The elegronic research identified 1091 articles and a further 34 articles were obtained from murual bibliographic reference. Overall 91 articles were included: that axemined CD25 expression in various entities of outaneous recipiarns and warthat the inclusion cribe'le.

Conclusion: Apart from catalagus CDSG-positive LFD, the last-studied group for CD30 expression was myconin fungoides (MF). CD30 pools (My www.found in 32% of classical (paints and plaque stage) and in 59.8% cases of transformed MF. CD20 was also frequently expressed in cultineous musticovteds (N6,5%), fir solid turnors, some single reports prescribe CD30 expression by turnor cells, but CD30 reactive tymphocytes were frequently observed in the turnor microecutronment [TME] especially in versioscanthuma (KA).

KEYWORDE

conclusions, lymphoesis, must suplants, represent fungations, sustained

INTRODUCTION

The transmirant prosts CD30 PG-1 or TNFRSF6) belongs to the turner reported factor receptor reperturille." CDSD, which is typically expressed by Reed-Steriders cells, was discovered in 1982." The CCCCC yealers/all with a resincular neight of 120 kD haw intracellulate. trummershows, and subspoolular domains.10 The CD30 Japani (CD30L) THESEL, or CDISO is a moritoire board untoline and use budetected on activated hymphyrytes, historistics, and granulosytes, ⁵⁴ A. subble furn of CDS0 hCDS0 ten she bean discreted."

CD30 is expressed on a small salese of T and 8 lymphocytes and is important for communication between these onlinges. Date

CD30 currence recurs premarie on CD4+/CD45RO+ and CD8+ nells, which produce TriZ-type cytokines, that nowe studies nim showed CDSD appropriate on Thill and This collection in B-lymphercates, COSO per also tic expressed in E-intranolities, which are locked at the edge of the gerninal tenter and in the estimatoral region. This Virus whereast Treath IntV, HTLV1-2) and 6-code IEBV also express CD30.25

CDS0 acts differently in writers signaling and ways." On the one hand, the captope attenuation of COM leads no receptor (them called and vigated them dustice through the includence of TNFR) dunor necessis factor receptor! 2:32 The signal is mediated by funor necrosic factor-receptor-associated proteins (IFAFL¹³ Especially

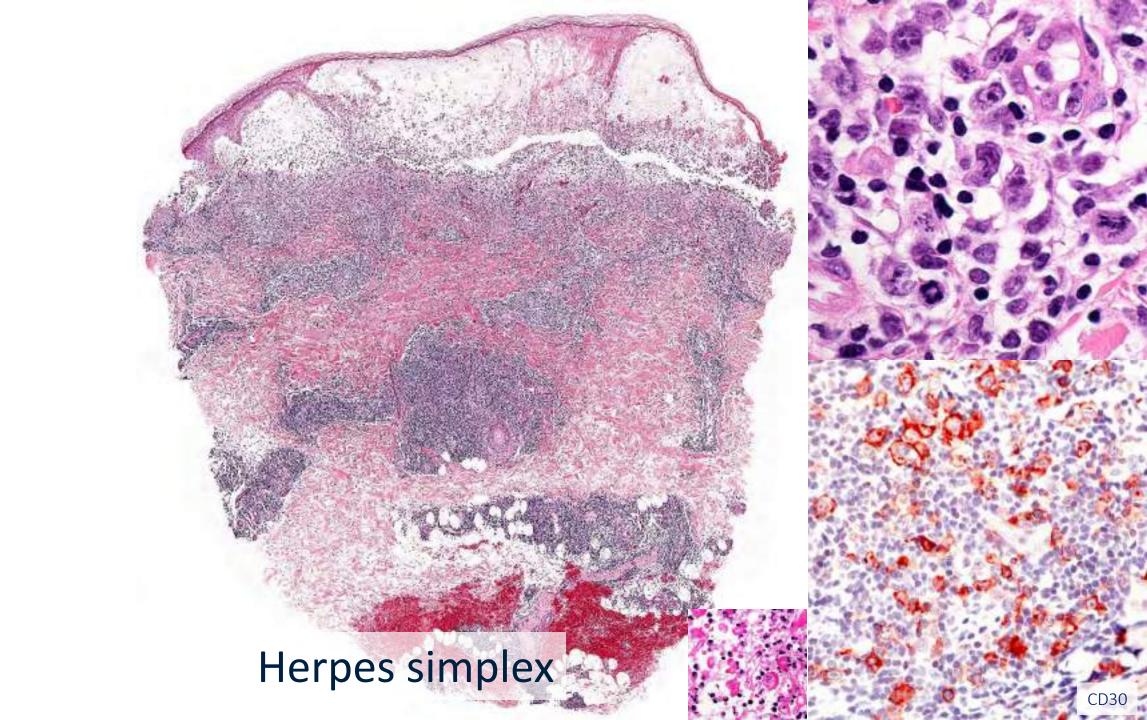
Apart from cutaneous CD30+ lymphoproliferative disorders, CD30 positivity was found in 32% of classical (patch and plaque stage) and in 59.4% cases of transformed MF

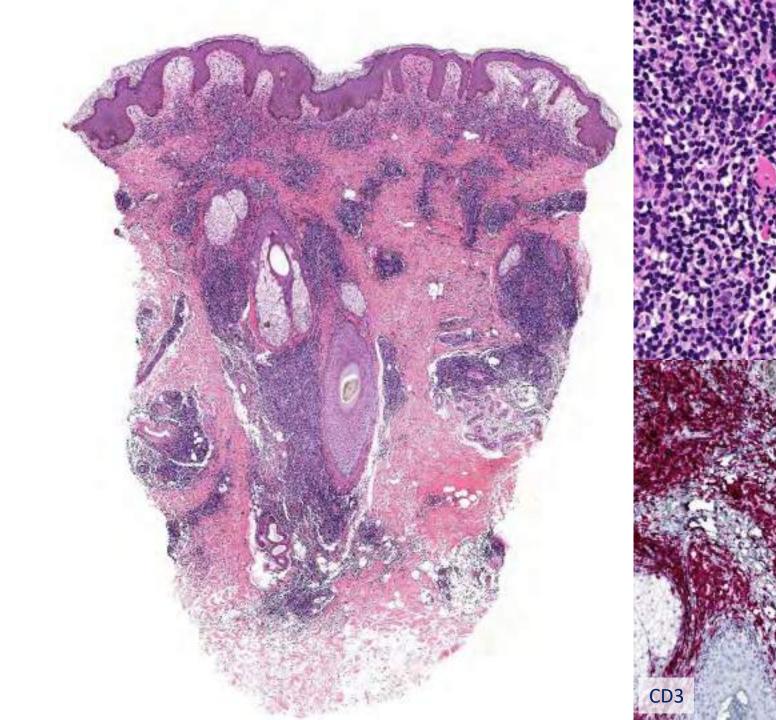
CD30 was also frequently expressed in cutaneous mastocytosis (96.5%).

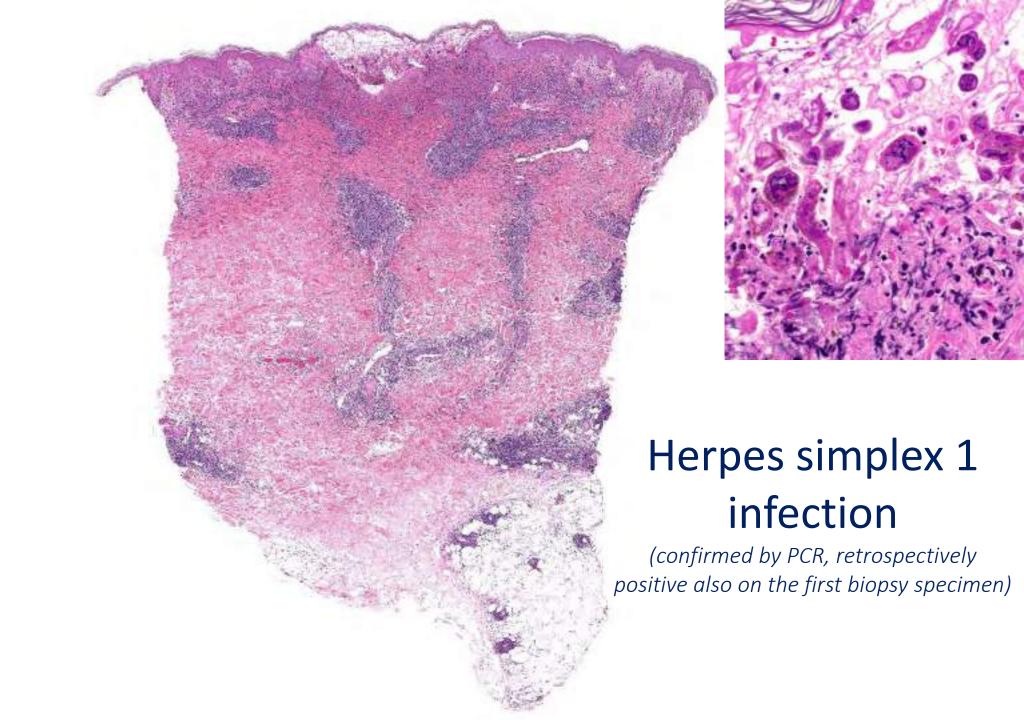
In solid tumors, some single reports describe CD30 expression by tumor cells.

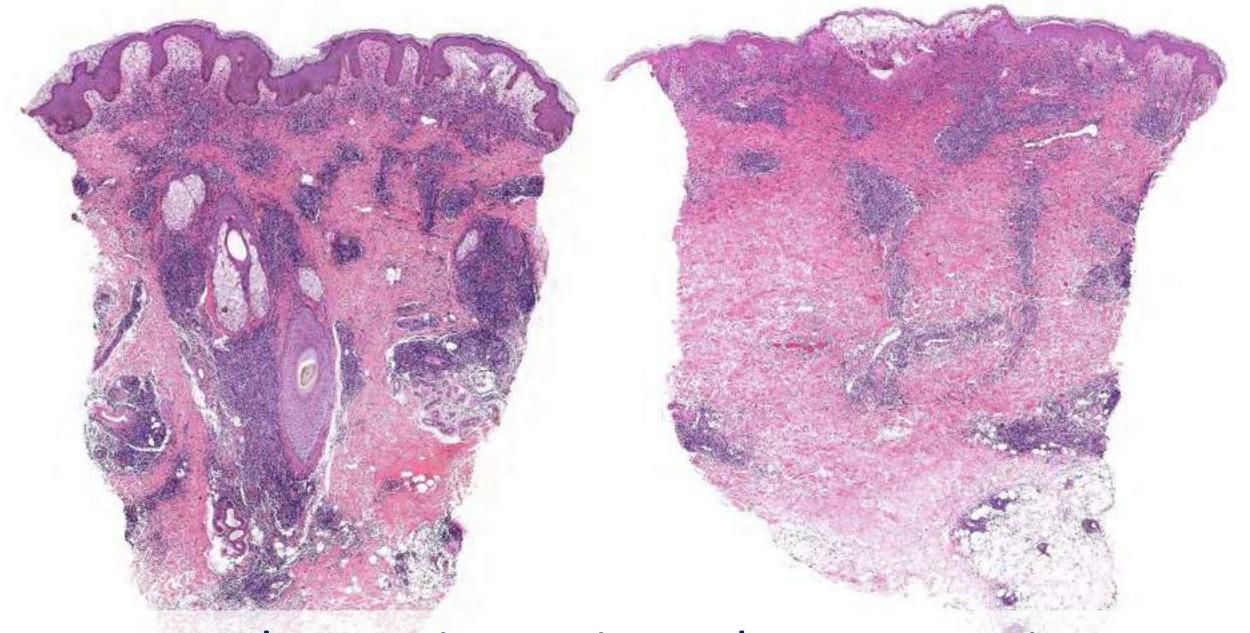
CD30+ reactive lymphocytes were frequently observed in the tumor microenvironment, especially in keratoacanthoma. (*)

(*) beware of "keratoacanthomatous" LyP and calcl!!









From herpes incognito to herpes cognito...

Histopathologic Features of Cutaneous Herpes Virus Infections (Herpes Simplex, Herpes Varicella/Zoster)

A Broad Spectrum of Presentations With Common Pseudolymphomatous Aspects

Bernd Leimseber, MD, Helmst Kerl, MD, and Lorenzo Cerront, MD

Abstract; Consens contains cased to hopes angles 1/2 (FNV-[7]) audicapes radecla/costr (VZV) reprome common demotorio-In some cases, they present with otypical ofinion! and/or histogethalogic features, including presence of dense hopphoid infiltrates with attribut I suplaces the strendiding automates lengtherers. In this study, we reviewed the trapey spengages of 65 patients CO radies. 32 introduct mean age, of 2 years; median age, 62 years; age major, 19 98 years) with common scriptions caused to DSV-1-7 or VZV. Histologic examination revealed several stypical hadrags, including presence of dense lymphoid infiltrent, origiotropism, and stypical hyphosytes simulating multipairs lymphorm. Invocatohistochemiamy performed at 22 cases showed a predominant Ticel infiltrate, in the majority of cases with variable matrices of CDMH and CDM uells. Two uses with a pseudoisraphomatous appearance and small aflesters of CTDD: palls monthly a record not population of T honphocytes by PCA analysis, anderburg the difficulties in classifying some of their cases correctly. Our stydy indicates that commons better Infortions our inhibit several atypical histoperhologic, intranohistocharacters), and molecular feetures, and that in given cause accounts cilinicogniticogic correlation and short-term following comols are necessary for differentiation from extragroup lymphonia-

Key Words: Impet tiagles, herpin varioribizates, subquess pourfelymplania

Cdar J. Surg. Physical (2016) (0:50-58)

Catagorus craptions caused by larges simples, 12 (HSV-1/2) and larges varicable/roster (VZV) regressed common detriators. In most cases, a cease, diagnosis can be made based on the characteristic elitical findings, and usually skin lesions are bropeied only to parients with uncommon children persentations. 140 In this context, it is well known that entrances better structures or motions with immunicipatessics or with infarrhous barrowschafe; silveness. 2002. In these matianues, the

cinimal diagnosis may be presterante, and the differential diagnosis includes commons lymphoras or pseudolymptourn among others. In addition, bisology of cuanterus harpes tections can very to a great extent, maping first lestors will purely epithelial involvement and sposse to absent informationly affiliates, we cases with a disaid pseudolymphonismus pattern simulating a miligram lymphoral atoms disair some analysis. Endosse-thenis et al uppored a case of an observation may in the tempolarymy caused by infection with IESV-LQ, with a clinical presentation simulating a meligrant sumer, and a perliminary pethologic diagnosis of extransical NK/Lettl lymphoras, meaningses.³⁴

Occasionally, patients without occasioning discuses persure with consensus MSV-1/2 or VZV attentions the display appeal clinical and bisologic findings suggestive of a restances jumphoma, habed, in the pass few months, one of as (L.C.) continued South areas for consultation tense cos. 27, 31, 49, 53, and 54), which had been previously mandagreesed as unalignent hypothoma (cutaneous CD30+) prophopolithication functions spacerum hypotheomorphic population insophatic large cell symphoma, in this study, we arish and crisispectively the histopathologic finiterior of 65 cases of cutaneous HSV-1/2 and VZV attentions.

MATERIALS AND METHODS

Bioptsy specimens from 65 potients (33 males, 32 formstar, maint age, 61.2 years; maditin age, 62 years; uponing, 19-06 years) with continents HSV-1/2 and VZV were included in the starb (Table 3). All cases were retracted from the files of the Division of Demanded ongs, Department of Demanded on the files of the Division of Demanded ongs, Department of Demanded on the rate of the cases had been sent as remarkation cases. All fragrates were reviewed by at lean two and position demanded on the case of the cases of the cases were based on clinical, tittelogie, intraumbehotsement, materials, and follow-up fars.

Histology

All hopey apocurery were fixed in 10% buffered formula, routinely processed, and tabbequestly embedded at periffic. Sections were suited with hermoxylin and easiand analyzed for the presented of several incommoding features lated in Table 1.

Am | Yung Petrial . Volume 35, Number 1, Benney 2006

Free St. Department of Denomining Musical Entransity of Stan, Gran, Academ

Longity & Mil's by London William & William

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									47707			
Case No.	CB3	CB4	CDS	CD20	CD36	CD56	TIAL	CD123	Herpes Type	TCR	198	
-1	1111	**			+/-	+/-	++		ND	ND	ND	
.5	ND	ND	ND	ND	ND	ND	ND	ND	VZV	ND	ND	
8		4/-	+	+	11-	4/-	++	-	ND	ND	ND	
11	1.44	+	14-	+	4/-	7	9.6	-	ND	ND	ND	
15		4	++-	+	+/-	41-	++	100	ND	ND	ND	
16	-110	++	++	+		45	++		ND	ND	ND	
17	+++	414	++	+	+/-	14/	++	-de	ND	ND	ND	
81	+++	++++	++	+	+/-	++	++	-	ND	ND	ND	
24	3146	4-6	6-6	94.	-	4	44	-	ND	ND	ND	
25	+++	+			+	-	++	-	ND:	ND	ND	
27	1111	ND	ND	4.7	+	*	ND	ND	HSV-1/2	P	2	
28	+++	++		44		.+	+++	-	ND	ND	ND	
29	ND	ND	ND	ND	ND	ND	ND	ND	HSV-1/2 & VZV	ND	ND	
31	1111		++-	+-	+5-	+	9.1	ND	VZV	P	7	
34	ND	ND	ND	ND	ND	ND	ND	ND	HSV-1/2	ND	ND	
36.	ND	ND	ND	ND	ND	ND	ND	ND	HSV-1/2	ND	ND	
37	+++			+ 1	+/	3	***	4-7-	ND	ND	ND	
39	+++		++	+	=	+/-	+		NIX	ND	ND	
40	*	+>-		+	4/-	-	+	-	ND	ND	ND	
43	1.11	++	11	+	#1-	+	9.6	-	ND:	ND	ND	
44	ND	ND	ND	ND	ND	ND	ND	ND	HSV-1/2 & VZV	ND	ND	
46	-14	+	++	44	+	41-	++	-	HSV-1/2	P	. 7	
48	+++	++	++	+	+	4/-	++	-	VZV	ND	ND	
49	ND	ND	ND	ND	+1	ND	ND	ND	HSV-1/2	36	1	
.58	+++	-44	++-	-	(4)	4	++	+/	MD	800	ND	
53	+++	4+	++	+	++		++	ND	H8V-1/2	M	7	
34	+++	44	+	+	4/-	ND	ND	ND	HSV-1/2	P	2	
56	++++	ND	NID	an or		ND	ND	ND	HSV-1/2	ND	ND	
61	NID	ND	ND	ND	NEE	ND)	ND	ND	HSV-1/2	ND	ND	
62	NIX	ND	NI	ND	ND	NIX	ND	ND	HSV-1/2	ND	ND	
63	ND	ND	ND	ND	ND	ND	ND	ND	HSV-1/2	ND	ND	
64	ND	ND	ND	ND	ND	ND	ND	ND	HSV-1/2	ND	ND	

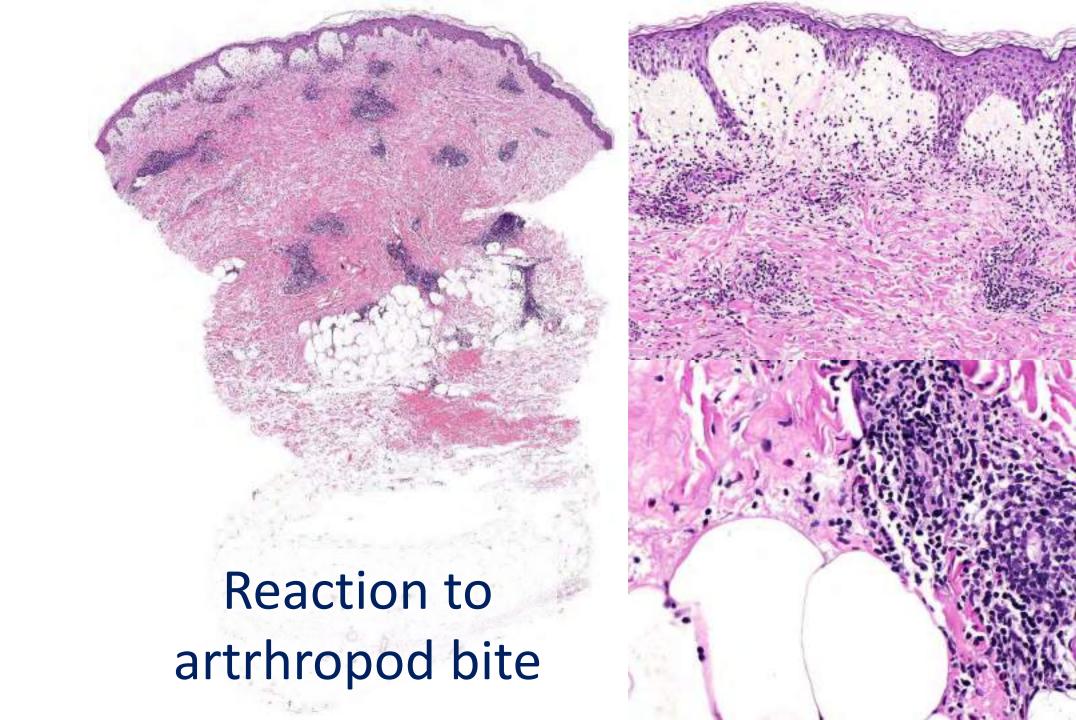
PCR

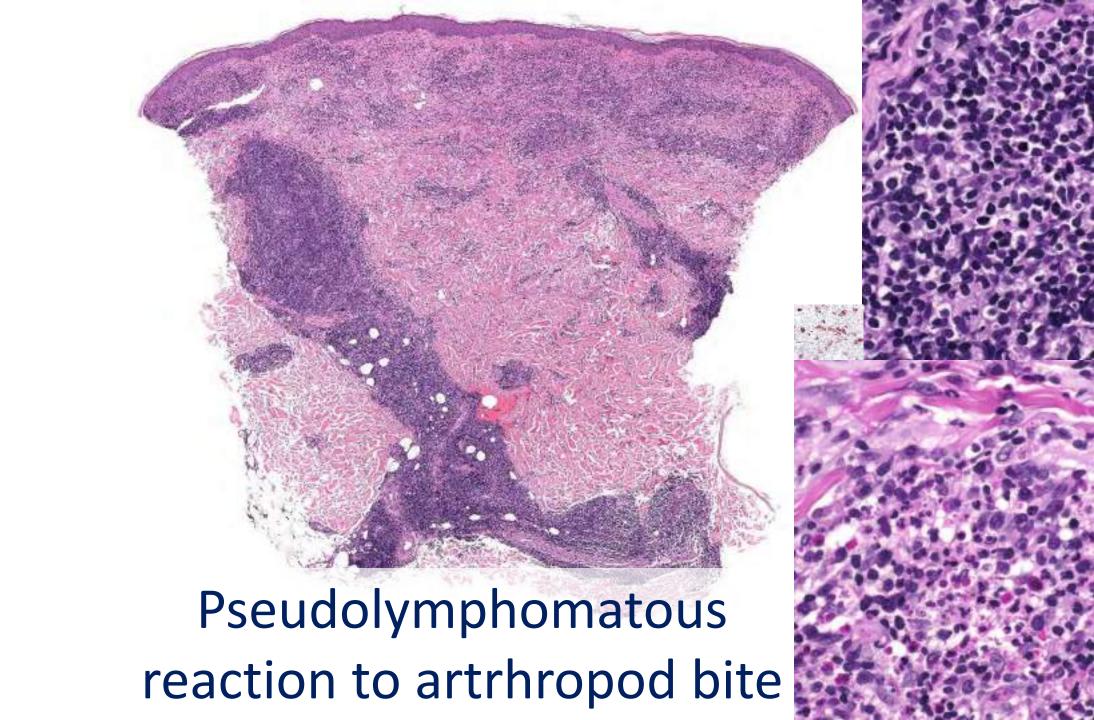
TABLE 2. Summary of Results of Immunohistologic and PCR Analyses

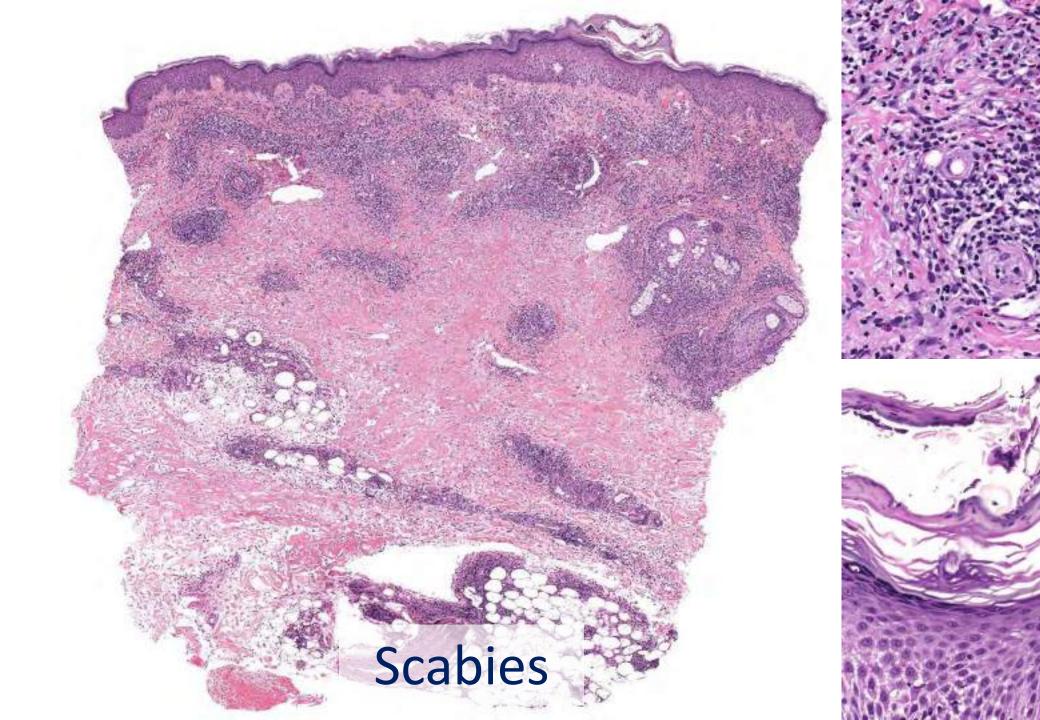
Immunohistochemistry*

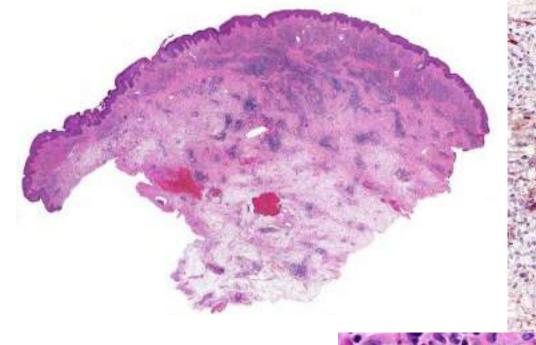
HSV-1/2, hepes simplex 1/2, VZV, variedla zoster virus, PCR, polymerate chain country. TCR, T-cell mospies: R polyclosal; M, monoclosal; ND, not determined country in a country of the country of the country of the country of the country cells.

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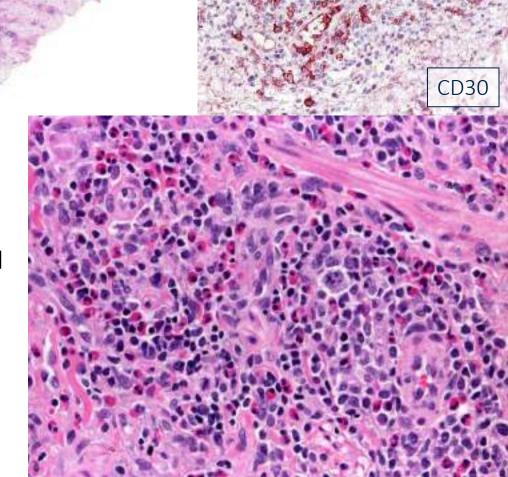


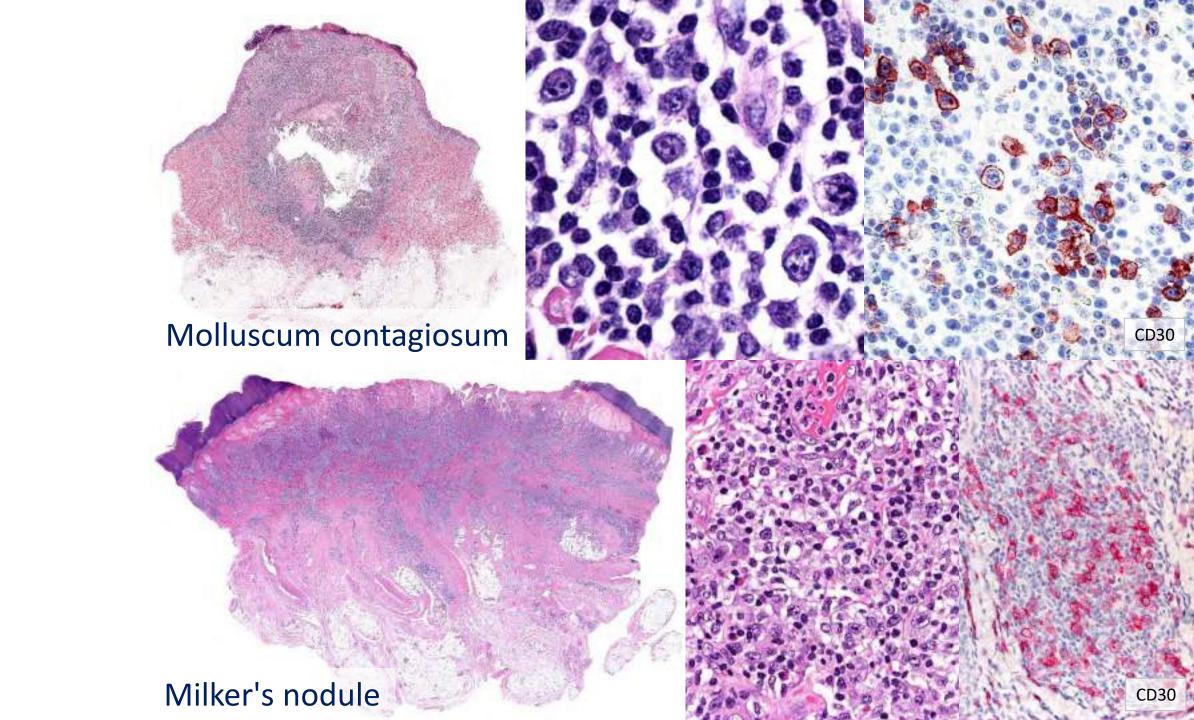


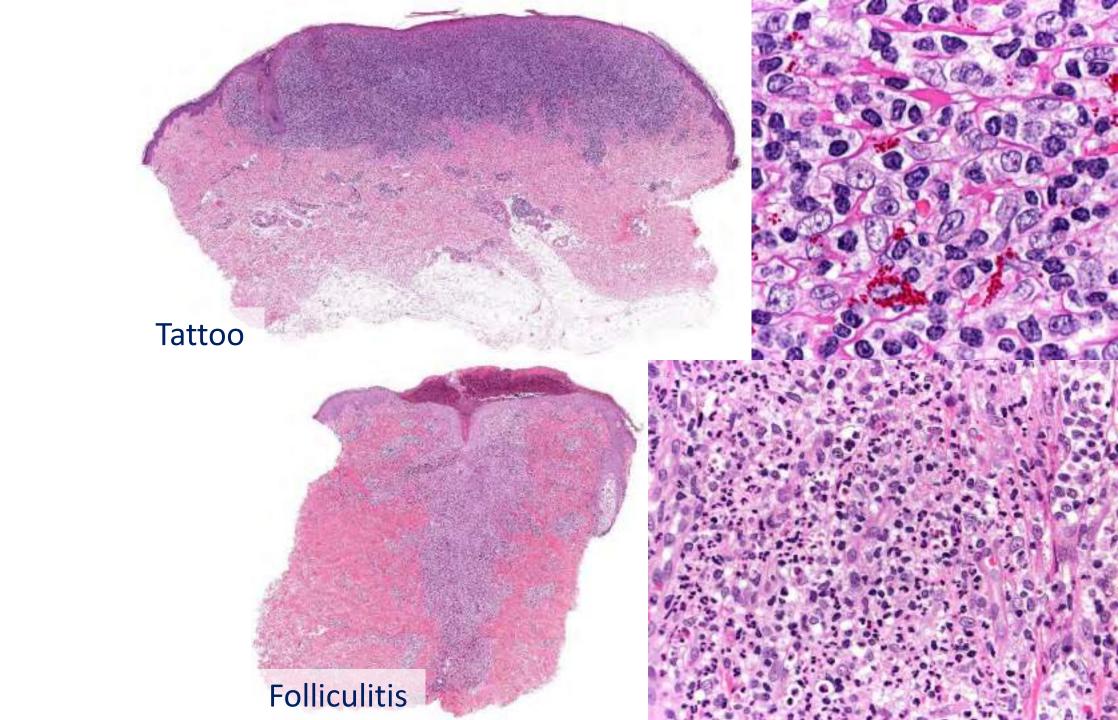


Nodular scabies

- Pruritic papules and small nodules with a predilection for the lower trunk, scrotum, and thighs; commonly observed in children
- May persist for several months and be not responsive to conventional treatment
- Mites are found in a minority of cases; it may represent a delayed hypersensitivity reaction similar to that found following other arthropod bites
- Activated, CD30+ cells may mimic lymphomatoid papulosis



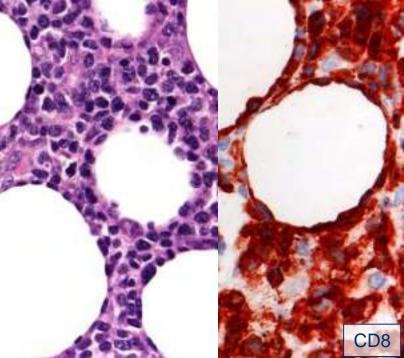




CD30+ pseudolymphomas – Histopathological clues

- Arthropod bites with CD30+ cells: infiltrate wedge-shaped, may resemble LyP type A but limited number of atypical cells; usually no clusters of CD30+ cells; sometimes central scale crust; intracorneal cuniculum in scabies (rare!)
- *Herpes infections:* necrotic keratinocytes within epithelial structures (sometimes confined to follicles, eccrine coils)
- *Parapox virus:* large areas of haemorrhage, dilated vessels, irregular epithelial hyperplasia with focal areas of necrosis
- Molluscum contagiosum: typical molluscum bodies (may be found only in deeper sections!)
- *Drug eruptions with CD30+ cells:* infiltrate superficial, may resemble MF but more "atypical" than early MF



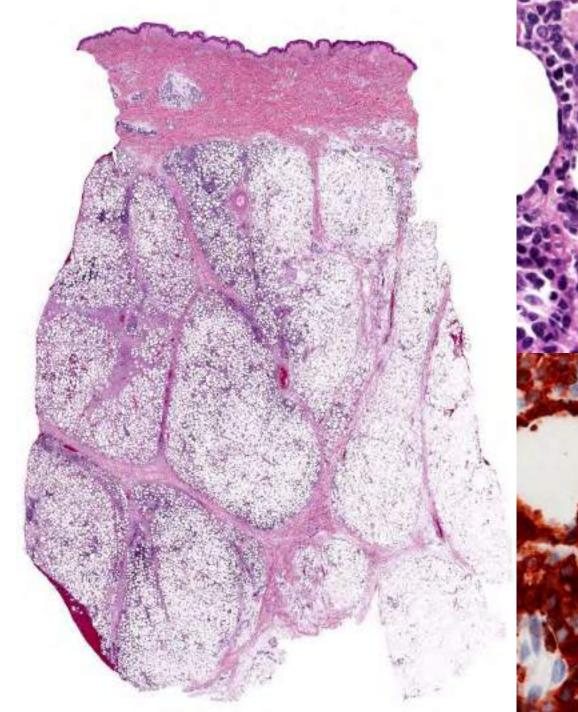


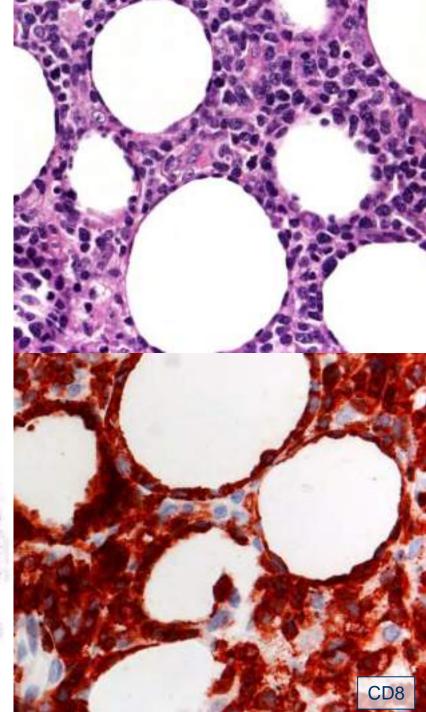
Subcutaneous panniculitis-like T-cell lymphoma

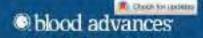
Exclusive involvement of subcutaneous fat (lobular panniculitis-like).

CD3+, CD4-, CD8+, CD56-, TIA1+, β F1+, TCR γ/δ -; monoclonal TCR genes rearrangement.

Mutations in *HAVCR2Y82C* associated with younger age, development of hemophagocytic lymphohistiocytosis, and short relapse-free survival.







Genetic profiles of subcutaneous panniculitis-like T-cell lymphoma and clinicopathological impact of HAVCR2 mutations

Jiwan Kiril, 1 Indon Lang ² Georgehan Mun ^{2,5} Chec/Line, 1 New Jeang Cha, ⁹ Young Ha Chi, ¹ Jin Man Kin, ⁸ Lin Ha Han, ⁸ Lin He Pak, ¹⁰ Author Cho, ¹¹ Young Hyoh Ko, ¹² Chan-Sik Pan, ¹² Heourgeong Go, ¹² Looyung Huit, ¹² Kwangsoo Kin, ^{10,12} Lind Yoon Reung Soor ^{12,16}

Key Points

- MAVC contract metation was found in 51% of SPTCL cases and was associated with younger upo, systems divess, and shurter 67S.
- HAVCR2 SPTCLs were enrithed in inflammatory agreeing, and HAVCR2 SPTCLs showed tigher COP4 expression in the microproviment.

