

LIVERPOOL DERMPATH UPDATE 2017

The ABC^{D,E,F}_^ of Lymphomatoid Papulosis

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Lymphomatoid papulosis

1st described in 1968 by Warren Macaulay to describe a continually self healing eruption that was clinically benign but histologically malignant.

Belongs to the spectrum of CD30 positive T cell lymphoproliferative disorders

Included in the WHO-EORTC classification of cutaneous lymphoma

Why LyP?

- Should a general pathologist diagnose LyP?
- Should all cases be referred to a specialist centre or specialist cutaneous lymphoma MDT for a second opinion?
- Can this entity be diagnosed histologically or is it more of a clinical diagnosis?

Clinical Presentation

- Crops of erythematous papules that develop over 3-4 weeks
- Can undergo necrosis and ulceration
- Heal spontaneously over weeks or months, may leave atrophic scars
- Typically lesions 'come and go', waxing and waning course





Disease Course



- Typically, lesions in different stages of evolution
- Overall disease course is chronic lasting years or decades
- Lesions can be limited and asymptomatic or widespread/mildly pruritic/disfiguring

Management of LyP

- Observation and follow up
- Topical steroids
- Low dose methotrexate
- PUVA

Excellent prognosis!!

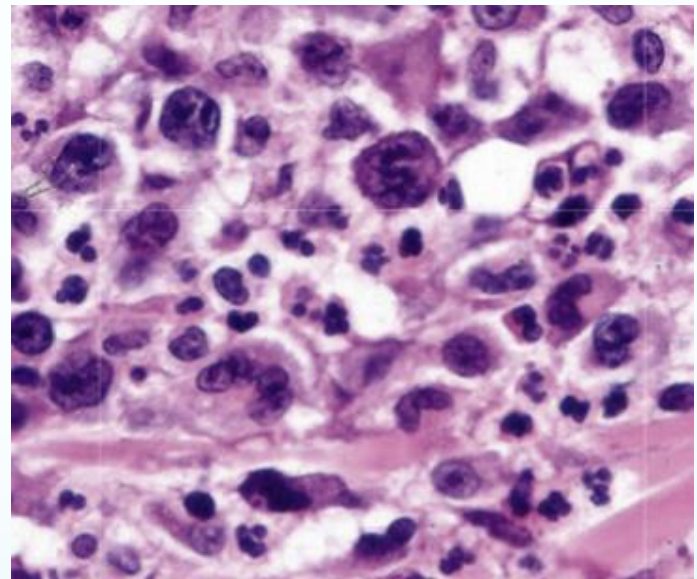
Why is LyP included in the WHO-EORTC
Classification of Cutaneous Lymphomas?

Why is LyP classified as Cutaneous Lymphoma?

1. 5-20% show association with a second malignant lymphoma (either preceding, concomitant, subsequent)
2. 40-100% of LyP skin lesions show monoclonal rearrangement of TCR genes.
3. ??

Histological Hallmark

- Large atypical CD30 + T cells (including bi and multinucleate forms).
- CD30 is cell surface cytokine receptor (belonging to TNF receptor superfamily)
- Large number of inflammatory/infective dermatological conditions and haematological malignancies express CD30

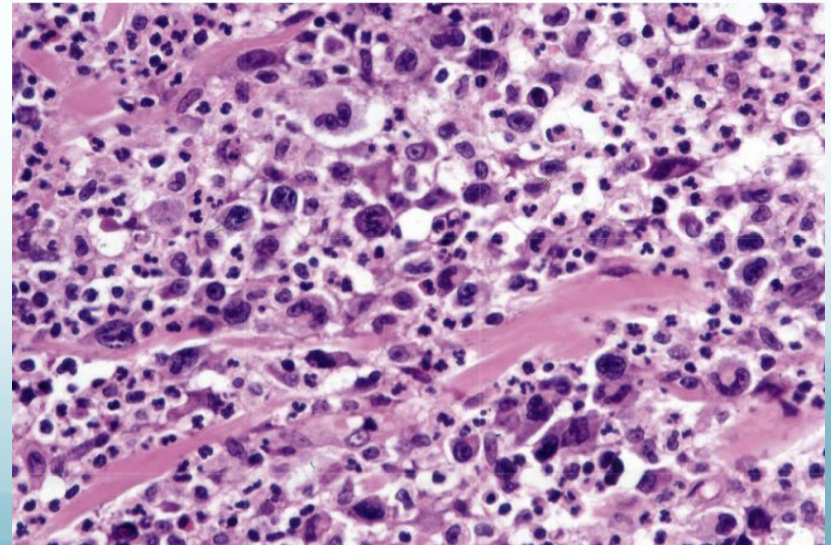
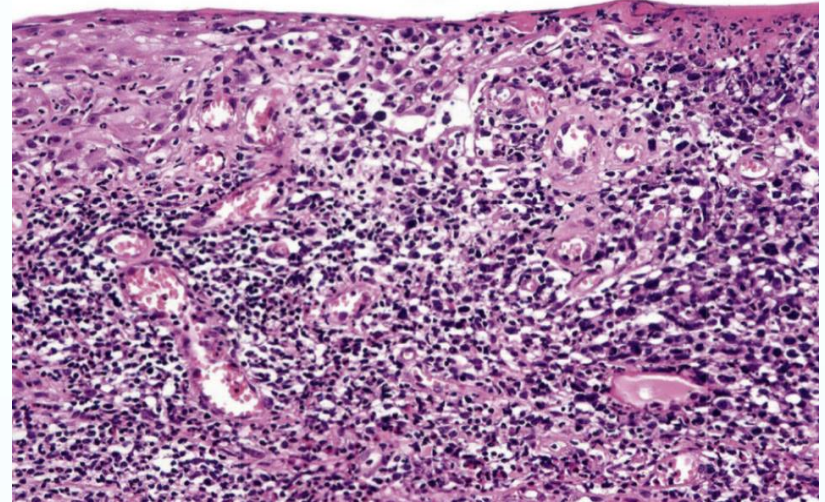


Histopathological Spectrum

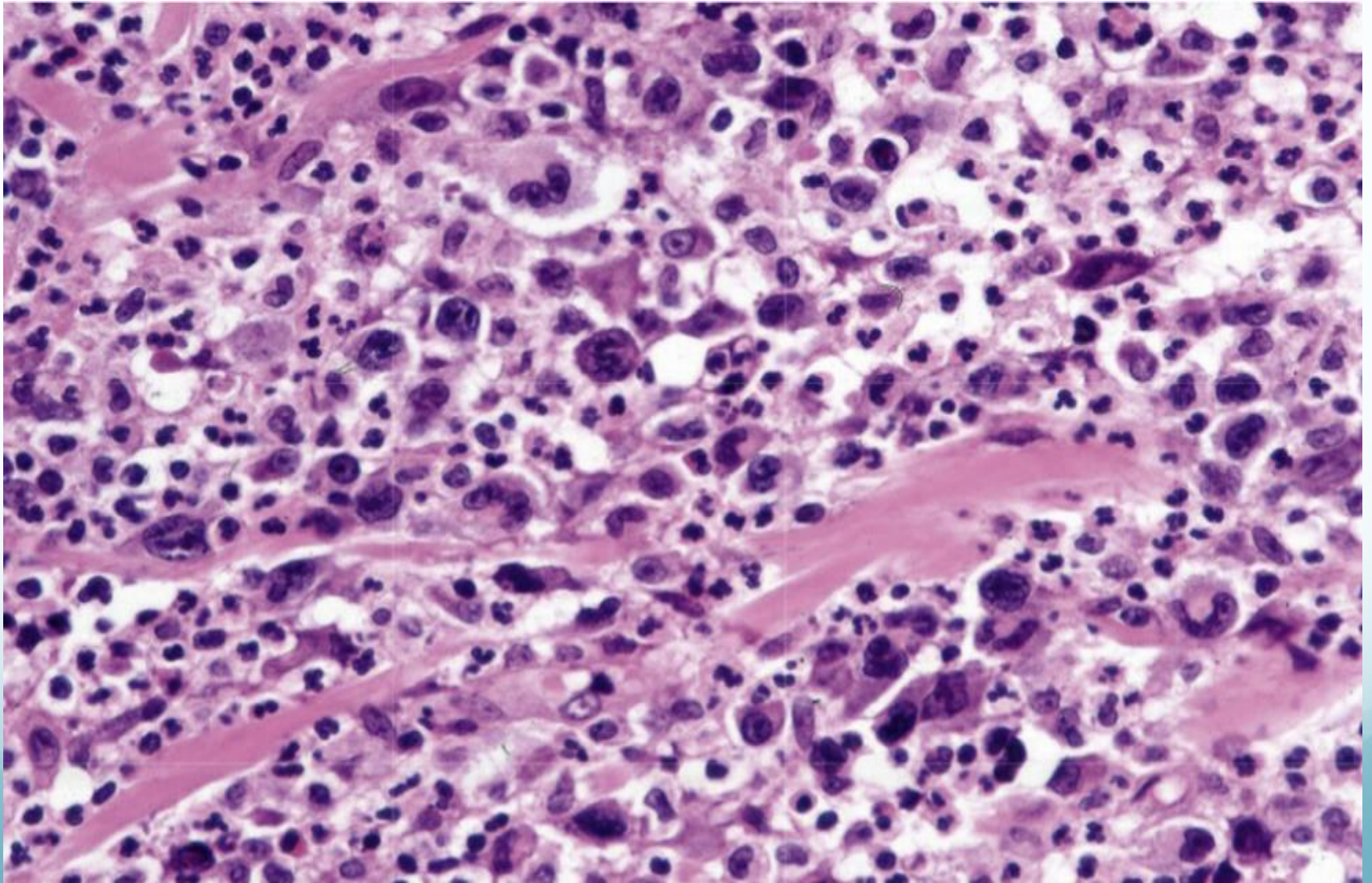
- Type A
- Type B
- Type C
- Type D (epidermotropic)
- Type E (angio-invasive)
- Type F (folliculotropic)
- LyP with 6p25.3 rearrangement

Type A

- Wedge shaped dermal infiltrate with/without surface ulceration.
- Mixed polymorphic infiltrate with large anaplastic cells (15-30 microns) with prominent nucleoli and abundant cytoplasm.
- Bi and multinucleate forms may be seen
- May resemble Reed Stenberg cells.

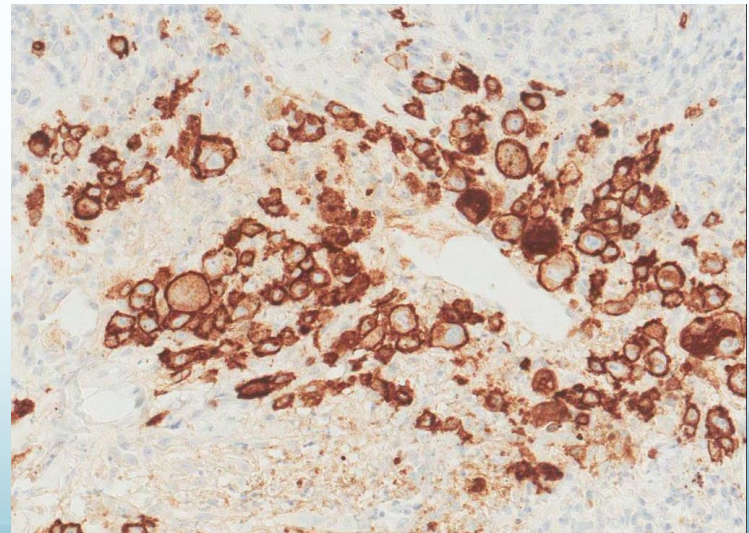
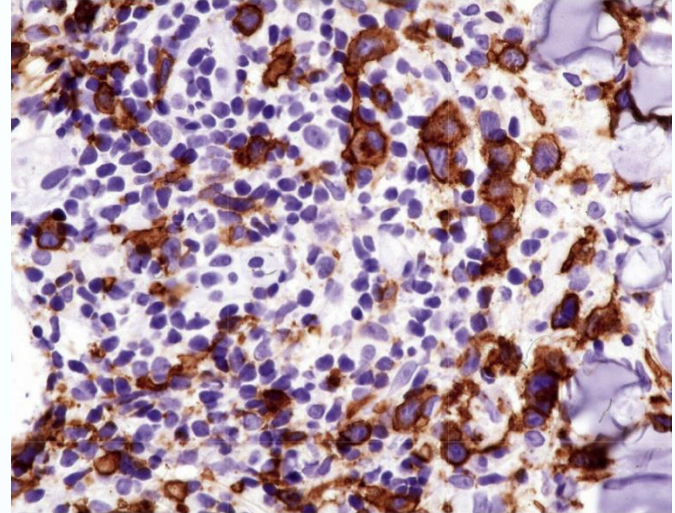


Type A



Immunohistochemistry

- Large cells are CD30 positive
- CD15, EMA, Alk1 negative
- Variable expression of pan T cell antigens (CD2, CD3, CD5, CD7)
- Usually CD4+/CD8-, but may be CD4-/CD8+, CD4-/CD8- or CD4+/CD8+



CD30

Histological D/D of Type A LyP

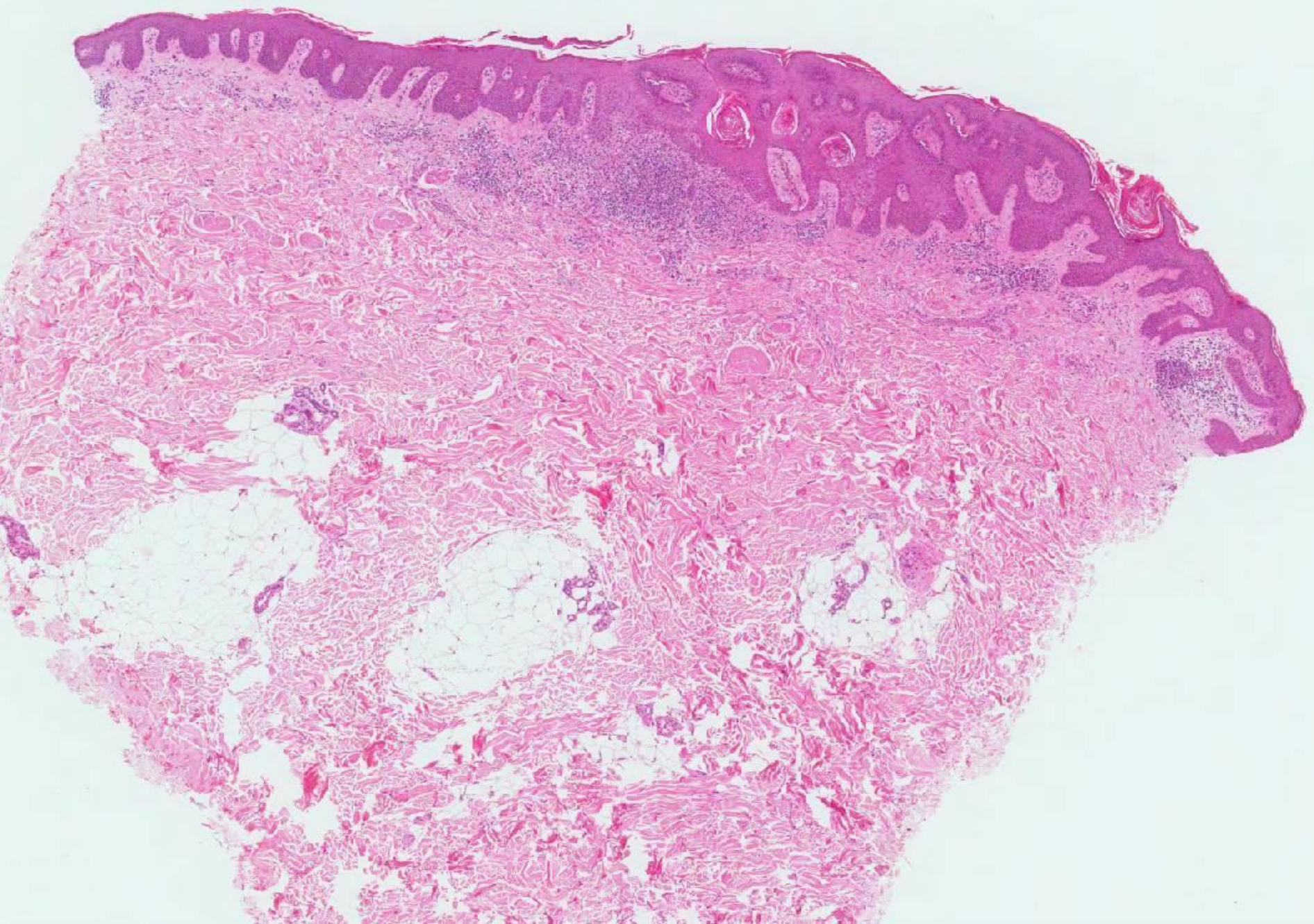
Inflammatory/Infective conditions with CD30 positive blasts:

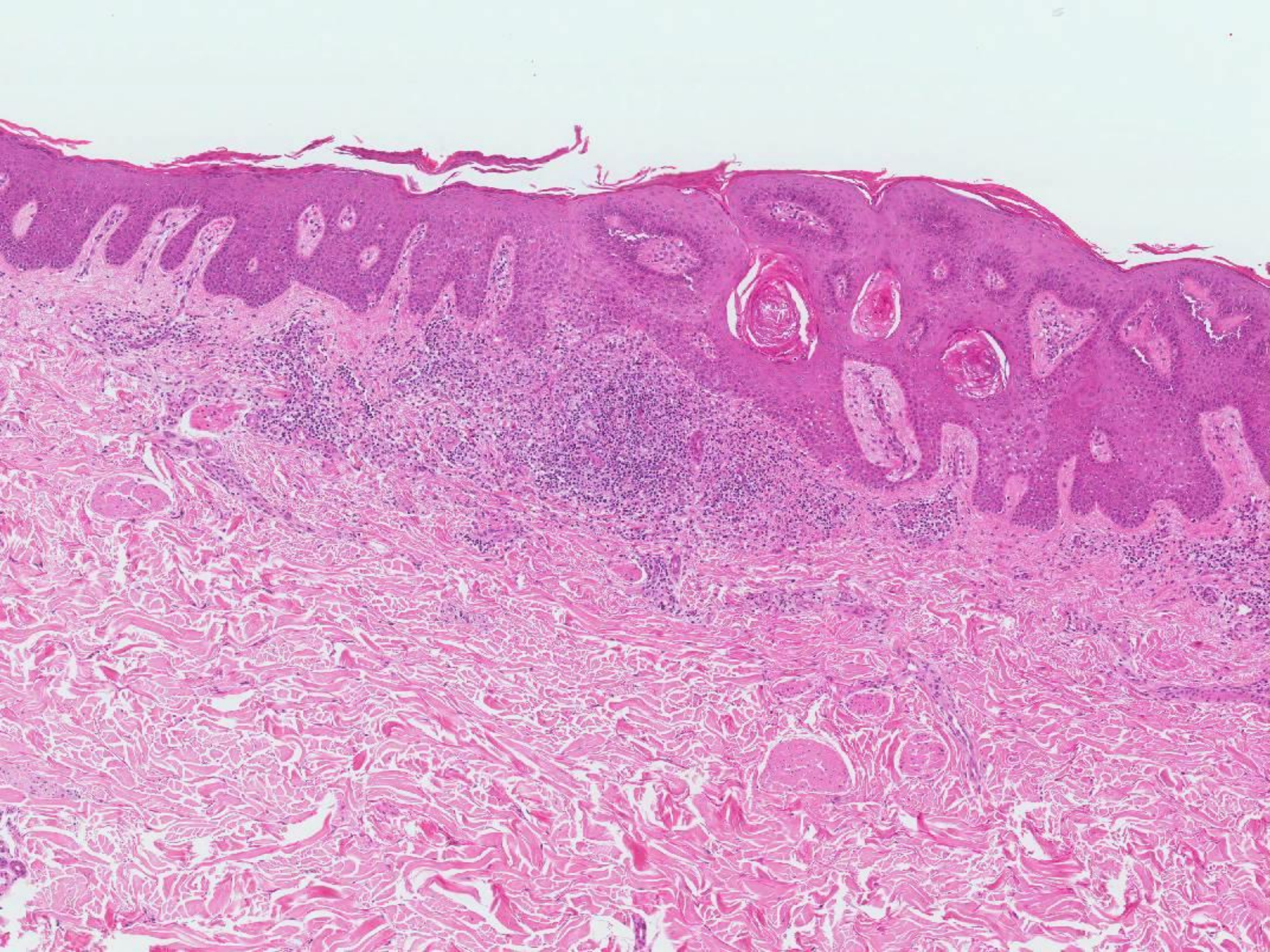
- Arthropod bite reactions
- Scabies
- Viral infections : parapox (Milkers nodule and Orf), herpes virus, molluscum contagiosum.
- Drug induced pseudolymphoma- CD30 rich infiltrates particularly described with Carbamazepine, gemcitabine, terbinafine, cefuroxime.

