Summer Academy 2025 Graz

# Cutaneous lymphoproliferative disorders and other disorders: a potpourri


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# blink

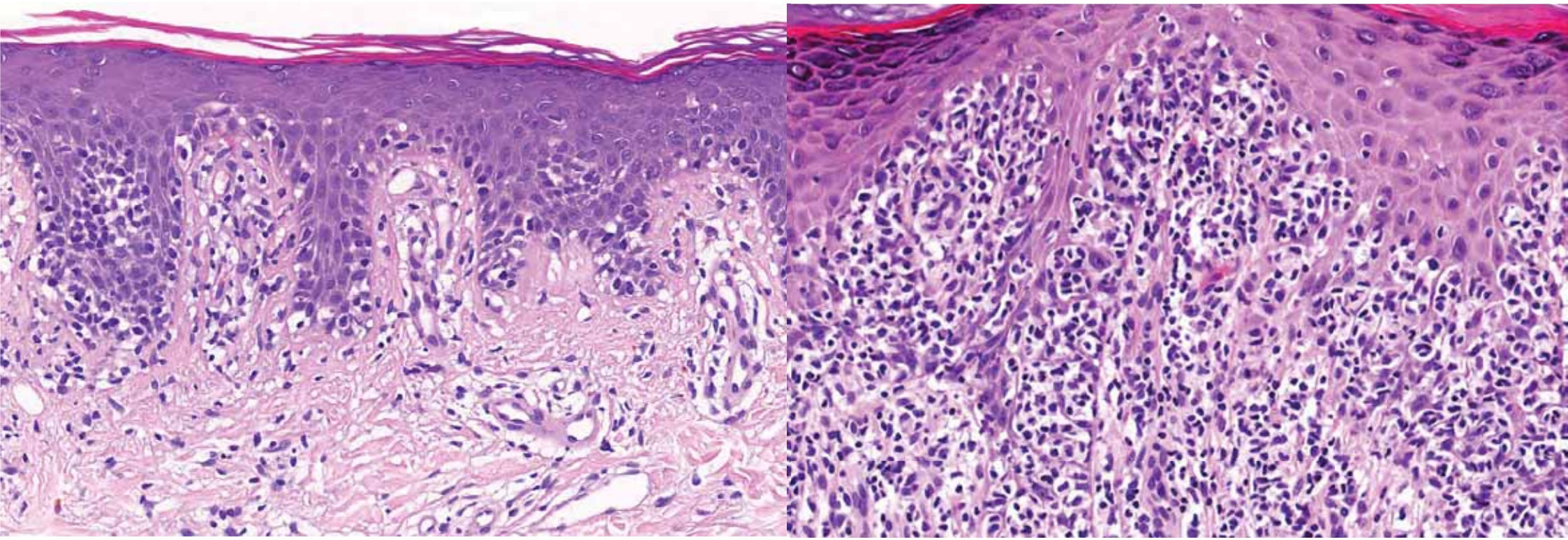
*by the author of* THE TIPPING POINT

*

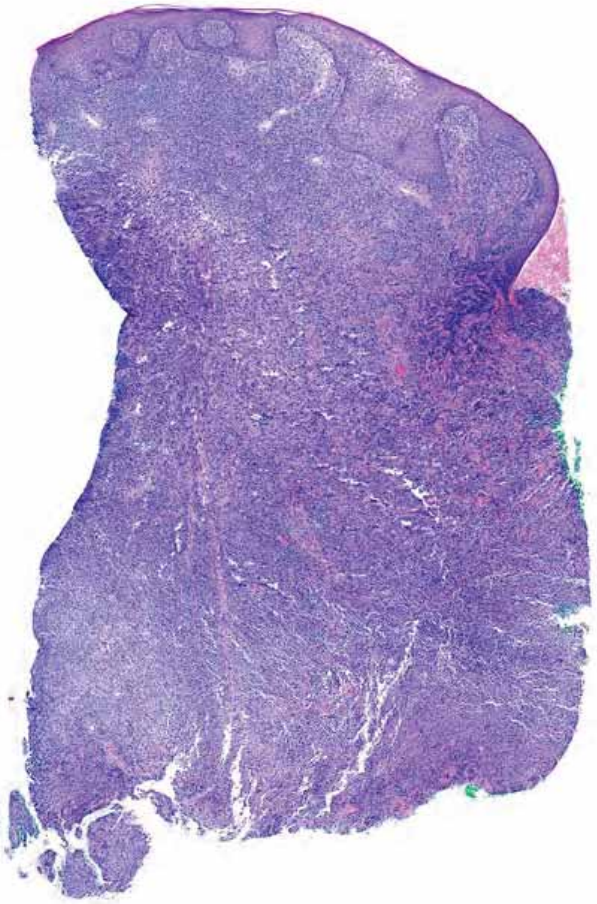
The Power of Thinking
Without Thinking

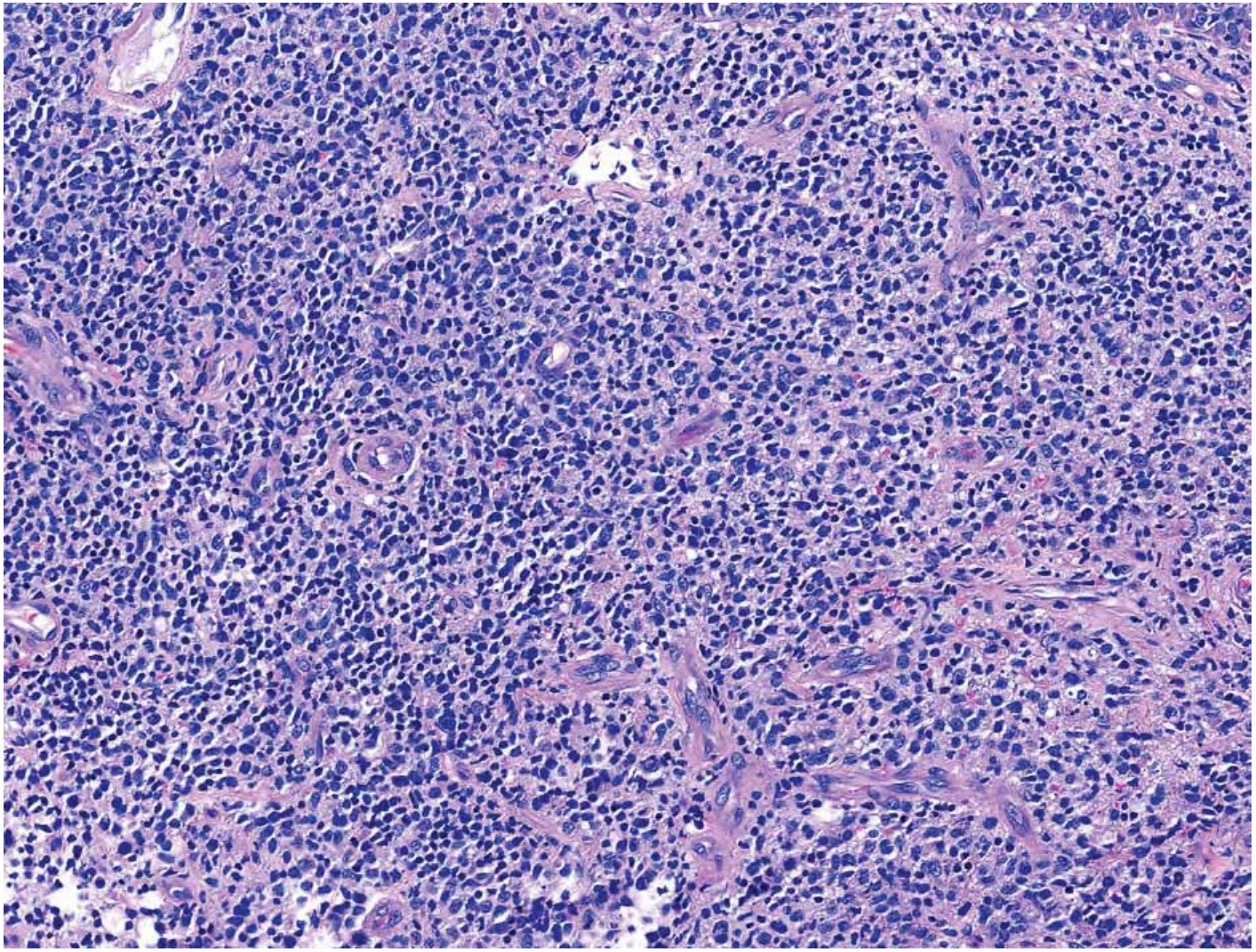
Malcolm Gladwell

"A real pleasure. . . . *Blink* brims with surprising insights about our world and ourselves." —*Salon*



67-year-old man with tumor (DM 5 cm) left inguina





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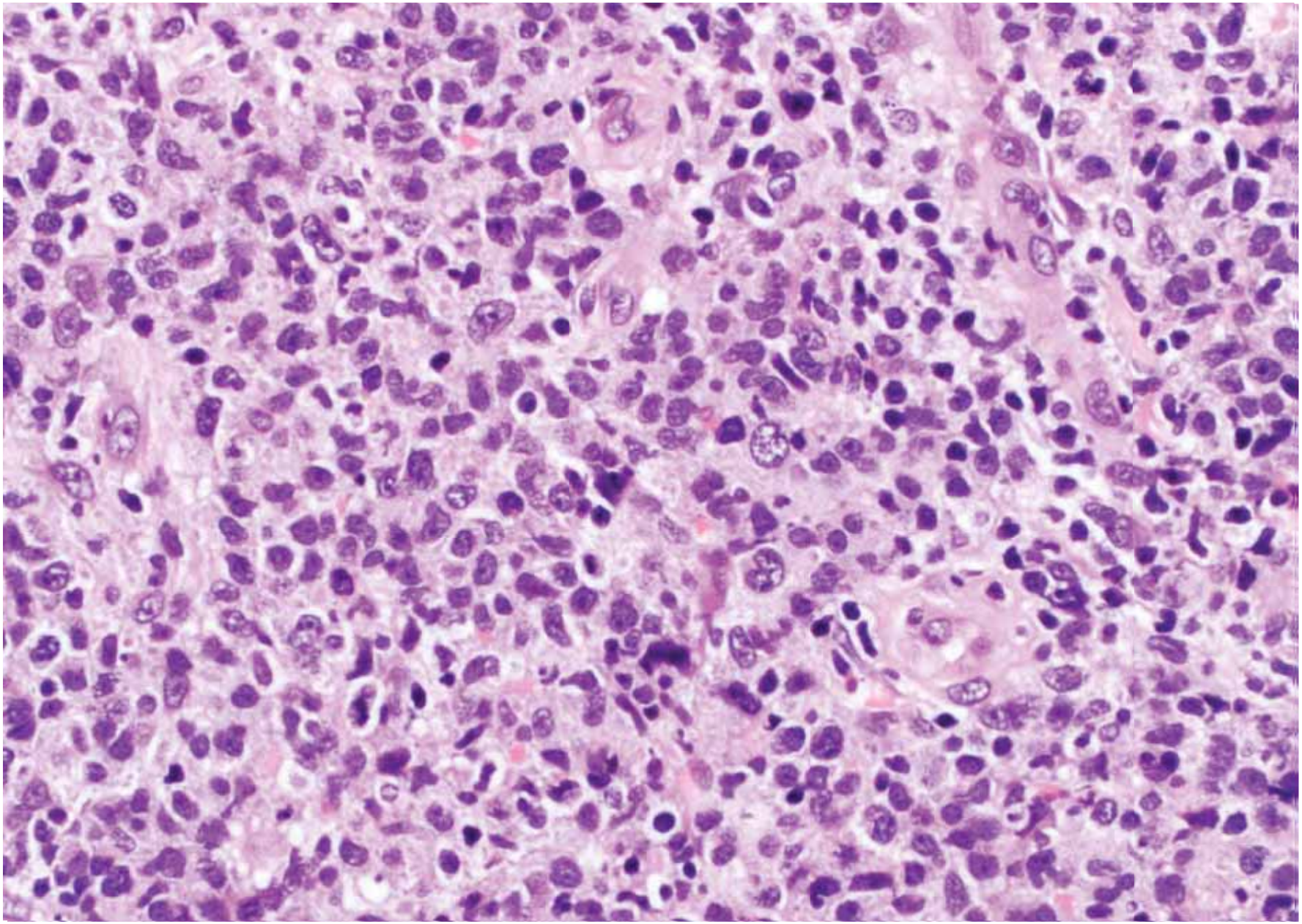

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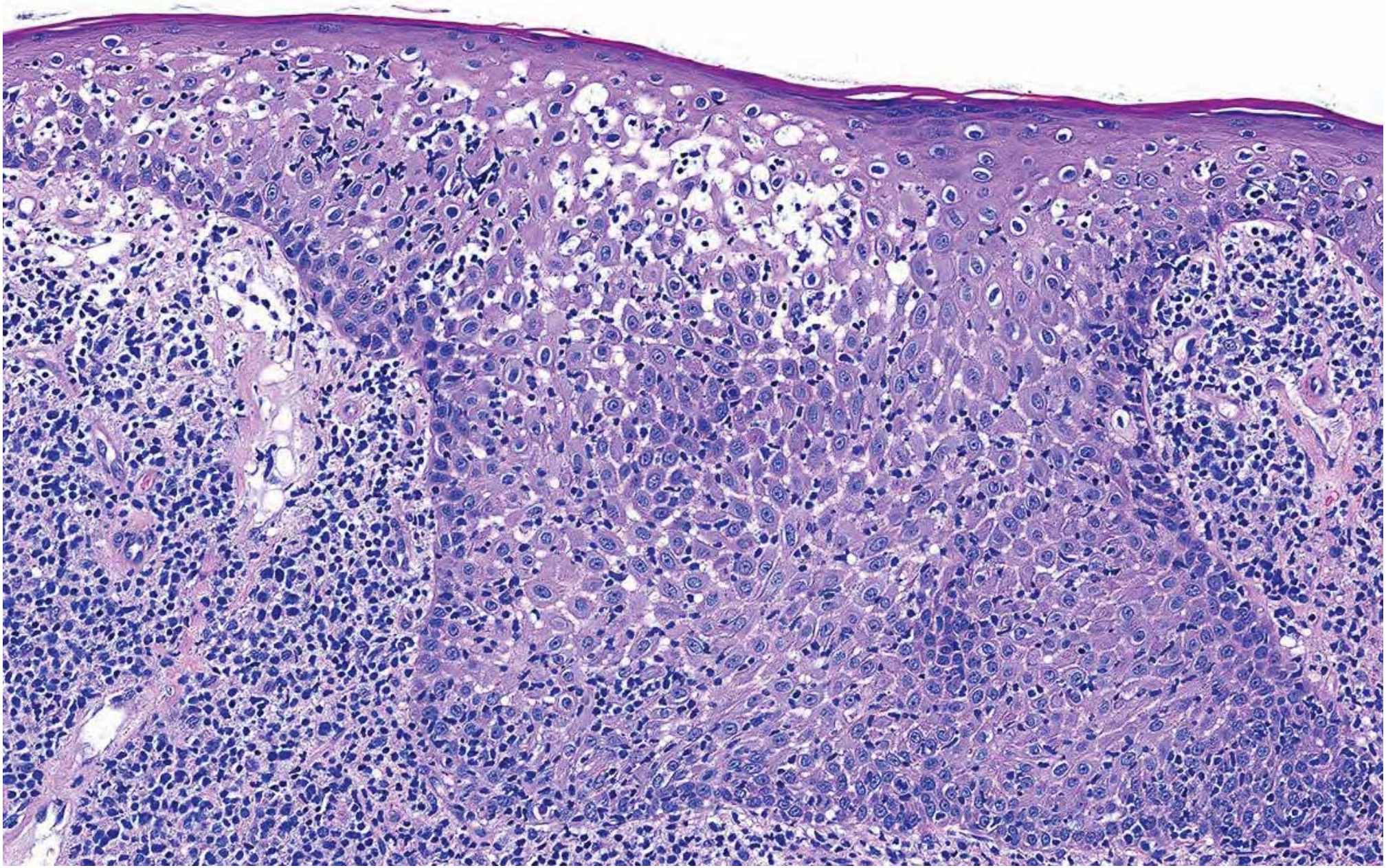
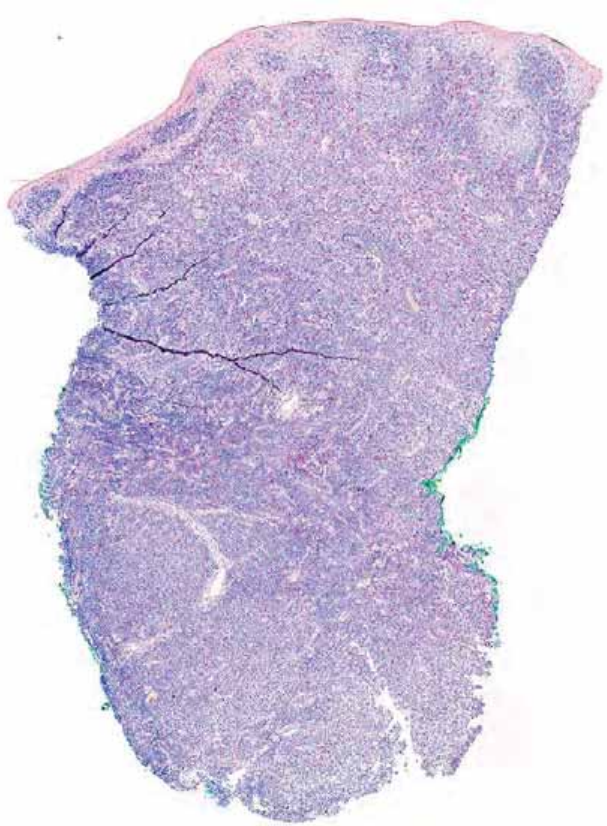
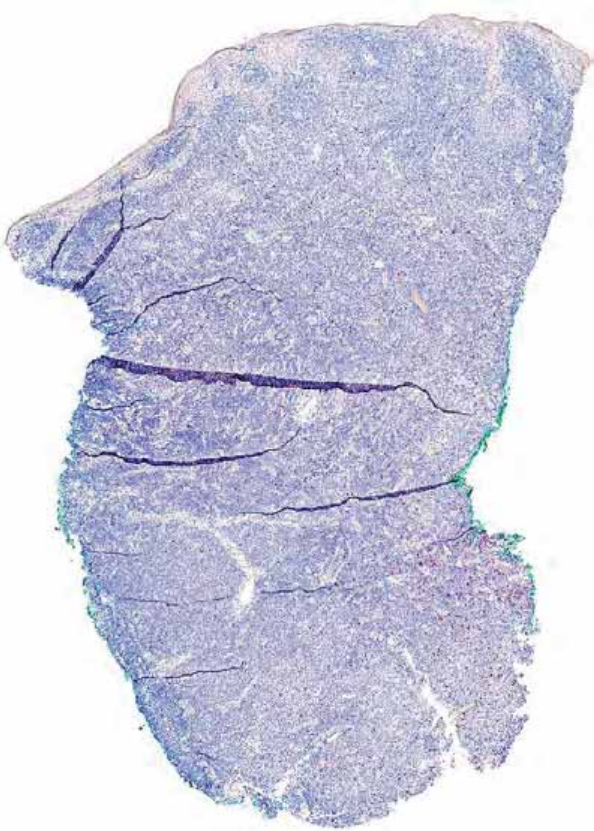


CD3



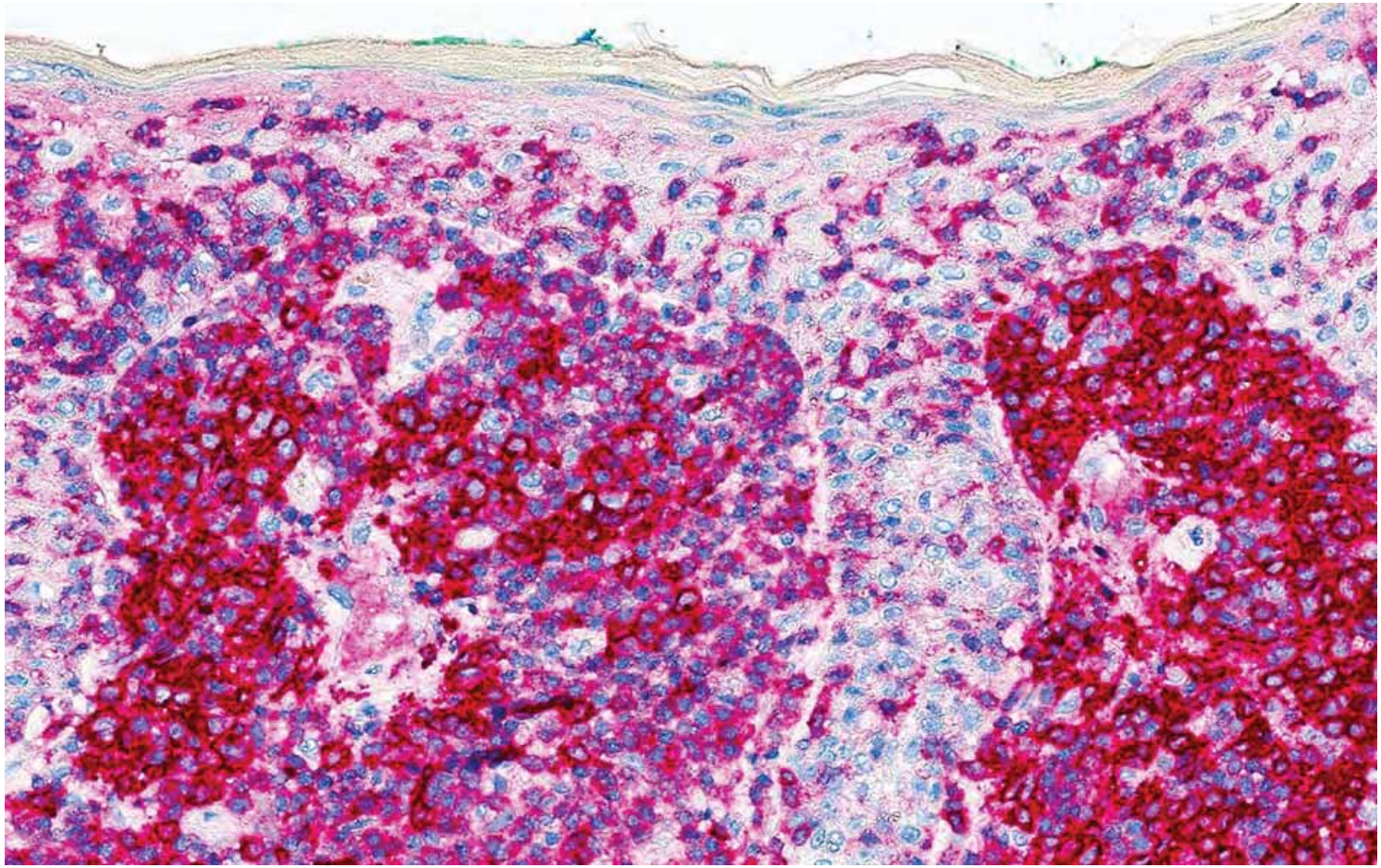
CD4



CD8

CD56, CD20 und CD79a: negative
TCR beta und delta: negative
ALK and EMA: negative

CD30



CD30

Mycosis fungoides with
large cell transformation

Patches – Plaques - Tumors

Cutaneous CD30+ ALCL

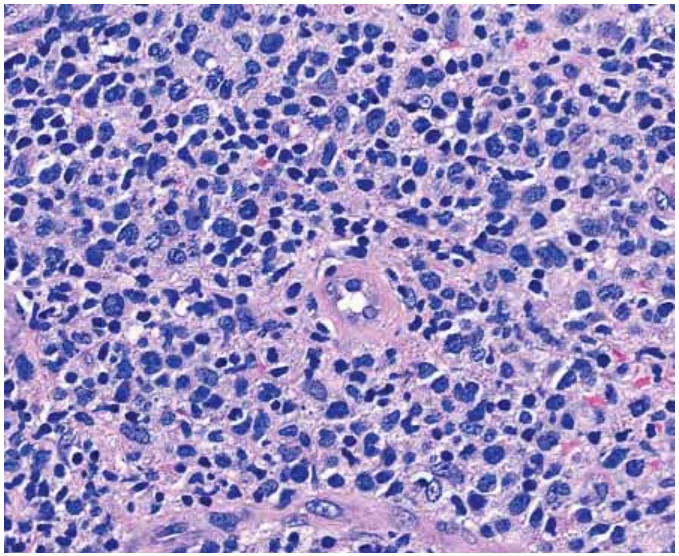
Solitary or grupped tumors

No Patches / Plaques

67-year-old man with tumor (DM 5 cm) left inguina

No preexisting patches and plaques

67-year-old man with tumor (DM 5 cm) left inguina

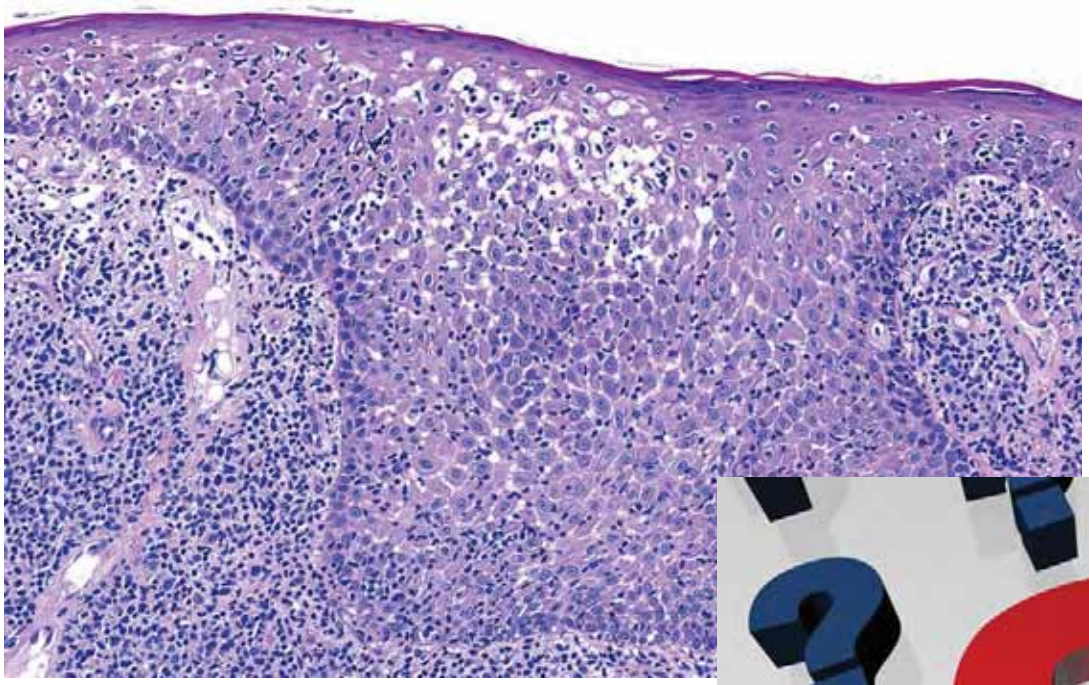


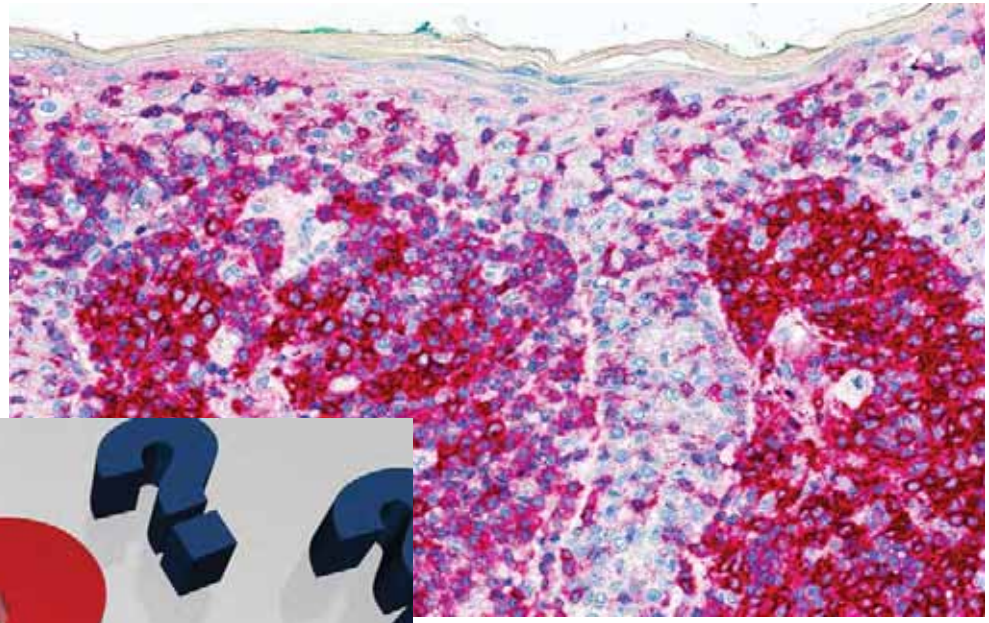
CD30

No preexisting patches and plaques

Staging negative

Primary cutaneous CD30-positive anaplastic large-cell lymphoma





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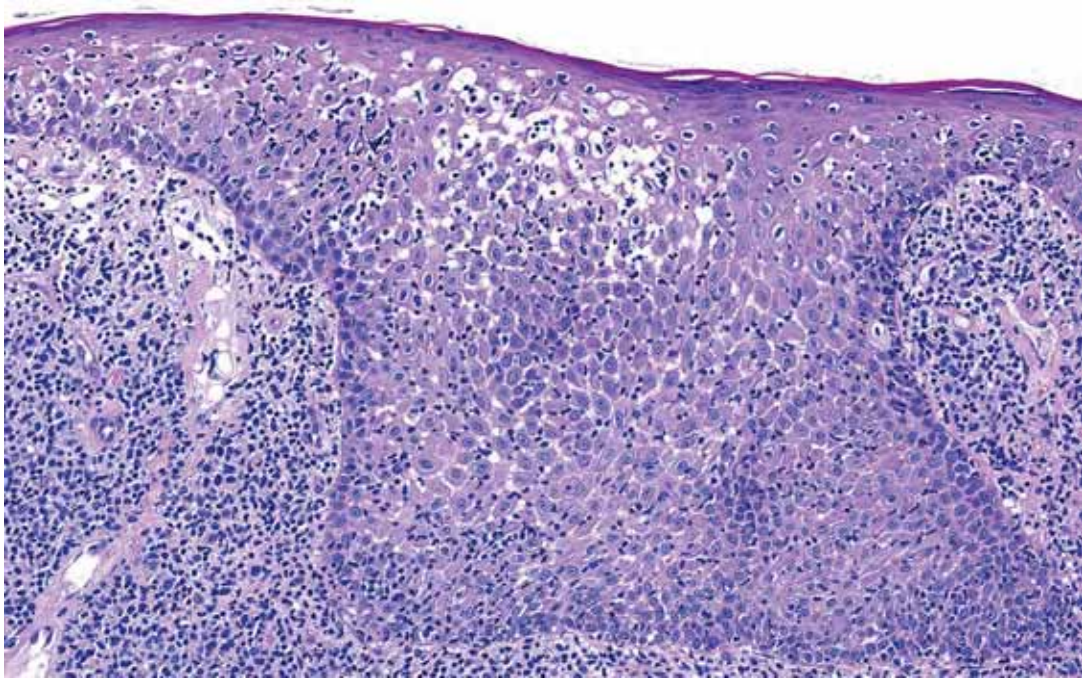
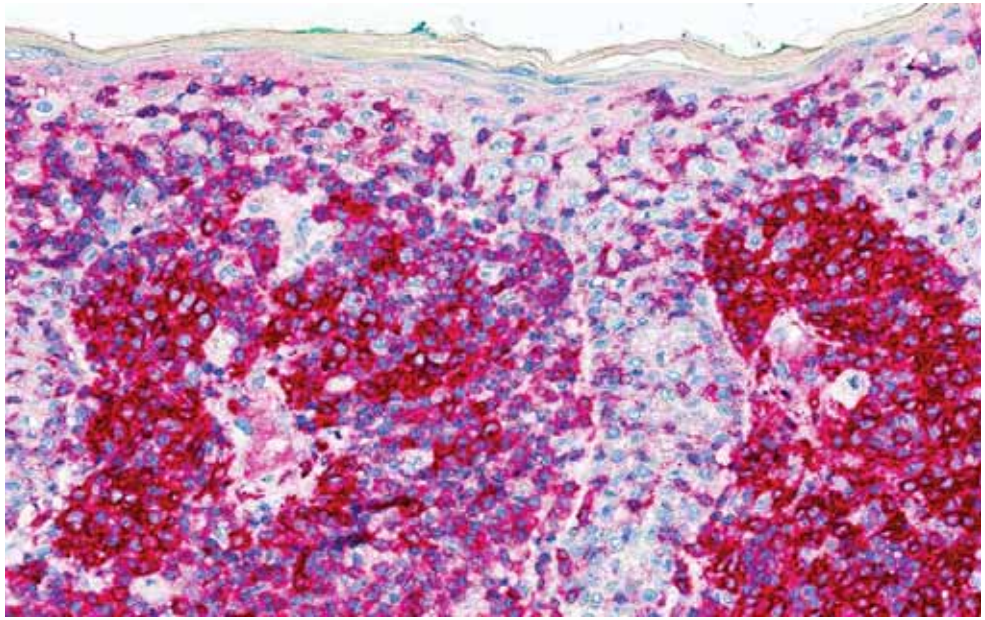
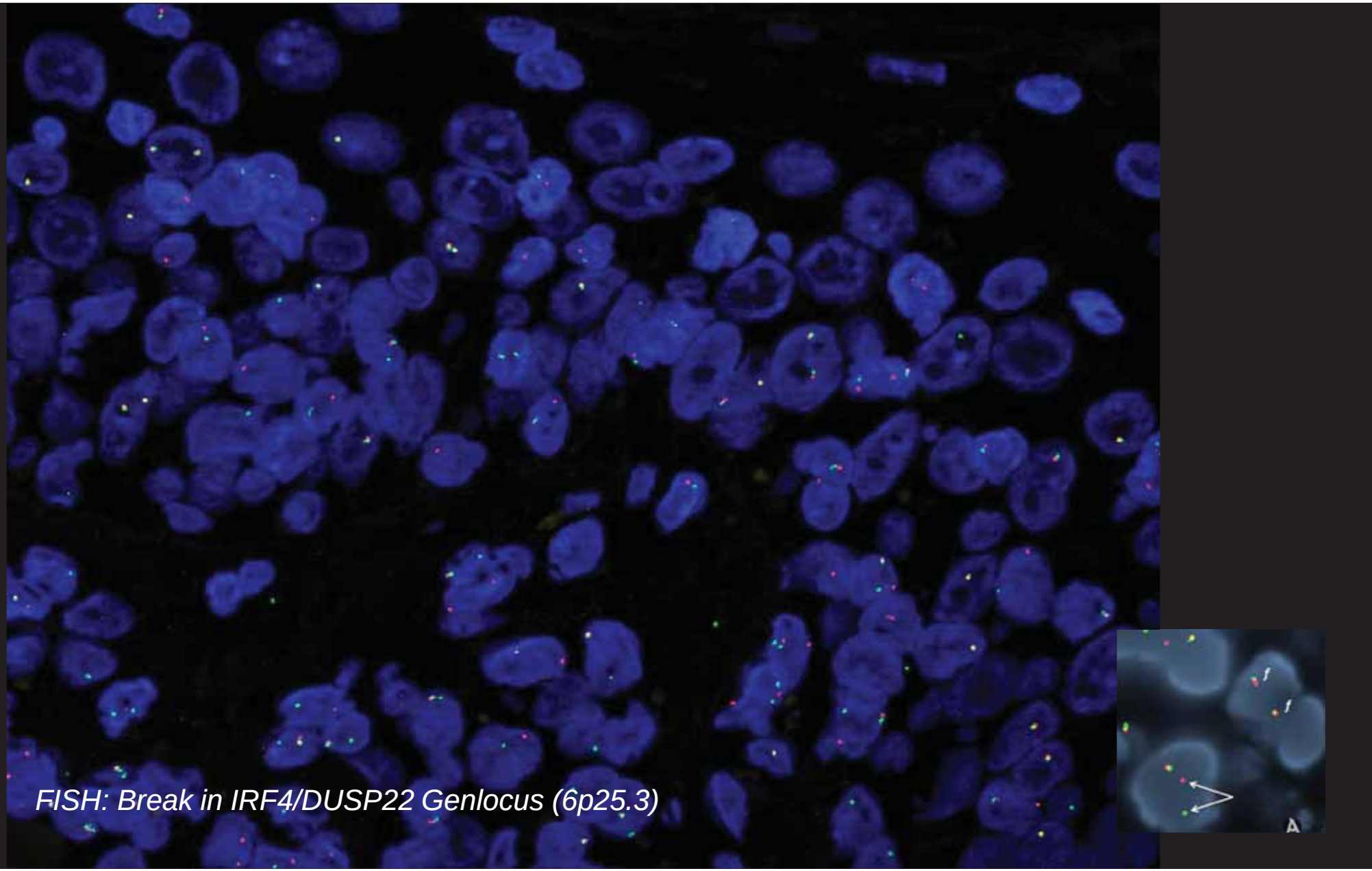




CD30

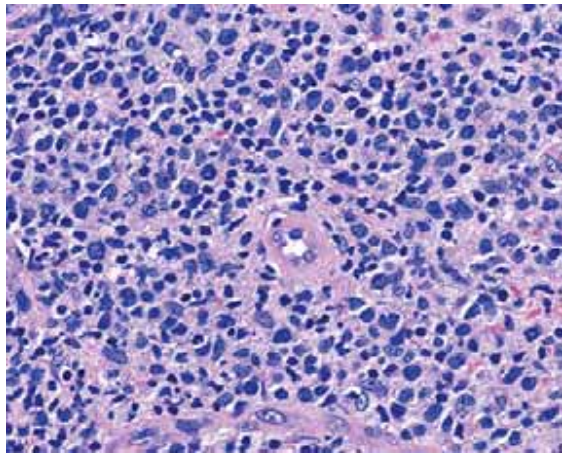
Biphasic pattern -> DUSP22 rearrangement

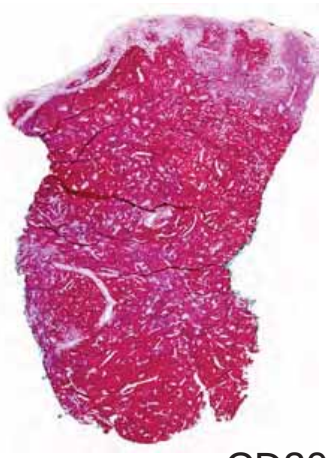
-> DUSP22/IRF4-FISH




*FISH: Break in IRF4/DUSP22 Genlocus (6p25.3)*

67-year-old man with tumor (DM 5 cm) left inguina





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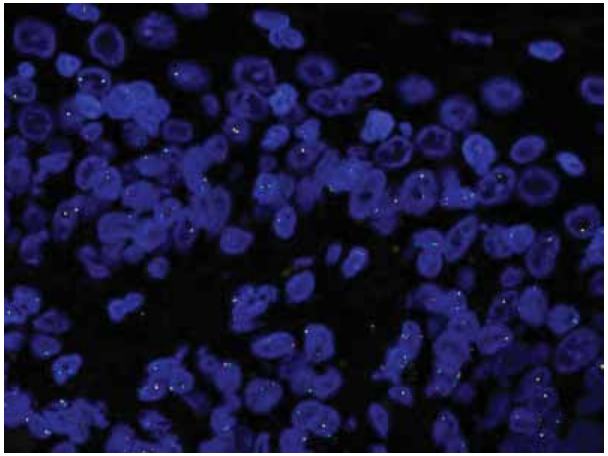

Primary cutaneous CD30-positive anaplastic large-cell lymphoma with DUSP22/IRF-rearrangement (6p25.3 locus)

# LEF-1 in DUSP22 rearranged C-ALCL

DOI: 10.1111/pin.13360

CASE REPORT

Pathology WILEY

## Constant small-cell changes and variable LEF1 expression in *DUSP22*-rearranged primary cutaneous anaplastic large-cell lymphoma: Analysis of the repeated biopsies of three patients

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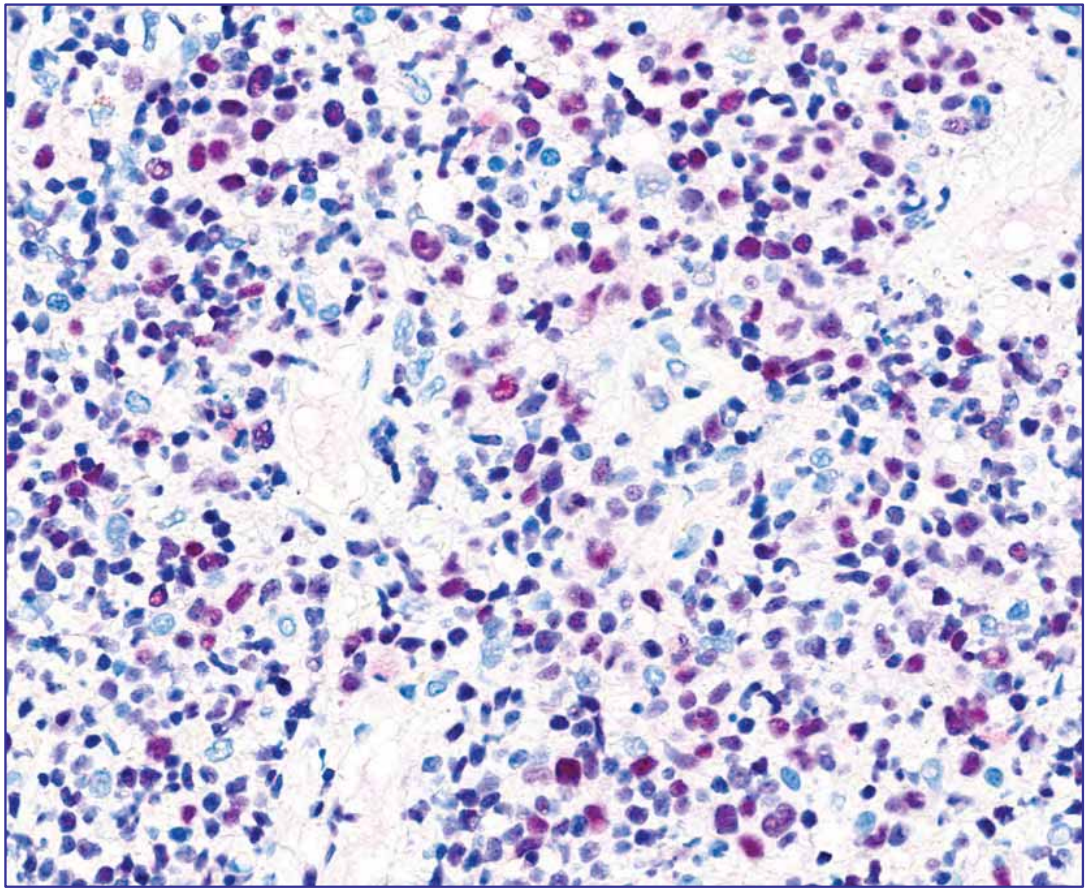
**Abstract**

*DUSP22*-rearranged primary cutaneous anaplastic large-cell lymphoma (pcALCL) has a biphasic histological pattern defined by large dermal atypical lymphocytes and epidermotropic small lymphocytes resembling pagetoid reticulosis, but the positivity rate of the biphasic pattern in *DUSP22*-rearranged pcALCL is unknown. Immunohistochemically, LEF1 expression in >75% of tumor cells is associated with *DUSP22*-rearrangement (*DUSP22*-R) in systemic ALCL. However, whether this association applies to pcALCL remains unclear. To analyze these pathological clues for screening *DUSP22*-R, we reviewed 11 skin biopsies from three patients with *DUSP22*-rearranged pcALCL. All specimens showed a biphasic pattern, of which three showed nonpagetoid infiltration of the epidermis. In all lesions, small-cell changes of tumor cells were observed not only within the epidermis but also under the epidermis. LEF1 positivity rates varied by lesion (range: 30%–90%, mean: 59.6%) with only three patients expressing LEF1 in more than 75% of tumor cells. In conclusion, the biphasic pattern was a constant finding in *DUSP22*-rearranged pcALCL, but it was not always pagetoid reticulosis-like. The recognition of small-cell change outside the epidermis may be helpful in diagnosing *DUSP22*-rearranged pcALCL. However, LEF1 expression was variable and its diagnostic usefulness may be limited.

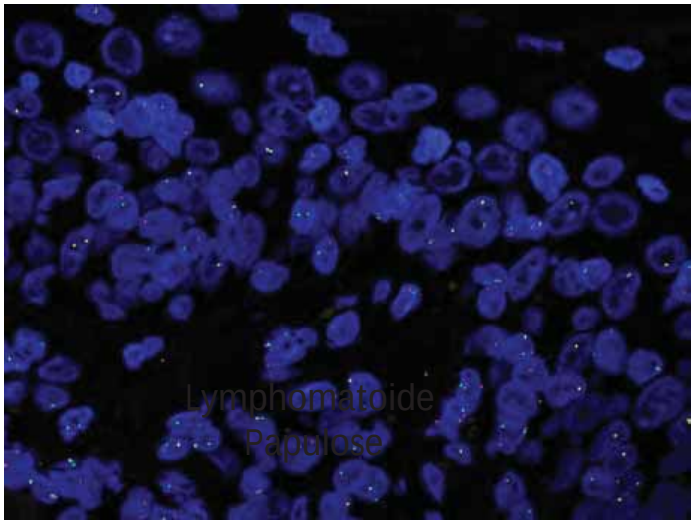
**KEYWORDS**

biphasic pattern, *DUSP22*-rearranged primary cutaneous anaplastic large cell lymphoma, LEF1, small-cell change



LEF-1

# IRF4/DUSP22 Genlocus (6p25.3) rearrangement in cutaneous T-cell lymphoma



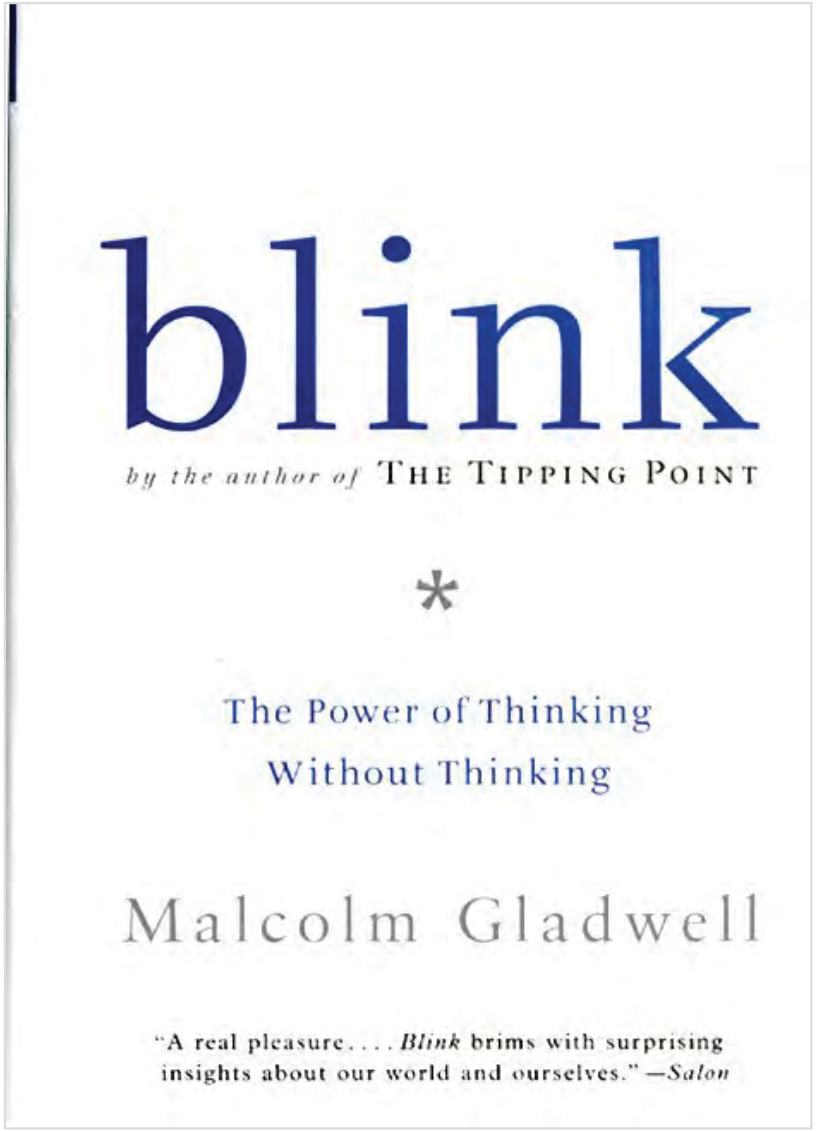

Break in IRF4/DUSP22 (6p25.3 locus)

LYP: rare (13 cases)

C-ALCL: rare (< 5%)
Systemic ALCL: 27-30%

Transform. MF: rare (10%)
Non-transformed MF: absent

Willemze et al. Blood 2019
Niu et al. J Cutan Pathol 2023
Sibon et al. Haematologica 2023


blink
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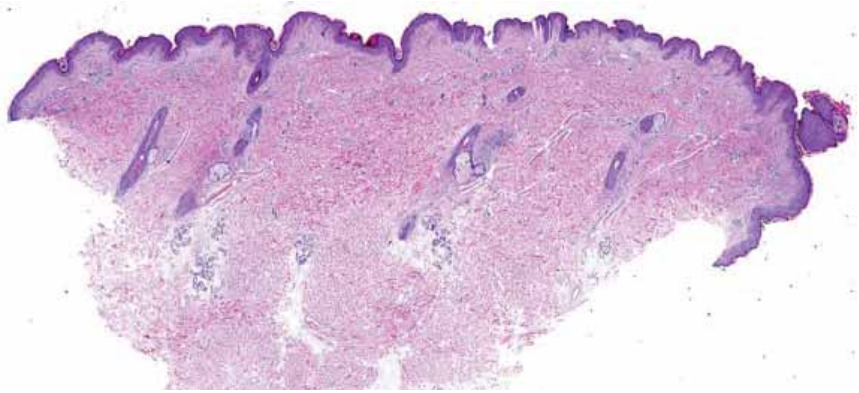
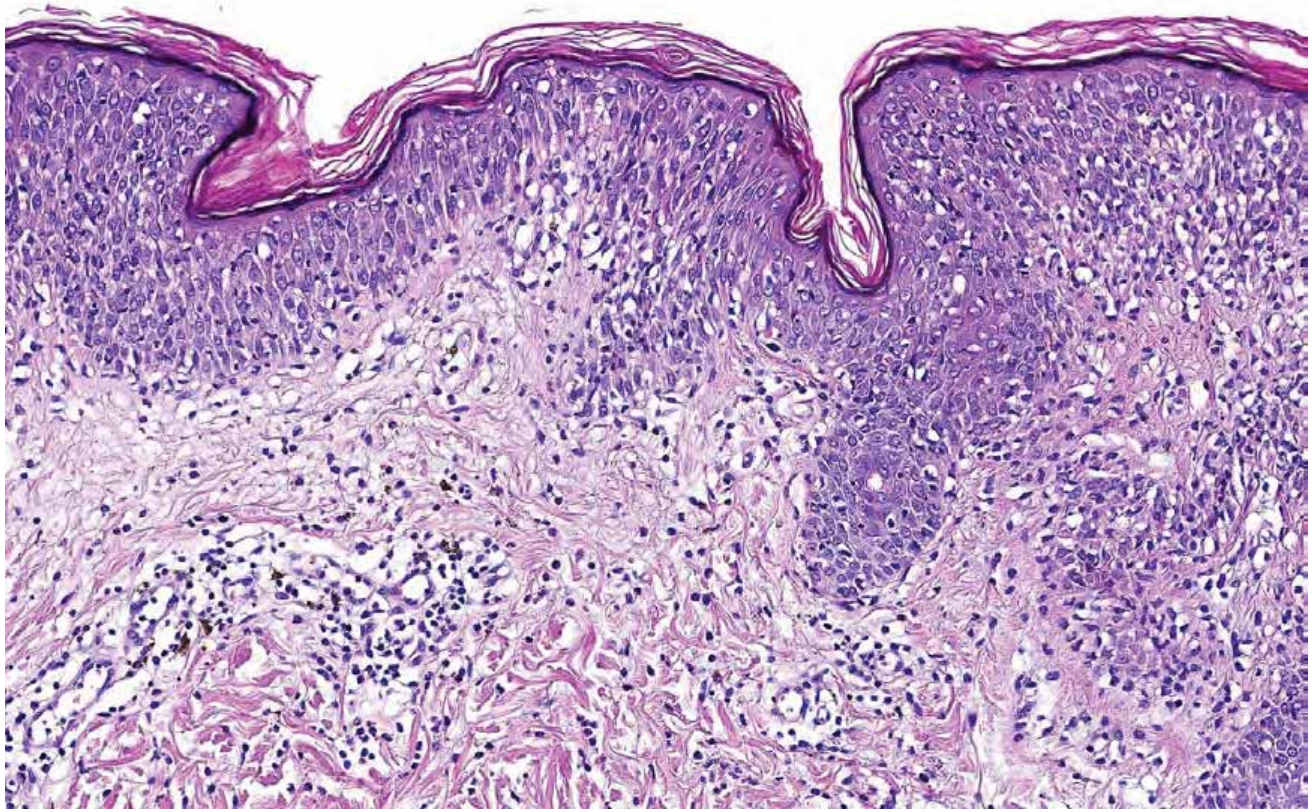
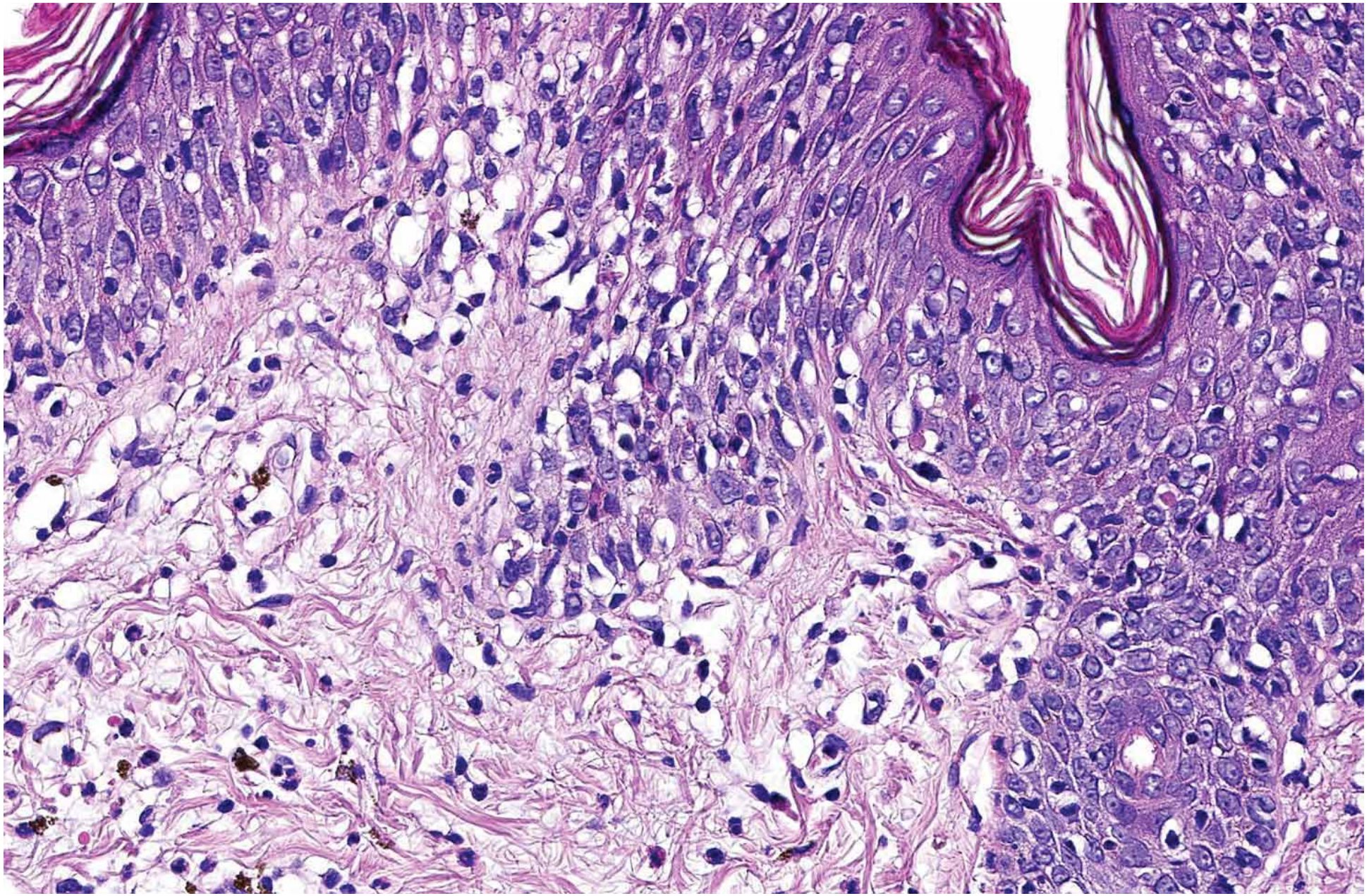
"A real pleasure. . . . *Blink* brims with surprising insights about our world and ourselves." —*Salon*

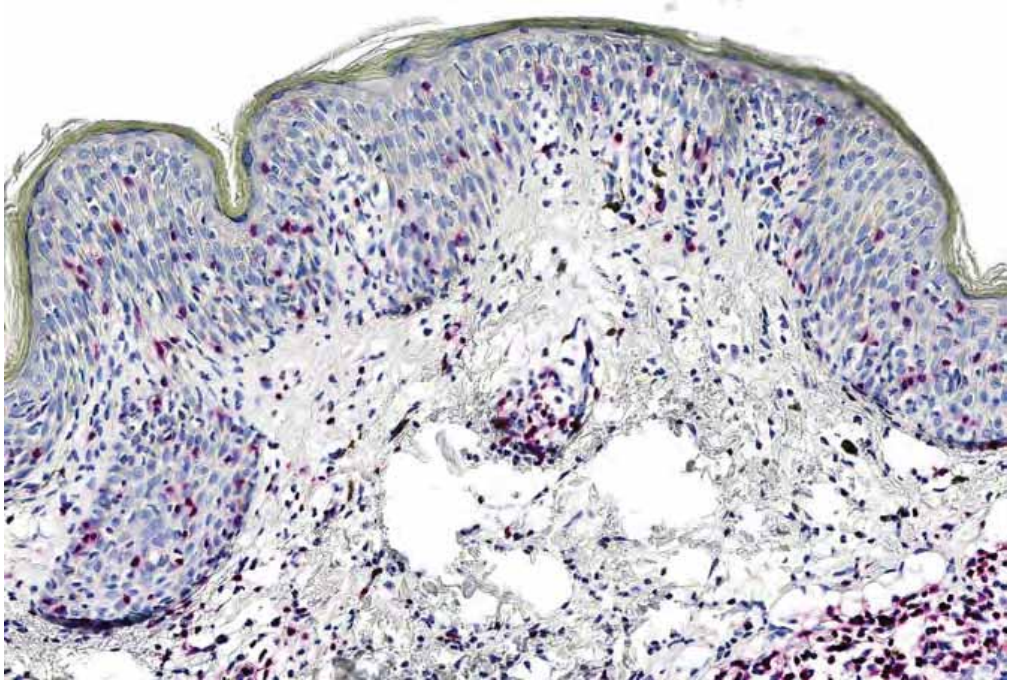
31-year-old man with two brownish, slightly infiltrated patches on the left thigh and right arm.