Recent studies identified germline mutations in IFAVCAC fee coding T-cell immunoglobulin much It is a generic factor that predisposes to suboutaneous panniculkis-like I'-odi lymphuma (SI'1CL). However, the differences between HAVCK2-mutared GRAVCK2****) and HAVCK2 wild-type CMAPCAS¹⁰⁰/SPTCL a rumain unclear. A nation wide cohort of SI parters; with SPTCL diagnosad at 8 Karean institutions was established. Whole-exome sequenting and RNA-sequenting were performed on Ripatients in the discovery set. In the validation set, targeted gene sequencing or direct sequencing of HAVGR2 vgs, performed, Of (9 patients with available HAVCR2 status, 23 of homophagocytic lymphohiotiocytosis or homophagocytic lymphohiatiocytosis-like systemic Binass (P < .801), and short religion-free survival (RPS) (P - .02%. Most trusted genes in SPTCLs were involved in immune responses, epigenetic modifications, and cell signalog. Munition in DNETSD, PLASS, and EMFIED were more frequent in HANCEST SPECIA. At the gene expression: level, FANDCR2***** SPTCTs overe enriched in genes involved in E.6-JAR-STATK signaling and in. names receives factors, signaling via NF-18. CCM was significantly apprepalmed in HAVCR2^{NT} SPTETs berhat the missenger RKA level and at the protein level. We usuablished a risk stratification system for SPECI, by integrating clinical and histopachological features, including ago and HAVER mutation status. This risk stratification system was strongly associated with RFS (9 = .031), to conclusion, the PANY/XX^{TSST} mentation was communical Korono patients with SFFC1. and was associated with unique clinicopathological and genetic features. Combining clinicopathological parameters could aid in predicting prognosis for patients with SPICL.

HAVCR2^{Y82C} was associated with younger age, development of hemophagocytic lymphohistiocytosis or hemophagocytic lymphohistiocytosis—like systemic illness, and short relapsefree survival (RFS).

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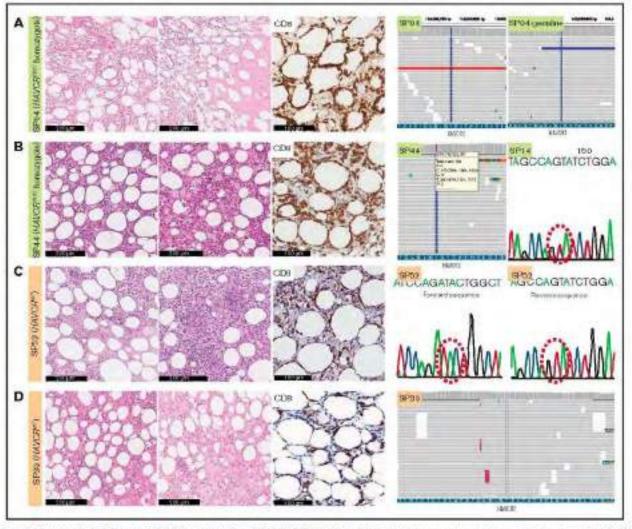
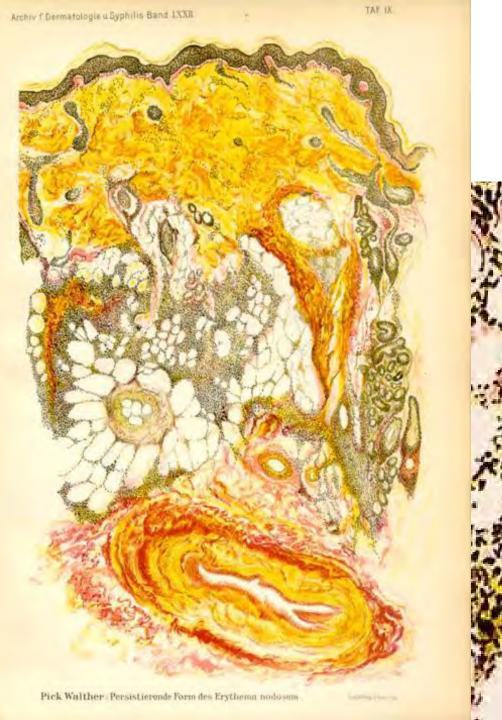


Figure 1. Histopathological features of SPTCLs and detection of HAVCR2**** mutations. (A) Excisional histopay specimen of a 16 year old himselpotium with an SPTCL. [SPG4] arbitrarily disprove immangely COS-positive lymphocytes along with preminent necessis. This potient was confineed by using WES to lace a germline because germline because an HAVCR2**** mutation. (B) Lipogranulorations in lumination was observed in a 64 year old harshopation (SP44), and TGS revealed harshopages HAVCR2*** mutations, which could be information on cluster president policy (C) A 45 year old formin potient (SP52) with the HAVCR2*** garacters and granulorate harshop and president policy (SP52) with the HAVCR2****.

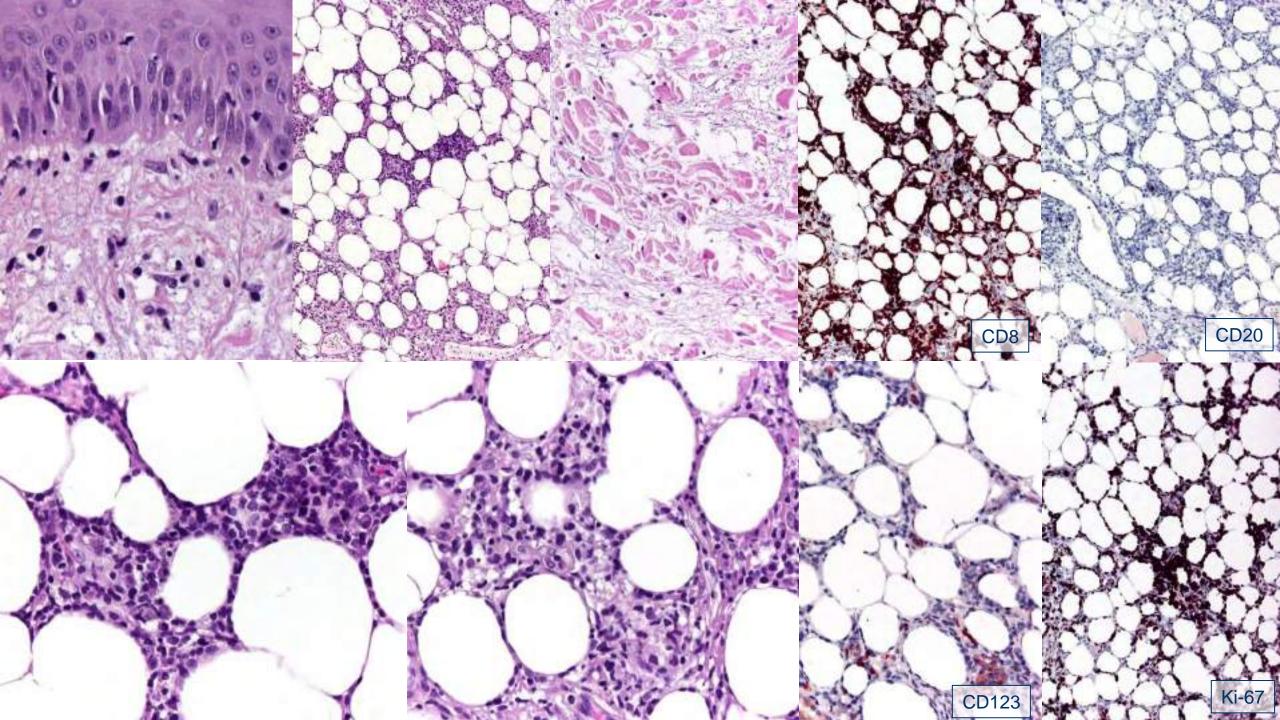


Pick W.
Persistent form of erythema nodosum
Arch Derm Syph 72, 1904

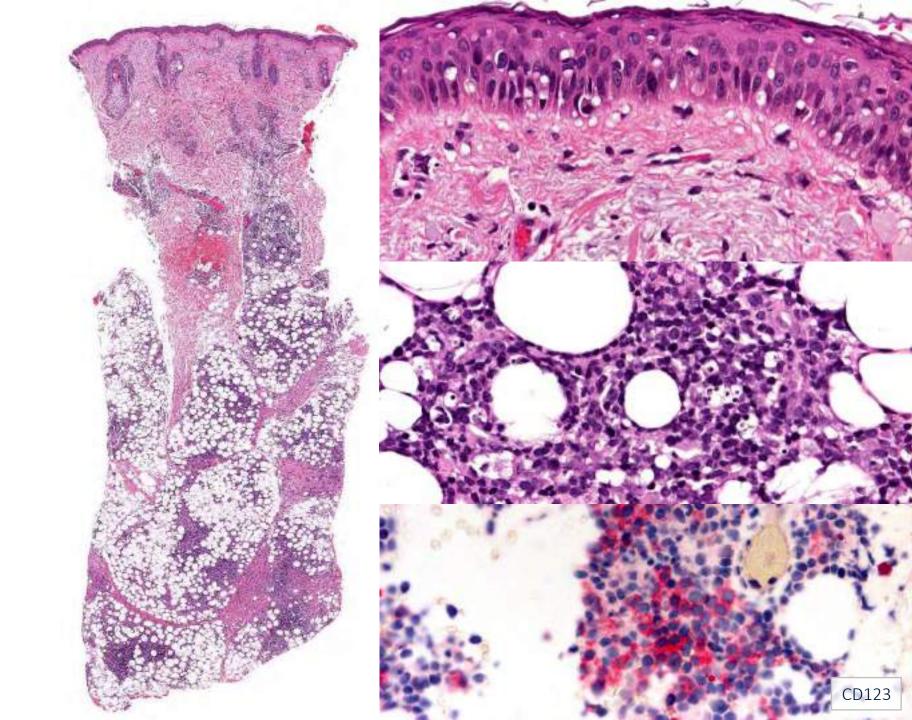


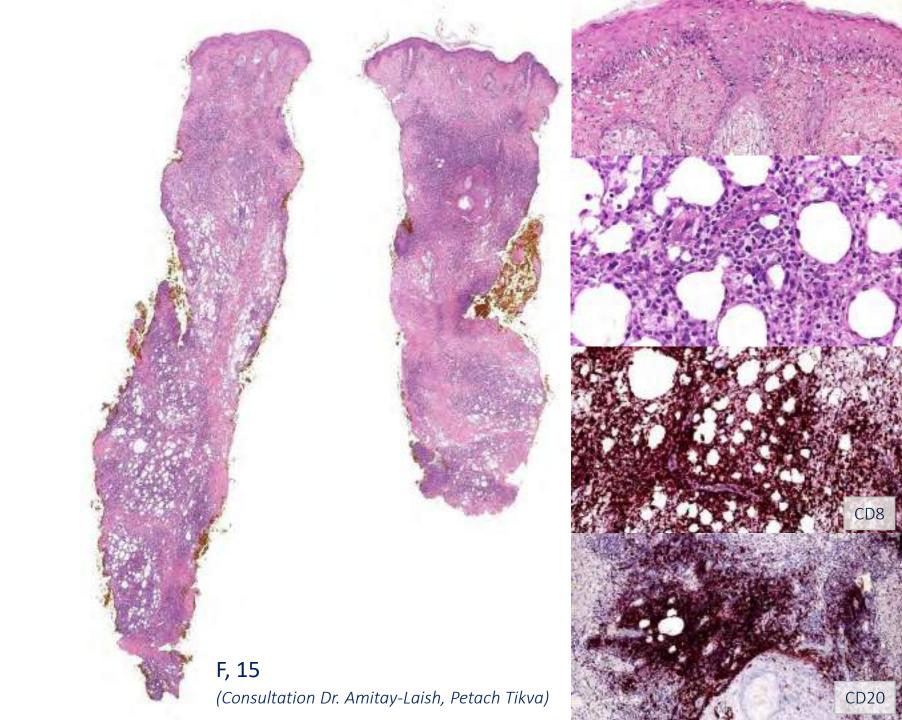
M, 36. Recurrent subcutaneous nodules, some with atrophic scars, for the last 14 years.











Journal of Cutaneous Pathology

Lupus erythematosus panniculitis (lupus profundus): Clinical, histopathological, and molecular analysis of nine cases

Background: The diagnosis of lupus erythematosus panniculitis (LEP) may be very difficult in cases in which involvement of the subcutaneous fat is the only manifestation of the disease. The main differential diagnosis is subcutaneous panniculitis-like T-cell lymphoma (SPTCL).

Methods: We performed a retrospective study reviewing the histopathologic features of 11 biopsy specimens from nine patients with LEP (M: F=2:7; median age: 48 years; range: 20-71 years). **Results:** Histopathologically, all biopsies revealed a lobular panniculitis, with concomitant septal involvement in 82% of them. Dermal changes included the presence of superficial and deep infiltrates (82%) and mucin deposition (73%). The majority of cases (73%) presented also some form of epidermal involvement. The subcutaneous infiltrate was composed of lymphocytes in all cases, admixed with plasma cells in 91% of cases. Lymphoid follicles with reactive germinal centers were detected in 45% of cases. Immunohistochemistry showed a predominance of α/β -T-helper and cytotoxic lymphocytes in 80% of cases admixed with B lymphocytes. The polymerase chain reaction analysis of the T-cell receptor (TCR)- γ gene showed a polyclonal smear in all cases.

Conclusions: Our study shows that the most useful histopathologic criteria for distinguishing LEP from SPTCL are the presence of involvement of the epidermis, lymphoid follicles with reactive germinal centers, mixed cell infiltrate with prominent plasma cells, clusters of B lymphocytes, and polyclonal TCR- γ gene rearrangement.

Massone C, Kodama K, Salmhofer W, Abe R, Shimizu H, Parodi A, Kerl H, Cerroni L. Lupus erythematosus panniculitis (lupus profundus): Clinical, histopathological, and molecular analysis of nine cases. J Cutan Pathol 2005; 32: 396–404. © Blackwell Munksgaard 2005.

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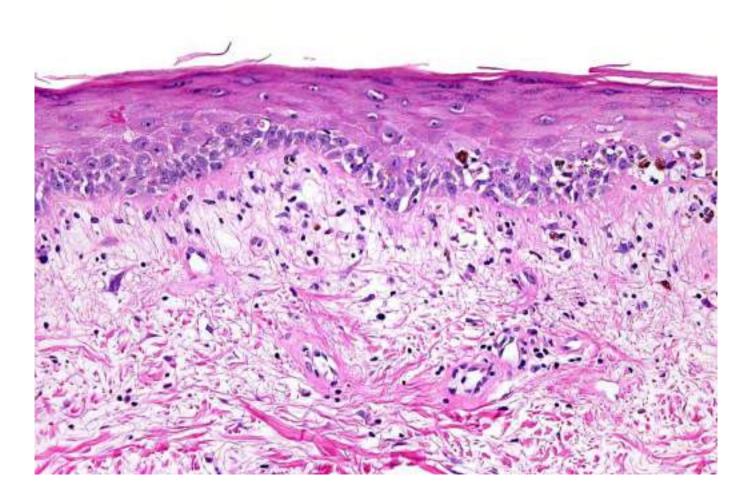
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Lupus erythematosus panniculitis (LEP) (lupus profundus) is defined as a specific involvement of the subcutaneous fat in patients with lupus erythematosus (LE). It is a rare manifestation of the disease, occurring approximately in 1–3% of patients with cutaneous LE. ^{1,2} It may be observed in patients with discoid lupus erythematosus (DLE) or systemic lupus erythematosus (SLE)^{3–5} or as an isolated phenomenon without systemic or other cutaneous findings.³ The diagnosis of LEP may be especially problematic

in cases in which the involvement of the subcutaneous fat is the only manifestation of the disease. Especially differentiation from subcutaneous panniculitis-like T-cell lymphoma (SPTCL) may be extremely difficult, and recently, Magro and coworkers suggested that LEP and SPTCL may belong to a spectrum of disease and introduced the term "subcutaneous T-cell lymphoid dyscrasia" to encompass these entities.

We performed a retrospective study on the clinical, histopathologic, and molecular features of nine



Epidermal involvement: 73%

Panniculitis in lupus erythematosus (lupus profundus)

- Patients with cLE may show prominent involvement of the subcutaneous fat (lupus profundus)
- May be concomitant to more conventional lesions of cLE (particularly CDLE but also SLE)
- The overlying skin may show features of cLE
- Histopathologically, pattern of a mainly lobular panniculitis with variable involvement of the septae ("mixed panniculitis") and with hyaline necrosis of the fat lobules
- Distinction from SPTCL is traditionally considered difficult; some biopsies show overlapping histopathological features of the two entities

Subcutaneous Panniculitis-Like T-Cell Lymphoma Versus Lupus Erythematosus Panniculitis: Distinction by Means of the Periadipocytic Cell Proliferation Index

Panitia Săthinanuevan, MD,* Penvadee Patianaprichakul, MD,7 Jimpa Treetipeath, MD,* Tavatchai Pongprunipun, MD,* Sanya Sukpanichanet, MD,* Laura B. Piacus, MD,2 and Timothy H. McCalman, MDZ

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Abstract: The distinction between inhermacous promodifie-like T-udl Employer (SPTCL) and logor enthronouses (CE) pursionhis is remobilly malerging. Rimmig by lymphosyes with mclosered Ki-07 cell multireation index has been forwarded as a potential diagnostic freding in hopsics of SPICL but has not been represely assurand with biopsies from persons with LEpopularitis. Nustrea and 17 symples of SPTCL and LE paniloslife, respectively, were evaluated for puriodipocytic meaning by Applicaytes expossing \$4-07, COS, and JPU and the attributes instended with Life including chairs of CD123-positive cells. The identification of partial operation overing using Ki-67, CDA unit \$61 hard sensitivity of 1996, 2000s, and 895% and specificity of 100%, 52.9%, and 88.2%, improtively (P < 101). CD123positive cells were in both distraters. Lit-like histogethalogy was connecely magazined in SPICC, in poschesia, in pleasal Ki-67 call problemature index with terratory a muttal for distinguishing SPTCL from LE passiculties Norshly, using fromocs of LE prominabilities our above by responsible of the SPTC'L.

Key Weeth: subcommone presidents like 1-cell (replane), teper or themstorn pumisable, penaltycette manag, Ki-67 (MB-1), CD123

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INTRODUCTION

Periodipscytic rimining, defined as a string of lymphocytes that entircle individual adoptoynes, is considered a tignificant degreesic flating but it not a publicytomorie, feating in subcutareous permiculitivities. F-cell lymphorus (SFFCL) because the feature can be seen in other cataneous lymphoruse' and is some forms of jumphocytic parametric, or particular legac crytheriatrons (LE) permiculities, in often dathening. As an illustration of this difficulty, cases

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On malties declar as conflicts of interest.

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with overlapping features of both of these critics base bean described. [57]

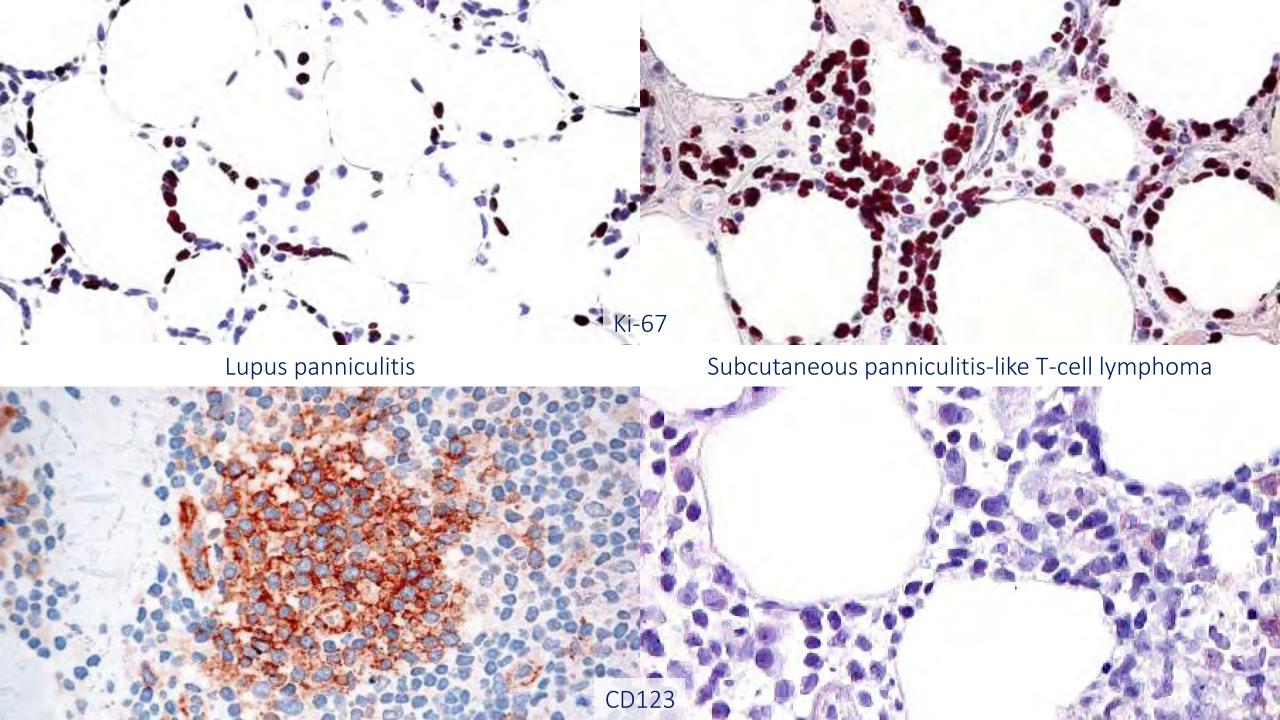
SPICI, is defined by the World Health Organization (WHO))the kinneeus Organization for Research and Treat-

Immunoreagents	SPTCL (n = 19)	LE (n = 17)	P	Sensitivity (95% CI) (%)	Specificity (95% CI) (%)	PPV (95% CI) (%)	PLR (95% CI)
Ki-67 periadipocytic rimming, n (%)							
Positive	15 (78.9)	0 (0)	< 0.001	79 (54.4–94)	100 (80.5-100)	100 (-)	
Negative	4 (21.1)	17 (100)					
CD8 periadipocytic rimming, n (%)							
Positive	19 (100)	8 (47.1)	< 0.001	100 (82.4-100)	52.9 (27.8-77)	70.4 (58.9-79.7)	2.1 (1.3-3.5)
Negative	0 (0)	9 (52.9)					
βF1 periadipocytic rimming, n (%)							
Positive	17 (89.5)	2 (11.8)	< 0.001	89.5 (66.9-98.7)	88.2 (63.6-98.5)	89.5 (69.6-96.9)	7.6 (2-28.2)
Negative	2 (10.5)	15 (88.2)					
CD123 positive in clusters, n (%)	50 NO.	-300 -300					
Positive	7 (36.8)	12 (70.6)	0.04	70.6 (44-89.7)	63.2 (38.4-83.7)	63.2 (46.9-76.9)	1.9 (1-3.7)
Negative	12 (63.2)	5 (29.4)					

protocol at the University of California, San Francisco (OCSF #1) (4000)

A search of the pathelogy tiles of the Department of Pathelogy, Paralty of Medicine Soring Heaptal, Medicida University was performed from Researy 1999 to December 2009 for cases of SPTCL and LE promodifies. The saidy occasion of 19 SPTCL and 17 LE parametries speciments aminosed from 16 and 17 patients, respectively.

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Lupus panniculitis

- Mostly lobular paniculitis
- Prominent necrosis
- Nuclear debris, degenerative changes
- Rimming of adipocytes by different cell types
- Nodules of B lymphocytes at the periphery of lobules
- Germinal centers frequent
- Mixed cell infiltrate; plasma cells frequent
- Fibrotic, enlarged septae
- Proliferation (Ki-67) low
- No proliferation "rimming"
- Clusters of CD123+ cells
- TCR: polyclonal

Subcutaneous T-cell lymphoma

- Mostly lobular panniculitis
- Prominent necrosis
- Nuclear debris, degenerative changes
- Rimming of adipocytes by atypical lymphocytes
- B lymphocytes few or absent
- Germinal centers absent
- Monomorphous lymphocytes; clusters of atypical cells
- Septae minimally or not enlarged
- Proliferation (Ki-67) high
- Proliferation "rimming"
- No (or small) clusters of CD123+ cells
- TCR: monoclonal

ORIGINAL STUDY

Subcutaneous Panniculitis-Like T-Cell Lymphoma With Overlapping Clinicopathologic Features of Lupus Erythematosus: Coexistence of 2 Entities?

Laura B. Pineus, MD,* Philip E. LaBoit, MD,* † Timothy H. McCalmont, MD,* † Roberto Rievi, MD, ‡ Carlo Buzio, MD, § Lindy P. Fox, MD,* Fergus Oliver, MD, † and Lorenzo Cerroni, MD

Abstract: We observed 5 patients with solutionarie paragraphics like T-red templature (SPTCL) who were unmost, to that they also edulated frames of hora eryticinetiess (LE). This observation is in keeping with a recent wish that reported on vicroised rate of nationaries disease, including automic lapse sepherorassis (NLE), uning priors with SPICL. In all more extincts edicating SETCL included an addition of happinoses with pleaninghic coclei analytes utanimeas labels solititus a graniste bott. (CDS*CDS*BEF*) immunostenativo. Additionally, is bigh pro-Efecution intrinsed a menocharal 1-cell economy year management were observed in reast ower. The manifestations at LE in these nations included a spectrum of clinical and bistoperhalisated shnormalities. Chipal maniforations of LT included, in some patients, morphologic evidence of lapus enthemotors, proximilitis (LEP) with suberbarrow quittles that bested with lipsuboutly in the face. in addition, all the potents individual resolution and the extraormerorus and-segre abnormalities som in parients with SUE, soft 2 parients having sufficient findings to meet American College of Rheumatollogy origins for SLE. Histopollokogical evidence of LE architect viscolar charge at the demail epiderral interface in 3 patients, 2 of relies ober shared grantitial deposition of moses in the reticular draws. One of these muleuts plan had findings of LEP in the inbcommunes friends; with chosens of \$17257. It raffs periodly account. within personal contain. In 2 patients in which reaffer the spidentes. nor denote was smallstile for review, histoporthological festures of LE arriaded to one patient, a few small charges of CDC15* plantage/end dealeric cells within the educate time and in the other ration. a politic discr instructionness to their land or chirally uninvolved and trainml shar. Our unity shows that name patients show overlap between SPIC3 and LE. We appear that those paints may after from both diseases uncontinuity. Furtienness, patients with EE, particularly EEE should be accommed for evolution.

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INTRODUCTION

A rough large European Organization for Research and Instances of Caster study of 63 patients with subcurfaceous pensionistics for local Symptoma (SPECL) indicated that 19% fast or associated automatume disease, including 4 with systemic lagus erystemisones. CELIL¹ We encountered 5 patients in research pension or at concatention who withhout typical features of SPECL but were around, in that they also had manufactations of lagus synthetimison (LE₂ The features of LE included a spectrum of findings from typical clusted numbers of spectrum of findings from typical clusted numbers are produced of SEE, to findings of LE seen on histographical sections from skin Nomice.

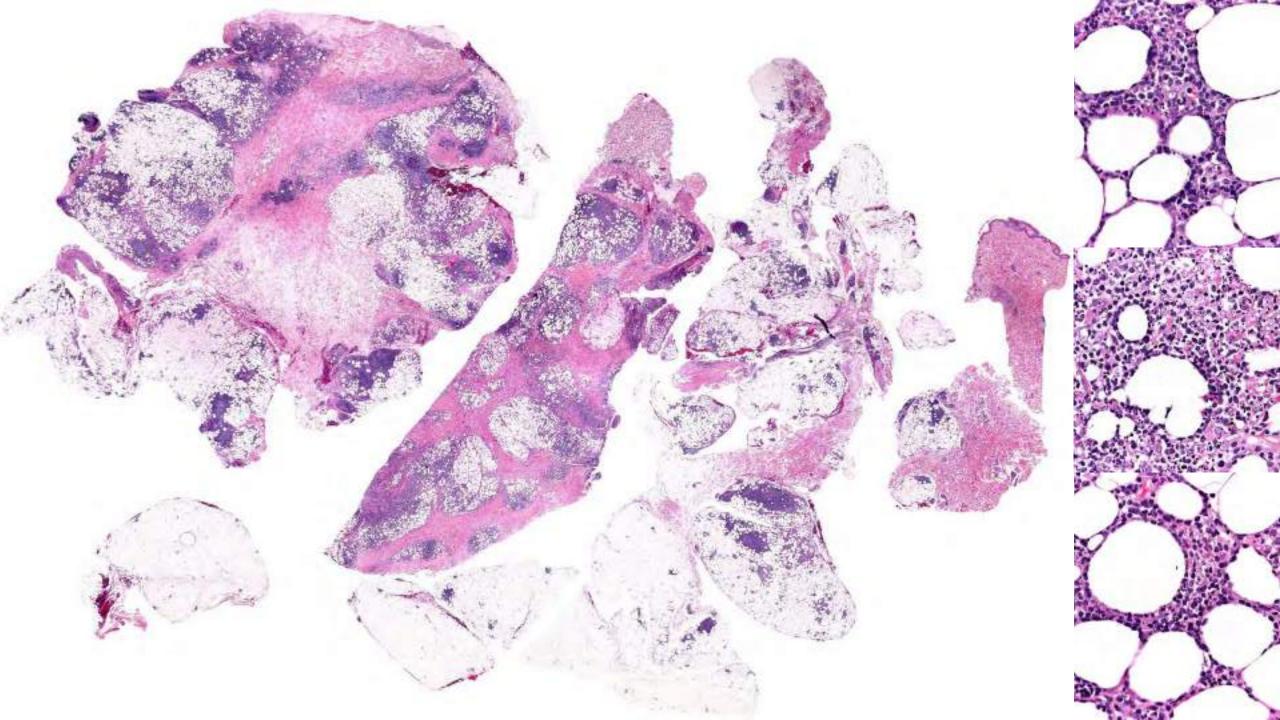
Reports addressing a relationship between SPICE, and LF bave finance primarily on delineating histographological and clinical festives that distanguish SPTCL from lapus erythematowes parmiculate (E.E.P).2 " Indeed, it can be very challenging to differentiate between SPECE and LEP on histoparhological grounds. Microscopically, LEP is typically characterized by a hypphocytic infiltante within subcutaneous lobules with little septal involvement, for necroses, and the presence of Instigestes containing terromitactic dates although these features can also be seen in SPYCL. Microscopic findings that can belo to dodingwish LEP from SPTCL include features typical of entancious LE in the epidernia and dentia, including vaccorbic clunge at the decreal-enidentual arrection, purisdiscual lengthocytic infiltentes, and measured deposition of much in the entirelia deemis. The presence in the subcutis of byrighaid Willicks with reactive permittal octoors, clusters of B lymphocytes, and a mixed suffirms with prominen plasmi cells also favors LEP* A recent by clued and plue to LEP is presented of charges. of CD125° plostostystid dendritic cells (pDCs) within the subamasson binds and if mesens within the donnal infiltration

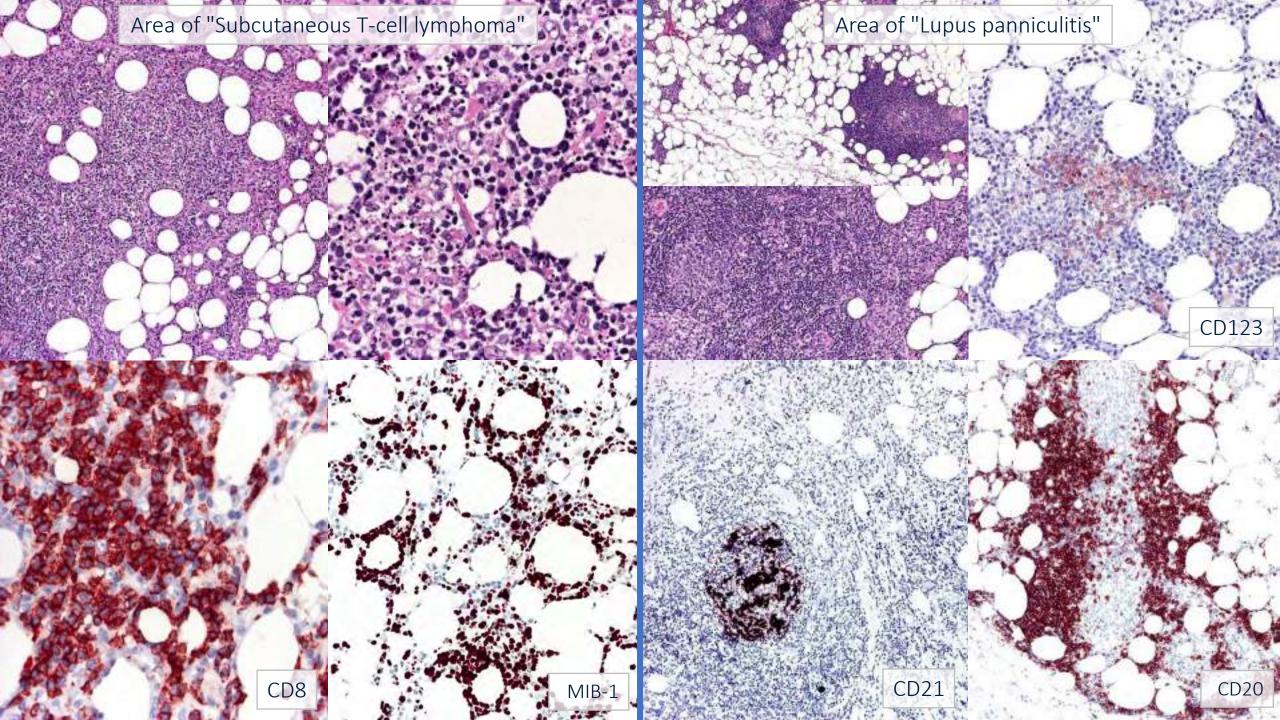
Am / Diamintopolina * Visione 31, Romber 6, August 2009.

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	Patient								
	1	2	3	4	5				
Age at diagnosis of SPTCL (yrs)/sex	52/F	22/M	22/F	20/F	20/F				
Age at first presentation of clinical lesions (yrs)	37	20	NA	NA	15				
Follow-up (mo)	A— (18): clinical remission after treatment with hydroxychloroquine 200 mg/d and methylprednisolone 1 mg/d	A— (19): clinical remission after treatment with hydroxychloroquine 200 mg/d	D+ (41)	NA	A= (30): clinical remission after treatment with vorinostat and currently on low- dose prednisone				
Location/morphology of skin lesions	Extremities and face/ "panniculitis" with evolution in lipoatrophy	Bilateral cheeks/facial swelling with evolution in lipoatrophy	Extremities and face/ "panniculitis" with evolution in lipoatrophy	Extremities/ subcutaneous lesions	Abdomen and extremities/ subcutaneous nodules; focal erosions				
Clinical features of LE	Skin lesions eventuated in lipoatrophy involving the face	Skin lesions eventuated in lipoatrophy involving the face	Skin lesions eventuated in lipoatrophy involving the face	dsDNA+	Episodic fevers				
	ANA+	Episodic fevers	ANA+ 1:2560		Elevated ESR				
	dsDNA+ (titer 1:80)	Lymphadenopathy	dsDNA+		Coombs-positive hemolytic anemia				
	Interstitial nephropathy with proteinuria	Anemia	Episodic fevers		IgA nephropathy				
	Anemia	Neutropenia	Renal failure requiring dialysis		Bilateral parotitis				
	Anti-Ro+ (meets ACR criteria for LE)		Coombs-positive hemolytic anemia (meets ACR criteria for LE)		ASMA + (1:40 titer)				
Histopathological features of LE seen	DIF: junctional deposits of IgM and IgG on	A few small clusters of CD123 staining pDCs	Interface dermatitis	Interface dermatitis	Interface dermatitis				
in skin biopsies	clinically uninvolved			Mucin deposition	Mucin deposition				
	and lesional skin			Substantial CD20 ⁺ B-cell population, partially arranged within germinal centers	DIF: junctional deposits of IgG and C3 on lesional skin				

A—, alive without signs of SPTCL; Anti-Ro, Anti-Ro antibodies; ASMA, anti-smooth muscle antibodies; D+, dead of hemophagocytic syndrome with SPTCL; ESR, erythrocyte sedimentation rate; F, female; M, male; NA, not available.





Lobular Panniculitic Infiltrates With Overlapping Histopathologic Features of Lupus Panniculitis (Lupus Profundus) and Subcutaneous T-cell Lymphoma

A Conceptual and Practical Dilemma

Francesca Basisio, MD,*+ Sebustiana Bai, MD,‡ Valentina Caputo, MD,§ Concetta Chlorelli, MD, § Fergus Oliver, MD, ¶ Roberto Ricci, MD# and Lorenzo Cerroni, MD*

Abstract: Superconsons particulate-like T-call lymphoms (SPTCL) is characterized by pouniculate infiltrates that may be difficult to distance in from inflantations disorders, particularly tupus envikematosas profinidas (LEP). We report on 11 patients (M/F = 550; minitian upor 49 y; sumper 20 to 75 y) producting with totally pagestile inflences showing histopathologic features of both SPTCL and LEF in different parts of the same biopsy specimen. The areas showing agreets of SFECL revealed dense infiltrates of small and medium-sized, atypical off T-cytotoria. tymphorytes with foral rimming of the adipocytes and tight profiferation. In other areas the authoric was composed of undales of B lympiocytes arranged characterizedly at the escriptury of the fits jobtain and in the segra and showing a law profference into CD123-peakive plamposysist dauditie selfaarranged in small clusters could be observed in J ones. One nieservation gains are important question conversing the relationship between SPTCL and LEP. A simple district overlap of 2. sont need pathologies some unlikely, as we could observe those noticeal features of 31 cases, couch those that mere chance would justify. Three other hypotheses may explain the featmesobserved in our partence (1) those are examples of SFTCL with fored histologic features mimicking those of LEP: (2) these seeaccomplist of LEP with focal anypical histologic features numseleng than, of SPTCL; (3) SPTCL and LEP may represent 2 ergly of a spectrum, a hypothesis that may be supported by the frequent association of the 2 diseases.