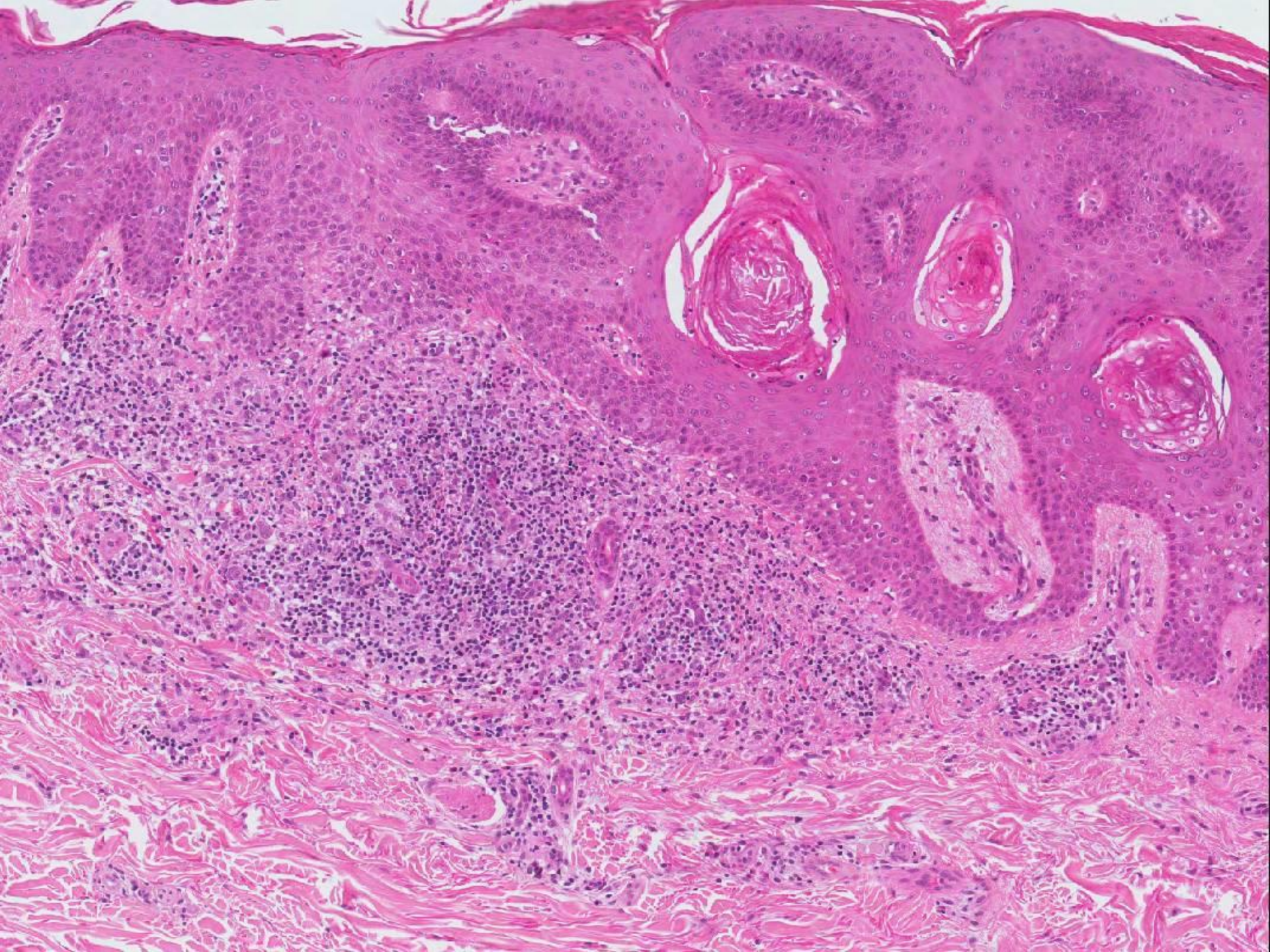
Case 1

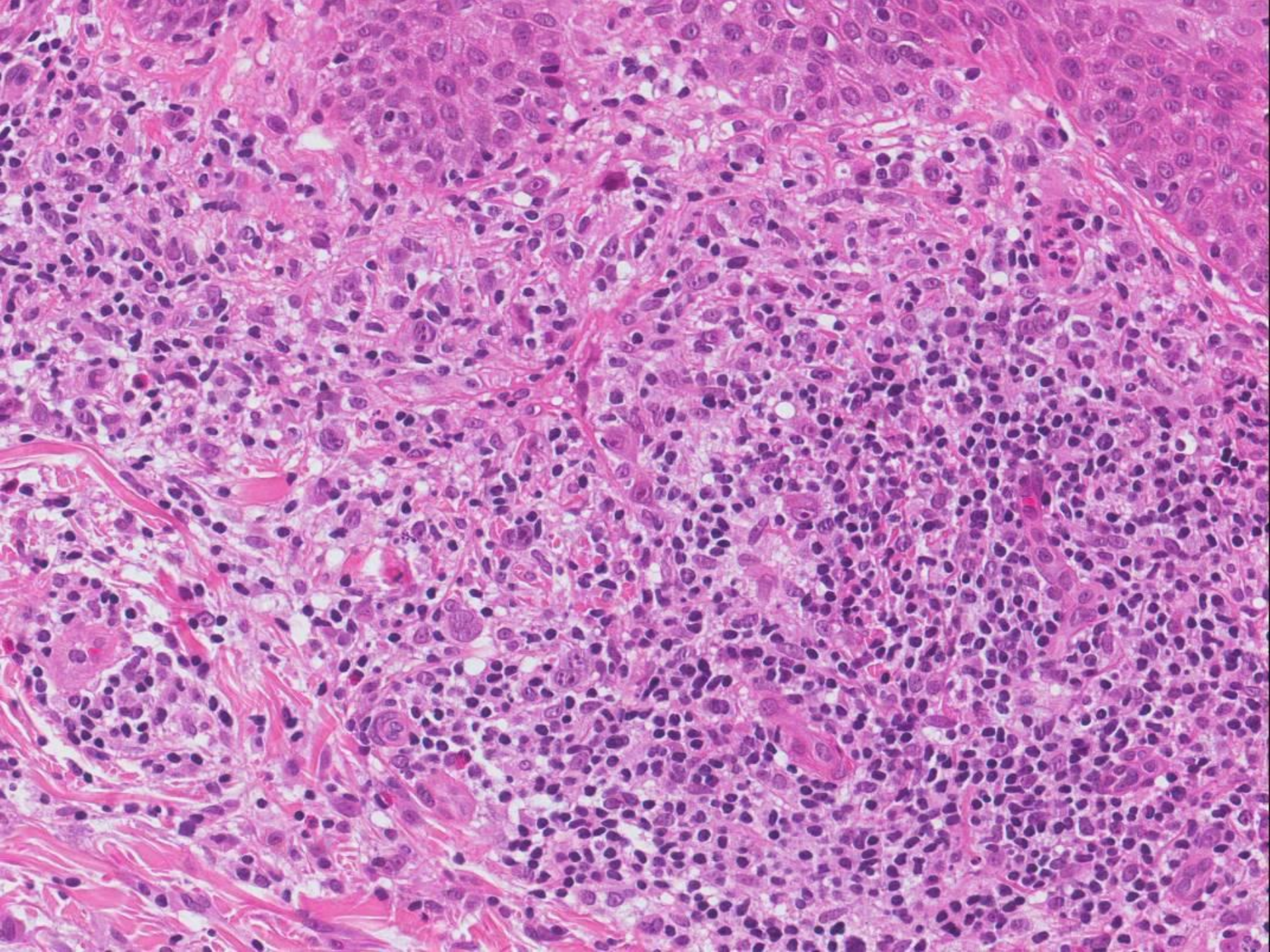
- 71/F, widespread polymorphic rash, very itchy
- Initially thought to be scabies.
- Patient and contacts treated, no response.
- O/E- erythematous papules (2-3mm) affecting forearm and trunk.

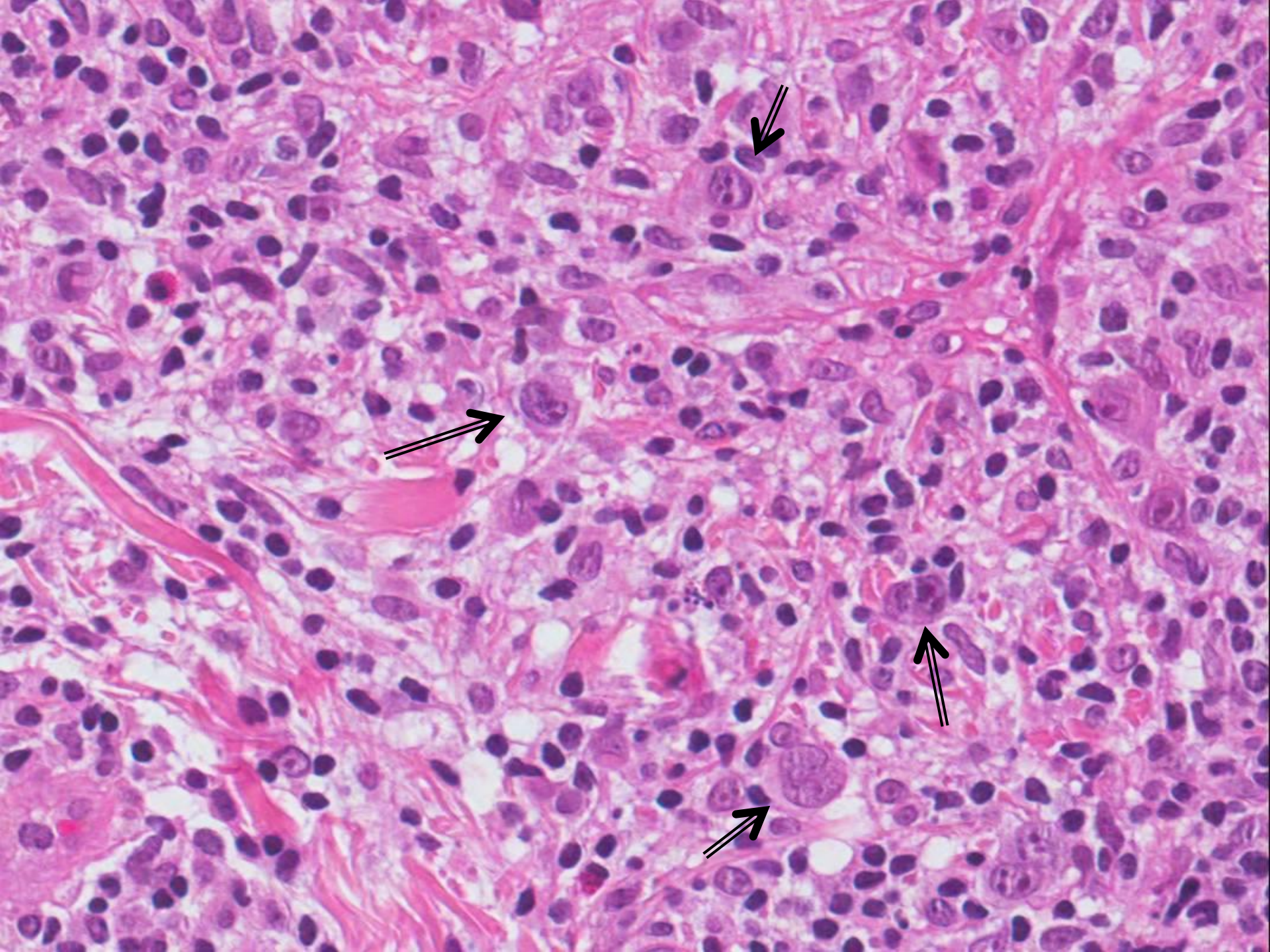




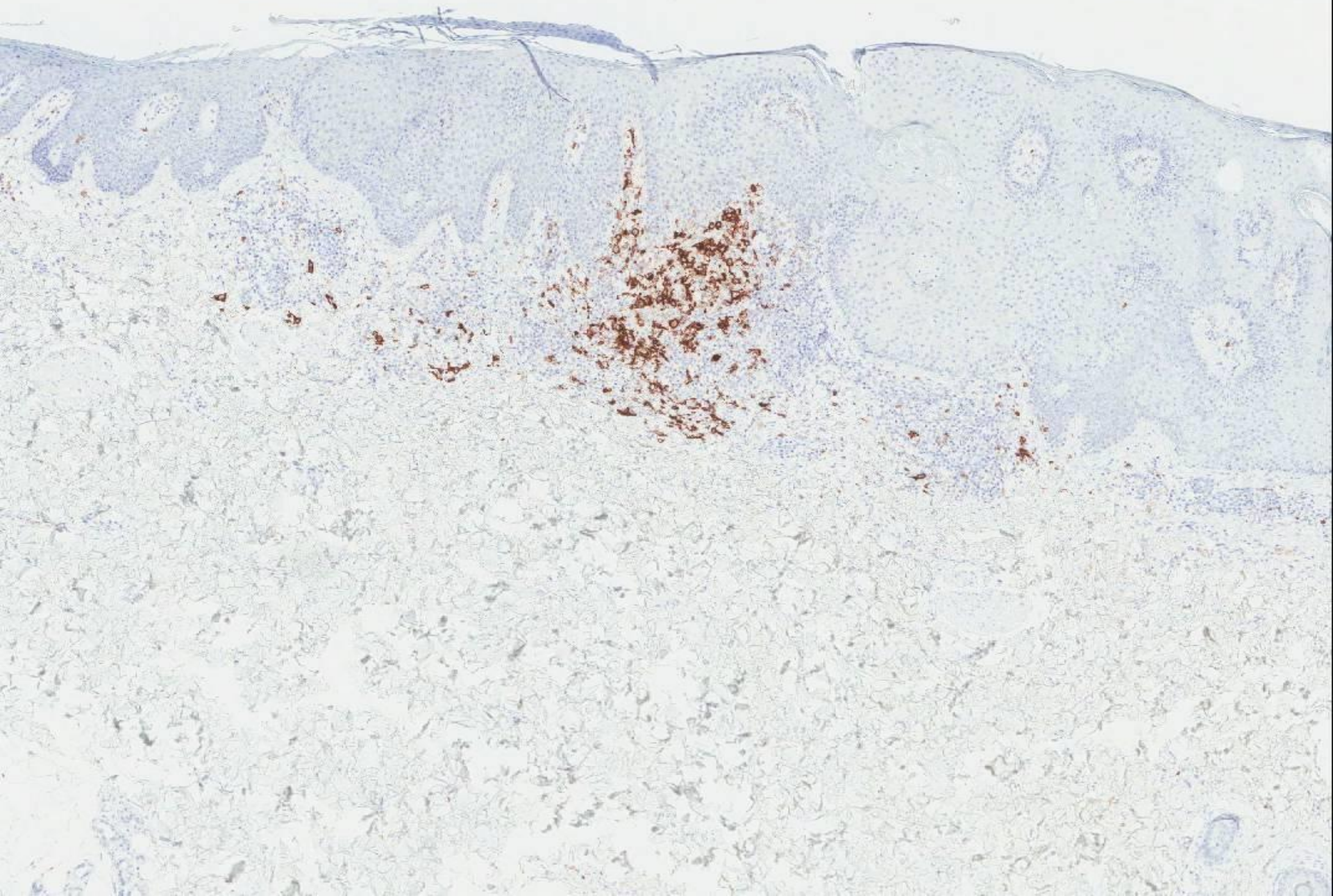


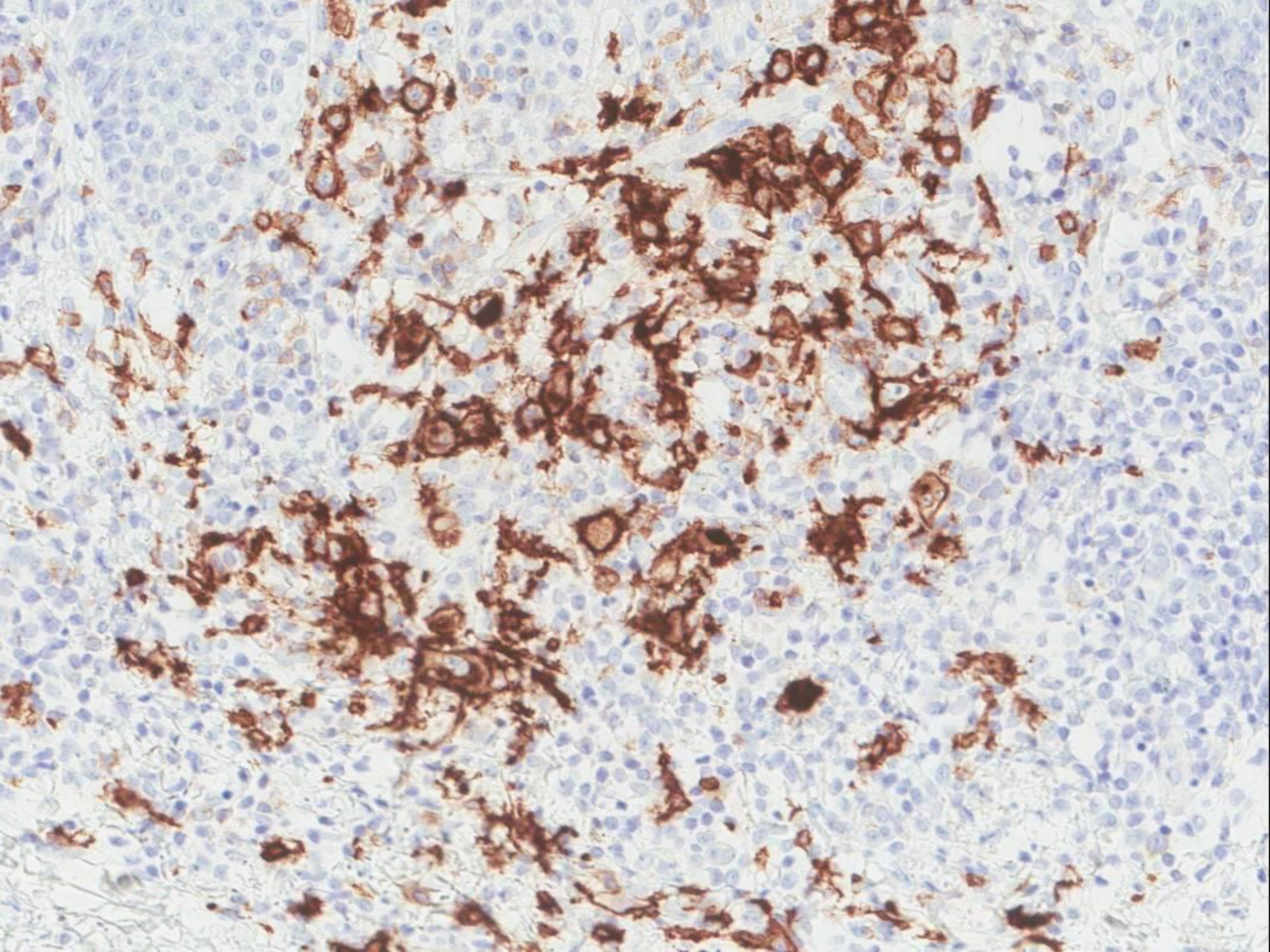






CD30

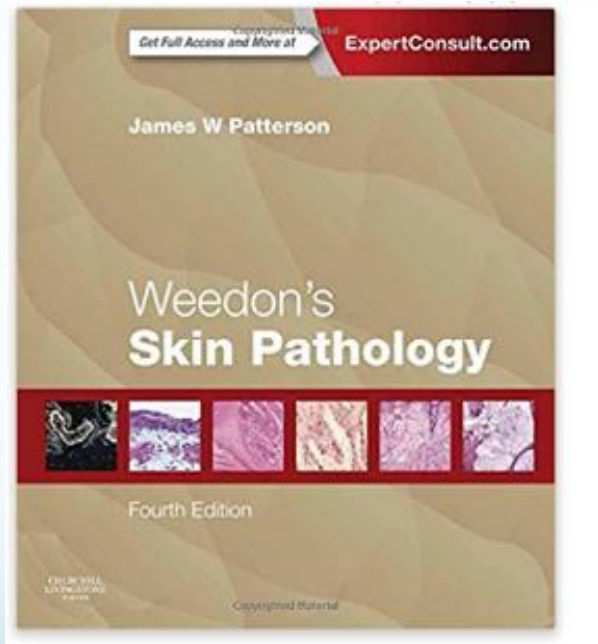




Diagnosis

- CD30 positive T cell lymphoproliferation suggestive of lymphomatoid papulosis, needs CPC
- CPC: other causes of CD30+ inflammatory/infective causes excluded.
- FINAL DIAGNOSIS: LyP (type A)