*Consultation case PD Dr. D. Helbig, Köln*

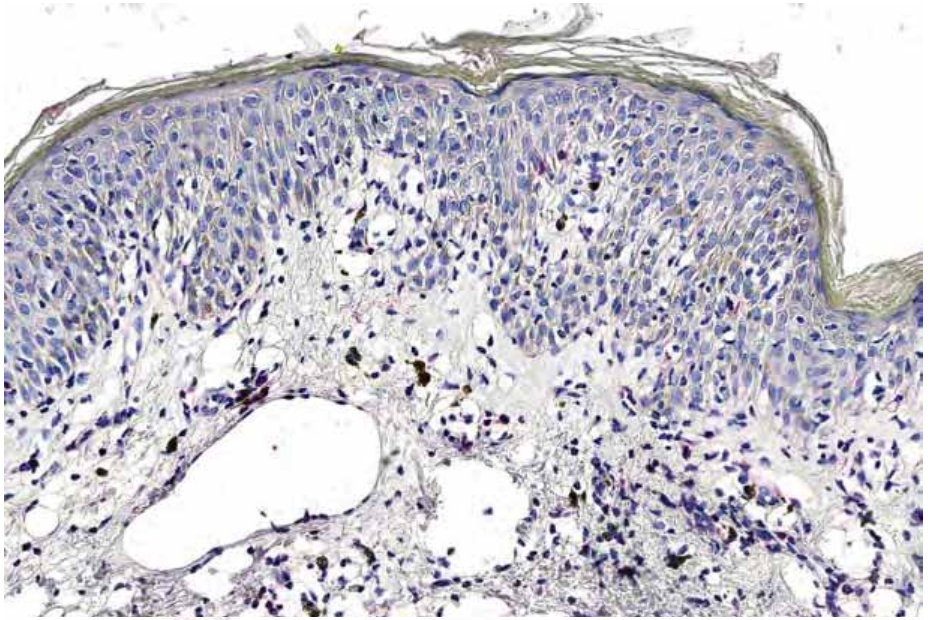




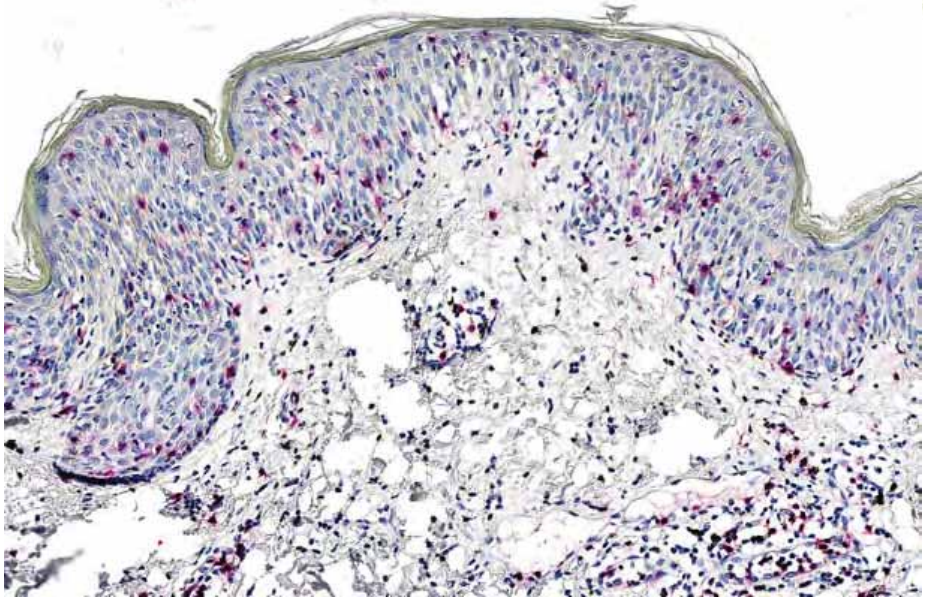




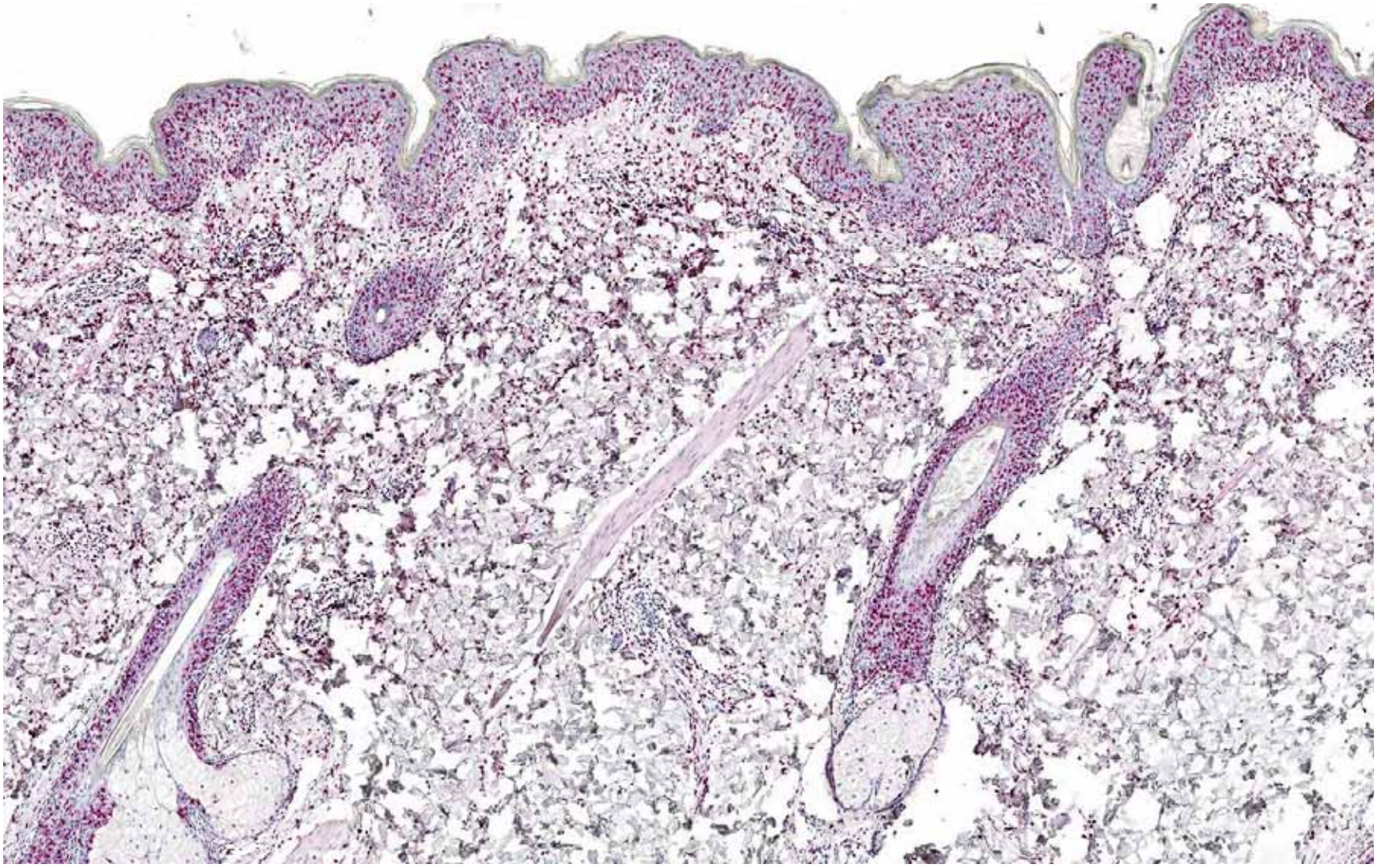
CD3



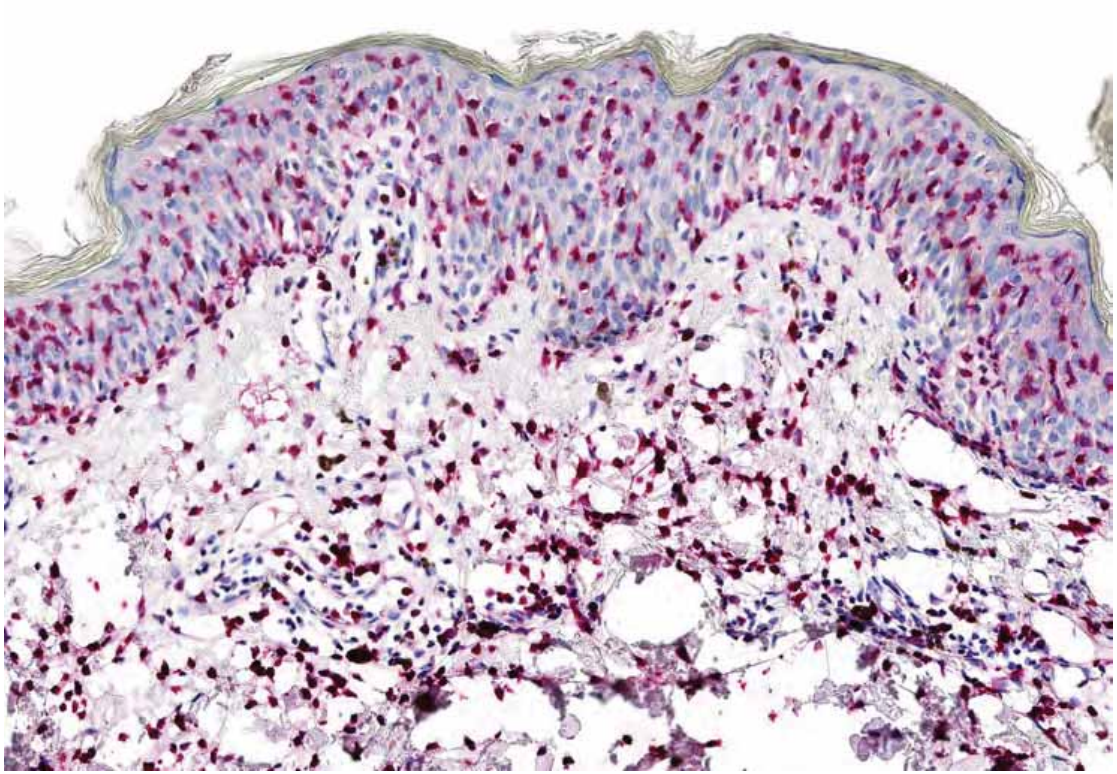
CD4

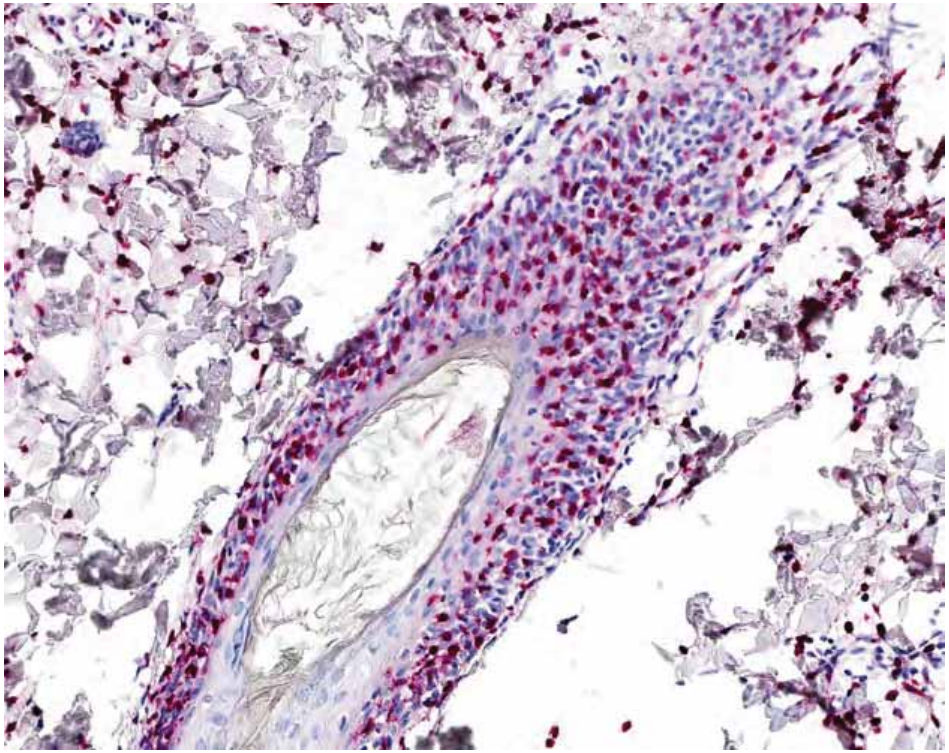


CD8



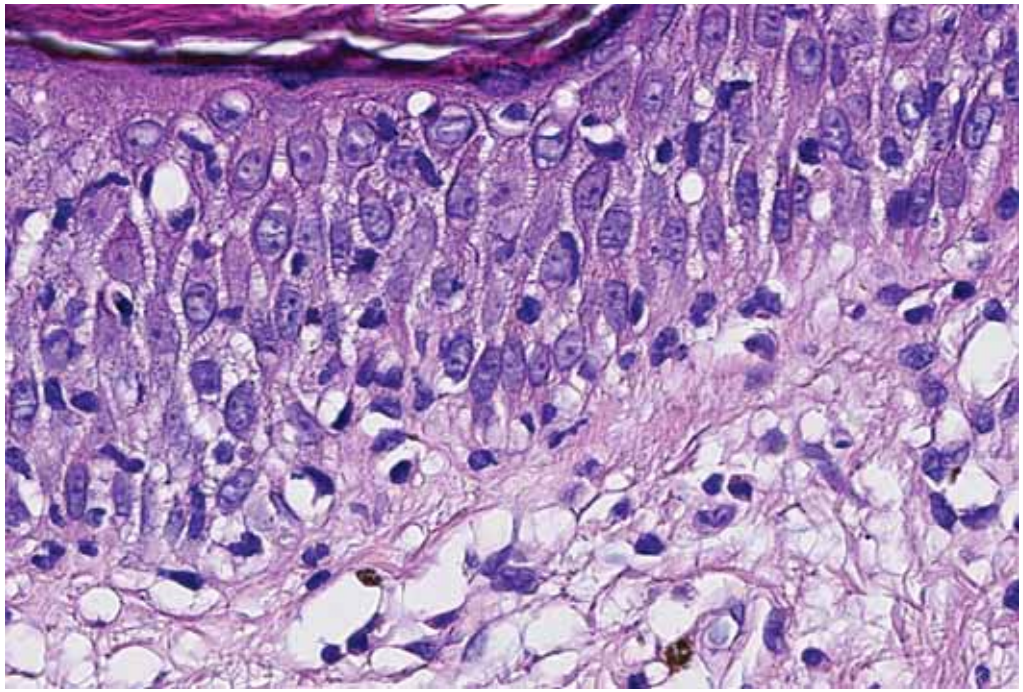
MPO

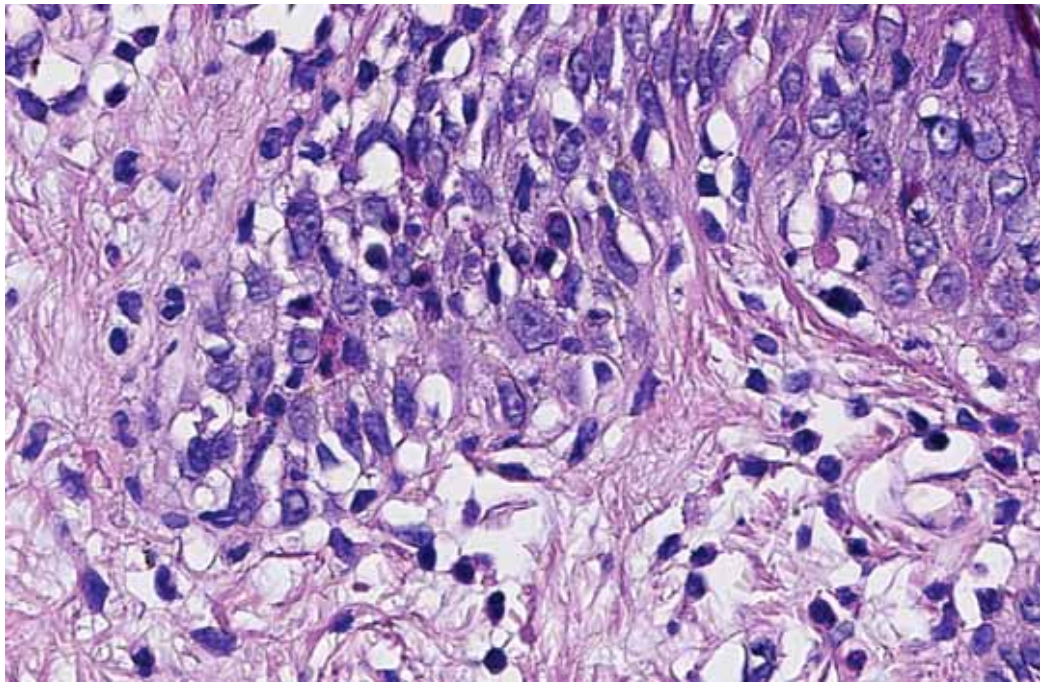




**MPO**

31-year-old man with two brownish slightly infiltrated patches on the left thigh and right arm.





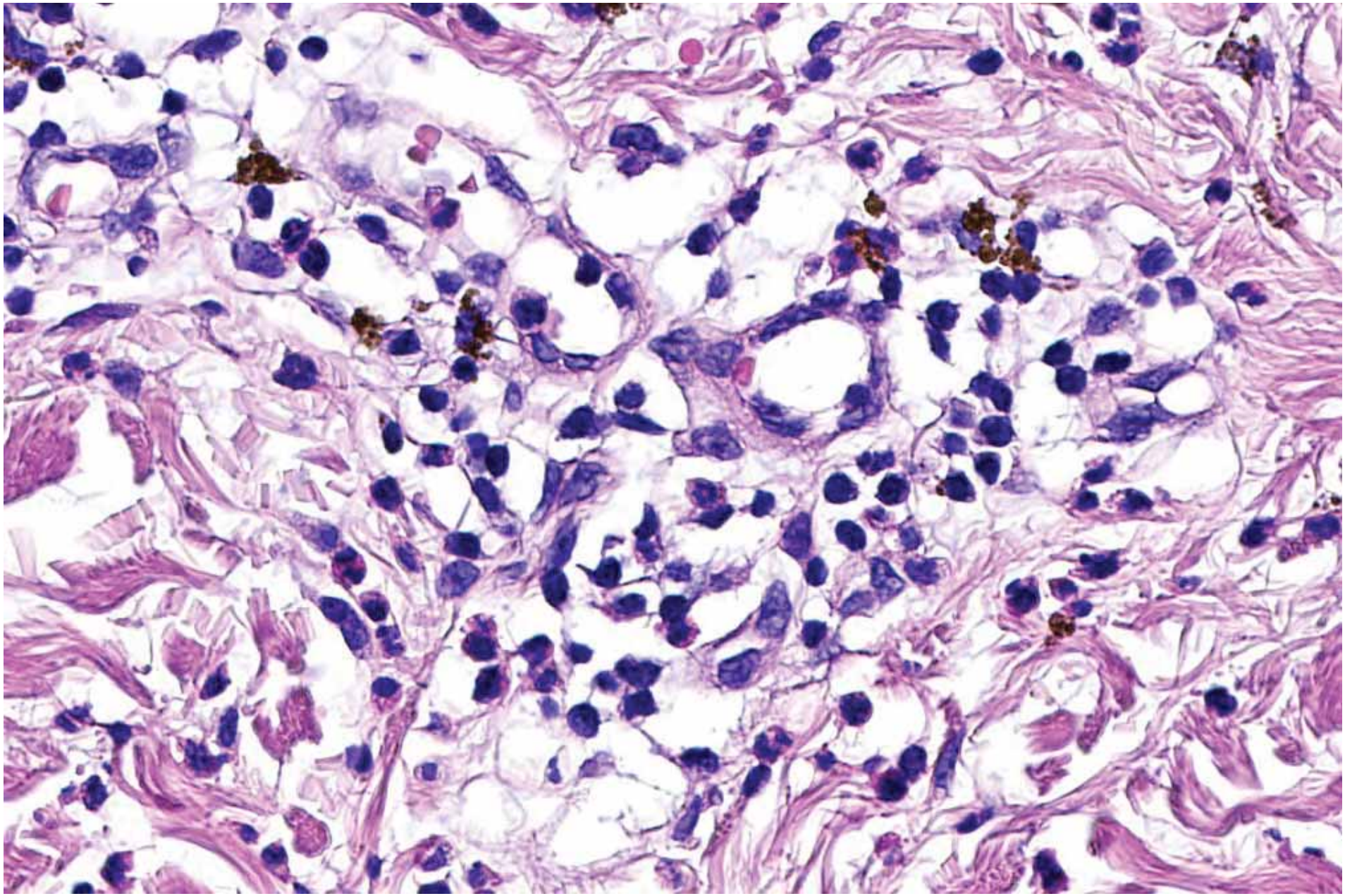


**TABLE 1.** Summary of Fixed Drug Eruption Cases

| No. | Age | Sex | Initial Presentation to Biopsy | Recent Onset to Biopsy | Neut. | Eos. | Pigment | Sites Involved | Bullous | Culprit Drug |
|---|---|---|---|---|---|---|---|---|---|---|
| 1 | 46 | F* | 2 y | 2 d | +++ | +++ | + | Neck, LE, UE, and back‡ | Yes | Carisoprodol |
| 2 | 32 | F* | 1 y | 1 d | ++ | +++ | ++ | Face, neck, chest, and back‡ | | Naproxen |
| 3 | 49 | F† | 5 d | 5 d | + | ++ | +++ | Gluteal‡ | Yes | Bactrim |
| 4 | 65 | M* | 1 y | 1 m | + | + | + | Chest‡ and penile | Yes | Valproate |
| 5 | 81 | F* | 4 m | 2 d | ++ | +++ | ++ | Face, chest‡, abdomen, and LE | | Naproxen |
| 6 | 33 | M† | 7 d | 7 d | + | ++ | +++ | Lip and UE‡ | Yes | Ibuprofen |
| 7 | 18 | F† | 1 y | 7 d | + | + | +++ | Lip, UE‡, and neck | | Metronidazole |
| 8 | 19 | M* | 2.5 y | 6 d | 0 | + | + | UE‡ and abdomen | Yes | Ibuprofen |
| 9 | 63 | F* | 10 d | 10 d | ++ | ++ | + | LE‡ | | Bactrim |
| 10 | 34 | F† | 3 d | 3 d | + | +++ | ++ | LE‡ | | Motrin |
| 11 | 36 | F* | 1 y | 3 d | ++ | +++ | ++ | Back, abdomen, UE‡, and LE | | Ibuprofen |
| 12 | 65 | M* | 6 m | 6 m | 0 | + | + | LE‡ | | Hydroxyurea |
| 13 | 66 | F* | 3 w | 3 w | 0 | ++ | ++ | Chest‡ | | Unknown |
| 14 | 72 | M* | 4 m | 4 m | 0 | ++ | ++ | LE‡ | | Unknown |
| 15 | 64 | M* | 3 m | 4 d | ++ | 0 | + | Face, chest, and LE‡ | | Aztreonam |
| 16 | 32 | F* | 11 m | 11 m | 0 | 0 | +++ | Abdomen‡ | | Unknown |

*Caucasians.
†African American.
‡Biopsy site.
d, day; Eos, eosinophil; F, female; LE, lower extremities; M, male; m, month; Neut., neutrophil; UE, upper extremities; w, week; y, year.

From: Li & Kazlouskaya Am J Dermatopathol 2022

# Neutrophilic fixed drug eruption

## Histological features

Neutrophils in FDE are relatively common in FDE (68.8%)

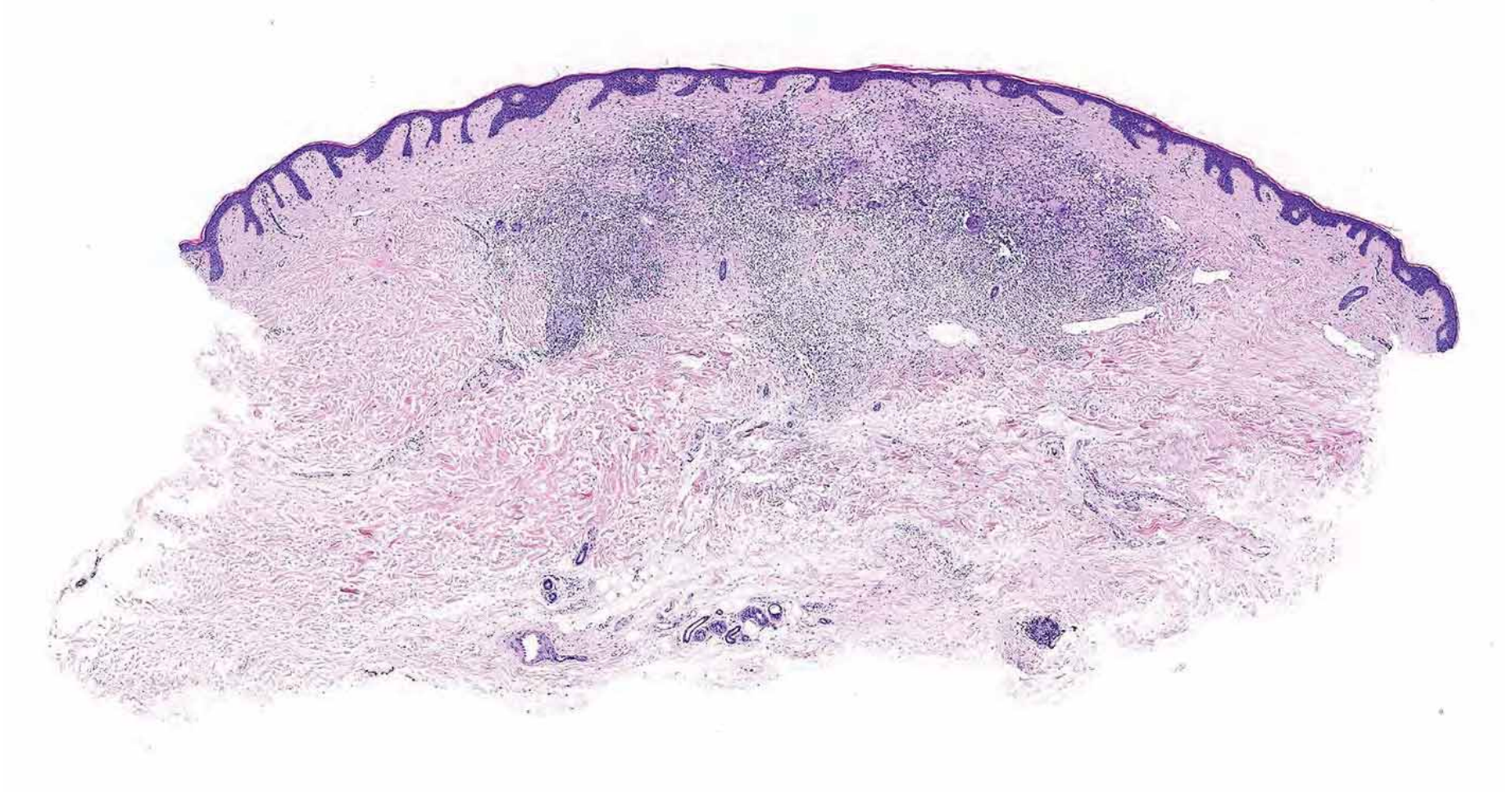
Abundant neutrophils in biopsies with shorter onset-to-biopsy interval
(3.7 vs. 16.9 days, $p < 0.023$)

Correlation with early phase and multiple lesions of FDE rather than a different entity

Li & Kazlouskaya Am J Dermatopathol 2022

41-year-woman with erythematous and slightly brownish papules and atrophy on the lower abdomen and right thigh since several years

*Referrral by Dr. Kathrin Bänziger, Zürich*



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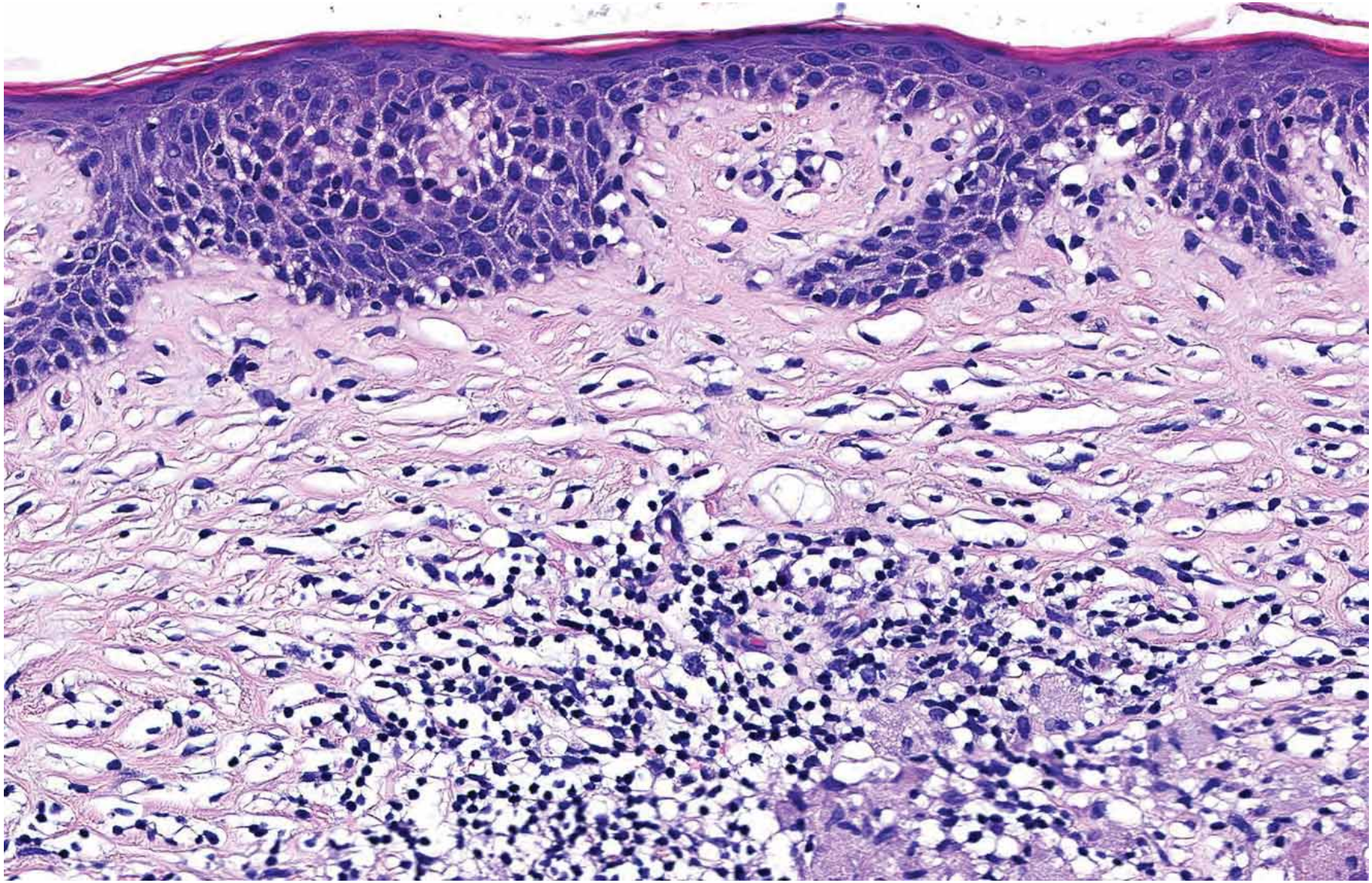

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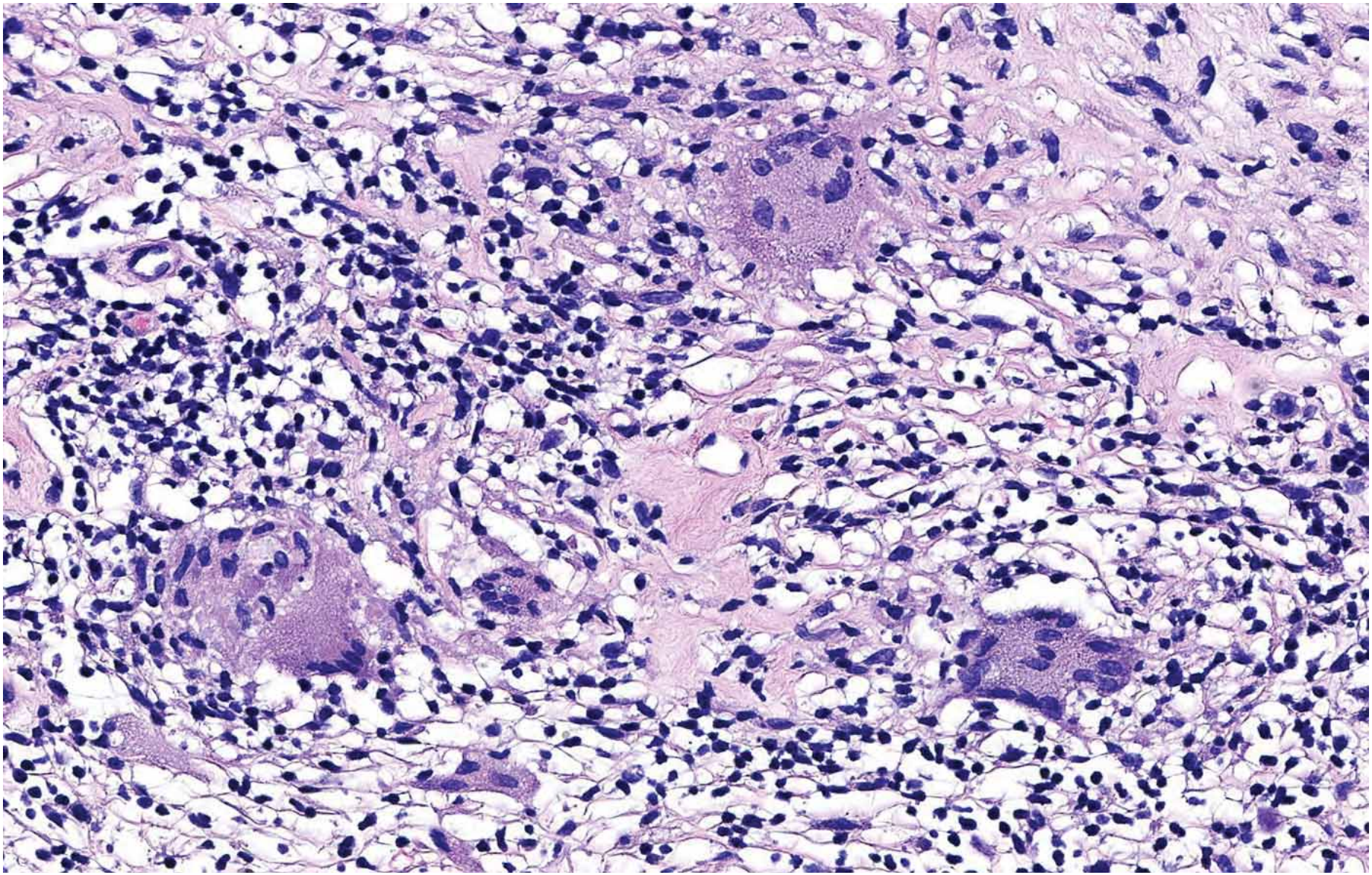

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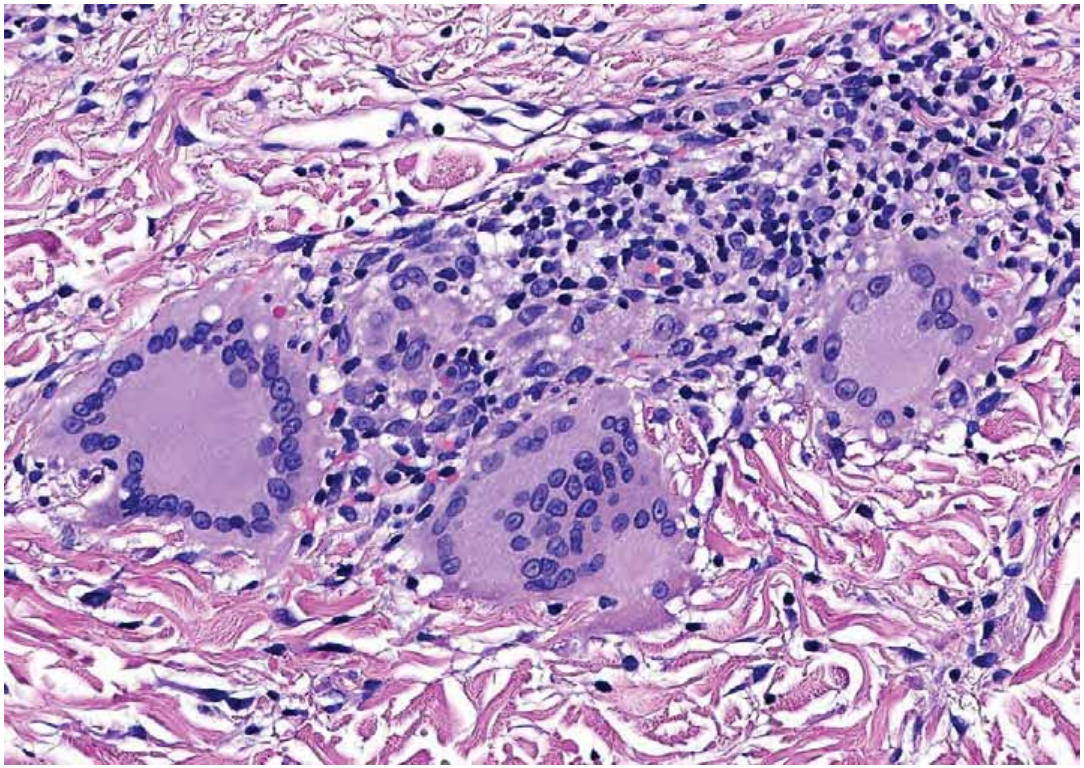
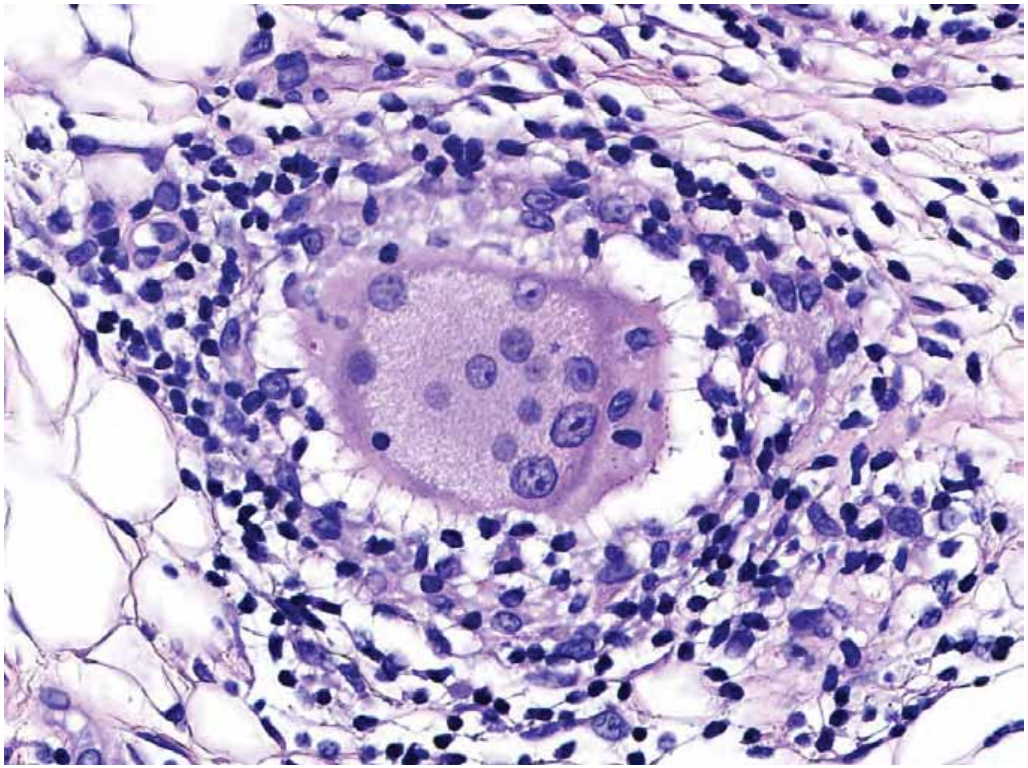
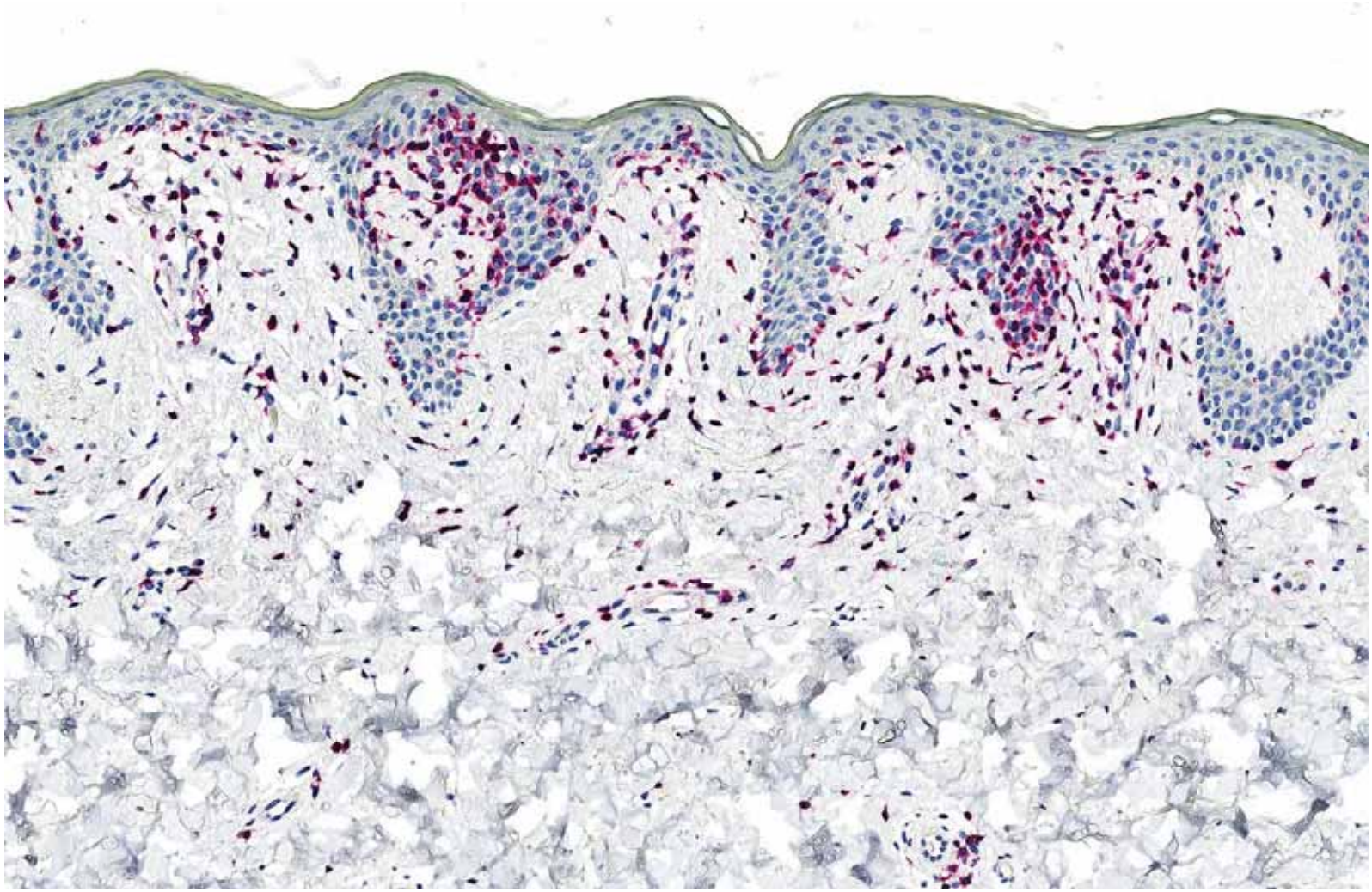


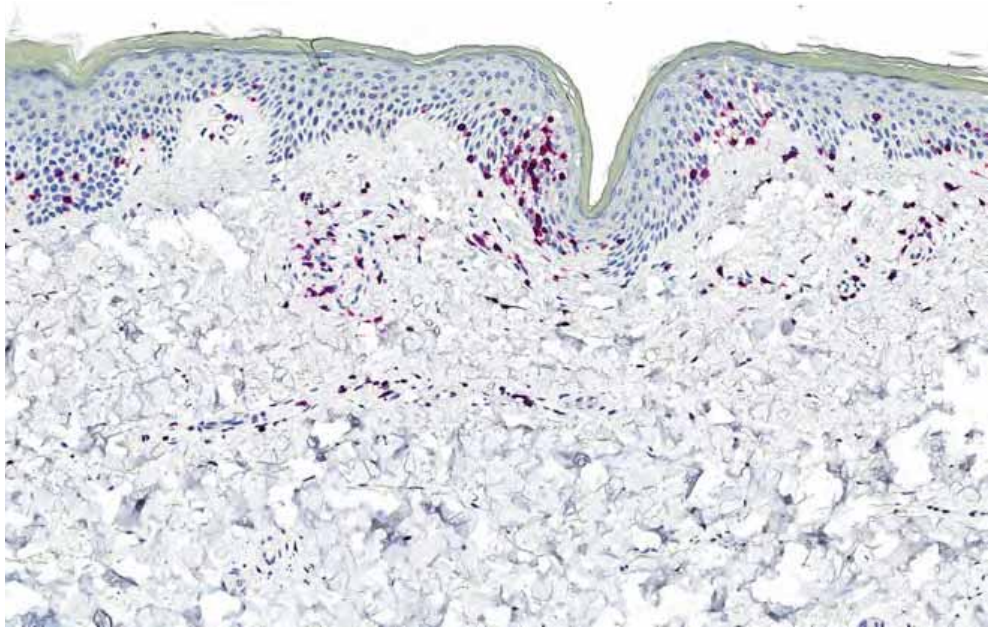


B23-69182

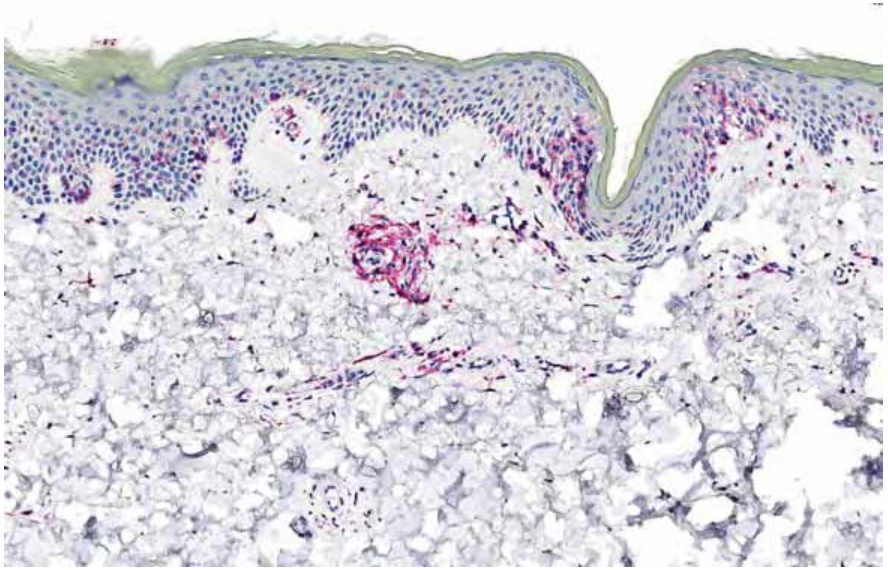


CD3

B22-88036



CD3



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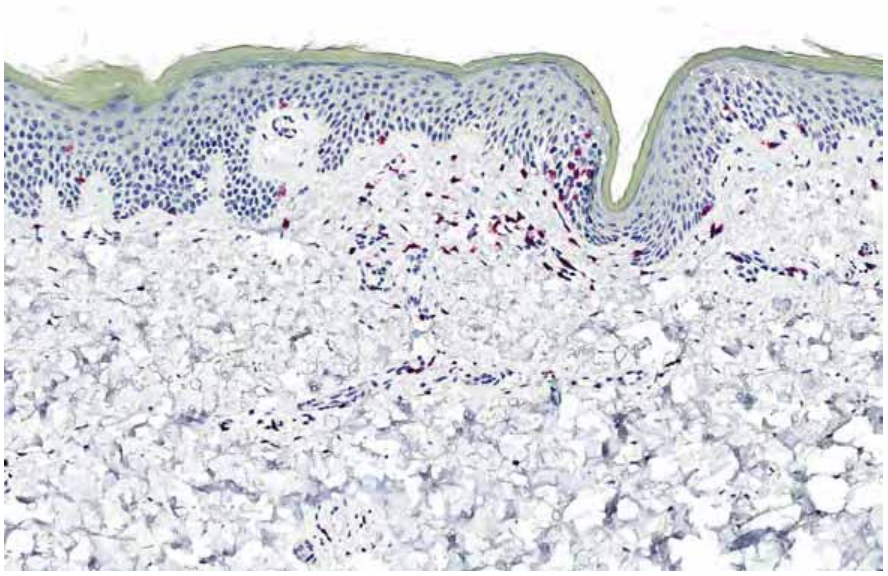
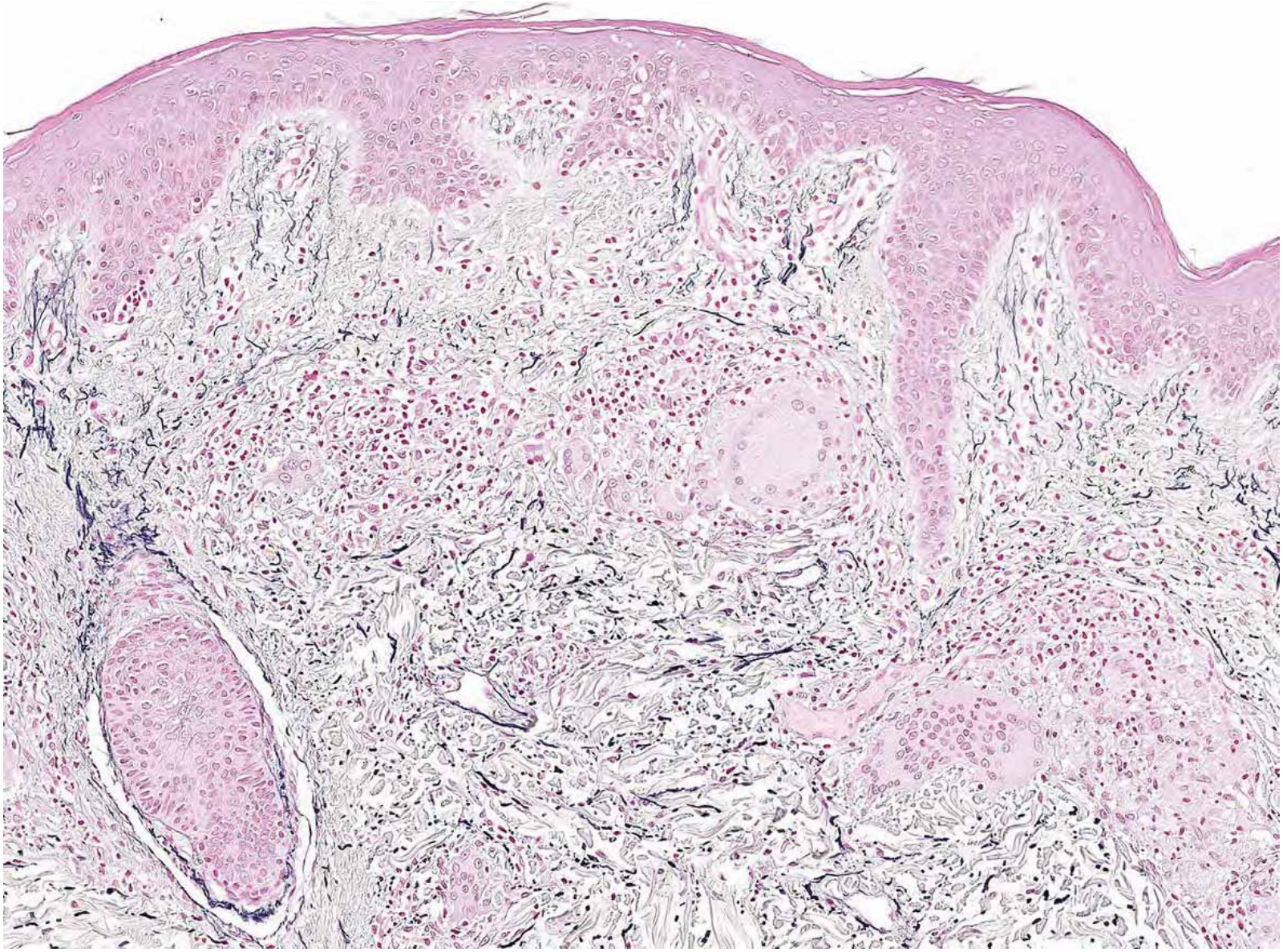