From the * Remark Unit of Demandagemology, Organization of Overmotivings, Markad Constraint of Gree, Cree, Assesse (Organization) of Sergood Scientis, Miland-Bottom University, Monac, Department of Federics, S. Classe Beognal, Green, W.D. Assisman Participies, Ovp. M. Mildon, Milanos (Demandar of Paltology, S. Martino Hospital, Britans, Oldic of Palto-logy, S. Martino Hospital, Britans, Oldic of Palto-logy, C. Osyanish Hospital of Porma, Porma, Lody, and *Louklond Scin and Carrier Frankholms, Assishani, Sew Joseph

Confries of Interest and Science of Frending: The authors into Gederald, that they have no significant reliable reliefs with, or financial racins to, any commercial comportic posterioring to this article.

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Key Words anterraceous possiculos-liku I-cell (turrhouslapus crystematieus, lupus parnietilius, lupus profundus, mytical httphocytic lobulor punneulius.

Little J. Stong Forthol 208:5:39:206-211)

ubcitamous sunnicultis-like I-cal hymhoma J CSPTCL's is defined in the World Health Organization (WHO)-European Organization for Research and Treatment of Canon (BORTC) dustification of primary cutaneous lymphomas and in the 2006 WHO obssilication of humans of humatopoietic and lymphoid tissues as a primary communes lymphones of Tredl Integer that involves the subcutameous tissue, expressing an a/B cyletoxic Tseell phenotype. 1,2 Lupus enthematosus profundos (I, EP) is abarrenorized by a lobaler panniouslins with aspects that may mimic those of SPTCL' and represents its most important differential diagnosis. A further problem is represented by the knowledge that is a distinct proportion of cases SPTCL is associated with various autoimmune disorders, 1.4 and that an interlace deraintitis has been observed in a minority of SPTCL cases. Thus showing that overlapping features between these 2 conditions may exist. However, historathologic analysis of army given biogen is aimed at differentiation of the 2 discases, and coerlapping histopathologic features on the some bropsy specimen have not been described. We report on 11 patients with localar panniculitic infiltrates showing fishings of both SPTCL and LFP and discuss the implications of this unusual finding.

PATIENTS AND METHODS

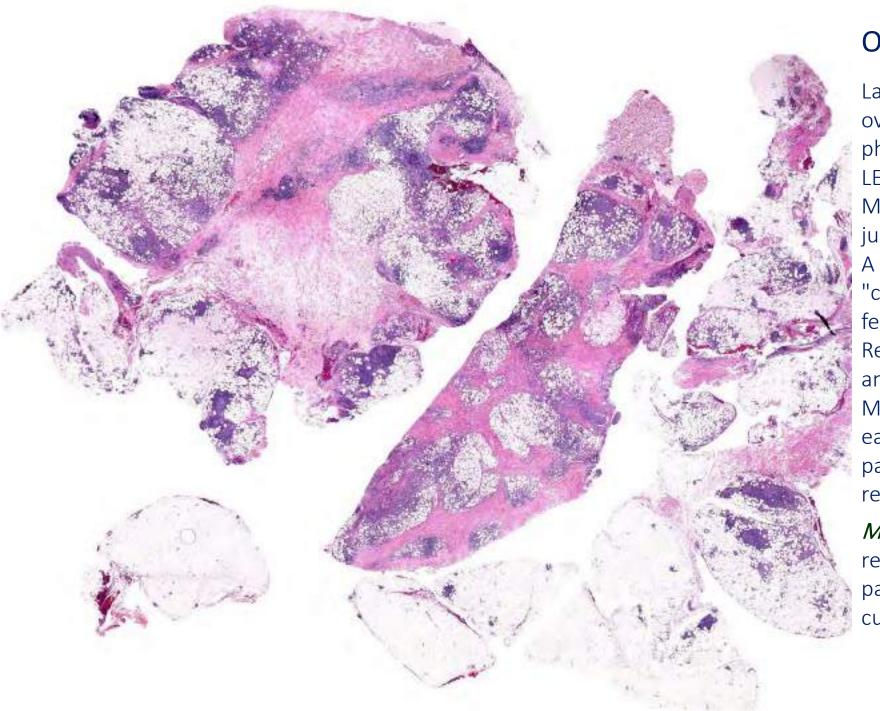
Patients

Data from 11 patients with overlapping histopathologic features of SPTC3, and LFP in the same buony specimen were collected from the files of the Research Unit Dermatopathology, Department of Dermatology, Medical Linucristy of Grae, Austria, When available, clinical and follow-up dara were obtained from the referring physicians. The study was approved by the Films Committee of the Medical University of Grae

11 patients

(M:F=5:6; median age: 49 y; range: 20 to 75 y)

A simple chance overlap of 2 unrelated pathologies seems unlikely, as we could observe these unusual features in 11 cases, much more than mere chance would justify. Three other hypotheses may explain the features observed in our patients: (1) these are examples of SPTCL with focal histologic features mimicking those of LEP; (2) these are examples of LEP with focal atypical histologic features mimicking those of SPTCL; (3) SPTCL and LEP may represent 2 ends of a spectrum, a hypothesis that may be supported by the frequent association of the 2 diseases.



Overlap SPTCL – LE panniculitis

Large biopsy specimens may show overlapping histopathologic and phenotypic features of both SPTCL and LEP.

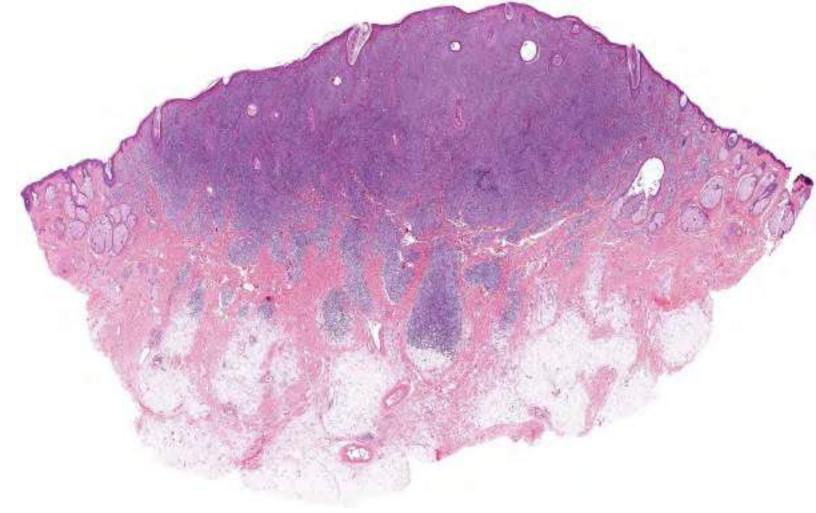
More cases than mere chance would justify.

A proportion of patients with "conventional" SPTCL shows clinical features of LE.

Relationship between the 2 diseases (if any) yet unclear.

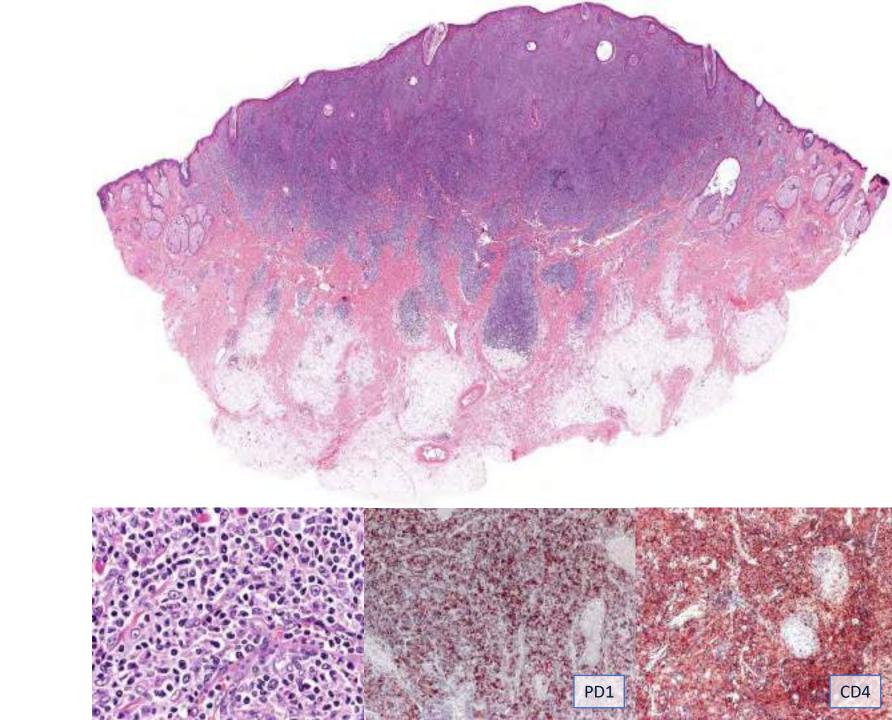
May represent cases of "atypical" LEP, or early stages of SPTCL developing in patients with LEP, or SPCTL and LEP may represent to ends of a spectrum.

My current approach: these cases represent examples of "atypical" LE panniculitis and do not progress to clear-cut SPTCL.



Cutaneous small-medium pleomorphic CD4+ T-cell lymphoproliferative disorder Solitary lesion (essential criterion) located mostly on the face. Mixed infiltrate with predominance of CD4+ lymphocytes with $T_{\rm FH}$ phenotype (PD1+).

Large cells should not exceed 20%; Ki-67 should be <30%. Indolent behavior, excellent prognosis.



Primary Cutaneous CD4* Small-/Medium-Sized Pleomorphic T-Cell Lymphoma: A Cutaneous Nodular Proliferation of Pleomorphic T Lymphocytes of Undetermined Significance? A Study of 136 Cases

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Solitary Small- to Medium-Sized Pleomorphic T-Cell Nodules of Undetermined Significance: Clinical, Histopathological, Immunohistochemical and Molecular Analysis of 26 Cases

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136 patients; 133 solitary lesion, 3 multiple (2 or 3 lesions)

Follow-up: 45 patients (median FU time: 63 months; range: 1-357 months)

41 CR (including 2 with multiple lesions)

4 persistent disease (2, 2, 4, and 16 months, respectively)

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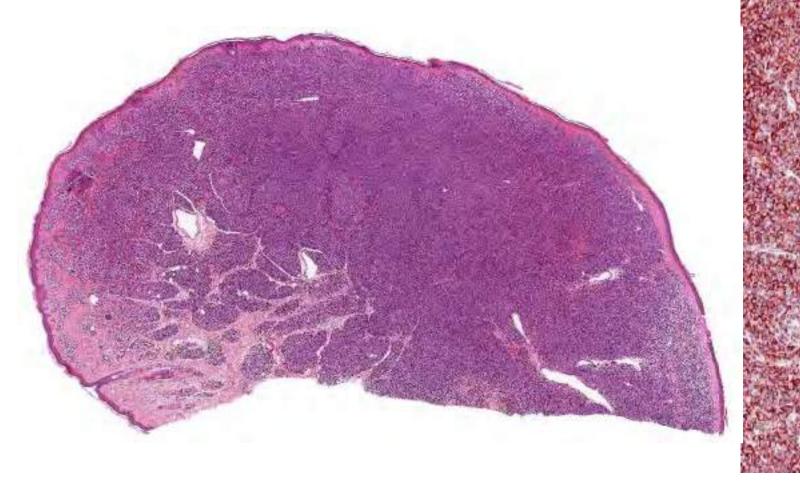
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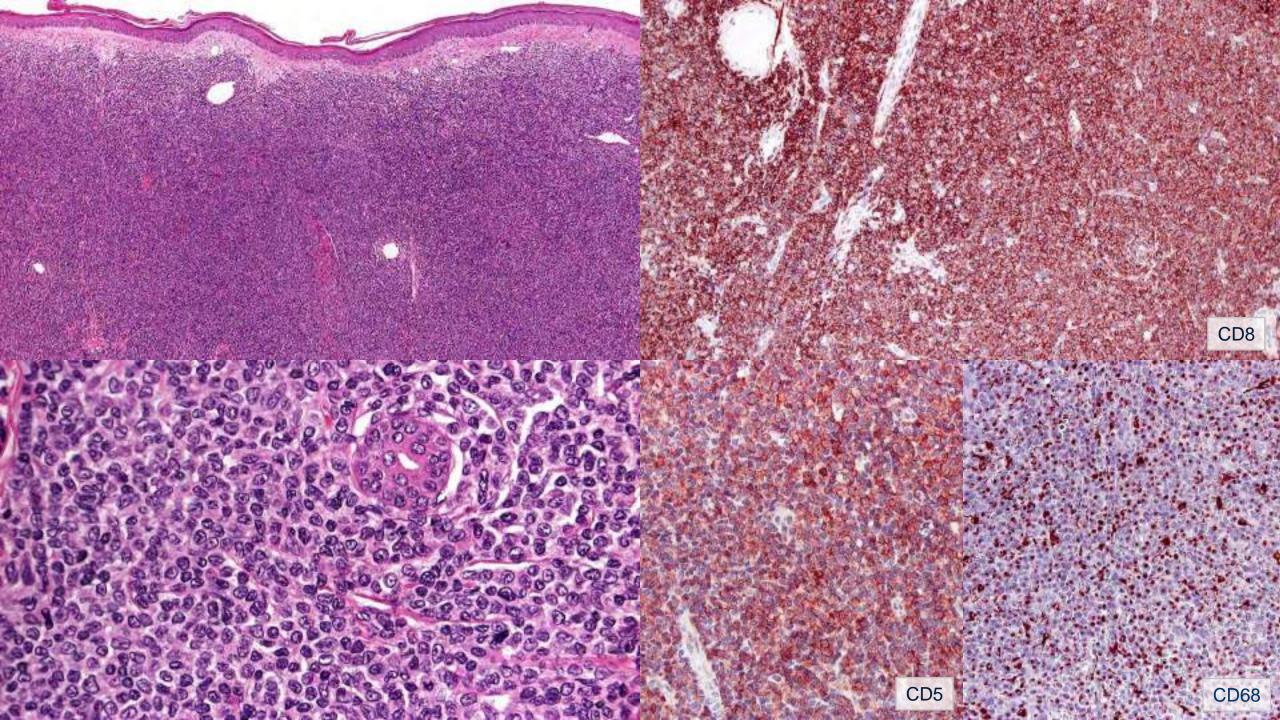
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Acral CD8+ T-cell lymphoproliferative disorder

Lesions located mostly on the ear/face.

Monotonous proliferation of medium-sized CD8+ lymphocytes; dot-like CD68-positivity. Main differential diagnoses: cutaneous CD8+ aggressive epidermotropic cytotoxic T-cell lymphoma (clinical features, prominent epidermotropism), peripheral T-cell lymphoma, NOS (different phenotype), pcCD4+SMPTCLD (CD4+, frequent TFH phenotype). Indolent behaviour, excellent prognosis.





MEDICAL DERMATOLOGY

BID. British Journal of Dermatology

Clinical, histopathological and prognostic features of primary cutaneous acral CD8⁺ T-cell lymphoma and other dermal CD8⁺ cutaneous lymphoproliferations: results of an EORTC Cutaneous Lymphoma Group workshop*

Linked Consumers, et al. Gru Sc J Sept 20 2325; 386,500 TF1.

Abstract.

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bulgions The difference diagnosis of atypical dermit none-jedemiotropic CD6* (amplicaçue inflicture tactades a teneroperature spectrum of (amphispical) tions with mentapping bistological and phototypic features, for divergent dinical manifestations and progressor. So these resoftence are rare, more data on their clinical action past presentation and more non-tended.

Obsten To seem be clinical, listeringical and transcriptorotypic features examined of; and differences between domal CBS* ymphogradifications.

Station Remocestre analysis of a series of 40 takents and bispotes by the intersumeral BORC Contribute (greenward Group.

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Garbern A consideration of district clinical, strapathologica and phenotypic frames allows discremination and augment of identic CDB' tribition into distinct disease entities. Framely custions seen CDB* lipinitions, assigned a prostored cauganty to commit impression strategistics, is a district and reproductive rathy A correct diagnosis is constain to avoid unancontainly aggressive treatment for videben CDB* lymphopolife science and so blendly cases with underlying transact districts or concern for descript or production.

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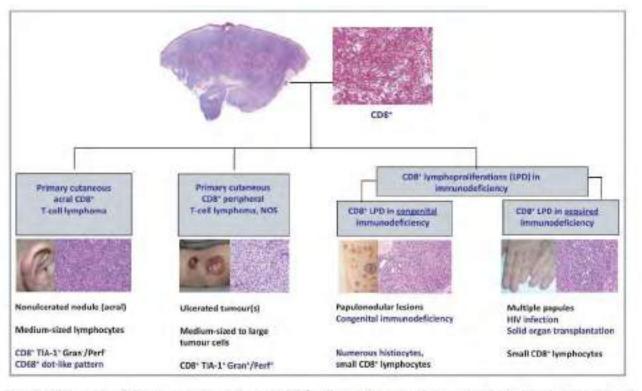
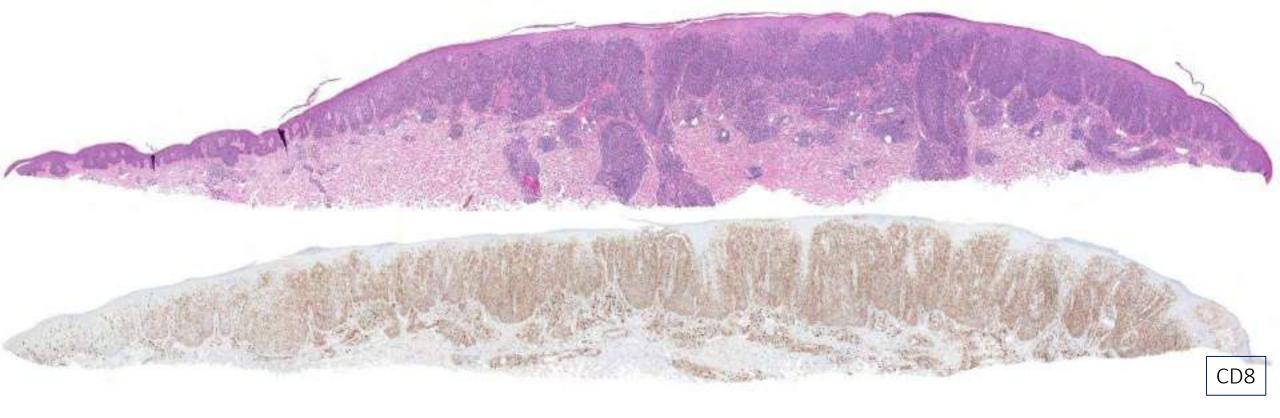


Figure 5 Differentiation of dermal small- to medium-sized CD8* infiltrates. Summary of the most relevant clinical, histological and immunophenotypic features for the differentiation of dermal CD8* infiltrates. Gran, granzyme B; NOS, not otherwise specified; Perf, perforin.



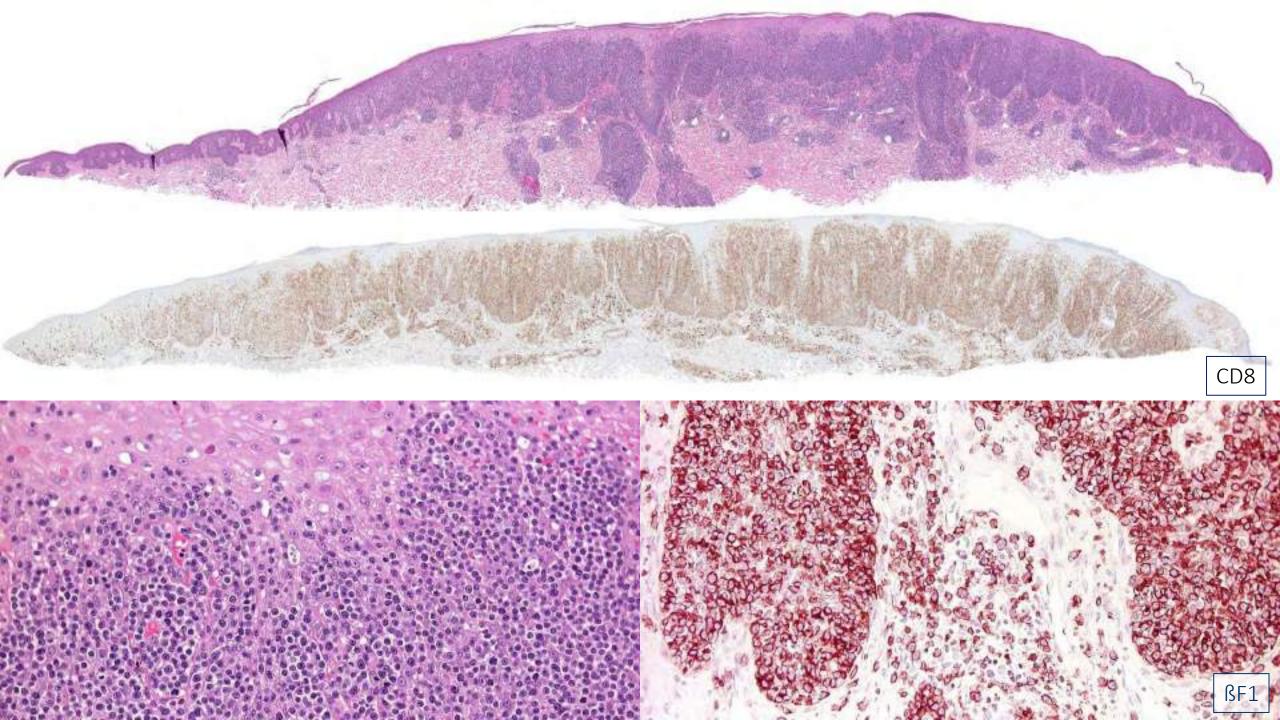
Aggressive epidermotropic CD8+ T-Cell Lymphoma

Clinically presents with the picture of so-called "generalized pagetoid reticulosis" (Ketron-Goodman).

Prominent epidermotropism (may vary with biopsy site, time); CD8 expression may be weak in some cases; CD2, CD5 often negative; CD30 usually not expressed.

Main differential diagnoses: CD8+ MF (history, clinical presentation), LyP-D (history, CD30+), cutaneous γ/δ T-cell lymphoma (TCR- γ/δ +).

Aggressive behavior.



Primary Cutaneous CD8-Positive Epidermotropic Cytotoxic T Cell Lymphomas

A Distinct Clinicopathological Entity with an Aggressive Clinical Behavior

Emilio Berti, * Cario Tomasini, *
Maarton H Vormoer, * Chris JLM Meijer, *
Elvio Alessi, * and Rein Willemze*

Probe the Business of Dermandique Science, and MCCN (opening Biogenest, Adian, Early, the Department of Dermandique) (opening the Adian Assista India, and the Department of Journal of the Adianage, "True ("Monthly Hughest, Association, The Mobbielessie).

Compeous T well lymphomas (CFCI) generally have the phenotype of CD3+, CD4+, CD4580+ memory T cells. CTCL expressing a CD8+ T cell phenotype are extremely rare and ill-defined. To elucidate whether these CD8+ CTCL represent a distinct disease entity, the clinical, histological, and immunophenotypical features of 17 CD8+ CTCl, were reviewed. None of the 17 cases expressed markers characteristic of natural killer cells or y/6 T cells. Nine of 17 cases showed the characteristic clinical and histological features to well as clinical behavior of well defined types of CTCL, such as mycosh fungoldes (2 cases), pagetold retieslosis (2 cases), lyeighomatoid papulosis (2 cases), and CD30+ large T cell lymphoma (2 cases), all of which wouldy express a CD4+ T cell phenotype, and I case of subcutaneous pauniculitis-like T cell lyanphoma. The other 8 cases formed a homogeneous group showing a distinctive set of clinicopathological and immunophenotypical features, not consistent with that of other well defined types of CTCL, Clinical characteristics included presentation with generalized patches, plaques, papulonodules, and tumors minucking disseminated pogetoid reticulosis; metastatic spread to unasual sites, such as the lung, testis, central nervous system, and oral cavity, but not to the lymph nodes; and an aggressive course (median survival, 32 months). Histologically, these lymphomas were characterized by hand-like infiltrates consisting of pleomorphic Y cells or immunoblasts, showing a diffuse infiltration of an acanthotic epidermis with variable degrees of spongiosis, intracpidermal blistering, and necrosis. The acoplastic cells showed a high Ki-67 proliferation tadex and expression of

CD5, CD6, CD7, CD45RA, BF1, and TIA-1 markers, whereas CD2 and CD5 were frequently lost. Expression of TIA-1 pointed out that these lymphomas are derived from a cytonoxic U cell subset. The results of this and other studies reviewed herein suggest that these strongly epidermotropic primary cutaneous CD8+ cytonoxic U cell lymphomas represent a distinct type of CTCL with an aggressive clinical behavior. (Am J Pathol 1993, 155:483–452)

Recently, the European Organization for Research and Treatment at Cancer (EORTC) Curaneous Lymphoma Group proposed a new classification for primary outaneous T (CTCL) and B (CBCL) call lymphomas. This classification is based on a combination of clinical. histological, immunohistochemical, and genetic criteria and contains a number of well defined entities as well as some provisional forms. Well defined entities within the CTCL group include classical mycosis fungoides (MF). folicular MF, pagetoid reticulosis, Sézary's syndrome (SS), CD30+ primary cutaneous large T pel tyrophomas (PC-LCL) and CC30 - PC-LCL. Together they constitute about the 96% of CTCL in the Dutch registry." In the overwhelming majority the neoplastic T cells have the phenotype of resting or activated CD4+ memory T cells (CD45RO+, CD29+). However, rare cases of CD9+ CTCL, with the dimographological features of MF or pagetoid reticulosis. 214 were also reported. In 1960. Jansen 11 described a furningnt MF-like case in which the reoplastic T lymphocytes were CD8+. Since that initial report, other aggressive cases have been reported."1111 However, because of the small number and the heterogenerly in clinical presentation and course of the cause published so far, CDB+ CTCL were not included as a separate group in the EORTC plassification for primary. cutamióus lymphomas.

In the present study we discuss the clinical, histological, immunohistochemical, and incleousir features of 17

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483

17 cases of CD8+ CTCL	
MF Pagetoid reticulosis Lymphomatoid papulosis cALCL SPTCL	2 2 2 2 1
Aggressive CD8+ CTCL:	8

CD2	2/7
CD3	8/8
CD4	0/7
CD5	2/7
CD7	6/7
CD8	8/8
CD30	0/7
CD45Ro	0/8
CD45Ra	7/8
TCRß	8/8
TIA-1	8/8
Granzyme B	2/8

Histopathology



Postmat/edgs 281 \$ 67, 425 441, 901-30.111 1/lac (287).

SPECIAL TOPIC

Aggressive epidermotropic cutaneous CD8⁺ lymphoma: a cutaneous lymphoma with distinct clinical and pathological features. Report of an EORTC Cutaneous Lymphoma Task Force Workshop

Alistair Robson, Chalid Assaf, 'Martine Bagot,' Ganter Burg, 1 Eduardo Calonje, Christine Castillo. * Lorenzo Cerroni. * Nicola Chimenti. * Pierre Dechelotte. * Frederic Franck. * Maria Geerts, Sylke Gellrich, John Goodlad, Werner Kempf, Robert Knobler, 19 Cesure Massone, 5 Chris Meijer, 11 Public Ortiz, 12 Tony Petrulla, 13 Nicola Pimpinelli, 14 Joelim Roewert. 5 Robin Rossell-Jones, Marco Santucci, 15 Mattias Steinhoff, Wolfram Sterry, 1 Janine Wechsler, 16 Sean Whittaker, Rein, Willemze 17 & Emilio Berti 18 St John's Institute of Dermitology, London, UK, "Department of Dermitology, Charite-University Medicine, Berlin, Germany, "Department of Pathology, University Paris, Puris, Proce, "Department of Dermatology and Consensing, University of Zorich, Zurich, Systerland, *CHRU, Life, France, *Department of Derimptology Medical, University of Unit., Gris., Austria. "Department of Demantology, University of L'Agulla. Rome, Italy. "Department of Pathology, Faturists of German-Ferrari Clement-Ferrard, France, "Agranment of Dermandon, Great Diversity Hoppid". Gont, Delglann, "Department of Poshology, Western General Hospital, Ethibarush, UK, 10 Department of Demastelique, Futurisity of Vienna, Vienna, Austria, 33 Department of Philhology, VII Engineraty Medical Contor, Amsterdam, the Natherlands, 12 Hogard Universitaria, Universidad Compiniorna, Madrid, Saain, 11 Department of Pathology, Discov. Enthersity (Longital, Dijon, Prense, **Division of Dermatology, Entersity of Florence Medical School, Plannice, Italy, Division of Pathological Anatomy, University of Florence, Process, Bulg, 16 Department of Pathology Reservation despertment. Hospital, University Perty-Val. dis-Alarse, Paris, Prance, 37 Department of Dermatology, Leider, Dalossong, Leiden, the Netherlands, and 38 Department of Dermitologic Fondestore 1907CS Co. Granda - Oqualois Maggiore Polisimics and Enterrotte degli Stinle di Aldens-Birovos, Abban, Itoly

Date of nationation 2.1 August 2013 Accepted for publication 12 Juneary 2014 Problems of national Artists disputed 18 Juneary 2014

Robson A. Assaf C. Regut M. Rurg G. Calonje E. Castillo C. Ceronni L. Chimenni N. Dechelotte P. Franck F., Geors M. Gelrich S. Goodind J. Kemgi W. Knobler R. Massonr C. Meijer C. Ortz F. Petrella T. Pimpelli N. Romert J. Bussel-Jones B. Santsart M. Steinhoff M. Sterry W. Wechster J. Whittaker S. Willeman B & Boot E. (2015) Histophylology 67, 425–441. DOI: 10.1111/bis.12371

Aggressive epidermotropic cutaneous CD8* lymphoma: a cutaneous lymphoma with distinct clinical and pathological features. Report of an EORTC Cutaneous Lymphoma Task Force Workshop

Ains: Aggressive epidermotropic culturerus CD8*
lyapphorus is currently affurded provisional status to the
WHO classification of tymphorus. An EDRTC Workship was conversed to describe in detail the features of

this putative reoption and evaluate its moningical status with respect to other cotoneous CW* lymphonius. Michael and results: Staty-one CDW* cases were antiseed at the workshort clinical details; often with photo-

Address for correspondence. Br A. Referen Department of Dermanopologically, 2nd Flore, Black C. Smith Weig, 8t John's Institute of Dermainlegs, 2t Turner: Hospital, Westerman Religio Erect, 371, 700 London, UK, e-mail: Allesteroburnjellerbergh.

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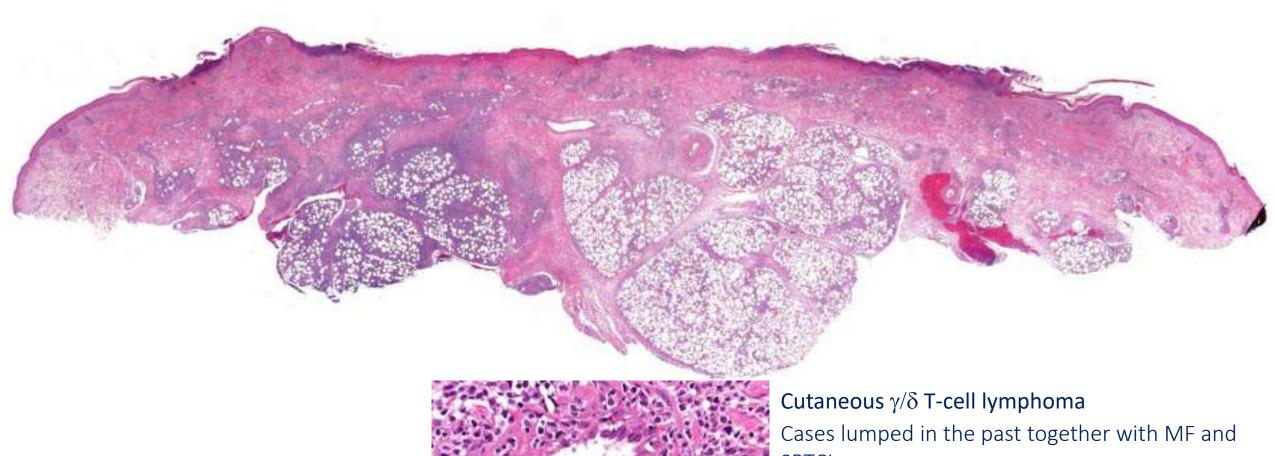
Eighteen cases had distinct features and conformed to the diagnosis of aggressive epidermotropic cutaneous CD8+ lymphoma.

The patients typically present with widespread plaques and tumors, often ulcerated and hemorrhagic, and have striking pagetoid epidermotropism histologically.

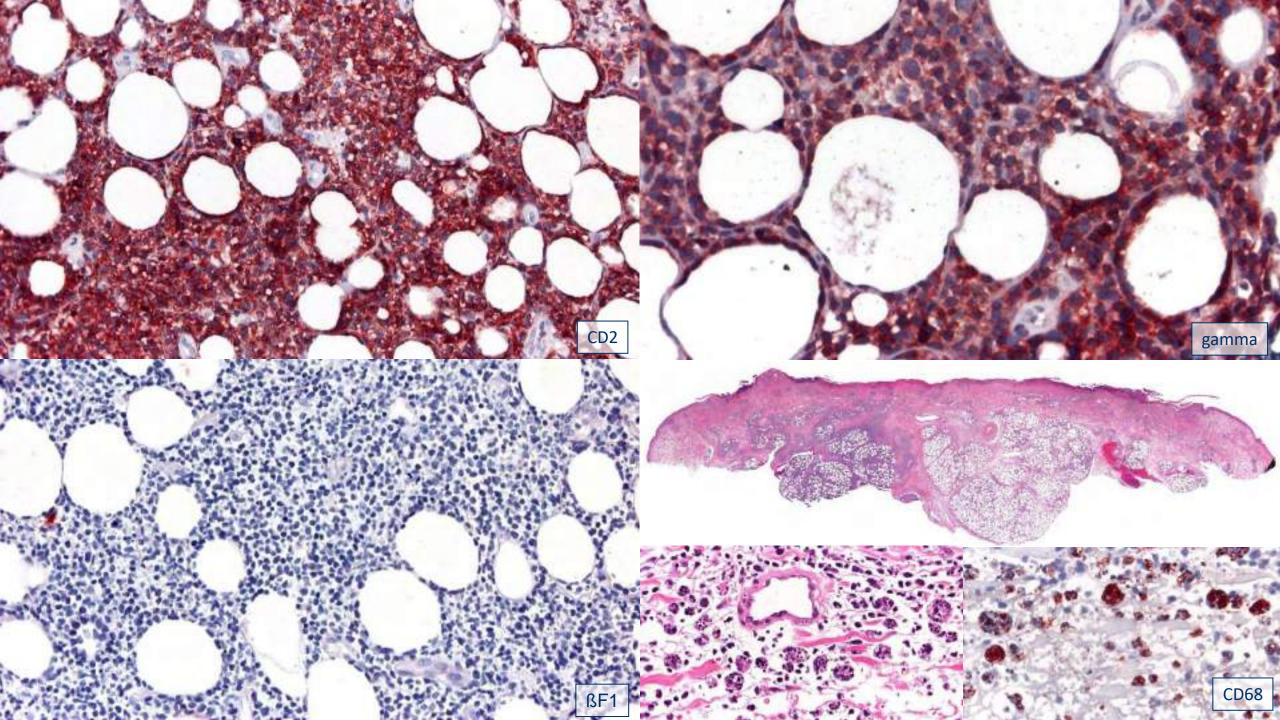
A CD8+ CD45RA+ CD45RO- CD2- CD5- CD56- phenotype, with 1 or more cytotoxic markers was found in 7/18 cases, with a very similar phenotype in the remainder.

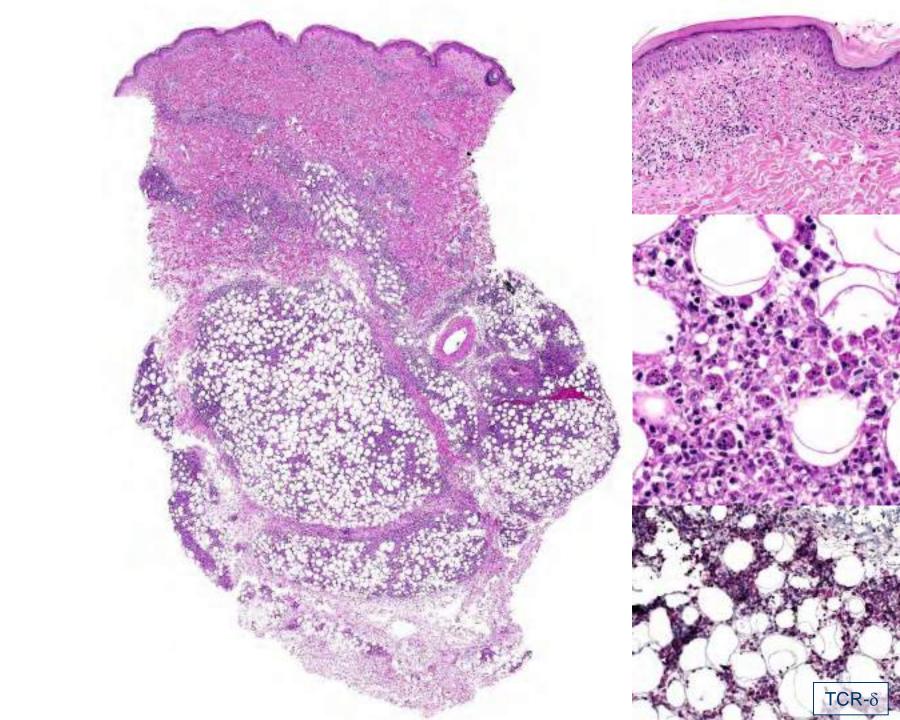
The tumors seldom involve lymph nodes but mucosae and central nervous system involvement is not uncommon.