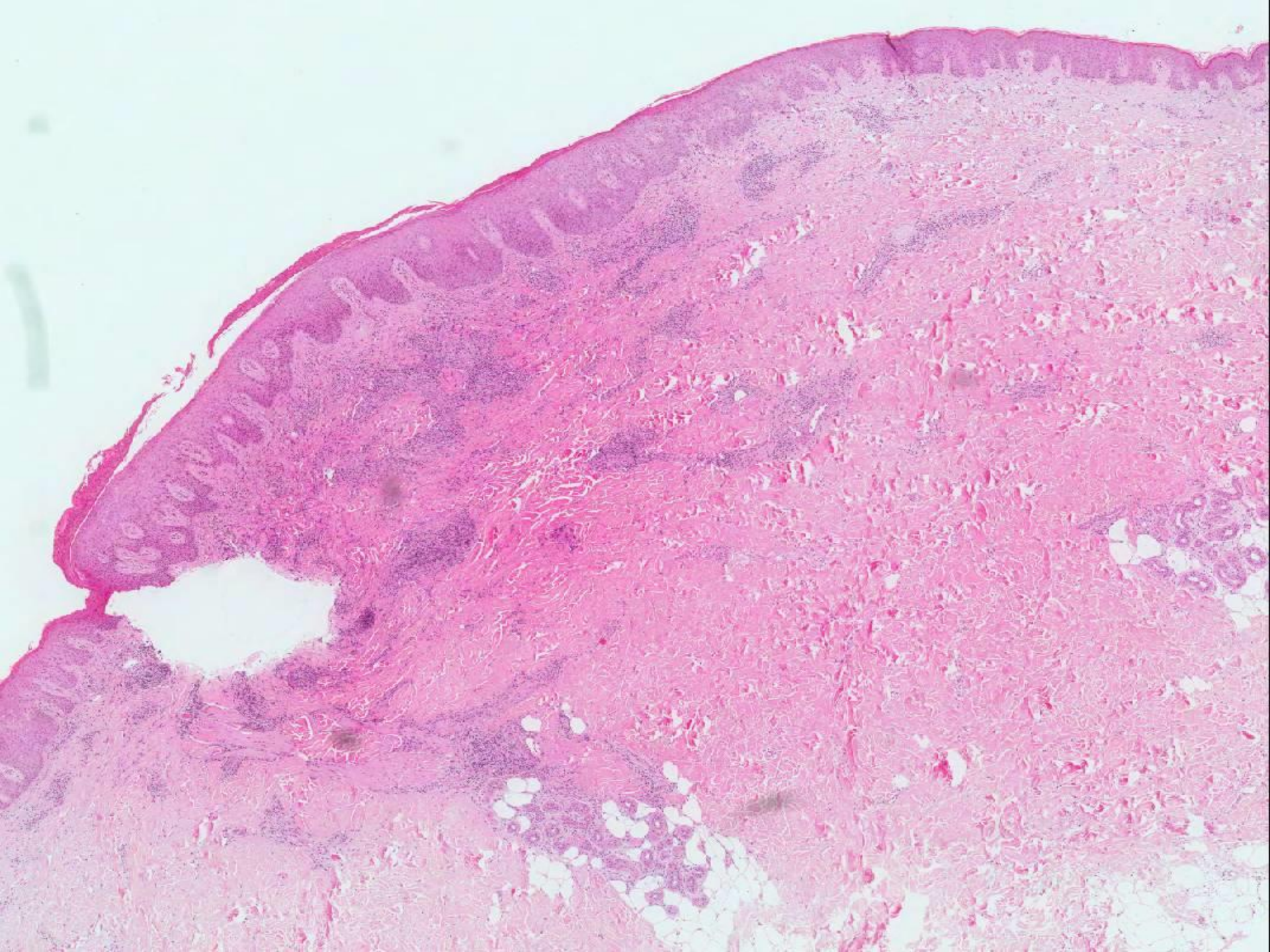
Scabies vs LyP

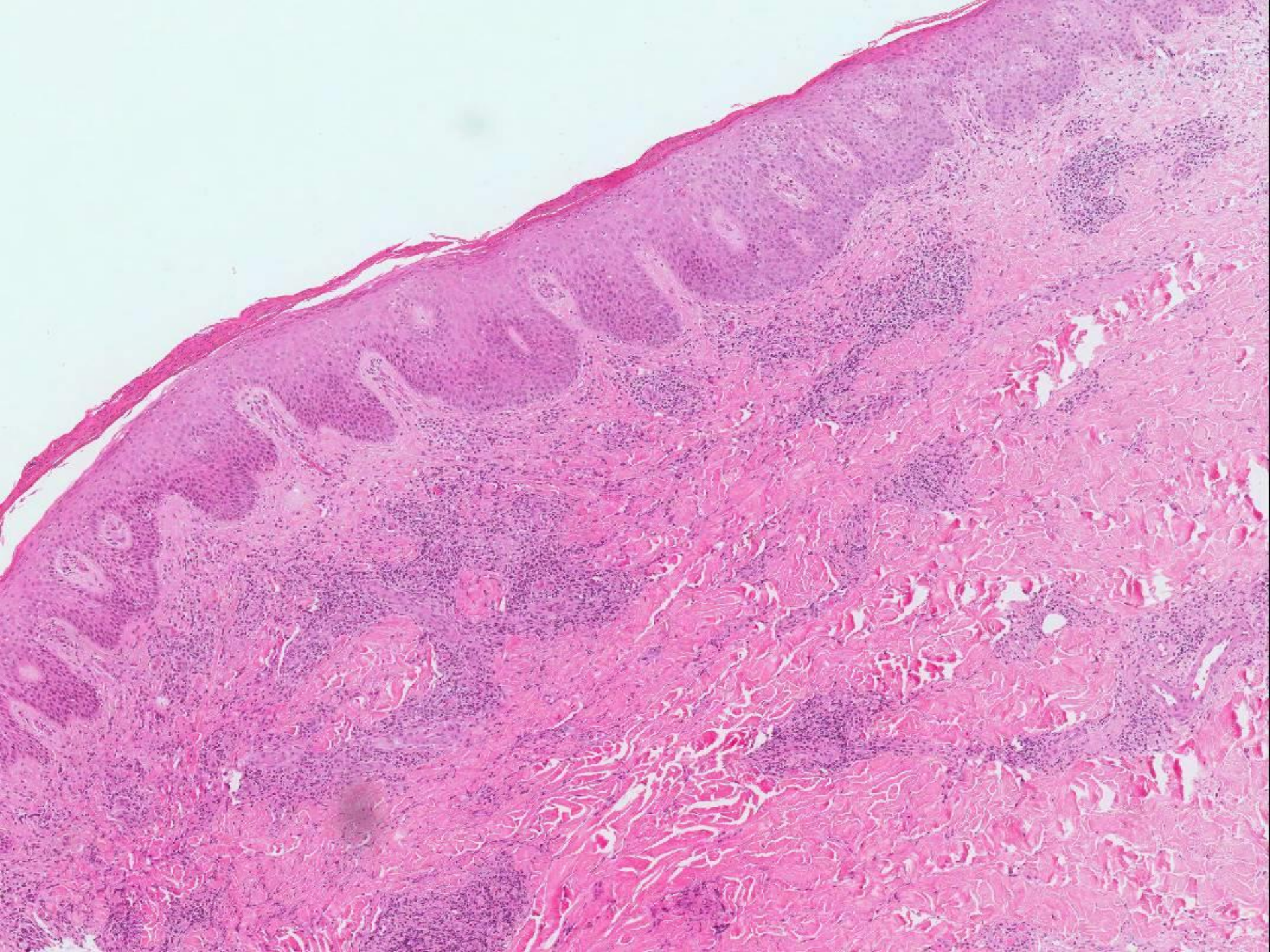


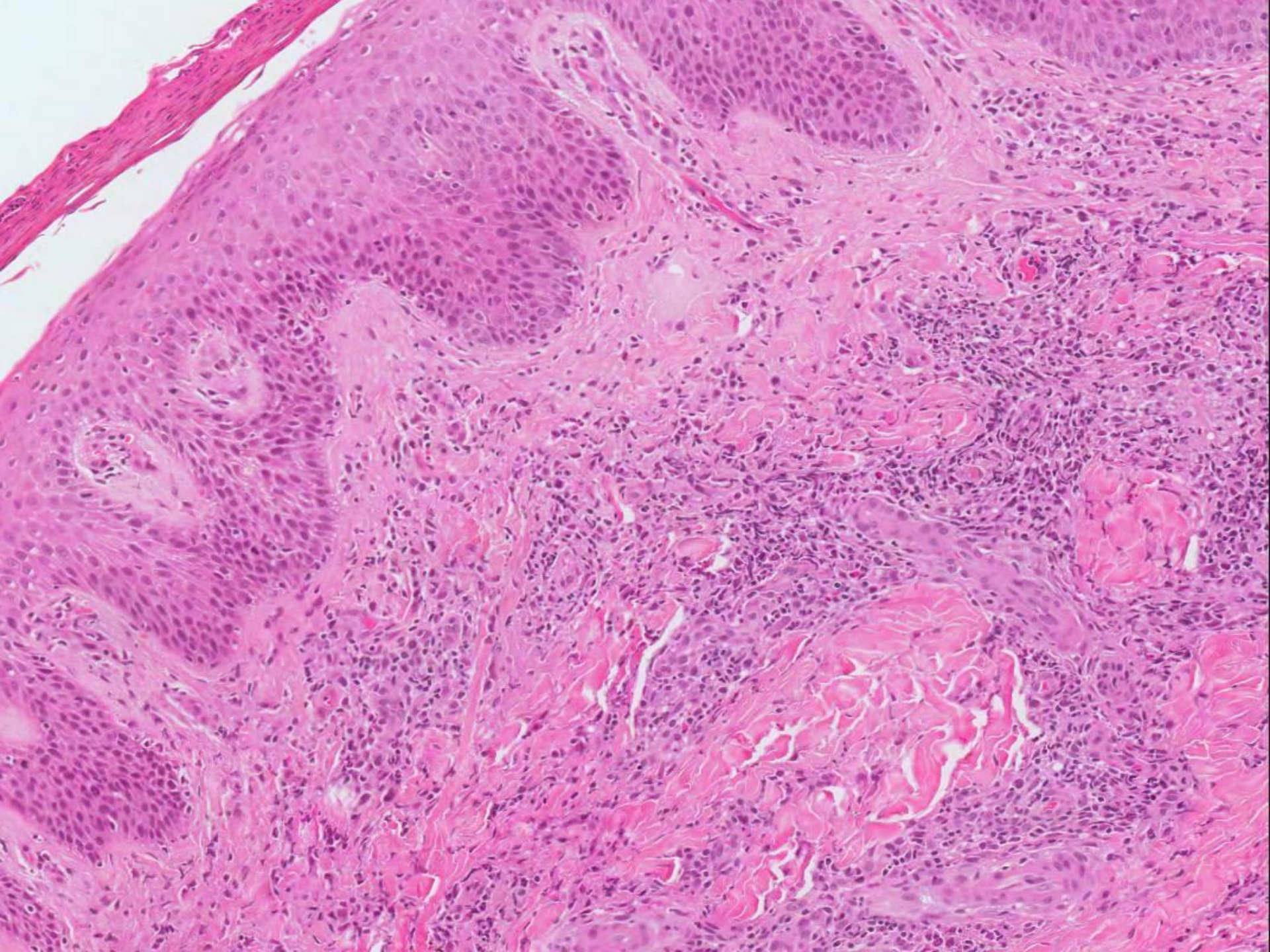
Weedon:
“the author
misdiagnosed LyP
on a superficial
shave bx of scabies
as a consequence of
large number of
CD30 + cell”

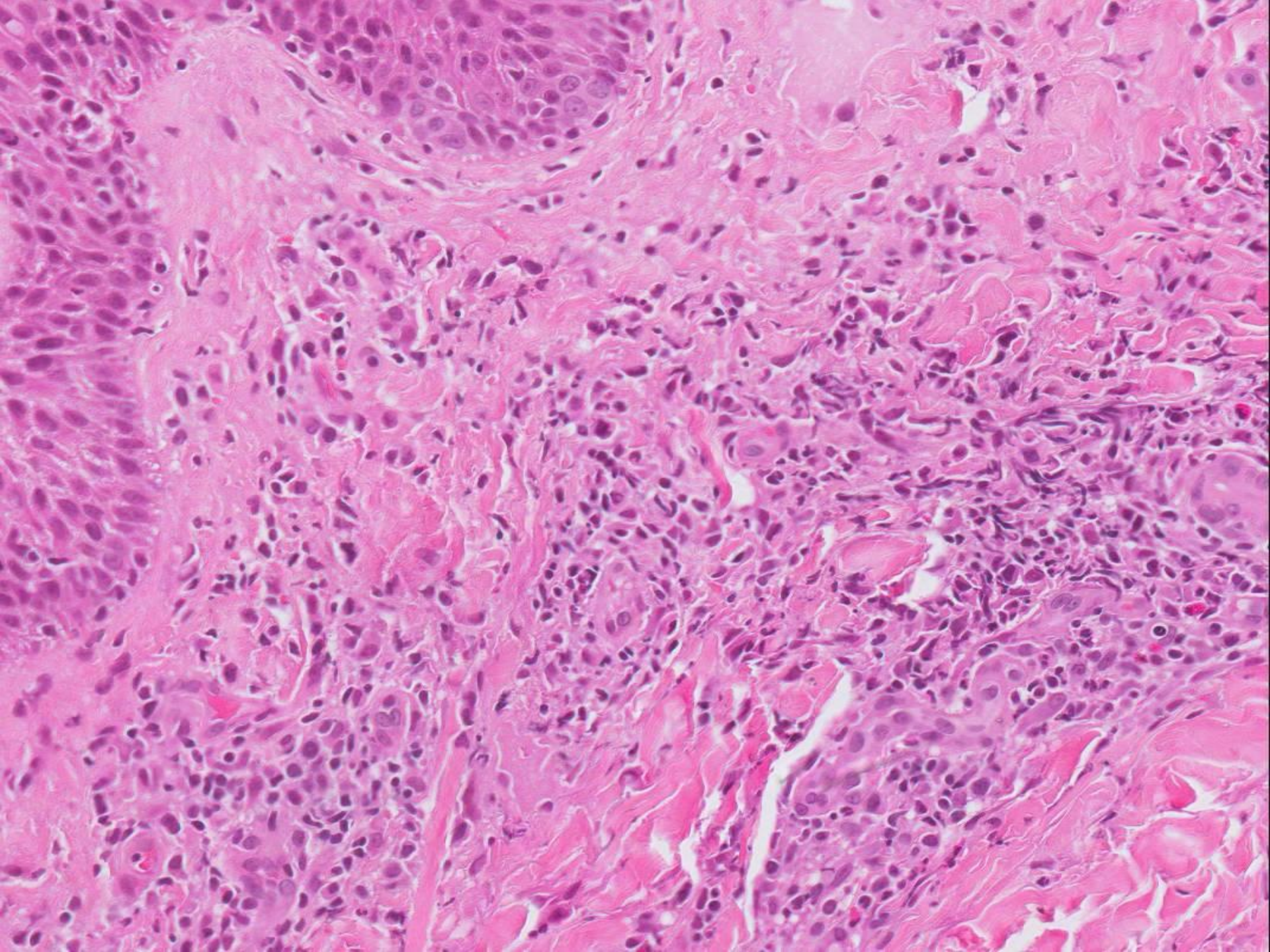
Case 2

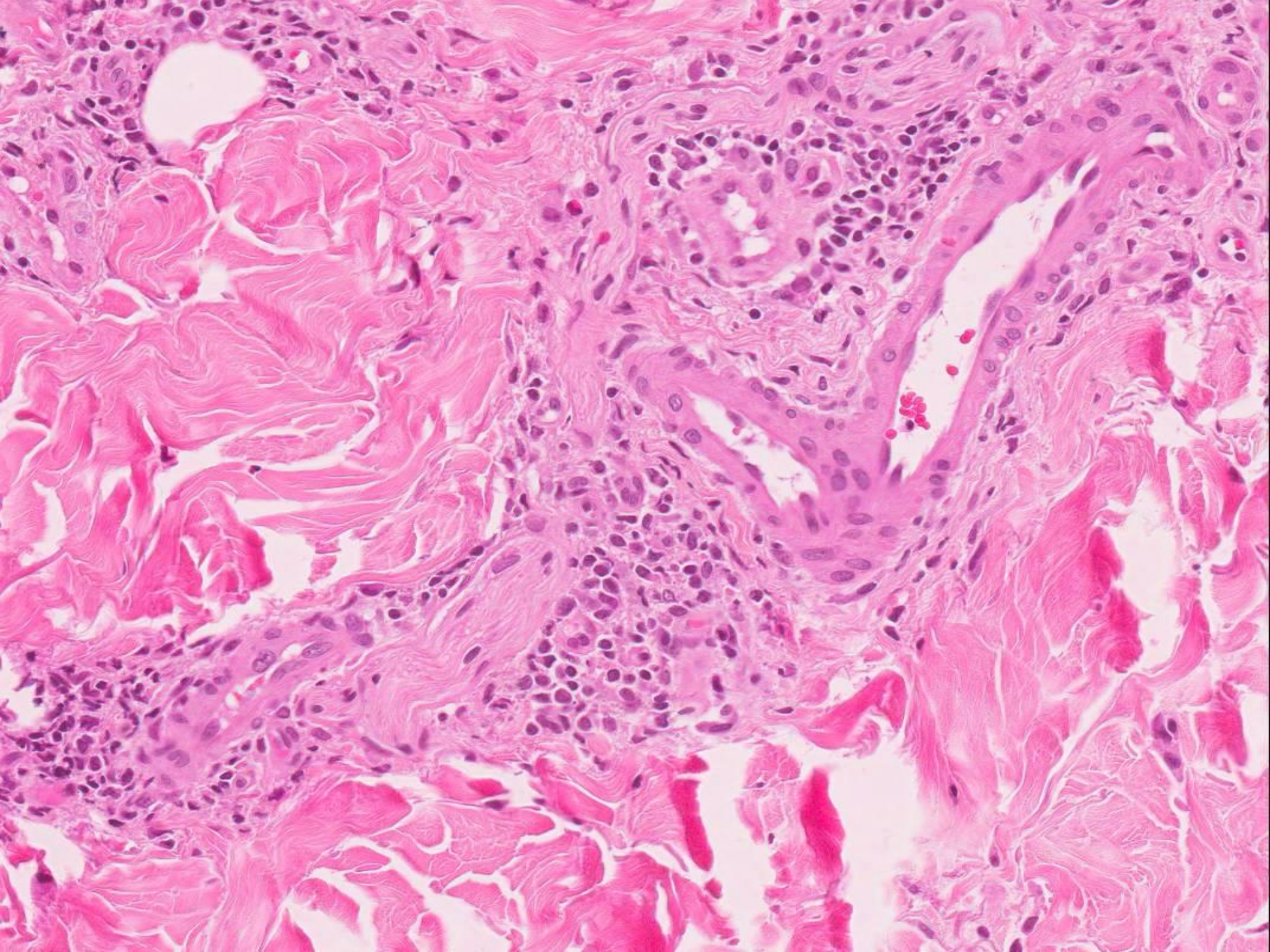
- 60/M
- Multiple purple erythematous nodules, trunk and legs
- Several biopsies in the past, no conclusive diagnosis
- Patient got fed up and stopped attending clinic.
- Came back in 2014 for excision of BCC and rash was rebiopsied