CD8

Identical T-cell clone in 3 biopsies

B22-88035



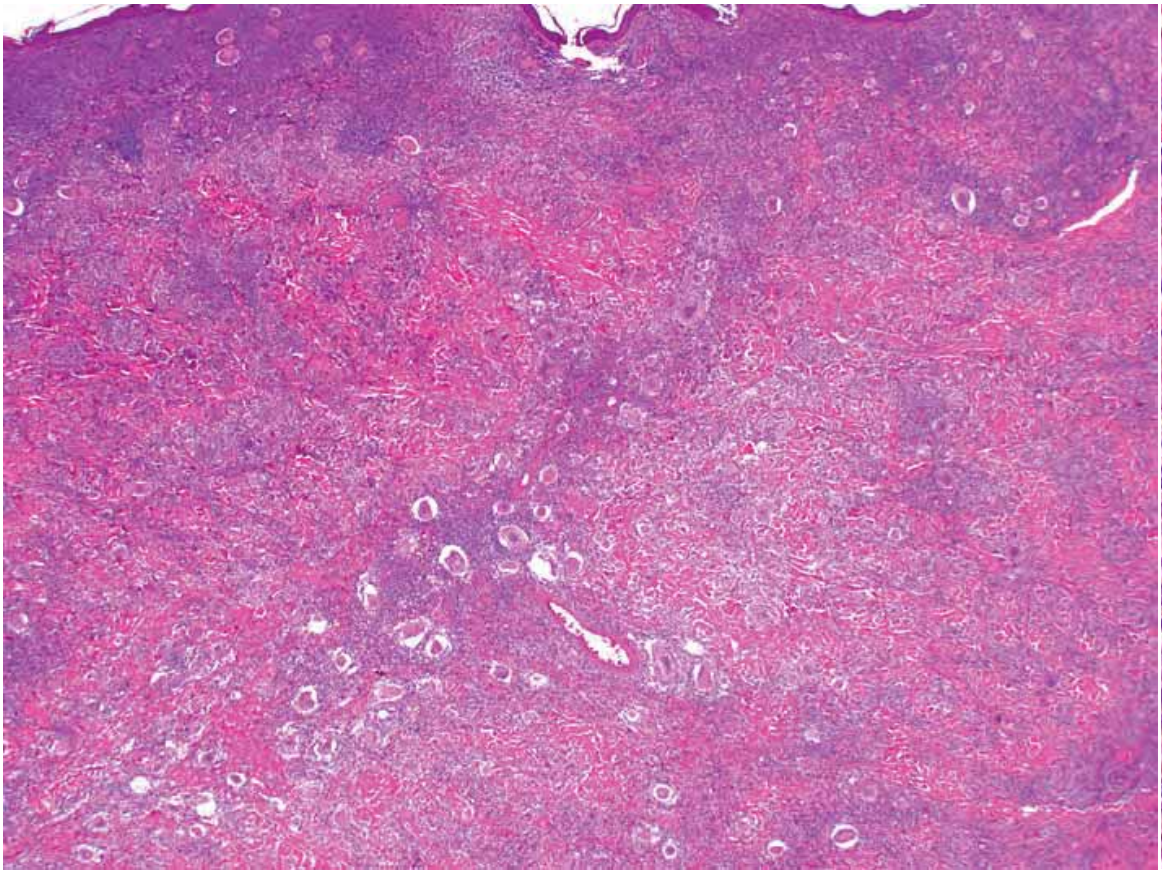
B23-69182

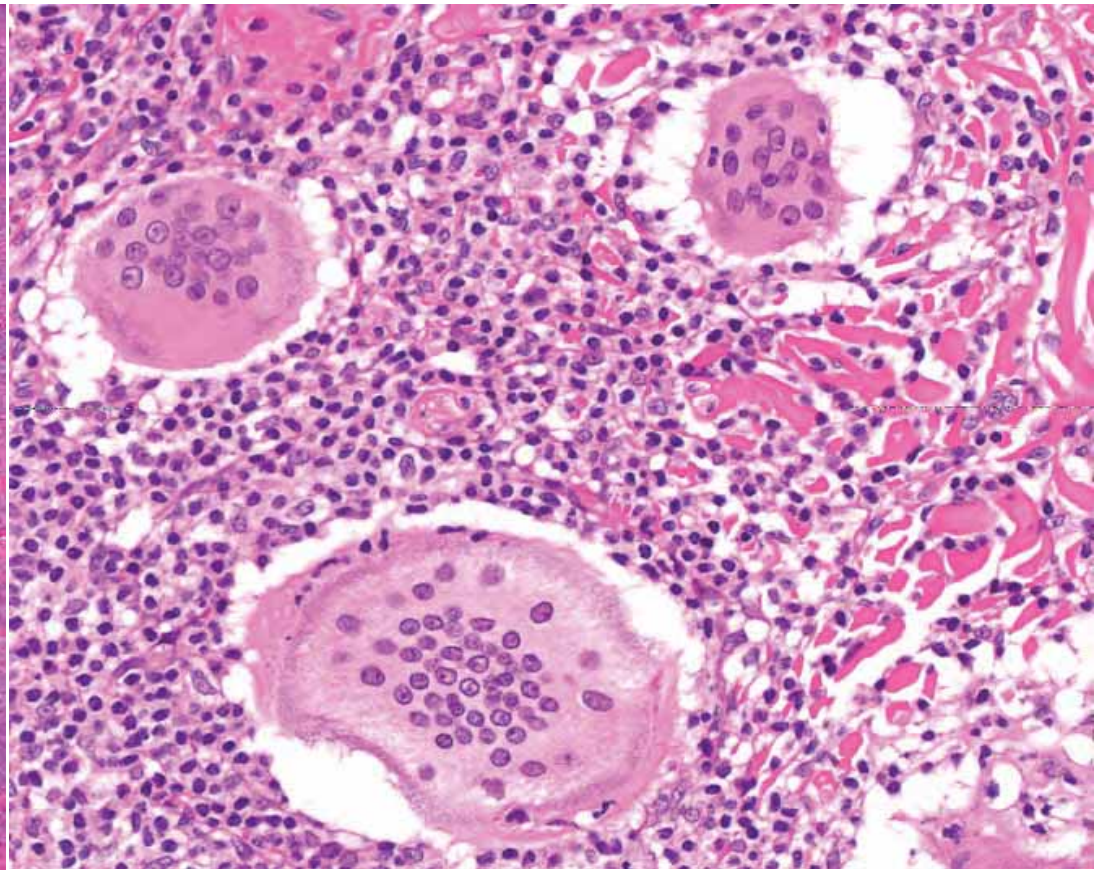
# Granulomatous slack skin

## Clinical features

- Poikilodermatous lesions
- Later cutis laxa-like
- Bulky skin folds

# Granulomatous slack skin

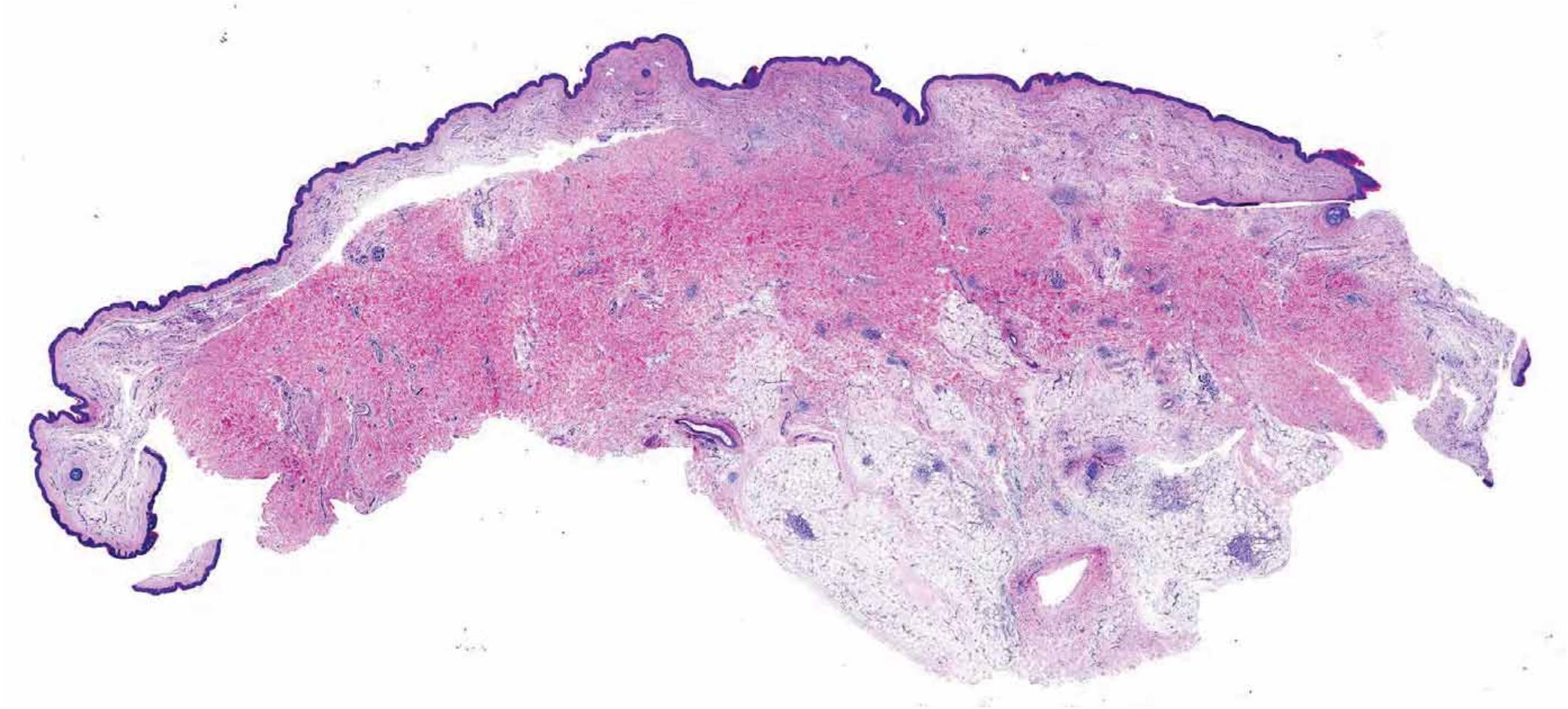




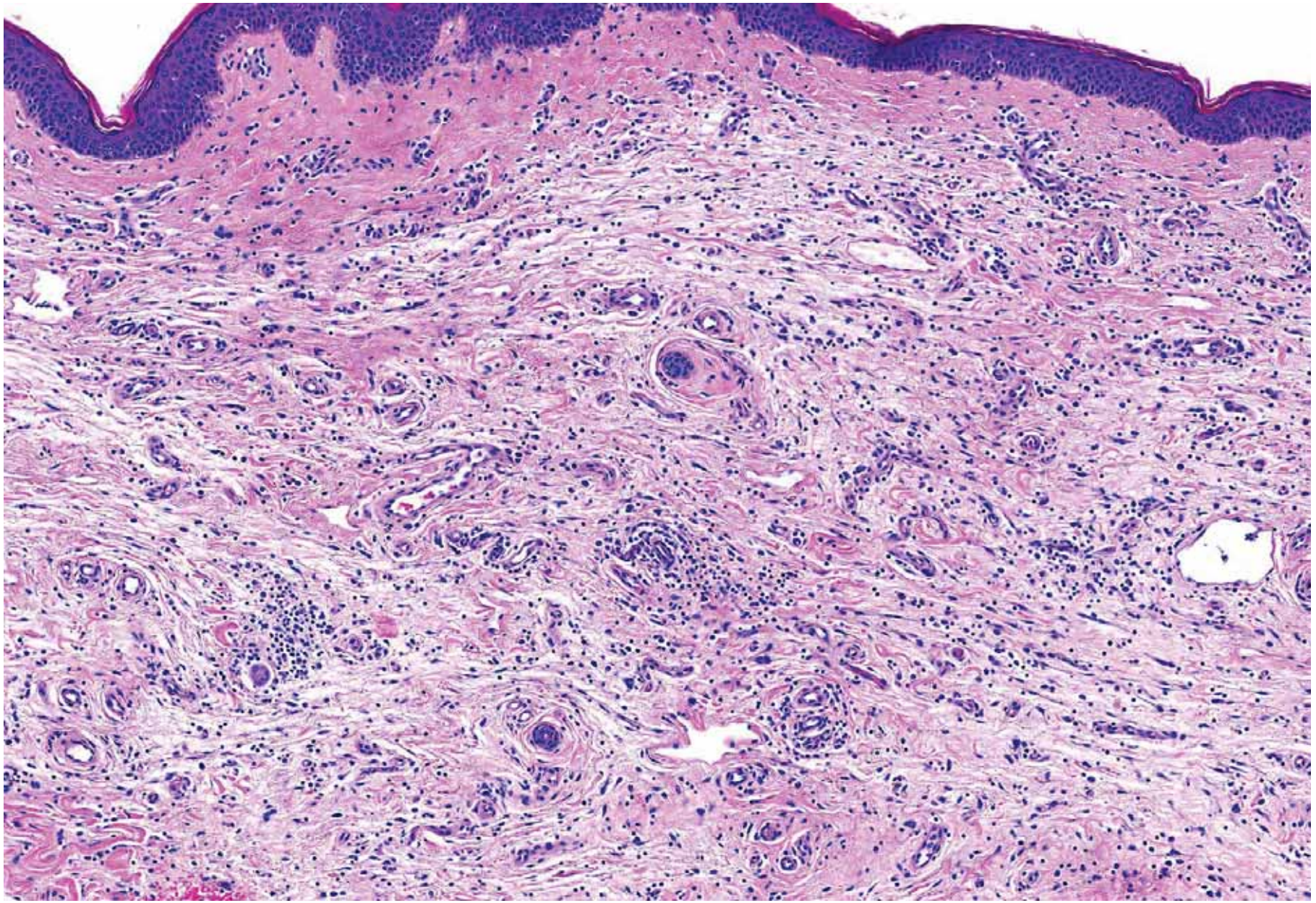
34-year-old woman with a slowly enlarging erythematous plaque since 10 years. Chronic borrelia infection?

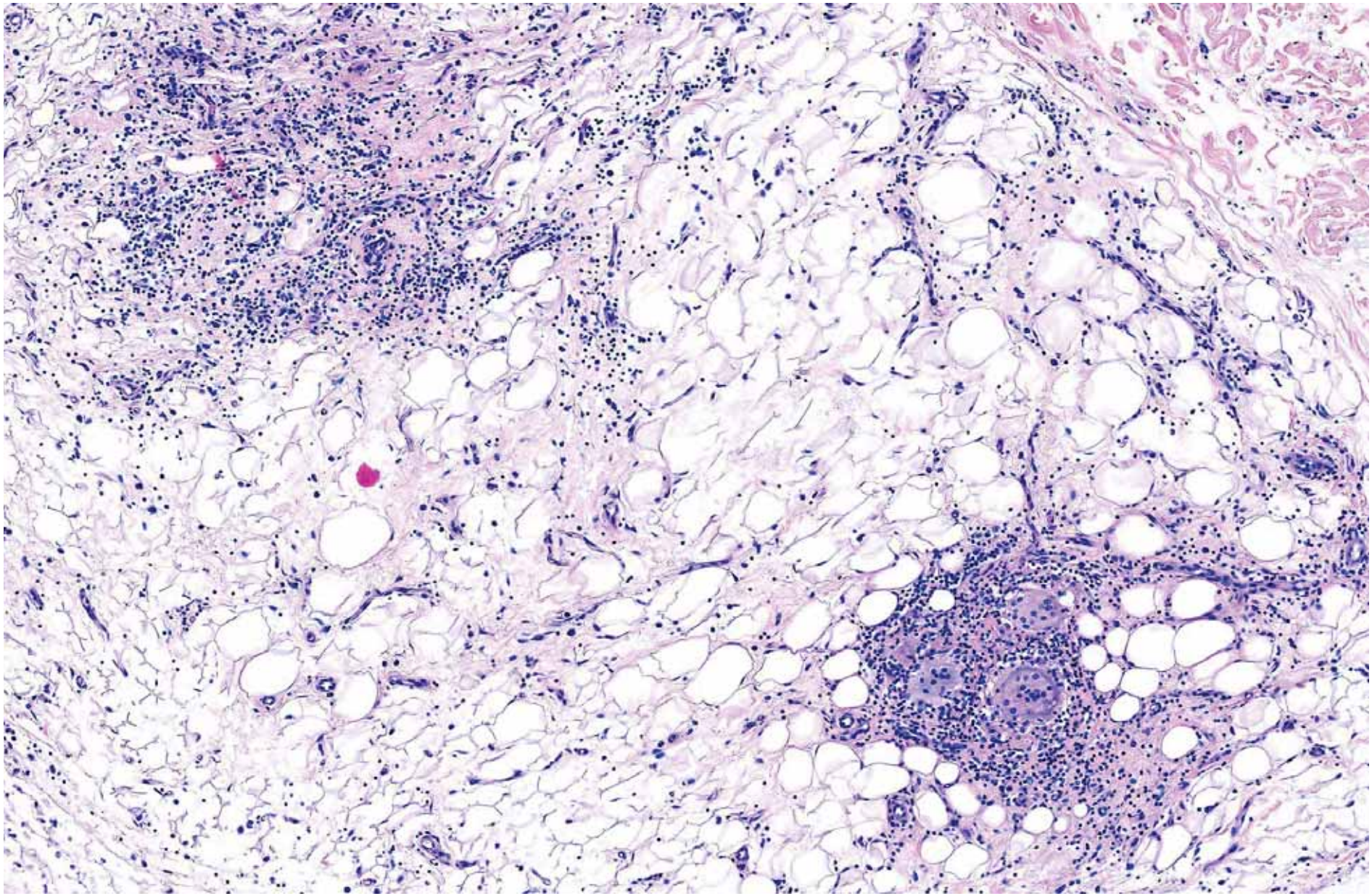
*Referrral by Dr. Ivo Weidenhoffer, Lenzburg*

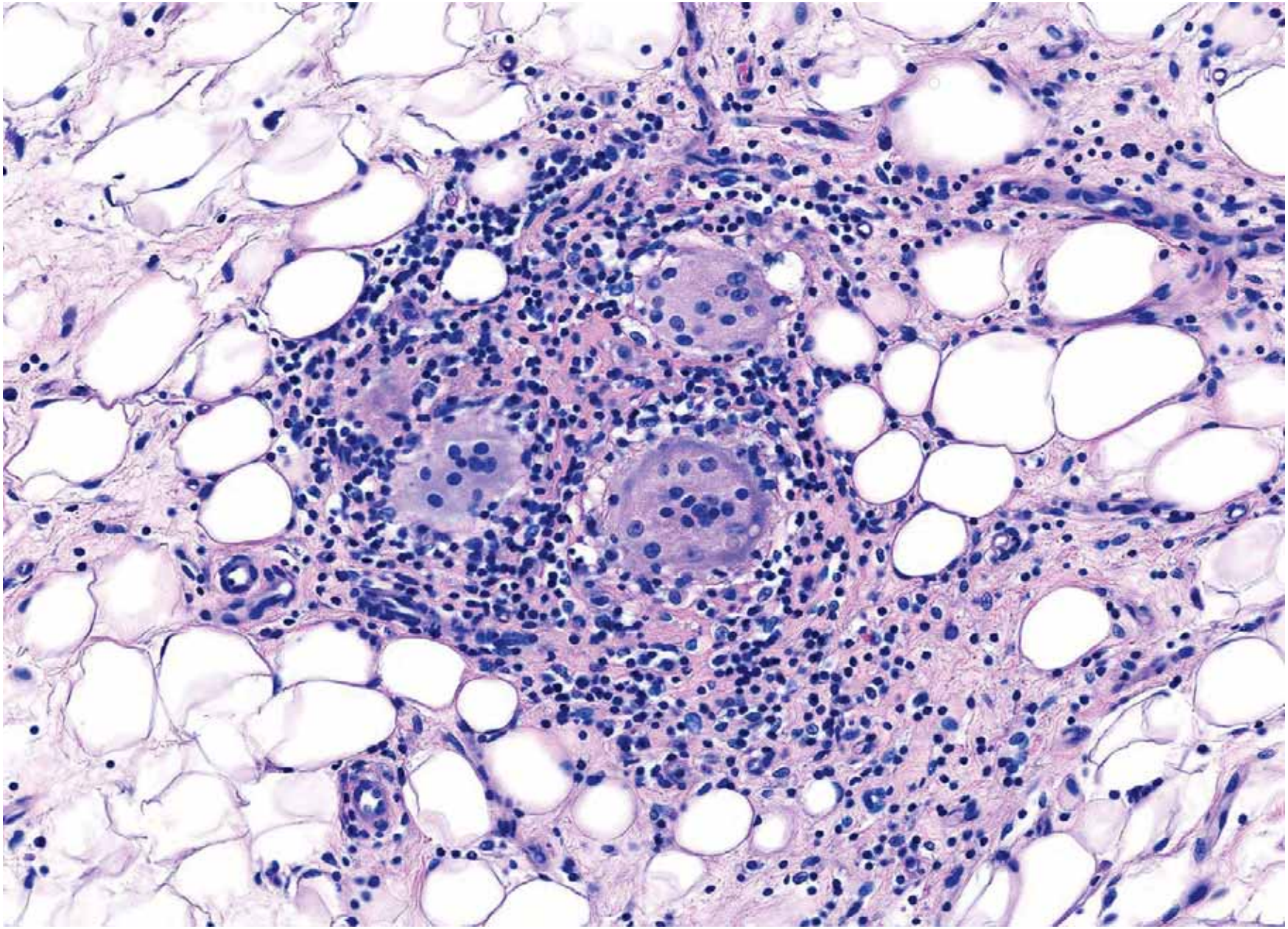
Central part of the lesion with folded skin

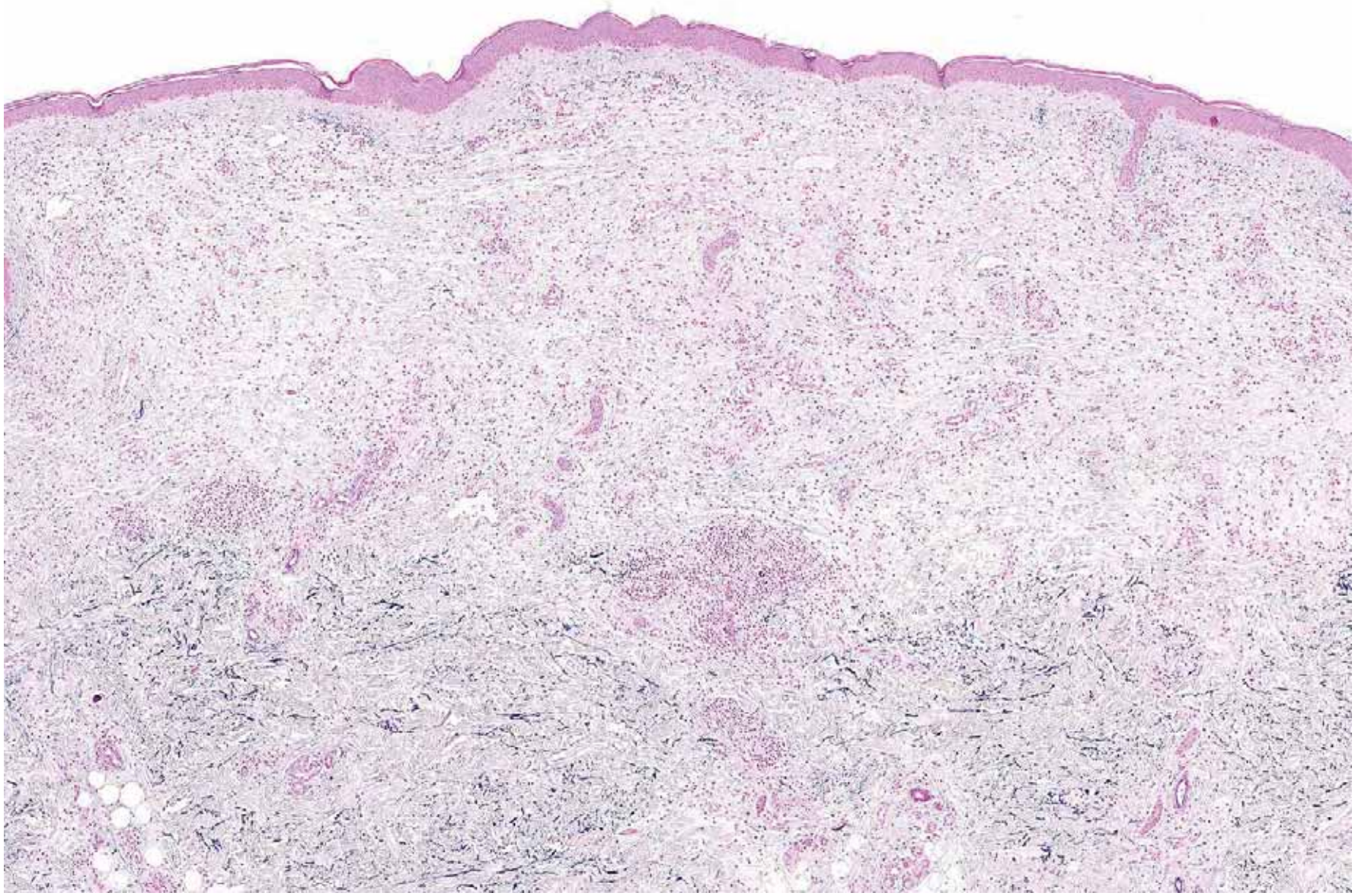


B25-19374



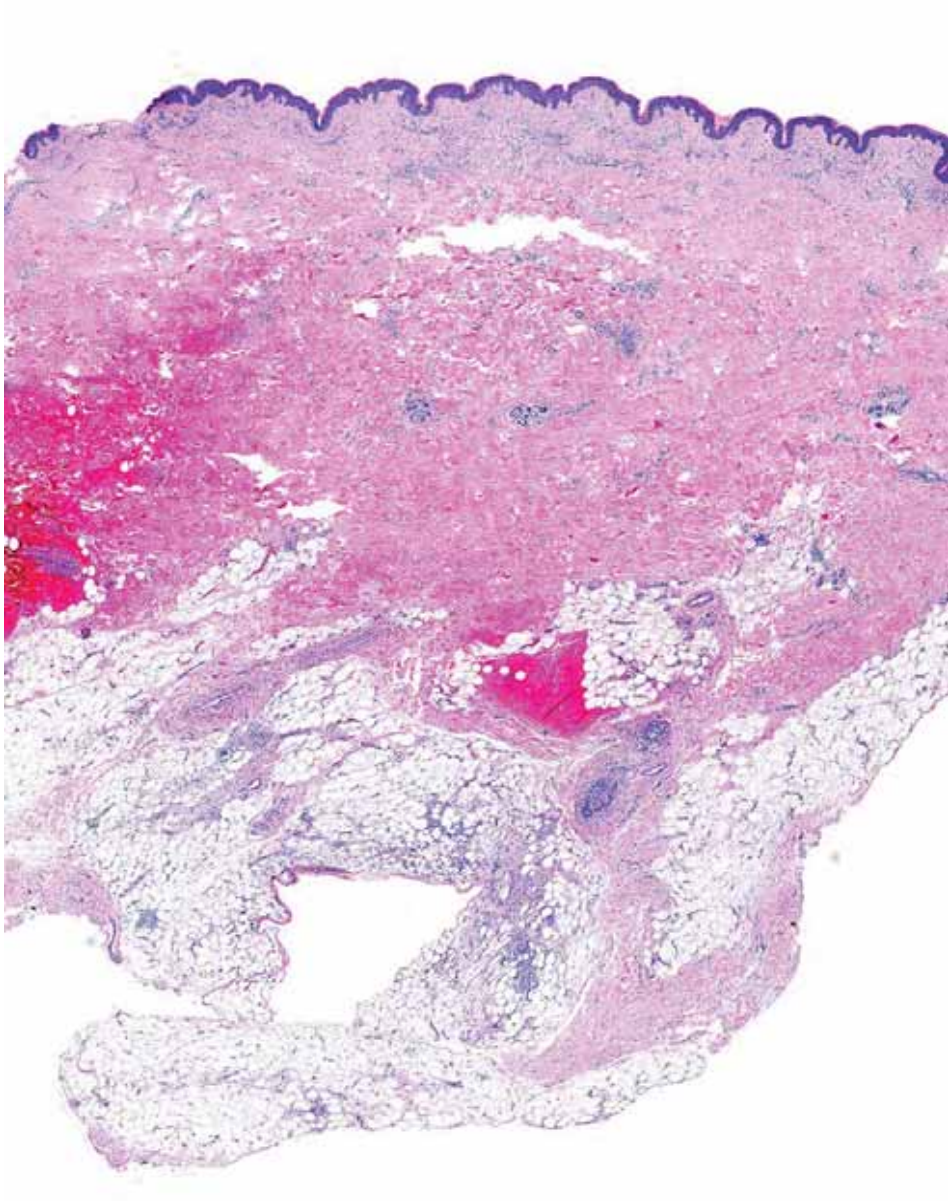






Elastica

# Margin

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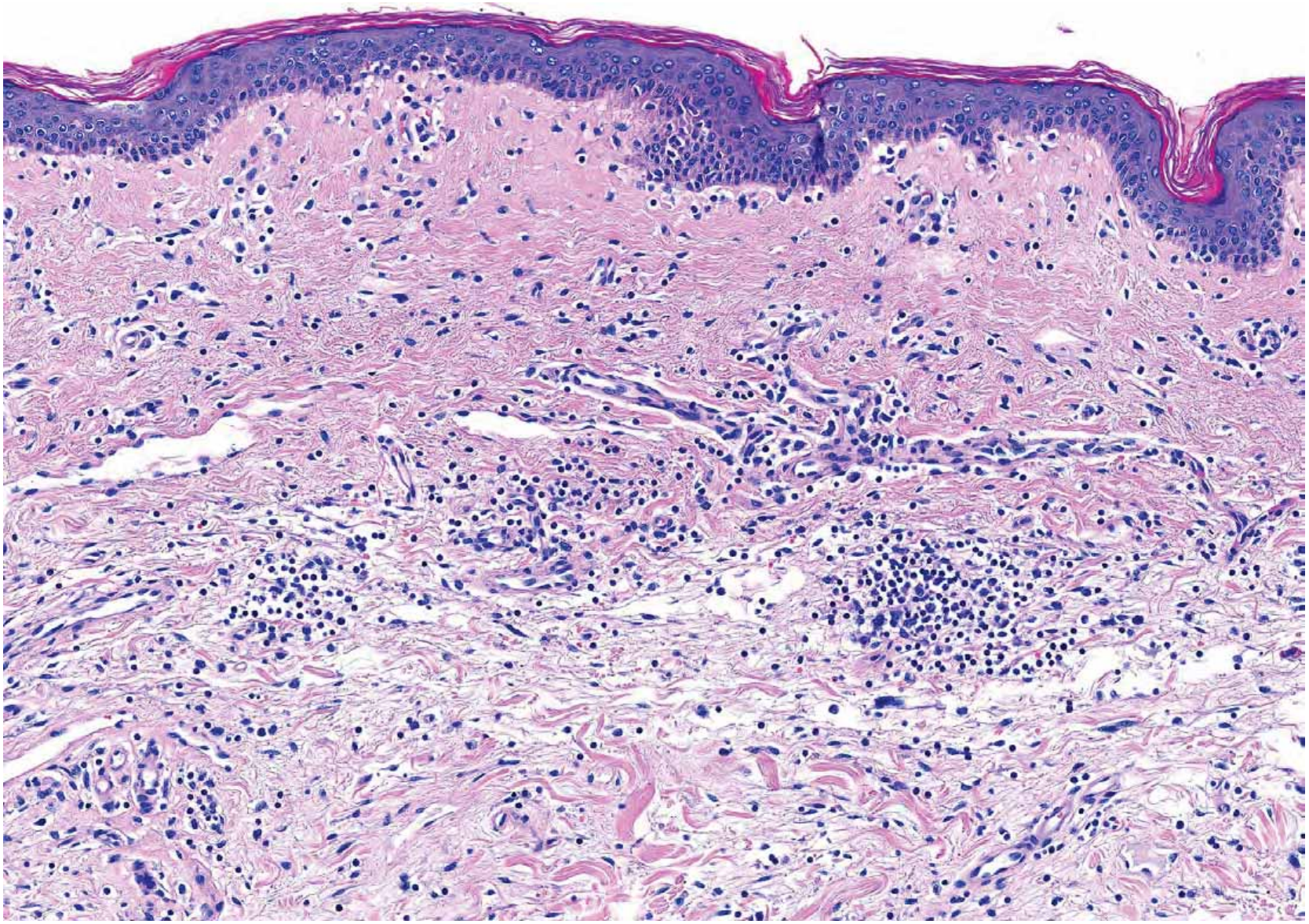

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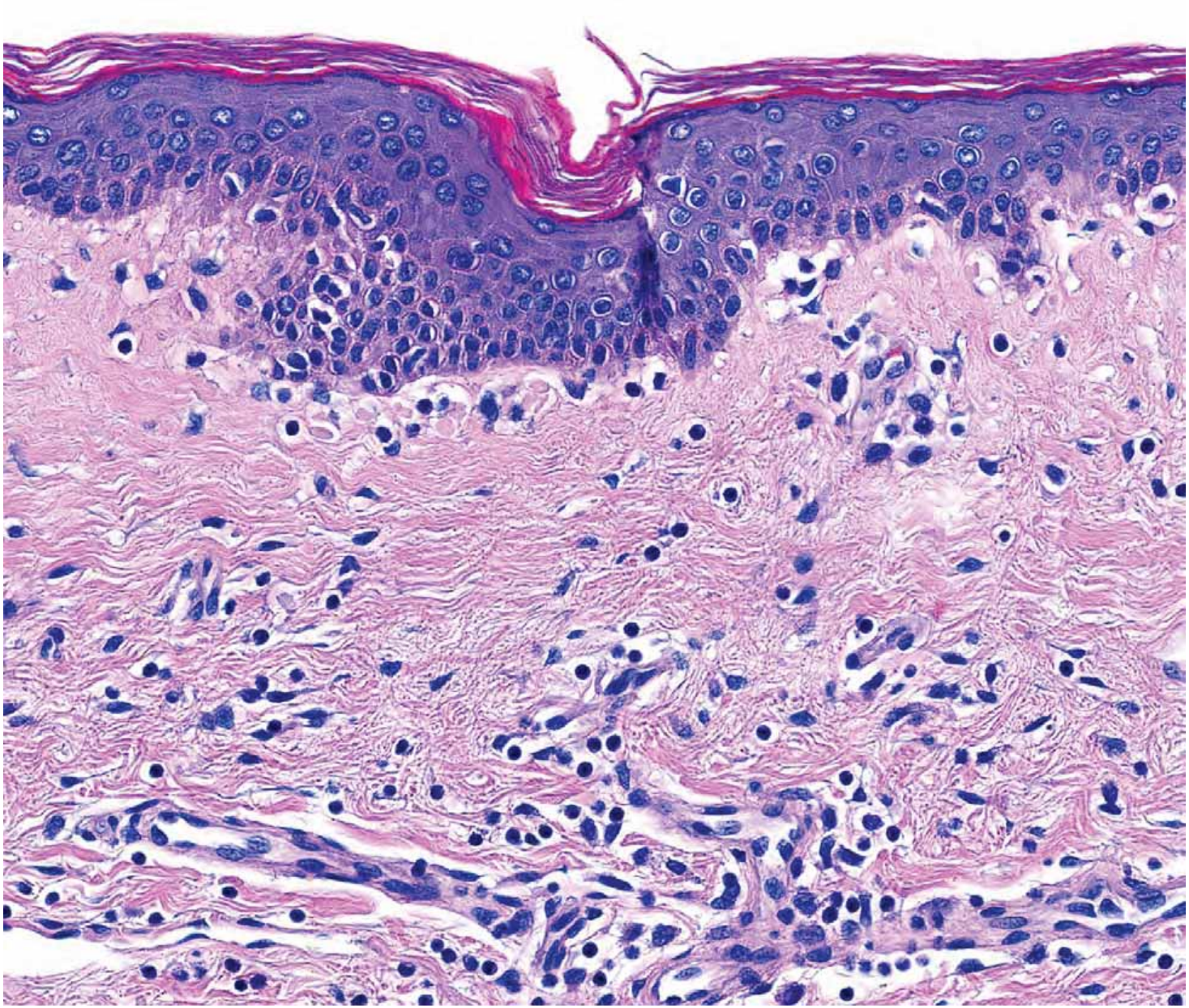
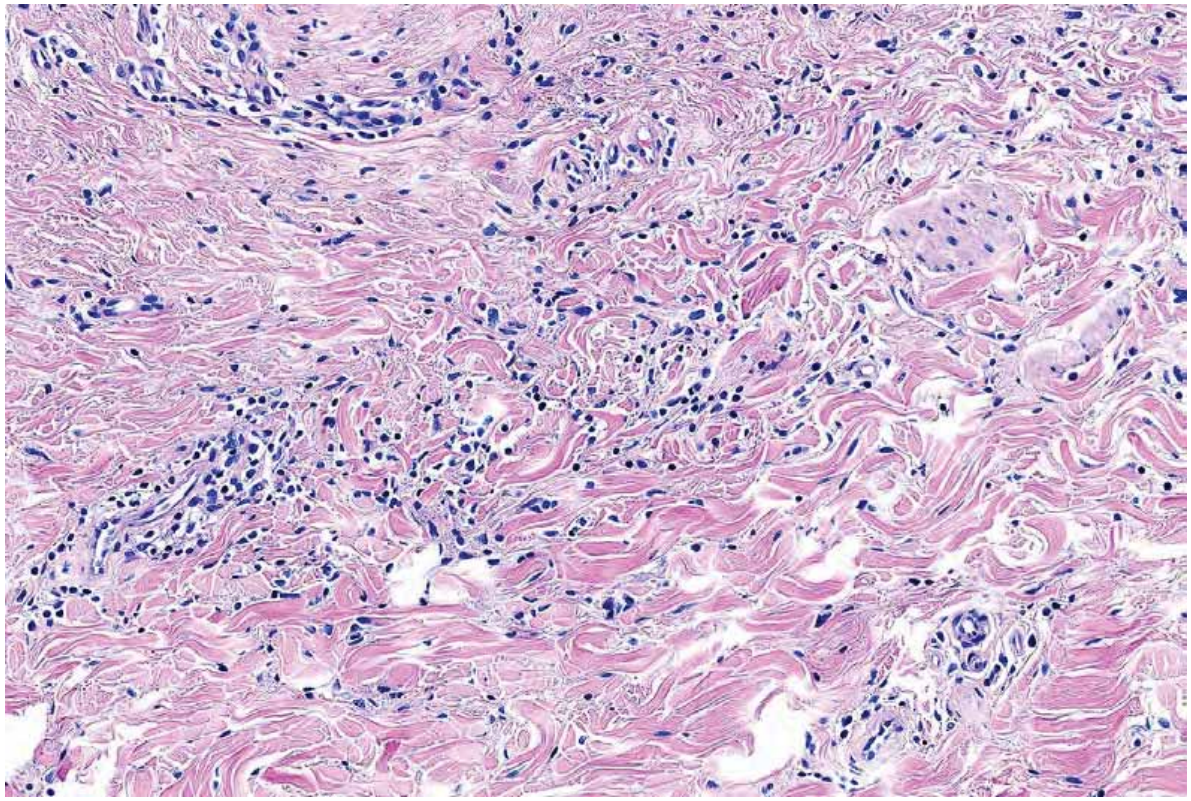
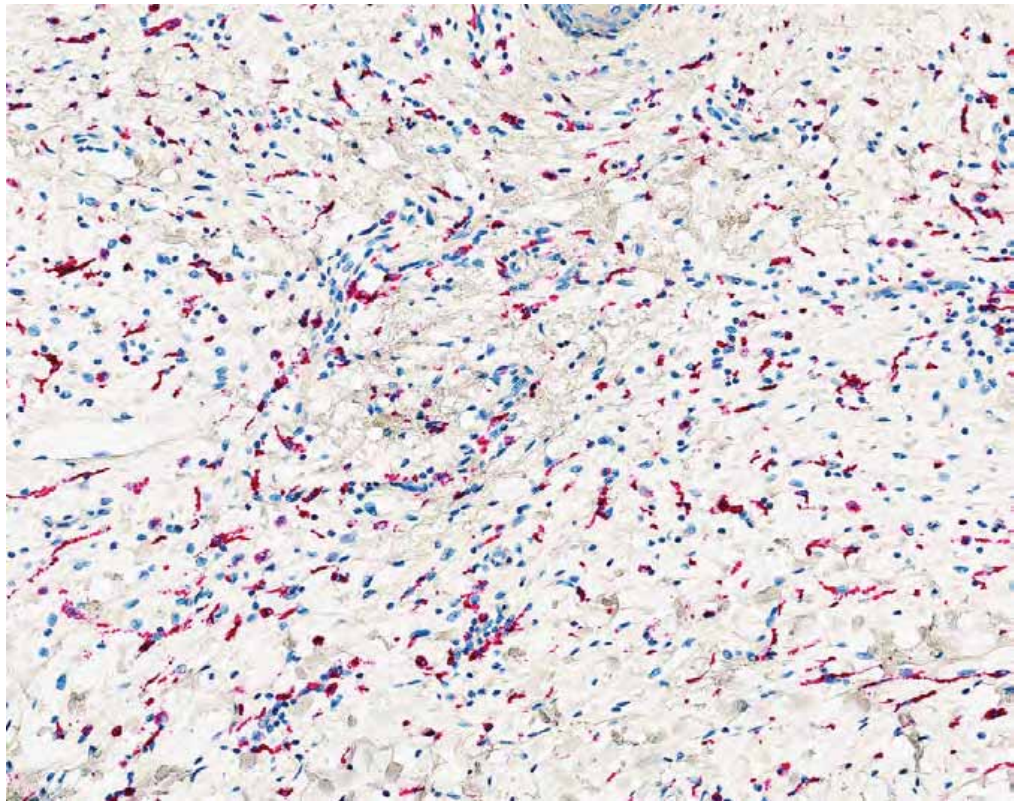
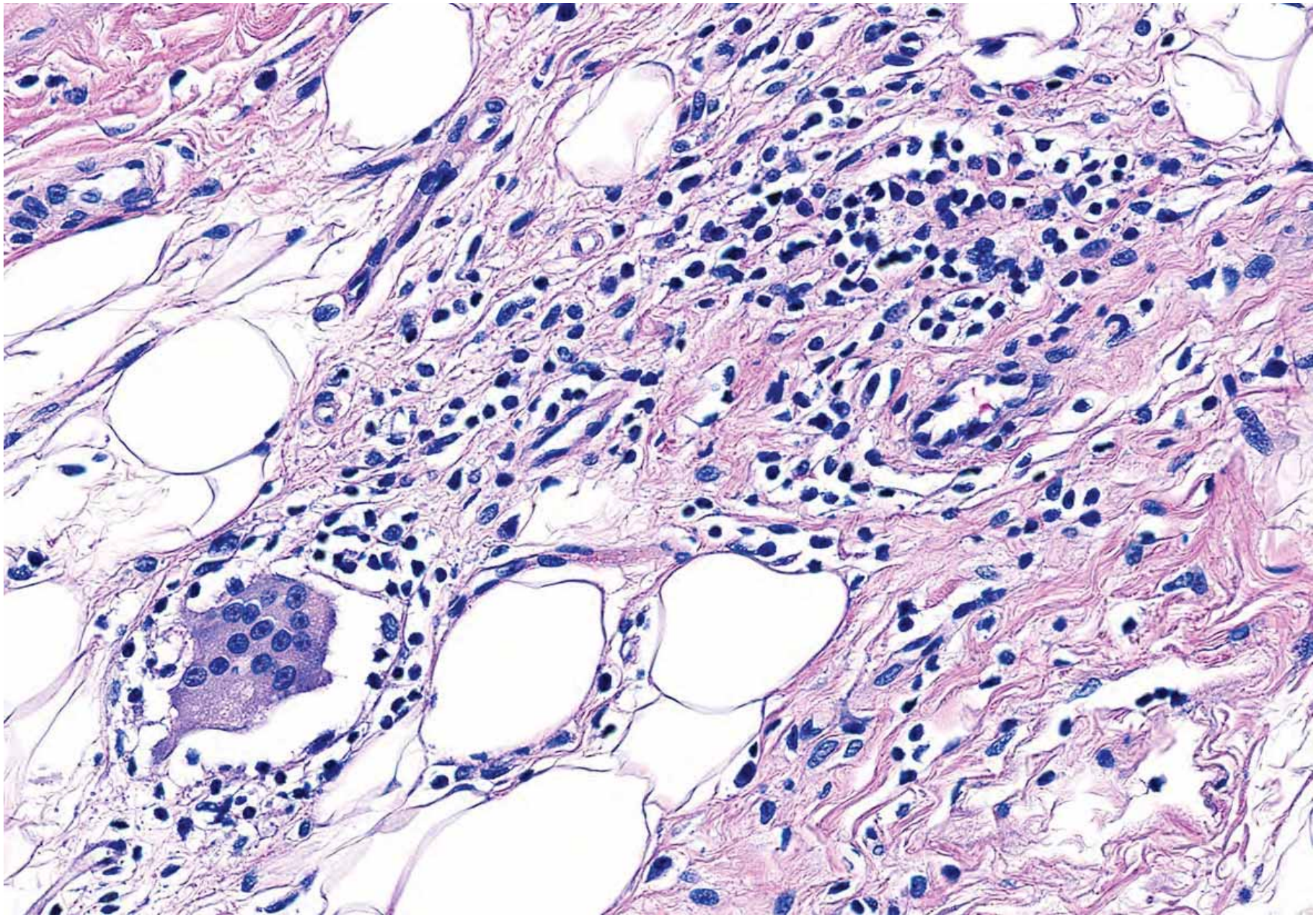
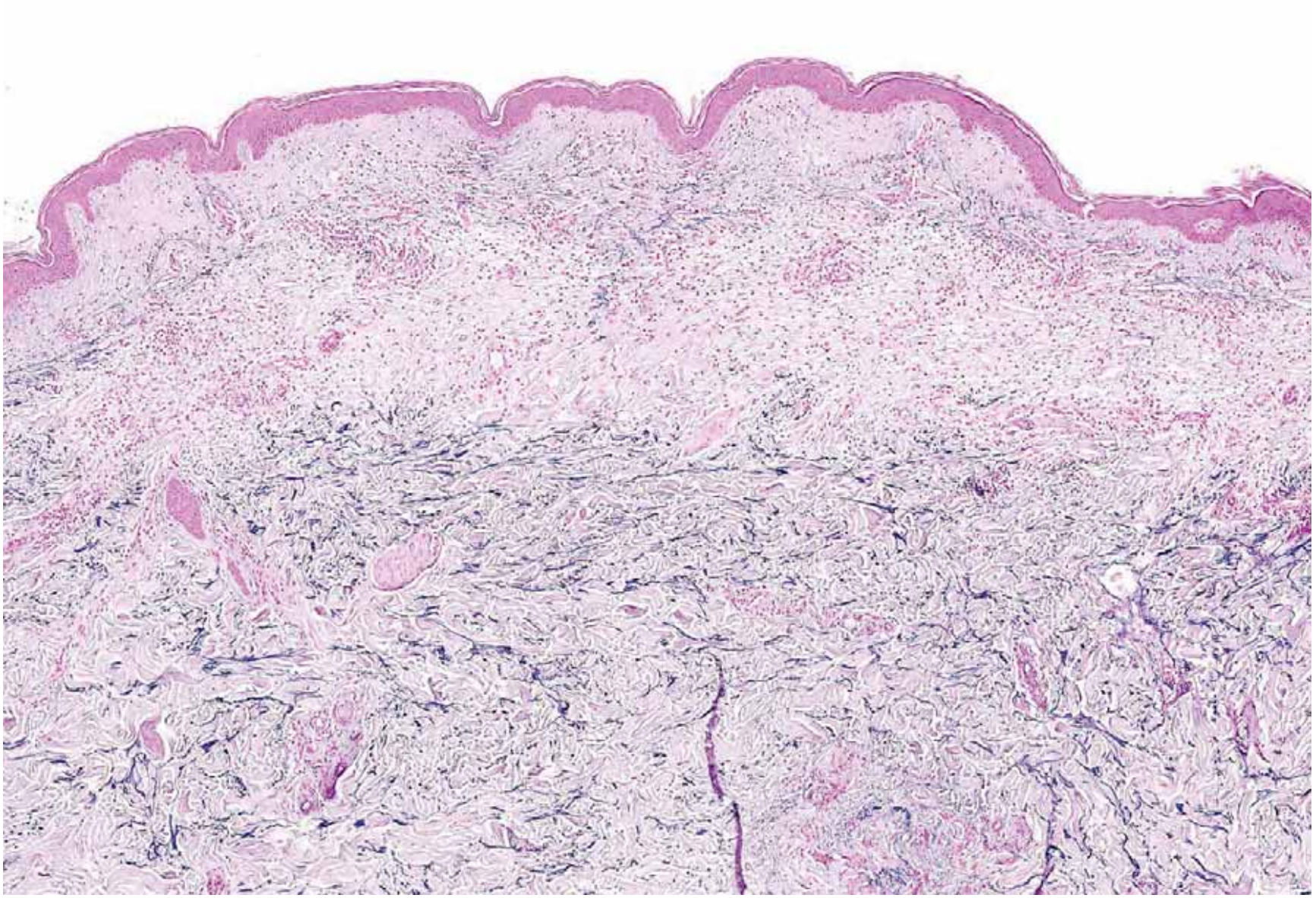






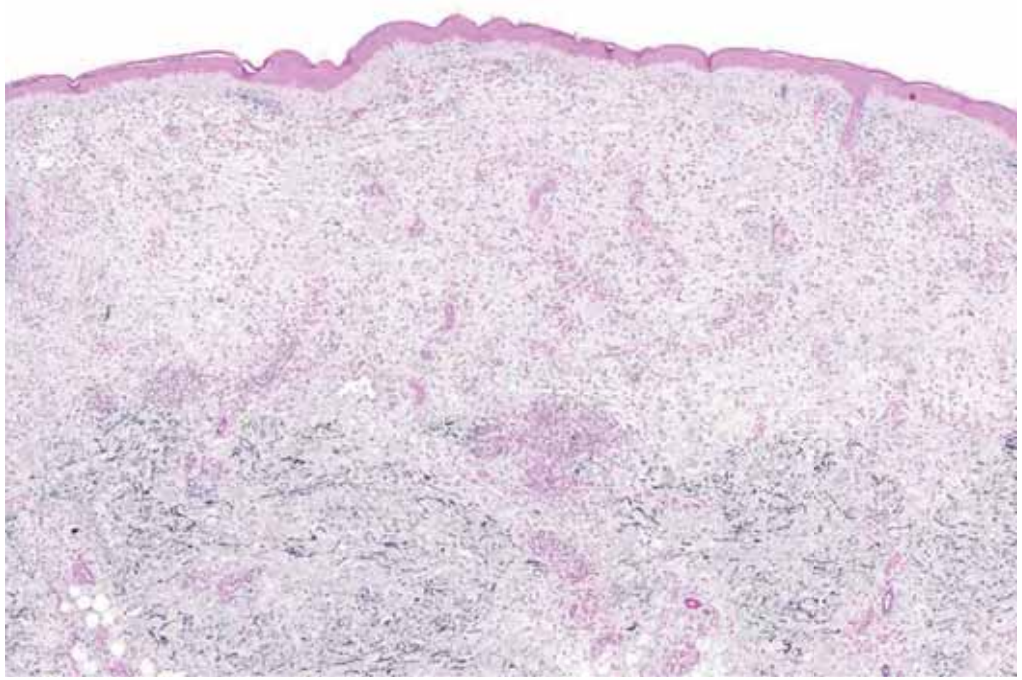
CD68



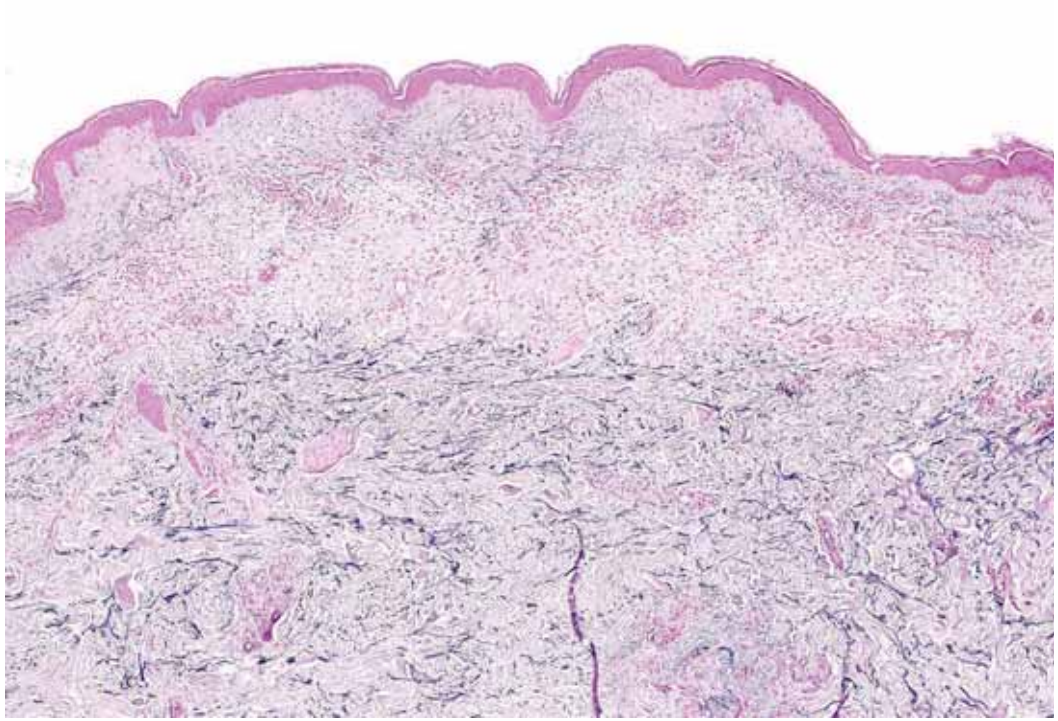


Elastica

Central area with folded skin



Margin with non-folded skin



Elastica

# Granulomatous cutaneous lymphomas

Granulomatous features rarely found in approx. 2% of cutaneous lymphomas

## Cutaneous T-cell lymphomas

- Granulomatous mycosis fungoides
- Granulomatous slack skin
- Sézary syndrome
- CD30+ lymphoproliferative disorders
- Subcutaneous panniculitis-like lymphoma
- Adult T-cell lymphoma/leukemia
- Peripheral T-cell lymphoma, NOS

## Secondary cutaneous lymphomas

- Angioimmunoblastic T-cell lymphoma

# Granulomatous MF

Hyperpigmented patches/plaques (40%)

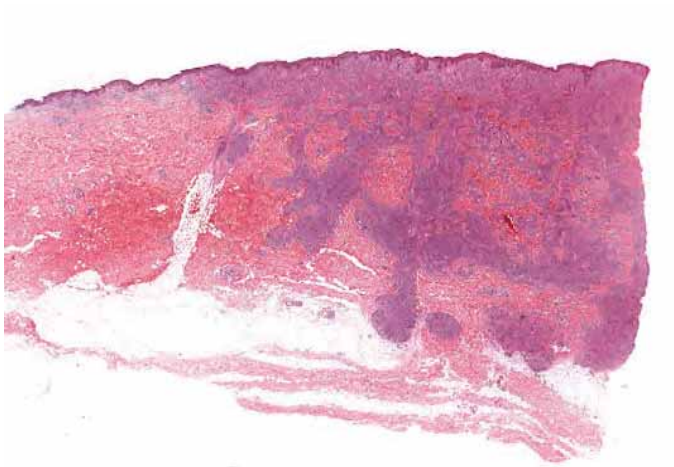
Diagnosis in granulomatous MF
often delayed - 6 years

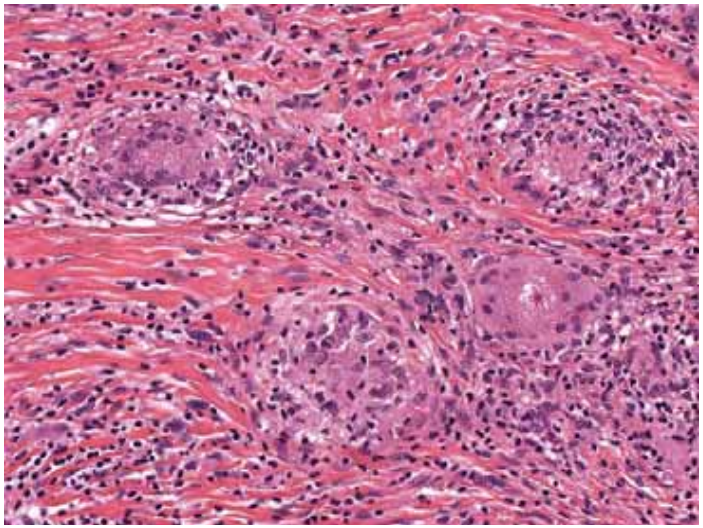
Prognosis worse than in classic MF
5-year-survival 66%.