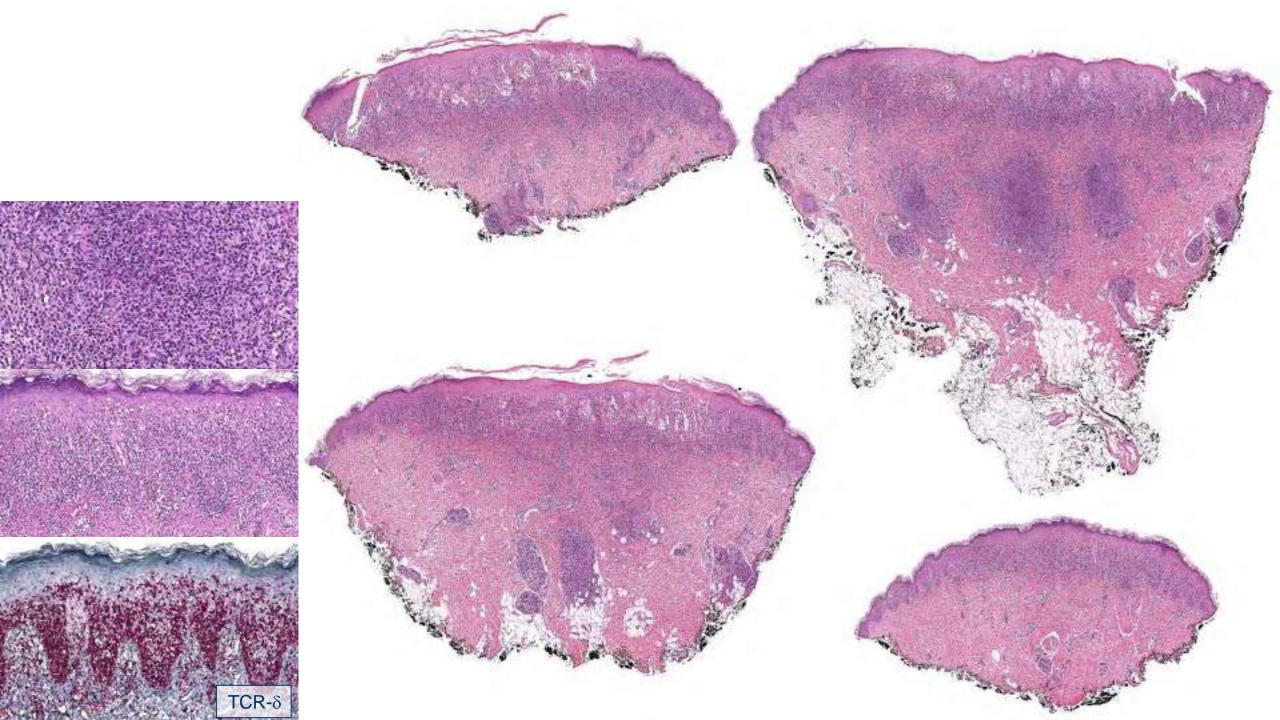
The prognosis is poor, with a median survival of 12 months.



Cutaneous γ/δ T-cell lymphoma Cases lumped in the past together with MF and SPTCL. A γ/δ phenotype is not unique to cutaneous γ/δ T-cell lymphoma (MF, LyP, ALCL), but is never observed in reactive conditions. Oft involvement of both epidermis and subcutaneous fat; angiocentricity / angiotropism; hemophagocytic syndrome (particularly in tumors involving the subcutaneous fat).









ARTICLE



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Cellular origins and genetic landscape of cutaneous gamma delta T cell lymphomas

Jay Daniels 17,18, Peter G. Doukas 118, Maria E. Martinez Escala¹, Kimberly G. Ringbloom¹,
David J.H. Shiho², Jingyi Yang¹, Kyle Tegtmeyer 1, Joonhee Parko¹, Jane J. Thomas¹, Mehmet E. Seli¹,
Can Alturbulakli¹, Ragul Gowithmian 16, Samuel H. Mo⁴, Balaji Jothshankar 17, David R. Pease 11,
Barbara Pro⁸, Farah R. Abdulla⁹, Christopher Sheo¹, Nidhi Sahni 18, Nidhi Sahni 18, Alejandro A. Gruin 18, Brian G. Riecco 14, Abner Louissaint 18, Joan Gultan 18, S. Jachyuk Choin 12, Kintik

Primary cutaneous ph T cell lymphoses (PCGOTLs) represent a heterogeneous group of uncommon but aggressive careers. Herein, we personn genome wide DNA, RNA, and I cell receptor (TCR) arqueously on 29 cutaneously interphonant. We find that PCGOTLs are not uniformly derived from V62 cells, restoad, the cell-of-origin depends on the tissue comportment from which the lymphomes are derived. Lymphomes arising from the outer layer of sion and derived from V62 cells, the predominant shift the apidemiss and derived, in conversit, punniculate lymphomes, arise from V62 rels, the predominant yfi T cell in the fat. We also show that TCR them usage in non-random suggesting common artigent for V61 and V62 hymptomas respectively. In addition, V61 and V62 PCGOTLs harbor smile genomic leadscapes with petentially targetable encagnetic mutations. In the LAC/STAT, MAPK, MVC, and determate modification pathways. Collectively, these findings suggest it paradigm for obsesting, staging, and treating these diseases.

^{**}Department of Terrecorps, Michaelman (in weath, Fair hory to bed in Michaele, Choogs, II, 1854, **Terrecord of Recomment and Michaela carrects, Modification (Michaela) (International States) (International Michaela) (In





 $V\delta1$ cells

 $V\delta 2$ cells

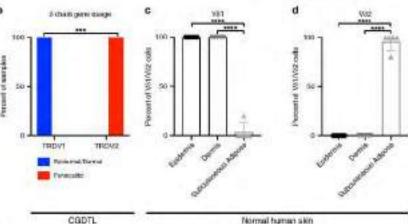
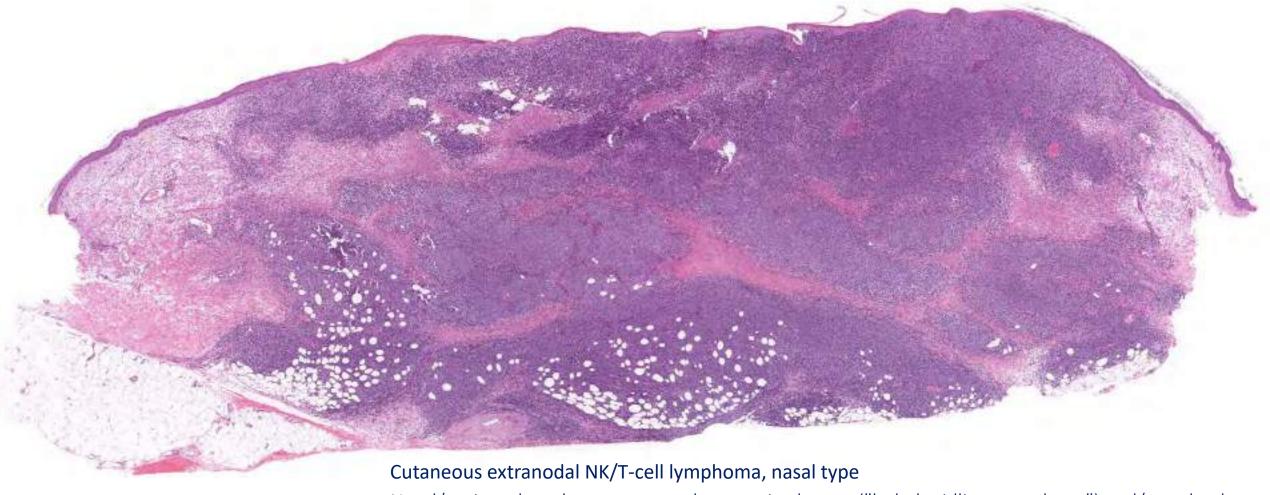


Fig. 1 Epidermal/dermal and parents/life CSDTLs derived from distinct cells of origin, a Schematic highlighting distinct chiesal and histological presentations of disease involving epidermis, dermis, or substanceus issue. Christal photographs of disease lossess, hereaterphic and easin staining of brookins, and yo 1 cell receptor immunostations. Whithour section) for representative patients with epidermal, dermal, and garneculate chases are shown. Ikin schematic created with BioRender. Scale for represents KO µm in bottom right epidermal panel, bottom right parents/life panel. 200 µm in top right epidermal panel, bottom right dermal sonel, and bottom loft parents/life panel. 200 µm in top right epidermal panel bottom right dermal sonel, and bottom loft parents/life panel. 200 µm in top right dermal panel and top right parents/life panel. Schematic panel. Schemat



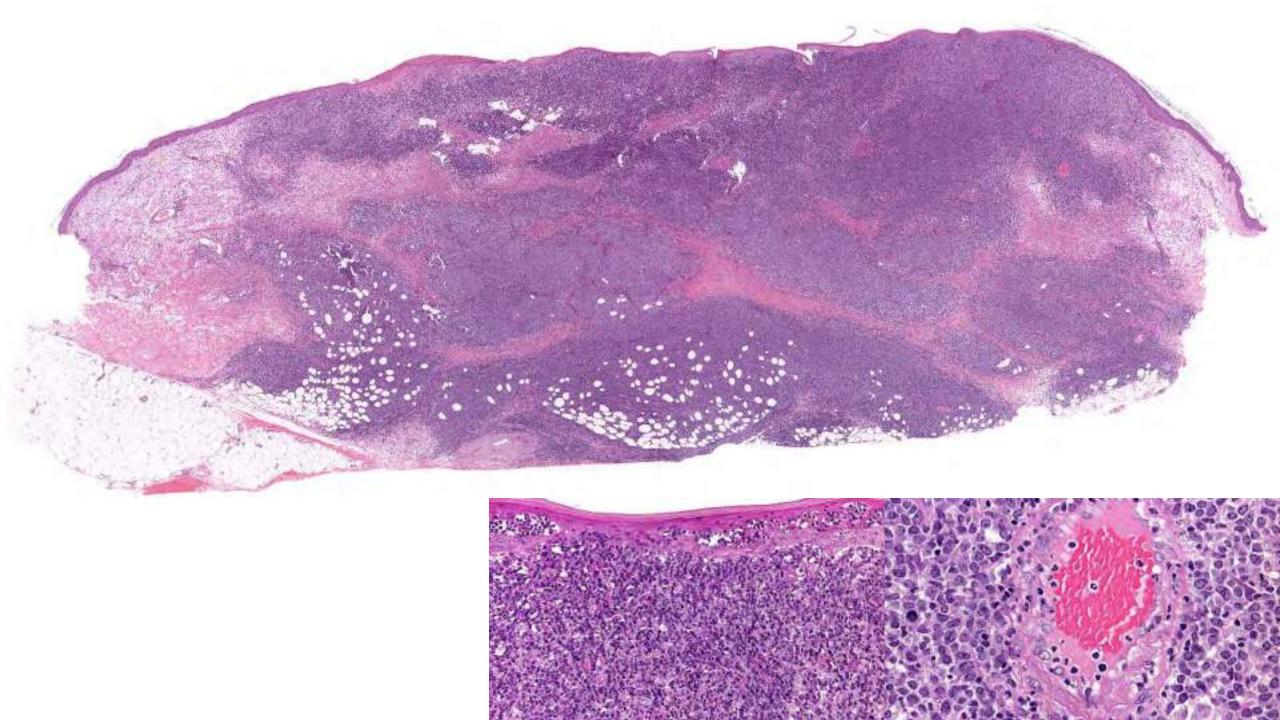
Nasal/perinasal erythematous, partly necrotic plaques ("lethal midline granuloma") and/or palatal ulcers; Persistent facial swelling is another typical presentation; non-descript patches, plaques and

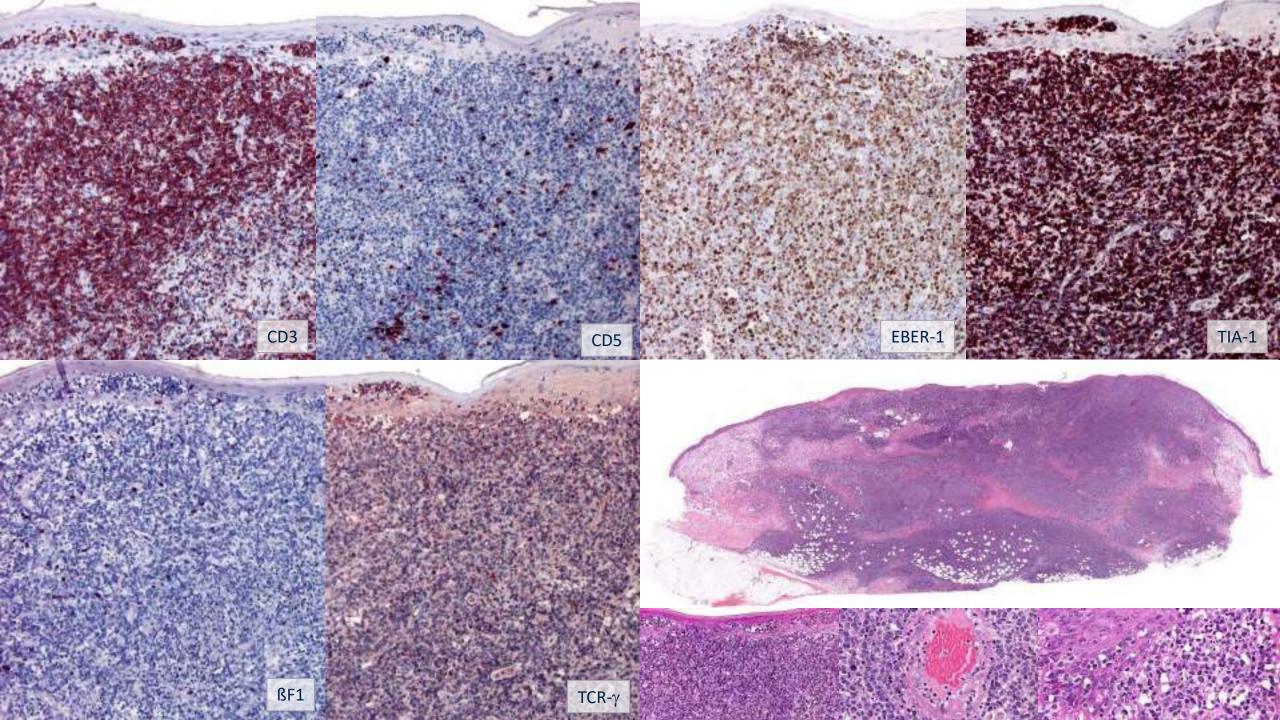
tumors on any region of the body.

Cell morphology variable (small, medium, large).

Phenotype: CD2+, CD3+, CD5-, CD4-, CD8-, β F1-, TCR γ / δ -, CD56+, TIA-1+, Skin often CD2-, CD56-; CD30+ in approx. 30% of cases.

EBV-positivity (EBER-1) and expression of cytotoxic proteins pre-requisites for diagnosis! TCR genes rearranged in 10-40% of cases.





Extranodal NK/T-cell Lymphoma, Nasal Type A Report of 73 Cases at MD Anderson Cancer Center

Shaoying Li, MD,* Xiaoli Feng, MD,* Ting Li, MD,† Shuang Zhong, MD,† Zhuang Zuo, MD, PhD,* Pet Lin, MD,* Sergej Konopley, MD, PhD,* Carlos E. Bueso-Ramos, MD, PhD,* Francisco Vega, MD, PhD,* L. Jeffrey Medeiros, MD,* and C. Cameron Yiu, MD, PhD*

Abstract: Estranodal NK T-adl Jourphous, usual type (ENKTL) is uncommon in the United States. We report 73 patients with ENKTL, including 49 mm and 24 women imedian age, 46y). Sixty-three patients had rused upper aerodigesting tract disease; 10 had extranged disease involving skin, small intestine, epiglotiis, testis, advend glands, kidney, and breast, Complete staging data were exadable for 68 patients: 44 stage J.H. and 24-stage IV. Fifteen of 60 (22%) bad lymphodenopathy and 1003 had bone marrow involvement. Histologically, 67:73. (92%) showed merous, and 48:39 (65%) had an angi-course. angiodostructive growth pattern. The neophysic sidls showed a wide spectrum; medium sized (n = 34); mixed small and large cn = 23), large cn = 13), and small m = 5), bu sine to bridication for Epsgein-Burr virus-encoded small #NA was positive in every case. Immunohistochemical studies should expression of cytissoxic markets (1809v), T-ber (903v), CD2 (963v), CD5 (903v), CD96 (90%), and ETS-1 (64%). K167 was > 60% in 46%. cases. Therapy was known for 64 patients: 14 accised only chemotherapy, 8 radiation alone, and 42 received combined radiation and chemotherapy. Median survival was 4.2 sears, and 5-year overall survival was 46% (medium follow-up, 3.5 y). Extravasal disease, high International Prognostic Index scoreand high problemation rate correlated with power prognosis. We conclude that ENKTL cases in the United States are similar to those reported in Asia and other countries. Absence of the angiocantric angiodomnicine pattern and prisoner of lymphadenopulity, features underemplusized in the literature, occurred in approciable subsets of patients. The International Prognostic Index score, varationtic site of disease, and proliferation rate bailprognosia; value in this patient cohora.

Key Words: extraordal NK.T-cell lymphoma, maid type, southern United States

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Extranodal NK-T-call lymphoma, mesal type (ENKTL) is a rare type of lymphoma that is endemic to Essi to 90%) partients present with most obstruction, strussifis, utcer, and epistaxis due to a destructive mass involving the middine facial visues. ENKTL most often presents us a localized disease, clinical stage I-II; however, wide-spread dissemination can occur in a subset of patients. Occasionally, patients with ENKTL present with only extranasal sites of disease, most often skin, lung, and gastrointestinal tract, but a variety of other extranasal sites have been reported. 1-4

Accurate diagnosis of UNKTL can be challenging, especially is small biopsy specimens or in frozen sections, as the neoplastic cells are often admixed with inflammatory cells and necrosis. An angiocentric and angiodestinetive growth pattern is common and has been emphasized in the literature, but this pattern is not invariable. Most cases of ENKTL are thought to be of NK-cell lineage or derived from an NK-T-cell procursor cell, but a subset of cases, meets the criteria for T-cell lineage. In the 2008 World Health Organization classification, presence of Epstein-Barr virus (EBV), usually shown by assessment for EBV-encoded small RNA (EBER), was included in the disease definition, and EBV has been implicated in disease pathogenesis. 10-12

Although the clinicopathologic features of ENKTL are well recognized, most current data are derived from partient populations in endemic regions, particularly East Asia, 2.5.7 Data on patients with ENKTL in developed countries are limited. In this study, we report the clinicopathologic and minumophenotypic features of a large series of patients with ENKTL at our institution in the United States.

MATERIALS AND METHODS

Case Selection

We searched the database of the Department of Hematepathology at The University of Texas MD Anderson Cancer Center from January 1, 1985 to March 21, 2012 for cases of ENKTL. The diagnosis was based on morphologic and immunophenotypic criteria as specified in the World Health Organization classification. Clinical information was obtained by review of medical records.

Art J. Surg Pathol . Volume 37, Number 1, January 2013

MATERIALS AND METHOD:

73 cases

(63 nasal / upper aereodigestive tract, 10 extranasal including skin)

32 cases with incomplete data, lineage could not be assigned

24 cases (59%) of NK-cell lineage 17 cases (41%) of T-cell lineage

All cases positive for EBV (EBER-1)

From the "Department of Hormoopedrology, The University of Texas MD Andrease Carner Center, Mounce, Try, and "Department of Bulledogs, Pelong University First Hospital, Beijing, Claim.

Conflicts of Intents and Source of Fauling: The authors have disclosed that they have no significant obtainings with, or Sanacial amount in, any commercial companies pertunding to this ornicie.

Conceposácio; C. Caracron Yue, N.D., PhD. Department of Hemotopathology, The University of Tesse MD Anderson Caracr Caracr, Bosson, 13, 7930 results, entireledadornous regi-

Cutaneous epidermotropic lymphomas

Mycosis fungoides and variants

Conventional clinical presentation or features of solitary pagetoid reticulosis Prominent ("pagetoid") epidermotropism observed mostly in cases with cytotoxic phenotype

Cutaneous γ/δ T-cell lymphoma (subset of cases)

Similar clinical presentation as advanced MF ("Ketron-Goodman" type of pagetoid reticulosis) TCR γ + or TCR δ + cytotoxic phenotype pre-requisite for diagnosis; TCR δ may be coexpressed Aggressive behaviour (cases reported as "indolent variant" indistinguishable from TCR γ / δ + MF)

Aggressive epidermotropic CD8+ cytotoxic T-cell lymphoma

Similar clinical presentation as advanced MF ("Ketron-Goodman" type of pagetoid reticulosis) CD8+ by definition (may be non-epidermotropic in given biopsies); TCR β + / TCR γ - / TCR δ - Aggressive behaviour

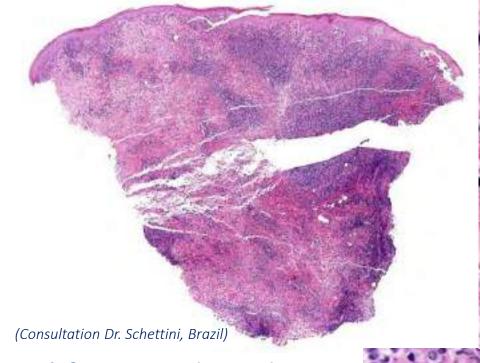
Lymphomatoid papulosis, type B or D

Waxing and waining papules and small nodules Positivity for CD30 and CD4 (type B) or CD8 (type D) a pre-requisite for the diagnosis

Extranodal NK/T-cell lymphoma, nasal-type (subset of cases)

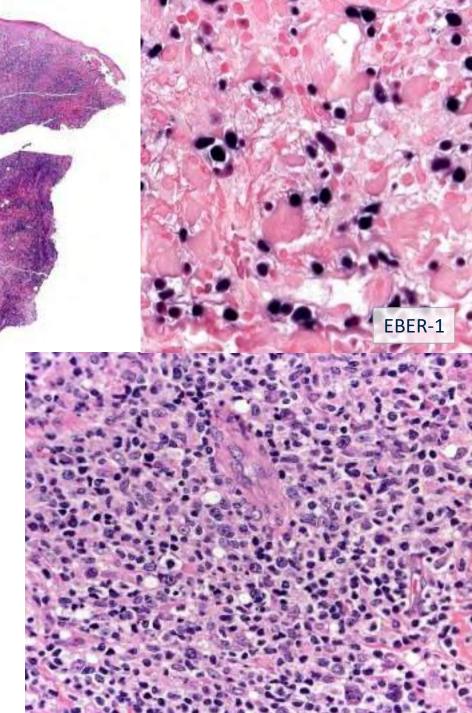
Positivity for EBV a pre-requisite for the diagnosis (EBER-1+) Epidermotropism less marked than in other epidermotropic lymphomas (may be absent) Aggressive behaviour in the majority of cases

... and others, including some cutaneous B-cell lymphomas



Hydroa vacciniforme lymphoproliferative disorder

- WHO 2024: included in the group of EBV+ T/NK-cell lymphoid proliferations and lymphomas of childhood
- Spectrum of clinicopathologic presentations from classic hydroa vacciniforme to severe hydroa vacciniforme and to hydroa vacciniforme-like T-cell lymphoma; genetic background plays a major role
- Hypersensitivity to sun and to insect bites
- Observed mainly in Asia, Mexico, Central- and South-America
- Primary cutaneous; variable clinical course but in HV-like T-cell lymphoma fatal outcome within 10-15 years



Clinicopathologic Features of Hydroa Vacciniforme-Like Lymphoma: A Series of 9 Patients.

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9 Mexican patients (M:F = 2:1; mean age, 14.5 years; median age, 13.3 years; age range, 4–27 years).

Facial edema in all cases.

No case with mosquito bite hypersensitivity. All cases with extracutaneous involvement at first diagnosis and survival <6 months.

Always cytotoxic phenotype.

3 cases CD8+; 4 cases CD4-/CD8-; 2 cases CD8- with some CD4+ neoplastic cells.

Cutaneous lymphomas

WHO 5ed

Mycosis fungoides & variants

Sézary syndrome

Adult T-cell leukemia/lymphoma

Cutaneous CD30+ lymphopr. disorders

Cutaneous anaplastic large cell lymphoma

Lymphomatoid papulosis

Subcutaneous panniculitis-like T-cell lymphoma

Cut. extranodal NK/T-lymphoma, nasal-type

Cutaneous γ/δ T-cell lymphoma

Aggressive epidermotropic CD8+ CTCL

SMPCD4+T-cell lymphoprolif. disorder

Acral CD8+ T-cell lymphoproliferative disorder

Systemic chronic active EBV disease

Peripheral T-cell lymphoma, NOS

Cutaneous marginal zone lymphoma

Cutaneous follicle center lymphoma

Diffuse large B-cell lymphoma, leg-type

Intravascular large B-cell lymphoma

EBV+ mucocutaneous ulcer

International Consensus Classification 2022

Mycosis fungoides & variants

Sézary syndrome

Adult T-cell leukemia/lymphoma

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Aggressive epidermotropic CD8+ CTCL

SMPCD4+T-cell lymphoprolif. disorder

Acral CD8+ T-cell lymphoproliferative disorder

Chronic active EBV infection

Peripheral T-cell lymphoma, NOS

Cutaneous marginal zone lymphopr. disorder

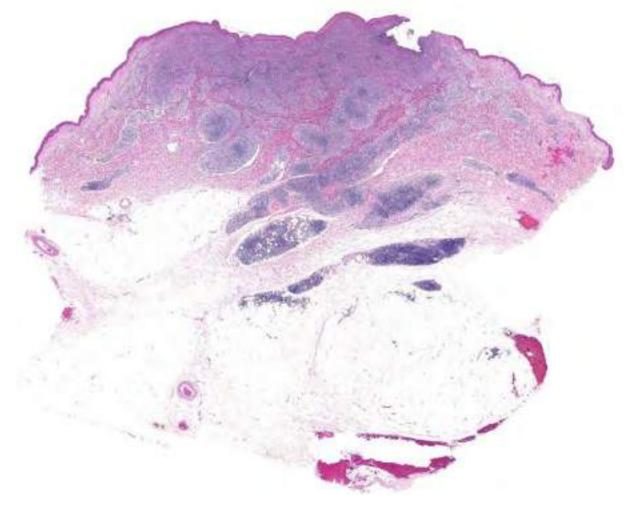
Cutaneous follicle center lymphoma

Diffuse large B-cell lymphoma, leg-type

Intravascular large B-cell lymphoma

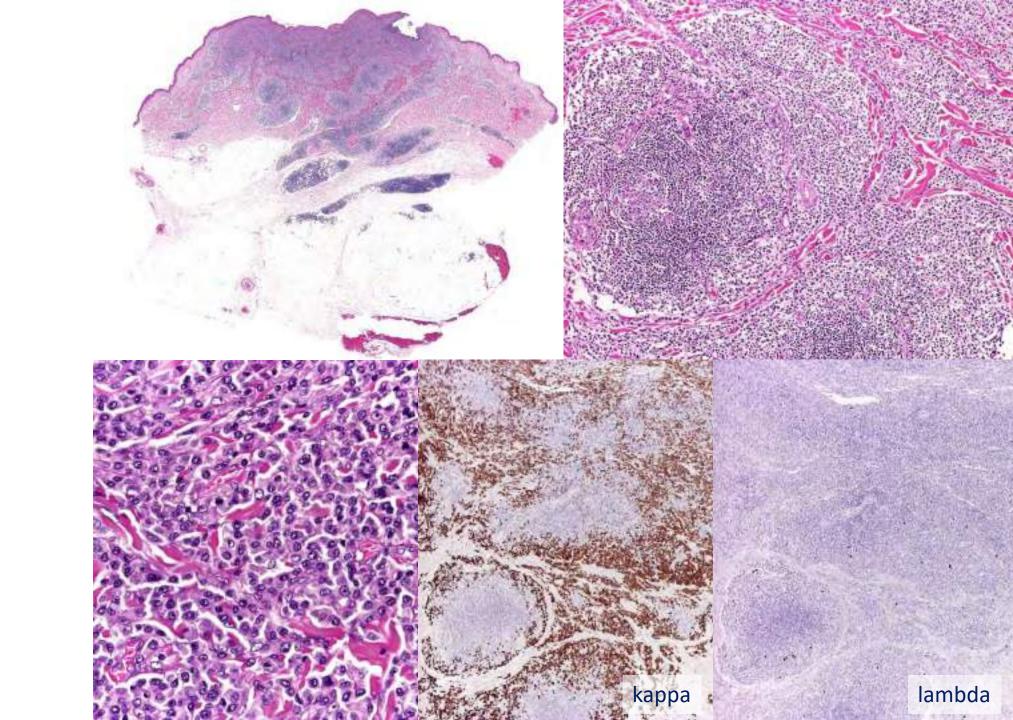
EBV+ mucocutaneous ulcer

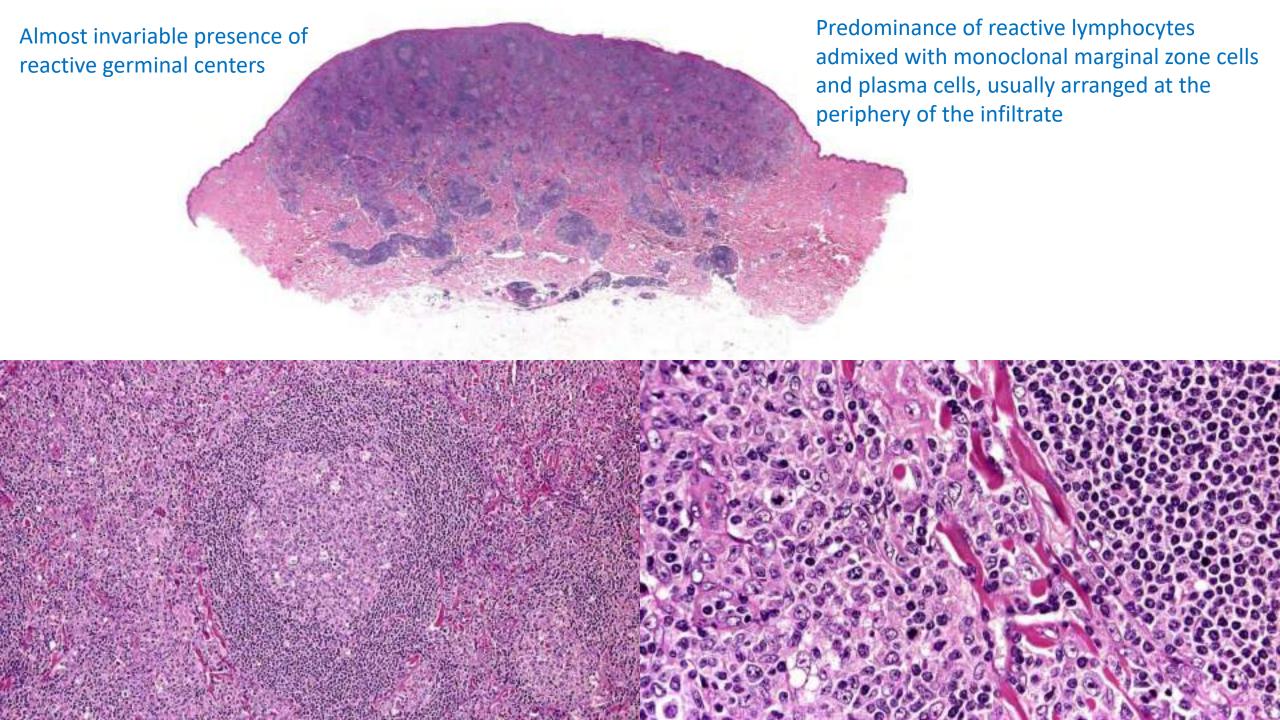
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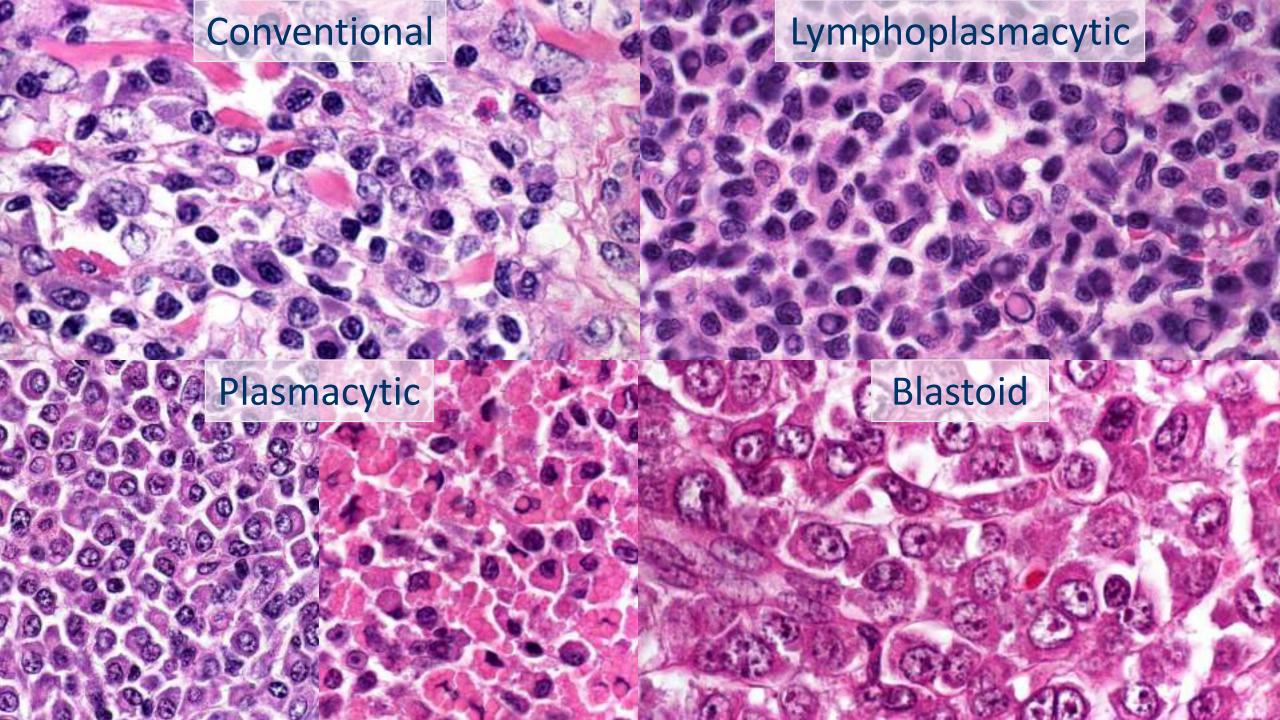


Cutaneous marginal zone lymphoproliferative disorder

(Young) adults; may occur in children. Predominance of any given cell type (marginal zone cells, lymphoplasmacytoid cells, plasma cells, blastoid cells) does not influence prognosis Conservative treatment; BM biopsy and staging investigations not necessary. Histopathological worrying features: blastoid features in sequential biopsies; monomorphous, IgM+ infiltrates (non-class-switched MZLD). Class-switched cases: excellent prognosis; IgM+ cases: excellent prognosis, but extracutaneous dissemination possible.









Infection by Borrelia burgdorferi and cutaneous B-cell lymphoma

to past years, association of primary cutaneous B-cell lymphoma (CBCL) with infection by Bornlin loogslarjer has been reported in a few patients. The evidence for a pathogenetic role was based on clinical grounds or raised acre of antibodies in serum. Both methuds, however, do not prove the association between the micro-organism and the CBCL, especially in countries where infection by Hornia burgdorin is endemic. Moreover, the exact percentage of Borrella Eurgsler/ers-positive CBCL is not known. We retrieved from our files 50 cases of CBCL to perform PCR analysis of Bertella burgdarferi DNA on paraffin-embedded tissue sections. Only patients with primary CBCL were selected. In all cases, monoclonality of the infiltrate was confirmed by intumunohistological pattern of immunoglobulin light chains or molecular analysis of Ingene rearrangement, or both. Specific DNA sequences of Bornfia hurgdorfor were identified in cutaneous lesions from 9 patients (follicle center lymphoma: 3/20; immunocytoma: 3/4; marginal zone B-cell hmphoma: 2/20; diffuse large B-cell lymphoma: 1/6). Specificity was confirmed by Southern blot hybridisation in all positive cases. We could show that Bornlin hurgdorferi DNA is present in skin lesions from a small proportion of patients (18%) with various types of CBCL. Our results may have therapeuric implications. In analogy to Helicobache pylori-associated MALT-hymphomas, which in some cases can be cured by eradication of Helicobacter falori infection, a proportion of CBCL may be cared with anobiotic therapy against Borwlin burgelorferi. Although yet speculative, adequate antibiotic treatment for patients with primary CBCL should be considered before more aggressive therapeutic options are applied, particularly in countries where infection by Bornha burgdorferi is codemic. PCR analysis of Barolin burgdorferi DNA is a fast test that should be performed in all patients with CRCL to identify those who more likely could benefit from an early antibiotic treatment.

Gerroni I., Zörhling N., Pötz B. Kerl H. Infection by Borelin Inegdorferi and cutaneous B-cell lymphoma.
J Cotan Pathol 1997: 24: 457–461. © Munkeguard 1997.

In pass years, association of primary cutmeous Brell lymphoma (CBCL) with infection by Berselia hospitosfer has been reported in a few patients (1, 2). The evidence for a pathogenetic role was based on clinical grounds (B-cell lymphomas arising on skin affected by accodermatitis chronica atrophicans) or raised titre of antibodies in serum. Both methods, however, do not prove the association between the micro-organism and the GBCL, especially in countries where infection by Borrelia Lorenzo Cerroni, Natalie Zöchling, Barbara Pütz and Helmut Keri

Department of Demonstrapy Conversity of Taxas Austria

Lorenze Televini, M.D., Depai transfel Commonlege, Lieuwesty of Groc, Auertraggeopticz, S. A. 8006 Groc, Apartia

Accepted April 30, 1987

hugdorfen is endemic. Moreover, the exact percentage of floredia hagglorfen positive GBCL is not known. We retrieved from our files 50 trees of CBCL to perform PCR analysis of floredia bagglorfen DNA on parallin-embedded tissue sections.

Material and methods

Solution of cases: Formalin-fixed, paraffin-embedded hispay specimens from 50 patients with prima-

REVIEW ARTICLE

Chronic inflammatory disease, lymphoid tissue neogenesis and extranodal marginal zone B-cell lymphomas

Richard J. Bende, Febe van Maldegern, and Carel J.M. van Noesel

Department of Pothology, Academic Medical Conter, University of Amsterdam, Anstendam, the Netherlands

ASSITUATI

Chrone autonomous or pathogen-induced immune reactions routing in lymphosts are associated with development of craftigrant lymphostsa, mostly extracodal magginal score B-cell lymphostsas (MZBCLa). In this review we address (i) the notice and adhesion coolecules involved in lymphost neogeneous (ii) the noticinument discuses and pathogens which are associated with development of B-cell lymphomas; (iii) the noticedar mechanisms involved in the initiation and progression of MZBCL; and (iv) 'potential' messes models for MZBCL.