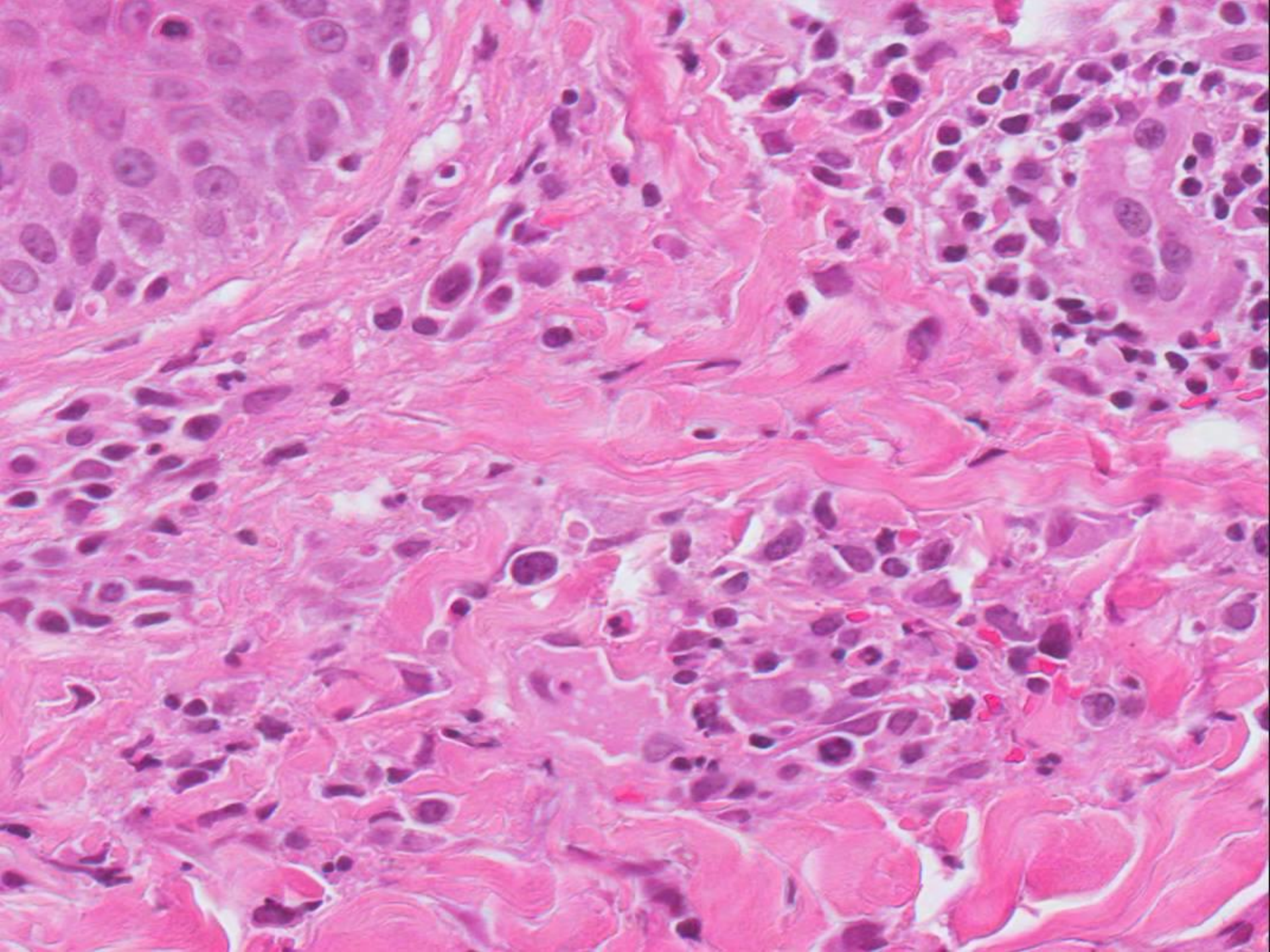


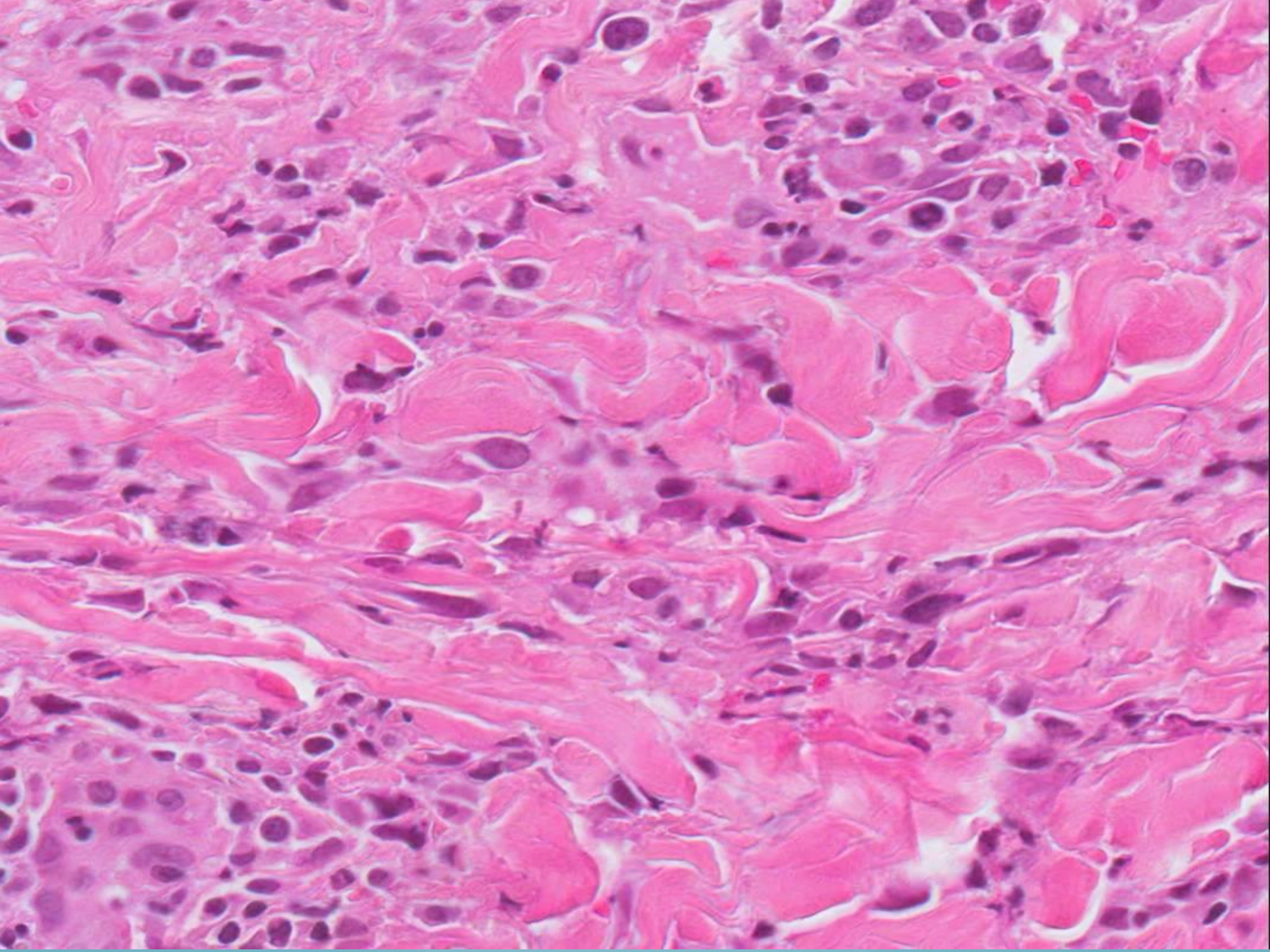




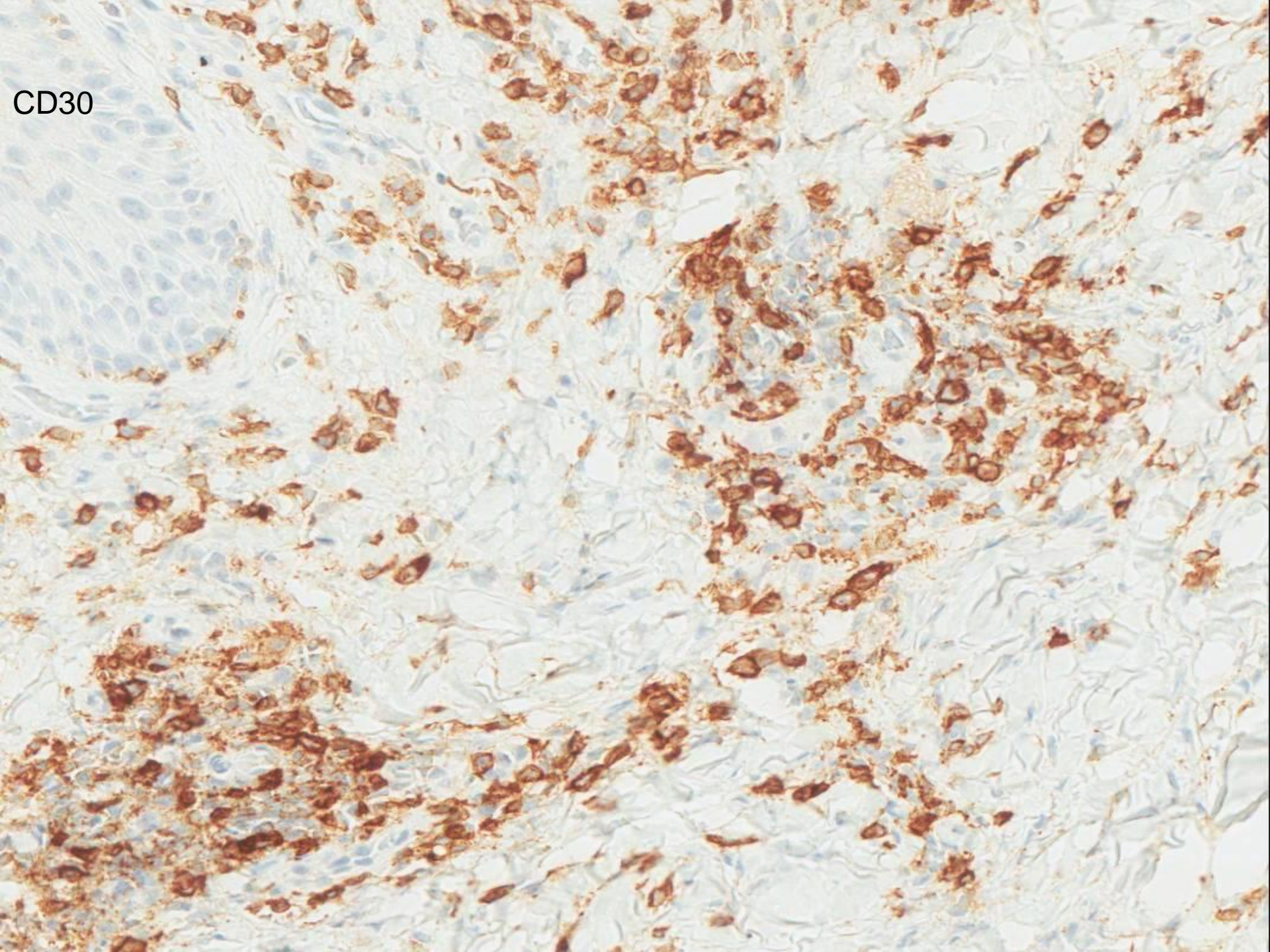








CD30

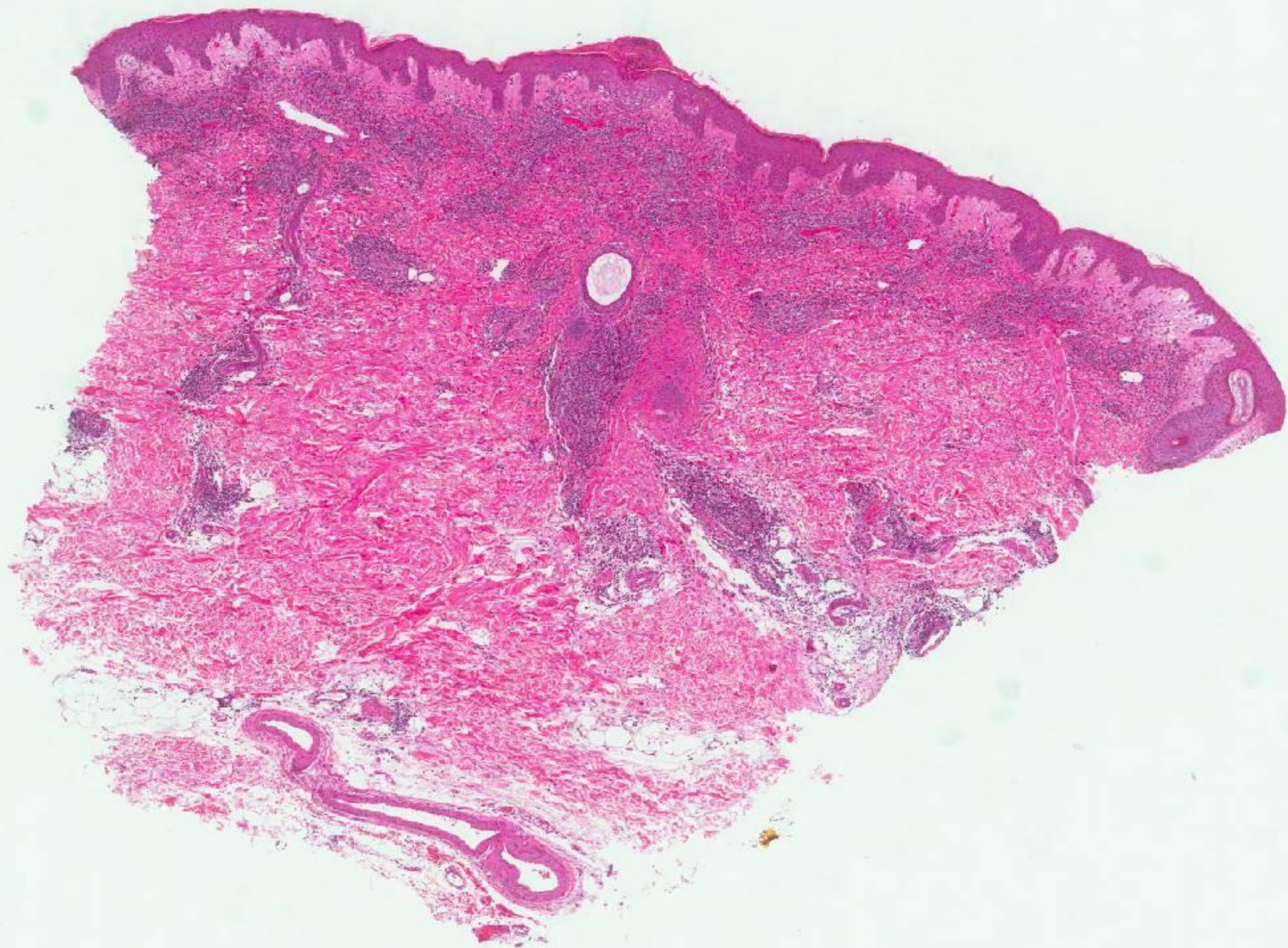


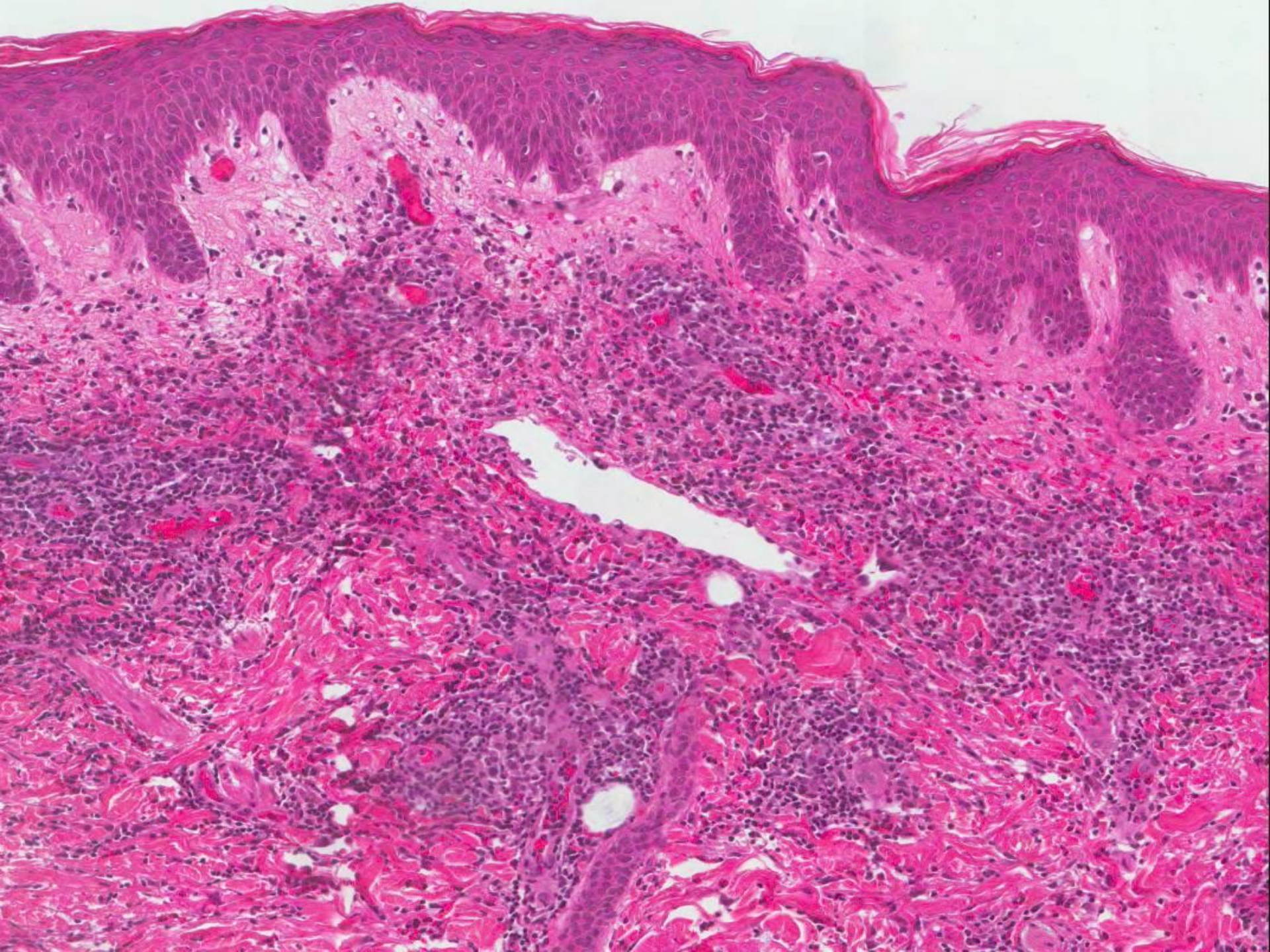
- CD30 rich T cell proliferation suggestive of Lymphomatoid papulosis, needs CPC
- More clinical history:
Fit and well, no B symptoms
Rash 'comes and goes', has been present for 20 years.

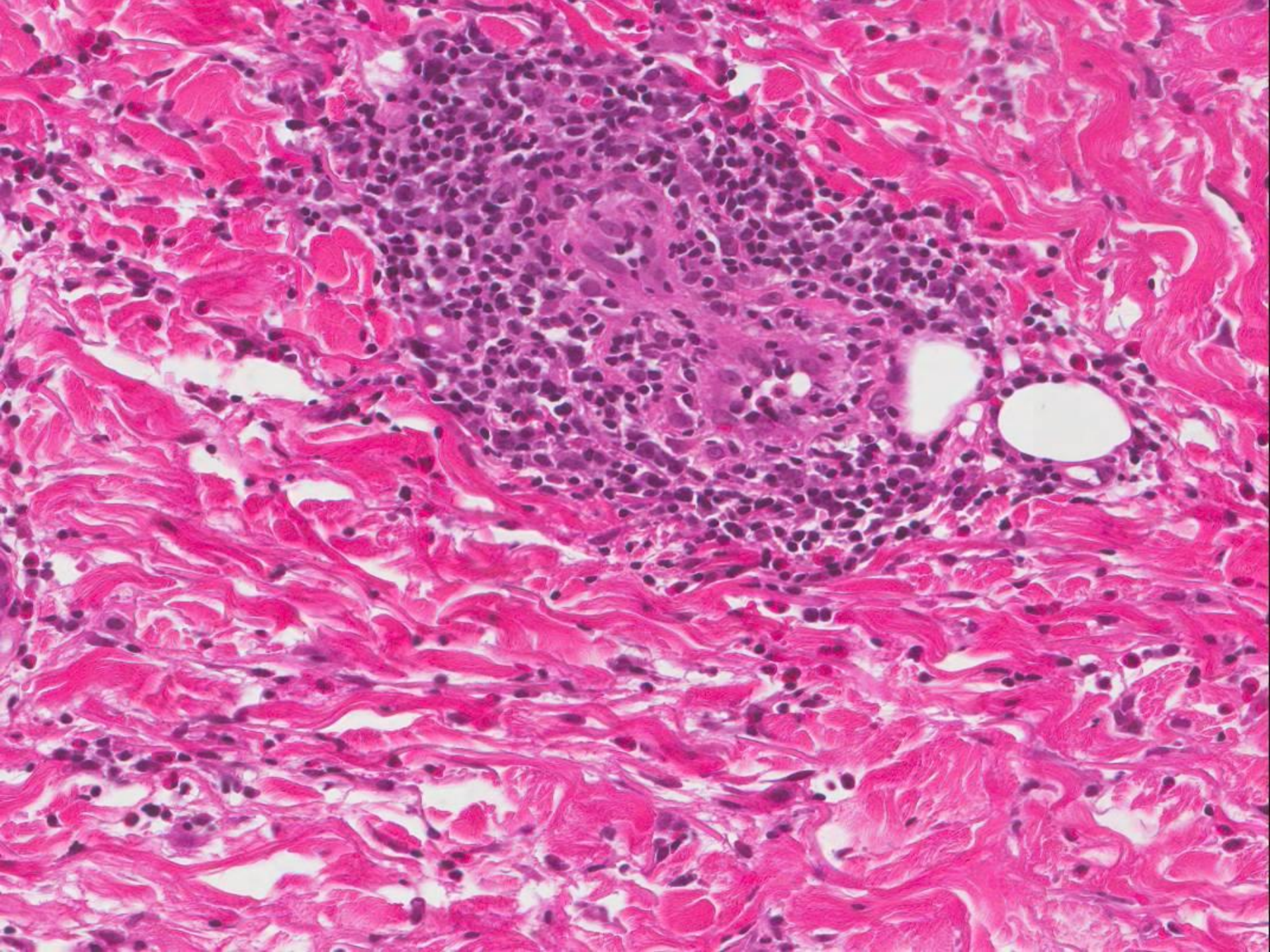
FINAL DIAGNOSIS: LyP (TYPE A)