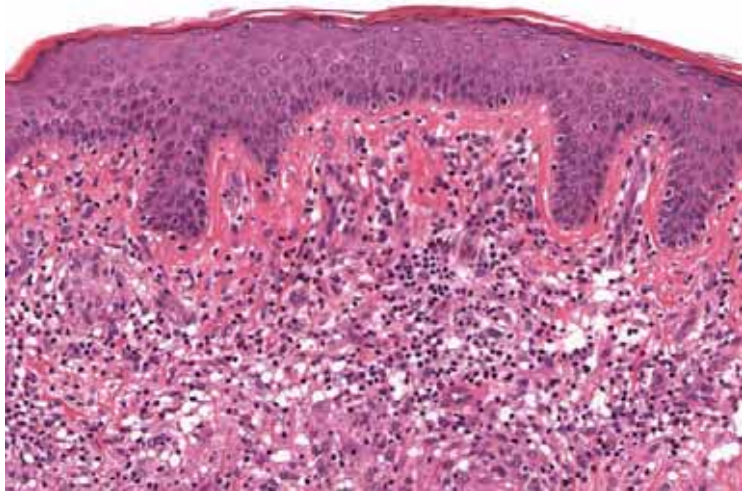
Kempf et al. Arch Dermatol 2008
Li et al. Am Acad Dermatol 2013

Second lymphoid neoplasias
Hodgkin lymphoma in 20-50%
of patients

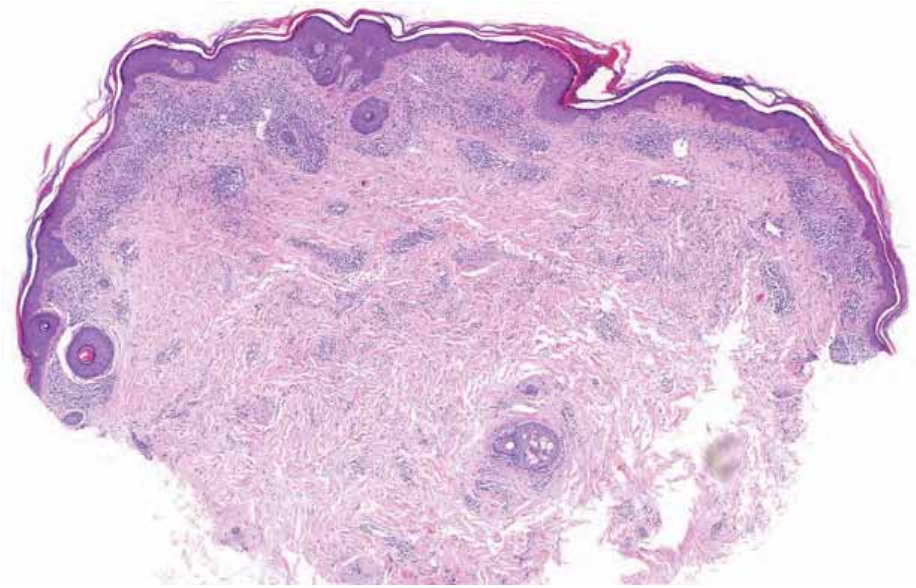
Van Haselen et al. 1998
Clarjis et al. 2003

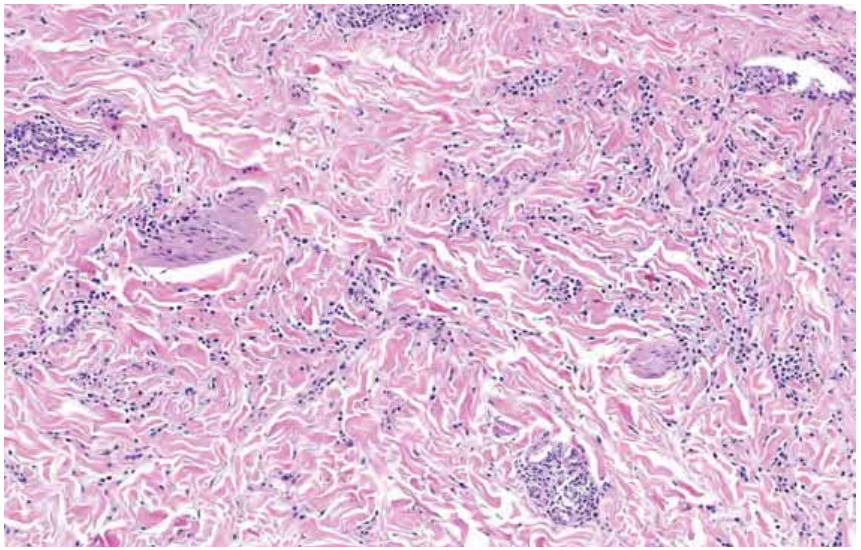


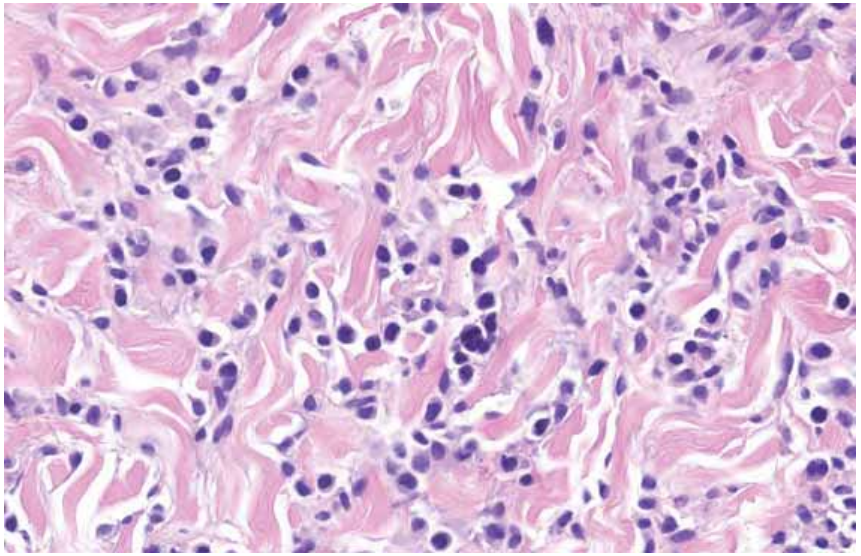




# Interstitial mycosis fungoides







Simulates interstitial GA, inflammatory morphea, and interstitial granulomatous dermatitis.

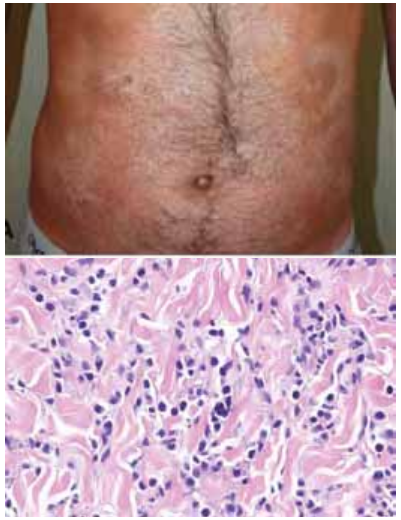
Frequently cytotoxic phenotype (50%)

In many cases a transient pattern in otherwise conventional MF

Clinically presenting with patches and/or plaques

Reggiani et al. Am J Surg Pathol 2016

# MF: Histiocyte-rich or granulomatous forms

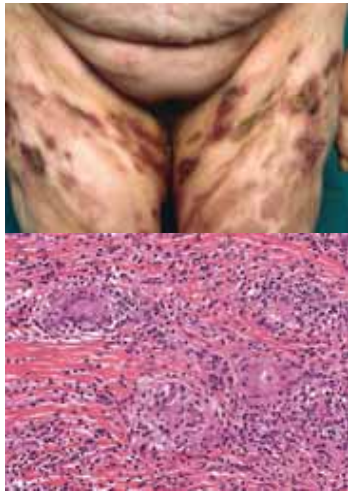


## Interstitial /histiocyte-rich MF

Patches

Interstitial lymphocytic histiocytic infiltrate

Prognosis as classic MF (5-y-SR: 90%)

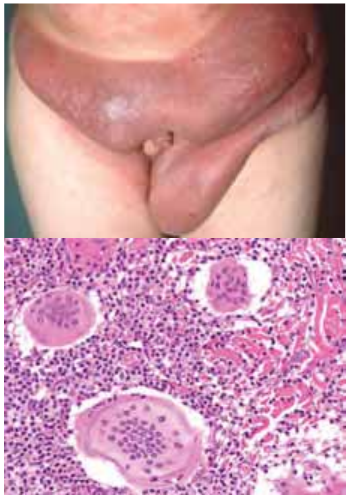


## Granulomatous MF

Hyperpigmented patches

Sarcoid/GA-like infiltrates

Prognosis (5-y-SR: 66%)



## Granulomatous slack skin

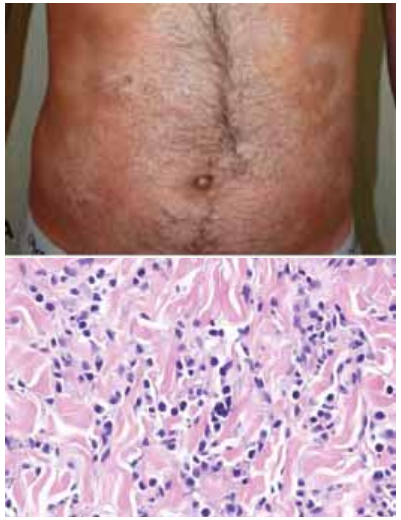
Bulky skin folds

Scattered multinucleated and histiocytic gaint cells

**Second lymphoid neoplasias**
Hodgkin lymphoma (20-50%)

Kempf et al. Arch Dermatol 2008
Li et al. Am Acad Dermatol 2013

# MF: Histiocyte-rich or granulomatous forms



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Patches

Interstitial lym
histiocytic infi

Prognosis as classic MF
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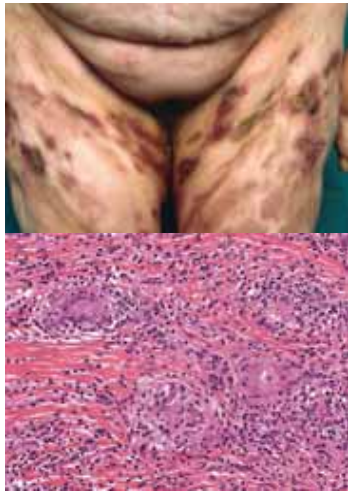

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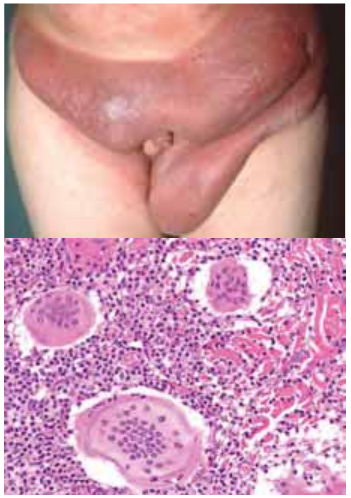
Hyperpigmented patches

e infiltrates

Prognosis (5-y-SR: 66%)



## Granulomatous slack skin

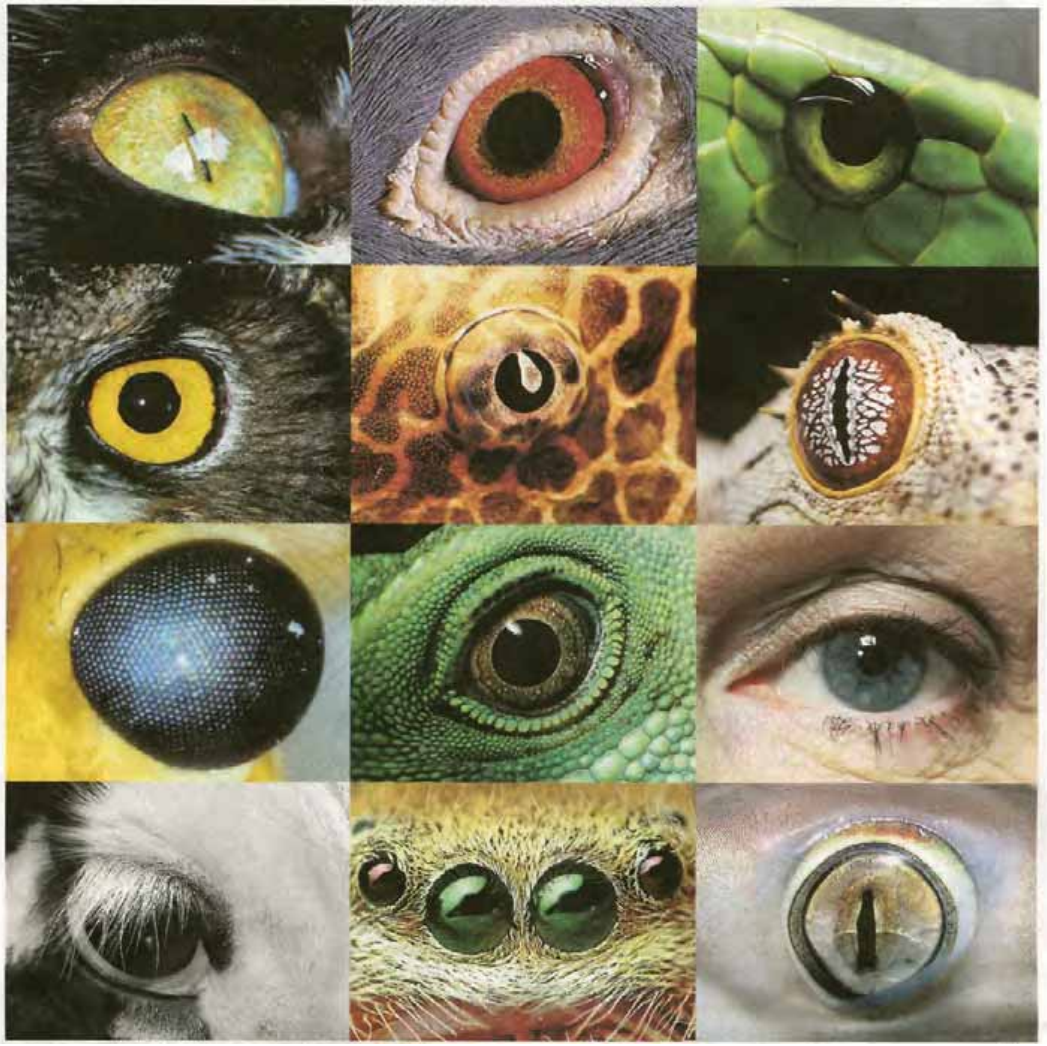
Bulky skin folds

Scattered multinucleated and
histiocytic gaint cells

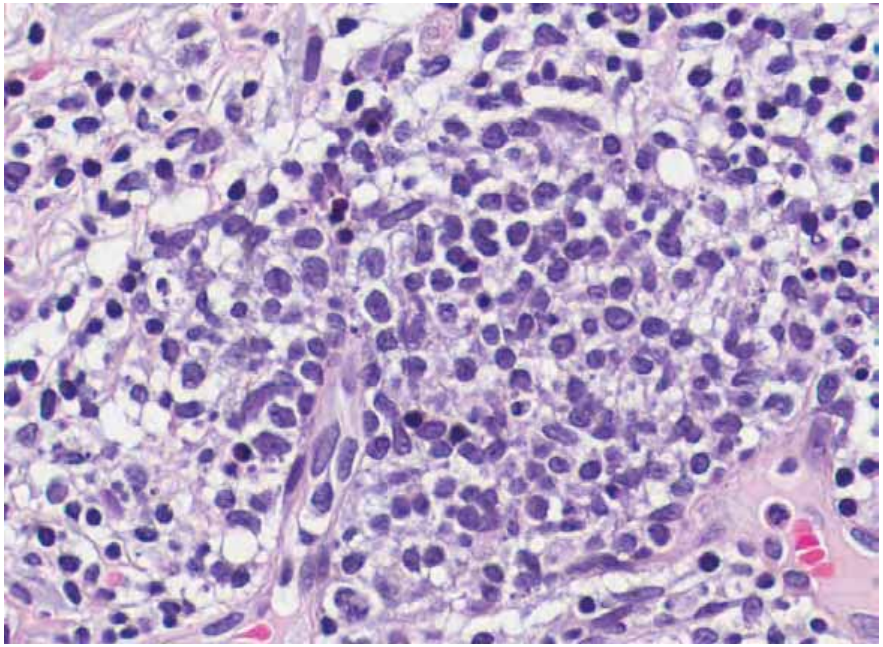
**Not distinct subtypes in WHO classification**

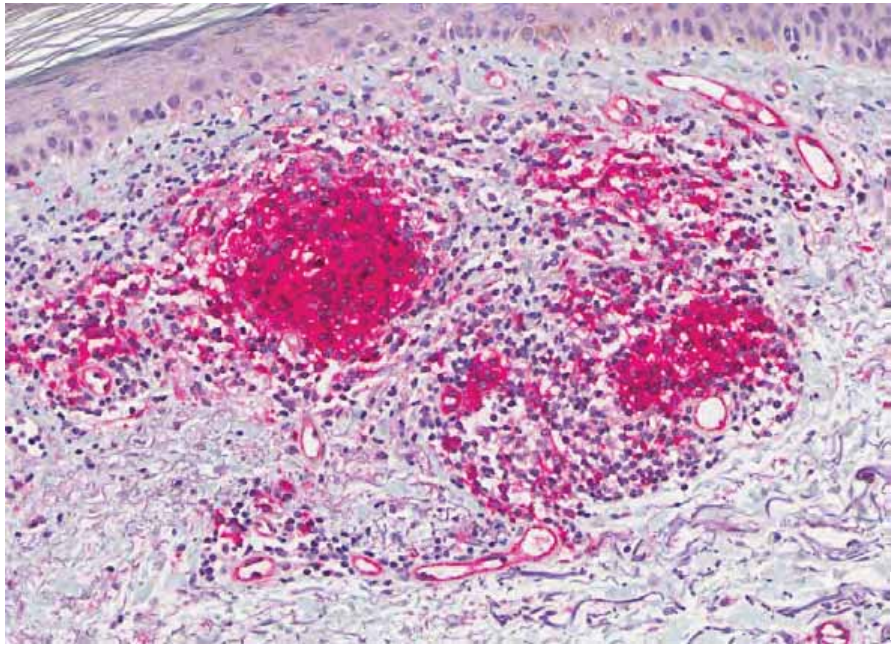
Second lymphoid neoplasias
Hodgkin lymphoma (20-50%)

Kempf et al. Arch Dermatol 2008
Li et al. Am Acad Dermatol 2013



# Plasmacytoid dendritic cells (PDC)





CD123

Monocytoid or plasmacytoid morphology

PDC in T-cell rich areas of lymphoid organs

CD123, CD2AP, BDCA-2 (CD303), TCF-4

Facchetti et al. Virchows Arch 2003
Marafitti et al. Blood 2008
Sukswai et al. Am J Surg Pathol 2019

# PDC - function

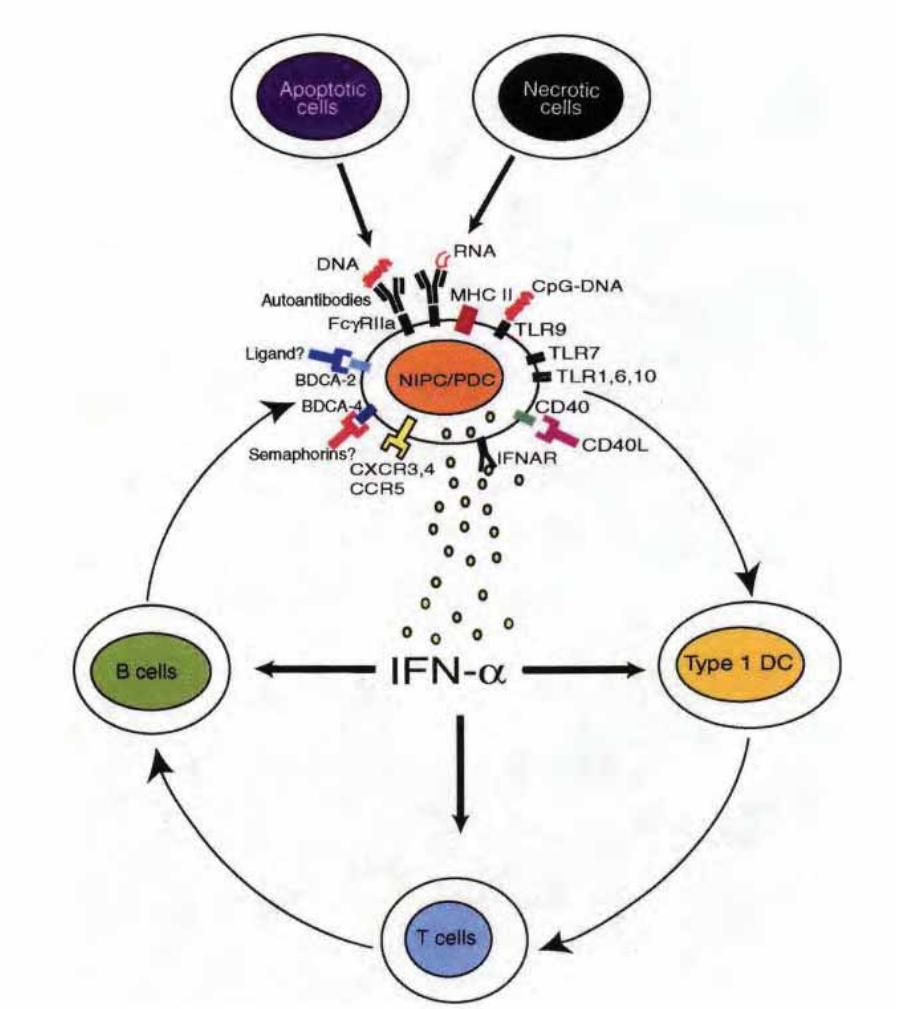
## Sensing nucleic acids in autoimmune diseases and viral infection

- Viral DNA/RNA
- Self DNA (high quantities)
- DNA-specific auto-antibodies
- Hypomethylated CpG islands
  (released from apoptotic keratinocytes)

# Plasmacytoid dendritic cells (PDC)

Sensing nucleic acids
in autoimmune diseases
and viral infection

Production of IFN alpha and beta
-> activation: NK cells, T and B-cells




from: Rönnblom et al. Autoimmunity 2003

# PDC in inflammatory skin diseases

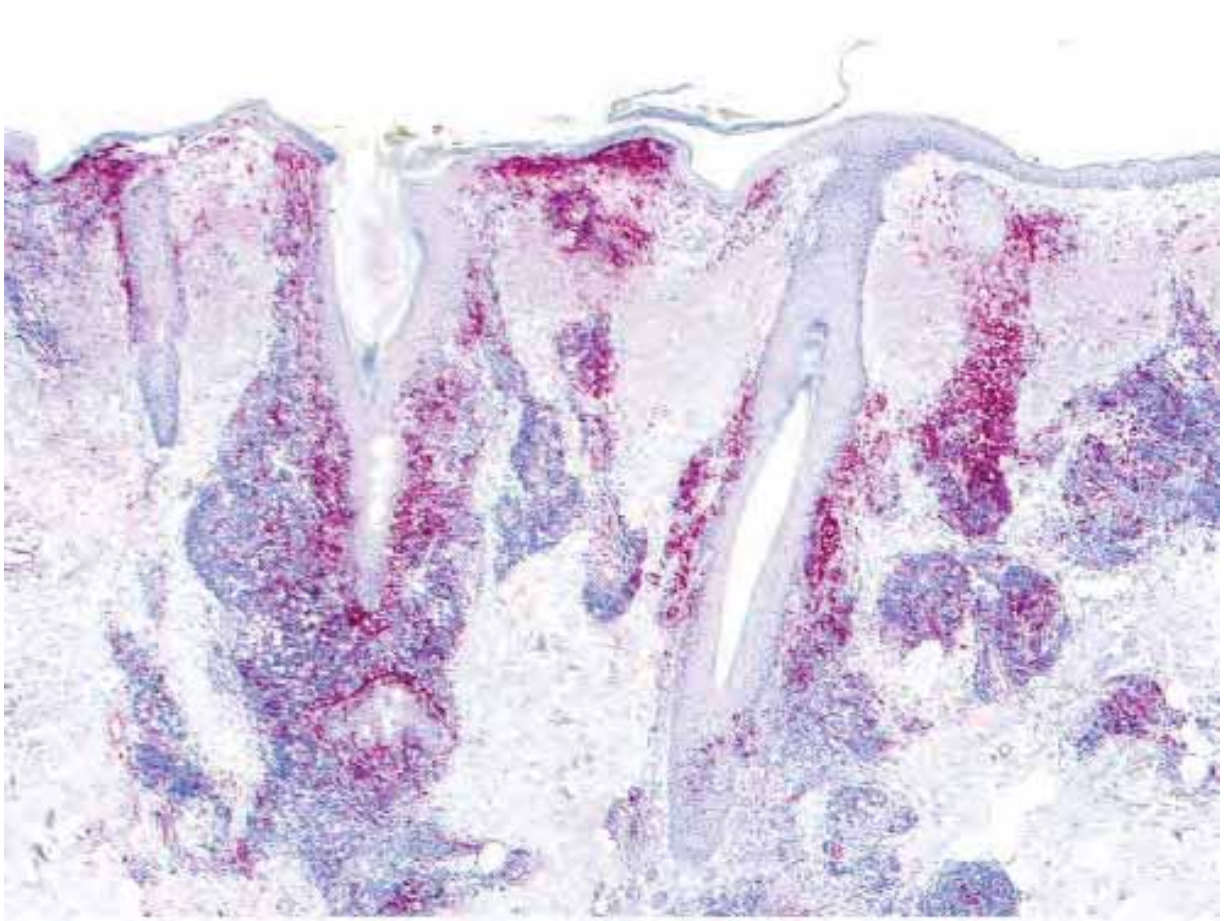
## Lupus erythematosus

Lymphocytic infiltration

Infectious diseases

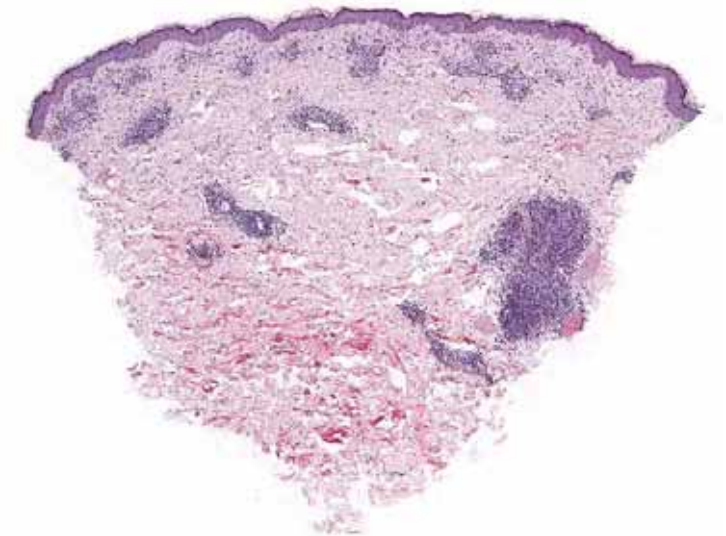
Facchetti et al. Virchows Arch 2003

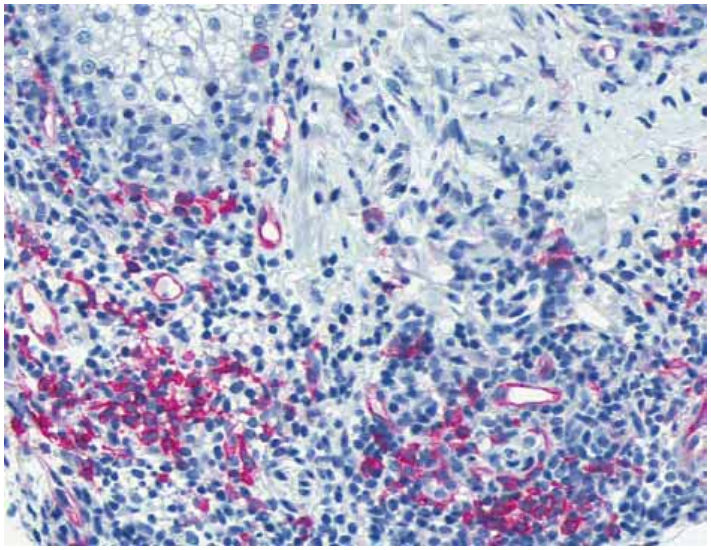
Tomasini et al. J Cutan Pathol 2010



CD123

63-year-old man with violaceous plaque on the left chest. Fatigue.





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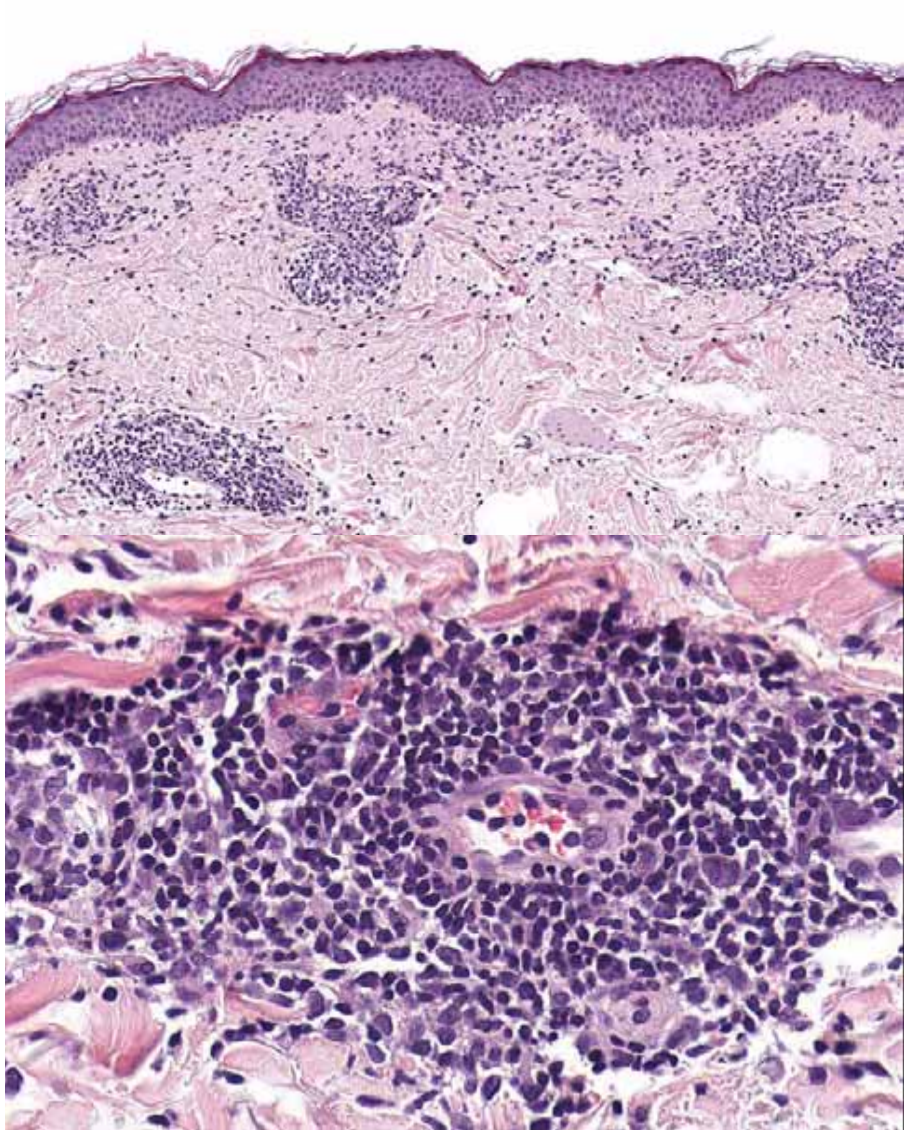
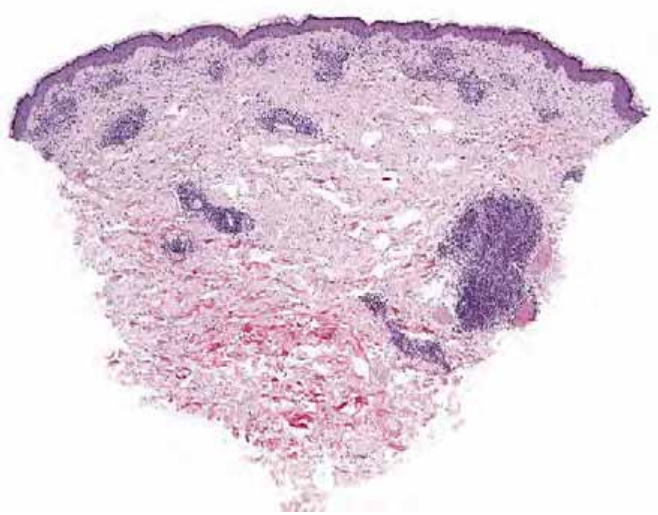
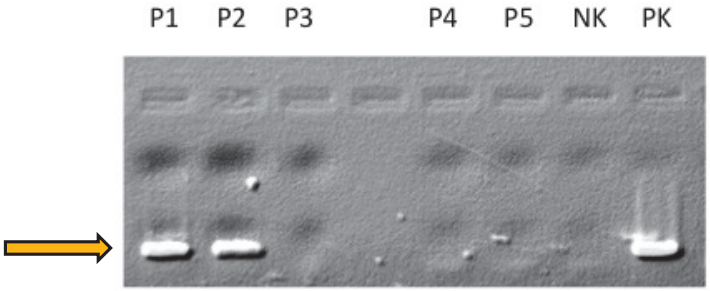
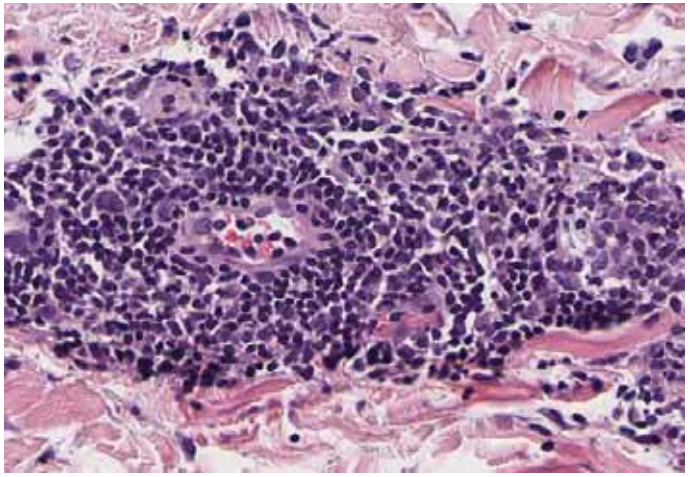


B09-361

# Herpes incognito





Detection of VZV DNA by nested PCR

Resolution of skin lesion and pain under treatment with valaciclovir (3x1 g per day for 7 days)

# Herpes incognito

No pathognomic epithelial changes of alpha herpesvirus infection (HSV, VZV)

Dense perivascular and sparse interstitial superficial and deep infiltrates of lymphocytes, sometimes assuming a patchy lichenoid pattern.

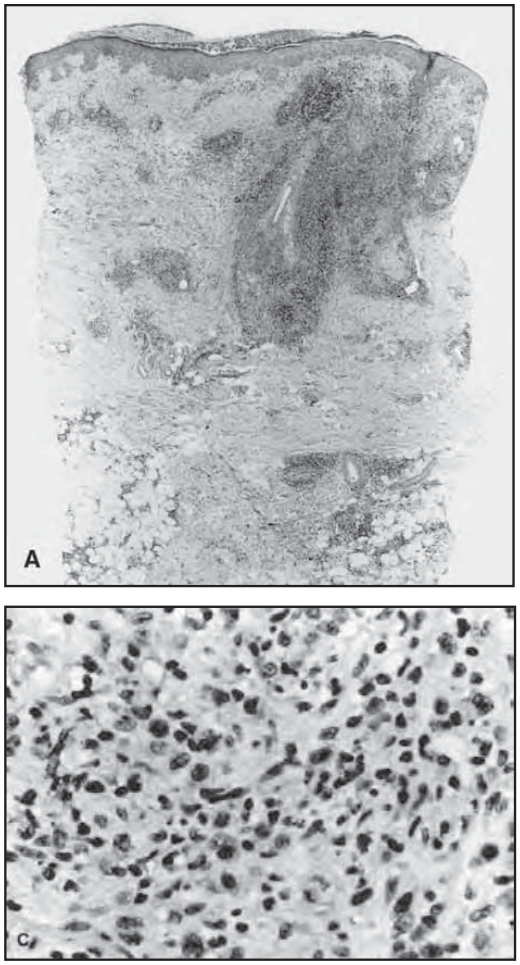
Infiltrates prominent in and around adnexal structures

Lymphocytes sometimes with large and polygonal nuclei.
Atypical lymphocytes were present in 32/45 cases.
Step section revealed diagnostic changes.

Resnik and DiLeonardo Am J Dermatopathol 2000
Boer et al. Am J Dermatopathol 2006

Diagnosis confirmed by PCR in 80% cases with non-specific histology.

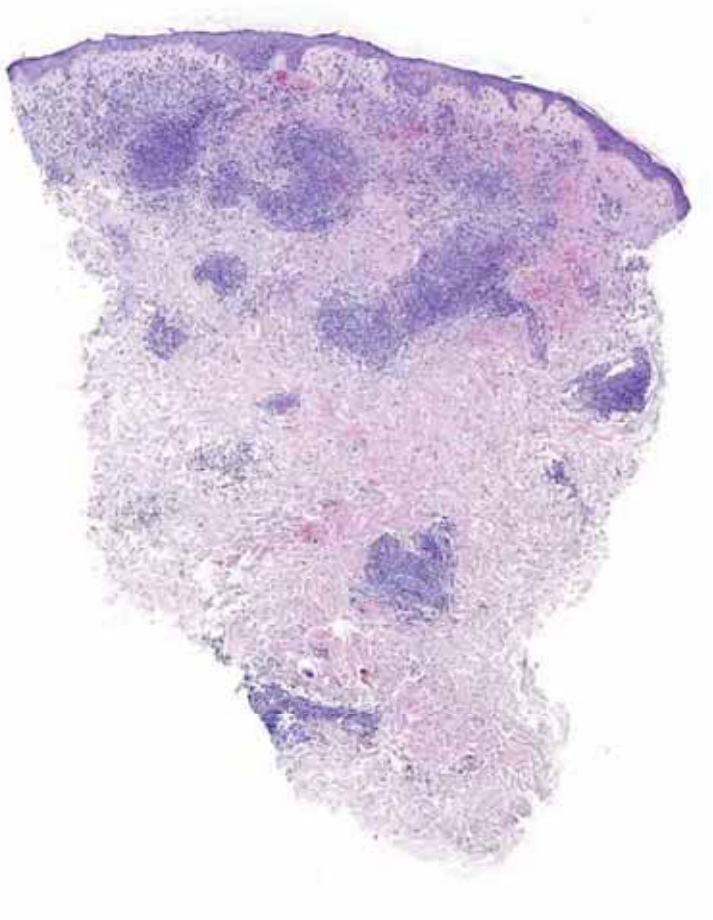
Jain et al. J Med Virol 2001
Kinonen et al. J Cutan Pathol 2012
Kempf et al. JDDG 2013

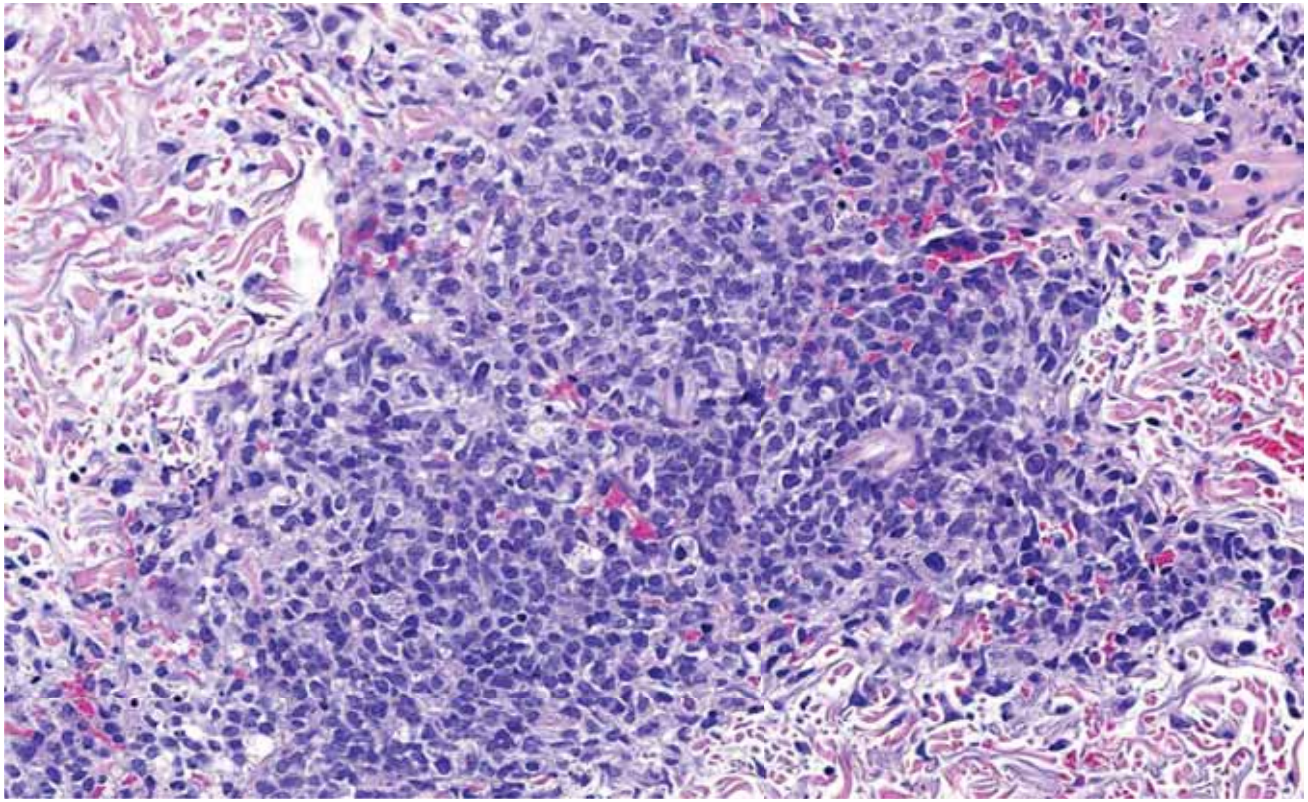



From: Resnik and DiLeonardo Am J Dermatopathol 2000

76-year-old man with AML and erythematous papules and small plaques on the chest.

B22-034742





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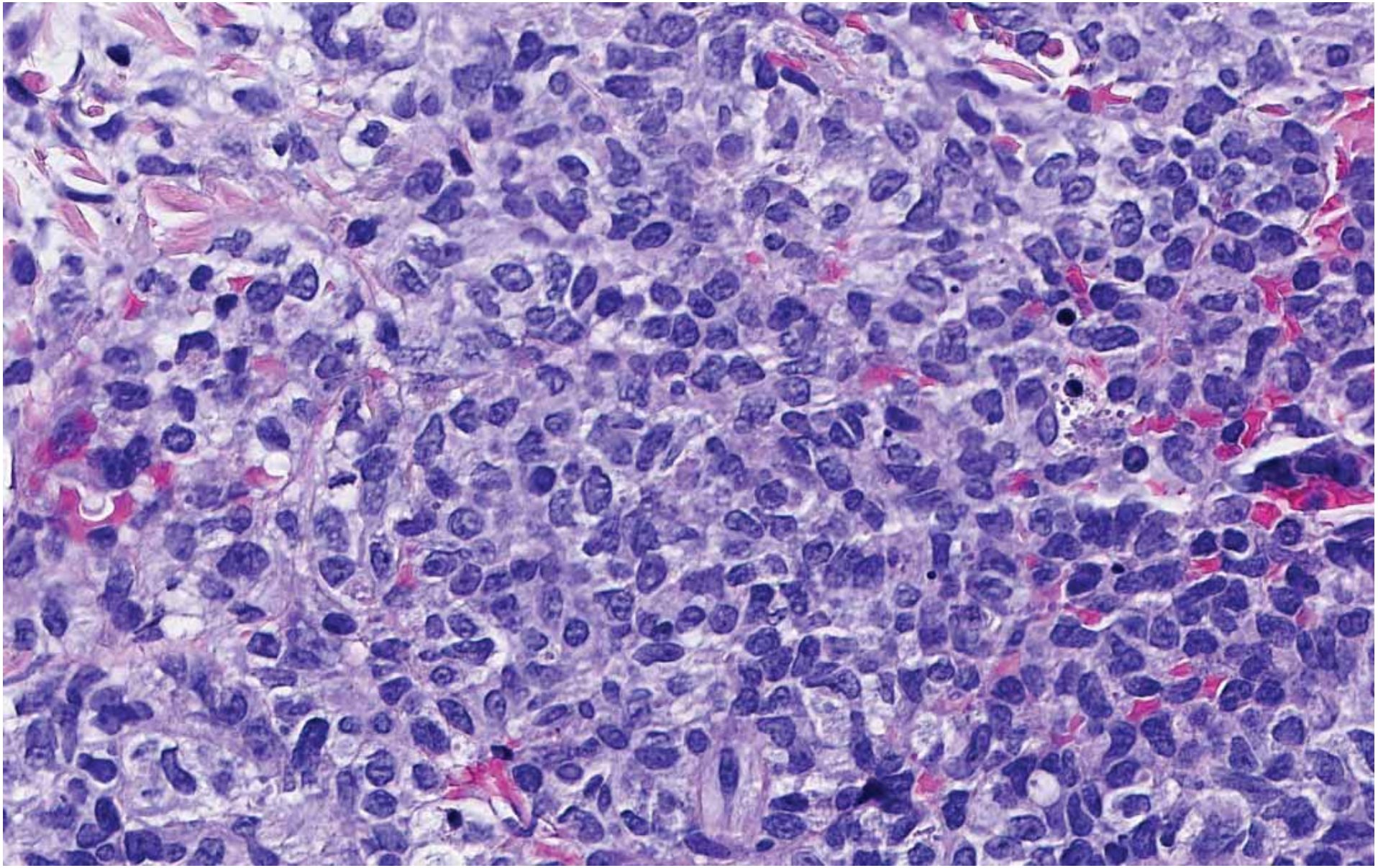

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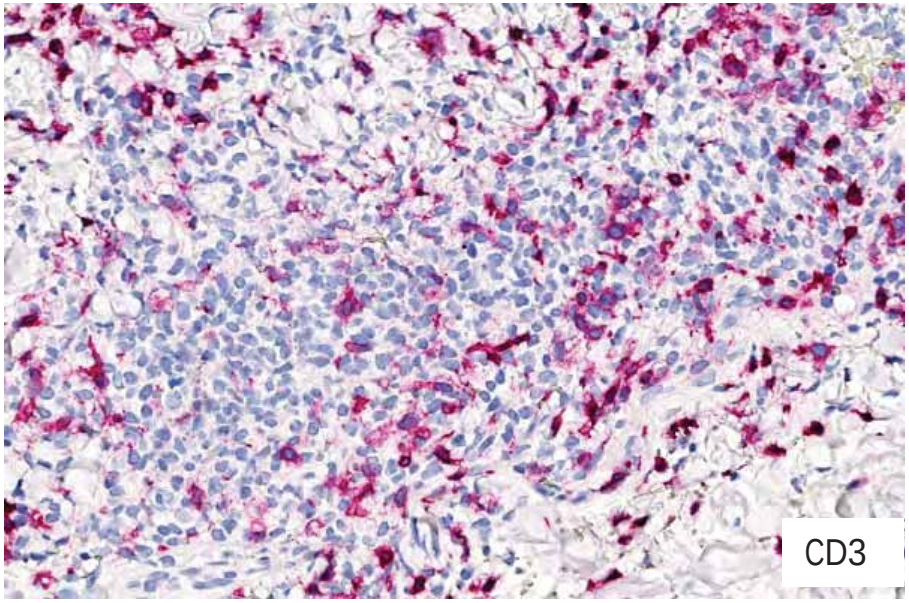