Key words B-cell non-Hodgkin's lymphoma, extranodal marginal zone B-cell lymphoma, immunoglobulin, B-cell antigen receptor, inflammation, lymphoid tissue neogenesis.

Circum: Beyle III, van Makingon E and van Norsal ClM. Chrons inflammant disease, hysplecid more recognisis and estimated marginal zone B off freedomes. Harmanlogus 2004-44:1103-1123. doi:10.1016/j.harmanl.2004.004482

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Lymphoid tissue neogenesis and ectopic germinal center formation

Inflammation is a local majories to callular argury and a mitsatted by macrophager and local epithelist and/or strongst cells? that selse microorganisms and cell damage by partern wonger." tion recomm, i.e. the Inf-like receptors (TLRs), achieve intracultular SCOO-bise receptors and RIG-like helicanes. The impgened cells respond by secretion of a plethou of inflammatory moliston such as histamine, pronaglordini, leukomenea, planet-activating factors and typical pre-oillammatory. chemokrass and cytoknes like II-III, II-6, II-6 (CXCIII) and TNE: These mediators, and in particular TNE, lead to enclothelist serivation and vascullantion followed by a local effice of circulating leakocytes. The first leakocytes among on site are grandocytes which combit the encyclud invades, while menocytea/maconfrager situri up dead sels, including apopturs: granulocytes and destroyed trave.1 In pandlel, dendrits cells (DCs) take up and process arrigers (Ag) from the intruder, manuer and migrate to a local lyingh node to set off an adaptive introduction temporate.

Chretic inflammatory conditions, that to improper smalleation of pathogens, auto-institute processes or chronic allogisal reportures, are associated with the general inflammatory of proposite dynphosid tissue. In second years, a member of key molecular determinants operating sharing the generation of tertiary lymphosid tissue, have been identified. In the complex sequence of events, TNF is again one of the key molecular as it induces the penduction of ECCL19 and CCL21 (SEC), which are important for the attraction of the and Tolymphocytes.

The affiltrating lymphosytes switch no expression of membrarie-board lymphomeus mile (inf. Tanfle) when activated sig. by Ag." High levels of millions lead to lymphotoxin receptor. (ETB-R) ligation on strongs cells and/or magnetyages and Induce CXCLIS (N.C.) production." The local production of CXCLI3 mediates homing of 5 cells and reduces the arrived 8. infli to further unregulate mil. Took and probably also TNE. The enhanced interaction of CXCL13-producing atomic refle with the TMF- and mLTm-B- producing B cells promotes differentiation of resident strengt cells into follogier dentime rela-(FDCs) which that expressing characteristic malecules to impimmine complexes, i.e. the complement acceptors CDE1 and CDS5 and the FcyR-IIB." Subsequent production of CXCL18 by FDCs establishes a positive feedback loop essential for ectopic lymphoid tissue development, angler to embryosic lympho organogenesis and normal folkde formation (Figure 1).100 The originatures of LT and TOF in this position has been demonstrated by transports expression of TOO, LTm and LTmBin the poncine and the Isdneys, leading to formation of anonized lymphoid tioner including TOC-containing foliates. "" Transperse expression of CCL21 alone, moulted in extensive lymphoid times development in the paramete." However, ectopic expression of CXCL12 (SDF), CCL19 or CXCL18 leads by attraction of symphocytes, some compating maigration but not to the genesis of FDC-containing fullicles."

Depending on the type of pathogon, i.e. differences in the Agjumentation made and the combination of continuistory molerates and cytokine ugrals, Ag-presenting cells (APCs) gaste Tsell differentiation into the doction of T-helper type 1 (T-11) or T-helper type 2 (To) cells. A Tol-polarised response dependin

Acknowledgeweits: we thank Rebbert Hospehoom and Region M. Relpment for critical reading of the manuscript.

Manuscript arrived on January 73, 2000, Revised terrisol arrived on March 73, 2009, Manuscript accepted on March 25, 2009.

Correspondence: Carel J.M. son Record, Department of Fathology, Assistance Medical Center, University of Amsterdam, Amsterdam, the Metheriansis.

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Cutaneous Marginal Zone Lymphomas Have Distinctive Features and Include 2 Subsets

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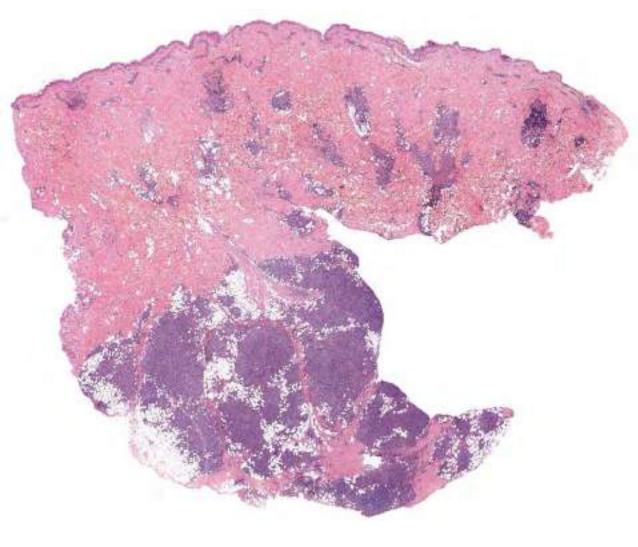
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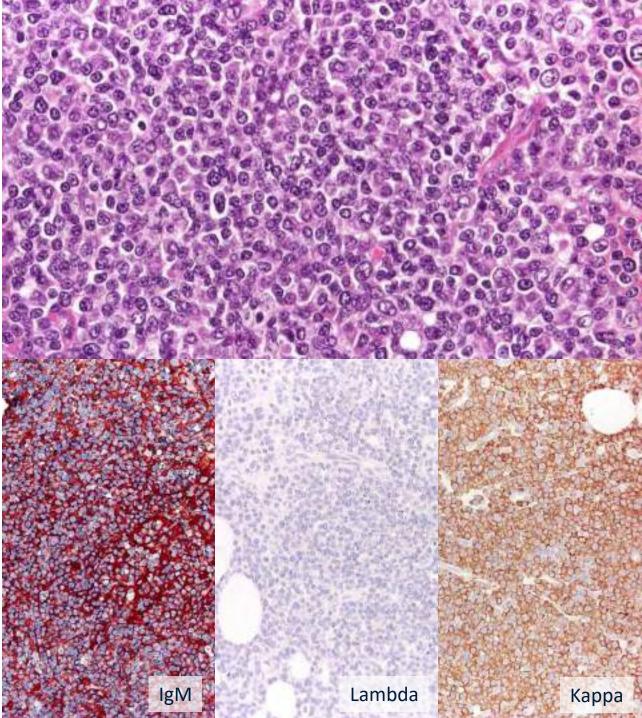
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These findings support the presence of 2 types of cutaneous MALT lymphomas with the class-switched cases being the most distinctive but still sharing significant features with MALT lymphomas from other sites.

The class-switched cases had a predominance of T cells in 22 out of 23 cases, usually showed nodules and scattered small B cells often with IgD+ apparently nonneoplastic follicles, never showed a totally diffuse growth pattern, and lacked extracutaneous involvement. The IgM+ cases showed a predominance of B cells in 5 out of 6, a diffuse proliferation of CD20+ B cells in all, and extracutaneous disease in 3 out of 6.

"non-class-switched" cutaneous marginal zone lymphoproliferative disorder (IgM+)





2022 CAC committee

Daniel A. Arber, MD Elias Campo, MD Robert P. Hasserjian, MD Elaine S. Jaffe, MD Attilio Orazi, MD Steven H. Swerdlow, MD

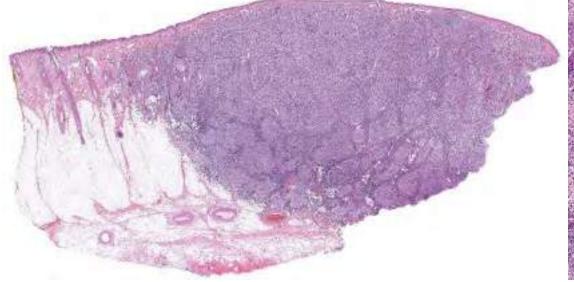
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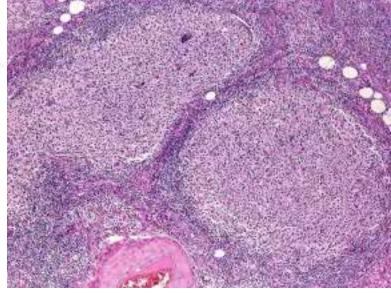
Steven H. Swerdlow, MD Lorenzo Cerroni, MD John Goodlad, MD Barbara Pro, MD Steven Rosen, MD

Cutaneous marginal zone lymphoproliferative disorder

- Segregated from other MALT lymphomas, based on clinicopathologic features including mutational landscape.
- Now considered as a lymphoproliferative disorder rather than overt lymphoma.
- Two subtypes recognized distinguished principally based on whether classchained switched or IgM+.
- IgM+ subtype requires greater concern about the possibility of concurrent or subsequent extracutaneous involvement.



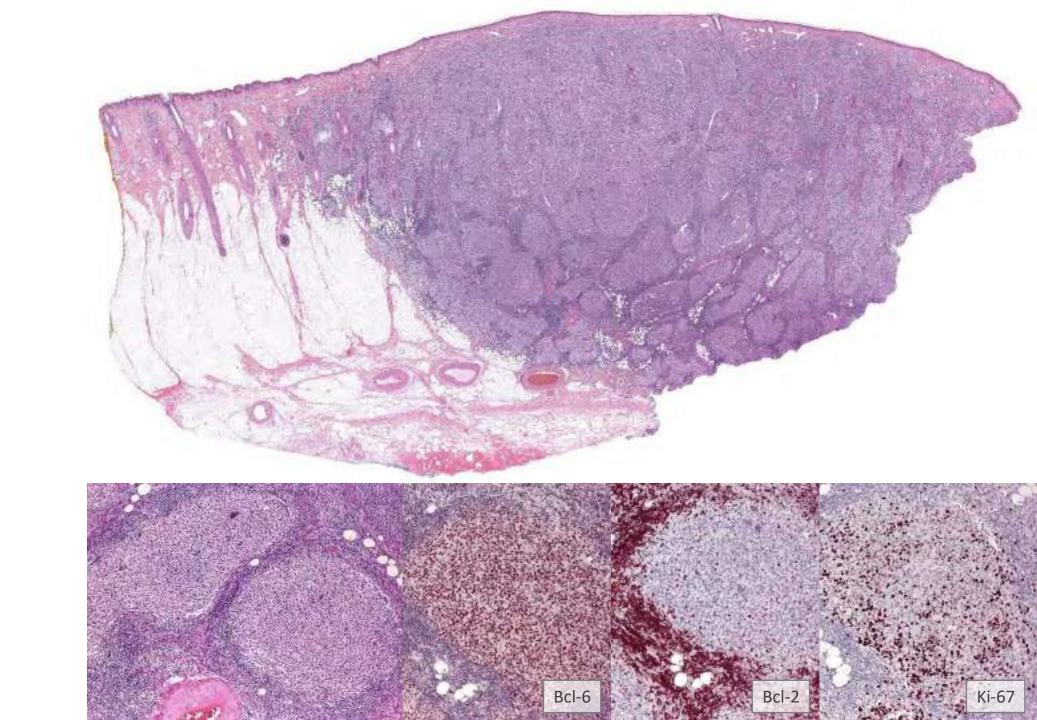




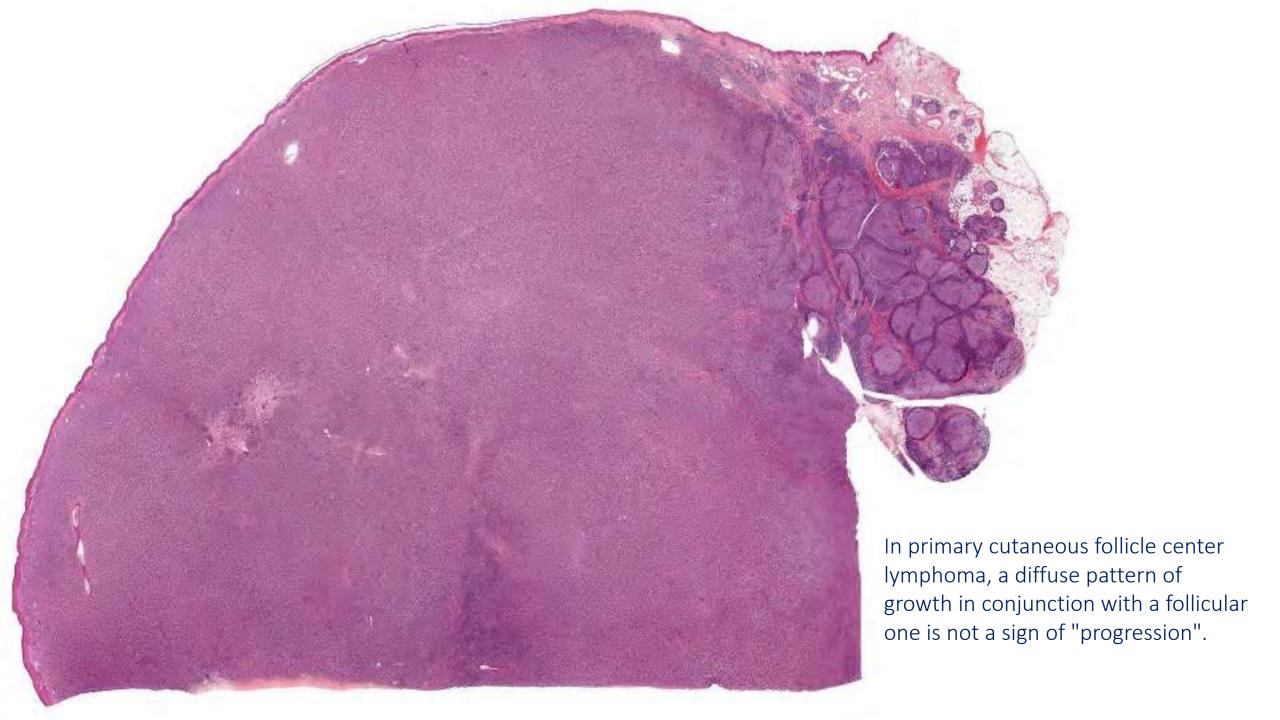
Cutaneous follicle center lymphoma

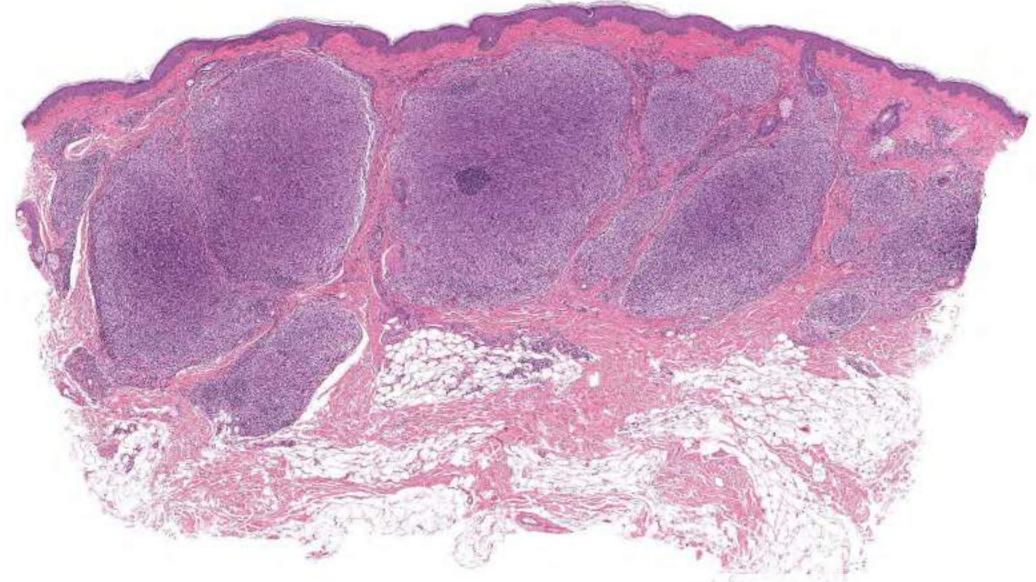
Most common type of cutaneous B-cell lymphoma. Adults; preferential locations: head & neck, trunk ("Crosti's lymphoma"). Staging mandatory; Bcl-2-positivity suspicious for (but not pathognomic of) secondary skin involvement. Indolent course irrespective of growth pattern (i.e., cases with diffuse infiltrates of large centrocytes are not classified as a high grade lymphoma). Differentiation from pcDLBCL, leg-type based on clinical presentation, cell morphology (predominance of centrocytes rather than of centroblasts & immunoblasts), and phenotype.

Deletion of chromosome 14q32.33 containing the oncogene *AKT1*, as well as the immunoglobulin heavy chain locus has been reported. Mutations in *CREBBP*, *KTM2D*, and *BCL2* much less frequently than in nodal follicular lymphoma. Mutations in *MYD88* and inactivation of *CDKN2A* and *CDKN2B* by deletion (9p21.3) or their promotor hypermethylation are not or only rarely found in PCFCL, in contrast to PCLBCL, leg type.

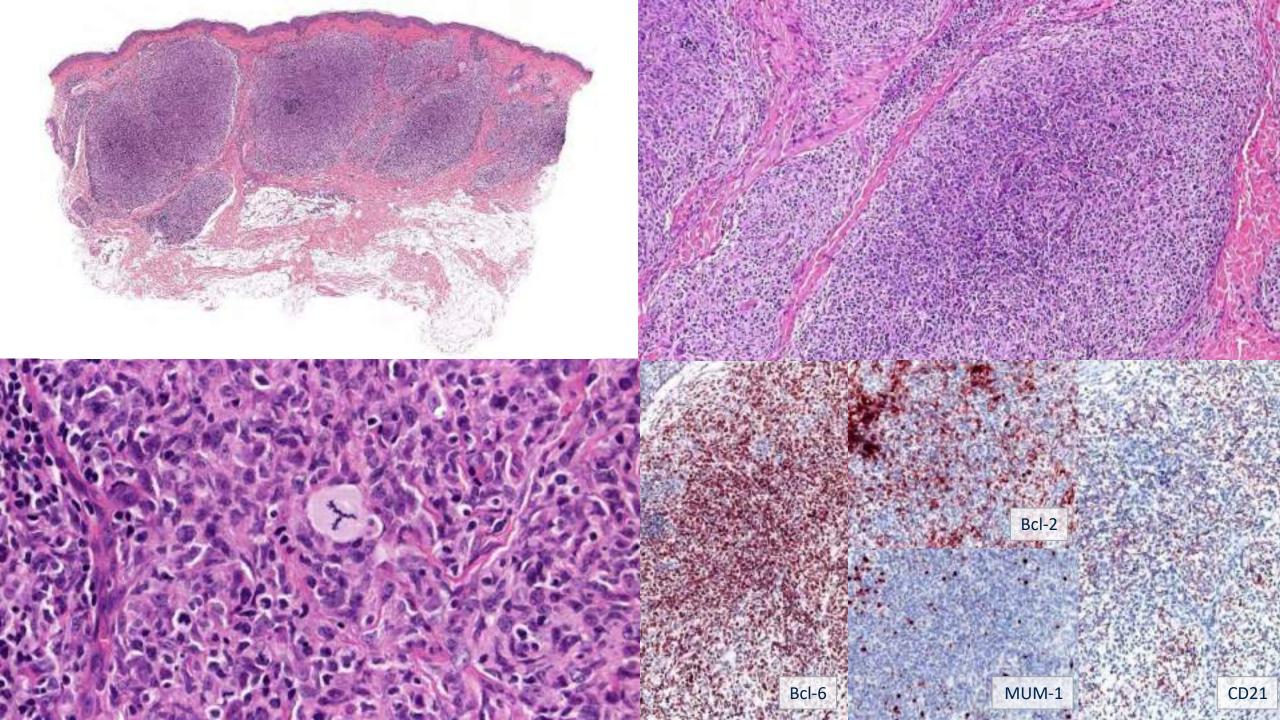




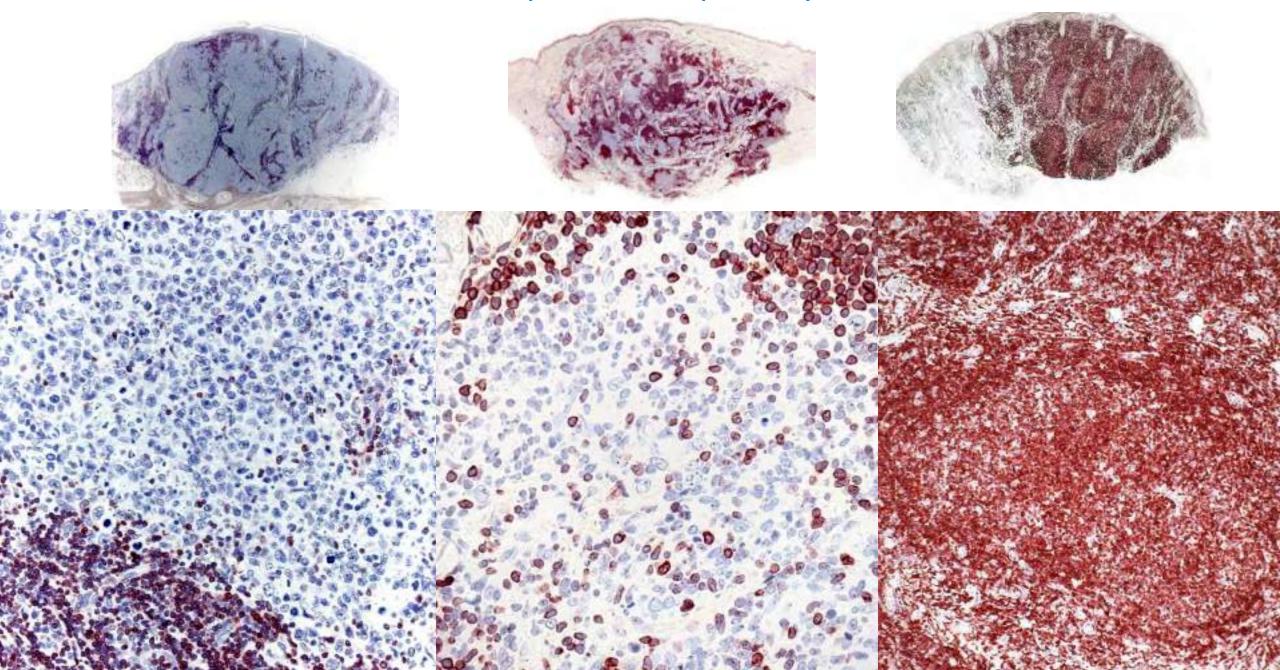


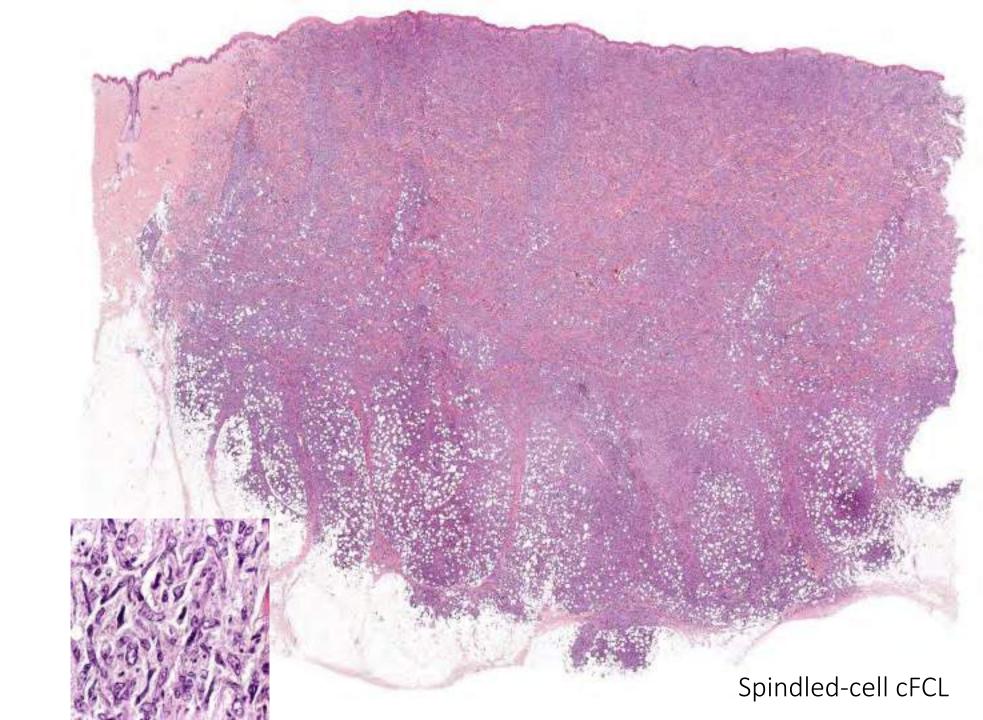


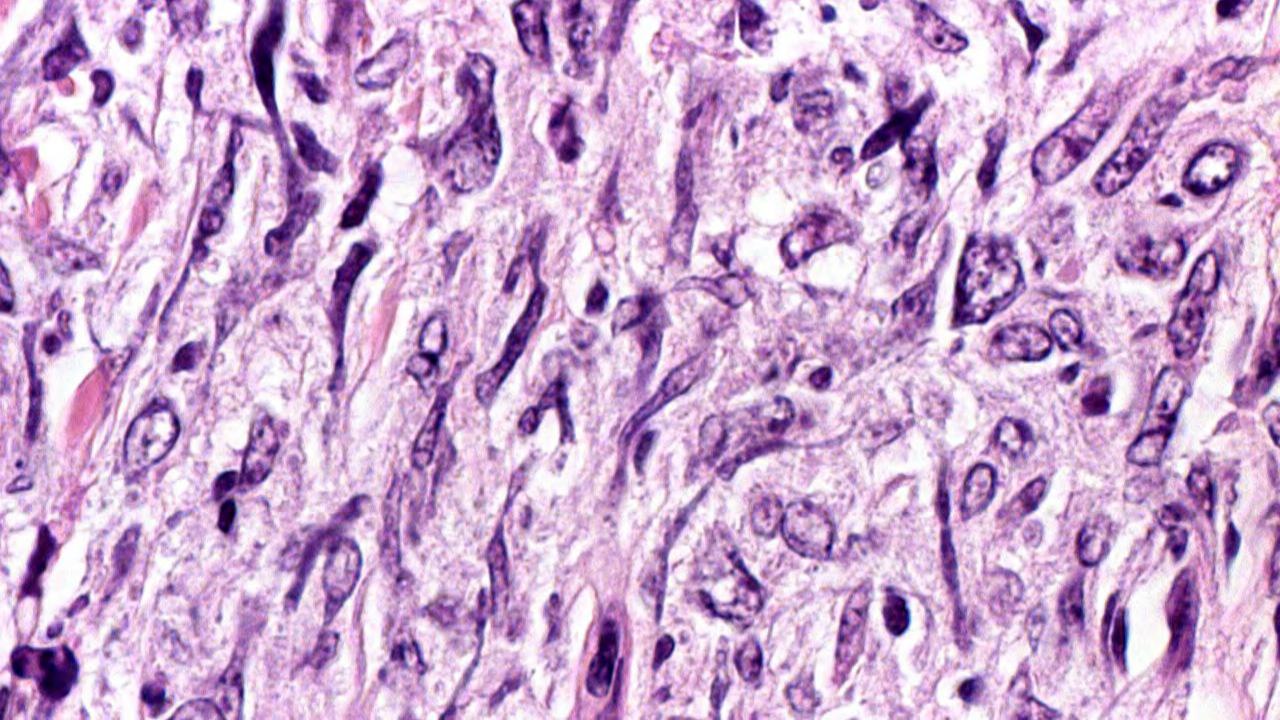
"Large cell lymphocytoma". In the past considered as a variant of the cutaneous pseudolymphomas; now included in the histopathological spectrum of cutaneous follicle center lymphoma. Almost exclusively on the head & neck area; clinically often localized miliary lesions (similar to miliary and agminated cutaneous FCL). No association with *Borrelia* infection.



Patterns of Bcl-2 expression in primary cutaneous FCL







Cutaneous Spindle-Cell B-Cell Lymphomas Afont are Neoplasms of Fallissian Center Cell Grigon

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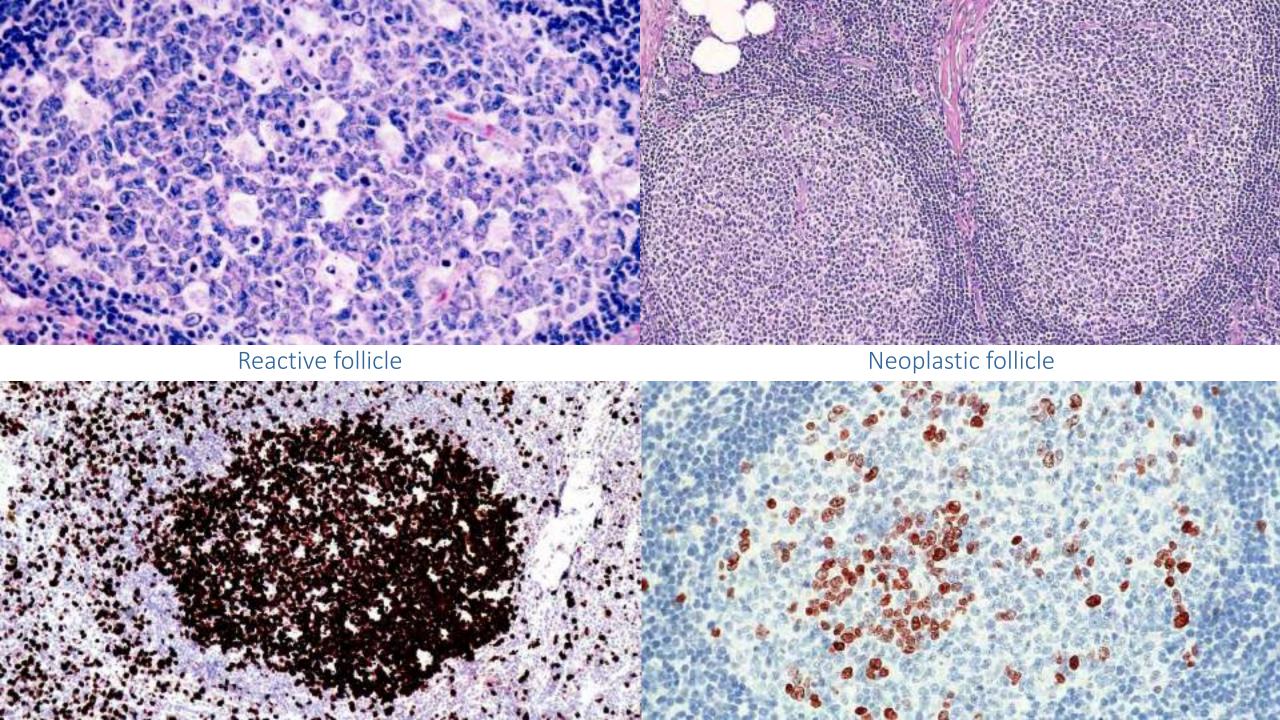
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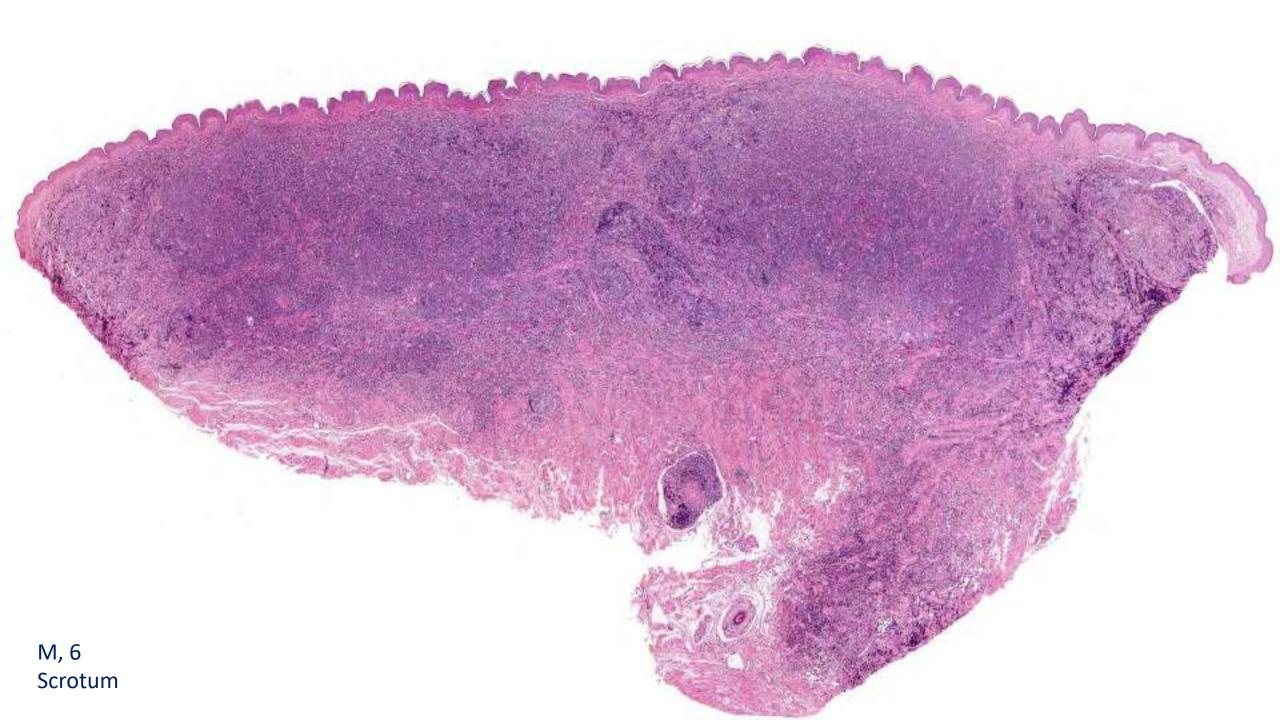
24 cases (M:F = 18:6) (mean age 55 years). Head (12), trunk (8), lower extremities (4).

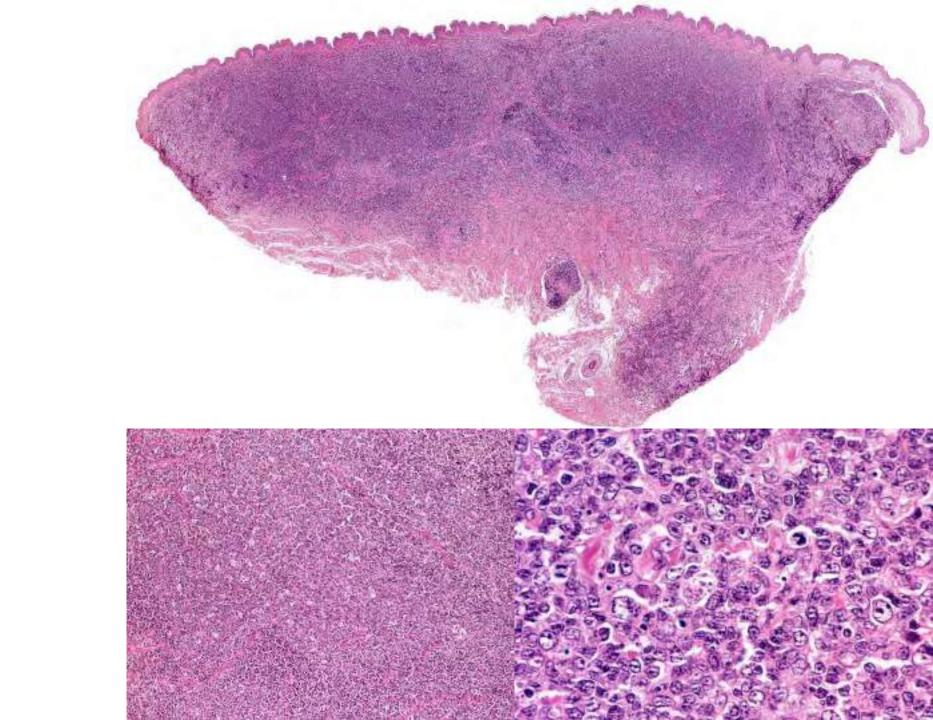
The neoplastic infiltrates comprised a mixture of medium-sized, visually prominent spindled cells (15% - 85% of the infiltrate) arranged in a fascicular pattern around nodular aggregates and admixed in a random manner between centrocyte/centroblast-like cells within these nodular collections. Immunohistochemical support for a follicular center cell origin was present in 22/24 cases, 1 was consistent with DLBCL-leg type and 1 defied precise classification, best fitting with intermediate-grade DLBCL-other.