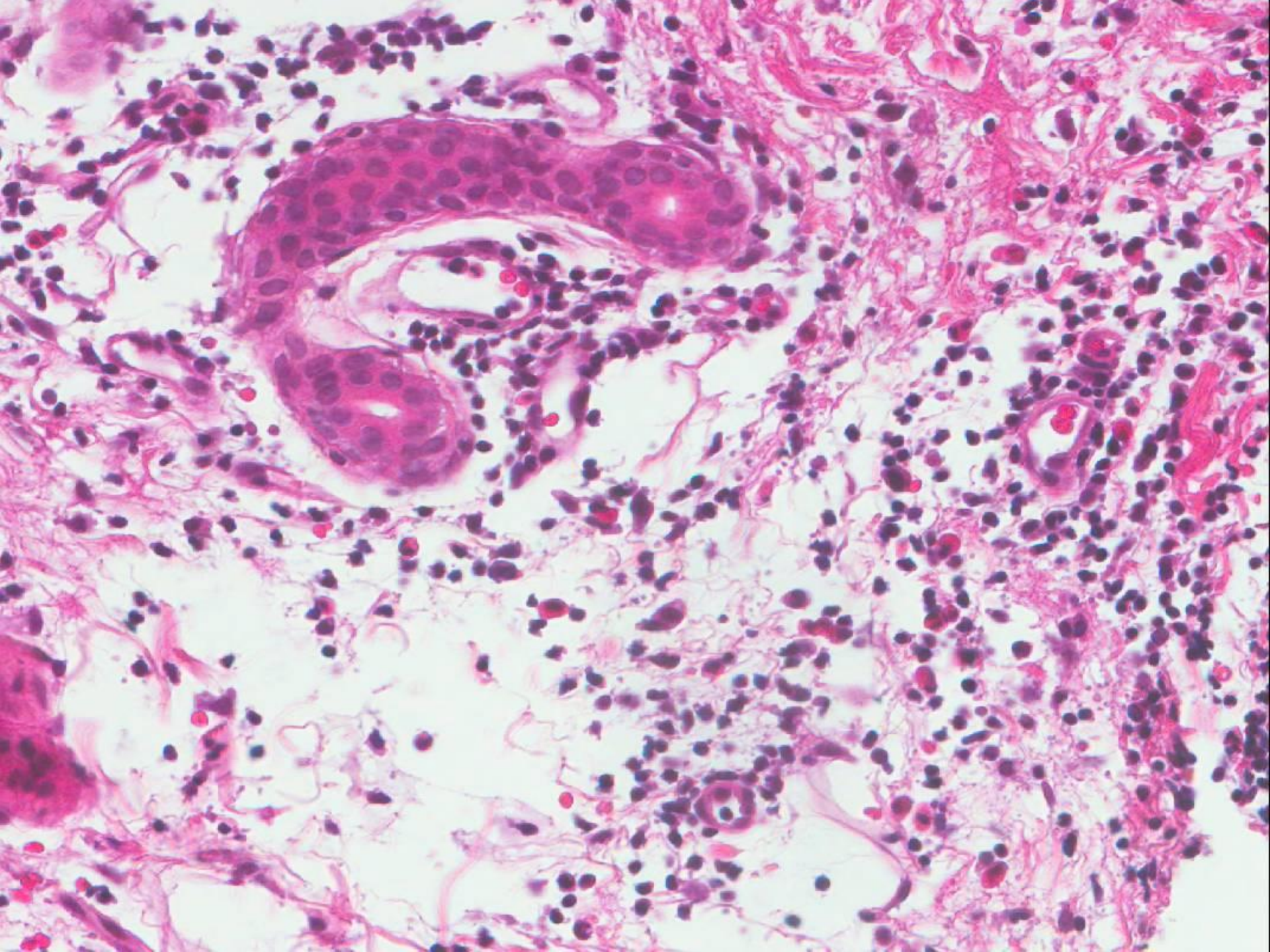
Case 3

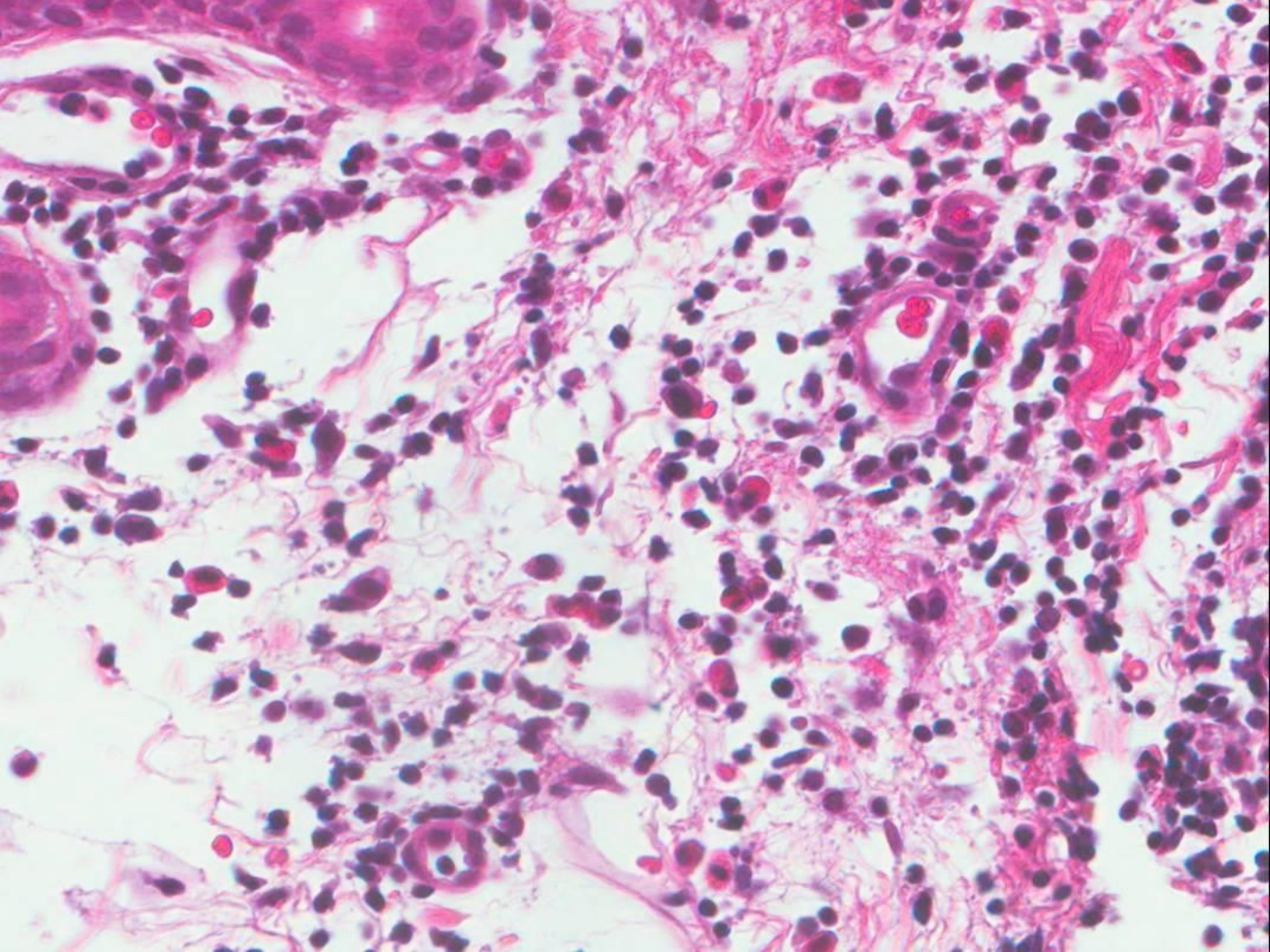
- 66/F
- Nodular erythematous urticated lesions buttocks and legs.
- Very itchy
- A few nodules in a linear distribution
- Do not ulcerate or heal with scarring
- Clinically: Insect bite reaction











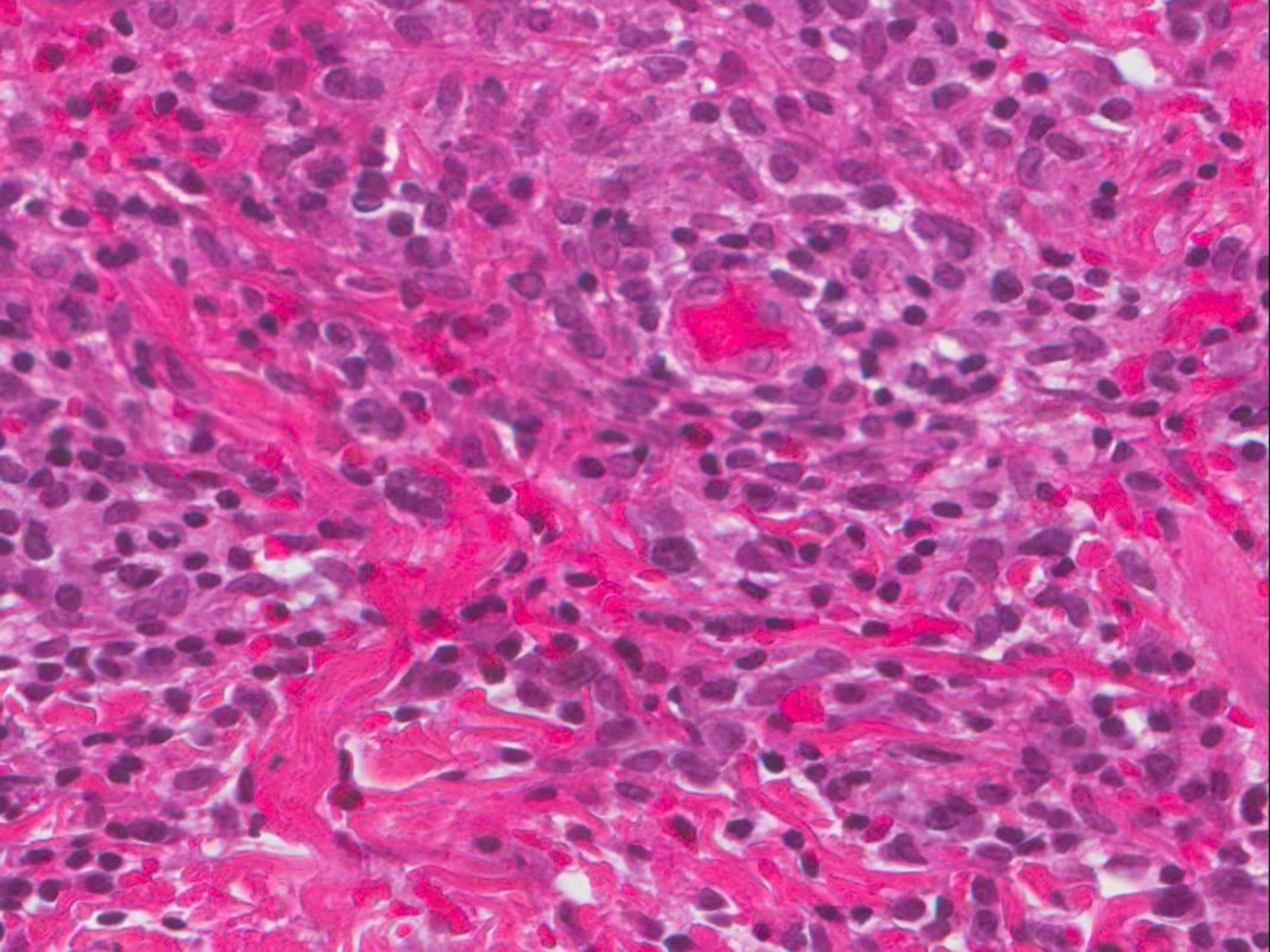
Diagnosis

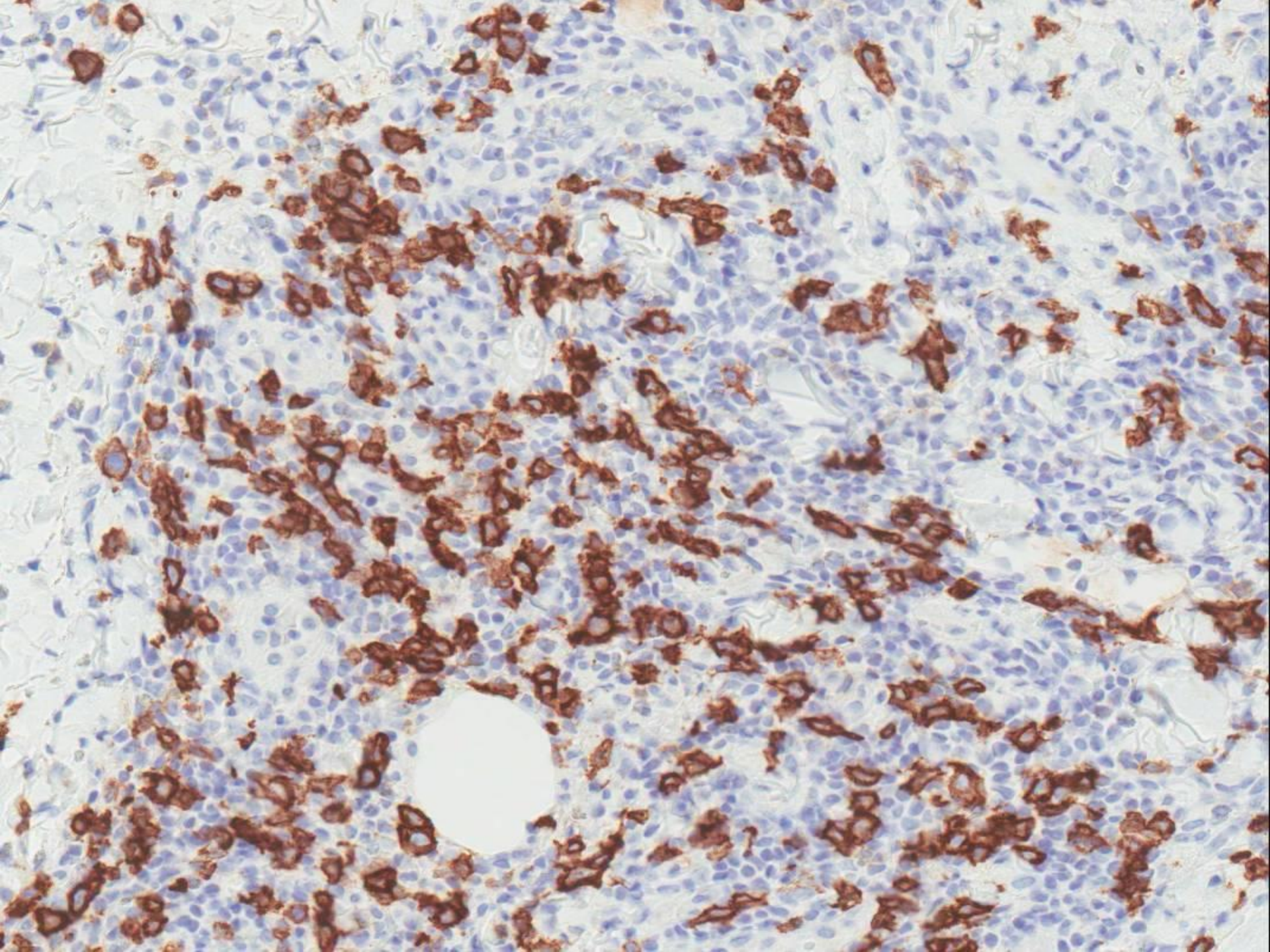
Insect bite reaction

CPC

- Patient very distressed by the itchy rash
- Not aware of insect bite
- Not been on outdoor activity or holiday
- Fumigated all her mattresses
- Stayed away from home for sometime, but lesions still keep appearing
- Finally, MOVED HOUSE

No response





? Insect bite reaction with CD30 + cells

? Lymphomatoid papulosis

Histological D/D of Type A LyP

Inflammatory/Infective conditions with CD30 positive blasts:

- Arthropod bite reactions
- Scabies
- Viral infections : parapox (Milkers nodule and Orf), herpes virus, molluscum contagiosum.
- Drug induced pseudolymphoma- CD30 rich infiltrates particularly described with Carbamazepine, gemcitabine, terbinafine, cefuroxime.
- **Pityriasis Lichenoides**

Pityriasis Lichenoides





[Am J Pathol](#). 1990 Apr; 136(4): 979-987.

PMCID: PMC1877642

Immunohistochemical distinction of lymphomatoid papulosis and pityriasis lichenoides et varioliformis acuta.

[F. J. Varga](#), [E. C. Vonderheid](#), [S. M. Olbricht](#), and [M. E. Kadin](#)

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This article has been [cited by](#) other articles in PMC.

Abstract

Lymphomatoid papulosis (LyP) and pityriasis lichenoides et varioliformis acuta (PLEVA) are benign self-healing cutaneous eruptions that may be clinically and histologically similar. However LyP has a 5% to 20% risk of associated lymphoid malignancy, whereas PLEVA does not. To determine whether the immunophenotype of lymphoid cells is useful in the distinction of these two disorders, the pattern of expression of lymphoid cell lineage and activation antigens in nine cases of LyP and seven cases of PLEVA were compared. In all cases of LyP most larger cells expressed the activation antigen Ki-1 (CD30) and lacked expression of the T-cell antigen CD7 and at least one other T-cell antigen (CD2, CD3, CD5). In contrast, CD30 antigen expression was rare or absent in PLEVA. CD3- and CD7 antigen expression was

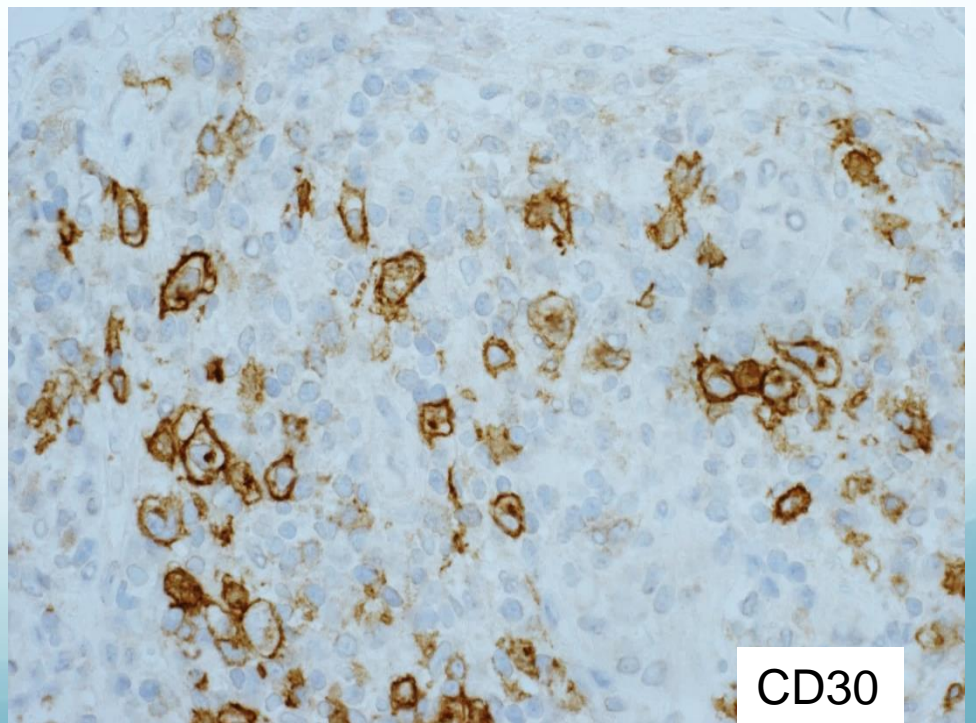
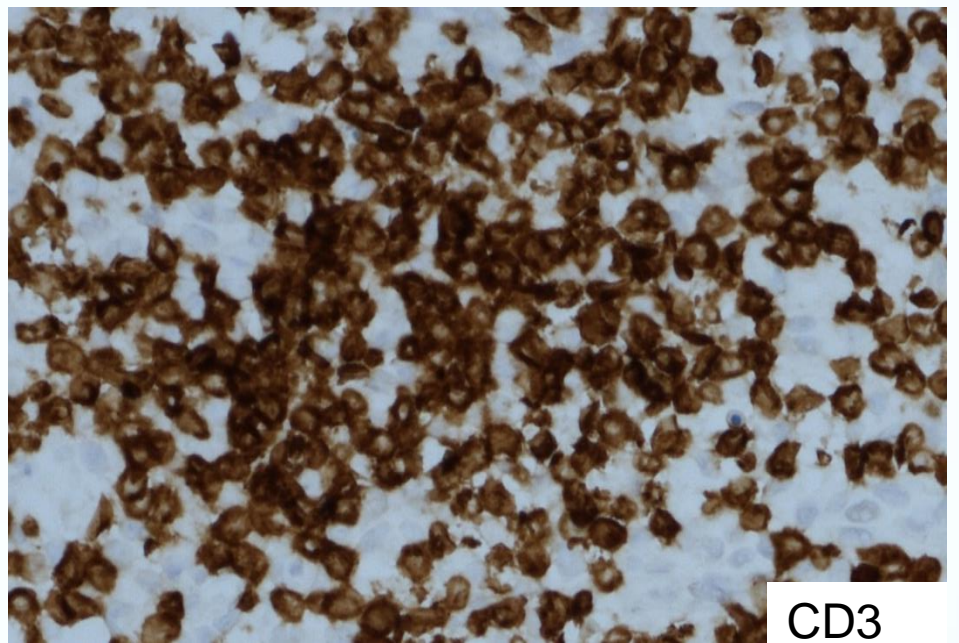
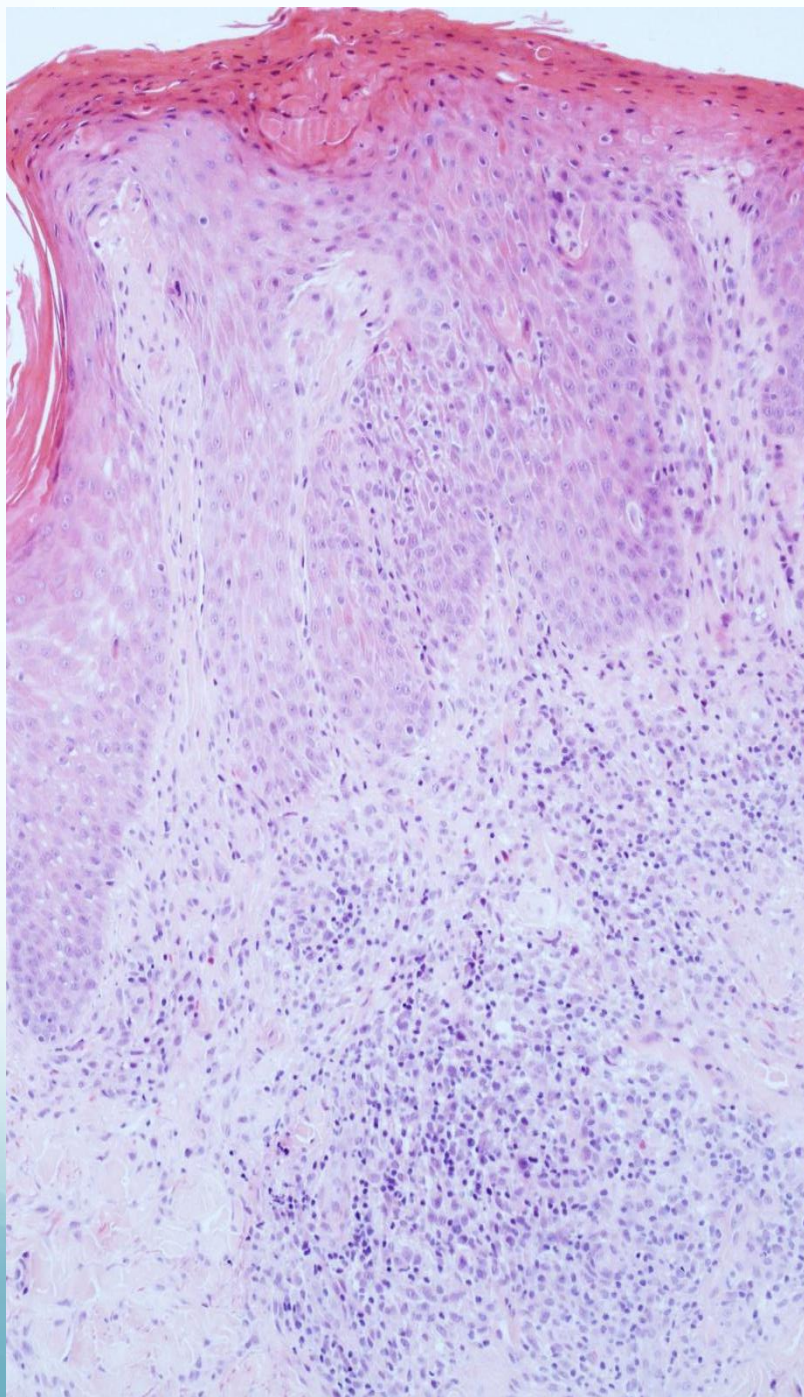
Pityriasis lichenoides et varioliformis acuta with numerous CD30(+) cells: a variant mimicking lymphomatoid papulosis and other cutaneous lymphomas. A clinicopathologic, immunohistochemical, and molecular biological study of 13 cases.