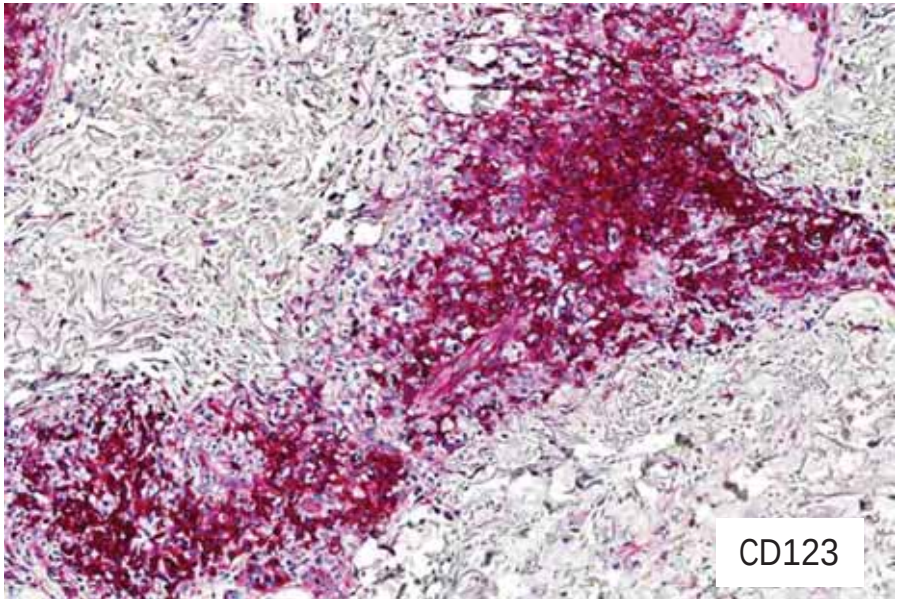


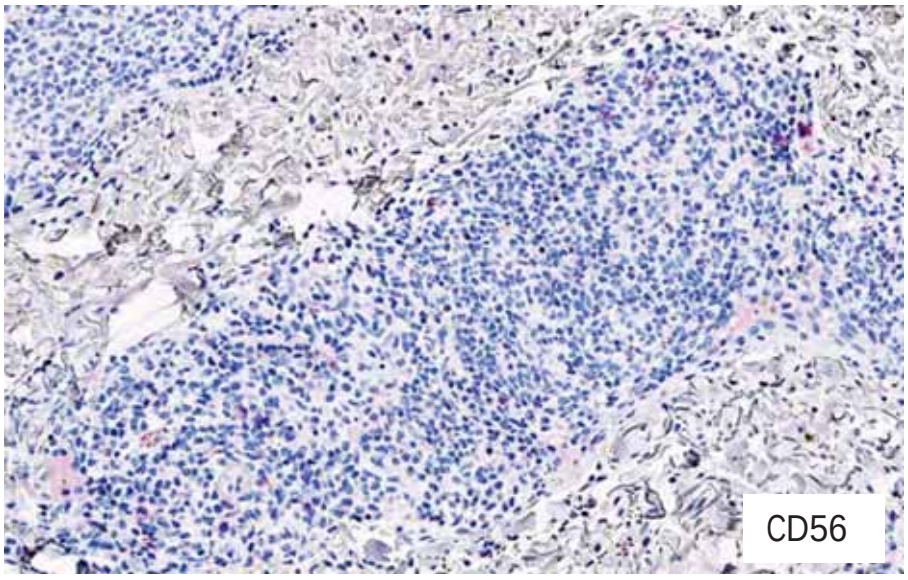


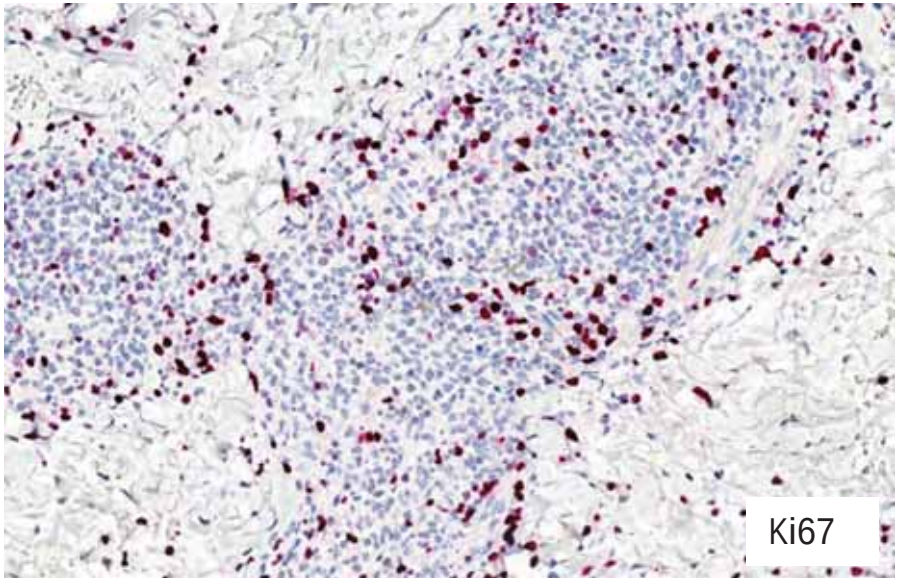


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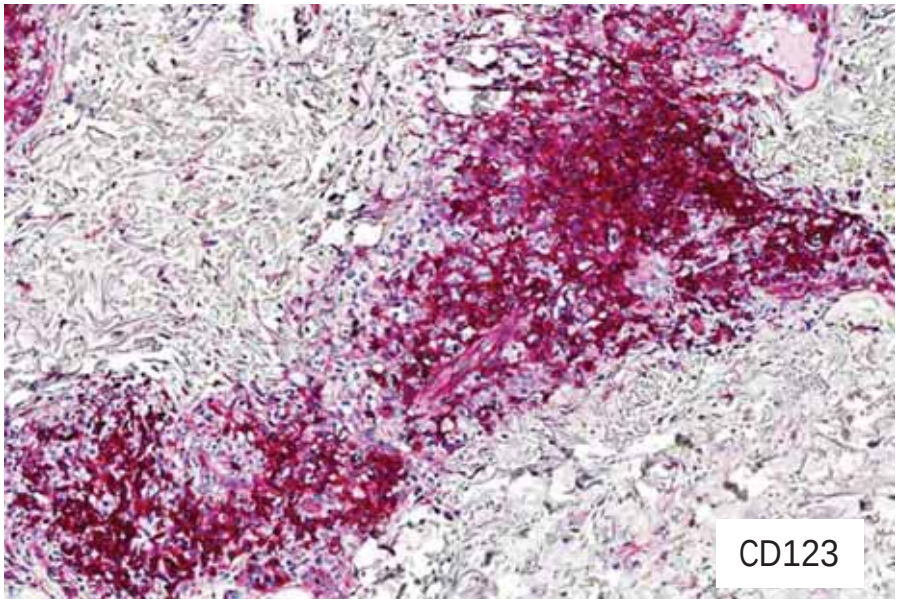
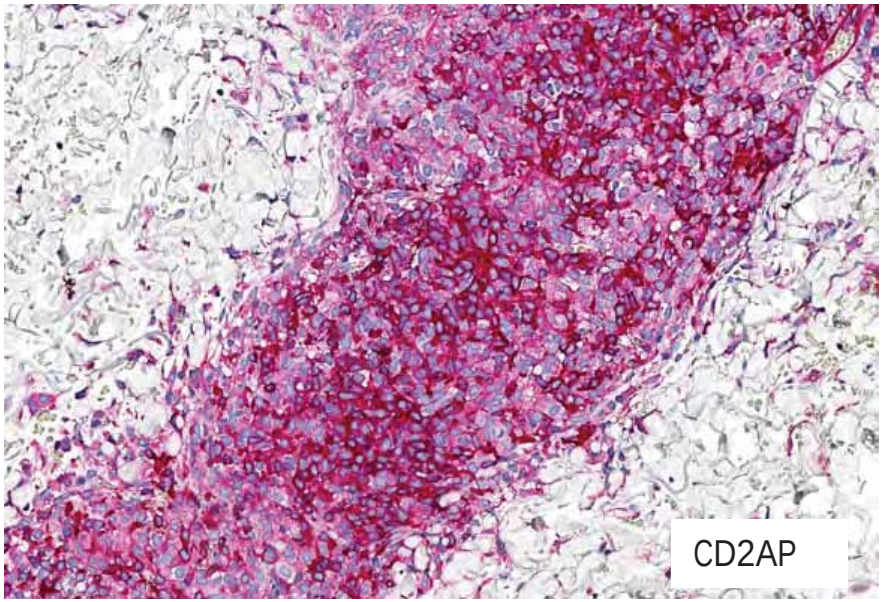


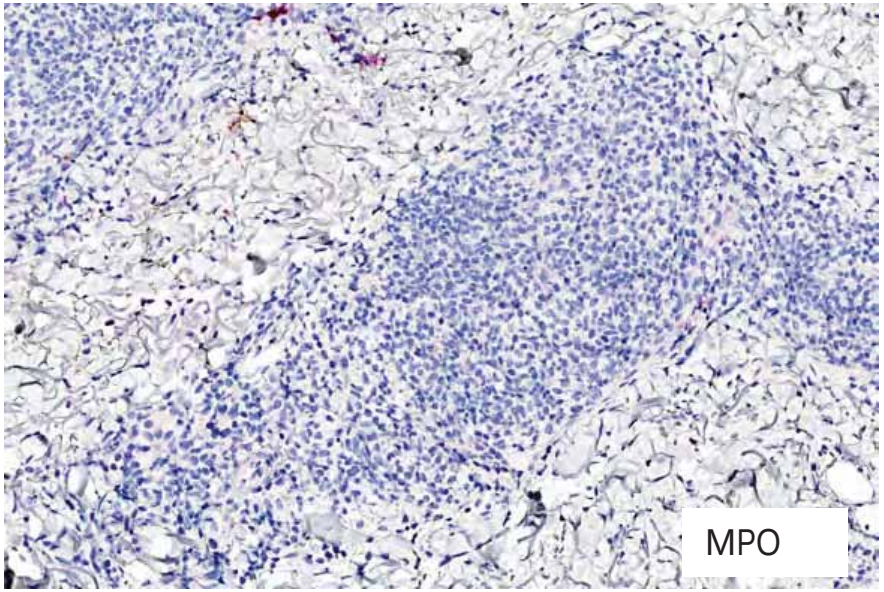




CD3+ CD4+ CD8- CD56-

CD123+ CD2AP+

MPO- CD33- CD117-

Ki67 low




B22-034742

# Differentialdiagnosis

Blastic plasmacytoid dendritic cell neoplasm (BPDCN)

Acute myelomonocytic leukemia with PDC phenotype

Mature proliferation of PDC associated with myeloid neoplasms

T/B-lymphoblastic leukemia/lymphoma

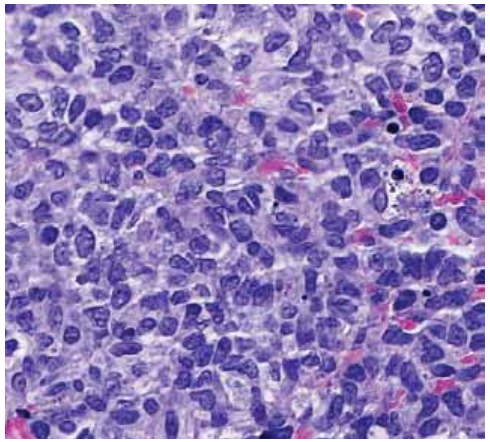
Diffuse large B-cell lymphoma

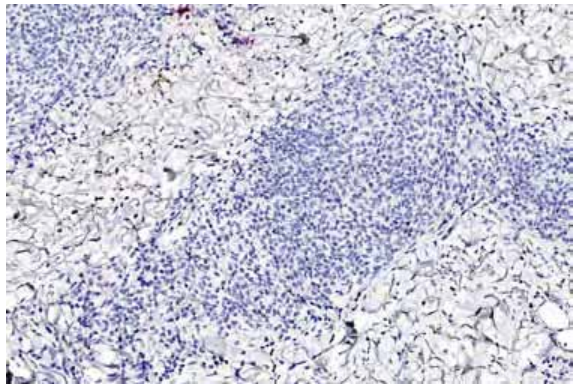
Mantle cell lymphoma

Extranodal NK/T-cell lymphoma

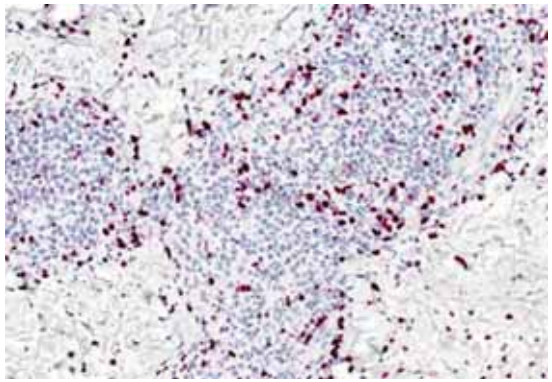
Merkel cell carcinoma

Ewing sarcoma



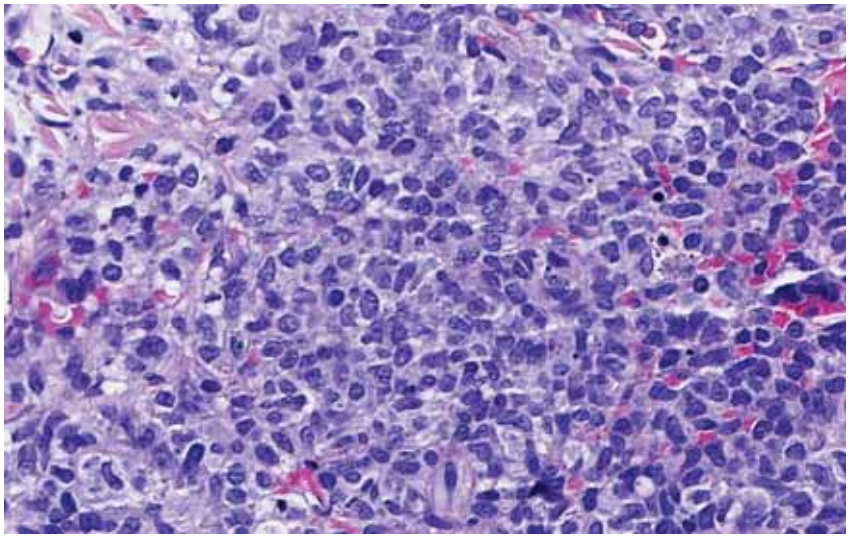


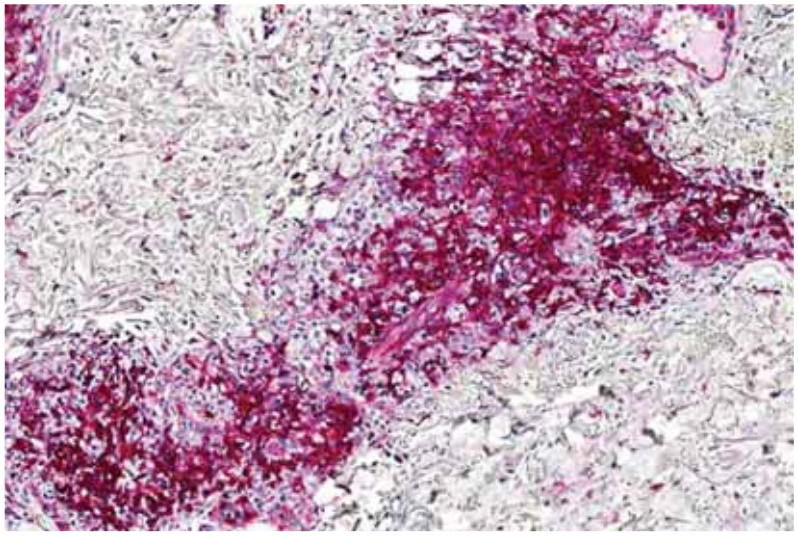
MPO



Ki67

76-year-old man with AML and erythematous papules and small plaques on the chest.





CD123

Mature PDC proliferation associated with myeloid neoplasms

*WHO 5th edition*

# Mature plasmacytoid dendritic cell proliferation associated with myeloid leukemias

Most commonly in acute or chronic myelomonocytic leukaemia
(approx. 5% of AML)

Skin: macules or pruritic papules
Bone marrow, lymph nodes (rarely)

Vitte F et al. Am J Surg Pathol 2012
Facchetti et al. Mod Pathol 2016

Indicator of poor prognosis, often heralds transformation to AML

Zalmaï et al. Haematologica 2021

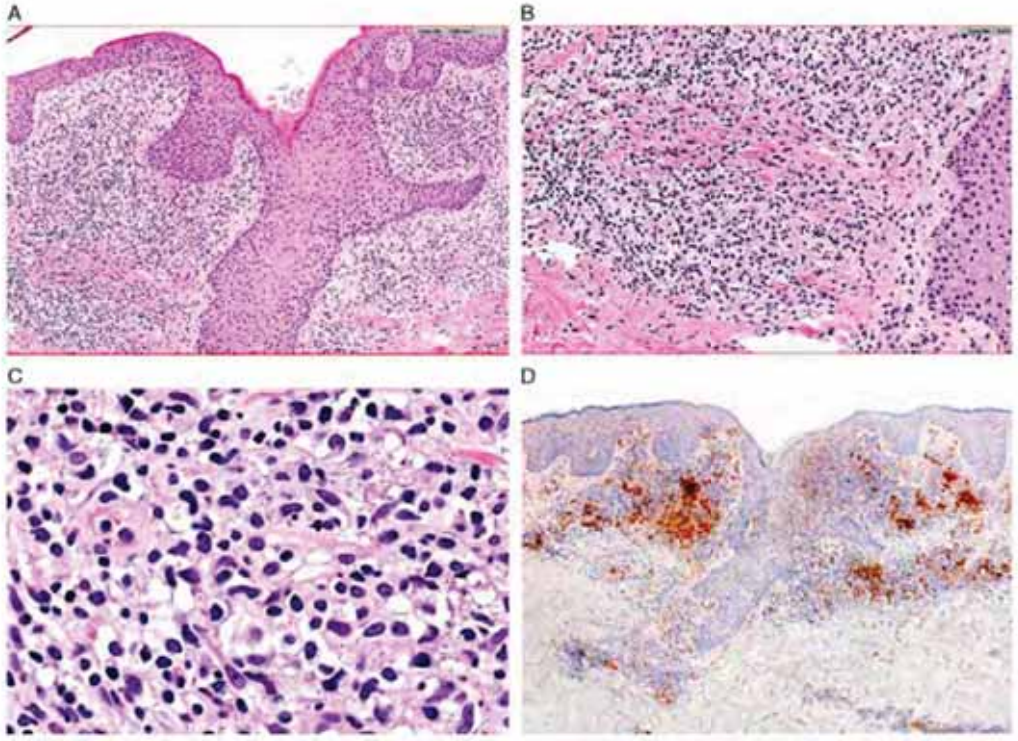
In WHO 5th edition included as separate entity:
Mature plasmacytoid dendritic cell proliferation associated with myeloid neoplasm

By courtesy Dr. L. Schärer

# Plasmacytoid Dendritic Cell Dermatosis Associated to Myeloproliferative/Myelodysplastic Neoplasms

*Salma Machan, MD, PhD,* Juan M. Alonso-Dominguez, MD, PhD,† F. Javier Sánchez Garcia, MD,‡ Rocio Nieves Salgado, MD, PhD,† Carlos Soto, MD,† Yolanda Castro, MD,§ Raquel Pajares, Tech,§ Rebeca Manso, PhD,§ Carlos Santonja, MD, PhD,§ Cristina Serrano del Castillo, MD, PhD,† Miguel A. Piris, MD, PhD,‡ Luis Requena, MD, PhD,* and Socorro M. Rodriguez Pinilla, MD, PhD‡*






(*Am J Surg Pathol* 2022;46:1623–1632)

# Mature PDC proliferation associated with myeloid neoplasm - phenotype

CD4+ CD8- CD56-

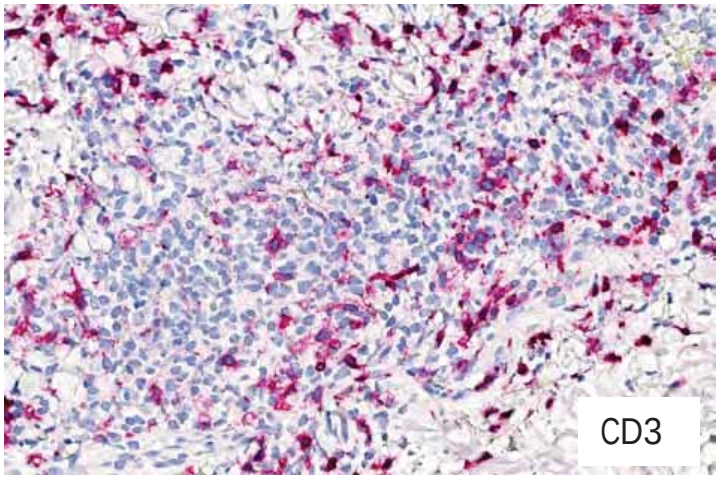
CD123+ CD2AP+

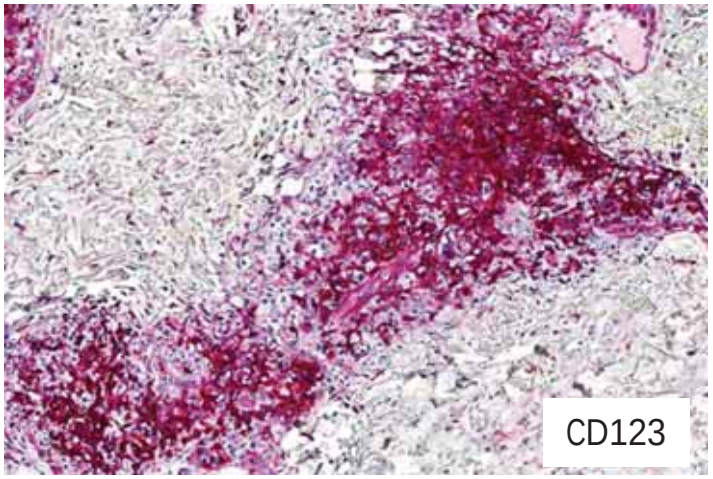
TCL-1- TCF-4+

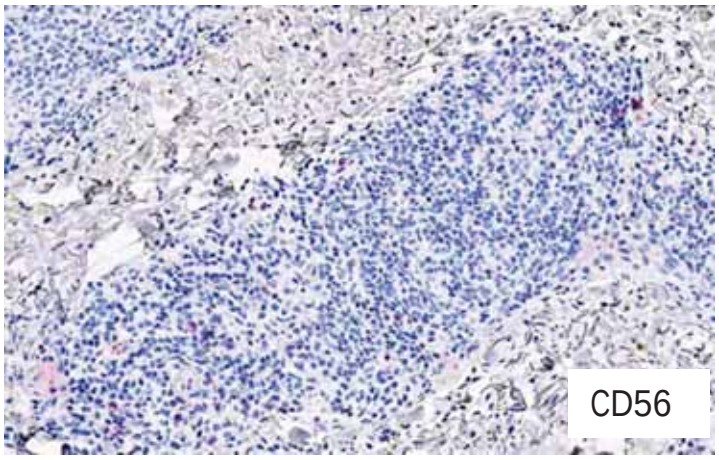
MPO- CD33- CD117-

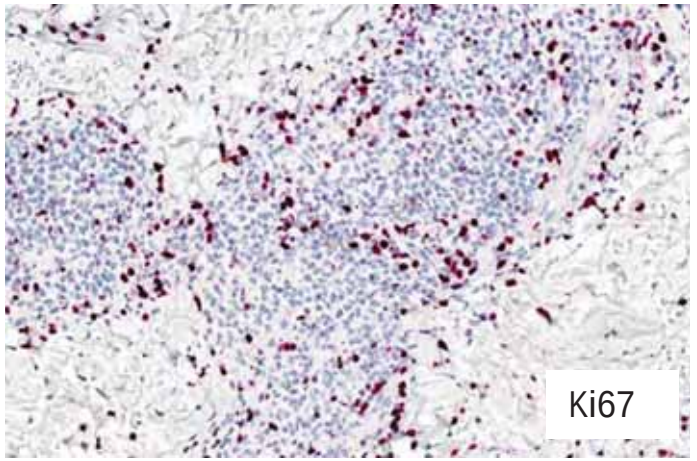
Bcl-2+ (30%)

Ki67 low (5-10%)



# Mature PDC proliferation associated with myeloid neoplasm

Association with myeloid leukemia: CMML > AML

Association with RUNX1 mutation

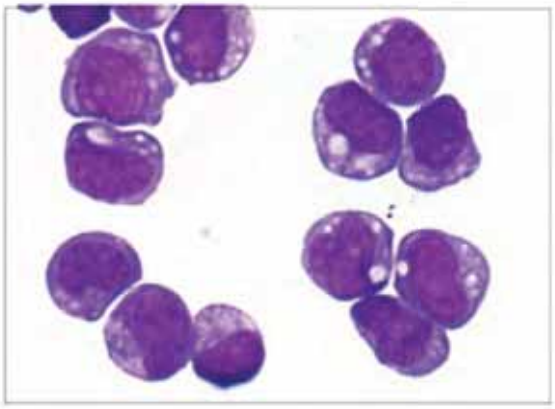
PDC clonally related and originate from to leukemic AML blasts.

Simon et al. Blood 2020

Xiao et al. Blood. 2021

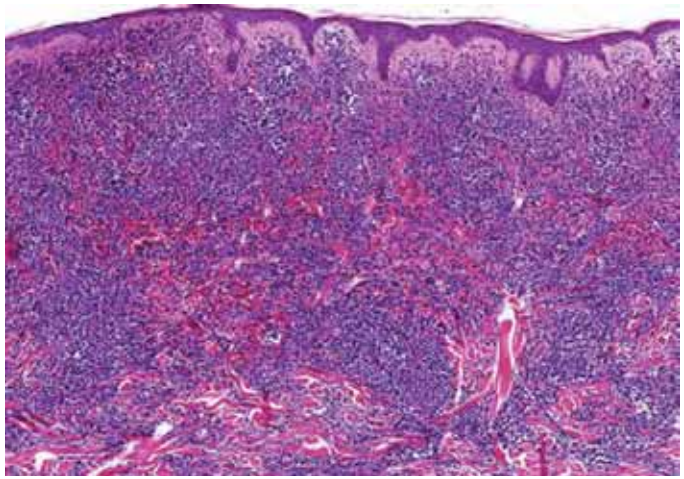
Leukemic blasts (AML)

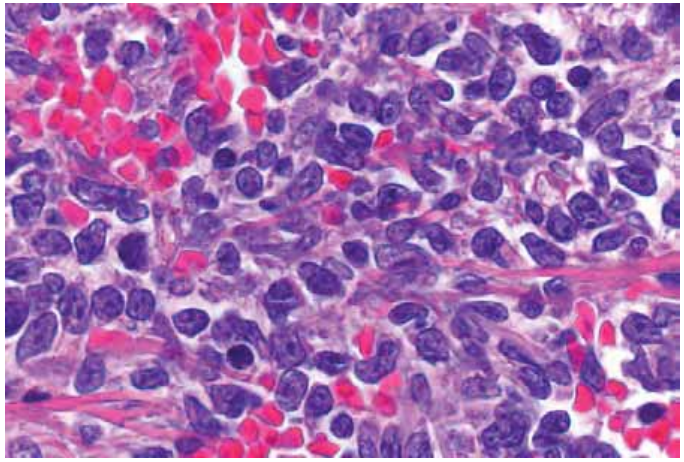
PDC

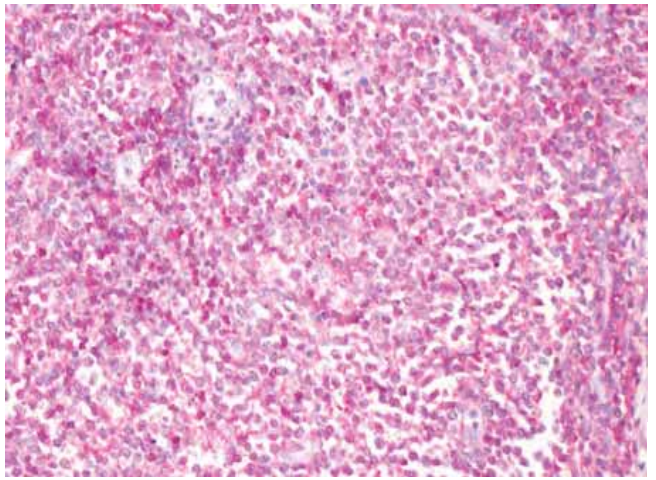


*Flow-sorted leukemic blasts and pDCs from pDC-AML. Giemsa stain (from Xiao et al. Blood 2021)*

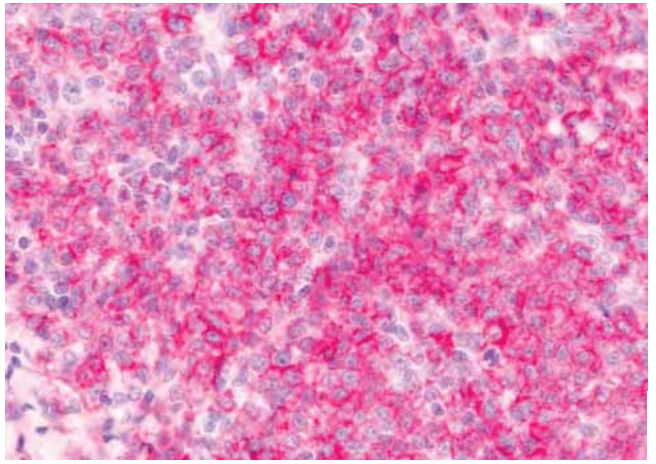
# Blastic PDC neoplasm







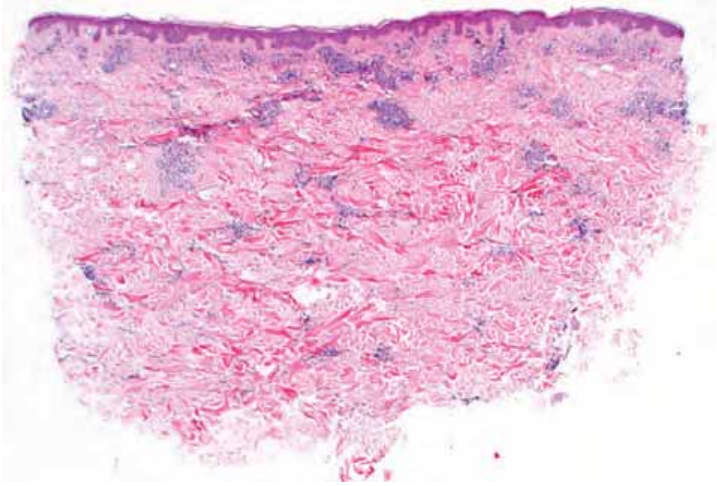
CD4

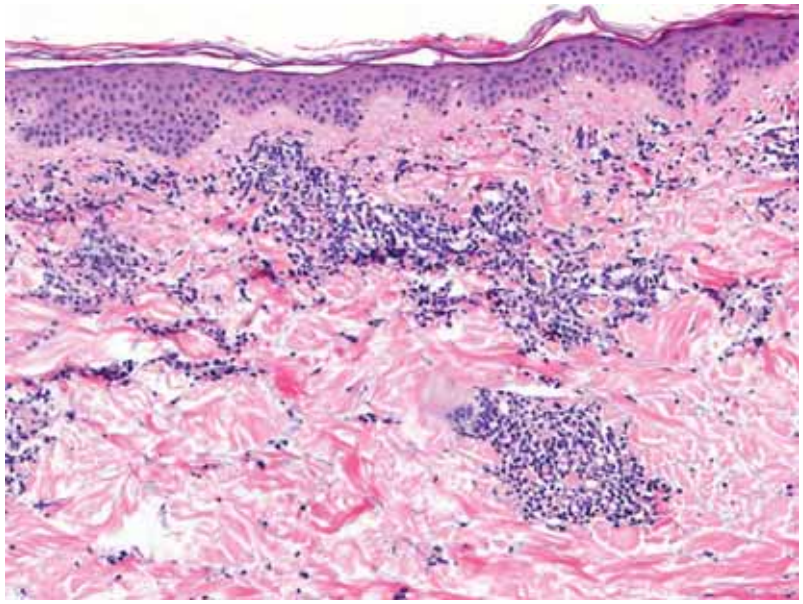


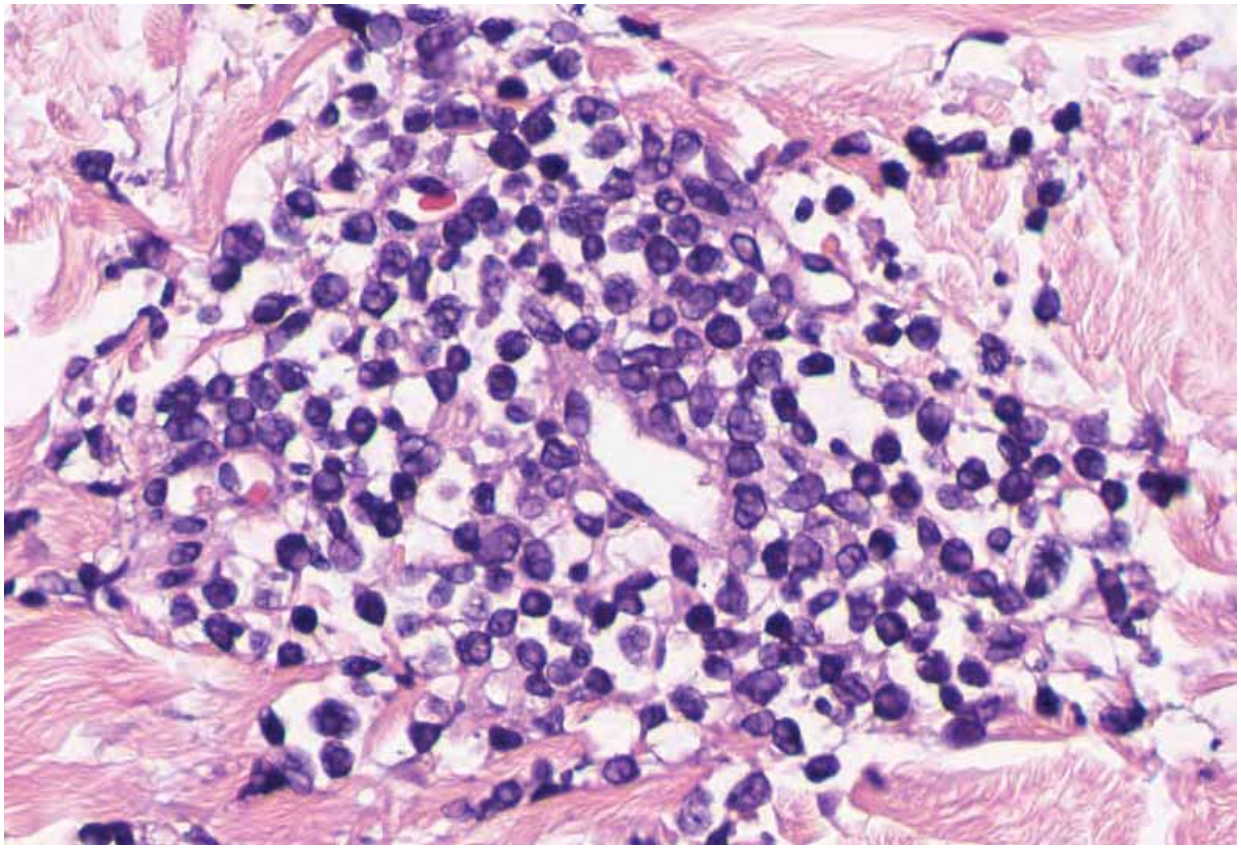
CD56

CD4+, CD56 +CD123+, BDCA2 + (CD303), CD2AP, TCL-1 +
MPO -, lysozyme -, CD34 –

60-year-old man - since 4 weeks slightly infiltrated plaques on the trunk.





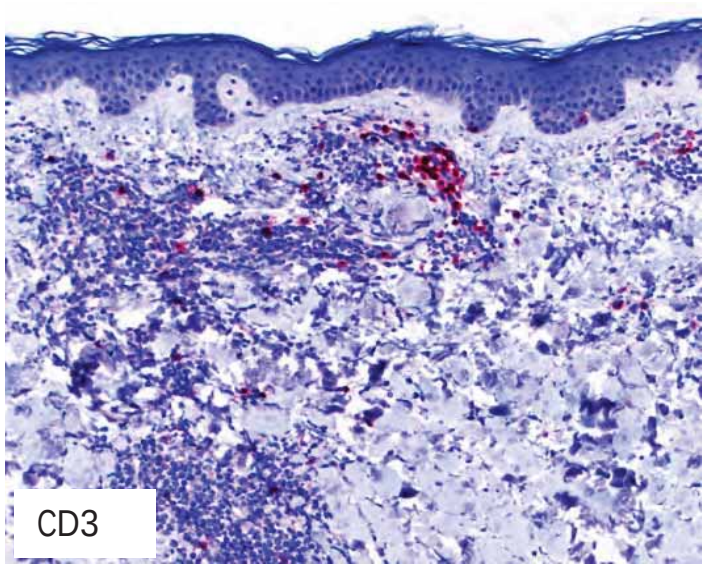


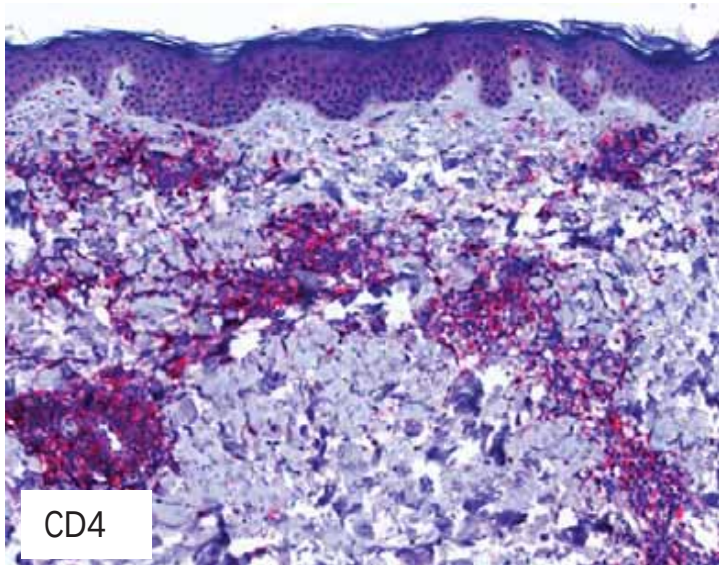
60-year-old man - since 4 weeks slightly infiltrated contusiform plaques on the trunk.

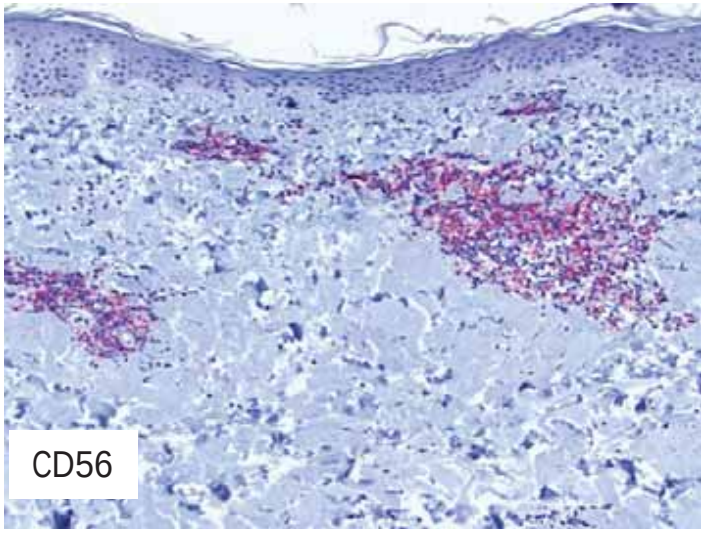
CD3- CD4+ CD8- CD30-
CD20- CD79a-

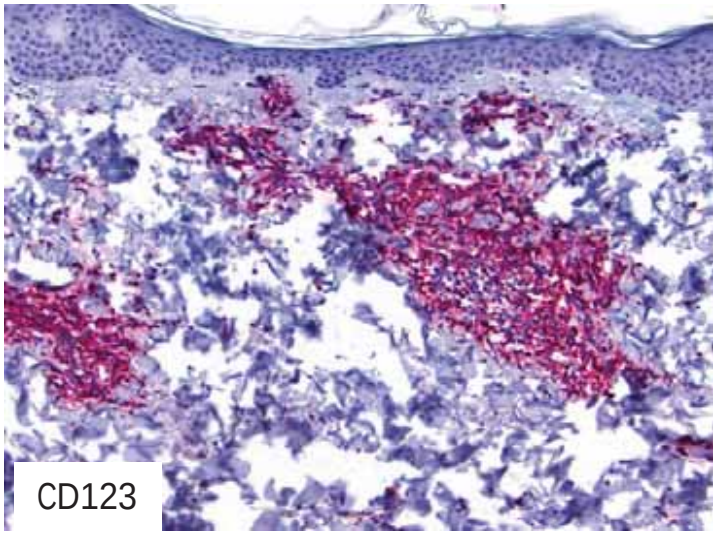
CD4+ CD56+
CD123+ TCL-1+ TCF-4 +

MPO- CD68-
CD117-



# Cutaneous Infiltrates of Acute Myelogenous Leukemia Simulating Inflammatory Dermatoses

*Marcela Martínez-Escanamé, MD,* Daniel Zuriel, MD,*† Shang-Ian Tee, MRCP,*‡ Isabella Fried, MD,* Cesare Massone, MD,* and Lorenzo Cerroni, MD**

**Abstract:** Some cases of specific cutaneous manifestations of acute myelogenous leukemia (AML) may mimic inflammatory dermatoses both clinically and histopathologically, presenting with an inconspicuous maculopapular eruption and with only sparse dermal infiltrates. The authors studied the histopathological and immunohistochemical features of 17 biopsies from 16 patients (11 men and 5 women, age range 15-85 years) presenting with minimal skin infiltrates as the first manifestation of AML or as first sign of recurrence after complete remission of the disease. In all cases, the diagnosis of leukemia has been confirmed by bone marrow examination. Two of these cases had been sent to one of us for second expert consultation. Patients presented with generalized, exanthematic maculopapular eruptions, sometimes with a hemorrhagic note, that were mostly interpreted clinically as drug reactions. Histopathologically, the lesions showed sparse, superficial, and mid-dermal infiltrates with minimal perivascular and periadnexal accentuation. Infiltrating cells consisted mostly of neoplastic monocytoid elements with only few reactive lymphocytes and histiocytes. Immunohistochemical stainings revealed in the majority of cases positivity for CD68 (14 of 16 patients), naphthol chloroacetate esterase (NaSDCl) (7 of 10 patients), and myeloperoxidase (6 of 9 patients). Other markers tested were positive only in a minority of cases. These cases represent a pitfall both in the clinical and in the histopathological diagnosis of cutaneous AML. Accurate morphologic and phenotypic correlation together with a high index of suspicion allows a precise diagnosis in these unconventional cases.

**Key Words:** acute myelogenous leukemia, CD68, inflammatory dermatoses

(*Am J Dermatopathol* 2012;0:1–6)

myelogenous cells have been observed in 11.6% of cases in a recent study.[7] Accurate identification of these cases is important for planning management, especially when skin lesions precede the onset of leukemia or when they represent the first sign of relapse after complete remission (CR).[8,9] Cases with minimal infiltrates may be mistaken for inflammatory dermatoses and represent a pitfall in the histopathological diagnosis of cutaneous manifestations of AML.

We studied histopathological and immunohistochemical features of specific cutaneous manifestations of AML with inconspicuous infiltrates, to identify diagnostic criteria in these difficult cases.

## MATERIALS AND METHODS

The study has been conducted at the Research Unit Dermatopathology, Department of Dermatology, Medical University of Graz, Austria, and has been approved by the Ethic Committee of the University. Files were searched for skin specimens with diagnosis of cutaneous manifestations of AML from 1972 to June 2011. Cases presenting with histopathological features characterized by sparse infiltrates resembling inflammatory dermatoses were included in the study. In all cases, the diagnosis of leukemia had been confirmed by bone marrow examination. Cases characterized histopathologically by "conventional" nodular/diffuse infiltrates were excluded from the study. From a total of 108 cases of specific cutaneous manifestations of AML, 16 met the criteria and were included in the study. Two of these cases (cases 5 and 13) had been sent to L.C. for second expert

CD4+ CD56+ coexpression (20-40%), CD123+

Myeloperoxidase (MPO)+ (cytoplasmic granulation)

CD13+, CD33+, CD34+ (immature forms)

CD43+, CD68+

AML: TCL-1 - (83%) vs. TCL-1 + (90%) in BPDCN

Petrella et al. Am J Clin Pathol 2004


**FIGURE 1.** Patient 2: (A) generalized hemorrhagic papules; (B) detail of clinical lesions. The provided clinical diagnosis was hemorrhagic drug eruption.

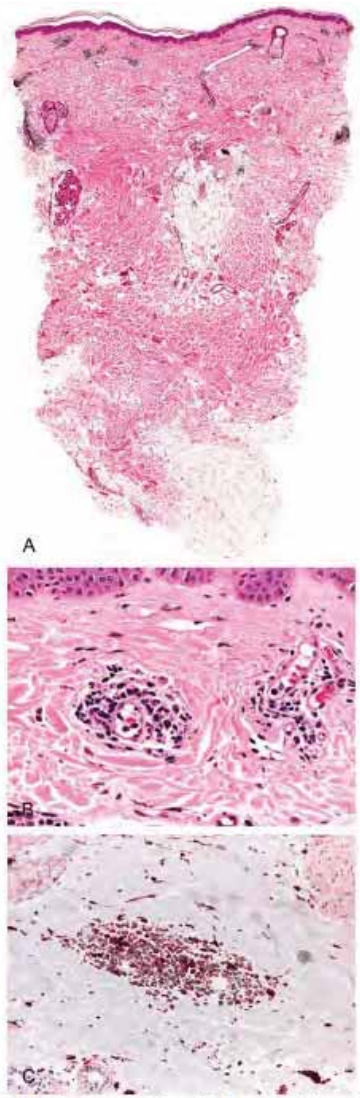



**FIGURE 4.** Patient 16: (A) Superficial and mid-dermal sparse perivascular infiltrates; (B) perivascular cells with monocytoid appearance; (C) neoplastic cells positive for CD68.

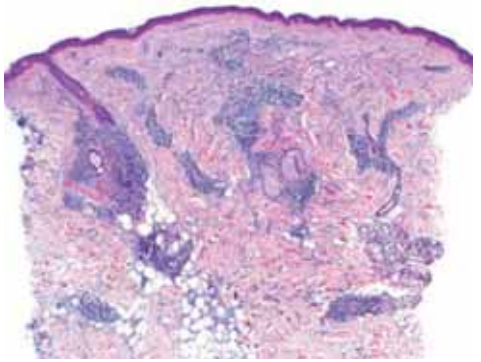
# PDC clusters - differentialdagnosis

*Lupus erythematosus*

Lesions in UV-exposed areas

Sleeve-like lymphocytic infiltrates, mucin

Smaller PDC clusters (CD56-)



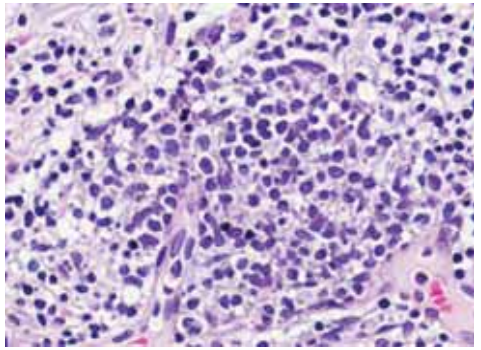
*Mature PDC proliferations in myeloid leukemia*

Pruritic skin lesions (esp. on trunk)

PDC nodules and lymphocytes

CD56-, low proliferation rate

Underlying myeloid leukemia (CMML, AML)

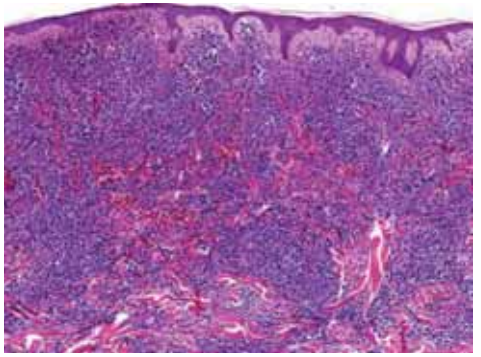


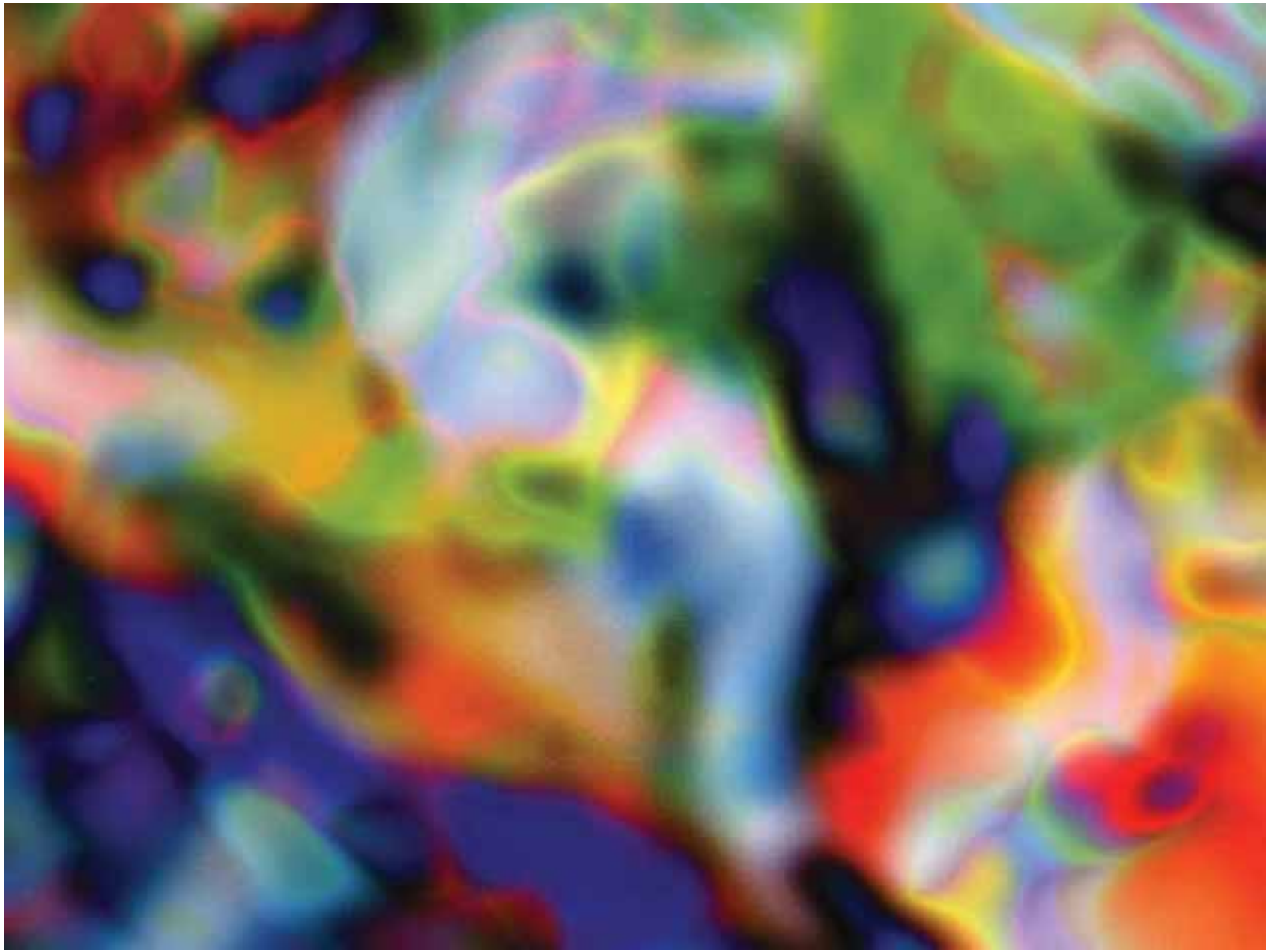
*Blastic PDC neoplasm (BPDCN)*

Contusiform skin lesions

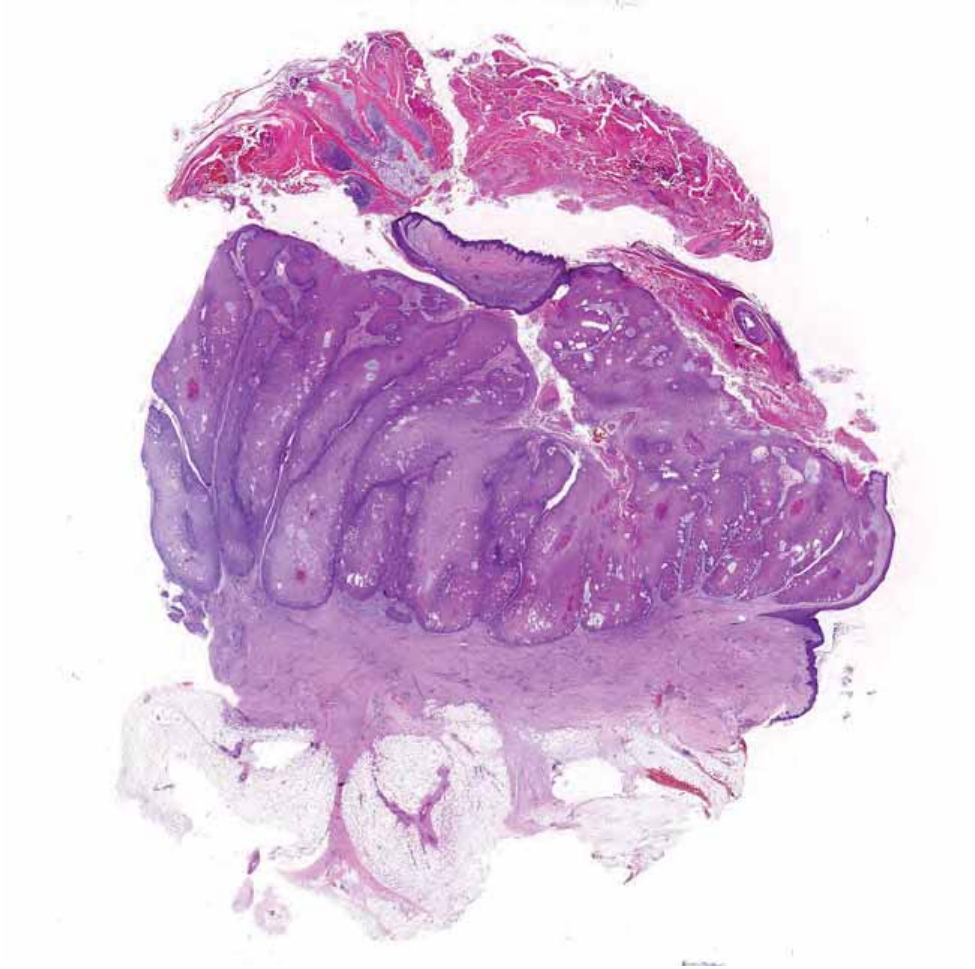
Diffuse "pure" PDC infiltrates (CD56+, Ki67 high)

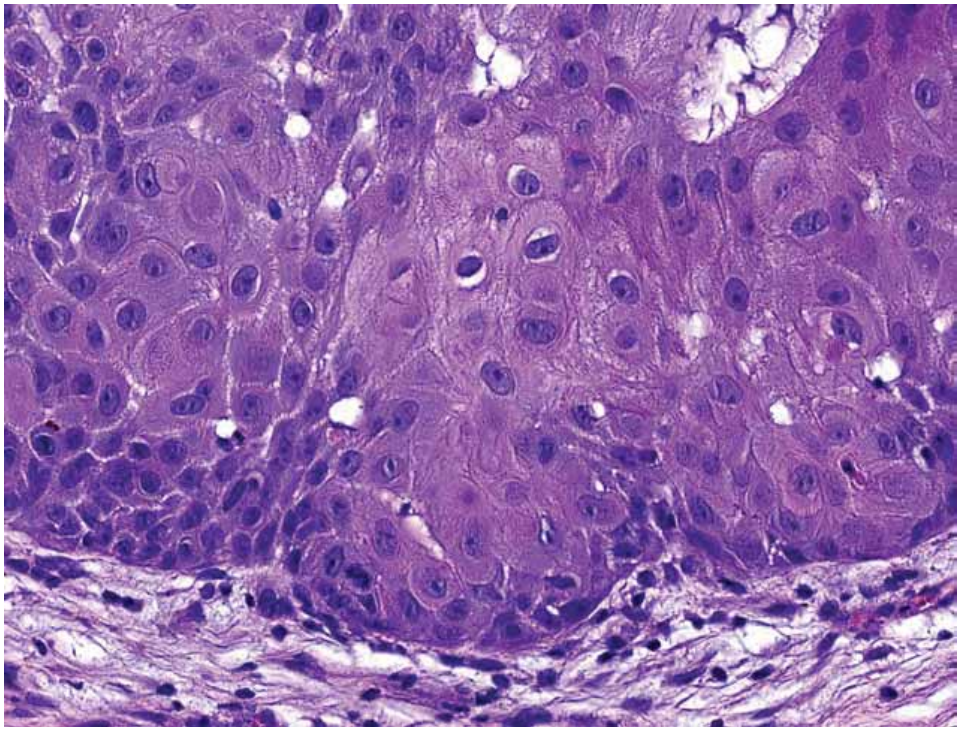
Leukemic phase (70%)





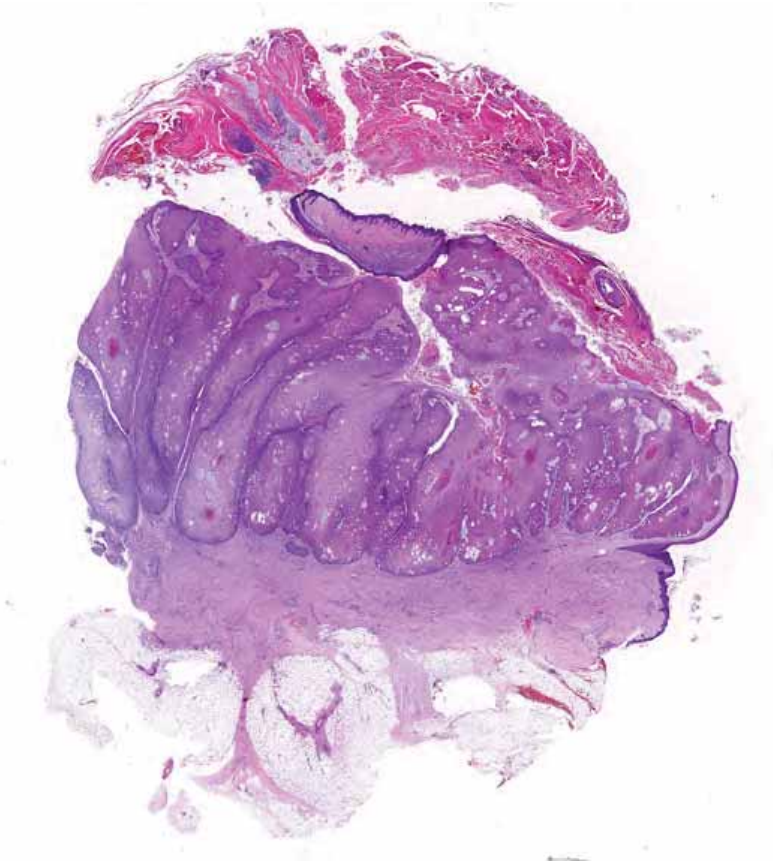
32-year-old man with krateriform tumoral lesion on the left perimammilary area since weeks.