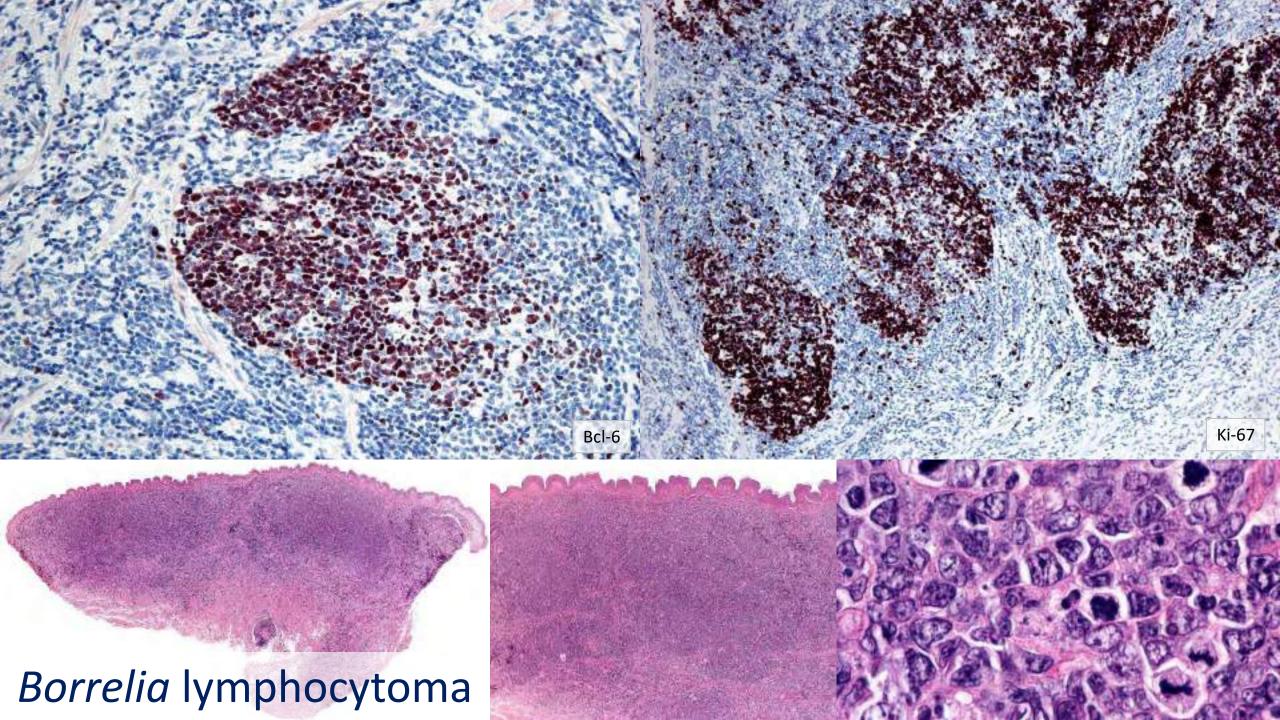
Differential diagnosis of cutaneous lymphoid infiltrates with follicular pattern

- Reactive germinal centers:
- Large numbers of tingible body macrophages and normal, well-formed mantle zone
- Clusters of Bcl6+ cells confined to the germinal centers
- High proliferation of the germinal centers
- Other clues specific to particular types of lymphocytoma (e.g., focal necrosis and histiocytes with a granular, basophilic cytoplasm in vaccination-induced pseudolymphoma)
- Beware of special locations in *Borrelia*-related lymphocytoma (e.g., earlobe, nipple, genital area)









Borrella burgdorfert-associated lymphocytoma cutis simulating a primary cutaneous large B-cell lymphoma

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"Because of this misleading histologic feature, a diagnosis of primary cutaneous large B-cell lymphoma was first suspected in both cases. In one case, successive recurrences led to aggressive therapies before the *B burgdorferi* infection was recognized."

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Fig 1. Case 1. Deeply infiltrated plaque on anterior part of scrotum.

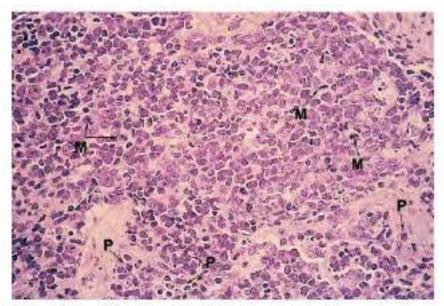
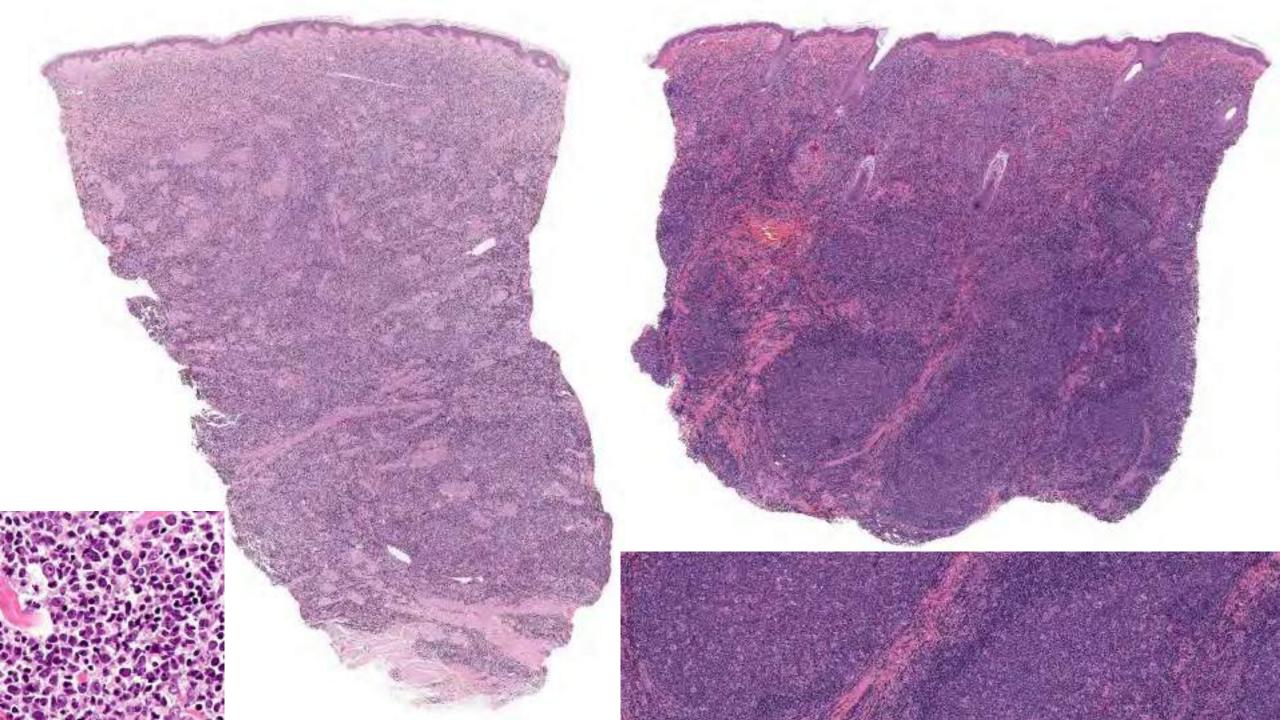


Fig 3. Case 1. Detail of Fig 2. Infiltrate is mainly composed of centroblasts; few immunoblasts and numerous mitoses (M arrows) are present. Some lymphocytes exhibit a plasmacytic differentiation (P arrows). (Hematoxylin-eosin stain; original magnification ×200.)

"A surgical cutaneous excision associated with a testis biopsy was performed. (...) After a 15-month disease-free interval, the patient presented in July 1997 with an infiltrated plaque of 15x10 mm in diameter on the anterior part of the scrotum. A biopsy specimen confirmed the recurrence of the previously diagnosed tumor. Radiation therapy was performed in September 1997 with 6 meV for a total dose of 44 Gy in 20 fractions and resulted in a slow and complete resolution of the skin lesion within 2 months. However, a local recurrence with similar histologic features occurred 3 months later in the radiation field. The patient received 6 cycles of cyclophosphamide, doxorubicin, vincristine, and prednisone chemotherapy. A complete response was achieved in July 1998. However, a scrotal nodule again reappeared in March 1999. (...) A complete resolution of the skin lesion was achieved after 3 weeks of therapy with amoxicillin, 3 g, administered daily. No relapse was observed after a follow-up period of 27 months."



Journal of Cutaneous Pathology

Borrelia burgdorferi-associated lymphocytoma cutis: clinicopathologic, immunophenotypic, and molecular study of 106 cases

Lymphorstoma rutis (LC) is considered as the stereospical example of the cutaneous B-cell pseudolymphorsus. It can be induced by sarious antigenic stimuli including arthropod bites, vaccination, and drugs among others. In endemic regions, Bomba karplodes is the principal causaire agent for LCL We studied retrospectively 108 biopsiot from 106 patients imale; female, 48: 58; mean age, 44.6; median, 31.3, range, 3-81) with A lenguages-associated LC retrieved from the files of the Department of Beneauology of the University of Graz (Austria). Only cases with a R. Mogarose eticling (regical) beatings, positivity of serologic and/or polymerate chain reacting PCR) tests, clinical history were included in the study. Lesious were located on the nipple 653 cases, earlobe (18 cases, pental region 9) cases), and trank or extremities (16 cases). PCR, analysis of B: barykofan DNA was positive in 34 of 80 cases resent (67.5%). In 47 cases, we rould remove data on sembane communition for it, longituding antibodies performed at the time of diagnosis of LC. Positivity was found in 45 patients digits / light , 5 cases, IgG / light , 57 cases; igG /lgM*, 5 cases; IgG /lgM , 2 cases. Histology revealed dense lymphoid infiltrates with prominent permisal censers (GCs) in all cases. Atypical insorphologic and/or immenophonocypic features of the GCs were commonly observed. In 5 cases, due to confluence of large follicles, the histopathologic pattern simulated that of a large Bcell Imphorus. PCR analysis of the IgH gene rearrangement performed in 35 cases showed a polytimal pottern in 31 cases and a monoclonal hand in 2. In company, B. hosperby-associated LC earpresent with reisleading himspathologic, immusophenotypic, and molecular features, and integration of all data is necessary for a correct diagnosis.

Call C, Leinverber B, Millegger R, Chour A, Kerl H, Cerroni L. Rossia largeleter-associated hymphocyteons cure: clinicopathologic, immunopherotypis, and arolembar surby of 10% const T Curan Puthol 2004; 31: 252-240. © Blackwell Municipantif 2011. Claudia Colli^{*2}, Bernd Leinweber¹, Robert Müllegger¹, Andreas Chott², Helmut Kert¹ and Lorenzo Cerroni¹

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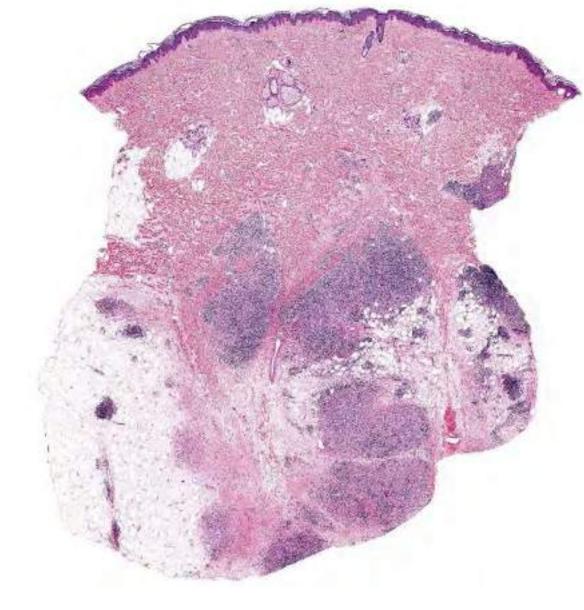
Lymphocytoma cuta (LC) is one of the most common types of cutaneous B-cell pseudolymphomin. In can be induced by various antigoric minute, to challing arthropoid bates, accommon, and drugs among.

others. In endemic regions, Bernáu is gainfan infection, is the most common cassative factor. These lesion are also resignant. Record lymphocytamic, and represent the least common numbersation within the

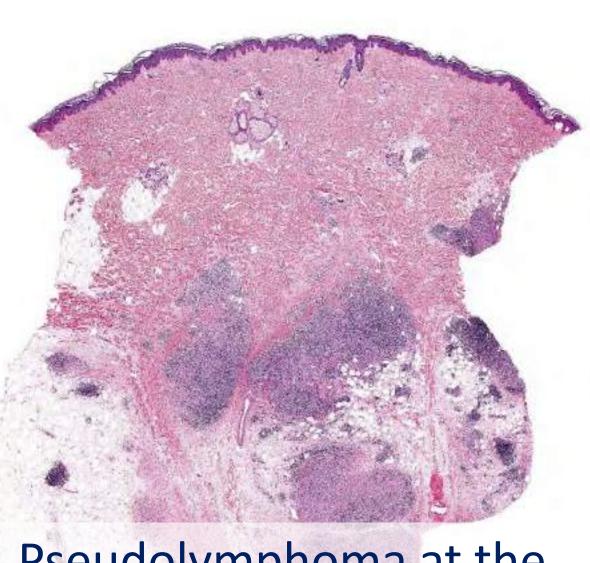
Nipple	59,4%
Earlobe	16,7%
Genital	8,5%
Other	10,0%

Exceptions to the rules

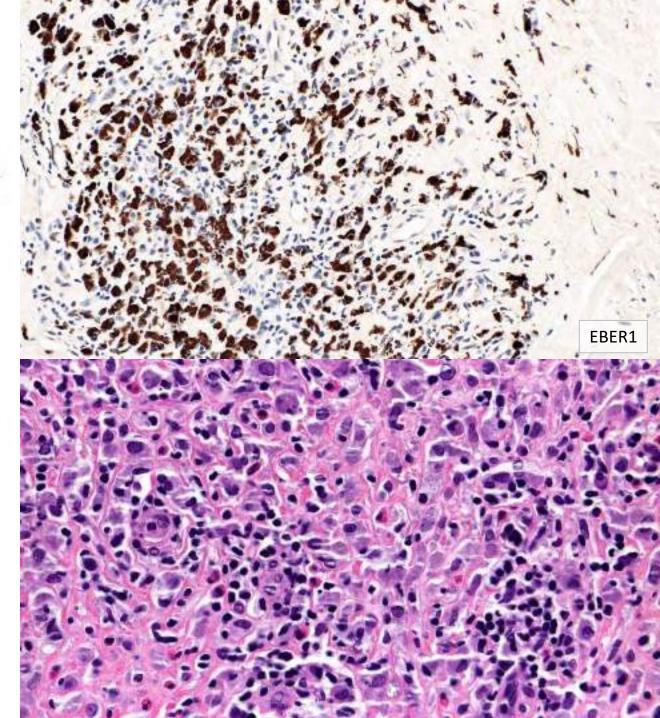
- Reactive germinal centers in Borrelia-induced lymphocytoma may miss a well-formed mantle and show confluence, mimicking the histopathological features of a diffuse large B-cell lymphoma
- High proliferation is usually a feature of malignant tumors, yet in lymphoid infiltrates with follicular pattern reduced proliferation of the lymphoid follicles is a clue for malignancy, whereas high (nearly 100%) proliferation is typical of reactive germinal centers

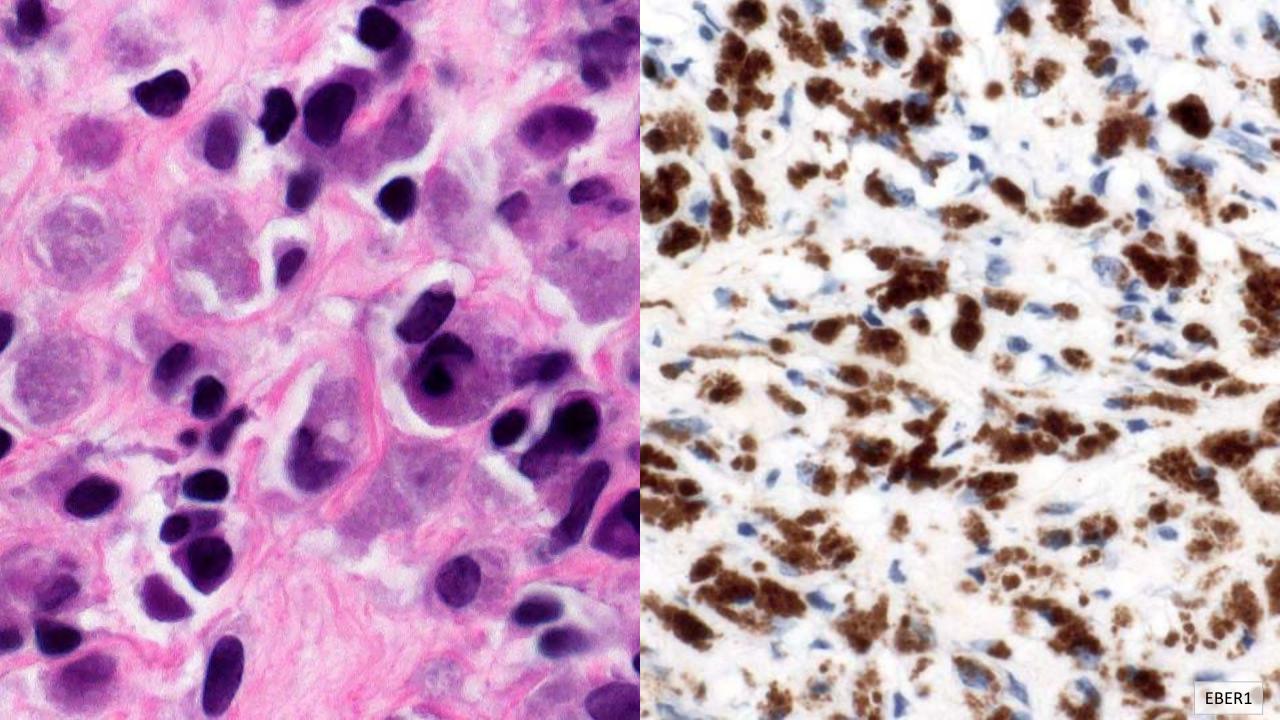


F, 42.Subcutaneous nodule at the site of a hyposensitivity treatment.



Pseudolymphoma at the site of vaccination





Cutaneous B-cell Pseudolymphoma at the Site of Vaccination

Lorenzo Cerroni, MD,* Riccardo G. Borroni, MD,*† Cesare Massone, MD,*
Andreas Chott, MD,‡ and Helmut Kerl, MD*

Abstract: Pseudolymphomas are a rare complication of vaccination, presenting with dense lymphoid infiltrates and prominent follicular pattern. We report our observations on 4 patients with vaccinationinduced B-cell pseudolymphoma (all females; age range 19 to 60 years; median: 34.5 years). Clinically 3 patients presented with subcutaneous nodules and 1 presented with a large, indurated, erythematous plaque. Histology revealed in all cases dense lymphoid infiltrates in the subcutaneous fat with prominent follicular pattern. The follicles displayed features of reactive germinal centers (normal mantle zone, presence of tingible body macrophages, normal proliferation). Necrotic areas surrounded by palisaded histiocytes were seen in 3 biopsies from 2 patients. A mixed-cell infiltrate with eosinophils and plasma cells was present in all cases. In addition, histiocytes with granular basophilic cytoplasm could be observed around the focal area of necrosis or within the inflammatory infiltrate. Follow-up was available for 3 patients. One patient was alive with persistent disease 6 months after the first observation. Two patients were treated with local radiotherapy and are alive and free of disease after 12 and 72 months, respectively. One of these two patients had a second pseudolymphoma on the contralateral arm after a new injection of vaccine. Cutaneous pseudolymphoma after vaccination should be distinguished histopathologically from low-grade cutaneous B-cell lymphomas (follicle center cell lymphoma, marginal zone lymphoma) and from other B-cell pseudolymphomas with prominent follicular pattern requiring different treatment (eg, Borrelia burgdorferiinduced lymphocytoma cutis).

Key Words: B-cell pseudolymphoma, vaccination, follicular pseudolymphoma, lymphocytoma, lymphadenosis benigna cutis

(Am J Dermatopathol 2007:29:538-542)

Adverse cutaneous effects of vaccinations include widespread and localized reactions. Mild erythema, edema, pain, and induration limited to the site of injection are commonly observed immediately after immunization and usually heal spontaneously. Less frequently, papules or subcutaneous nodules arise at the site of vaccination and may persist for months or years.^{1,2} Histopathologically, they are characterized by either granulomas or lymphoid infiltrates with prominent germinal centers.^{2–7} Typically, pseudolymphomas at the site of injection have been reported following administration of vaccines or allergens adsorbed to aluminum.^{1,6,8,9}

We describe the clinical, histopathologic, immunophenotypic, and molecular biologic findings of 4 patients who developed cutaneous B-cell pseudolymphoma at the site of vaccination.

PATIENTS AND METHODS

Patients

Four patients with a diagnosis of pseudolymphoma occurring at the site of vaccination were included in the study. The diagnosis of pseudolymphoma was based on clinicopathologic features. Association with previous vaccination was documented in all patients.

Histology, Immunohistology, and Molecular Biology

All biopsy specimens were fixed in 4% buffered formalin, routinely processed, and subsequently embedded in paraffin. For routine histopathologic analysis, sections were stained with hematoxylin and cosin. All histopathologic sections were reviewed by at least two of us (L.C., R.G.B.). The following features were analyzed: location of the infiltrate, presence or absence of necrosis, sarcoidal or tuberculoid granulomas, germinal centers, degenerative fat changes, cosinophils, plasma cells, and histiocytes with granular basophilic cytoplasm. Standard immunohistology and molecular biology techniques [polymerase chain reaction (PCR) analysis of immunoglobulin (Ig) H gene rearrangement] were used as described previously. [1,11]

RESULTS

Clinical Features

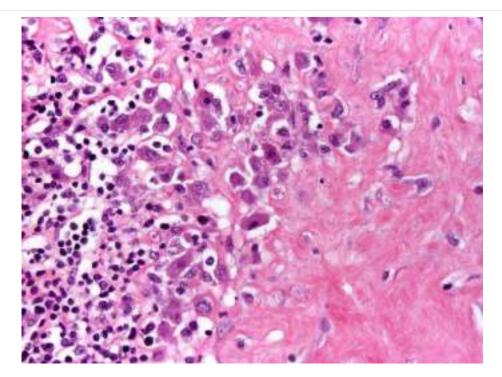
The clinical features of our patients are summarized in Table 1. All patients included were women. Age ranged from 19 to 60 years (median: 34.5 years). The vaccine administered was for early summer meningoencephalitis (ESME) in 2 of 4 patients, tetanus in 1 patient, and hepatitis B virus in 1 patient. The site of injection, thus the site of occurrence of skin lesions, was the upper arm in all patients. Patient 2 presented with a pseudolymphoma after ESME vaccination on the left upper arm. She subsequently received a second injection of the

TABLE 2. Histopathologic Features of Pseudolymphomas at Site of Vaccination

Patient	Necrosis	Sarcoidal or Tuberculoid Granulomas	Germinal Centers	Eosinophils	Plasma Cells	Histiocytes With Granular Basophilic Cytoplasm	Degenerative Fat Changes	Polymerase Chain Reaction
1	_	_	+	+	+	+	+	P
2	_	_	+	+	+	+	+	P
2*	+	_	+	+	+	+	+	ND
2†	+	_	+/-	+	+	+	+	P
3	_	_	+	+	+	+/-	_	P
3*	+	_	+	+	+	+	+	ND
4	_	_	+	+	+	+	+	P

ND, not done; P, polyclonal smear.

"Histiocytes with a granular, basophilic cytoplasm were observed in clusters and scattered throughout the infiltrates in all cases."



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^{*}Persistent lesion at the same location.

[†]New lesion on the contralateral arm after a second injection of vaccine.



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DRIGINAL ARTICLE



EBER in situ hybridization in subcutaneous aluminum granulomas/lymphoid hyperplasia: A diagnostic clue to differentiate injection-associated lymphoid hyperplasia from other forms of pseudolymphomas and cutaneous lymphomas

Verena G. Frings¹ | Sabine Roth² | Andreas Rosenwald² | Matthias Goebeler¹ | Eva Geissinger^{2,3} | Marion Wobser¹

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Abstract

Background: Subcutaneous vaccination or desensionation may induce persistent normalise at the injection stee, Without the knowledge of prior injection, fundapathological work up may be childrightn.

Objective: Aim of this stury was to costribute to the hydopathological work up of unclear subquitaments modules, especially their differentiation from cutaneous verphores.

Methods: We represent you would clinical opts and histopathological sides of four patients with executaments naturing which were suspected to further from outs record. They Blood lymphoms. Sections of these possiumed 12 regalize controls were stained with hemotoxylin and exem and a standardized immunohistochemical poset of Blood Those markets including EBER in situ hybridization as well as electron microscopy.

Results: If all cases, targe histocyces with grenum cytoplains competitive with Intracellular analytical trycholder years present. EBER in site hybridization revealed and three staining of these granular histocytes white staining was passent in regative controls.

Unitations: Post for completion of medical history revealed that secondary or specific immunochampy had been applied before at the bloppy sile in only times out of hour patients: one patient was best to fellow-up.

Conclusion: EBER in alls hybridization is an adjunctive time to differentiate startistian induced granulareally/replaced hyperplants from other forms of operation/mohorta-and/outsisess B- or T-cell (implicates).

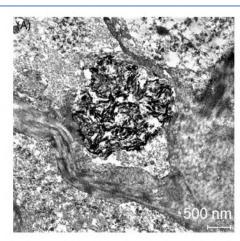
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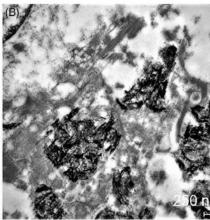
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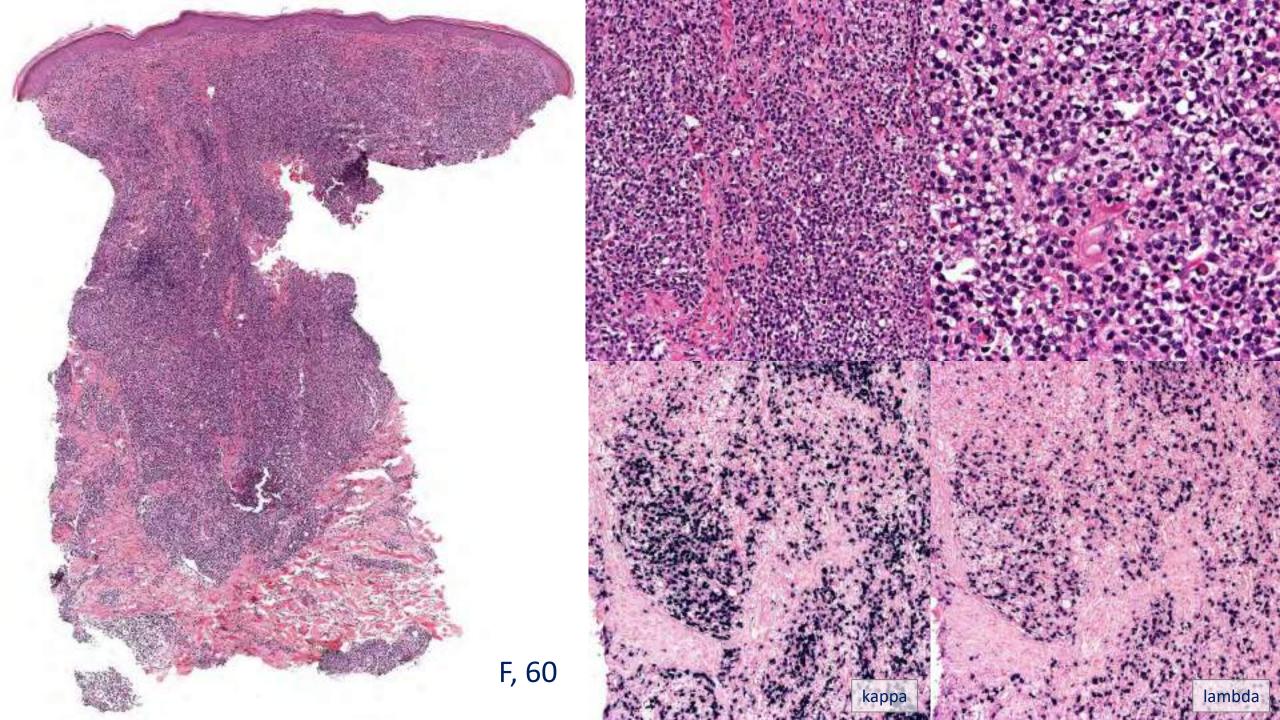


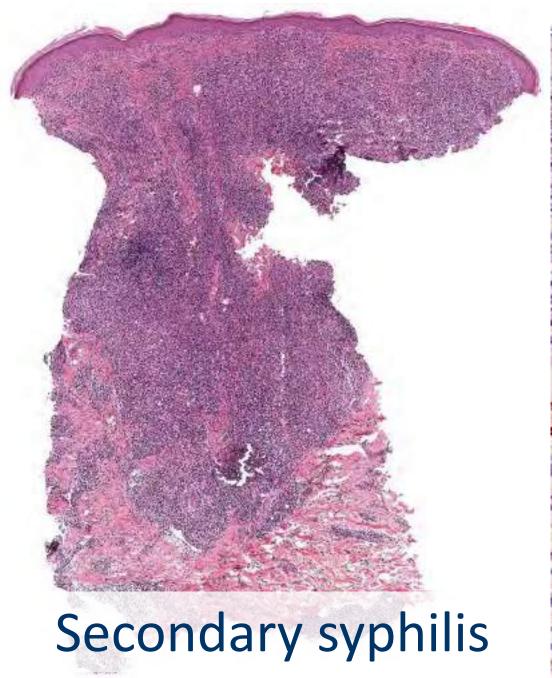
granuloma. Electron microscopy exemplified by case 1. (A, B) In the cytoplasm of the histiocytes there are interwoven, filamentary or crystalline structures that correspond to the EBER positive signals

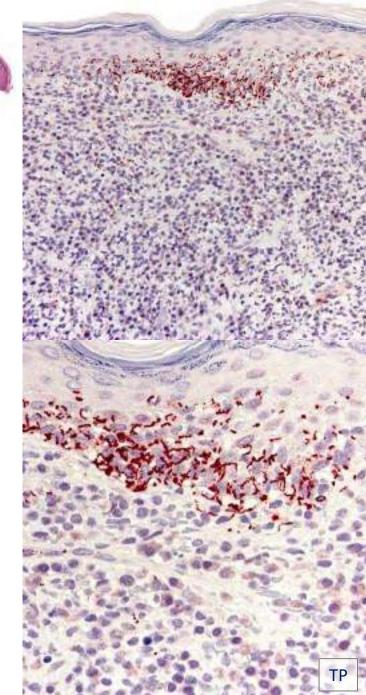
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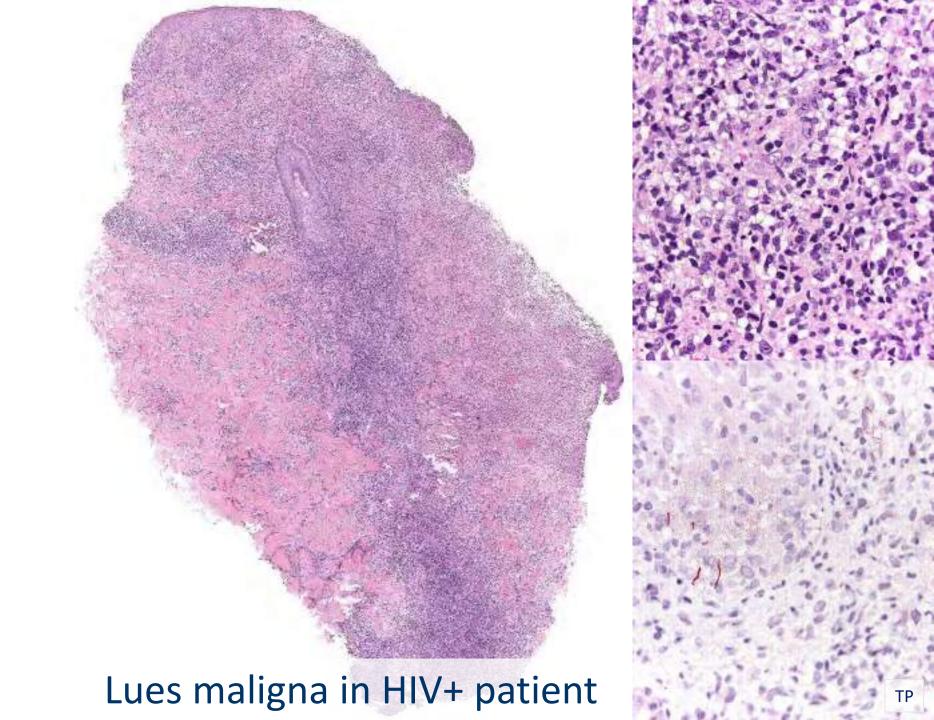
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^{*}First other Ingold art. Ingold art. German









Secondary Syphilis Misdiagnosed as Lymphoma

D. R. Goffinger, M.D., C. Hoyt, M.D., and J. R. Eltringham, M.D., Stenford

In 1968 Sensions reviewed the histologic moternal of 500 patients with an initial history diagnosts of Hodgkin's disease and found that three of the patients actually had either primary or autismy syphilis as the correct diagnosis. However, 25 years have elapsed sixed the generalized lymphodenogathy of secondary syphilis was last reported to have been misdiagnosed as one of the lymphomas, in particular gians follicle lymphomas.

Since 1944 a new generation of physicians has been trained, some of whose have rever seen a rose of secondary applilis. Therefore, attention is again called to the fact that syphilis is still a common disease that should be considered in the differential diagnosis of generalized lymphedenopathy. This report describes two patients seen recently, both of whom had syphilis, mindiagnosed in one case as glant follole lymphedens and in the other confused with Hodgian's disease.

Report of First Case

Case J. A 31-year-old Negro man noted tender right inguised lymphodotorpothy in January 1968, but no peakle leatons were present and a VSKL report was negative. Brythnomycin was given osalby for two days with prempt disappearance of silpalpuble lymph modes.

The patient was then well until October 1968 when a slightly practite widespread papular skin eruption appeared, followed in shour two weeks by generalized lymphademopody. The skin lesions were treated with comstanth soals. Biopsy of material from axillary and inguinal nodes in November was interpreted as giant follote lymphoma, and the potient was subsequently referred to the Division of Radiation Thorapy at Stanfard University Medical Center for further evaluation and

treatment. He was taking no medications, had not used Dilastin® and had no history of monomicleosis, cit scratches, sweats, or fevers.

The patient, who was healthy-appearing, had generalized lymphadenopathy, including palpublic epitrechlers nodes, of less than 2.5 cm in size. There was a generalized pagulo-squamous eraption, most premium and trunk. The remainder of the examination including neurological, disclosed to absormative.

The Venereal Disease Research Laboratory Test (vipel.) was reactive to 1:128 dilution and the Fluorescent Treponeme Antibody Test (AFTA) was also positive. The Stanford surgical pathologists were of the opinion that the lymph node biopsy sections showed assented hyperplasis.

The petices was sent back to the referring physician with a diagnosis of accountry applicia. A Jerisch-Herzheimer reaction developed during particilin therapy, and pulpoide adecupathy disappeared within these weeks. A repeat your was nomencular within these weeks.

Report of Second Care

Care 2. A 41-year-old single white man were well until Jamary 1968 when he flow noted and it publics, slowly enlarging masses on both sides of the neck. A generalized, crythematous and practice skin emption was also noted. It cleared completely, without treatment, in a few days. There was no history of fevers, sight sweats, diphenylhydantein (Dilantin®) larake, cat scratches, monomodeously, or people lesions. A visu, test had been negative in 1966, but she pattent admitted to having both homosexual and betweenval relations since that time.

After a March 1969 cervical lymph node biopsy was interpreted as showing Hudgkin's disease, the patient was transferred to the Palo Alto Veterans. Administration Biosphal for crossideration of radiotion therapy.

Except for generalized lyexpludesopathy, including pulpable spitrochiese nodes, no abnormality was mosel on physical exemination. All modes were less than 2 cm in dismeter. The Ever and spices were not palpable, and there were no skin legions.

Results of blood cell count, urinalysis, determination of blood urea nitrogen, soon and electrolyte contents, and an x-ray film of the chest wore all within normal familia. A visu, test was reactive at 1:128 dilution and an PTA test was also positive.

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British Journal of Dermatology (1976) 95, 251.

Histology simulating reticulosis in secondary syphilis

KEBECCA E.I.GOCHRAN,* JOHN THOMSON, K.A.FLEMING* AND ALEXANDRA M.M.STRONG

Department of Dermanningy, "University of Glasgow, Department of Dermanningy, Royal Informacy, Glasgow, and "University Department of Pathology, Royal Informacy, Glasgow

Accepted for publication 5 January 1976

SUMMARY

Three cases of secondary syphilis are described in whom a skin biopsy was performed. In all, the histology bore a striking resemblance to that of malignant lymphoid acoptages.

The classical cutaneous munifestations of accordary syphilis are availly easy to diagnose, especially when there is a good clinical history and the appropriate investigations are positive. If, however, the truption is not characteristic, a skin biopsy may be carried out. We should like to report three cases where the histological appearances in inclation would have been misleading.

CASE REPORTS

Case t

The patient, a 16-year-old girl, was admirted to hospital with a pyrexia and symptoms suggestive of a urinary tract infection. She was noted to have a widespread crythematous papular cruption involving face, trank and limbs, which had been present for 3 weeks. Their were no masosal lesions. The inguinal lymph nodes were palpuble.

Specific serology was as follows: VDRL slide test—positive. Cardiolipin Wassermann reaction—positive. Reiter protein complement fination test—positive. A skin biopsy was reported as follows: The epidermis is hyper—and parakeratoric with marked epidermotropism of mononuclear lymphoid arills which are forming micro-obscesses in areas. There is inter—and intracellular ocalema in the epidermis. In the dermis there is a dense infiltrate which predominantly is perivascular. There is no evidence of a vascular lesion. The infiltrate is composed of histocytic cells, mononuclear cells, plasma cells and occasional neutrophil polymorphs. Scattered throughout there are large pleomorphic mononuclear cells with hyperchromatic nuclei and prominent nucleut. Mitotic figures are occasionally found. These findings in the absence of a clinical history are compatible with the diagnosis of cutaneous lymphoid neoplasm.