Kempf W¹, Kazakov DV, Palmedo G, Frailtag S, Schaerer L, Kutzner H.

- 13 cases- all had significant numbers of CD30+ cells
- Non of the cases had a 'waxing and waning' course on follow up.

Case 4

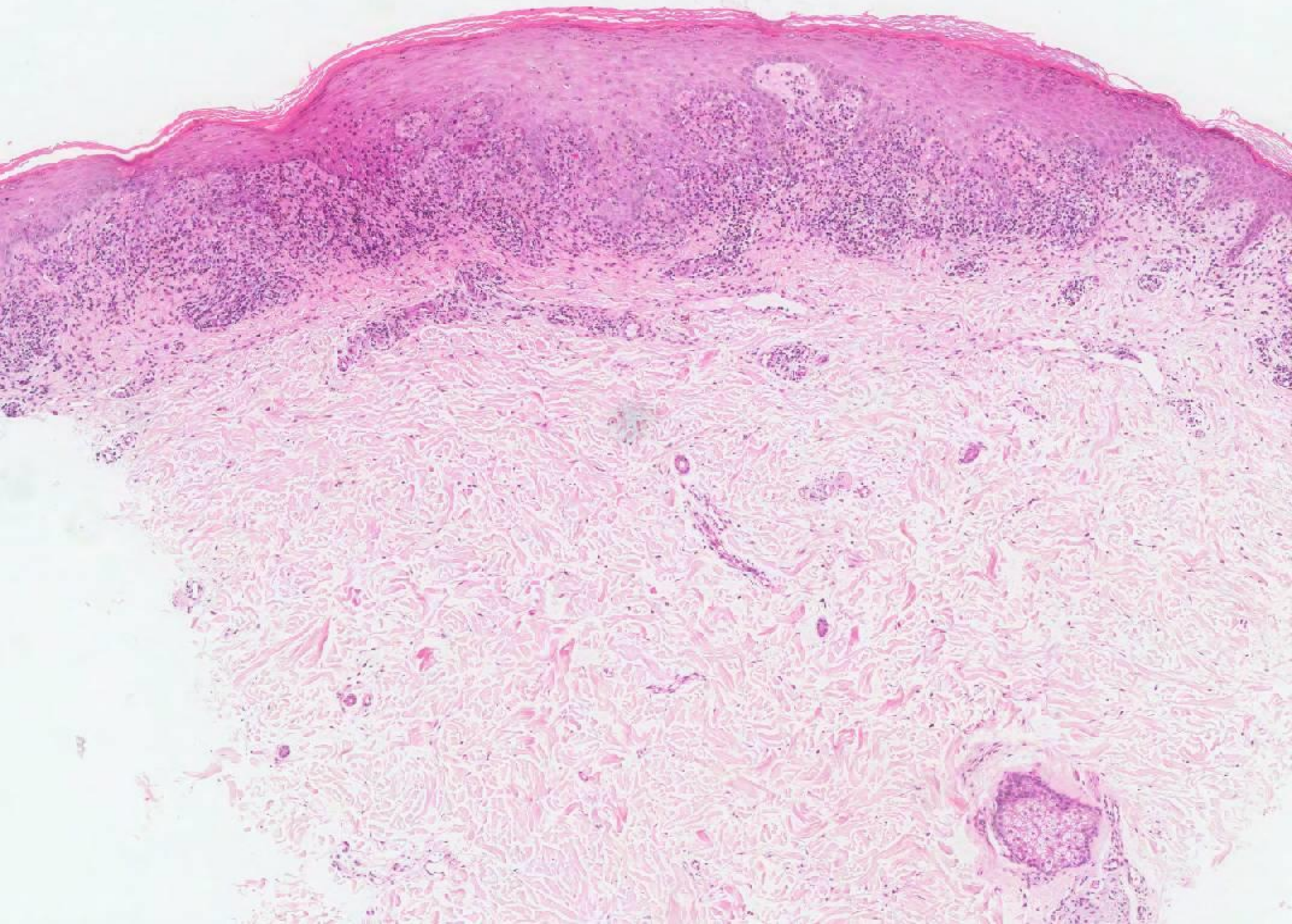
- 3yr/boy presented with multiple excoriated papules on trunk and limbs
- Otherwise fit and well
- Clinical d/d- insect bite reaction, pityriasis lichenoides

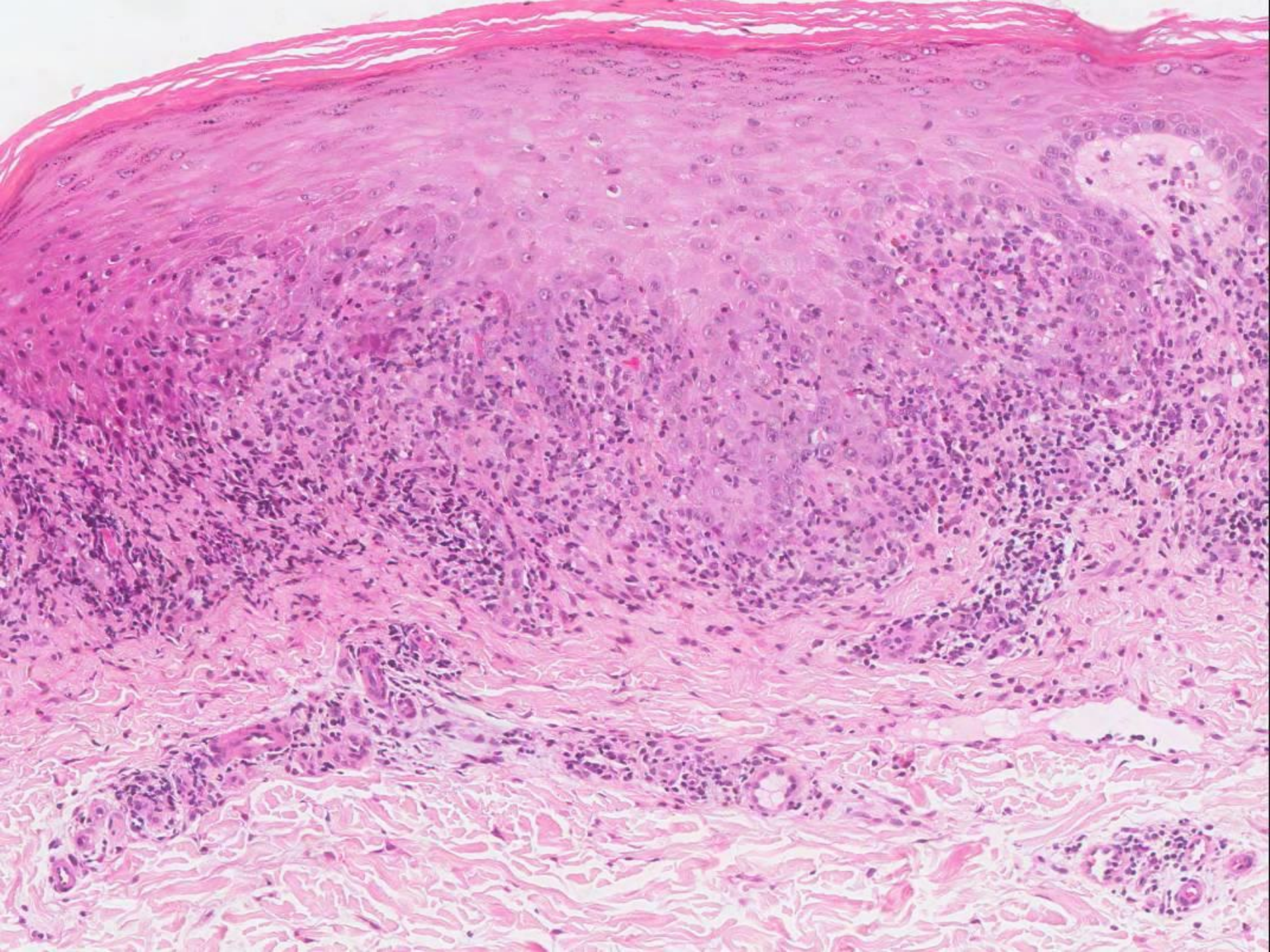


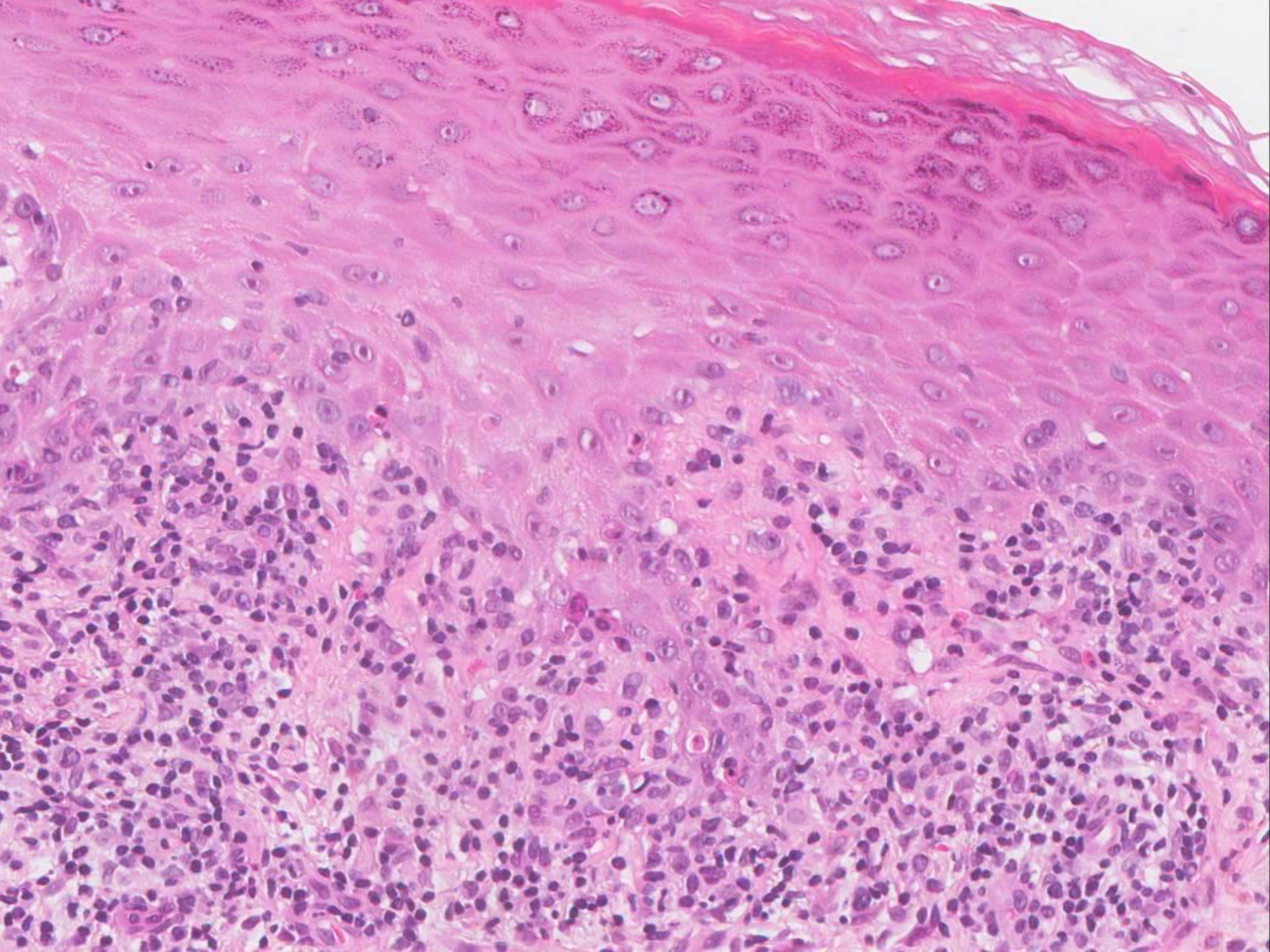
Case 5

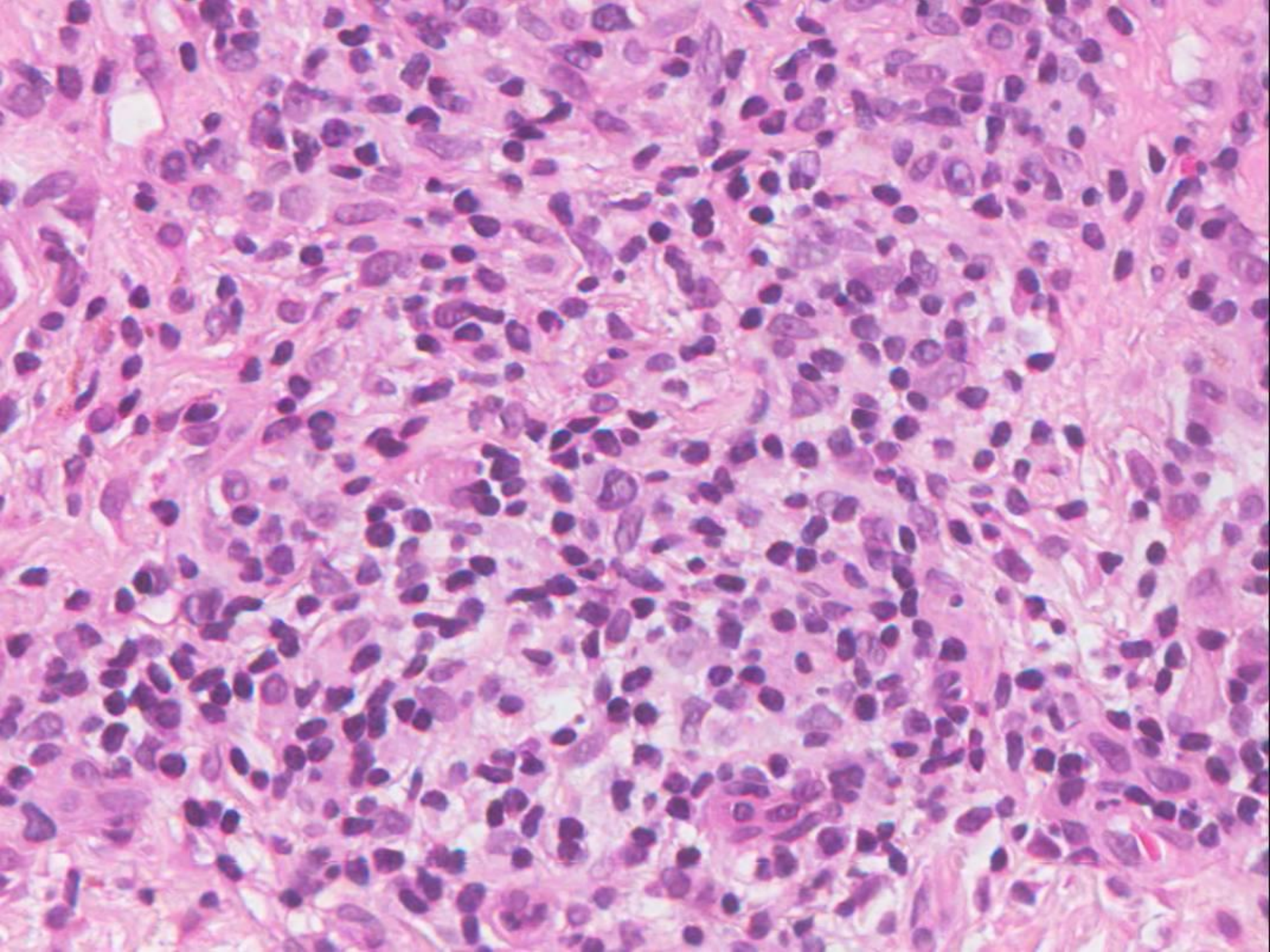
- 34/F, papular rash
- Occurs in clusters
- Heals with scar