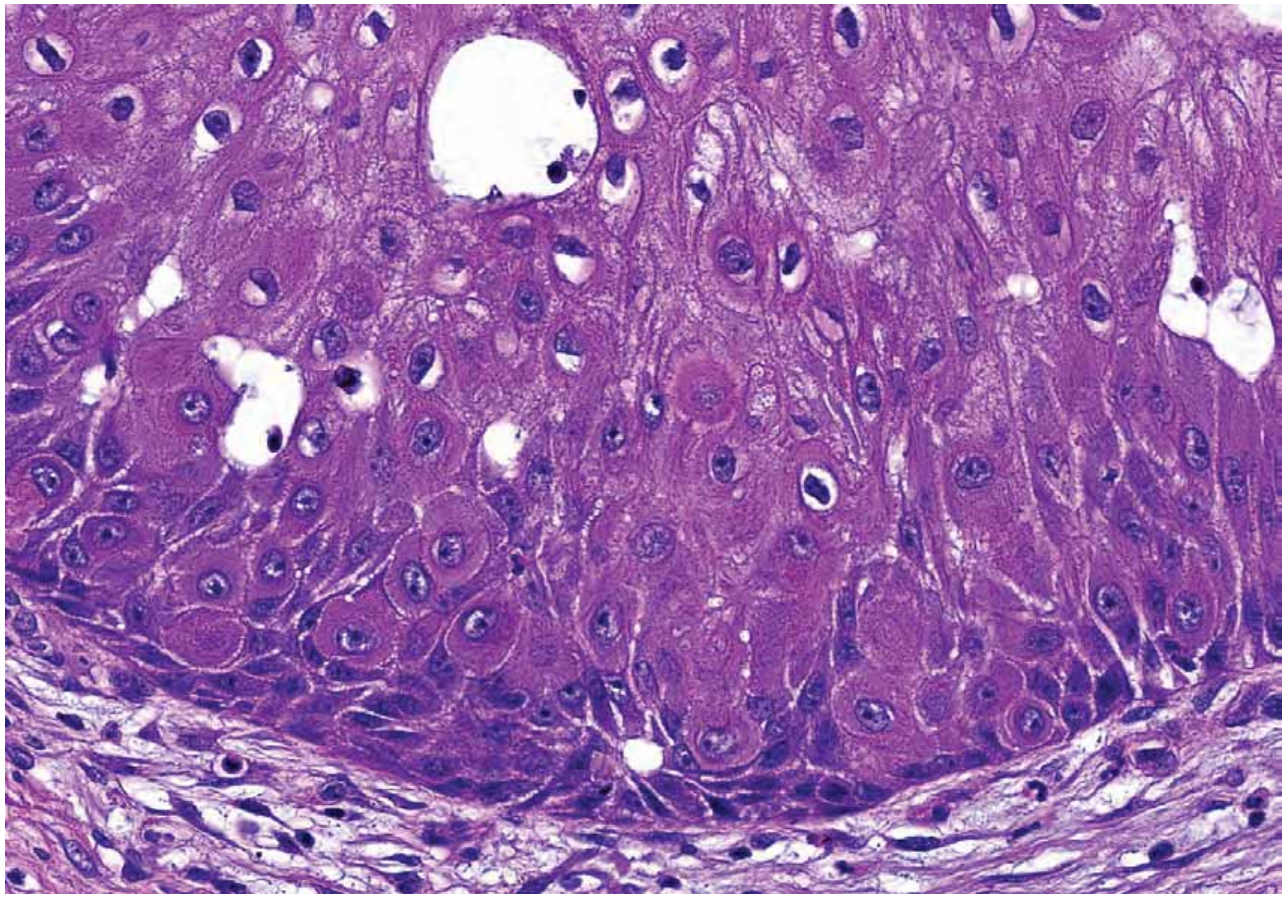




B24-87806

By courtesy Dr. Jung, Dept. Dermatology STZ, Zurich





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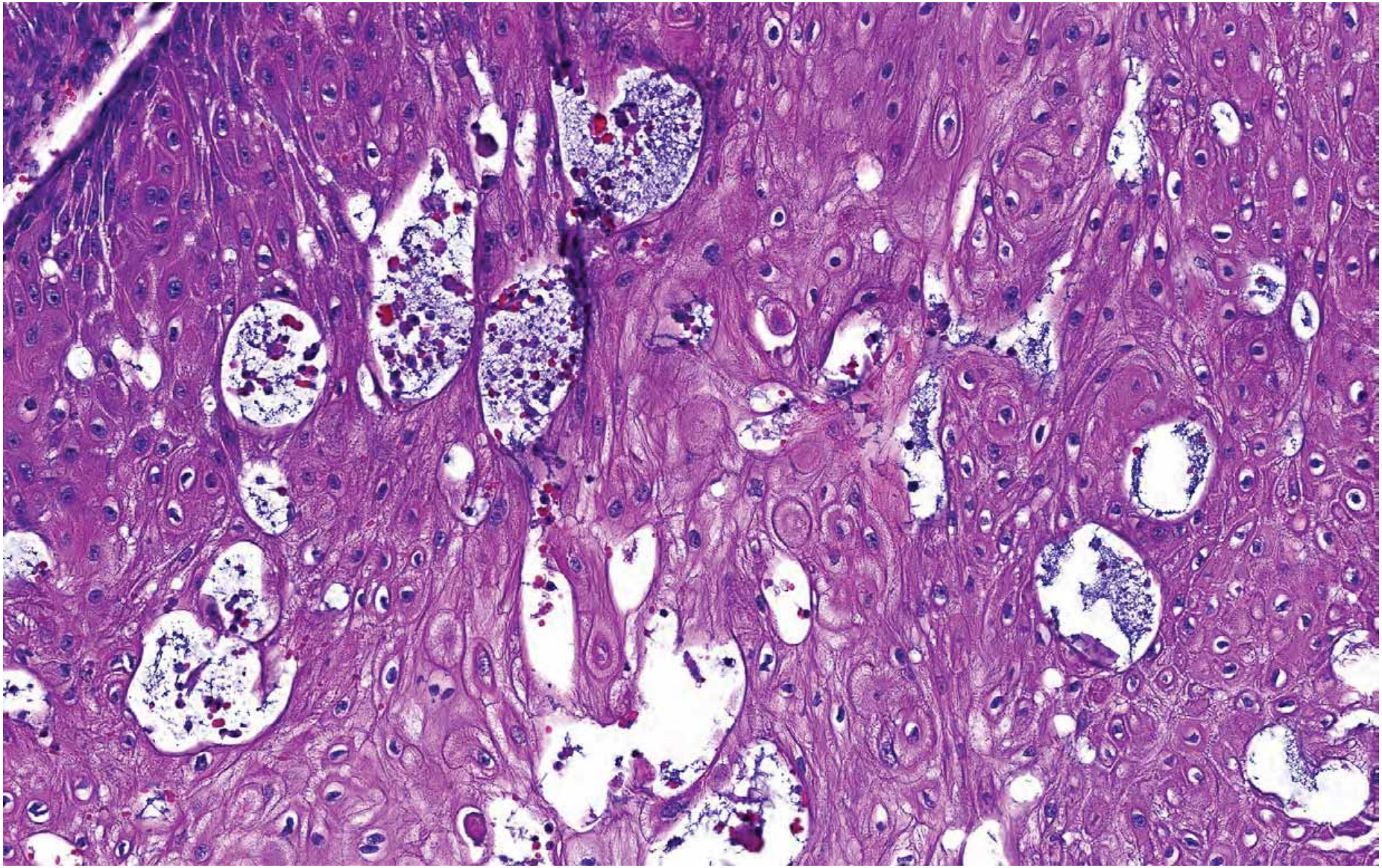

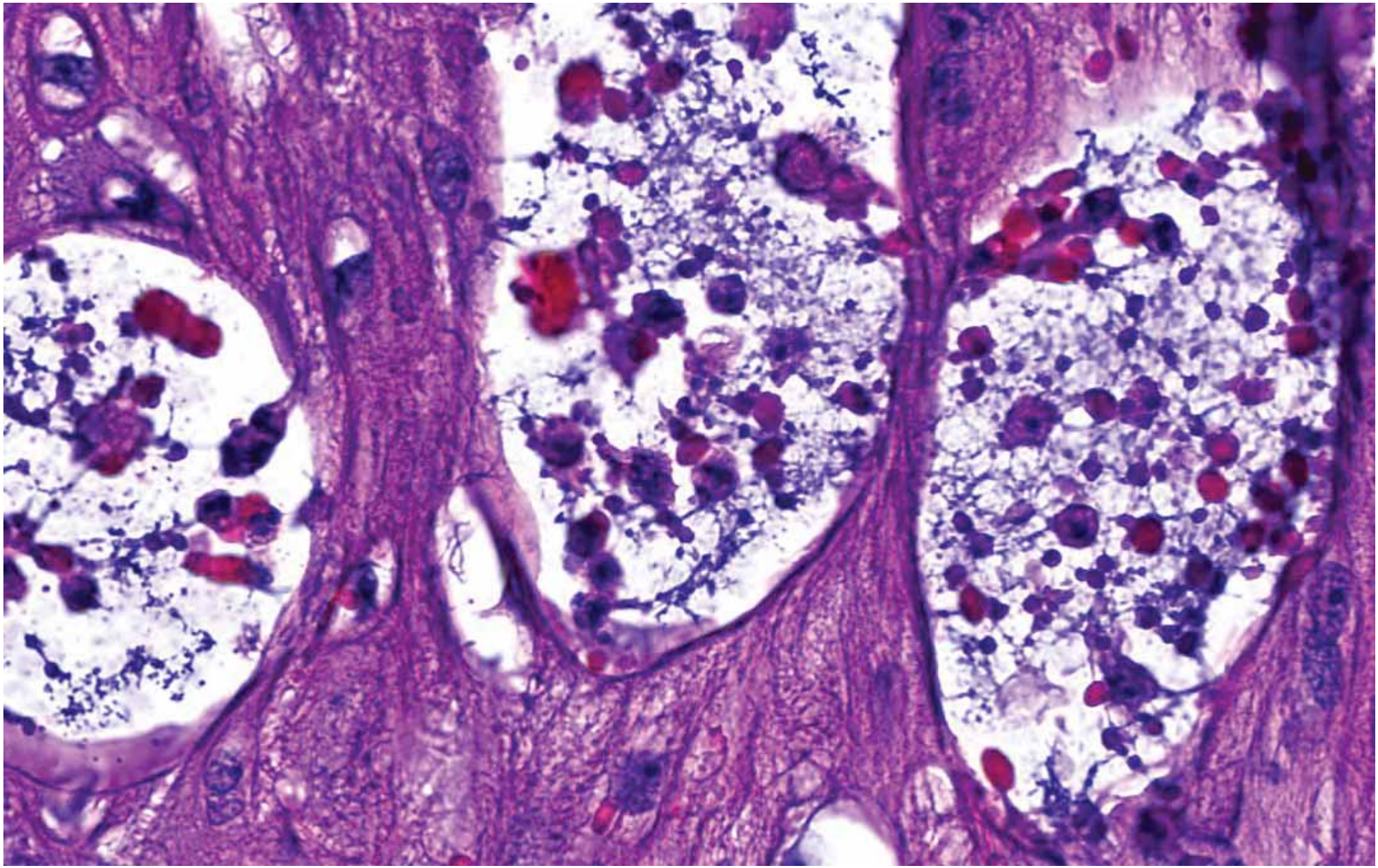

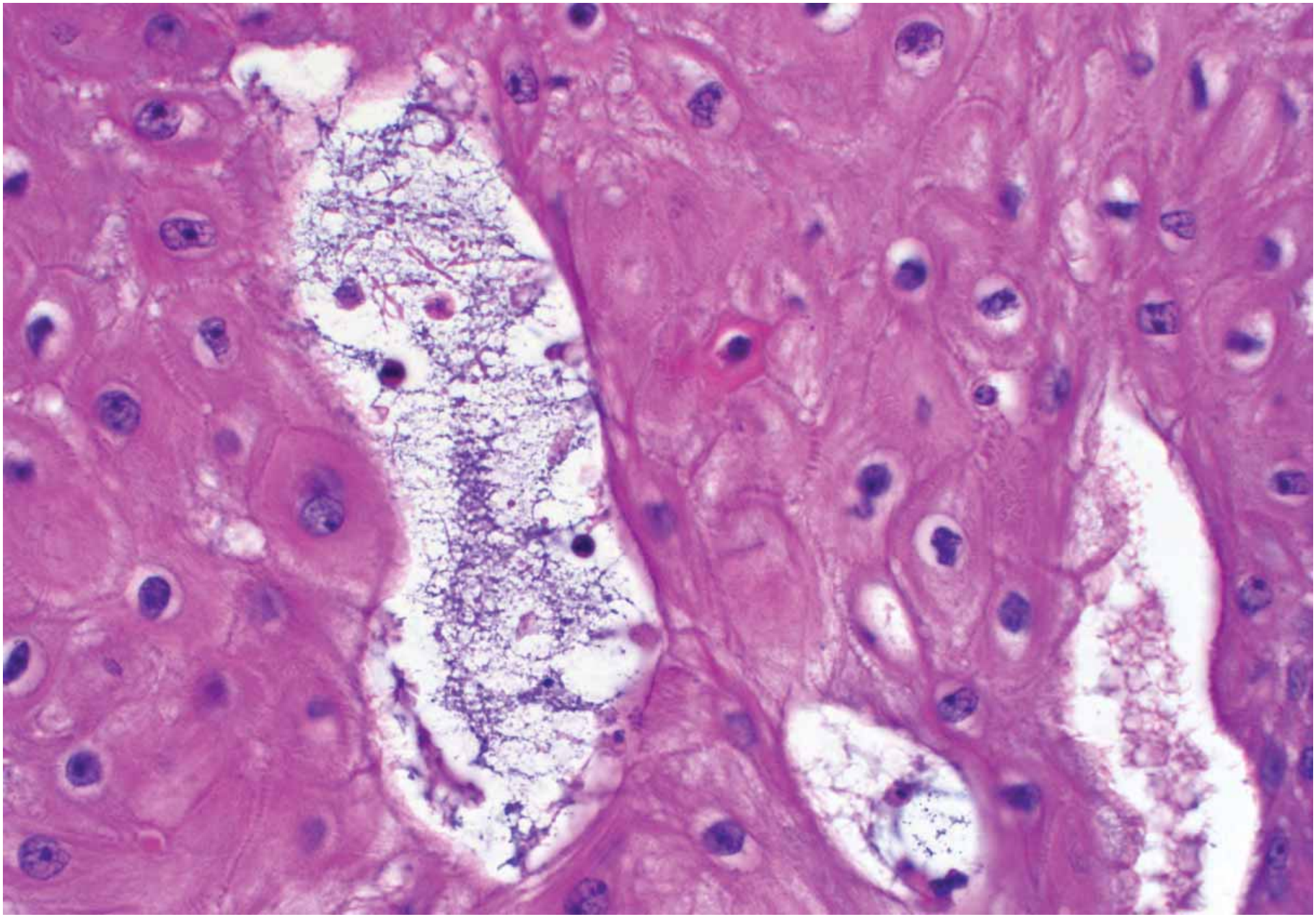

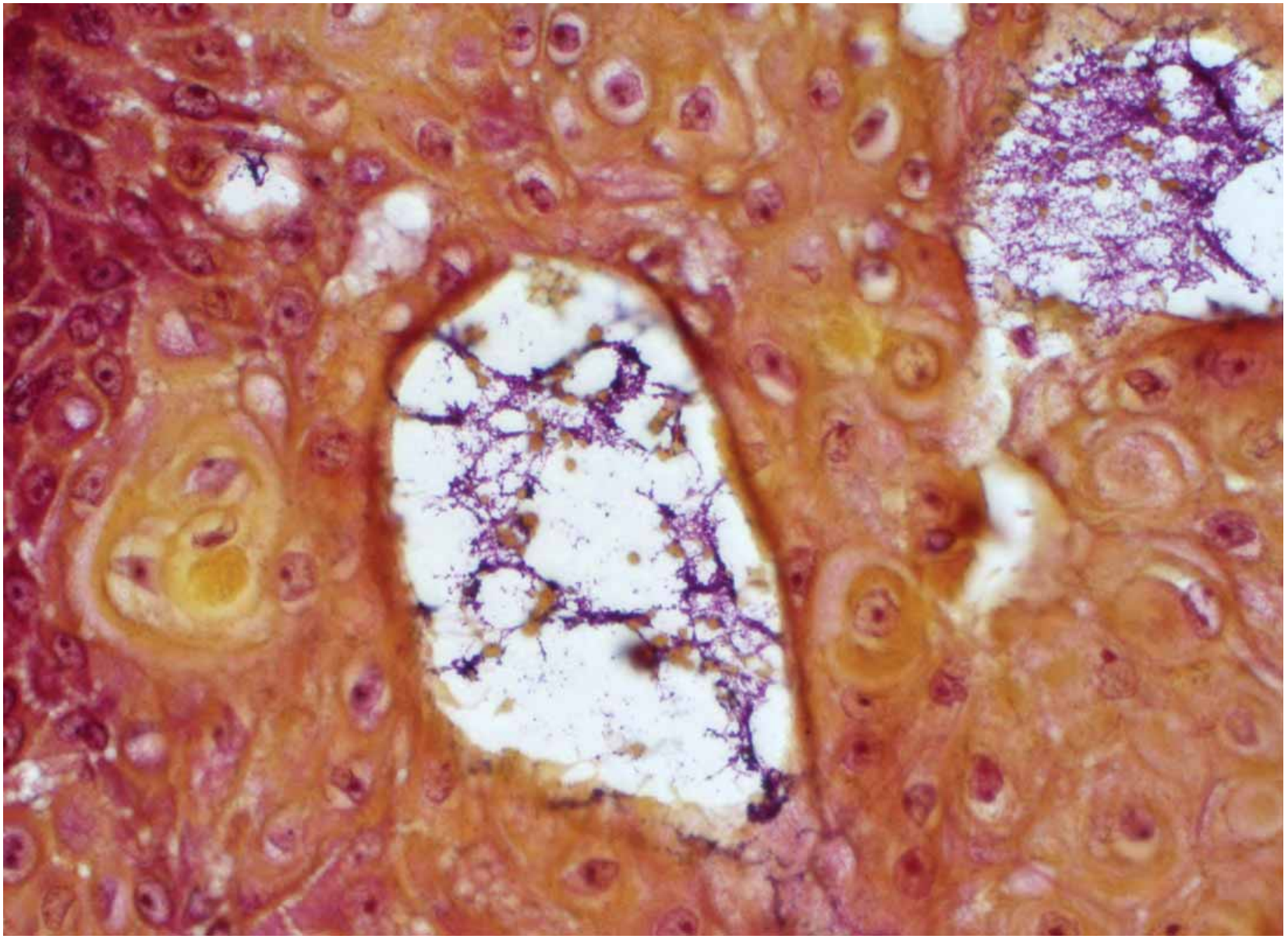

Brown Brenn Gram stain

# Tumor-like manifestations of actinomyces infections

Case Reports Singapore Med J. 2012 Jan;53(1):e9-e11.

## Actinomyces turicensis infection mimicking ovarian tumour

C Ong [1], S Barnes, S Senanayake

Affiliations
PMID: 22252197
Free article

### Abstract

This case report explores an unusual presentation of a commensal organism, Actinomyces, which mimicked a presentation of ovarian cancer. A 73-year-old woman presented to a tertiary level hospital with persistent left iliac fossa abdominal pain, anorexia and fever lasting over one week, with a three-month history of bright rectal bleeding. Imaging was suggestive of malignancy. Fine needle aspiration of an enlarged lymph node was non-diagnostic. Blood cultures taken at presentation became positive after two days for Gram-positive rods, which were most likely Actinomyces. The patient was treated with penicillin 1.8 g four hourly with rapid improvement. Actinomycosis is frequently misdiagnosed as malignancy initially due to its relatively indolent course. Lesions often resolve with antibiotics, without the need for surgical intervention.

Case Reports Nihon Kokyuki Gakkai Zasshi. 2002 Jun;40(6):525-9.

## [A case of pulmonary squamous cell carcinoma coexisting with pulmonary actinomycosis]

[Article in Japanese]
Tetsutaro Nagaoka [1], Yasuhiro Setoguchi, Masashi Muramatsu, Noriyuki Honma, Takashi Danbara, Hideaki Miyamoto, Hiroshi Izumi, Toshimasa Uekusa, Yoshinosuke Fukuchi

Affiliations
PMID: 12325341

### Abstract

A 71-year-old man was referred to our hospital complaining of cough. Chest radiography revealed a mass opacity in the right upper lung field. A transbronchial biopsy specimen revealed non-specific inflammatory changes. Percutaneous lung aspiration biopsy under ultrasound guidance demonstrated gram-positive rods, suggesting actinomyces. On the diagnosis of pulmonary actinomycosis, the patient was treated with penicillin-G and his symptoms were relieved. In a three-month follow-up, the mass shadow in the right upper lung field was found to have increased in size. Squamous cell lung cancer was diagnosed on the basis of repeated transbronchial tumor biopsies, and right upper lobectomy was performed. Most cases of pulmonary actinomycosis have been diagnosed from post-surgical tumor specimens taken on suspicion of the presence of lung cancer. However, the lung cancer in this case was difficult to diagnose because the lung cancer was co-existent with pulmonary actinomycosis.

# Fatally invasive actinomycosis masquerading as a tonsillar carcinoma

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**ABSTRACT:** *Background.* Actinomyces is a bacterial rod found in the normal oral flora. It can gain entry to the submucosa via trivial wounds and ultimately lead to slow growing lesions which may mimic cancerous lesions.
*Methods and Results.* We present the case of an elderly, immunosuppressed woman who presented with a herald bleed from a tonsillar lesion. Despite initial operative arrest of the hemorrhage, she died of a carotid blowout. At autopsy, no sign of cancer was found, but rather an invasive actinomycosis.
*Conclusion.* Although actinomycosis of the tonsil is well known and has even been described as mimicking tonsillar cancer, this is, to our knowledge, the first report of a carotid blowout secondary to actinomycosis. © 2014 Wiley Periodicals, Inc. *Head Neck* 36: E129–E130, 2014

**KEY WORDS:** actinomycosis, tonsillar cancer, herald bleed, carotid blowout, squamous cell cancer, immune suppression

## INTRODUCTION

We report the case of a 75-year-old woman who presented with a herald bleed from the tonsillar fossa. A working diagnosis of tonsillar cancer/lymphoma was made, but before the patient could undergo staging and before the results of biopsies became available, she died from a carotid blowout. Autopsy showed no sign of cancer, but rather an invasive actinomycosis that had eroded through branches of the external carotid artery. This is the first report, to our knowledge, of carotid blowout secondary to actinomycosis infection.

## CASE REPORT

A 75-year-old woman presented to a neighboring hospital with oropharyngeal bleeding. She was immediately transferred to the University Hospital Zürich with a working diagnosis of bleeding from a right-sided tonsillar cancer. On arrival, the bleeding had stopped and the patient was fluid resuscitated including transfusion of 2 units of packed red blood cells.

Clinical history revealed that she had lost 8 to 10 kg in the previous 3 months, which she attributed to a worsening trismus and odynophagia radiating to her right ear. Of further note, she had polyarthritis for 20 years and been variously treated with nonsteroidal anti-inflammatory drugs and methotrexate. She had to stop the latter because of extensive oral/anal ulceration and been switched to Leflunomide (a pyrimidine synthesis inhibitor disease-modifying anti-rheumatic drug). She was a nonsmoker and nondrinker.

Shortly after admission, the patient started to bleed again intraorally and she was taken to the operating room for an endoscopy and surgical arrest of the hemorrhage. After an awake transnasal intubation, inspection showed a large ulcer in the right tonsillar fossa infiltrating the tongue base. Hemostasis was achieved with bipolar coagulation and multiple biopsies were taken. Neck palpation revealed several enlarged lymph nodes.

Later that afternoon, the patient was informed of the operative findings, consistent with a diagnosis of tonsillar cancer. Further staging was planned and the results of the biopsies were awaited. The patient had an advanced resuscitation directive and her resuscitation status was further discussed with both the patient and her family. It was agreed that no mechanical resuscitation would be attempted in the event of cardiac arrest. The possibility of additional radiological embolization was considered, but surgical control in the event of further bleeding was preferred because of the high likelihood of radiotherapy was assumed.

Later that night, the patient had a carotid blowout and died within minutes.

Contrary to the clinical diagnosis of tonsillar carcinoma, autopsy showed no sign of cancer. An invasive actinomycosis had eroded branches of the external carotid artery leading to fatal hemorrhage (Figure 1). The neck lymph nodes showed chronic lymphoplasmacellular inflammatory changes.

## DISCUSSION

Actinomyces is a facultative anaerobic, gram-positive, non-acid fast, branched filamentous bacterial rod found in normal oral flora.[1] It has an incidence of 1 per 100,000 in Europe, and men are 3 times more likely to be infected than women.[2] It is commonly found in tonsillar crypts

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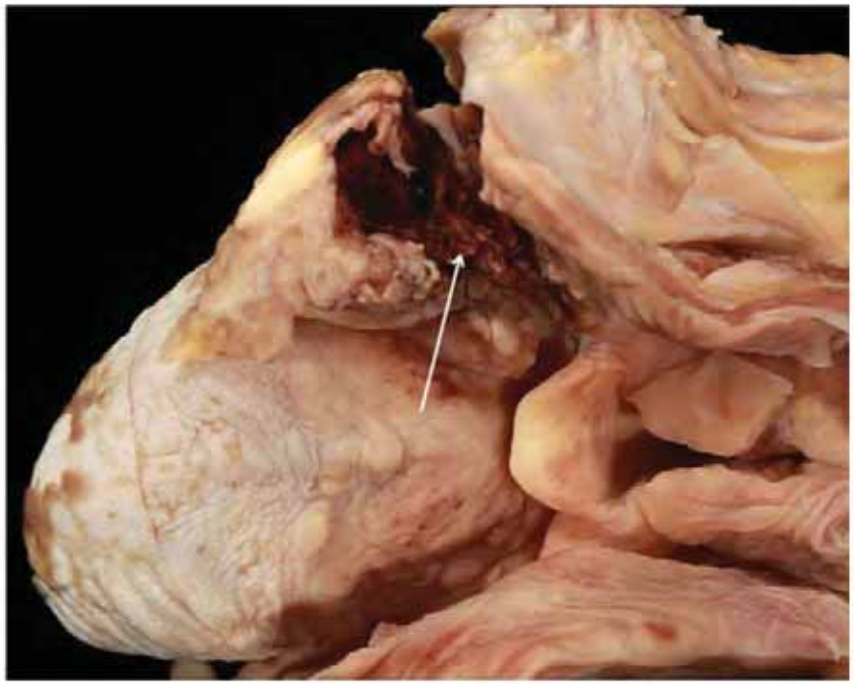
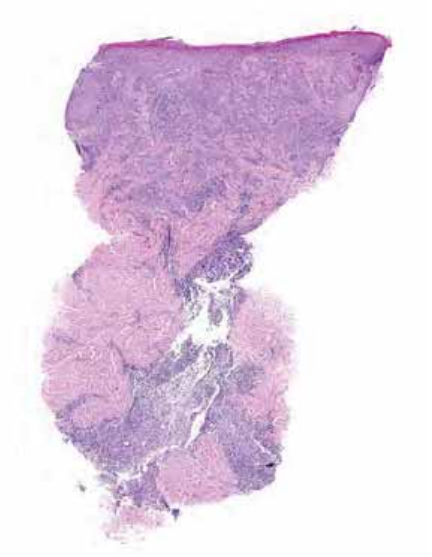
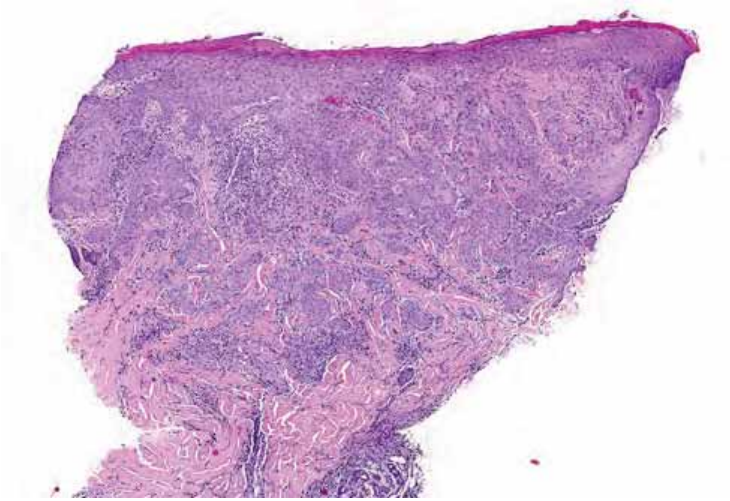


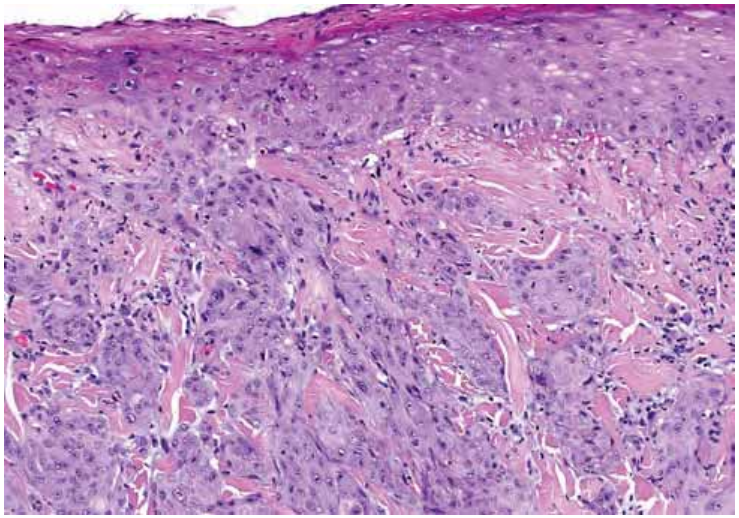
FIGURE 1. Autopsy specimen showing an axial view of the tongue, vallecula, and trachea. The right tonsilla fossa (arrow) can be seen completely eroded. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

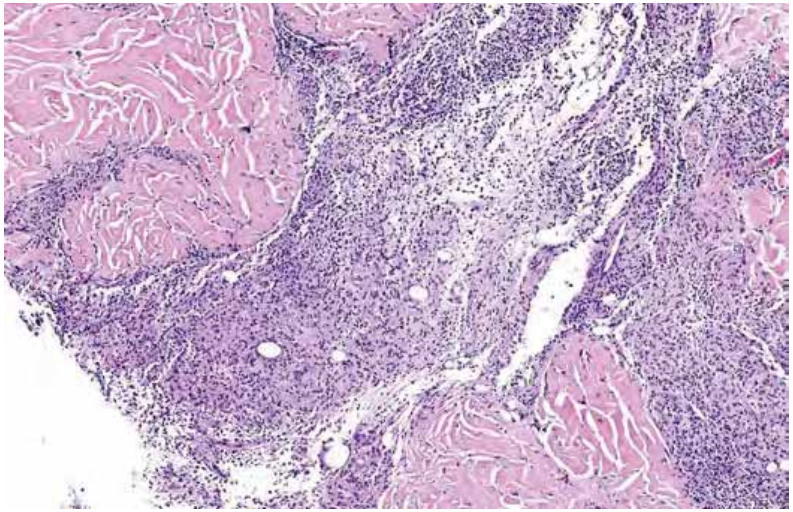
# Cutaneous tularemia

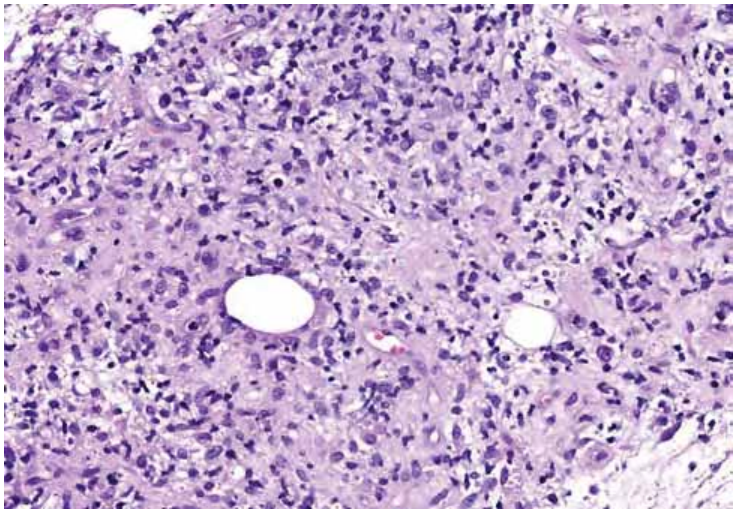
57-year-old man with a solitary ulcerated nodule since 4 weeks on the right upper arm:







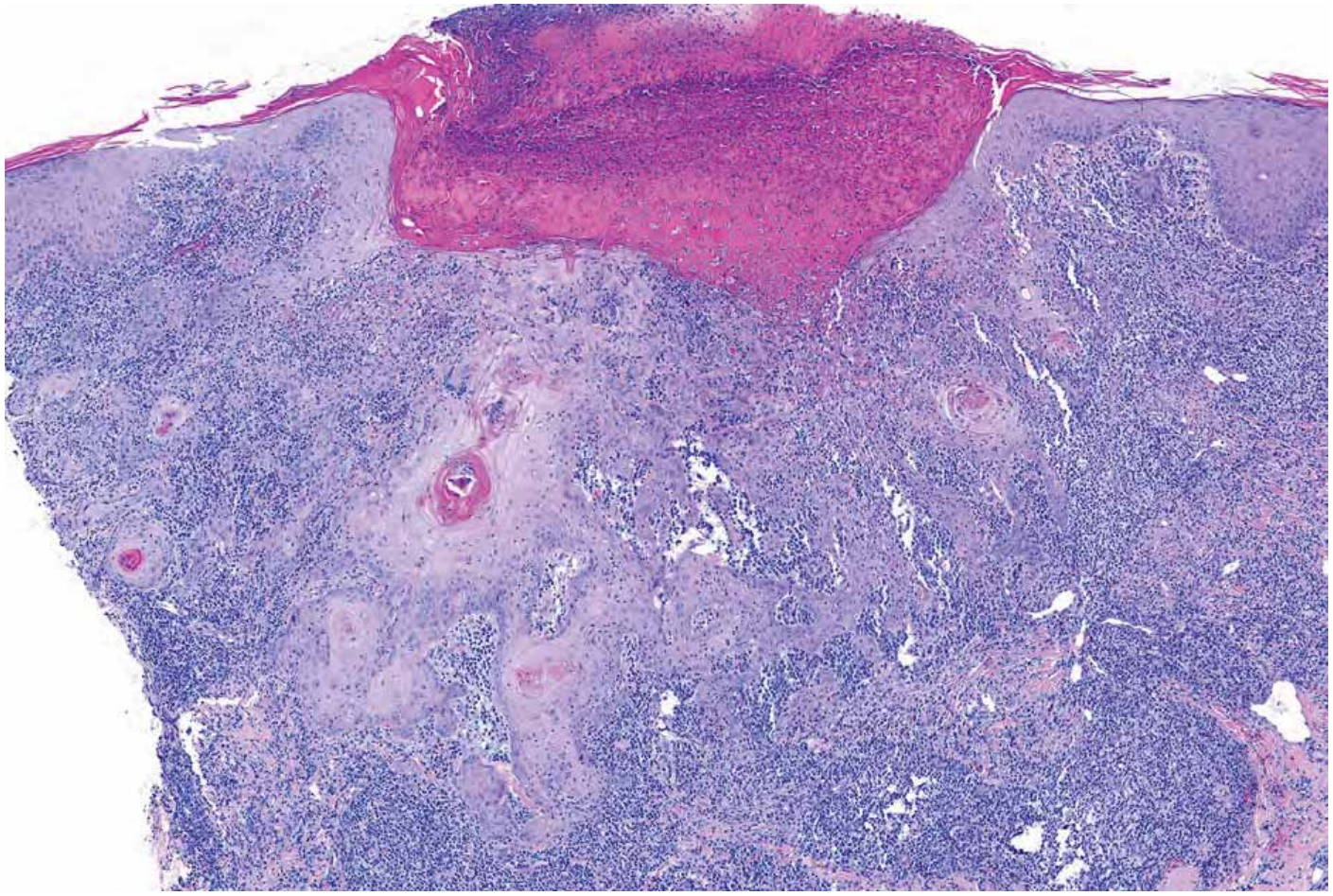


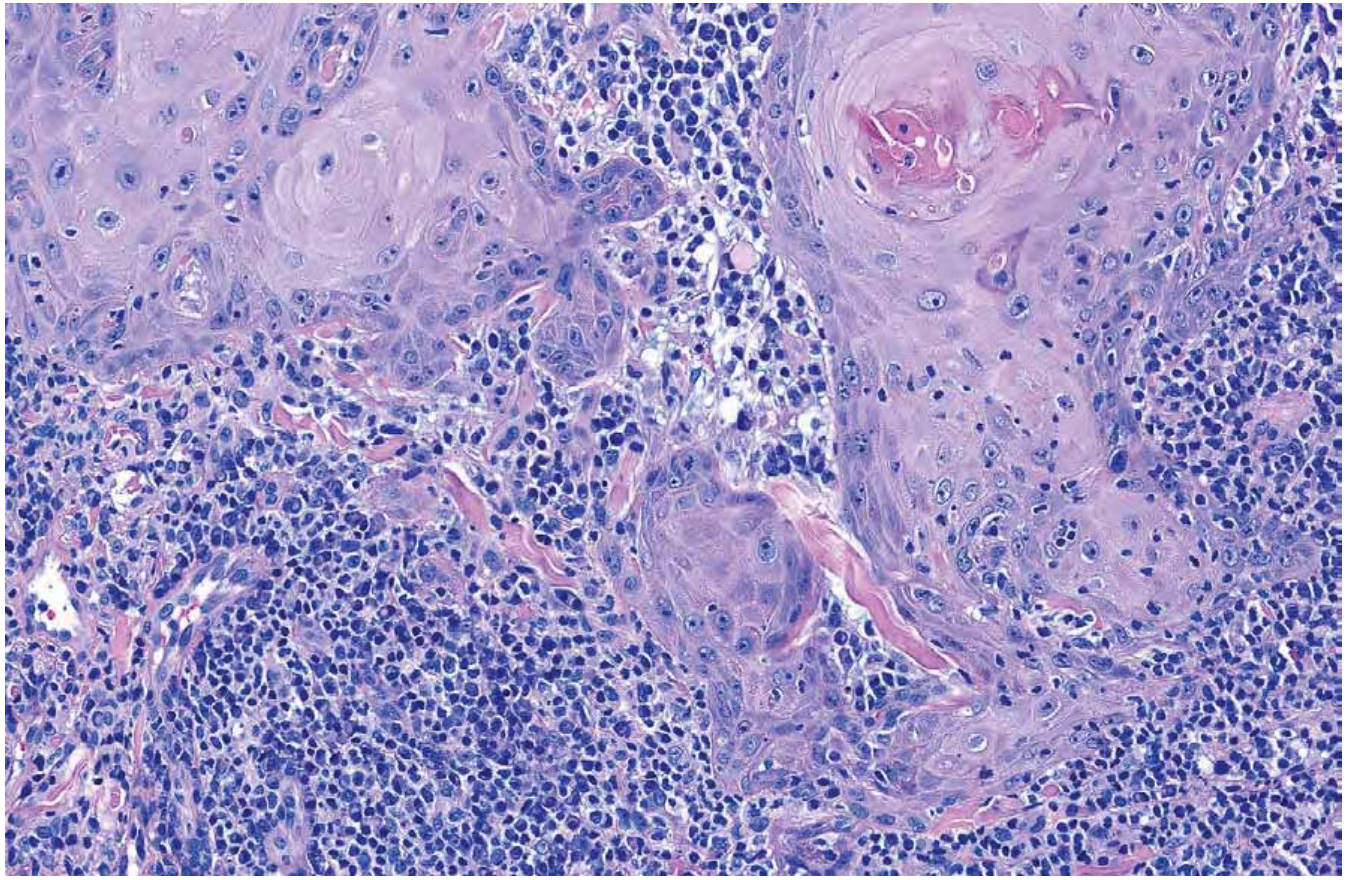


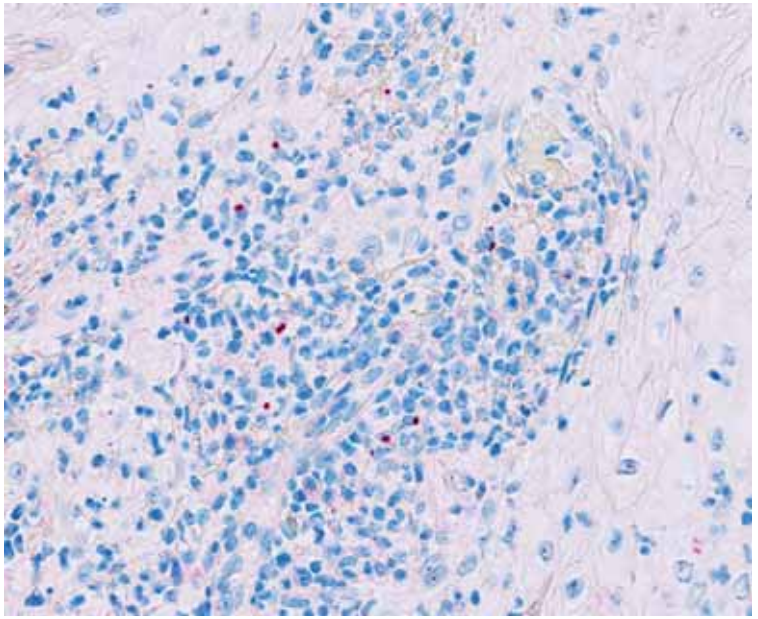
# Leishmaniasis

## Leishmania tropica ("Old World")

Photo: Dr. med. Daniel Zuder, St.Gallen, Switzerland

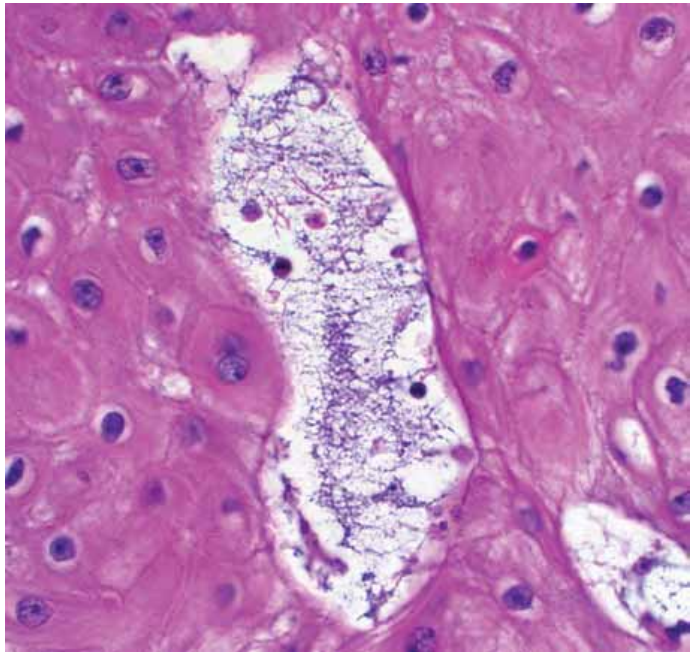




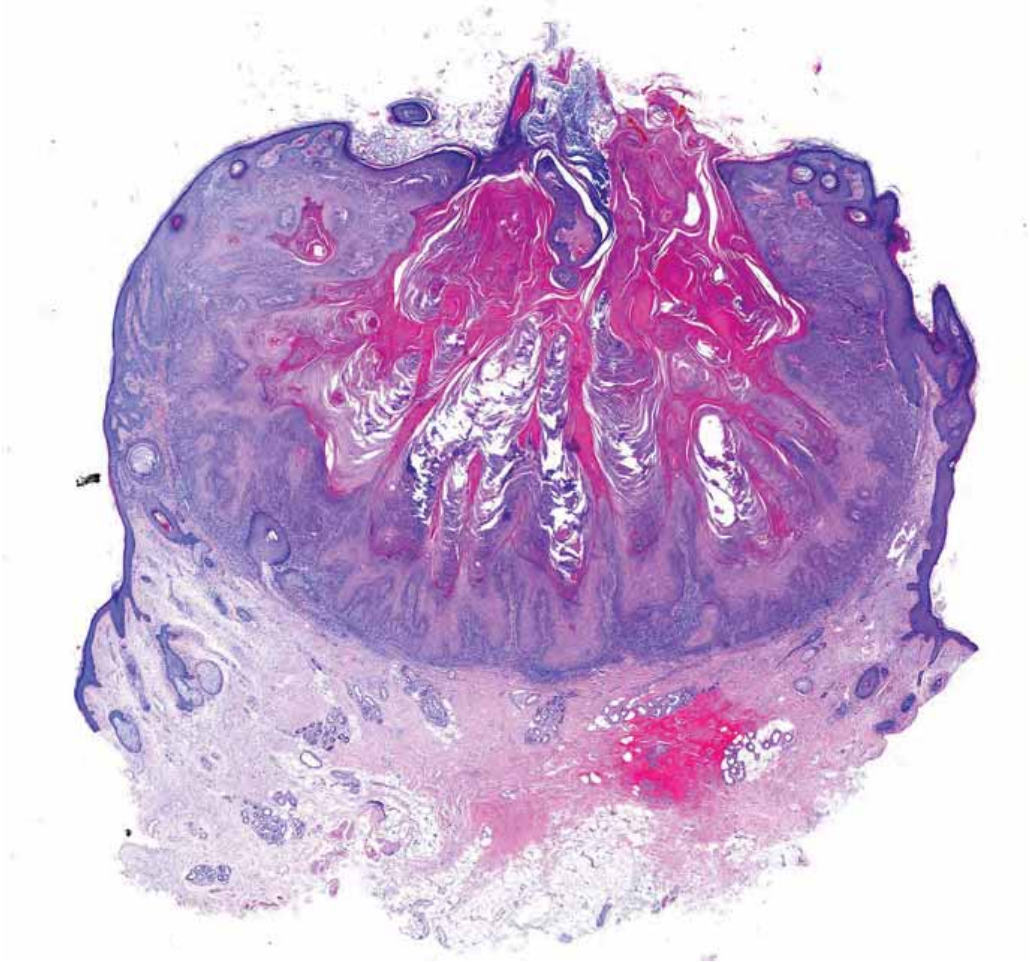


Leishmania-IHC

25-28212

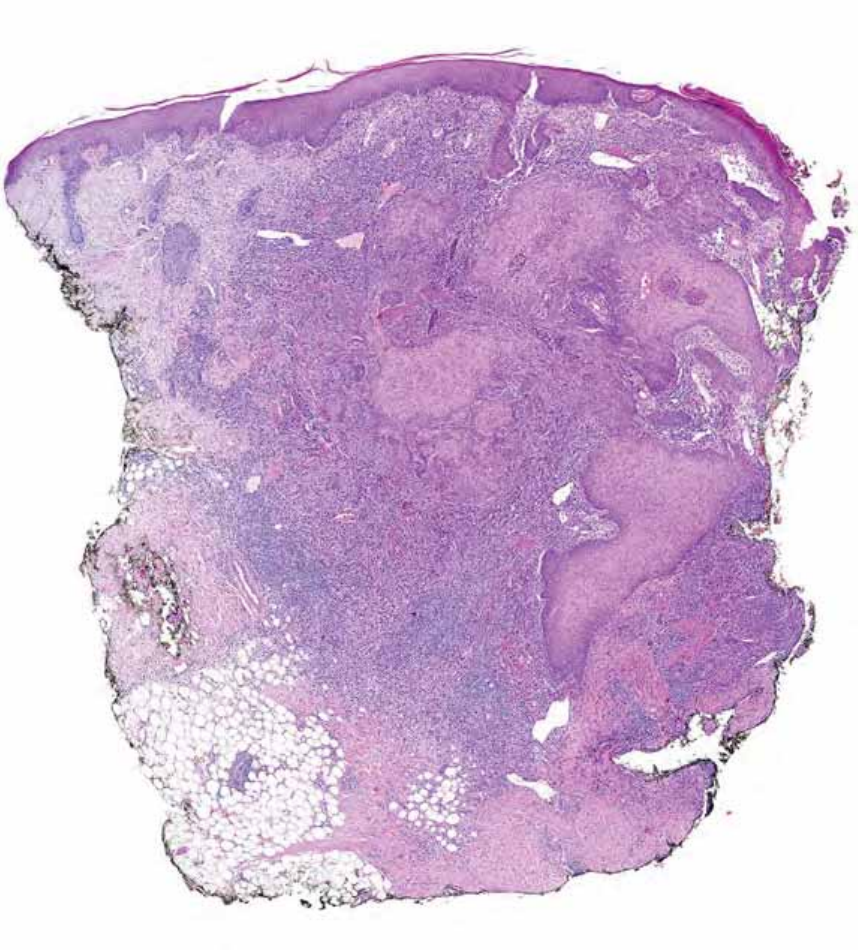


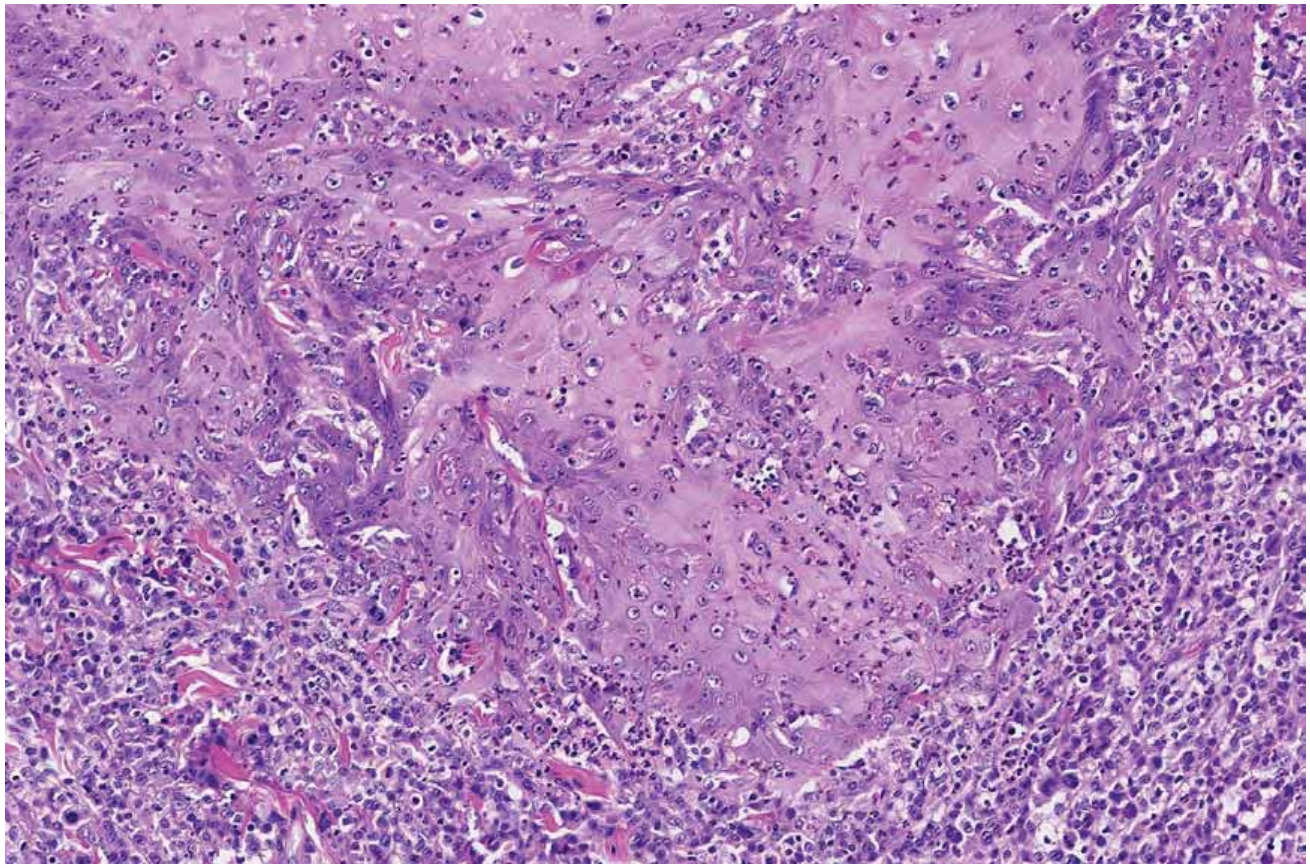
Keratoacathoma-like pseudocarcinomatous hyperplasia in actinomyces infection
or
keratoacanthoma superinfected with actinomyces (unknnown source)



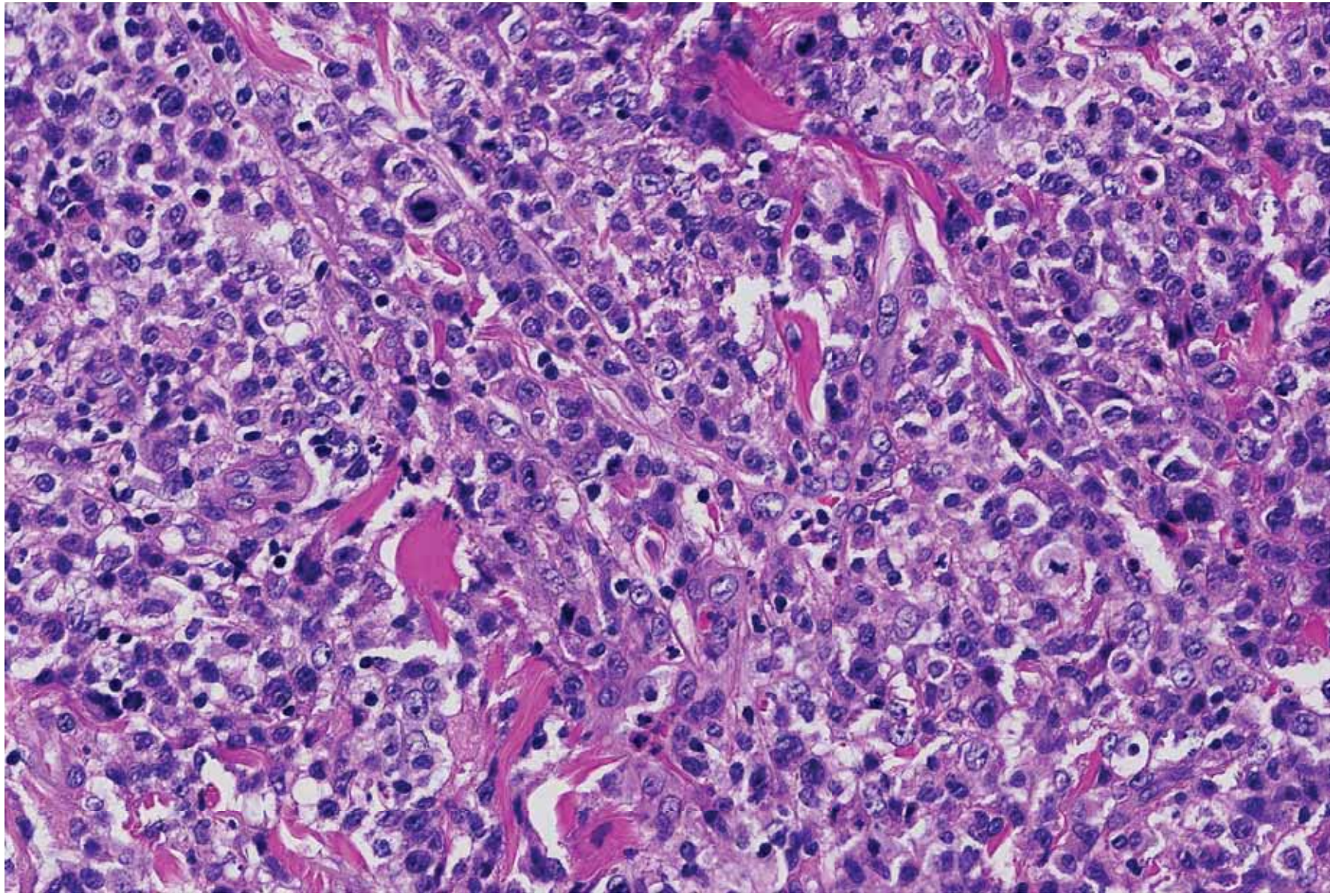
Is keratoacanthoma a process driven by an infectious agent?