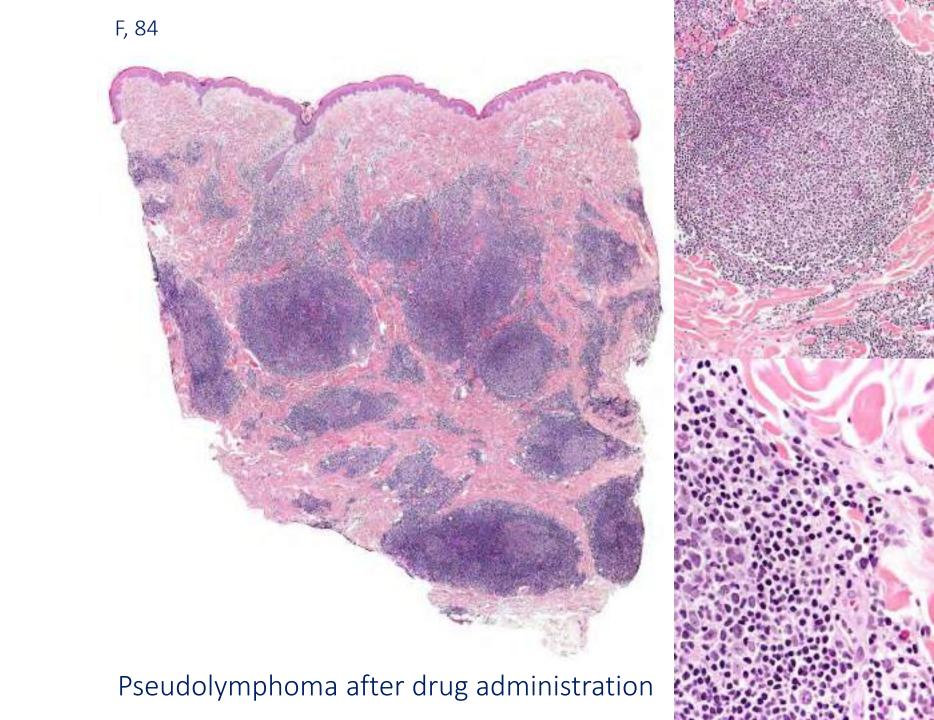
Skin biopsies interpreted as lymphoma

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Pseudolymphomatous syphilis

- Rare clinicopathologic presentation of secondary syphilis
- Solitary (rarely) or multiple papules, nodules and small tumors; may simulate MZLD, but plasma cells polyclonal
- In HIV+ patients with low CD4+ count may simulate a T-cell lymphoma (lues maligna)
- Some ulcera of primary syphilis may also be characterized by florid, pseudolymphomatous infiltrates
- Staining for Treponema pallidum represents a useful tool, but microorganisms may be only a few



Lymphomatoid drug eruption (B-cell pattern)

- Drug eruptions may occasionally mimic a cutaneous B-cell lymphoma (FCL-like or MZLD-like); The B-cell pattern is much less frequent than the T-cell pattern of drug-induced pseudolymphoma
- Sudden onset, localized or generalized distribution; Resolution upon discontinuation of the offending drug
- Cases with B-cell pattern present with nodular infiltrates, either with germinal centers or with clusters/sheets of monotypic plasma cells
- The germinal centers reveal reactive morphologic and phenotypic features



DESCRIPTIVIDE DIRECTORS

Australapan Journal of Dermatology REVIEW ARTICLE



Drug-induced cutaneous pseudolymphoma: A systematic review of the literature

Ifa Etesami MD, MPH | Yasamin Kalantari MD12 | Soheil Tavakolpour PhD300 Hamidreza Mahmoudi MD¹ Maryam Daneshpazhooh MD¹

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Abstract

Drug induced caraneous pseudolymphums (CPL) is a common form of pseudolymphons, and there are numerous drugs associated with it. In this study, we performed a systematic review of the literature by searching PubMed/Medline and Finhase dualisses to determine the most common drugs responsible for CPL and to define the demographic, clinical, histopathological and lemminopathological characteristics of potents (updated up 30 December 2020). From 883 initially found anticles, 36 studies (89 reported cases) were included. The mean age of patients was 54.4 ± 17.7 (ranging 8-10) years, and 46 (\$1.7%) were men. The median time interval between drug intuke and CPL occurrence was L20 days (range 1-7300 days). The shortest median time interval besween taking the drug and the onset of the disease was observed among patients taking antidepressants (Midays) (range 7-540) and the longest modium time interval was observed in individuals using immunumodulators (300 days) (range 3-7300). The most-reported drug caregories causing CPI, were anni-hyperturshes (17.9%), anniconvoluents (14.9%), monoclosal and bodies (13.4%) and unitdepressons (41.2%). Moreover, the mast common drugs were pleasytein (6.7%), amind/plus (8.6%). flurisatine (5.6%) and earhomizzepine (4.4%). Histopathological evaluation of 76 cases revealed 62 (81,9%) reports of T cell infiltrations. Furthermore, positive reports of CD4 (44.0%), CDR (93.0%) and CD30 (87.5%) were noted. The lowest previdence of CD30-positive reports was observed among manufornal antibudies. In corclision, anti-hypertonshes, anti-convulsants, monoclonal antibodies and unti-depressions are the most common drugs respondible for CPL. It mostly presants in middle-aged patients with almost no gender difference as prantic papities, nodules and plaques

REYWORDS

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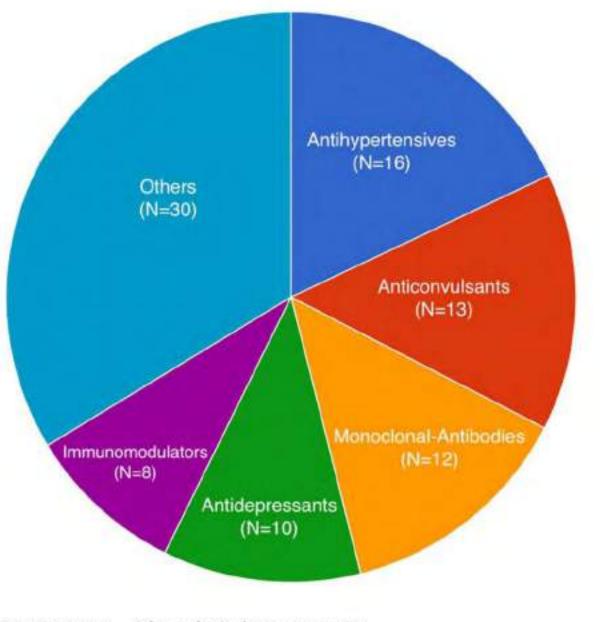
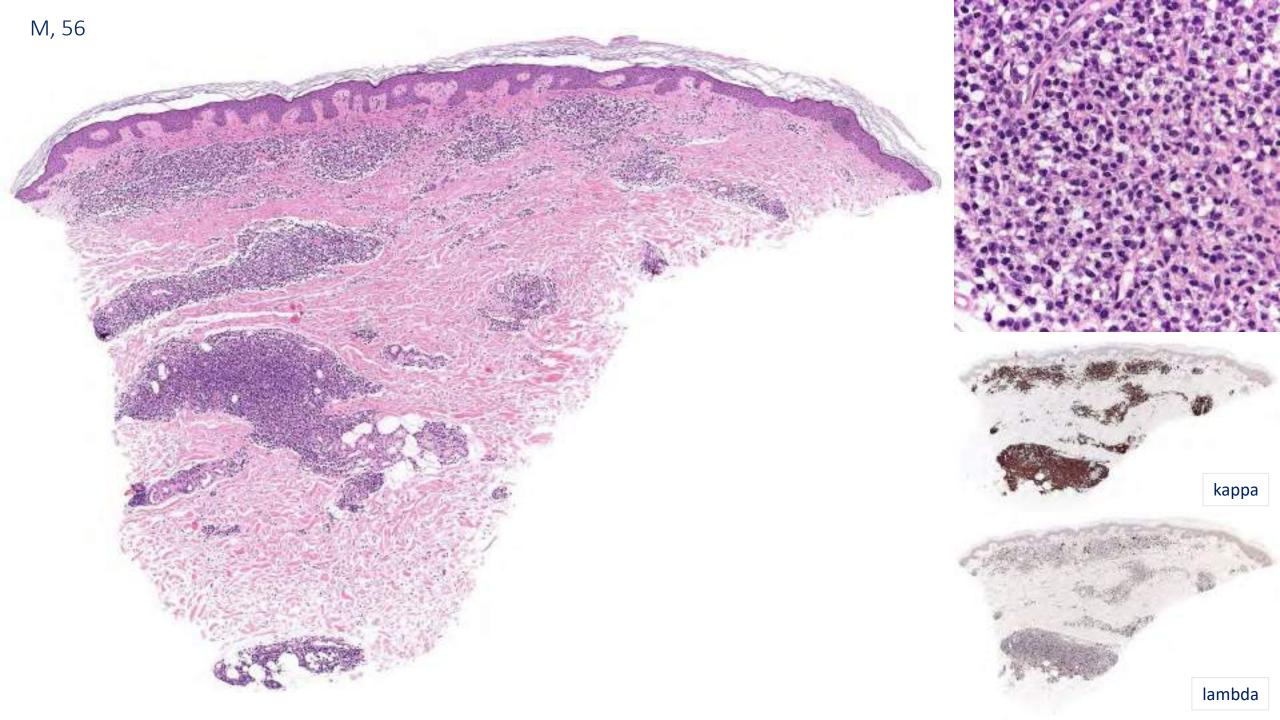
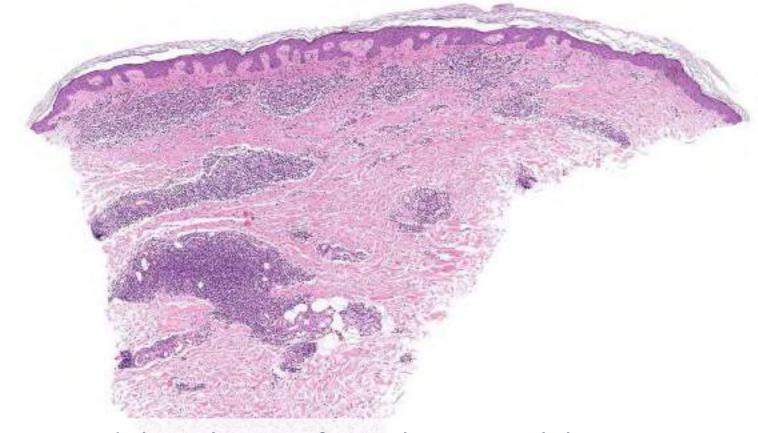


FIGURE 1 The culprit drug categories





Pseudolymphoma after talimogene laherparepvec treatment for metastatic melanoma





Letters to the Editor (200)

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DOMESTING SECTION

Talimogene laherparepvec can initiate plasma cell invasion into infiltrated melanoma lesions - a case series

Talkrogere leherpungwee (T. VB), (is a genetically engineered. herpes supplies virus type I (HSV I) and used in locally arlianced rectinions patients. To mode of artists is not fully anderstood, 12 We present three cases where TADE cassed reproctoral as well as polyclonal fi-cell infilmation.

Care D.A.99 year-old male potient presented with several firm. black blank payaks or his right upper sent after a history of modeliar stellaturus (2.95 mir.) on his right bovor and 2 years prior (Fig. 1st. Histopathology movehal extension: 2001) state restated maluranta extintions. Due to rea signs of distant metalases, material with T-VDC (IMINIAC®) was adminiantibling behaviorate to godorca yllavoicalized have Within 4 mostle, all beions represed leaving flat gressly and tiles that were mened ting. It is

Histology recolail drate infinites composed alreast entirely of mature places with isomed in the mater deprise and squeetcial subcatis (Fig. 1c). Pocal Eboosis and superficial dumers of melanophages were observed, and completes of inelanocetes were absent (Fig. 3d'). By in una hybridization and immunohistochemieny, the planea cells sons closed, suprouting light chain trappe and horsy chain IgG (Fig. te.J. Nine munits later, uso new papeles on the right apper and were recised. They showed the same infiltrate as mentioned above. Serum and times protein electrophoresis was polestous! Quartification of JoS. ItA and 16M increaned obdies as well as resourcement of the senior free light clums herists and kappy showed no pathologic fracings. A.

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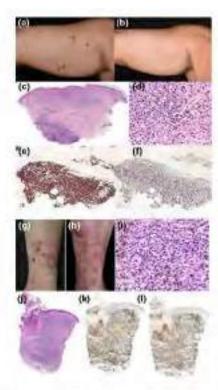


Figure 1 Clinical images and immunohistochemical pictures of case 1 and 2. (a) Black-bluish papules on right upper arm representing outaneous melanome metastases in December 2016. (b) Regression of all marked lesions in May 2017, (c) Histology showing dense infiltrates composed almost enfrely of mature plasma. cells located in the entire dermis and superficial subcutis longinal magnification 20 x). (d) Focal fibrosis and small clusters of melanophages admixed with plasma cells, but no complexes of melanocytes (original magnification 200 x). (e) Plasma cells are positive for kappa light chain (in situ hybridization; original magnification 100x). (i) Plasma cells are mostly negative for lambda light chain in situ hybridization; original magnification 100 s.). (g) Red and black-bluish macules and papules on the left lower leg representing outaneous melanoma metastases in August 2018, (h) Regressive lesions in Mai 2019. (i) histology showing dense infiltrates composed almost entirely of mature plasma cells located in the entire dermis (original magnification 20x). (i) Focal fibrosis and small plusters of melanophages admixed with plasma cells and lymphocytes, but no complexes of metanocytes (original magnification 200x). Polyclonal aspression of kappa (k) and lambda (l) light chains of plasma cells (in situ hybriotzation; original magnification 20xlx

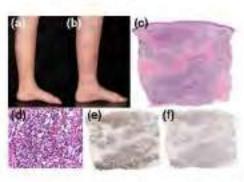
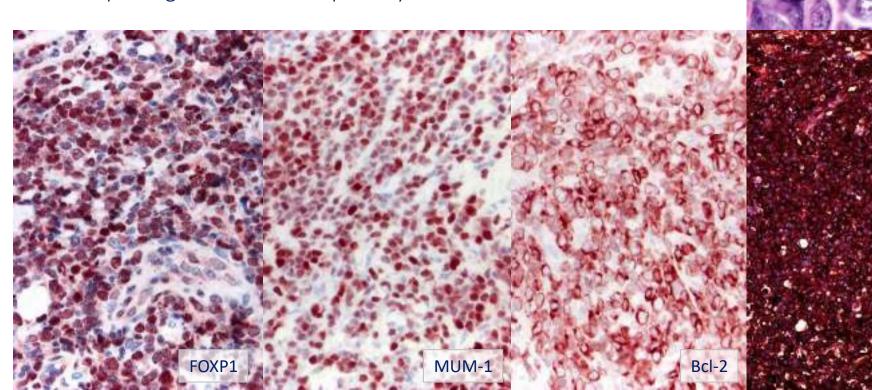


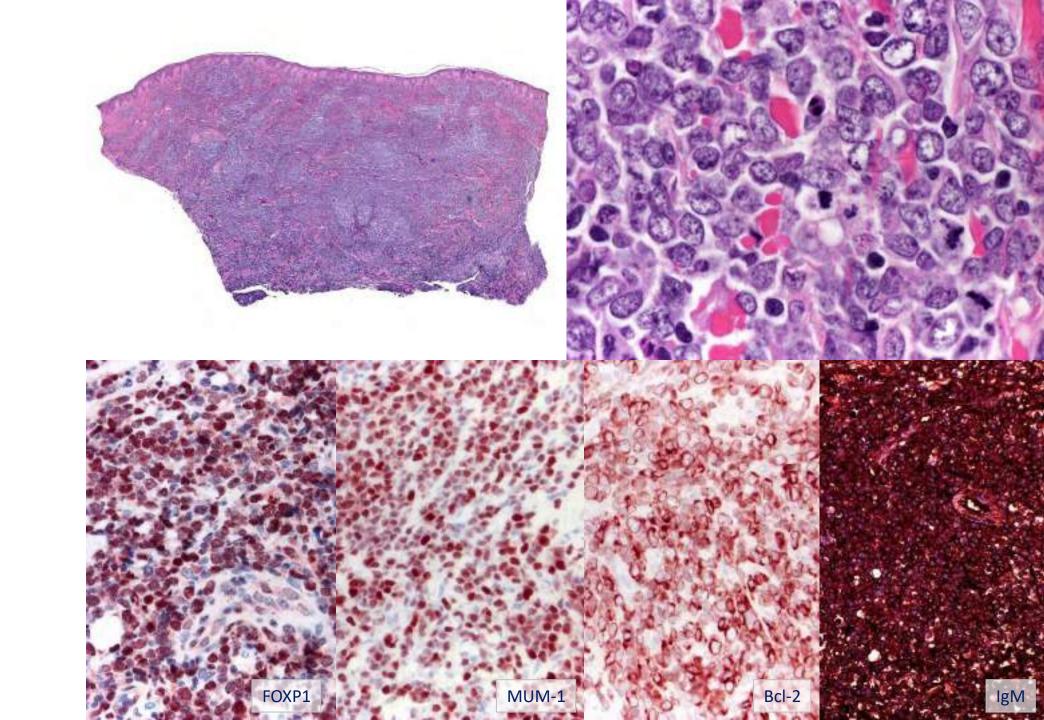
Figure 2 Clinical images and immunohistochemical pictures of case 3. (a) Black-bluish papules on the left lower leg representing cutaneous melanoma metastases in December 2017. (b) Regressive lesions in December 2018. (c) Histology showing dense infiltrates composed almost entirely of mature plasma cells located in the entire dermis (original magnification 20x), (d) Focal fibrosis and plasma cells, but no complexes of melanocytes (original magnification 200 x), (e) Plasma cells are positive for kappa light chain (in situ hybridization; original magnification 20x), (f) Plasma cells are mostly negative for lambda light chain (in situ hybridization; original magnification 20x).

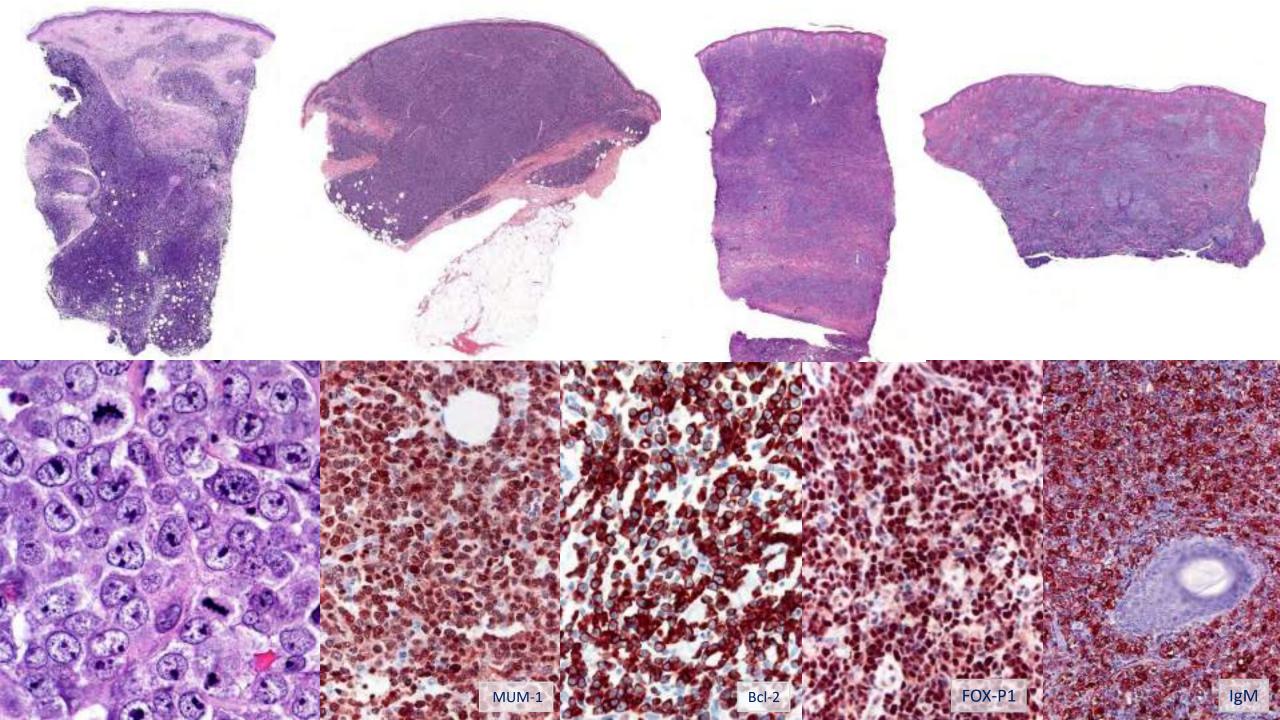
Primary cutaneous diffuse large B-cell lymphoma, leg-type

Edlerly patients; in >80% of cases located on the leg(s). Sheets of centroblasts and/or immunoblasts. Bcl2+, MUM1+, Bcl6+/-, FOXP1+, IgM+, MYC+/-, CD10-(+).

Chromosomal translocations involving *IGH* in 50%, *MYC* in 5-43% and *BCL6* in 23-50% are reported, as well as "double-hit" lymphomas with *MYC* and *BCL6* translocations (not of *BCL2*). Highly recurrent hotspot mutations in the adaptor molecule of the Toll-like receptor *MYD88* are found in ~70-75% of cases. The gene expression profile of PCLBCL-LT resembles activated B-cell–like DLBCL, similar to lymphomas arising in immunoprivileged sites such as primary DLBCL of the CNS and testis.







Follicle center lymphoma, diffuse type Non-aggressive treatment

Diffuse large B-cell lymphoma, leg type Aggressive treatment

Applical elinicopathologic presentation of primary cutaorous diffuse large il-cell lymphoma, leg type

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Fig 1. Primary cutaneous diffuse large B-cell lymphoma, leg type. Patient 1. Annular lesion on the leg. A small scar represents the site from which the biopsy specimen was obtained,

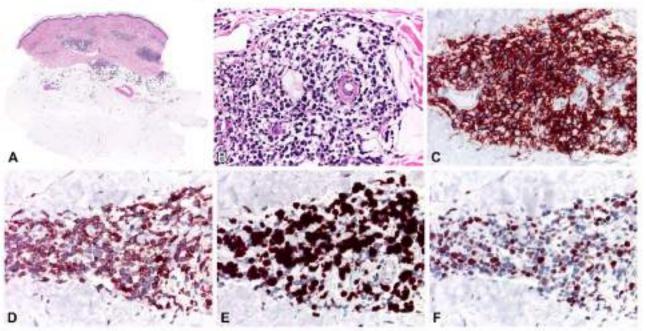
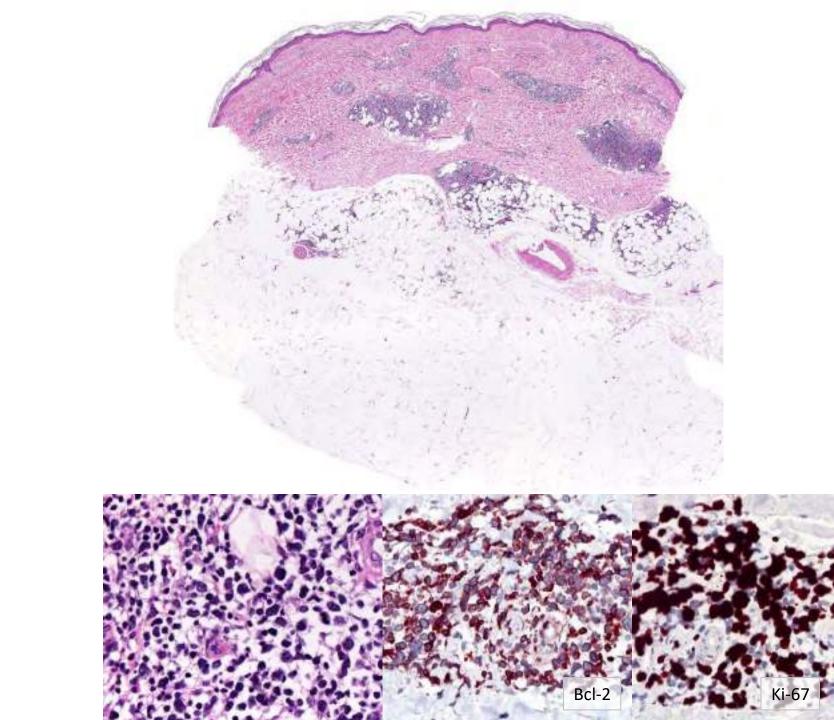
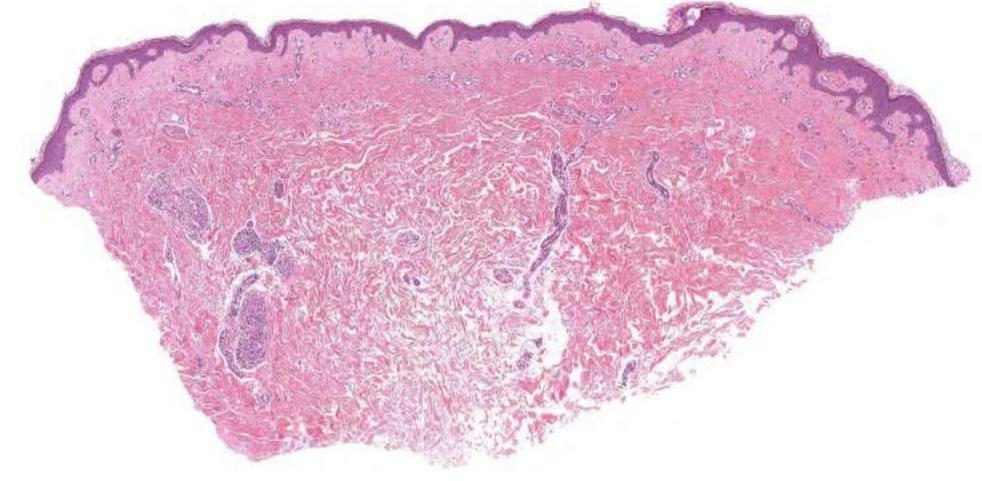


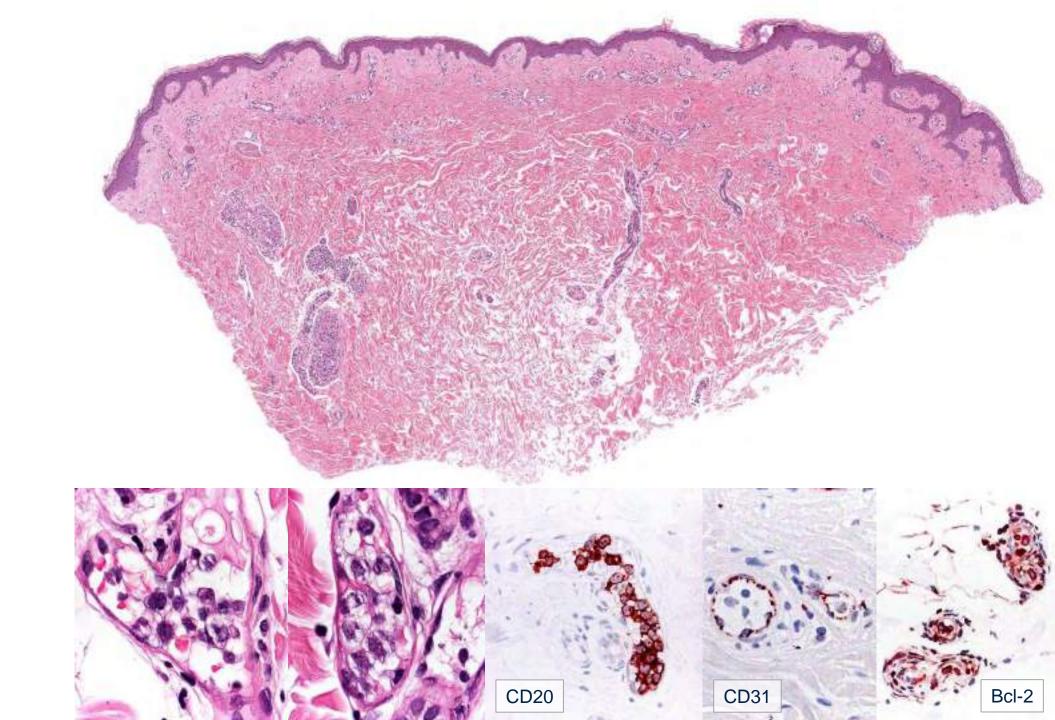
Fig 2. Primary cutaneous diffuse large B-cell lymphoma, leg type. Patient 1. Histopathologic and phenotypical studies reveal (A) a moderately dense, perivascular infiltrate (B) characterized by small lymphocytes admixed with several large cells. The cells are positive for (C) CD20, (D) Bcl-2, and (E) MUM-1 and (F) show a high proliferation as detected by the antibody Ki-67.



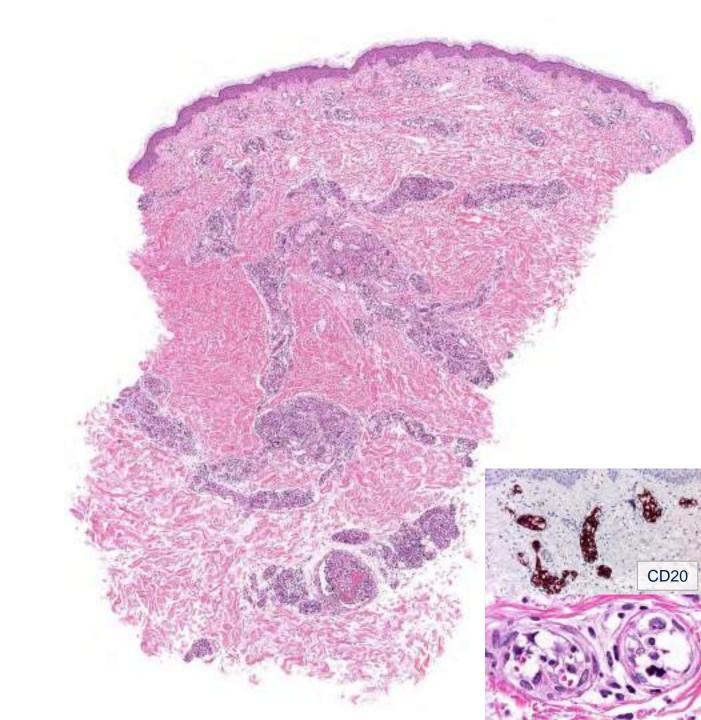


Intravascular diffuse large B-cell lymphoma

Rare variant of large B-cell lymphoma confined to the lumina of small blood vessels. Common involvement of skin and CNS ("Western variant"); multiorgan failure, haemophagocytic syndrome ("Asian variant"); a purely cutaneous variant, observed only in Western women, has a better prognosis. Sometimes diagnosed by "random" skin biopsy; located within haemangiomas in more cases than mere chance would explain. *MYD88 and CD79B* hot spot mutations are reported in 50% and almost 70% of cases, respectively. Morphologically indistinguishable from IV-NK/TCL.



F, 56
(Consultation Dr. Müller, Homburg/Saar)





Dermutology 2004;200:79-89 DOI: 10.1199/000079597

Hemangiomas with a (Bad) Surprise

Lorenzo Cerroni

Department of Dermornlogy, University of Graz Medical School, Graz, Austria

Few lesions are less eye-eatching for dermatologists and demastorathologists than senile (cherry) hemangiomas. For one, they are among the most common benign neoplasms in the adult and elderly population, and two, they are devoid of any particular clinicopathologic or therapeutic problem; they are straightforward clinically, a glance diagnosis histopathologically, and treatment, if desired, is easy as well. In short, they are hardly the source of particular interest. And yet, in this issue of Decoratology 2 cases of cherry hemongrouns or hemongrouna-like skin changes draw the attention to these unremarkable neoplasms, showing that behind their innocent appearance sometimes the nevil can hide. Our case [1] and that reported by Motegi et al. [2] show two different faces of the 'hemangiomas with a surprise'; one characterized by colonization of precisiting therry hemangiomas by neoplastic cells of an intravascular large 8-cell lymphoms and the second showing an eruption of hemanajoma-like skin lesions representing in truth skin involvement of angioturpic lymphoma. In both cases, the diagnosis was completely unexpected and represented a surprise, unfortunately a bad one, for the clinicians, the dermatopathologists and the patients.

Intravascular large B-cell lymphoma (also termed angatropic lymphoma) is a muligrant proliferation of large Hlymphocytes within blood vessels. It was first described by Pfleger and Tappeiner in 1959 [3] and was formerly classified as a vascular recipiasm (malignant angioendotheliomatosis) [4]. It is considered as a subtype of extranodal diffuse large B-cell lymphoma [5]. This peculiar dis-

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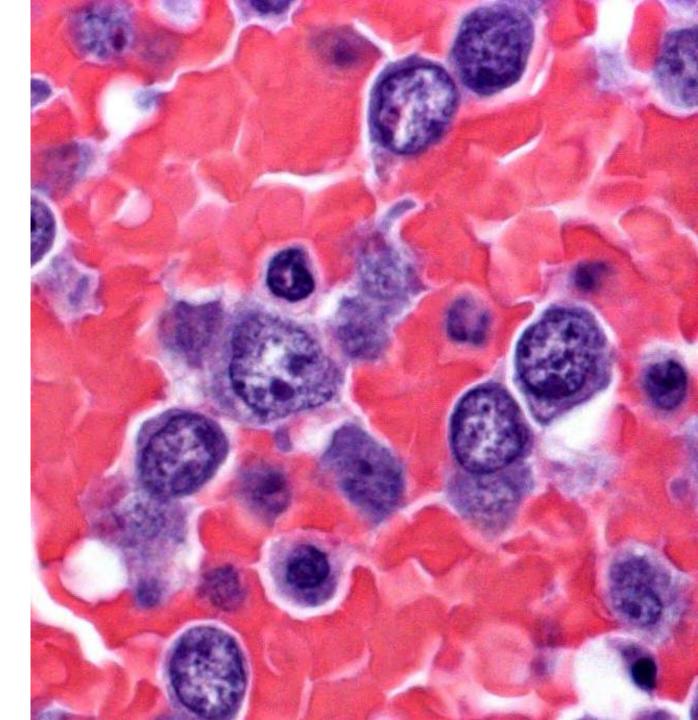
case may arise de novo or in patients with precasiting entancous or, more often, nodal large B-cell lymphoma, in the latter strance probably representing a recurrence of the original malignancy rather than a second lymphoma [6, 7]. Neoplastic cells are positive for B-cell-associated markers, but a very rare T-cell variant of the disease has been reported [8]. Prognosis is usually very poor, with a median survival of about 12 months. The prognosis of cases limited to the skin may be better than that of the generalized (multiss stem) disease, but only a very limited number of patients has been followed up to date.

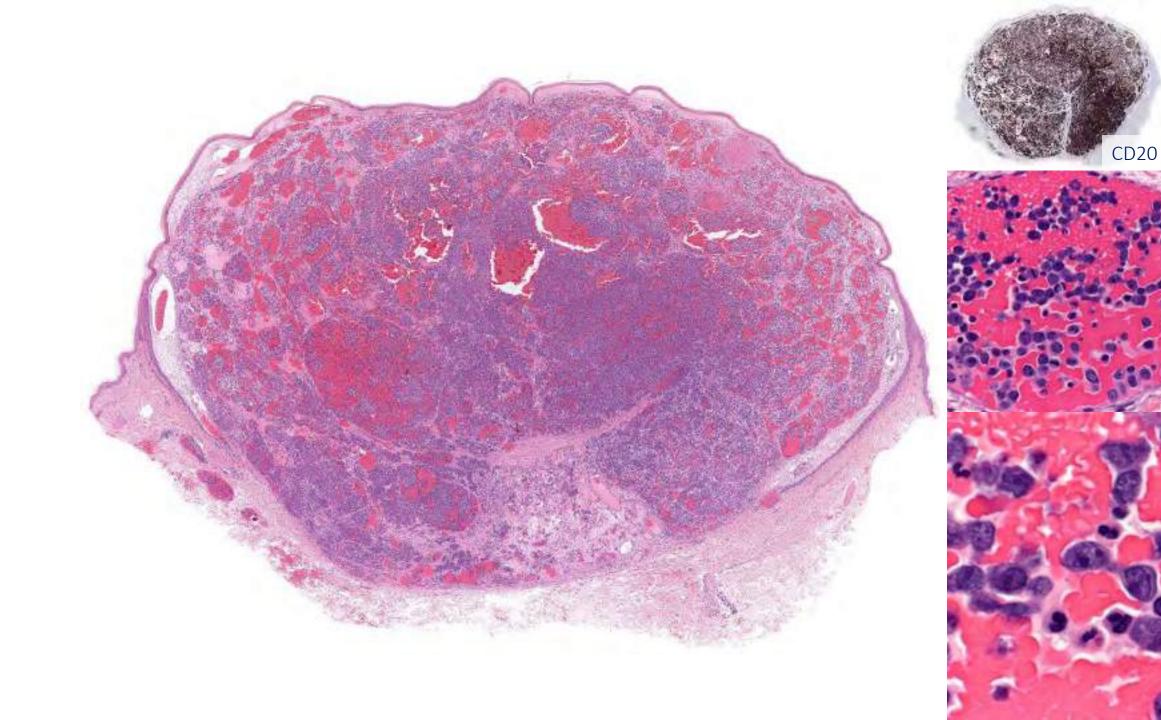
The most common clinical presentation of intravascufar large B-cell lymphoma is characterized by industed. erythematous or violaceous patches and plaques, preferentially located on the trunk and thighs. The clinical appearance is not typical of lymphoma and may staggest a diagnosis of punniculitis or of purposa [9-13]. In rare cuses, the skin may be the only affected site (primary cutaneous intravascular lange B-cell lymphoma), though more often the lymphoma is disseminated, and neumlogic symptoms as a sign of involvement of the central nervous system are commonly present [14]. Other organs that are frequently involved are the liver, lungs and kidneys. Sestemic symptoms due to specific manifestations at extractitansous sites are more likely to be caused by clots within the blood vessels and subsequent infarction of rissue than by destructive reophistic growth.

Colonization of preexistent cutaneous herrangiomas, similar to that observed in our patient, has been described in 2 other cases [15–17]. Although this is an exceptional

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Demacdagy 2004;209:122-134 DOI: 10.1159-0000070580

Intravascular Large B-Cell Lymphoma Colonizing Cutaneous Hemangiomas

Lorenzo Cerroni Iris Zalaudek Helmut Kerl

Department of Dermatology, University of Graz Medical School, Graz, Austria

Intravagia lar large B-od l lympt-onta : Cherry hemongiums

Abstract

intravolucator Sirger B-cell fyrrginums to a malignant moploers characterized by the proiferation of large Boels (rarely of Throughtrytest confined within the triood neesels. All though the disease can be invited to the skin, insolvement of other organs to common. We report a case of intravascular large B-cell temphoma cotoniging the vessels of presisting cutateous cherry herrangin-

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Intravescular large B-cell lymphoma (formerly maligrant angioendotheliomatosis. angietropic (saughorna) is a molignost recoplant characterized by the profferation of showed that these edis were positive for large B cells (turely of T lymphocyles) cros- CD45, CD20 and CD79s, and negative for lined within the blood vessels. Although the CD3 CD5 and CD30. They were also requialsesse can be limited to the skin, involvement of other organs, aspecially the coroni. 45, Motor-Ayand for creckmatin. Based on nervous restem, is common. We report a clinicopathologic features, a diagnosis of insase of intravescular large B-cell lymphona - may acolor large B-cell lymphona autorizsolonizing the vessels of propositing turn-ing a prossition himsegions was made. neous cherry horsangioesas.