?lymphomatoid papulosis ?PLC

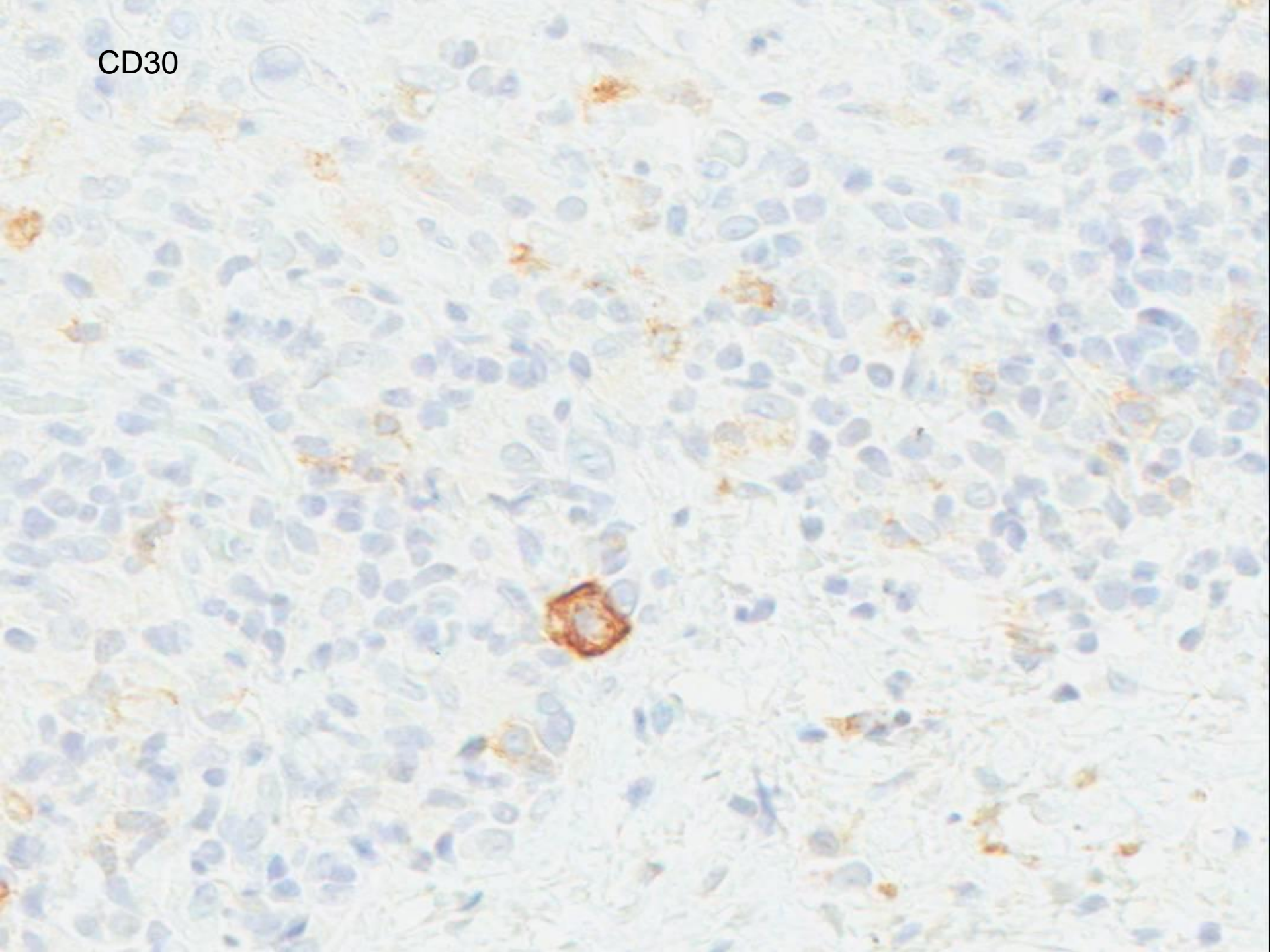




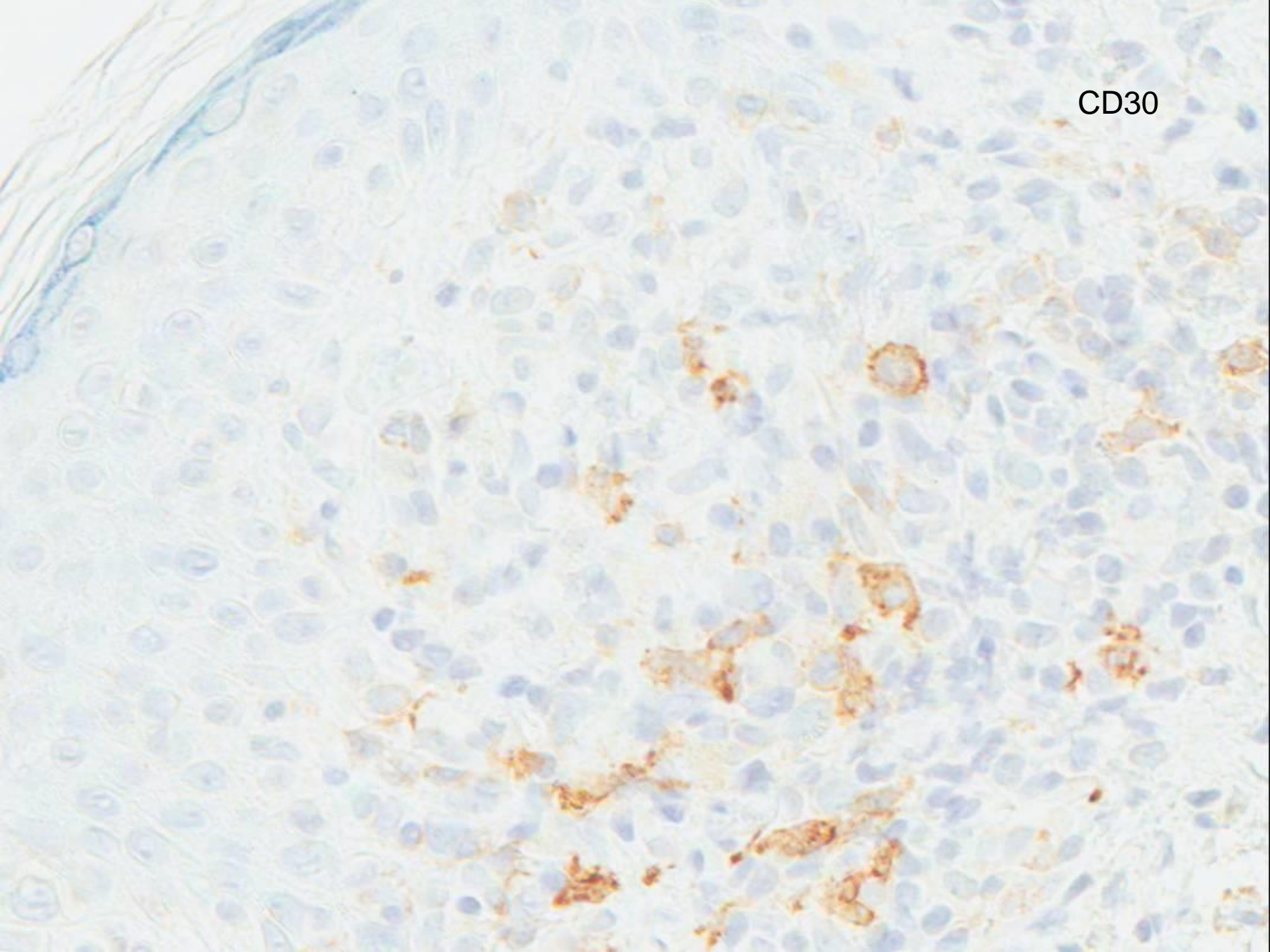




CD30



CD30



Are lesions self resolving?

- Difficult to decide if first presentation
- Patients usually started on topical medication.
- Lesions of PLEVA/PLC can also subside spontaneously
- Follow up- presence/absence of waxing and waning course.

Histological and Clinical Overlap

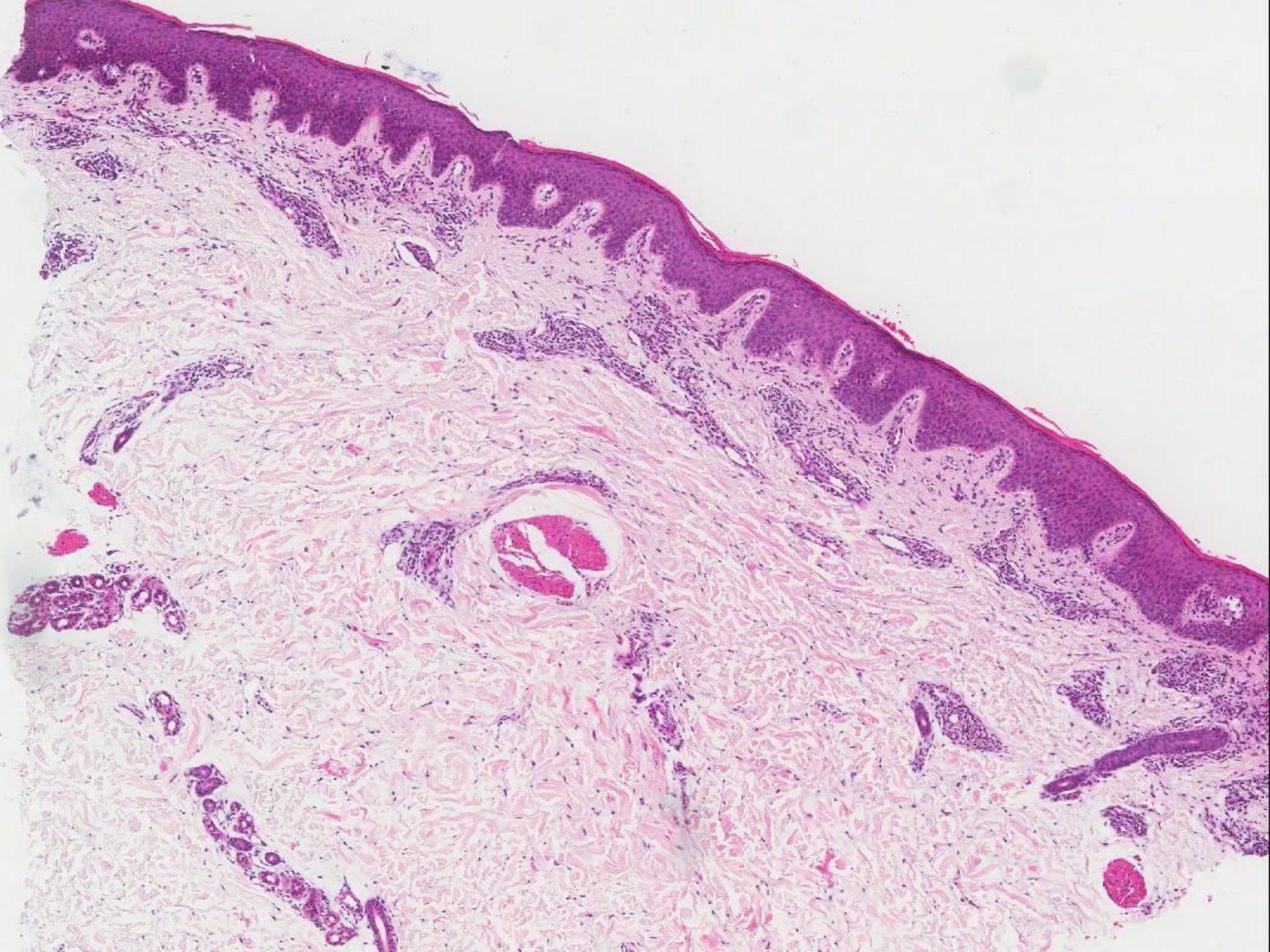
- PLEVA and LyP could be more closely biologically related, than previously thought
- Probably lie on a clinico-pathological spectrum

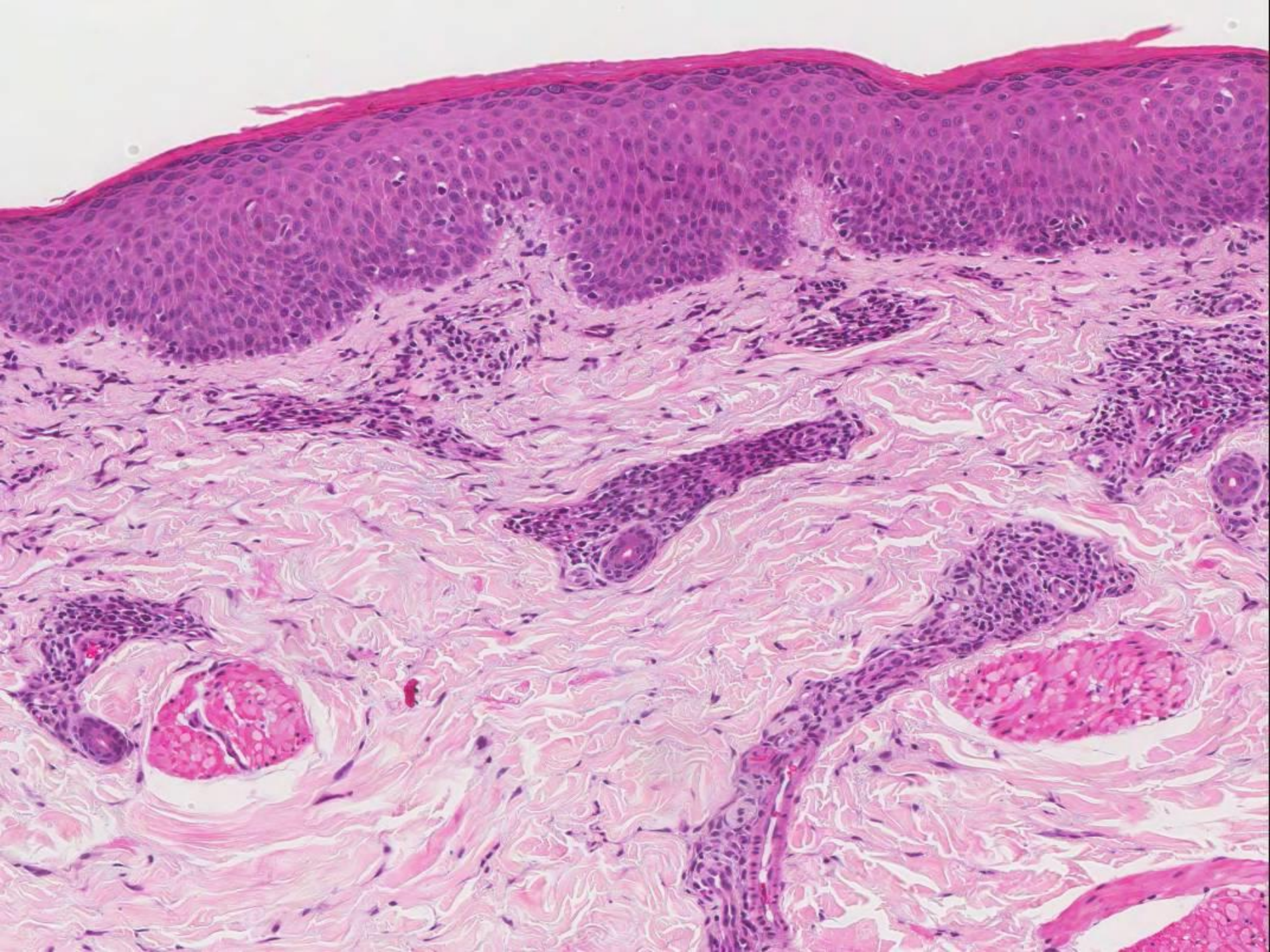
Histopathological Spectrum

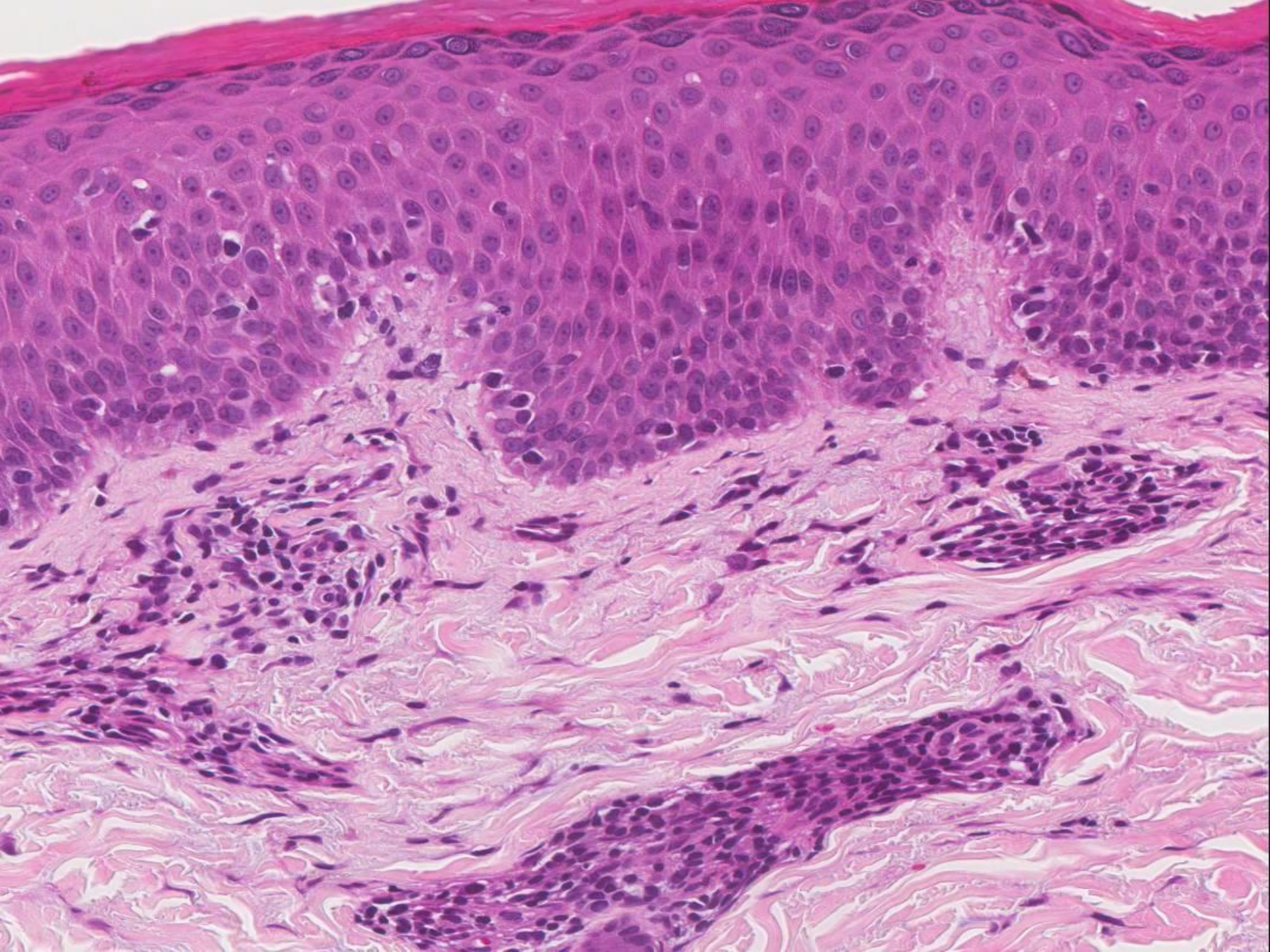
- Type A
- Type B
- Type C
- Type D (epidermotropic)
- Type E (angio-invasive)
- Type F (folliculotropic)
- LyP with 6p25.3 rearrangement

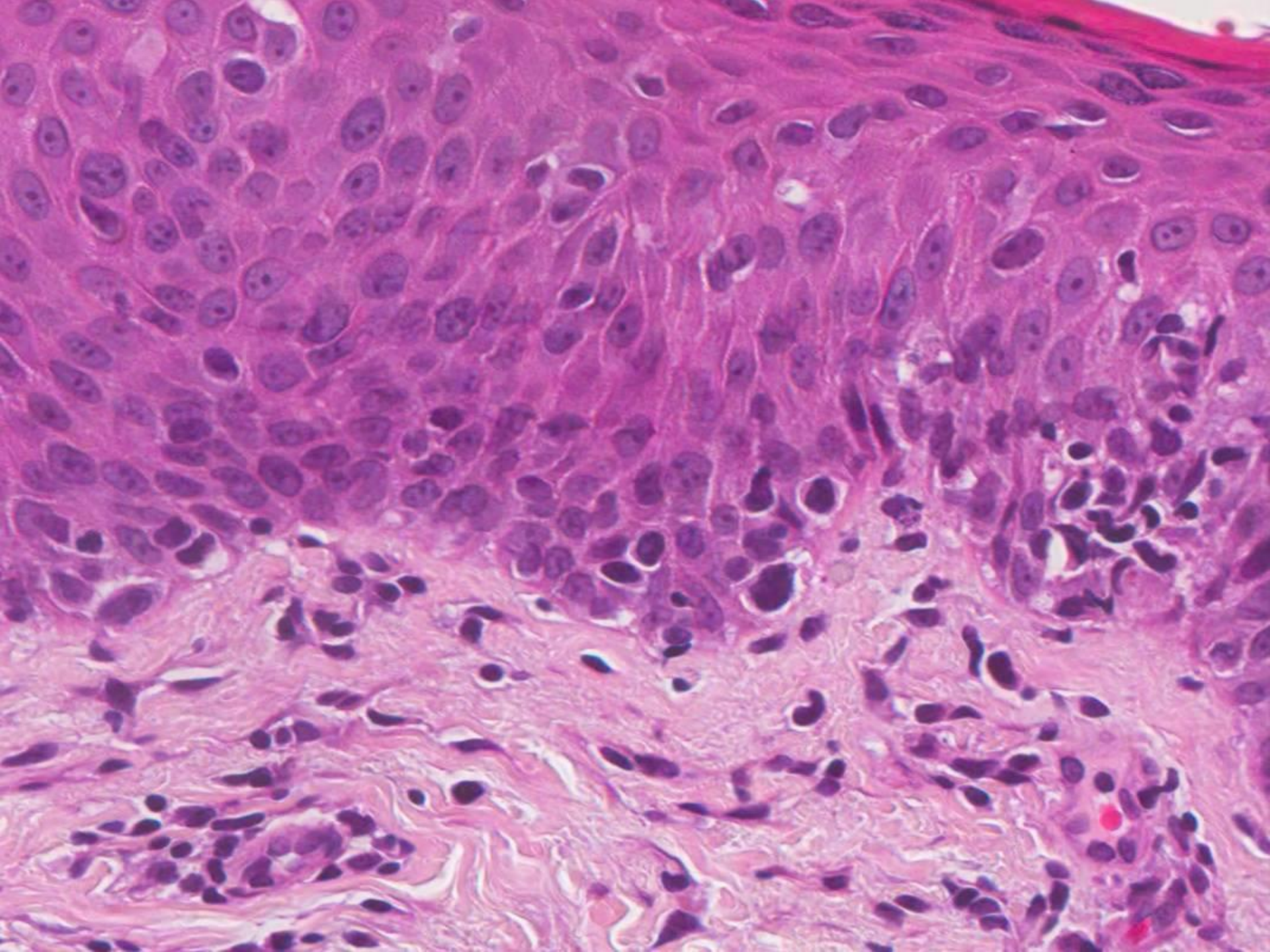
Case 6

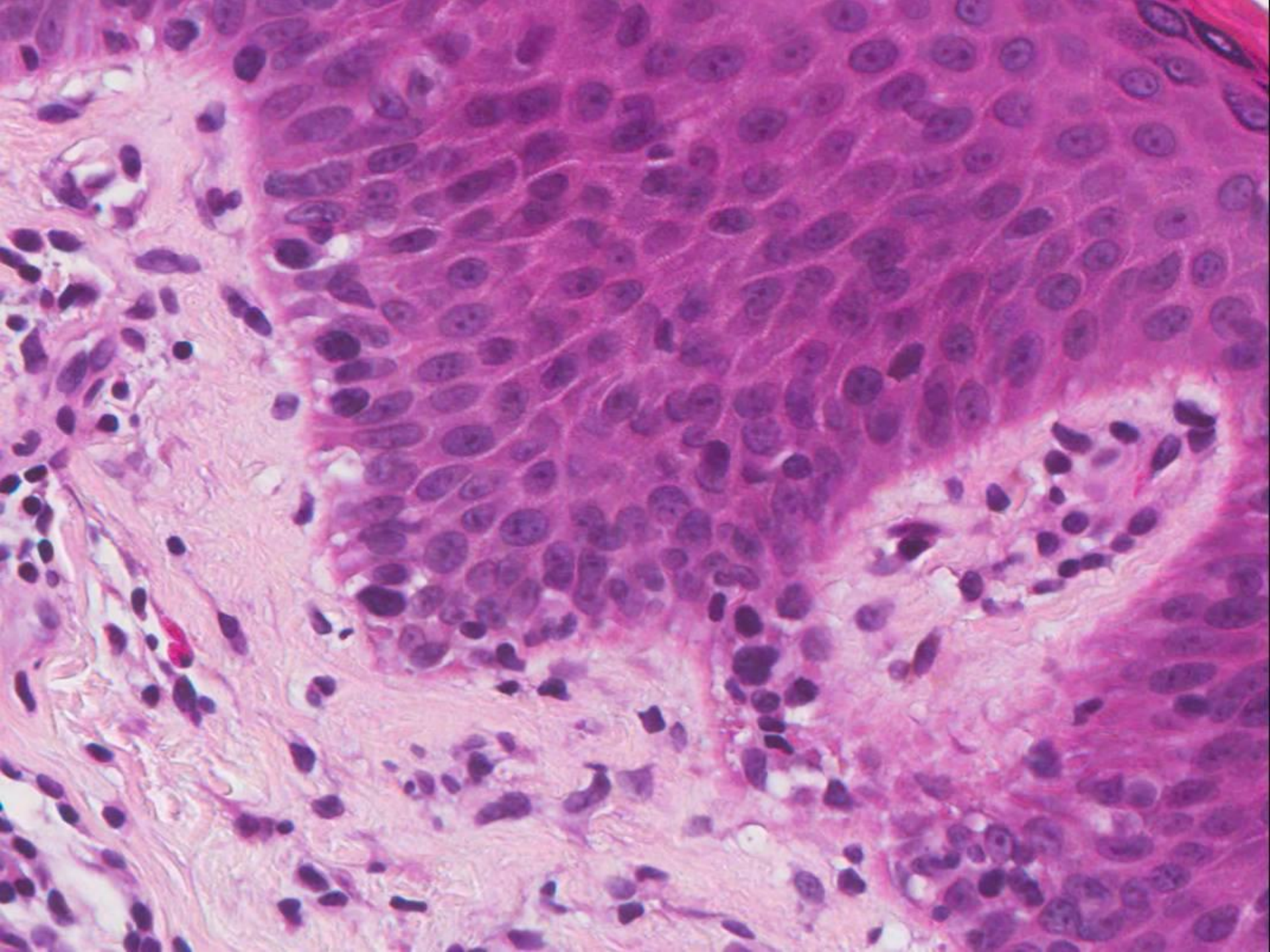
- 45/M
- Widespread papular rash and 2 nodules on arm and forehead