65-year-old woman with rapidly growing tumor on the left cheek.

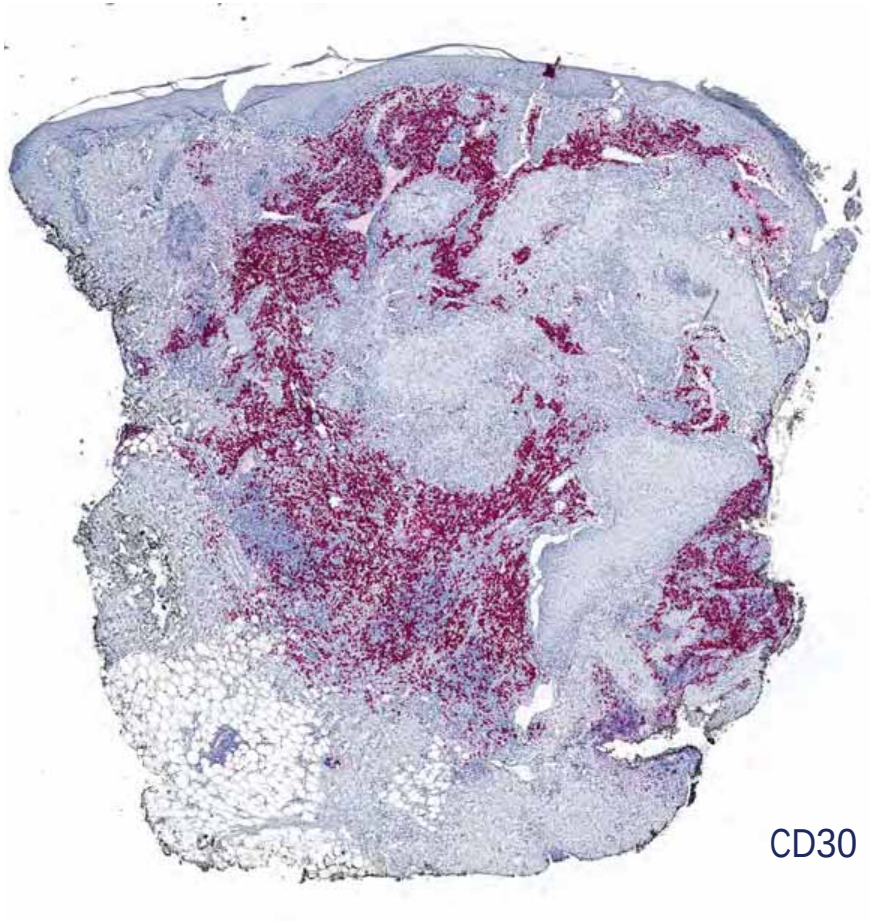




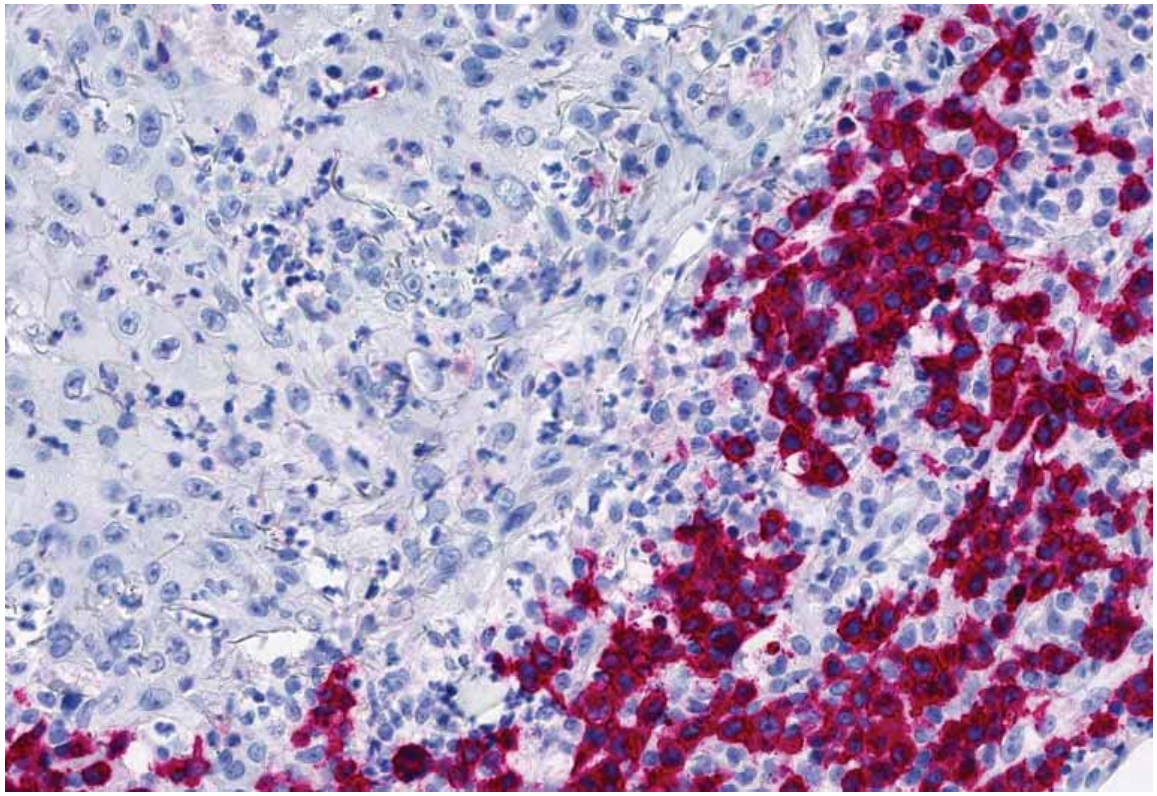
K11-340



K11-340



CD30

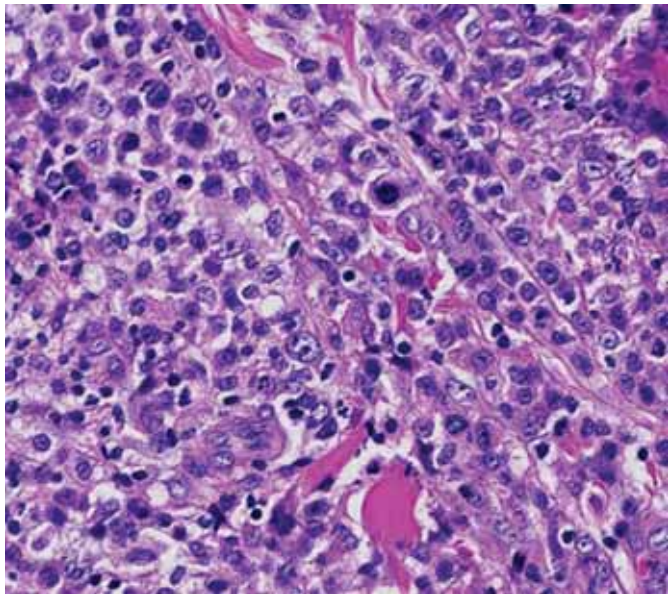


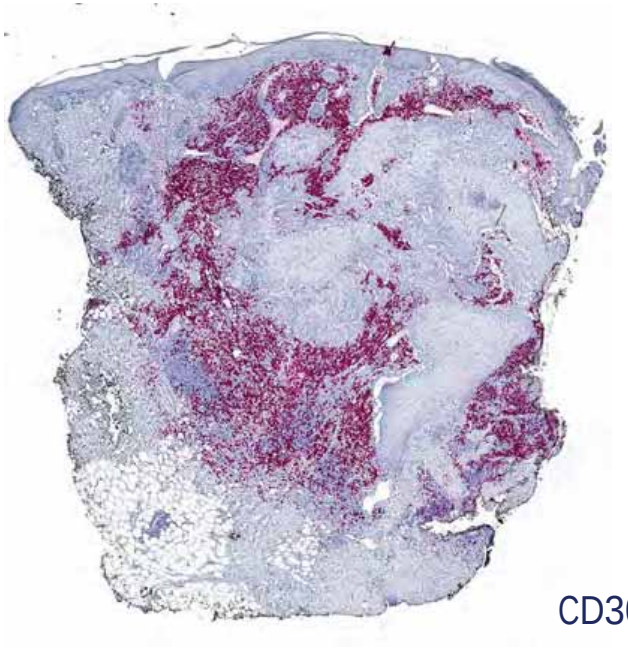
CD3- CD4+ CD8- CD30+ ALK- EMA-

Monoconal rearrangement of TCR gamma genes

K11-340

65-year-old woman with rapidly growing tumor on the left cheek.



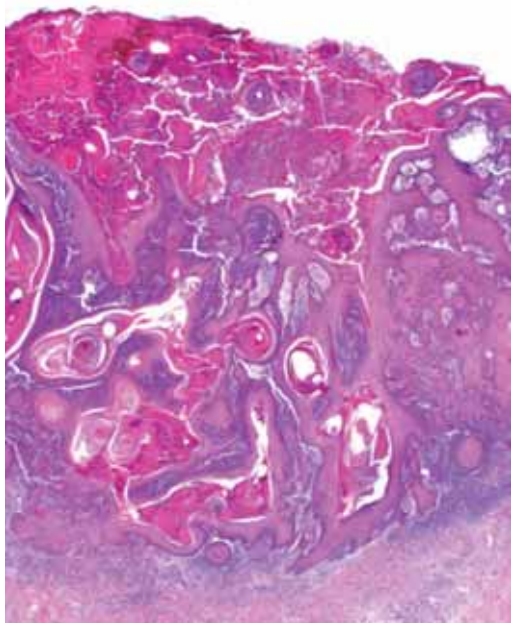


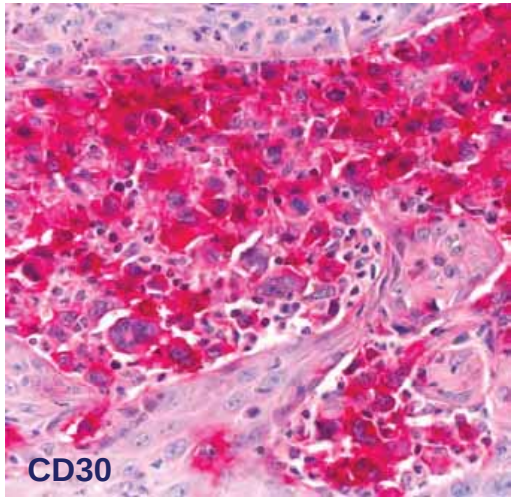
CD30

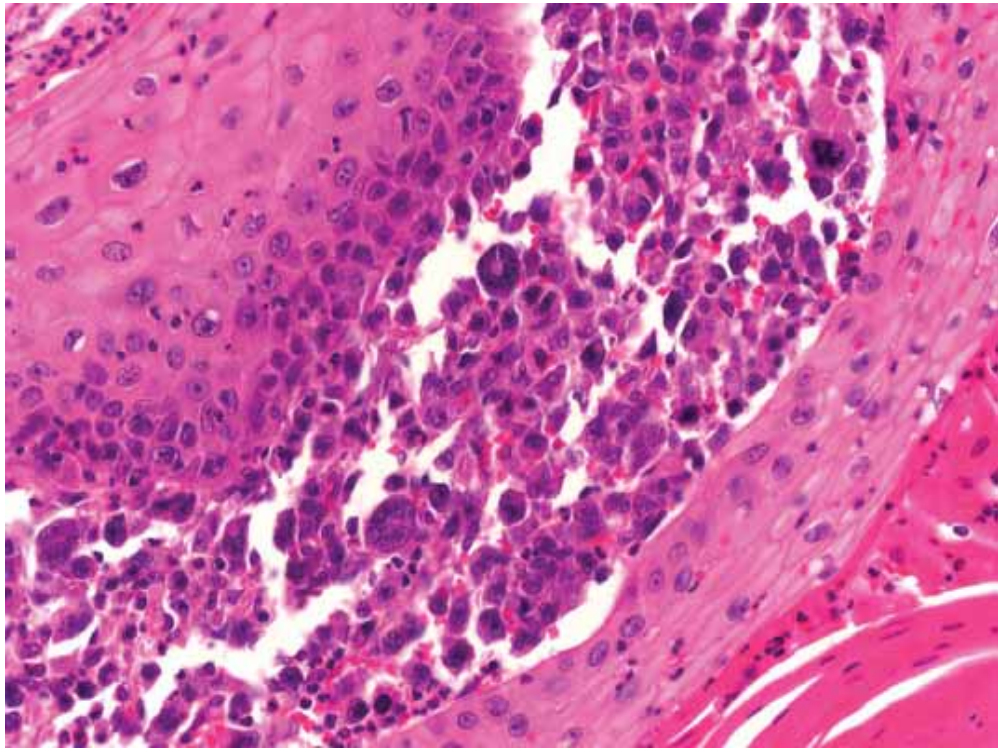
Primary cutaneous CD30-positive anaplastic large-cell lymphoma with pseudocarcinomatous hyperplasia

K11-340

# PC-ALCL





Clin Exp Dermatol. 2007 Nov;32(6):668-71.

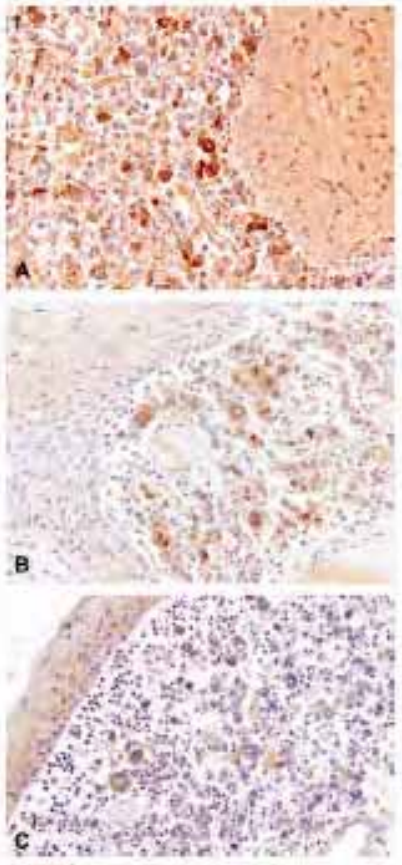
**Primary cutaneous CD30+ anaplastic large-cell lymphomas mimicking keratoacanthomas.**

Martín JM, Ricart JM, Monteagudo C, Alcácer J, Pinazo I, Tomás L, Rausell N, Jordá E.

Department of Dermatology, Hospital Clínico Universitario, Valencia, **Spain**. jmmart@eresmas.com

# CD30$^+$ cutaneous lymphoproliferative disorders with pseudocarcinomatous hyperplasia are associated with a T-helper-17 cytokine profile and infiltrating granulocytes

Joan Guitart, MD,[a] Maria Estela Martinez-Escala, MD,[a] Janyana M. D. Deonizio, MD,[a] Pedram Gerami, MD,[a] and Marshall E. Kadin, MD[b,c]
*Chicago, Illinois; Boston, Massachusetts; and Providence, Rhode Island*


IL-17

IL-22

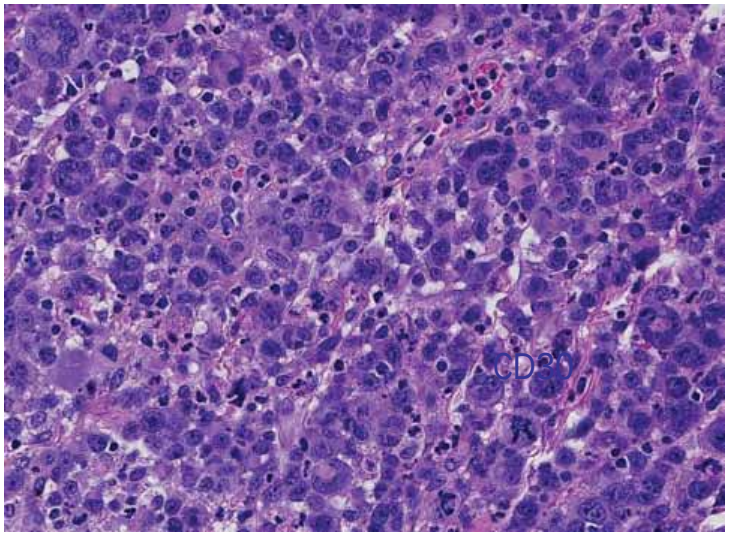
Th17-TF

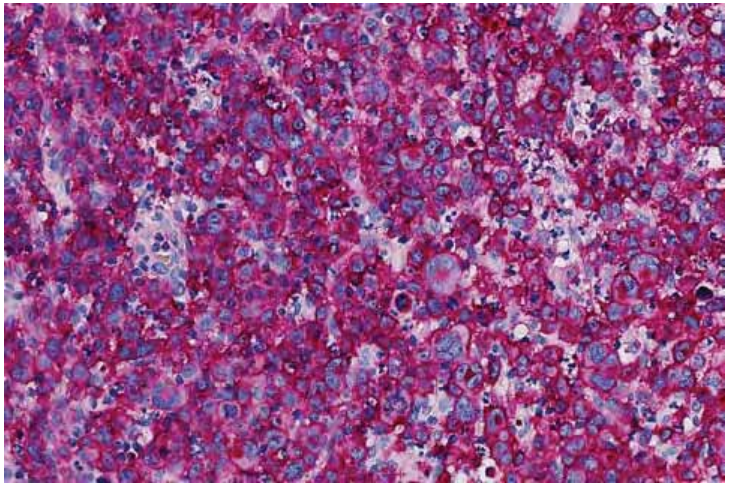
14 / 25 cases with neutrophil- or eosinophil-rich infiltrates

Th17/Th22 cytokine pattern expressed by CD30+ cells

Guitart et al. J Am Acad Dermatol 2014

11 years later rapidly growing nodule on the back.





CD2+ CD3- CD4- CD5+ CD8- CD30+ EMA (+)

Identical T-cell clone like KA-like C-ALCL 11 years ago

CD30

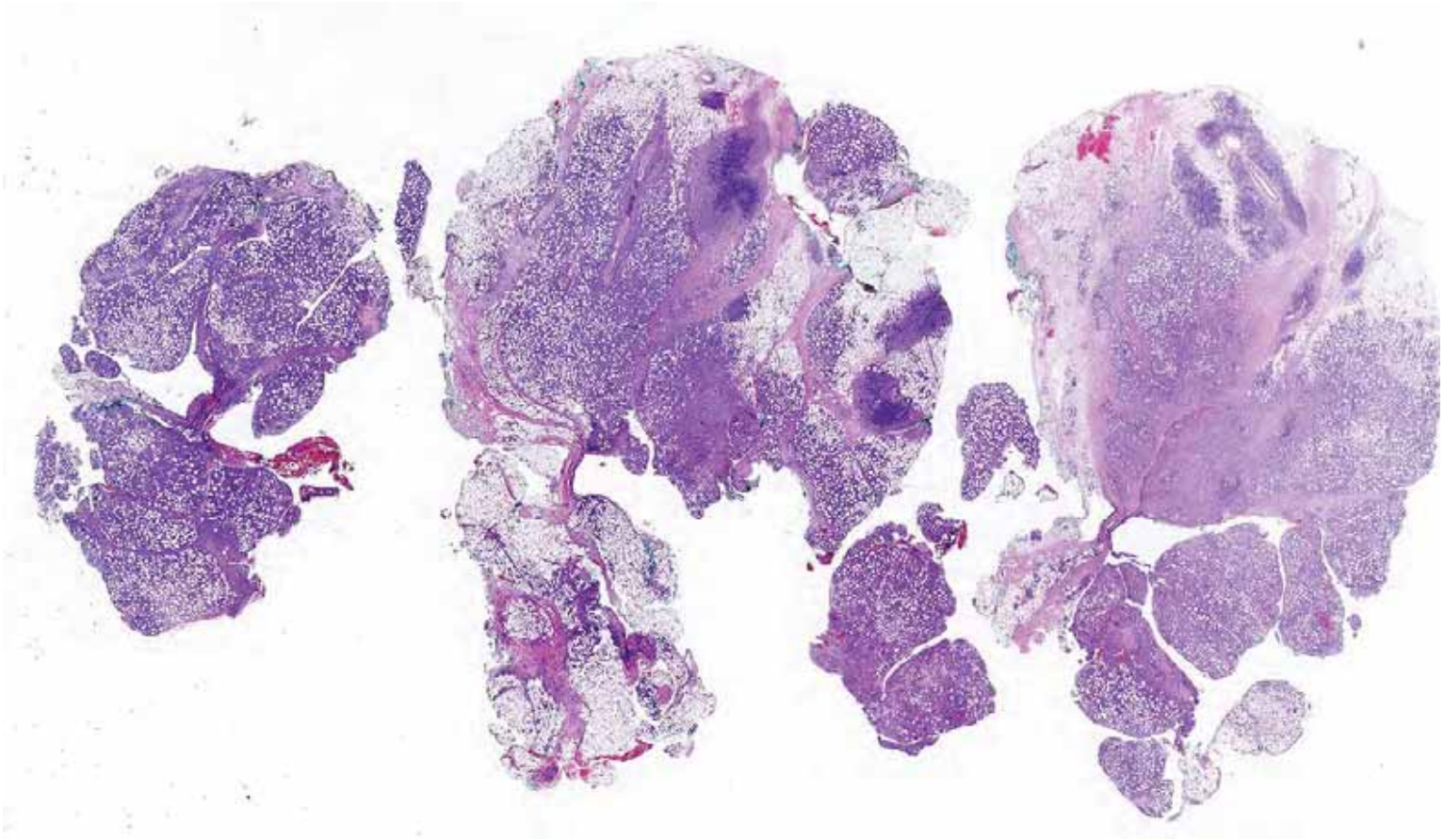
B22-71613

*Tarantel Nebula in the large Magellan cloud (via James-Webb telescope)*

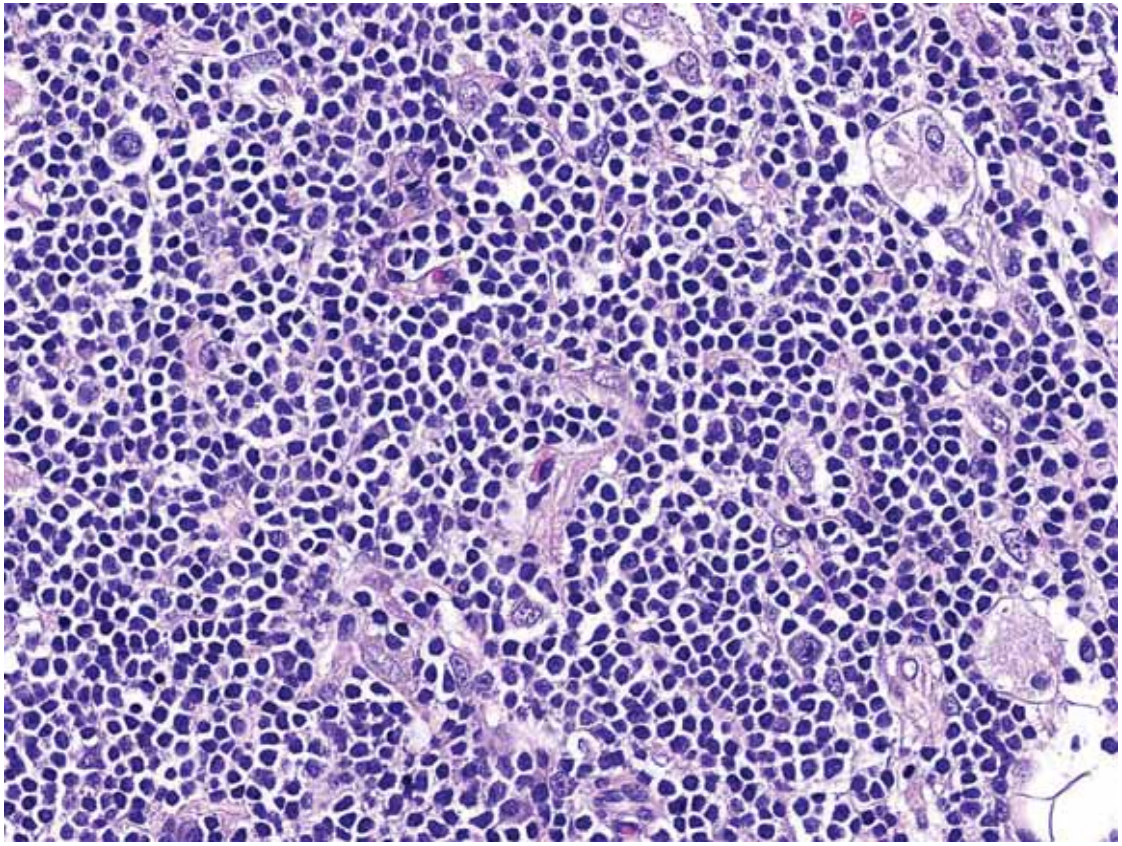
NASA/ESA/CSA

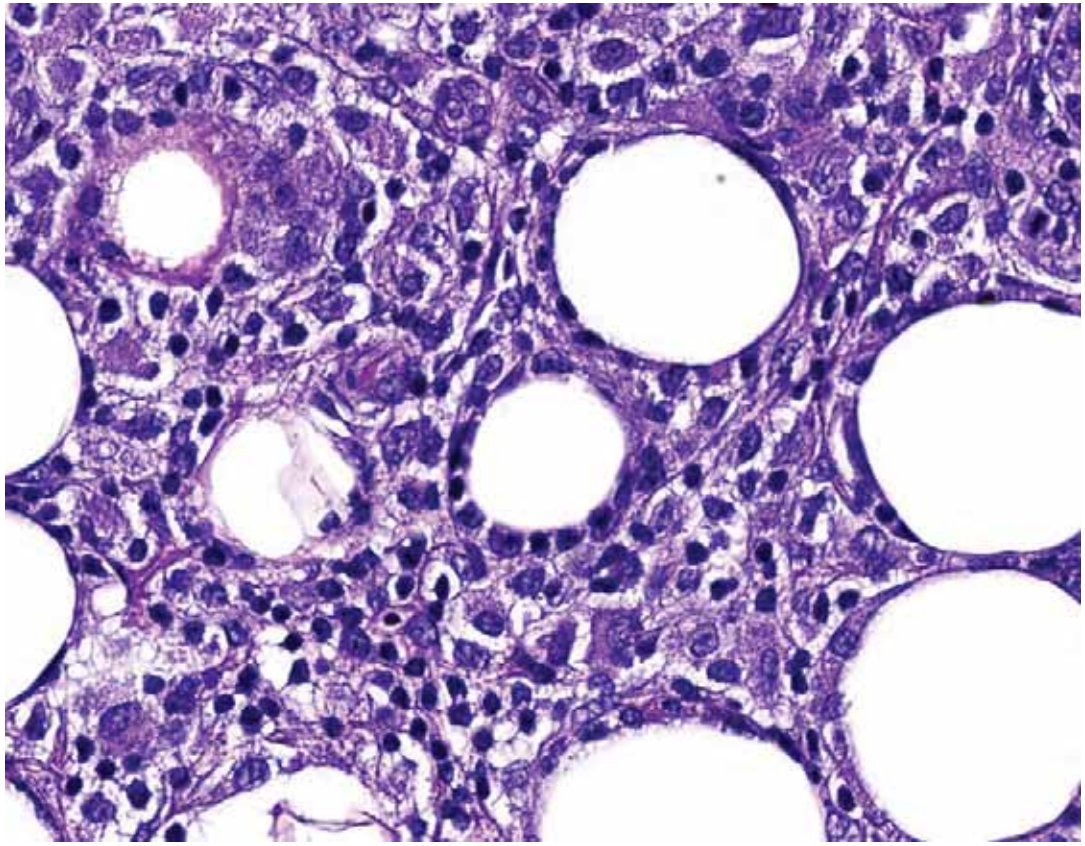
38-year-old woman with deep dermal and subcutaneous infiltration (right arm)

*Consultation case: Prof Dr Daniea Mihic Probst, Dept. Pathology, Univ. Hospital Zürich*



K24-133





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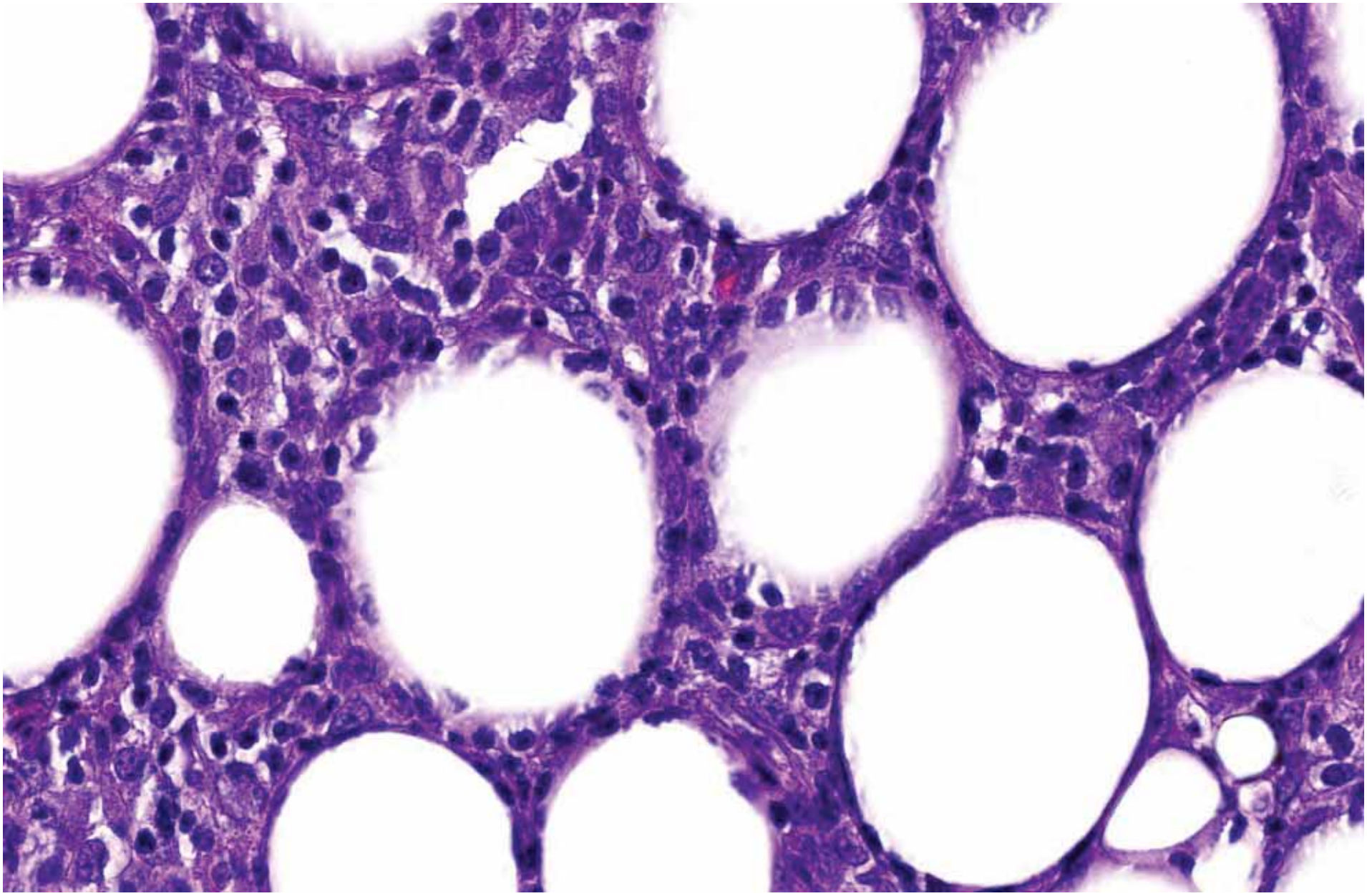
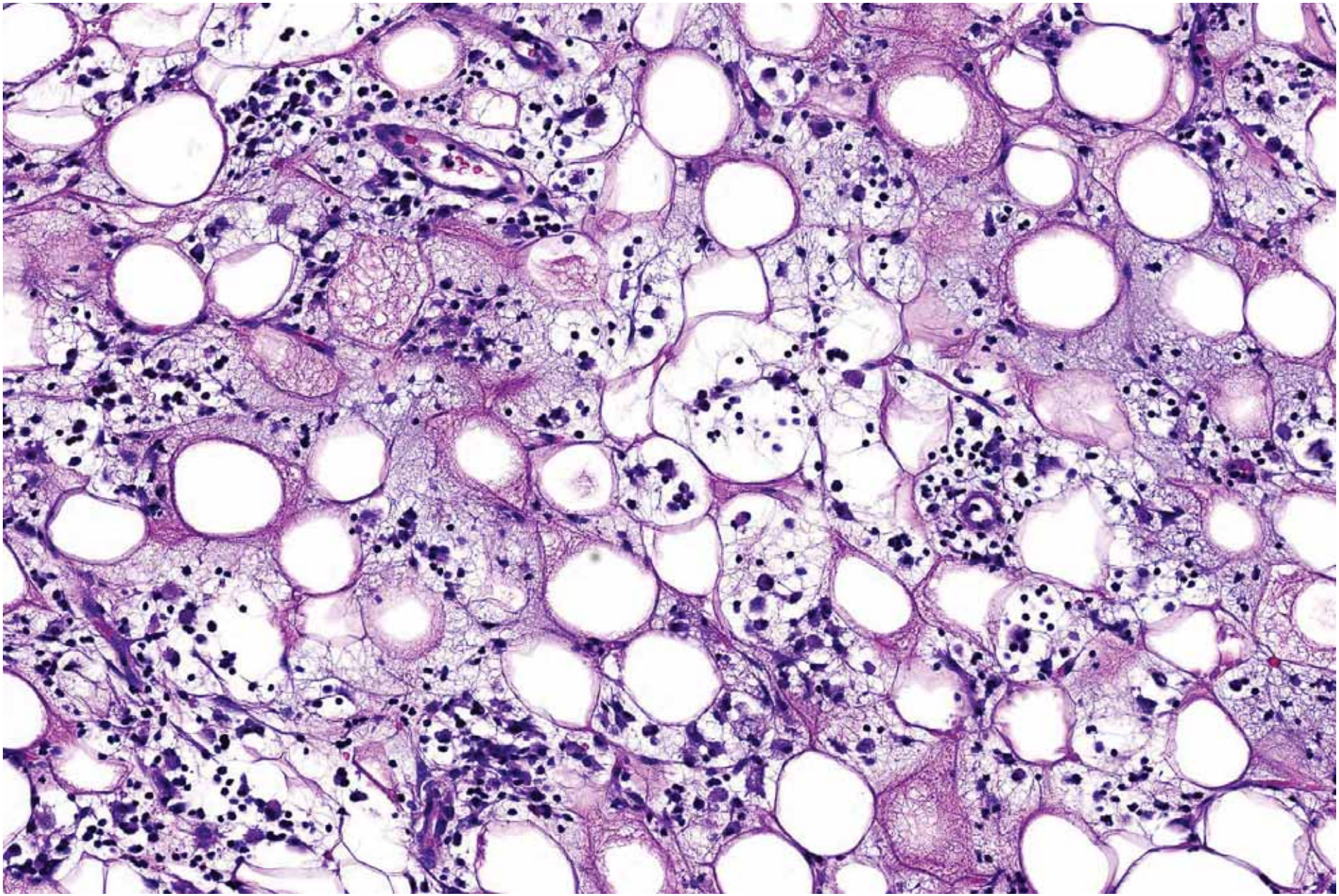
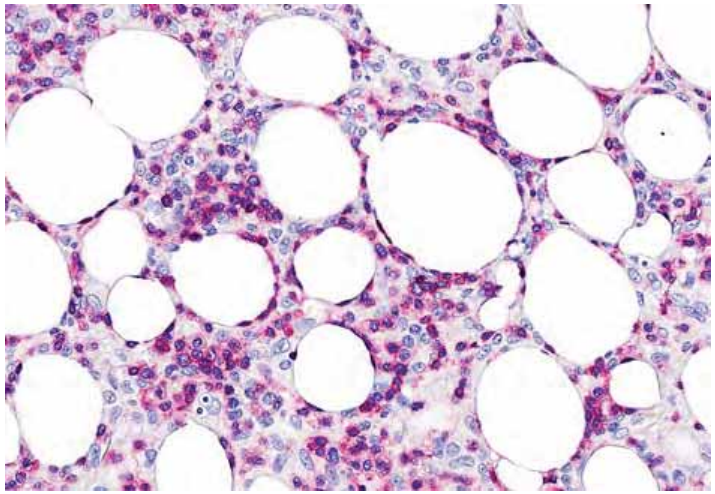
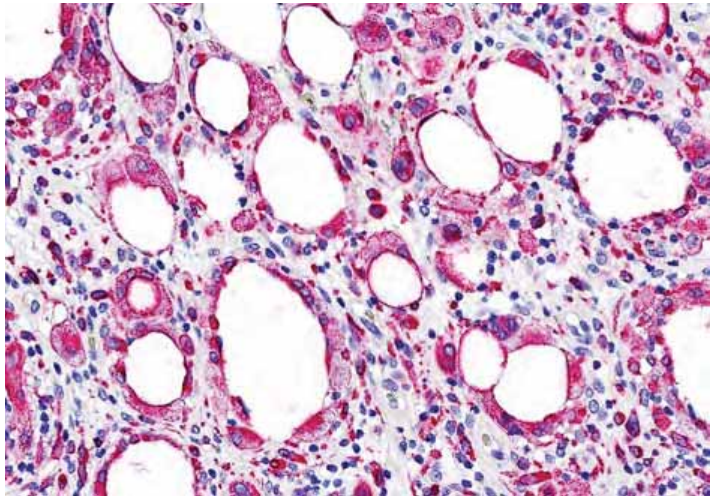




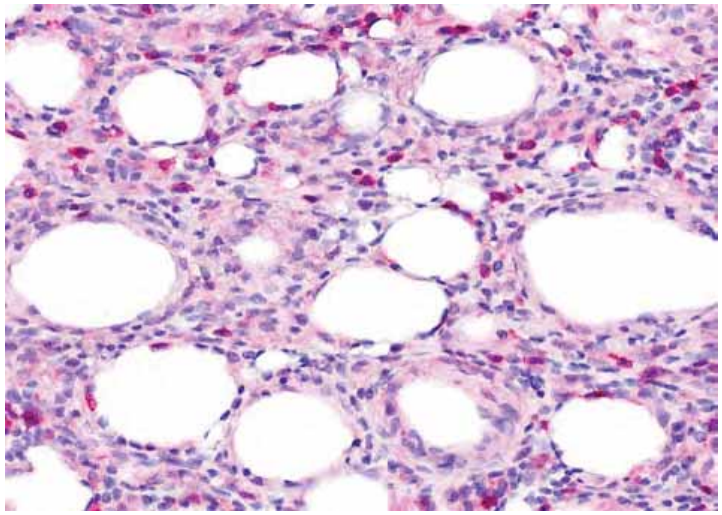
CD3

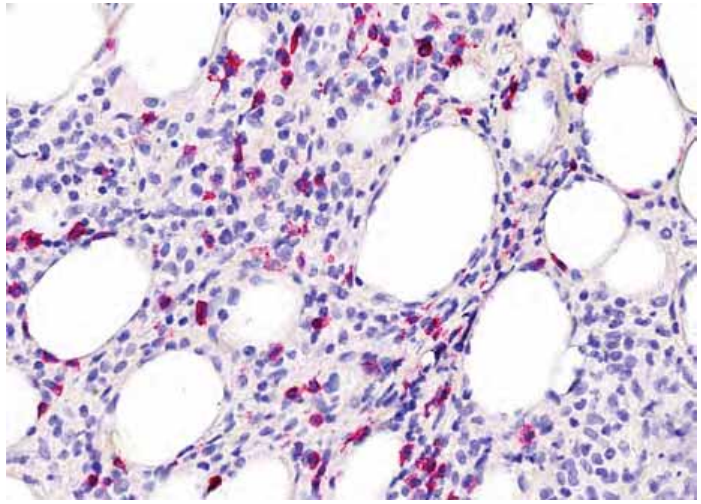




CD68

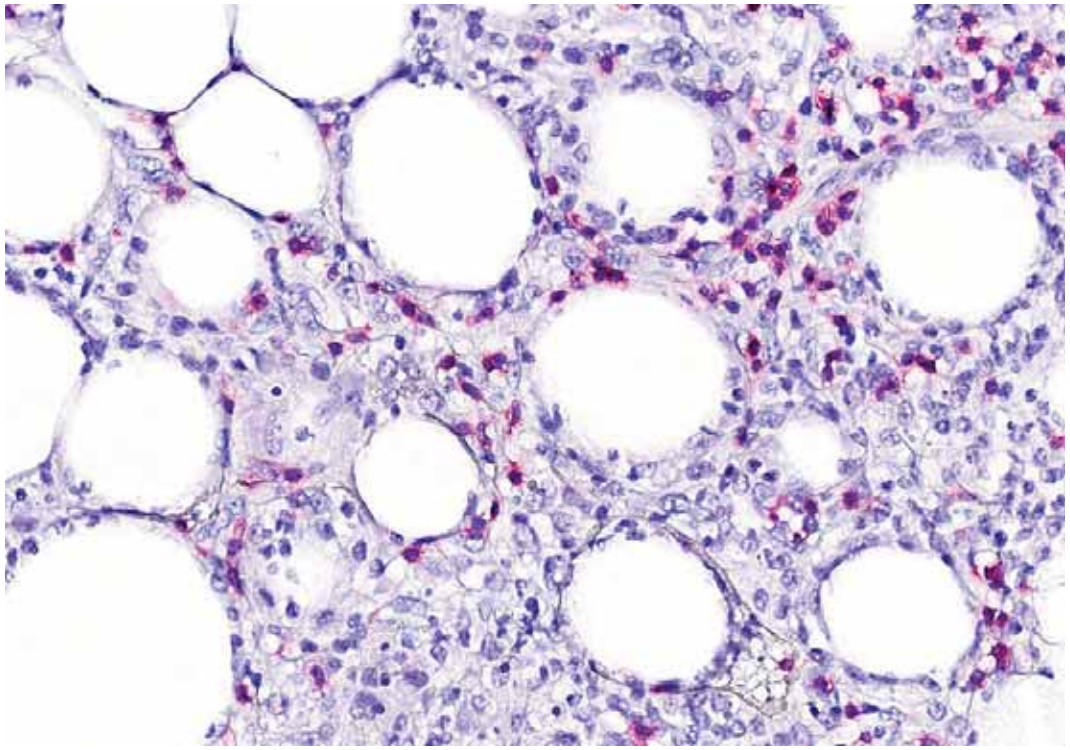
CD4



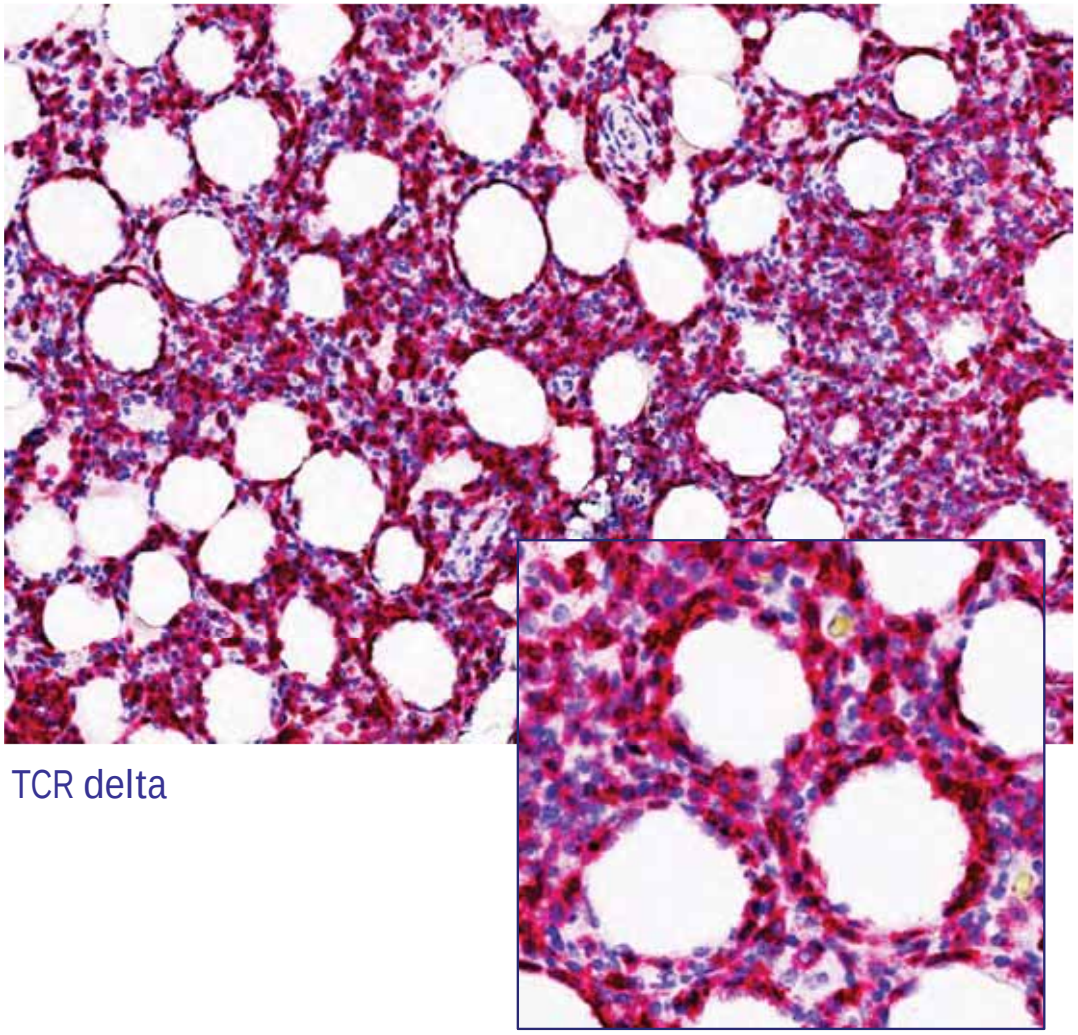


CD8

CD3+ CD4- CD8- CD30- CD56- CD123- CD138 (+), Ki67 low (< 5%); Germinal centers with B-cells

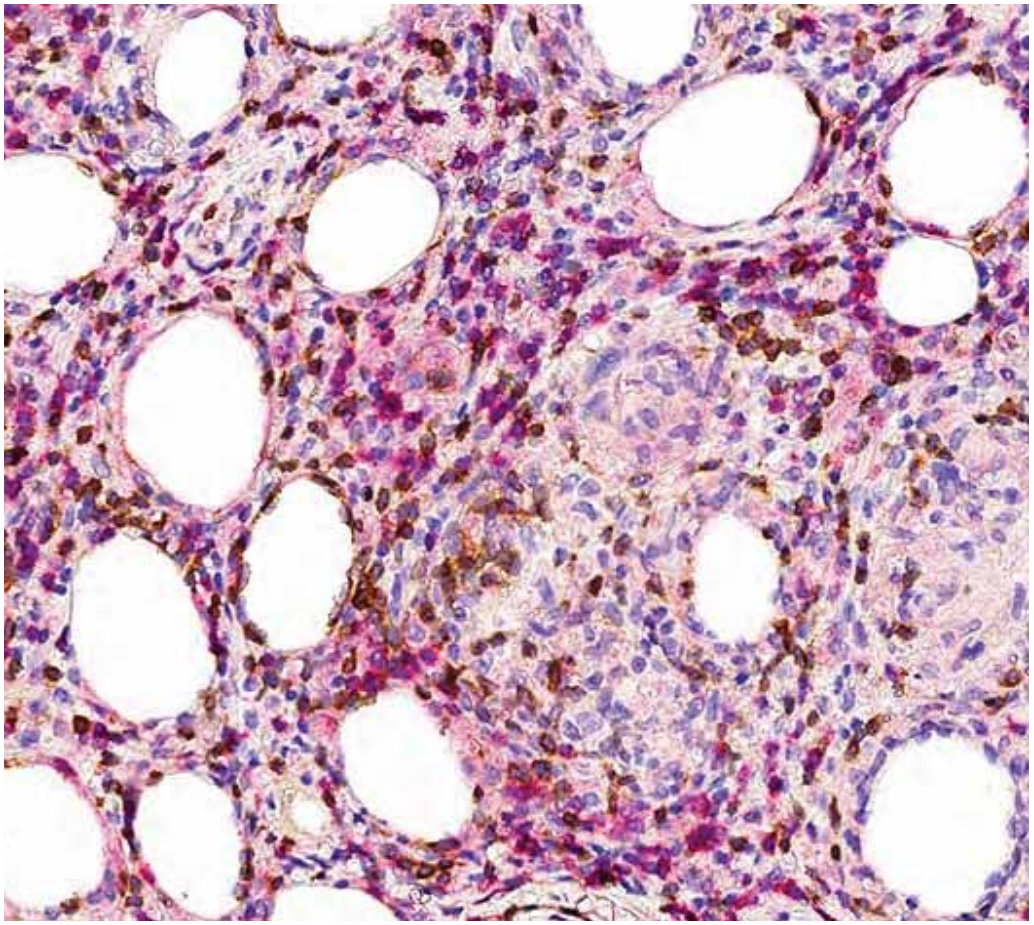


TCR betaF1

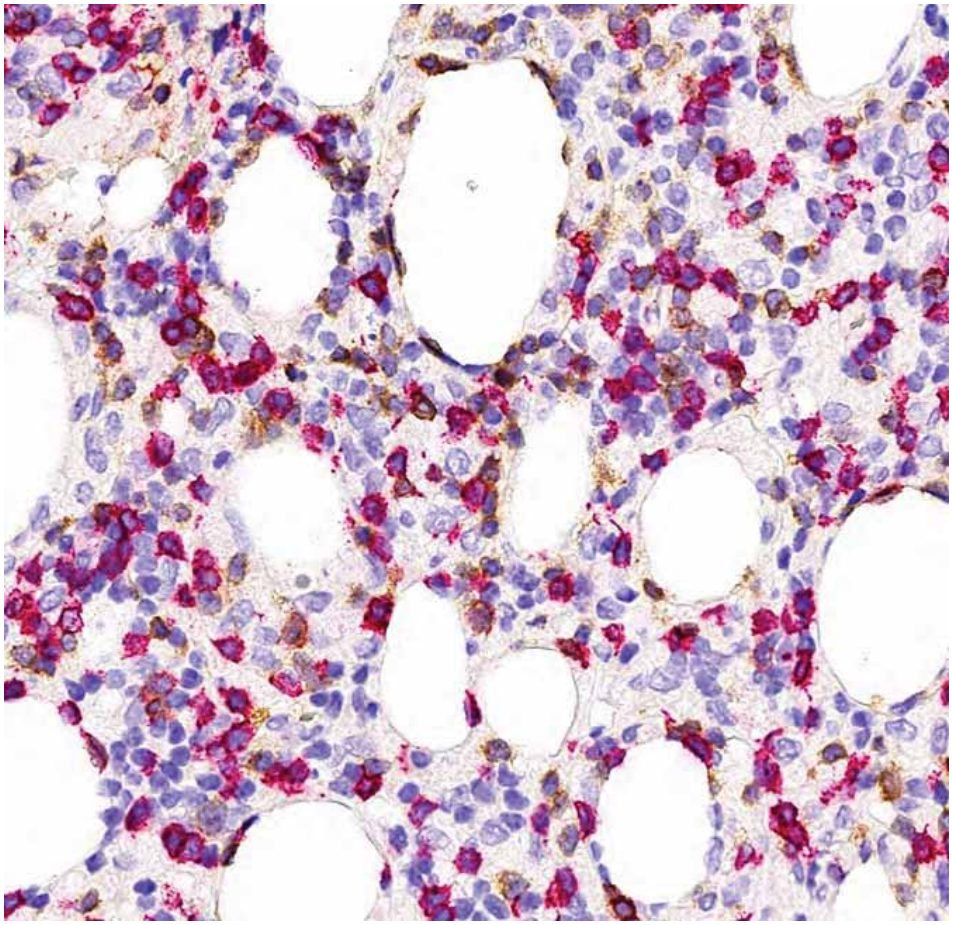


TCR delta

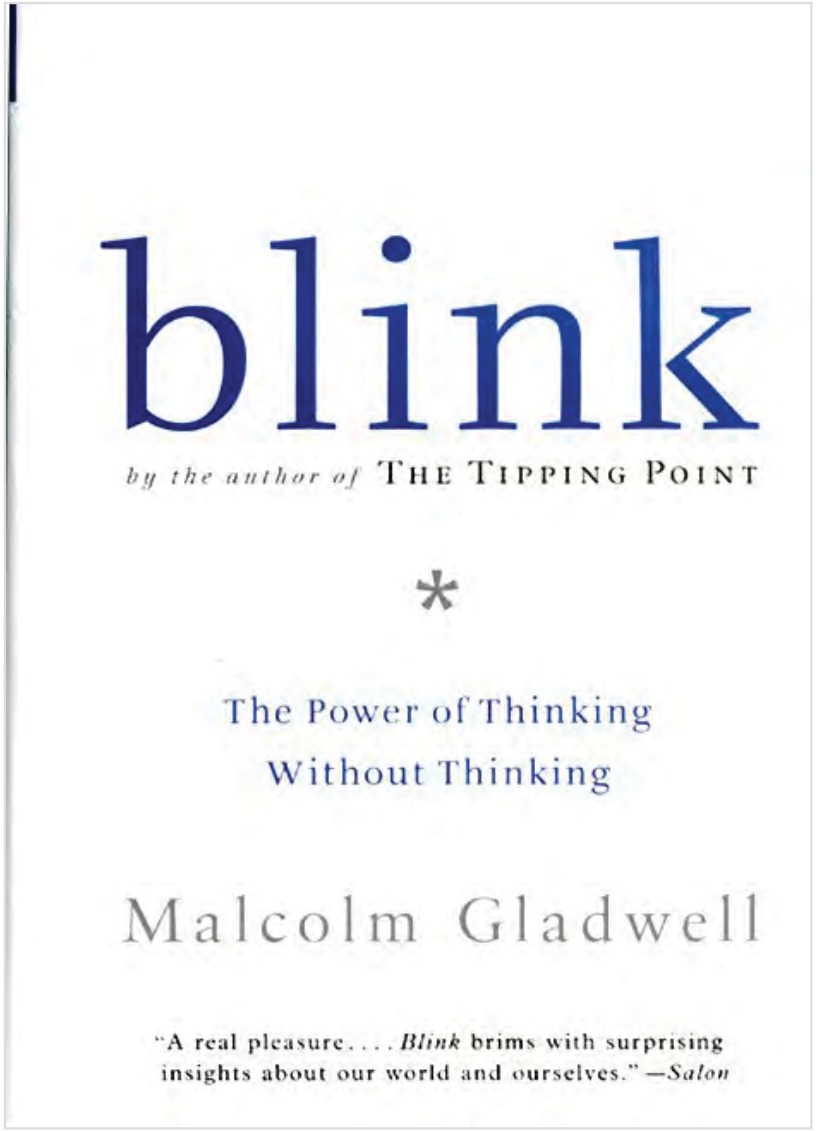
Monoclonal T-cell rearrangement of TCR gamma genes