Report of a Case

An 31-year-old woman with a furtury of mangnant mekanima in 1999 Damor thickmess 4 mm; no extracutaneous involvement) gresented to our department in April 2002 for a number softwoop examination. Physical experimention did not show any sign of recurrence of stutonoma. She had soverall usual mesile (chiney) bermangiorean which had been present for none years. However, she had noticed that one of them located on the left upper arm had been dightly enlarging in the last few morths and asked to have it removed for connectiv reasons (fig. 1). The herrorgiona was surgically removed, fixed in formalin and enfected in parallin for matine histogethologic experiestion. Historogy revealed the overall architecture of a capitary homogeoms. However, the vessels went filled with large attribud cells with cutamorphologic features of controbiasts and emmunoblests trig. 2). Immunohistology tive for melanocytic merices (\$-100, HMB-

The parient was submitted to staging asvestigations than failed to noteal any extracttimeous involvement. Five more cataneous terrangional were surgically emount fall

of them located at the trunks. Histografiologic avidence of introvoceidar large B-odl. lymphoria andd be found in 2 of them (fig. 3). In contrast to the first loom, coloninotion of the Blood vessels in these 2 was only partiet and limited to a part of the berningerius. Bergical excisam of 5 Justiere. clinically disgressed as liponta revealed the histopathologic features of angempores. withour any malignant lymphoid collewithin or outside the vessels.

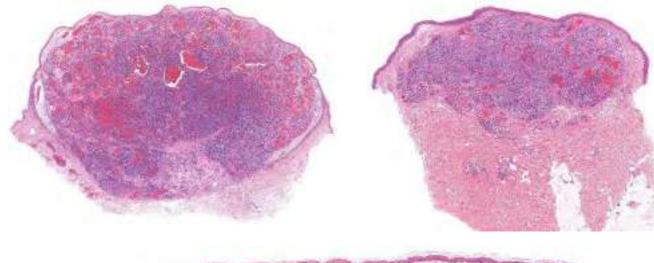
The petime declined any treatment, but was attending regular follow-up controls. At the last follow-up examination 9 months after the first diagnosis she complained of increasing farigue, but did not show any contral nurrous system or systemic symptoms. She died at home 12 months after presentation, and the relatives desind authorization.

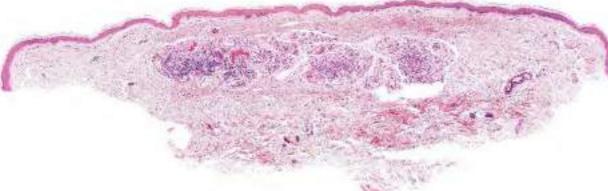
Intravescular large 8-cell Irrephorus is a year rant various of large Head by easternafrequently involving the skin, first described by Pfloger and Tappainty in 1979 Ht. Citalcally, lesions are often incompanious purpusic marsles and players, and reay be randingnoted as purpose or 'parmiculate'. Colonization of processors harrangionas has been described rarely to those patients and some to be a prestkar efinicopathologic manifestabiox of this unusual temphono (2, 3).

IVLBCL in 3/6 angiomas.

5/5 angiolipomas negative.

Normal skin at the side of involved angiomas did not show histopathological signs of intravascular lymphoma.





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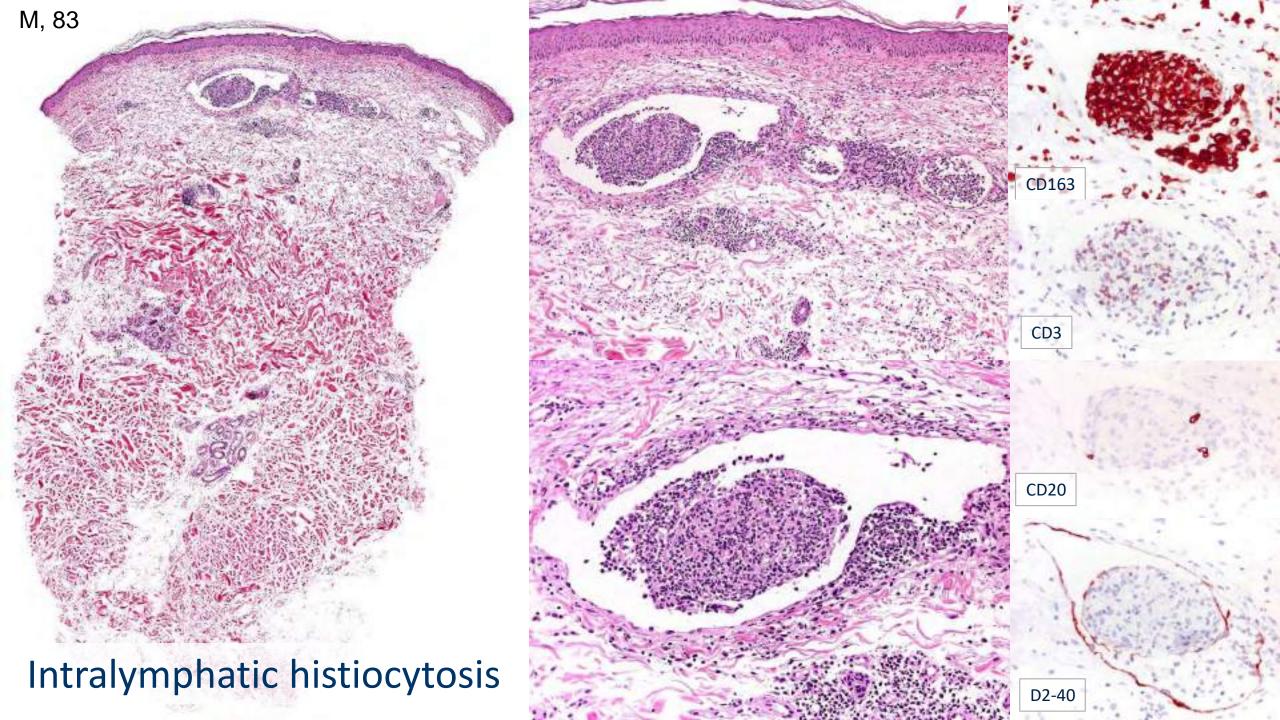
Main "intravascular" proliferation of cells

Within blood vessels

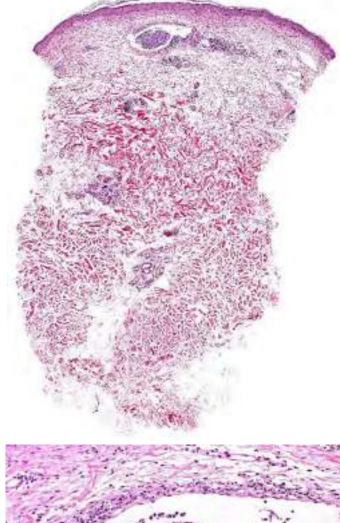
- B- and NK/T-cell intravascular diffuse large cell lymphoma
- Diffuse large B-cell lymphoma with intravascular component
- Intravascular angiosarcoma
- Reactive angioendotheliomatosis
- Rare cases of intravascular histiocytosis
- Merkel cell carcinoma (rare)

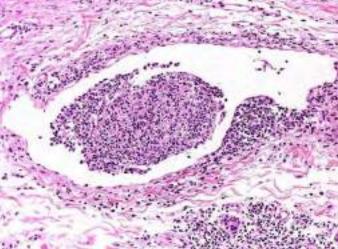
Within lymphatic vessels

- Intralymphatic cut. anaplastic large cell lymphoma / lymphomatoid papulosis
- Benign intralymphatic proliferation of large T-cell lymphoid blasts
- Intralymphatic histiocytosis
- Merkel cell carcinoma (common)
- Metastases of different types of carcinoma and of other malignant neoplasms



- Known seronegative chronic polyarthritis
- Elevated CRP (111,1 mg/L)
- Duration of the skin lesions unknown





Intralymphatic histiocytosis

- Clusters of histiocytes within lymphatic vessels; may mimic intravascular large cell lymphoma (but it is intralymphatic)
- Cells CD68+, CD163+ and negative for lymphoid markers;
 vessels positive for podoplanin
- Association with rheumatoid arthritis more common than mere chance would explain (part of a macrophage activation syndrome?)
- "Localized" cases observed in different settings (particularly in chronic recurrent infections / inflammation, e.g. recurrent erysipelas)

Intralymphatic Histiocytosis. A Clinicopathologic Study of 16 Cases

Luis Requena, MD, * Luila El-Shabrawi-Caelon, MD,† Sarah N. Walsh, MD,‡§¶
Sonia Segura, MD, † Mirjana Ziemer, MD,** Mark A. Hurt, MD,¶
Omar P. Sungüeza, MD,‡§ and Heinz Kutzner, MD††

Abstract: lattalymphatic bisineytosis is a nee condition chandserized by the prosence of diluxed (ymphatic results certaining aggregates of measuredcen biologytes (manusophages) within their busines. The phenomenon seems to occur almost exchangely within the noticelar domain. Although its pathogonalis minutes automatic limitings expand on the previously described morphologic and aumanotialochamized features of introspecture histocytosis. We also decays the possible relationship between intralymphonic histocytosis and the se-called relative intercapatiful angiocendetholiomatoris.

Key Words: intralymptanic hisrocytosis, intralymphatic murn-

TARIF 1	Clinical	Data of	16 Patients	With Intral	vmphatic	Histiocytosis

		Age (yrs)	Lesion Location	Clinical Features	Associated Diseases or Findings	Follow-up
1	F	79	Thighs, knees	Erythematous violaceous confluent patches		
2	Γ	46	Left lower leg	Poorly demarcated erythema	Rheamatoid arthritis Klippel-Trenaunay syndrome	N/a
3	M	48	Left chest, left thigh	N/a	N/a	N/a
4	F	84	Right arm	Indurated plaque: intravascular lymphoma?	None	Lesions have persisted
5	F	57	Left thigh	Erythema and induration		
6	M	79	Abdominal skir.	Multiple excoriated papules: scabies?	None	N/a
7	F	69	Right breast	Erythema on the surgical scar: carcinoma erysipeloides?	Previous right breast carcinoma	N/a
8	F	85	Left upper arm	Livic erythema: cermatomyositis?	PCR negative for Borrelia, Streptococcus, Siaphylococcus, and Bartonella	N/a
9	F	66	Left breast	Livid erythematous patch	Excision of left breast carcinoma 9 yrs ago	N/a
10	F	78	Right elbow	w Scaly induration: granuloma None armulare, allergie eczema, herrses simplex?		N/a
11	M	63	Right hip	Indurated crythema of the The lesions developed on the scar after hip surgical scar joint replacement with a metal prosthesis		N/a
12	F	75	Right upper arm			N/a
13	М	65	Right thigh	The lesions developed on the surgical sear after hip joint replacement with a metal prosthesis		N/a
14	F	84	Right upper arm	Persistent reticulate erythema	Rheumatoid arthritis, PCR negative for Borrelia, IgH and TCR clonality	N/a.
15	M	68	Upper eyelic	MelkerssorRosenthal syndrome?	Melanoma in situ in the overlying epidermis Unilateral eyelid swelling histopathologically showing suppurative granuloma	N/a
16	M	73	Left upper arm	Large vascular radiating patch present for 2 months: angiosarcoma, in:llammatory carcinoma, Kaposi's sarcoma?	Rheumatoid arthritis, malignart melanoma S/P lymphadenectomy	N/a

HHV-8, human herpesvirus 8; N/a. Not available; PCR, polymerase chain reaction; TCR, T-cell receptor; EBV, epstein-barr virus.

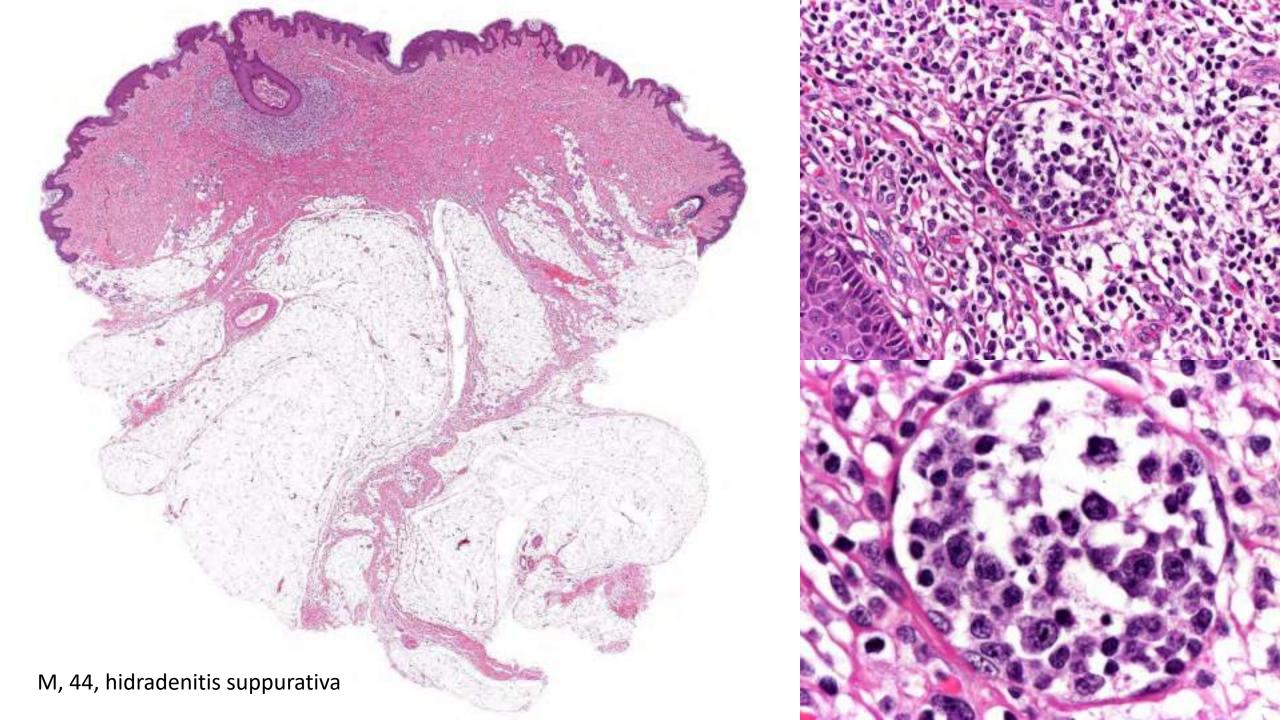
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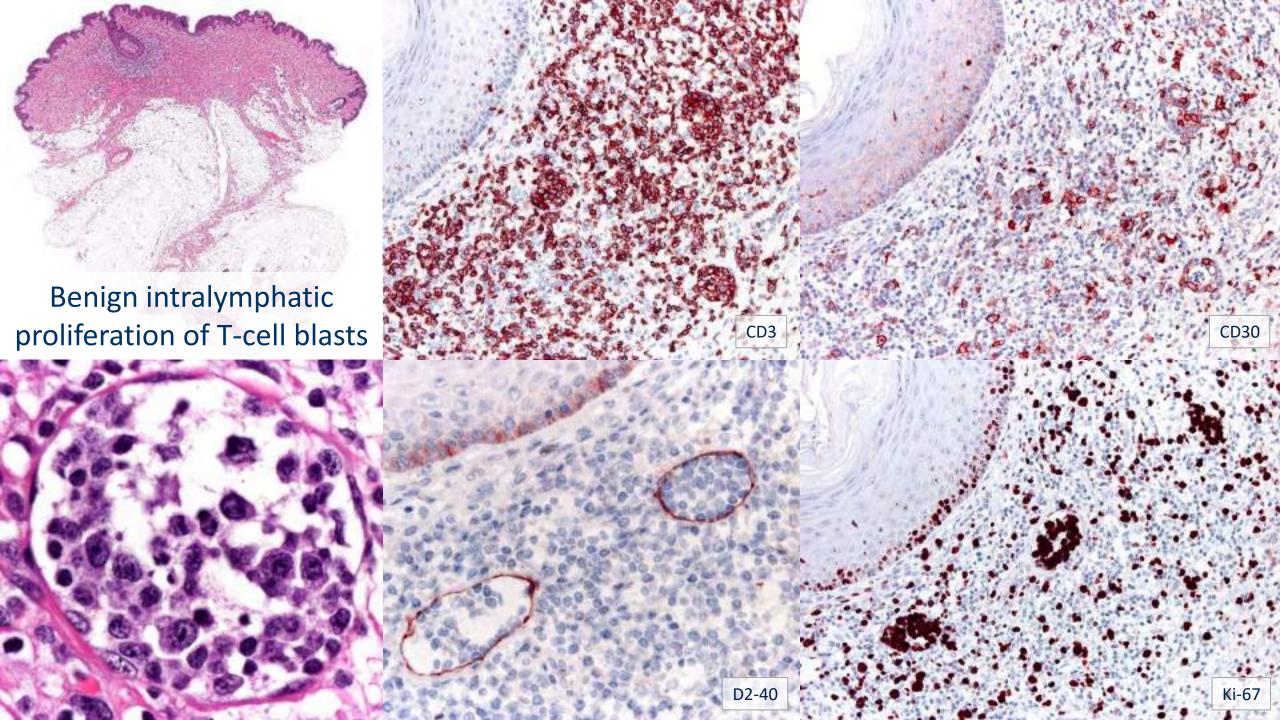
Am | Demotopothol • Volume 31, Number 2, April 2009

TABLE 2. Summary of the Cases of Intralymphatic Histiocytosis Previously Described in Literature

Case, Reference	Age (yrs)/Sex	Clinical Diagnosis	Histopathology/Immunohistochemistry	Associated Diseases
I, O'Grady et al ¹ 70/F		Erythematous rash below the left knee	Intravascular collections of histiocytes (Mac 387 and Kp1 + histiocytes and F-VIII + endothelial cells)	ND
2, Rieger et al ²	80/F	Red macules and plaques on face and arms	Intravascular collections of histiocytes (Mac 387 and PGM1 + histiocytes and CD31, F-VIII, and Ulex europaeus + endothelial cells	Cardiac insufficiency osteoporosis, positive rheumatoid factor
3, Rieger et al ²	77/F	Violaceous patches with livedo-like erythema on both elbows	Intravascular collections of histiocytes (Mac 387 and PGM1 + histiocytes and CD31, F-VIII, and U. europaeus + endothelial cells)	Rheumatoid arthritis, bilateral breast cance
4, Pruim et al ³	63/M	Violaceous lesions with livedo-like erythema on the left elbow	Intravascular collections of histiocytes (HAM 56 and CD68 + histiocytes and CD31, CD34 + endothelial cells)	Rheumatoid arthritis
5, Pruim et al ³	59/F	Erythematous rash on the left wrist	Intravascular collections of histiocytes (HAM 56 and CD68 + histiocytes and CD31, CD34 + endothelial cells)	Rheumatoid arthritis
6, Magro and Crowson ⁴	82/M	Contact dermatitis on shoulder	Intravascular collections of histiocytes	Rheumatoid arthritis
7, Magro and Crowson ⁴	46/M	Urticaria on buttocks, thighs, and lower back	Intravascular collections of histiocytes	Rheumatoid arthritis
8, Magro and Crowson ⁴	41/F	Lymphoma on forearm	Intravascular collections of histiocytes	Rheumatoid arthritis
9, Takiwaki et al ⁵	69/F	Indurated erythema and papules on the elbow	Intravascular or intralymphatic collections of histiocytes (CD68 + histiocytes and CD31, CD34, and F-VIII + endothelial cells)	Rheumatoid arthritis
10, Takiwaki et al ⁵	74/ M	Livedo-like crythema on the elbow and forearm	Intravascular or intralymphatic collections of histocytes (CD68 + histocytes and CD31, CD34, and F-VIII + endothelial cells)	Rheumatoid arthritis
ll, Takiwaki et al ⁵	66/F	Livedo-like crythema on the elbow and forearm	Intravascular or intralymphatic collections of histocytes (CD68 + histocytes and CD31, CD34, and F-VIII + endothelial cells)	Rheumatoid arthritis
12, Takiwaki et al ⁵	62/F	Erythema and confluent papules on forearm	Intravascular or intralymphatic collections of histocytes (CD68 + histocytes and CD31, CD34, and F-VIII + endothelial cells)	Rheumatoid arthritis
13, Okazaki et al ⁶	52/M	Livedo-like erythema with vesicles on lower leg	Intralymphatic collections of histiocytes (CD68 + histiocytes and D2-40 + endothelial cells)	Rheumatoid arthritis
14, Asagoe et al ⁷	17/M	Painful induration of the scrotum	Intravascular collections of histiocytes (CD68 + histiocytes and CD31 + D2-40 endothelial cells)	Tonsillitis
15, Catalina-Fernández et al ⁸	50/F	Erythematous plaques with livedo-like pattern on shins	Intralymphatic collections of histiocytes (CD68 + histiocytes and D2-40 + endothelial cells)	Rheumatoid arthritis, fibromyalgia
16, Okamoto et al ⁹	75/F	Violaceous, infiltrated erythema on left forearm	Intralymphatic collections of histiocytes (PGM-1 + histiocytes and D2-40 + endothelial cells)	Rheumatoid arthritis, lymphedema
17, Mensing et al ¹⁰	68/F	Reticular, bizarre-shaped livid macules on the face, livid macules on the face, back, and thighs	Intravascular collections of histiocytes (CD68 + histiocytes and CD31, CD34, and F-VIII + endothelial cells	Heart attack, diabetes
18, Waranabe et al ¹¹	75/M	Erythematous nodules on the left knee	Intravascular collections of histiocytes (PGM-1 + histiocytes and D2-40 + endothelial cells)	Orthopedic metal implants

F-VIII, factor-VIII-related antigen; F, female; M, male; ND, not described.





Intralymphatic Proliferation of T-cell Lymphoid Blasts in the Setting of Hidradenitis Suppurativa

Paola Calamaro, MD*†2 and Lorenzo Cerroni, MD*

Abstract: intolyophnic problemies of T-cell (surplaid blass) (IPTCLBs) is a rare, occurrly described critis, associated with examents inflammatory conditions and characterized by intralymphotic prolifection of highly prolifering, blossed T lymphosytes expressing CDNs, thus ministing as intoxusually longhous. In all aground esses, the removinghatic posification was ansecuted with an underlyog inflammatory condition, with no closed T-cell exceptor reterangetient, no agra of systemic or entancies hypphorus, and exectlers prognosis. The authors procest a new case of WTELH ensure in a patient with hidrodyness supportion. Histological currination revested a diluted foliate embedded within a fibrour strong surrounded. by a dense temphoral infiltrary characterized by the presence of dilated. bound look spel-reminen lexion thin helds seem land hosphocytes expressing a CDF T phonoripe. There was also expressist of CDM, his requirely for expense markers and Testers-Timvirus. The proliferation index was high and the viruals showed expresuses of DC-40, confirming their Symphatic nature. No sums of systemic Periphorno could be deticted after rowthe investigations, and the nation ivaling and in pool general health. IFFCLB is a turn horizoneitry that pesens with working, potentially moleculing hotopathological featury that martic drose observed in introducidor legistromic Capital hatelogical and phototypic to origination and complation with the clinand feetings are rangeousy for a people discription.

Key Words: mentiorephatic problemics of T cell lymphoid Yasas, improsecular large cell lymphorta, antidymphatic histocytosis, T-cell pseudolymphorta.

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attalymphatic proliferation of T-cell lymphatal blant (IPTC Lfm) is far meanth described entity observed by the presence of large, inhated T lymphatic willin lymphatic vessels, often with C D00 expression. Although a metacs blookogically as interested by the abertagn condition because of the leck of clinical signs of lymphorm, the lack of clinical signs of lymphorm, the lack of clinical signs of lymphorm, the lack of clinical rearrangement of the TCR genera, and the incoming to-low-up.

To date, only few cases of IPTCLB have been reported in the Isterature, associated with different inflammatory

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conditions.2 We present a new additional case occurring in a young rule patient in the setting of hidrackentic supportation.

CASE REPORT

A 35-year-old man with long-tracking hidradonite temperation of the ingarnal regions was referred to our department for surgical mattern. Headogical treatment of the biopsy speciment revealed typical feature of hidradonite apparative, characterized by cystic-schaud has follows resectated with filterial and variably dense perficilipated niferrates composed mainly of lymphocytic and listington.

In one of the specimens, a dilater follow embedded within a fibratic strong was remunded by a deme lymphotic infiltrare (Figs. 1A, B), abuncterized by the presence of diluted small vocats filled with appeal medium/o-lime sized bloosed frombacours (Figs. 16; D). The atopical calls were possible for CD2, CD3. (Fig. 1A), CD4 (Fig. 2B), CD8, and bea-F1, and regative for CD8, TIA-L CD96, TCR-grimms, and CDQ9, Expression of CD39 was observed in turns of the drystal lymphocytes (Fig. 2C). Egisting Bur virus-encoded small 80vA (ESER-1) in anti-hybridienton was regative. Starring for Ki-67 revealed is high proliferation indea-(200%) of the introdynghole calls (Fig. 2D). The applical hyphaevies were arranged within \$2.40-posteric vessels (Fig. 3), thus posfaming the intolymphatic distribution of the cults. Besides the mesharphite bloomledly a desse militate of gredeminantly until hytebocytes almised with some laterr blasteid eells was present around the diluted foliole (Figs. 1A-17). The phenotype of these cells sess samply to the of the intuly-replicate open, and some of them were positive for C030 as well (Figs. 2A-C). The Ki-67 index in this component was lower approximately 20%; chig. 20%.

Routine investigations were negative. The potient is alone in good general leasts 7 months after presentation.

DISCUSSION

Our patient showed on IPTCLB in the setting of clomic inflammation because of hidradesitis suppurstiva. IPTCLB is a benign condition characterized by the probleration of large. atypical lymphoid cells within lymphatic vessels. Although the histopathologic features may arise the suspicion of intravascular large cell lymphoma, all reported cases occurred in the background of an inflammatory disorder, without clinical signs of lymphoms and with a favorable osteonic.37 So far, only 7 cases of IPTCLB have been reported, 6 of them with retuncous localization, and 1 ansing within an endometrial polyn (Table Ft.2.5 Although the first description is considered to be that by Bryani et al. in 2007.1 Ackerson and Tamaki" described a similar case in 1977 under the term "pseudoleraceria estis." The pseudolymphomatous inflammatory infiltrate was arising in the background of multiscum contagissum, and the poetures presented in their report show histapathological features circuitly alerment to those observed in

Am.) Demonopathol . Volume 38, Number 7, July 2016

TABLE 2. Histopathologic Criteria for the Diagnosis of ILPTCB

Presence of histopathological features of an inflammatory skin disorder (eg, lichen sclerosus, granuloma pyogenicum, etc)

Clusters of large atypical lymphoid cells confined to D2-40 + lymphatic vessels; scattered atypical extravascular cells common

T-cell phenotype without aberrant features (no loss of pan-T-cell markers; no aberrant double positivity/negativity of CD4 and CD8)

Lack of positivity for Epstein-Barr virus (EBER-1 negativity)

Polyclonality of the infiltrate as detected by polymerase chain reaction

Rignini, Limnar Central, MD, Recent Ulti of Demonspoliology, Department of Demonstrap, Stellar University of Gast, Australia, Solid Cons., Australia, Consult International Consultation (Inc.).

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Benign intralymphatic proliferation of blasts

- Most reported cases observed in a "microorganism-rich" environment (also at extracutaneous sites!)
- May be related to a local infection triggering the activation and proliferation of a T-cell subclone trafficking to and from the regional lymph nodes
- Usually CD30+ T-cell phenotype with high Ki-67; cytotoxic markers negative;
 no association with EBV; polyclonal pattern of the TCR genes
- Positive staining for podoplanin in affected vessels rules out intravascular NK/T large cell lymphoma
- Presence of a prominent inflammatory response outside of the affected vessels rules out intralymphatic cALCL (LyP may remain a differential diagnosis, but features of the background condition usually allow a clear-cut distinction)

PSEUDOLEUKEMIA CUTIS

Report of a Case in Association with Molluscum Contagiosum

A. BERNARD ACKERMAN, MD, AND EUGENE V. TANSKI, MD

Histologic sections from a solitary cystic cutaneous lesion that showed atypical mononuclear cells in the dermis and within blood vessels were diagnosed by several general pathologists and dermatopathologists as leukemia cutis. The patient, who had no other cutaneous lesions, was consequently submitted to an extensive investigation for leukemia, which proved negative. Additional and deeper sections from the original block revealed that the cellular infiltrate so suspicious of leukemia cutis was secondary to rupture of a lesion of molluscum contagiosum. The correct histopathologic diagnosis, therefore, was pseudoleukemia cutis. The lessons of the case are that 1) further study of the specimen, solitary as it was and asymptomatic as the patient was, would have obviated worry and the expense and inconvenience of an extensive systemic investigation, and that 2) the diagnosis of leukemia cutis should never be made solely on the basis of histologic sections of skin, but rather after examination of blood and bone marrow.

Cancer 40:813-817, 1977.

PERTAIN CAVEATS PERTAINING TO THE INTERpretation of histopathology of the skin cannot be emphasized too firmly or too often. One such caution relates to making an unqualified diagnosis of leukemia cutis solely on the basis of histologic findings in a lesion of the skin. The consequences of such premature conclusions are here reported in a case that may be as instructive to others as it was to us.

CASE REPORT

A 37-year-old woman had a "cyst" of 11 months duration on the right lower eyelid. It was removed in toto by surgical excision and histologic sections were interpreted by a general pathologist as leukemia cutis. For greater certainty, the slides were sent in consultation to the Armed Forces Institute of Pathology (AFIP Accession No. 1475626) where a diagnosis of "malignant neoplastic infiltrate, probably granulocytic leukemia, eyelid" was also made. A diagnosis (#1122-74) of "metastatic lesion, lymphoma or lymphomatoid papulosis" was rendered by the Department of Eye Pathology of the Northwestern University School of Medicine. The Dermatopathology Section of the Skin and Cancer Unit of New York University School of Medicine also interpreted the

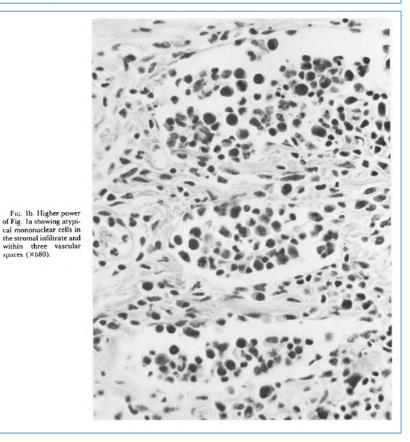
Despite the fact that the cutaneous lesion was solitary, and solely on the basis of the histologic diagnosis of leukemia cutis, which had been concurred in by most of the pathologists who had examined the tissue, the patient (a doctor's wife) was admitted to the M.D. Anderson Tumor Institute for thorough systemic investigation. Findings of complete routine examination and special studies of the blood and bone marrow were completely normal.

Perplexed by the contradiction between the dire histologic interpretation and the negative clinical and other laboratory findings, we obtained the original block of the cutaneous specimen and cut deeper sections through it. To our amazement, and embarassment, those sections revealed molluscum bodies within the cornified cells of an epithelial, cyst-like structure (Fig. 2) that had ruptured. In these sections, too, within the lumina of the dilated blood vessels surrounding the cystlike lesion of molluscum contagiosum, there were many of those atypical mononuclear cells that were previously so misleading (Fig. 3a & b)

Discussion

One may only wonder worriedly about the phenomenon of rupture of a lesion of molluscum

Perplexed by the contradiction between the dire histologic interpretation and the negative clinical and other laboratory findings, we obtained the original block of the cutaneous specimen and cut deeper sections through it. To our amazement, and embarassment, those sections revealed molluscum bodies within the cornified cells of an epithelial, cyst-like structure (Fig. 2) that had ruptured. In these sections, too, within the lumina of the dilated blood vessels surrounding the cystlike lesion of molluscum contagiosum, there were many of those atypical mononuclear cells that were previously so misleading (Fig. 3a & b)



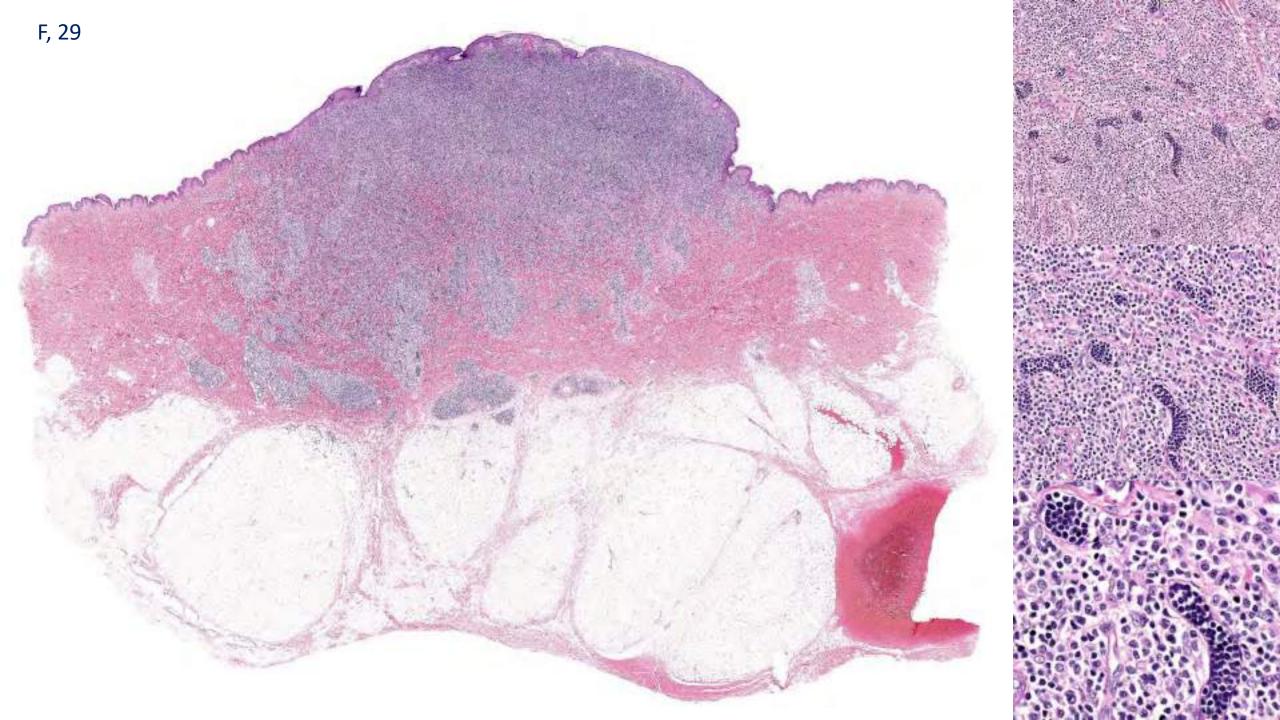
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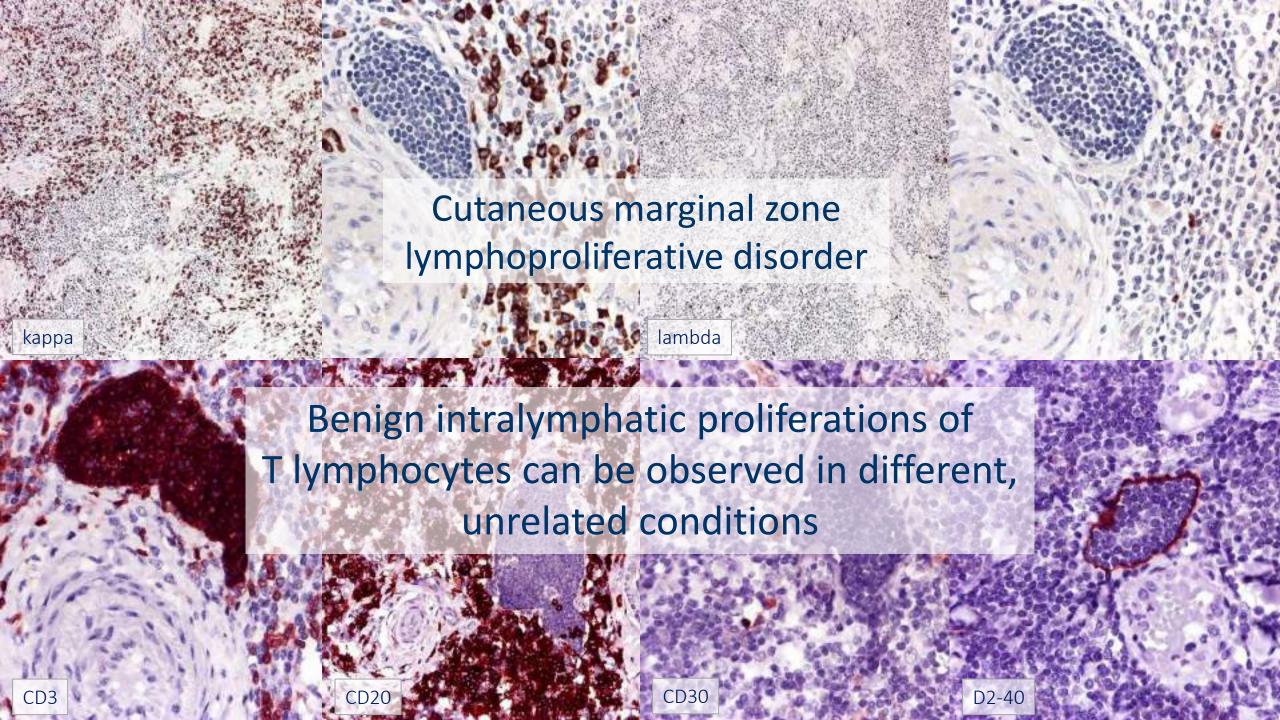
changes as those of leukemia cutis. All saw a moderately dense, mixed infiltrate of lymphocytes, histiocytes, plasma cells, eosinophils, and especially atypical mononuclear cells throughout the dermis. In addition to their interstitial distribution, the atypical mononuclear cells were found in large numbers within widely dilated endothelial-lined spaces (Fig.

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Approach to diagnosis of intraluminal cells