TCR delta/CD4

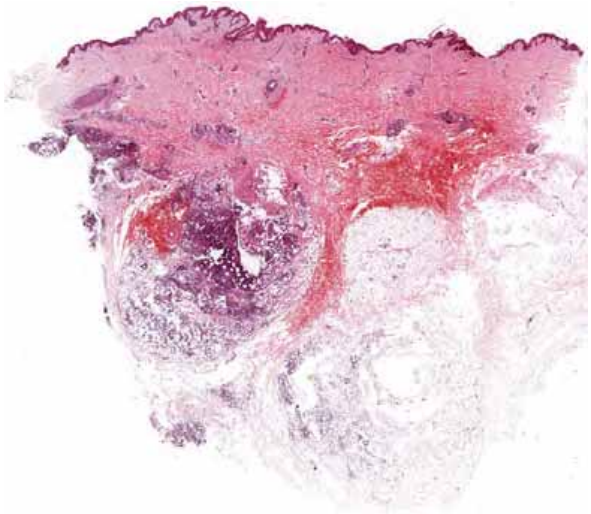


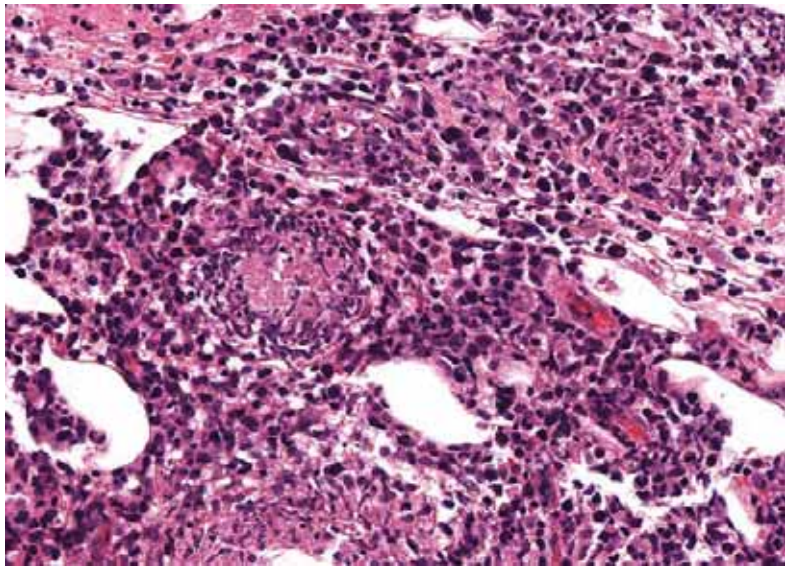
TCR delta/CD8


blink
by the author of THE TIPPING POINT
*
The Power of Thinking
Without Thinking
Malcolm Gladwell
"A real pleasure. . . . *Blink* brims with surprising insights about our world and ourselves." —*Salon*

# Cutaneous gamma delta T-cell lymphoma

Nodules and plaques
with ulceration





Epidermotropic, dermal and/or subcutaneous lobular infiltrates

Atypical lymphocytes of variable size

Nuclear pleomorphism

CD3+ CD4- CD8- CD56+

TIA-1+ Granzyme B +

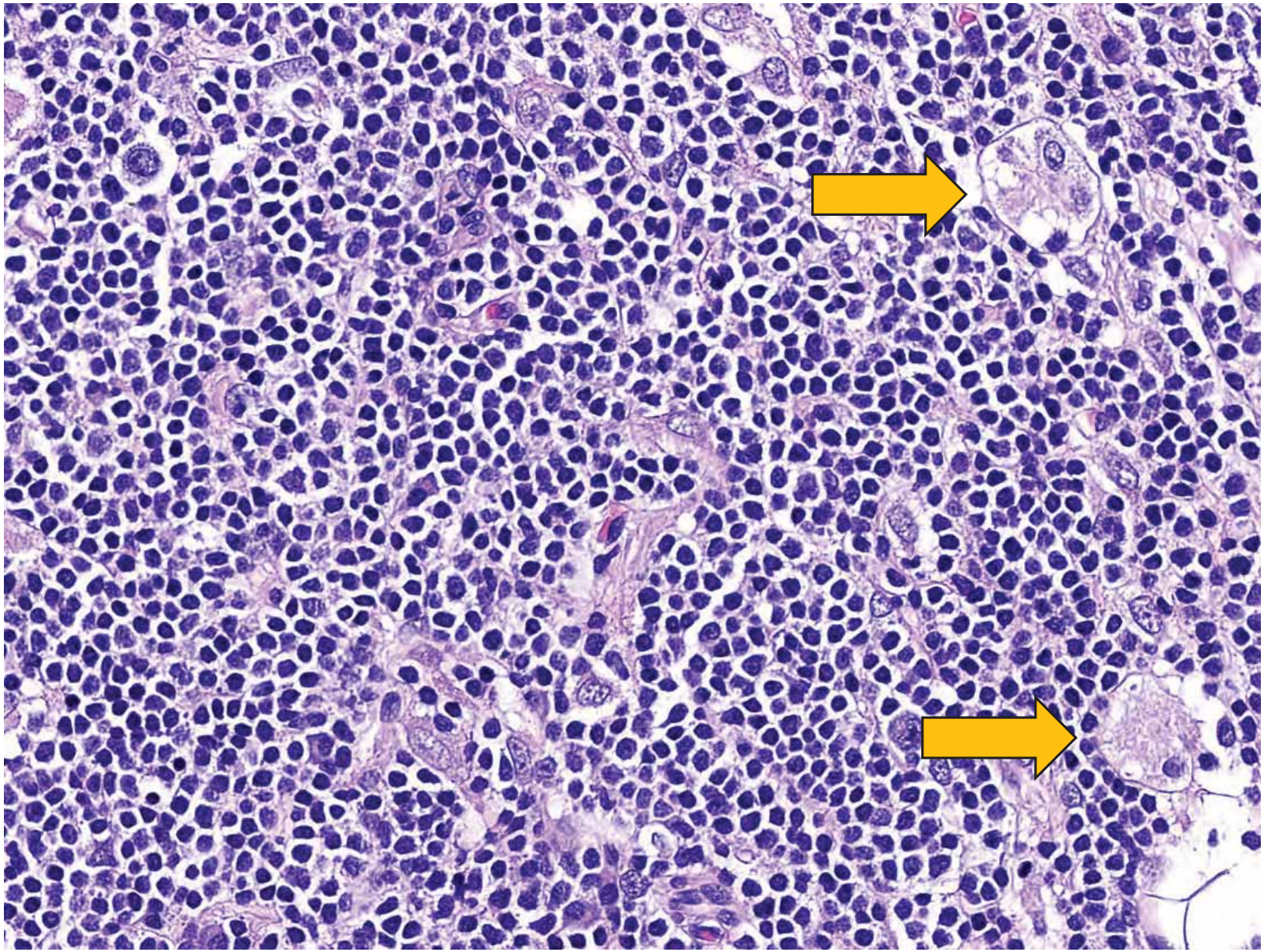
beta F1-

TCR gamma / delta +

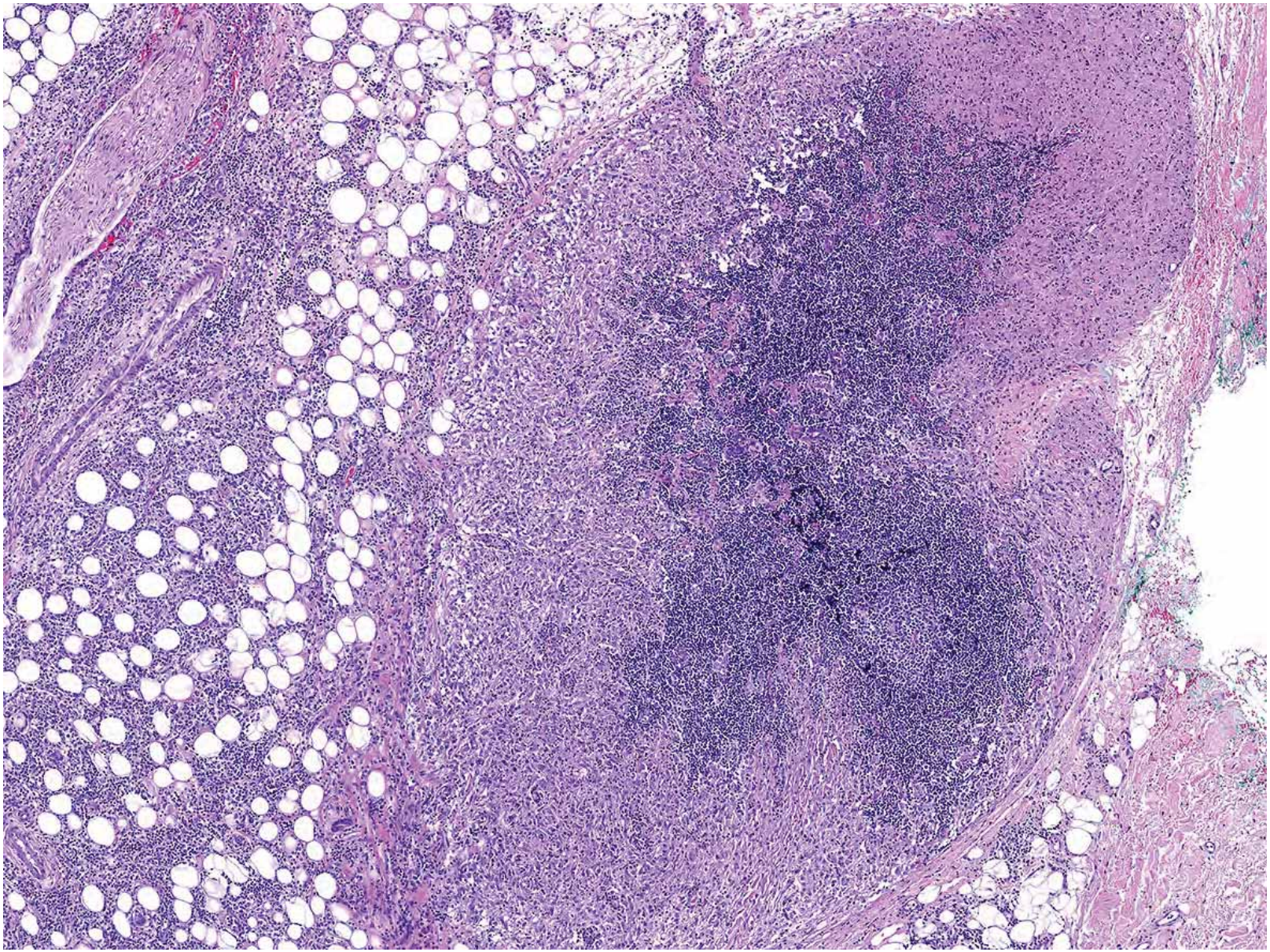
TCR alpha/beta -

EBER-


THE GOOD
THE BAD
AND THE UGLY



K24-133



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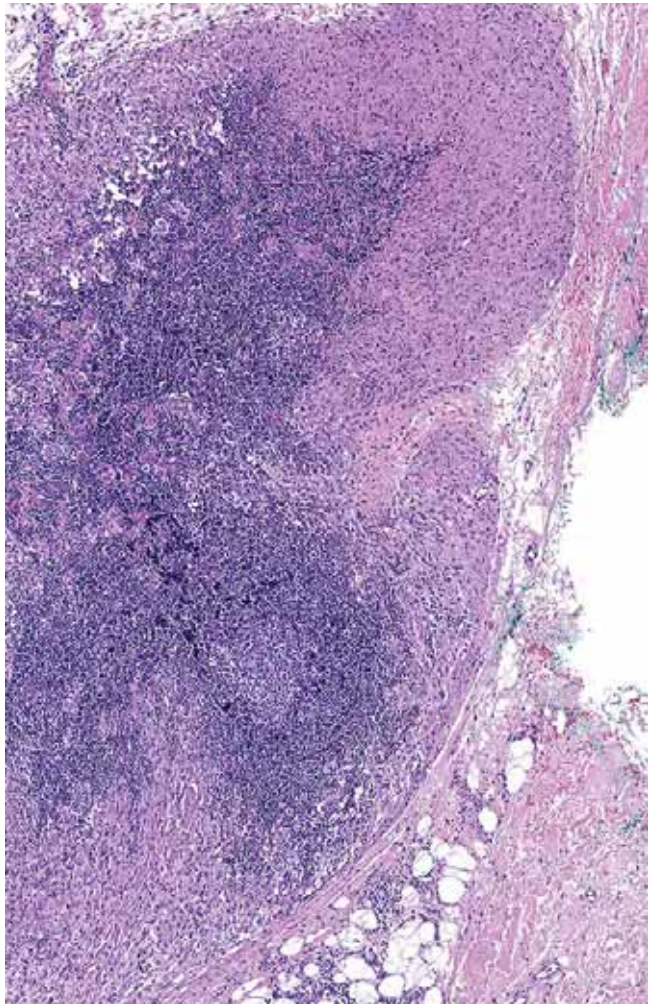
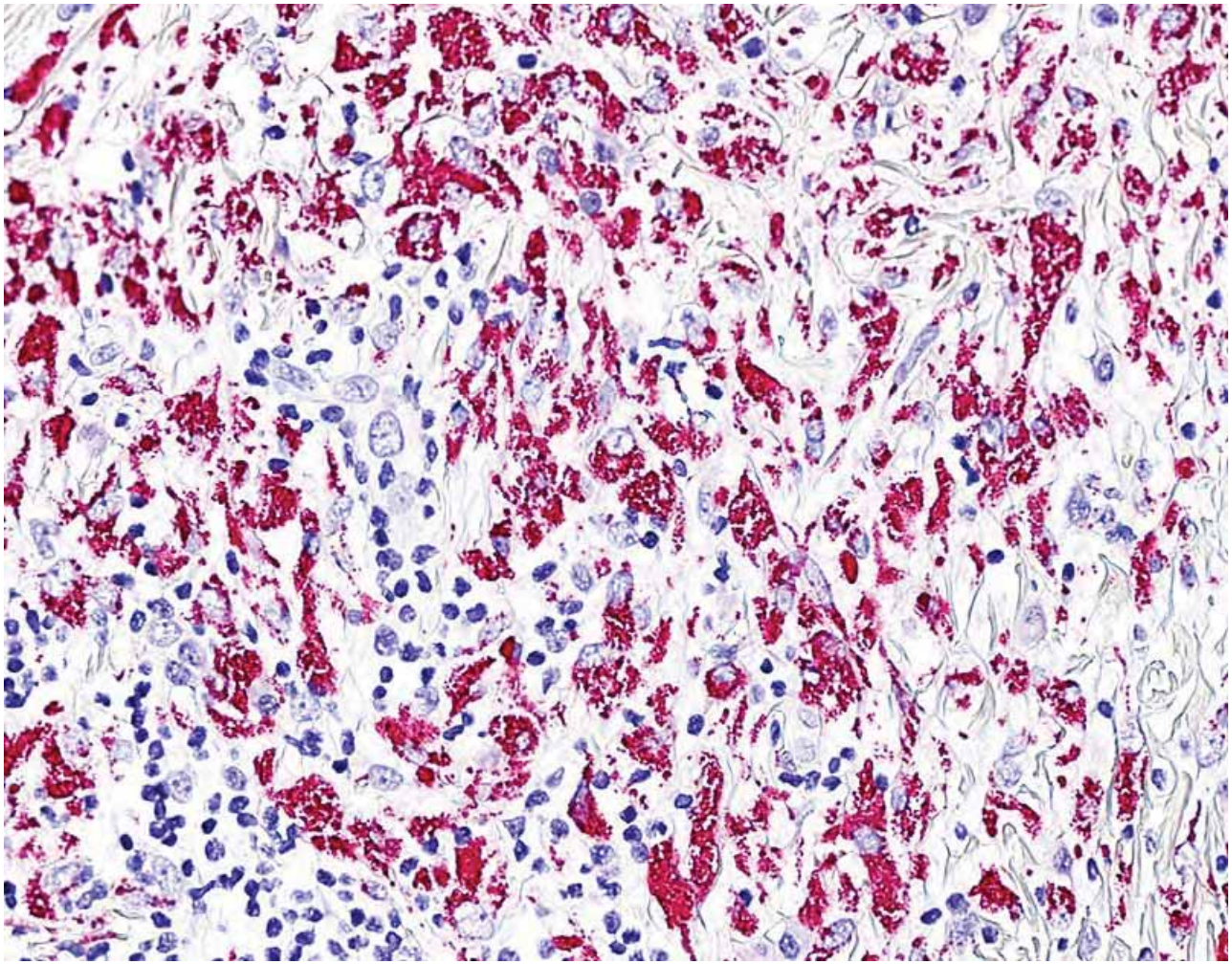
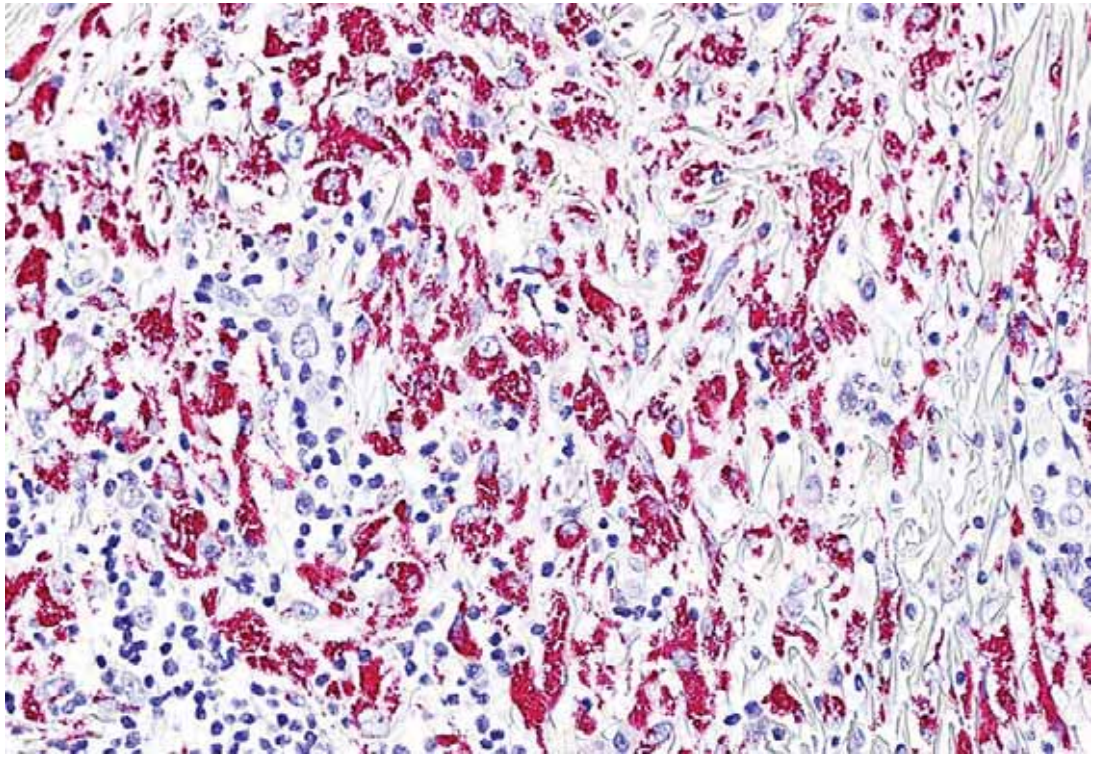




EBER



EBER

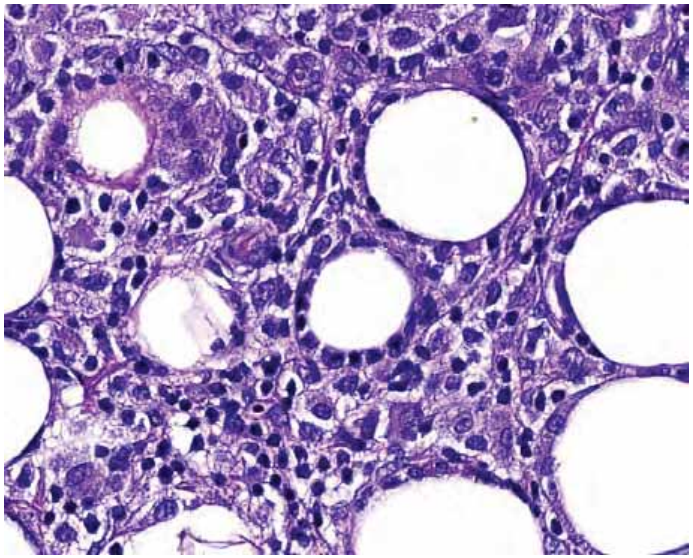
FULL TEXT LINKS

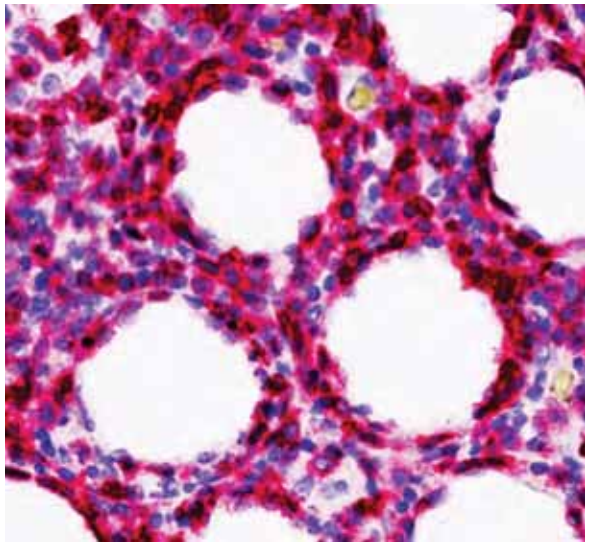
WILEY Full Text Article

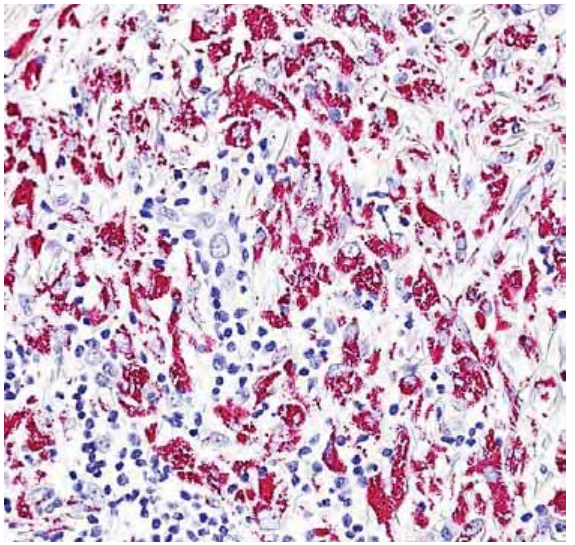
J Cutan Pathol. 2021 May;48(5):625-631. doi: 10.1111/cup.13972. Epub 2021 Feb 11.

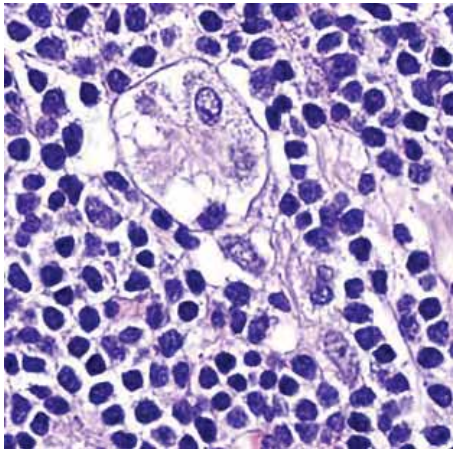
# EBER in situ hybridization in subcutaneous aluminum granulomas/lymphoid hyperplasia: A diagnostic clue to differentiate injection-associated lymphoid hyperplasia from other forms of pseudolymphomas and cutaneous lymphomas

Verena G Frings [1], Sabine Roth [2], Andreas Rosenwald [2], Matthias Goebeler [1], Eva Geissinger [2 3], Marion Wobser [1]

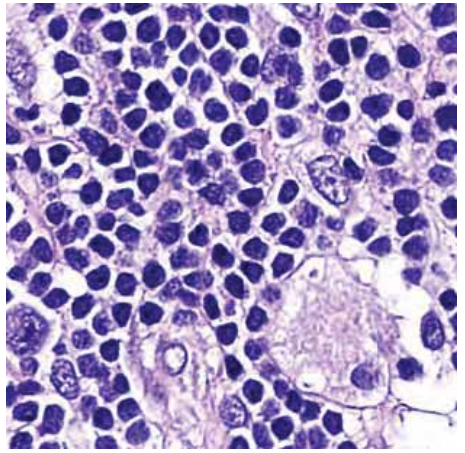




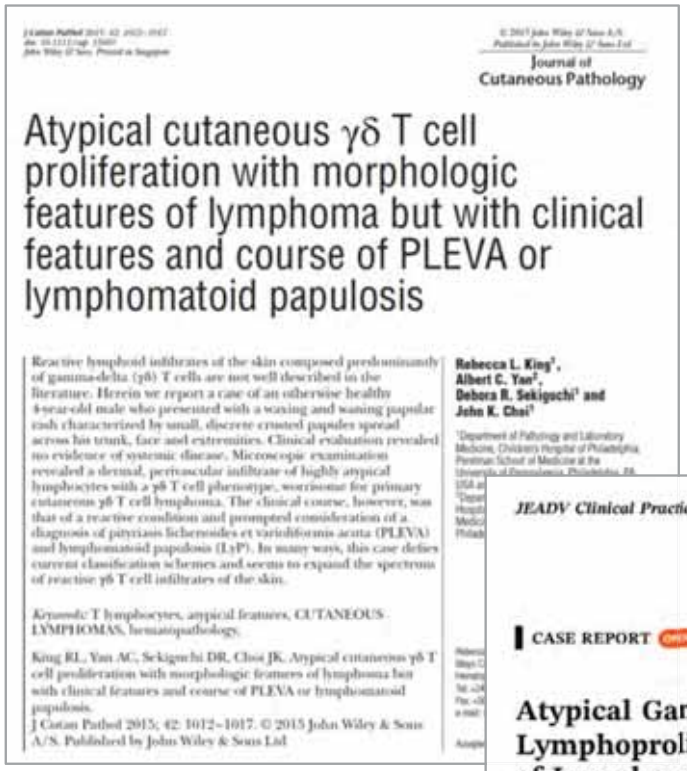




Reactive gamma/delta T-cells lymphoid infiltrate after vacciantion (aluminium hydroxide granuloma)



# Gamma delta T-cells in inflammatory reactions



Journal of Cutaneous Pathology

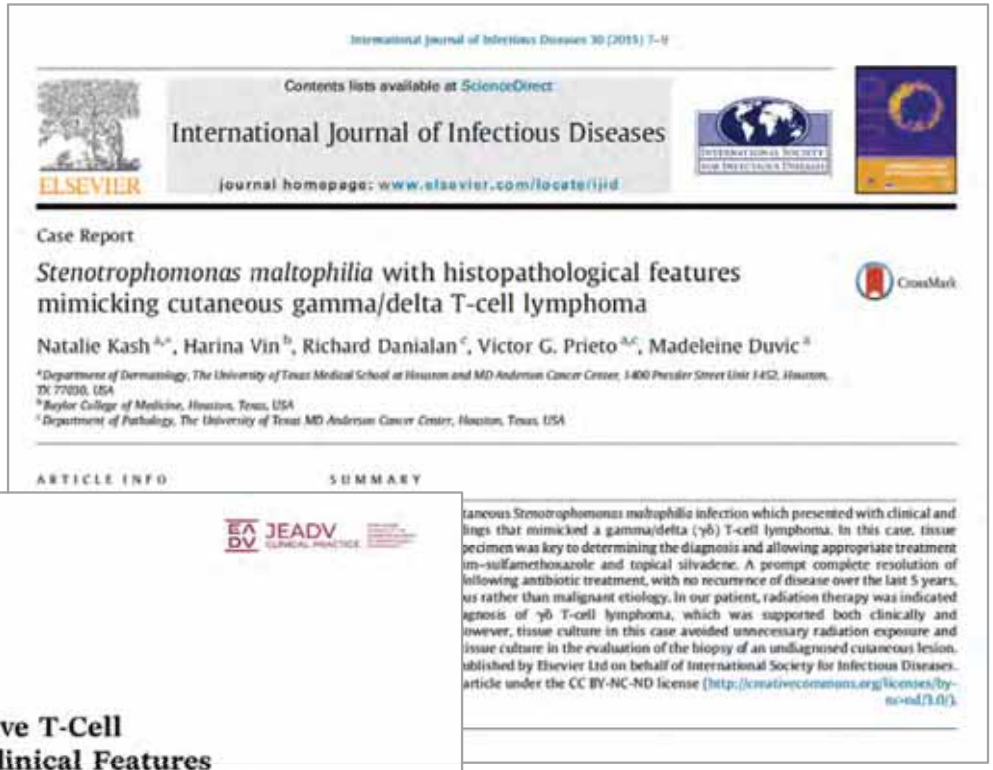
## Atypical cutaneous γδ T cell proliferation with morphologic features of lymphoma but with clinical features and course of PLEVA or lymphomatoid papulosis

Rebecca L. King[1], Albert C. Yan[2], Debora R. Sekiguchi[3] and John K. Choi[1]

Reactive lymphoid infiltrates of the skin composed predominantly of gamma-delta (γδ) T cells are not well described in the literature. Herein we report a case of an otherwise healthy 4-year-old male who presented with a waxing and waning papular rash characterized by small, discrete crusted papules spread across his trunk, face and extremities. Clinical evaluation revealed no evidence of systemic disease. Microscopic examination revealed a dermal, perivascular infiltrate of highly atypical lymphocytes with a γδ T cell phenotype, worrisome for primary cutaneous γδ T cell lymphoma. The clinical course, however, was that of a reactive condition and prompted consideration of a diagnosis of pityriasis lichenoides et varioliformis acuta (PLEVA) and lymphomatoid papulosis (LyP). In many ways, this case defies current classification schemes and seems to expand the spectrum of reactive γδ T cell infiltrates of the skin.

*Keywords:* T lymphocytes, atypical features, CUTANEOUS LYMPHOMAS, hematopathology.

King RL, Yan AC, Sekiguchi DR, Choi JK. Atypical cutaneous γδ T cell proliferation with morphologic features of lymphoma but with clinical features and course of PLEVA or lymphomatoid papulosis. J Cutan Pathol 2015; 42: 1012–1017. © 2015 John Wiley & Sons A/S. Published by John Wiley & Sons Ltd



International Journal of Infectious Diseases 30 (2015) 7–9

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Case Report

## *Stenotrophomonas maltophilia* with histopathological features mimicking cutaneous gamma/delta T-cell lymphoma

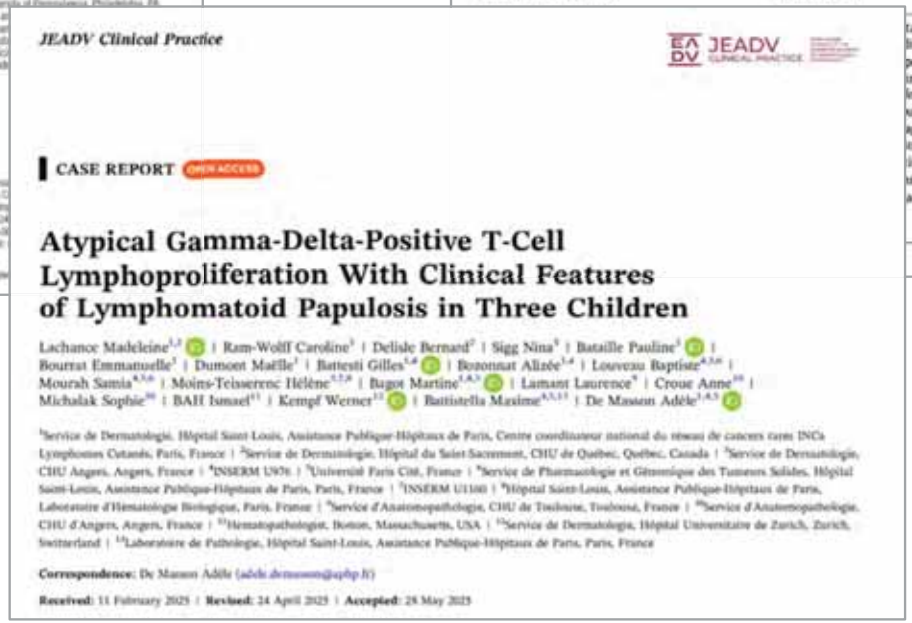
Natalie Kash[a,*], Harina Vin[b], Richard Danialan[c], Victor G. Prieto[a,c], Madeleine Duvic[a]

[a] Department of Dermatology, The University of Texas Medical School at Houston and MD Anderson Cancer Center, 1400 Pressler Street Unit 1452, Houston, TX 77030, USA
[b] Baylor College of Medicine, Houston, Texas, USA
[c] Department of Pathology, The University of Texas MD Anderson Cancer Center, Houston, Texas, USA

ARTICLE INFO

SUMMARY

taneous Stenotrophomonas maltophilia infection which presented with clinical and lings that mimicked a gamma/delta (γδ) T-cell lymphoma. In this case, tissue pecimen was key to determining the diagnosis and allowing appropriate treatment m–sulfamethoxazole and topical silvadene. A prompt complete resolution of llowing antibiotic treatment, with no recurrence of disease over the last 5 years, us rather than malignant etiology. In our patient, radiation therapy was indicated agnosis of γδ T-cell lymphoma, which was supported both clinically and owever, tissue culture in this case avoided unnecessary radiation exposure and issue culture in the evaluation of the biopsy of an undiagnosed cutaneous lesion.

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CASE REPORT OPEN ACCESS

## Atypical Gamma-Delta-Positive T-Cell Lymphoproliferation With Clinical Features of Lymphomatoid Papulosis in Three Children

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# Shiitake (Lentinula edodes)

Second most common edible mushroom linked to umami taste.

Natural medicine in China and Japan

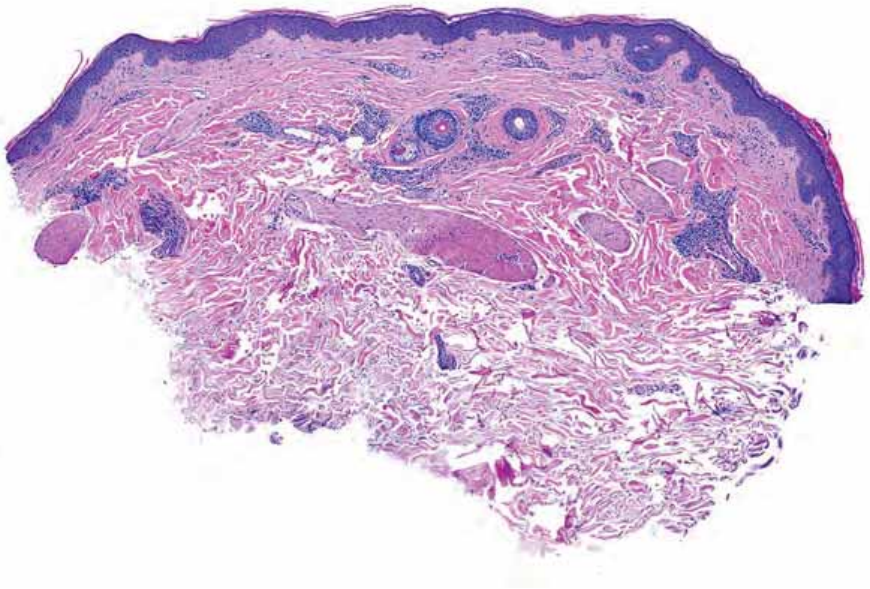
From: Wikipedia

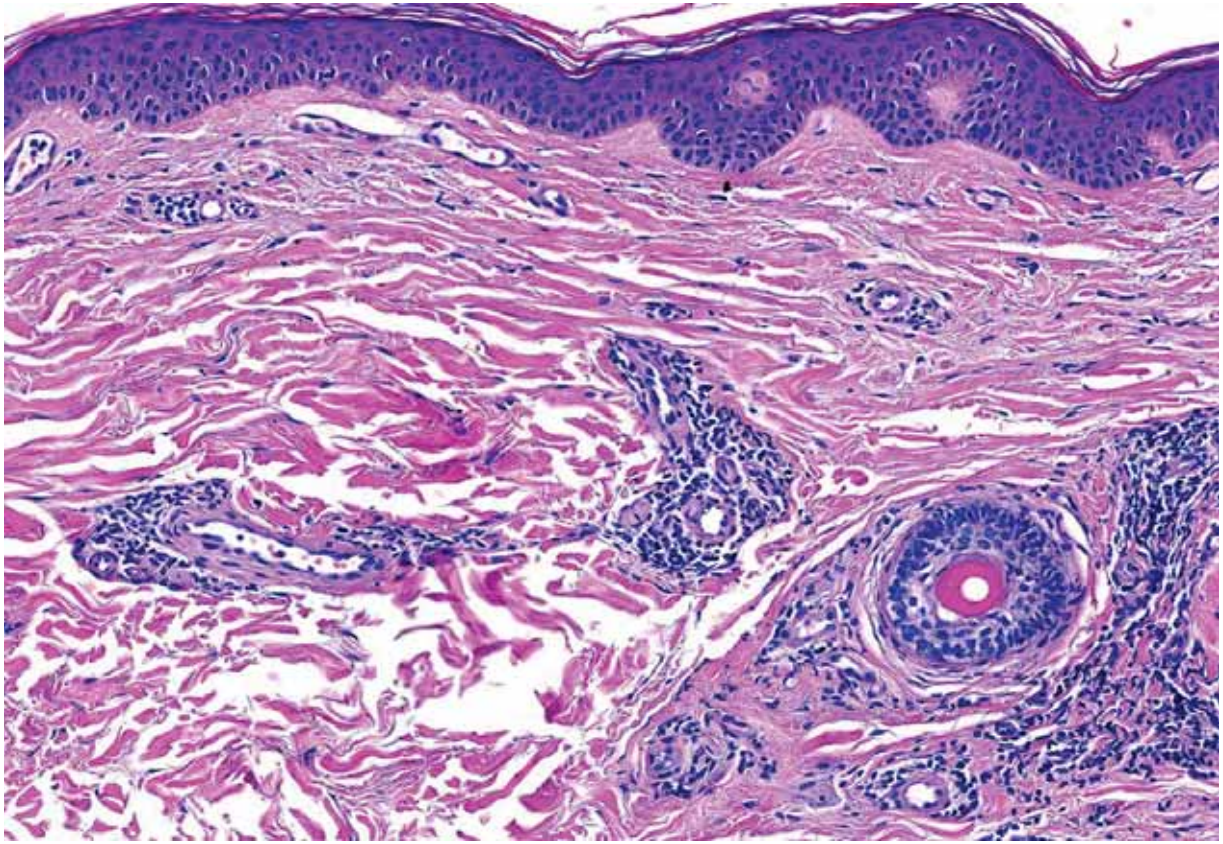
From: asiastreetfood.com

# Shiitake Dermatitis



Images: Dr. med. Daniel Mahler, Lucerne





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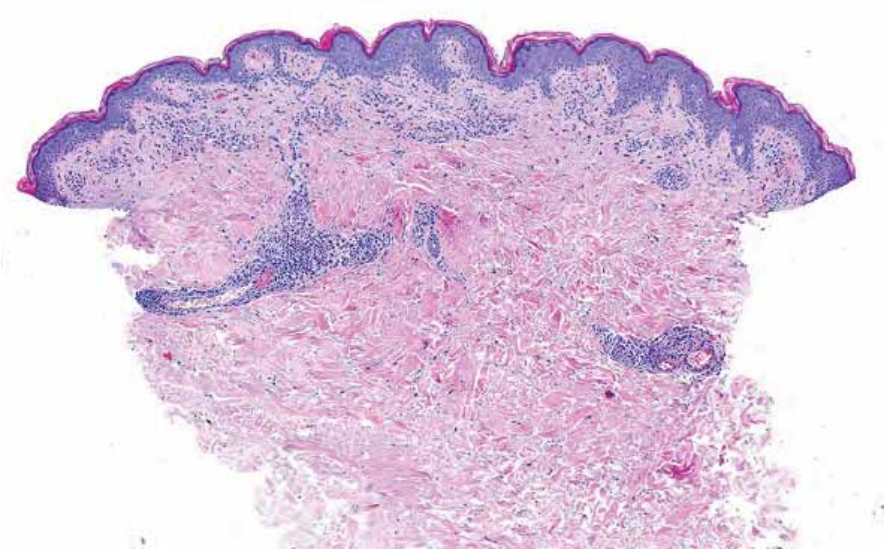

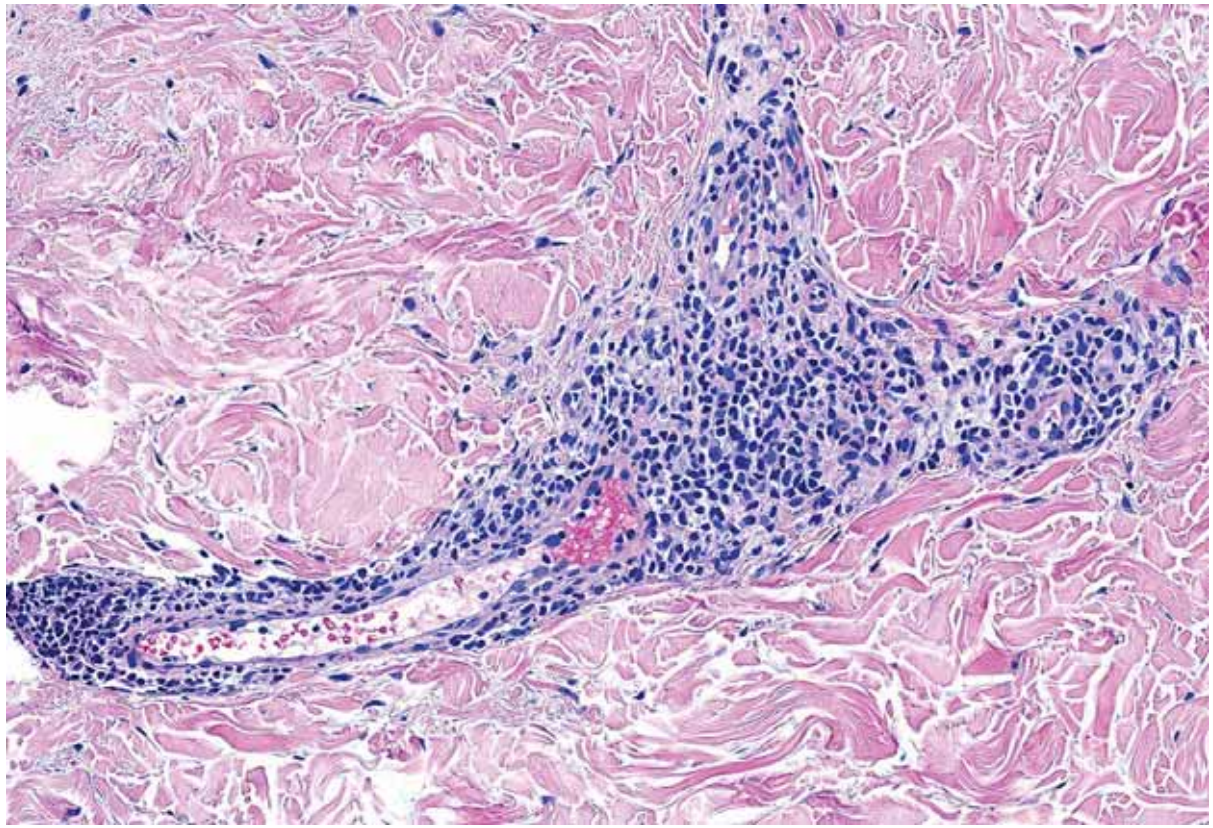

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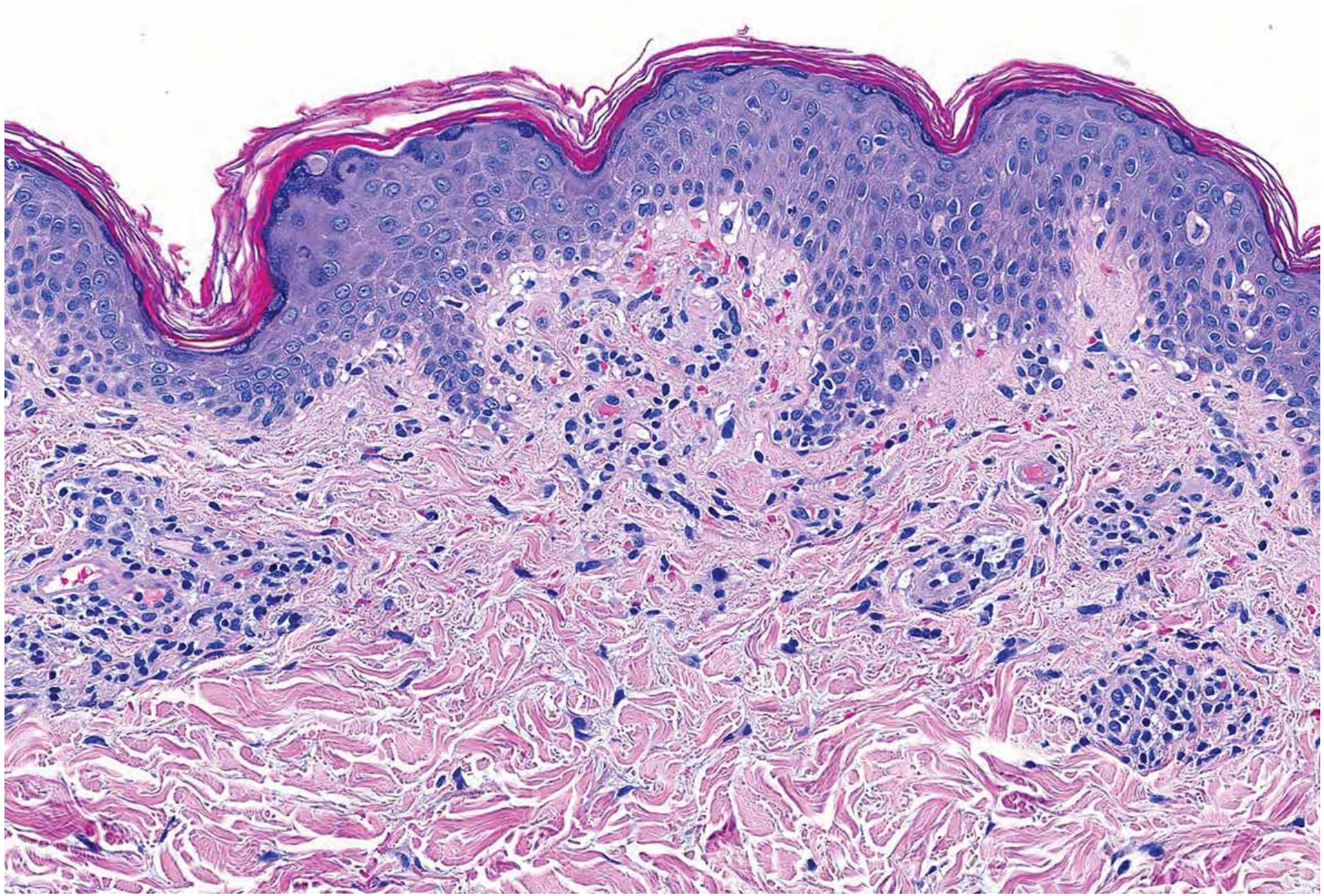

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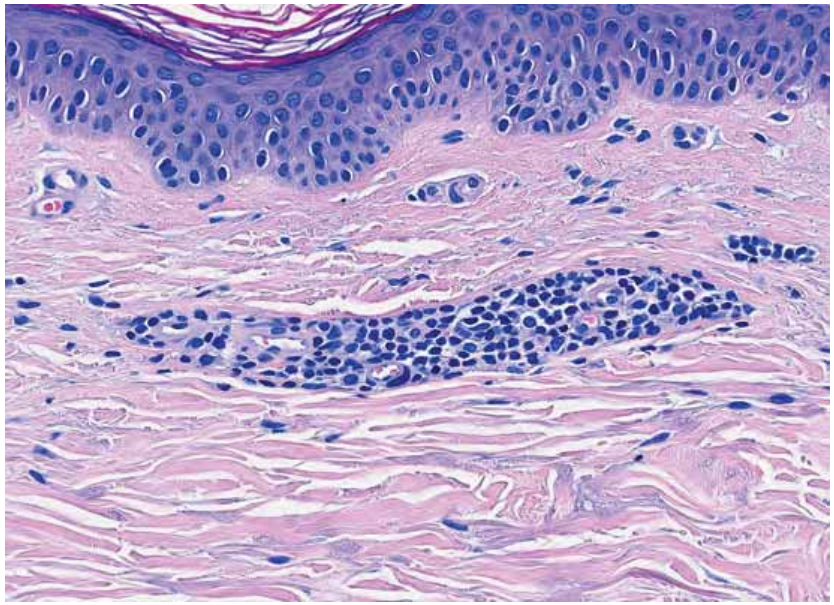
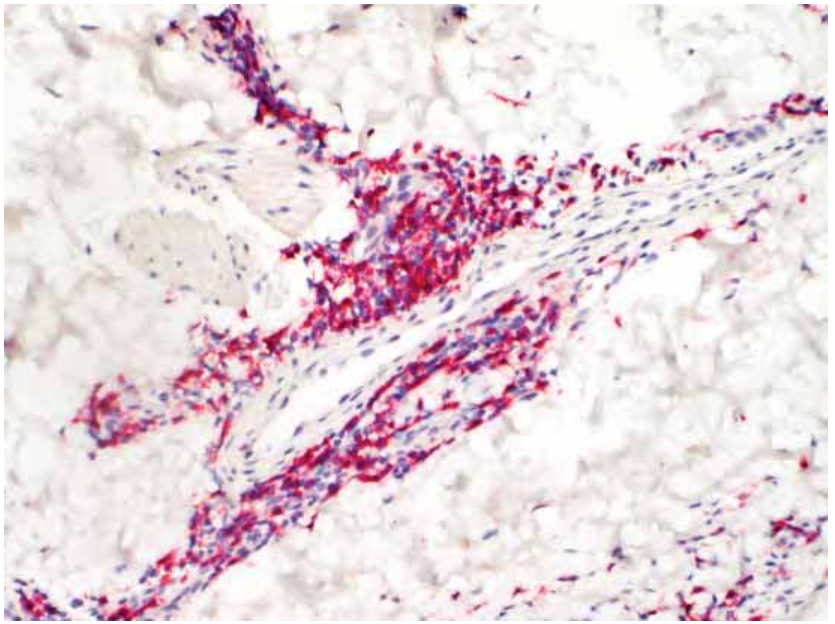
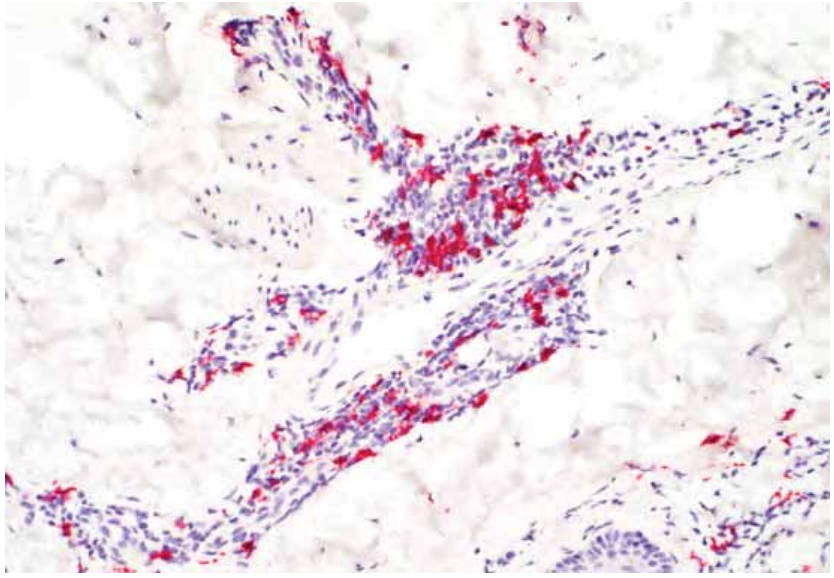
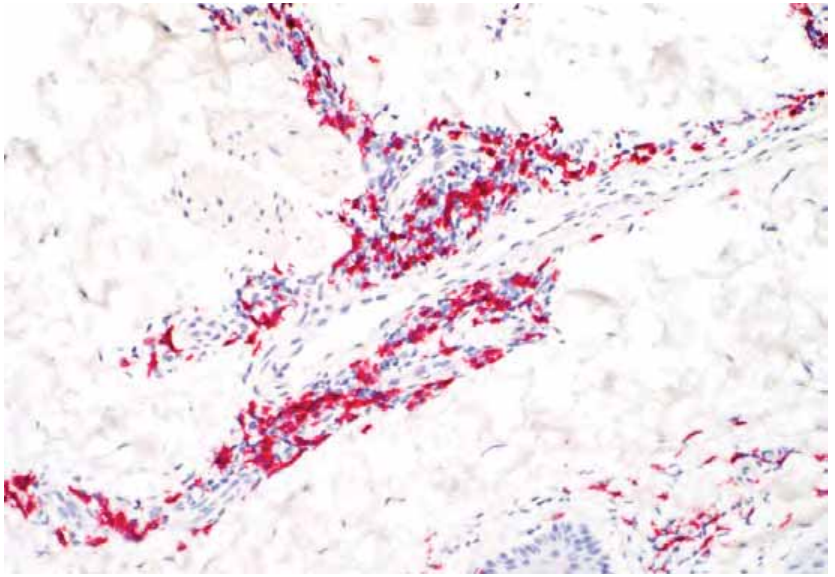




CD4

CD20





CD8

# Shiitake dermatitis

First reported case outside Asia in Finland in 1998

Skin: Flagellate linear pattern on trunk, extremities and neck
Oral mucosa: erosions without a linear pattern.

Histology
Spongiosis
Superficial dermal cuff-shaped perivascular lymphocytic infiltrate

DDx:
Flagellate drug reactions due to bleomycin and trastuzumab
Phytophotodermatitis
Adult-onset Still's disease

Course:
Resolution usually within 8 weeks. No long-term sequelae.

Stephany et al. Am J Clin Dermatol 2016

*Fully cook (20 min.) shiitake prior to ingestion!*

From: Janusonyte & Pünchera N Engl J Med 2023