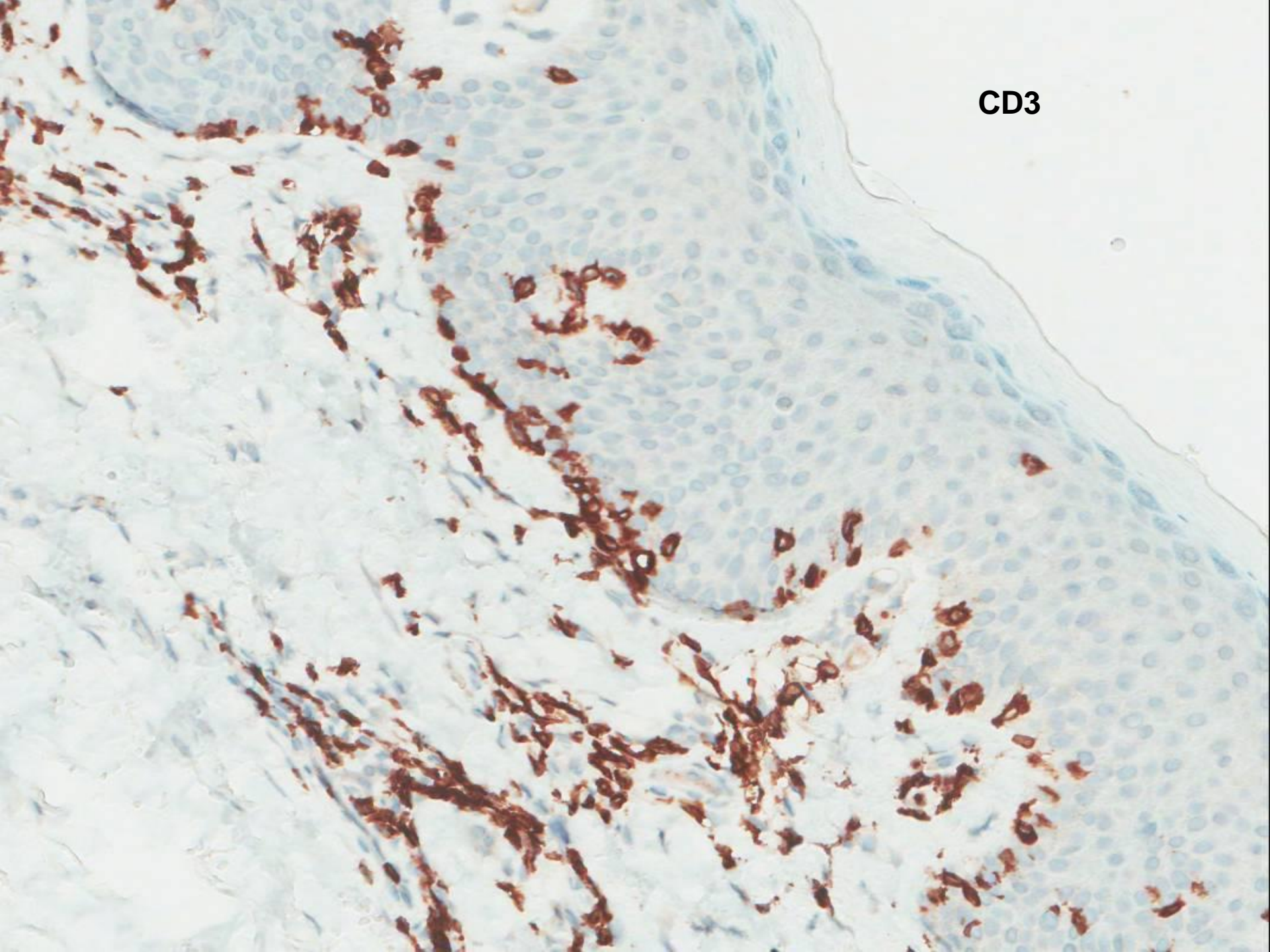




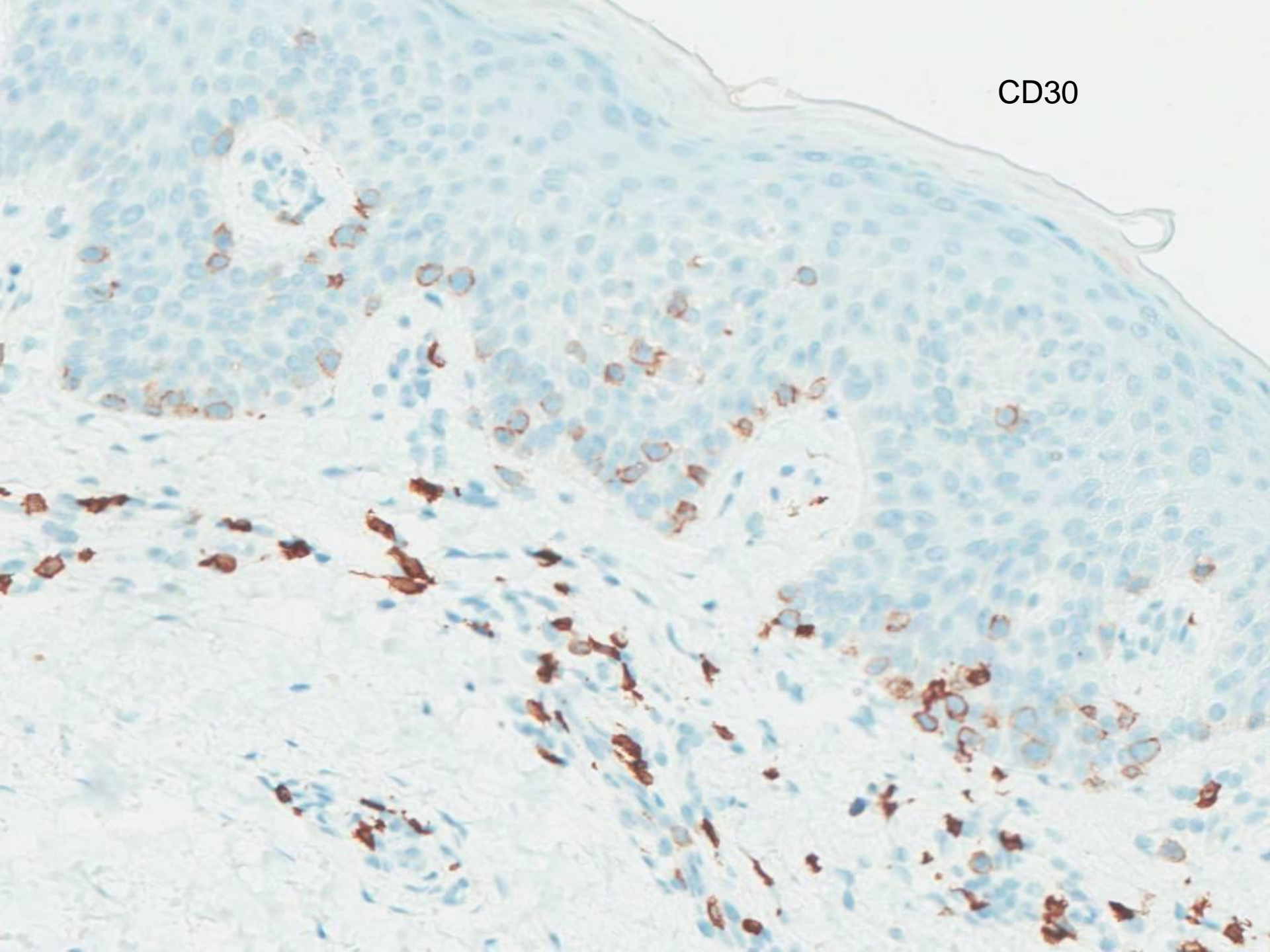




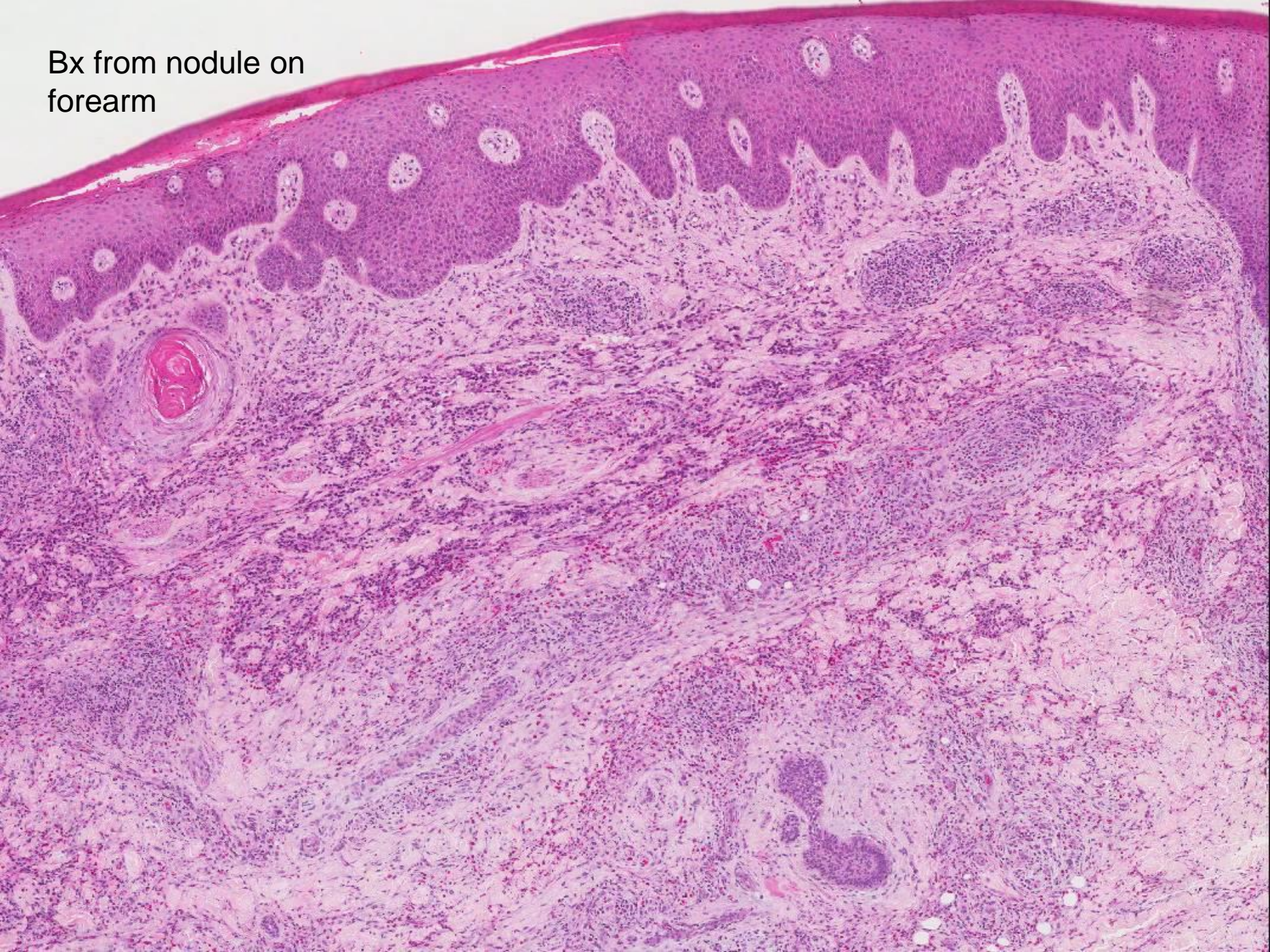
CD3

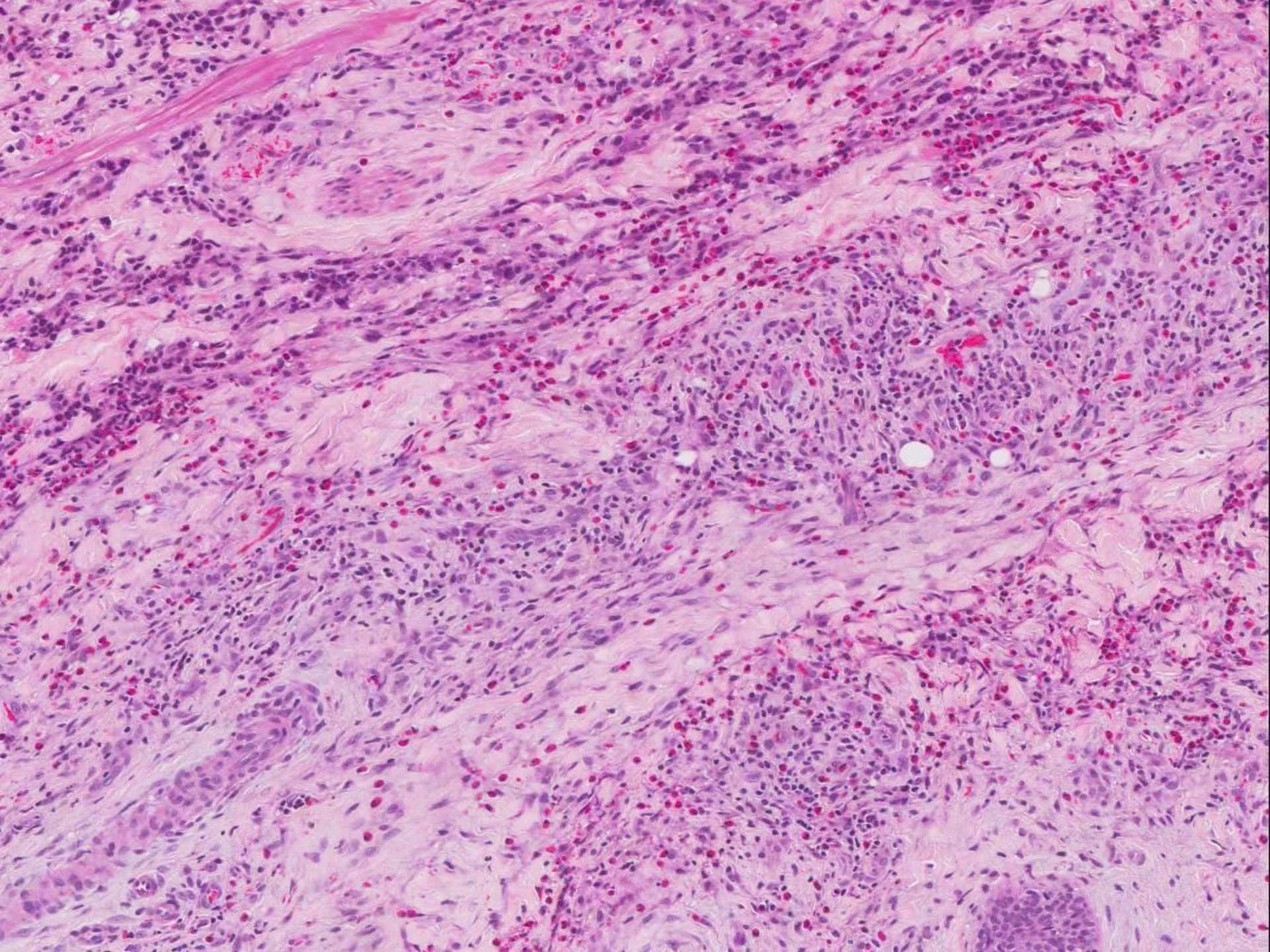


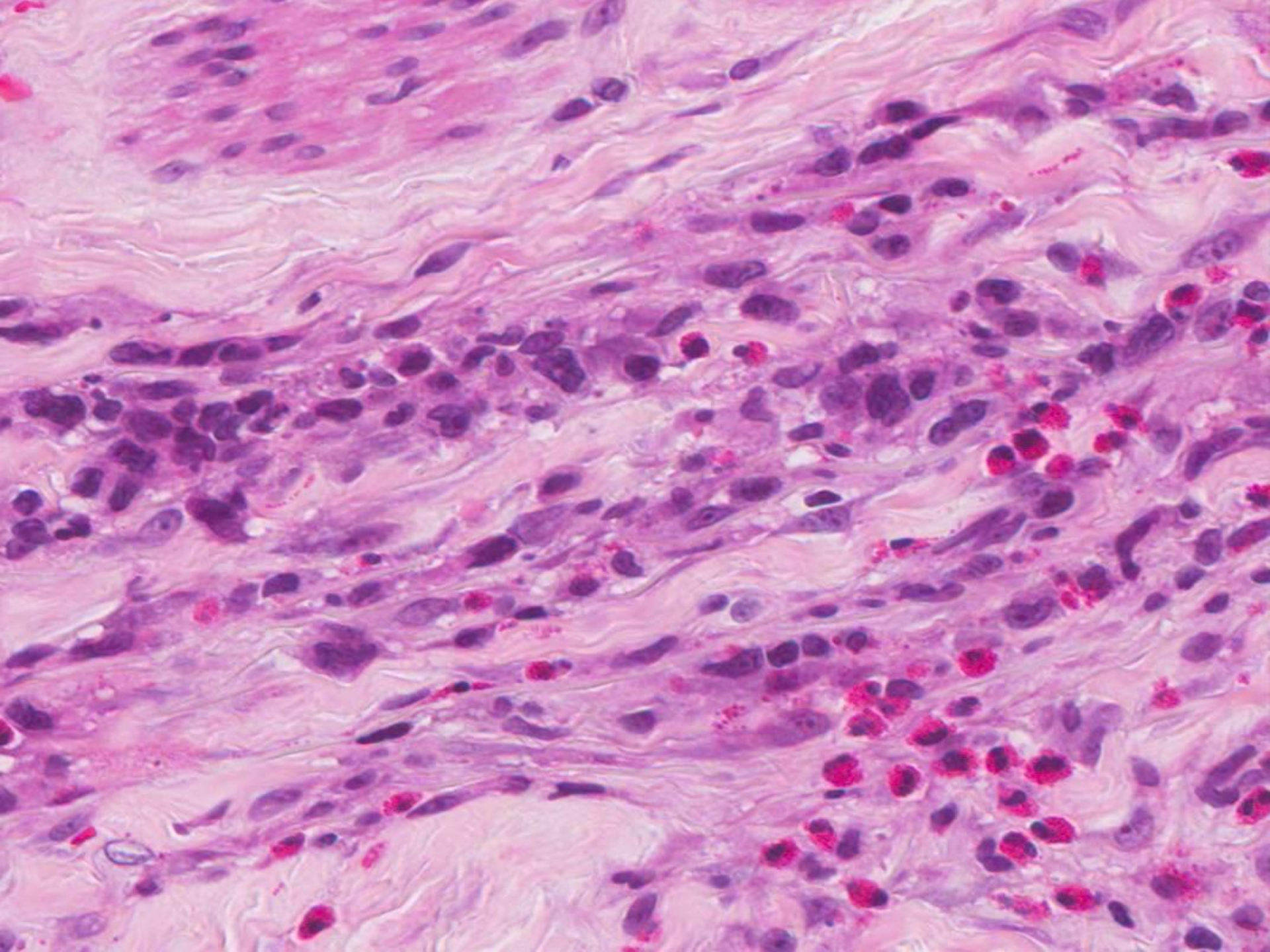
CD30



Bx from nodule on
forearm







Patient referred to specialist lymphoma MDT

Lesions showing signs of spontaneous resolution

Final Diagnosis

Lymphomatoid papulosis (Type A and Type B)

Mycosis
Fungoides

Type B LyP

- Indistinguishable histologically from mycosis fungoides, distinction entirely on clinical grounds
- Few, if any, large atypical blast cells seen.
- IHC:
CD4+CD8-
CD30 blasts often absent



LyP

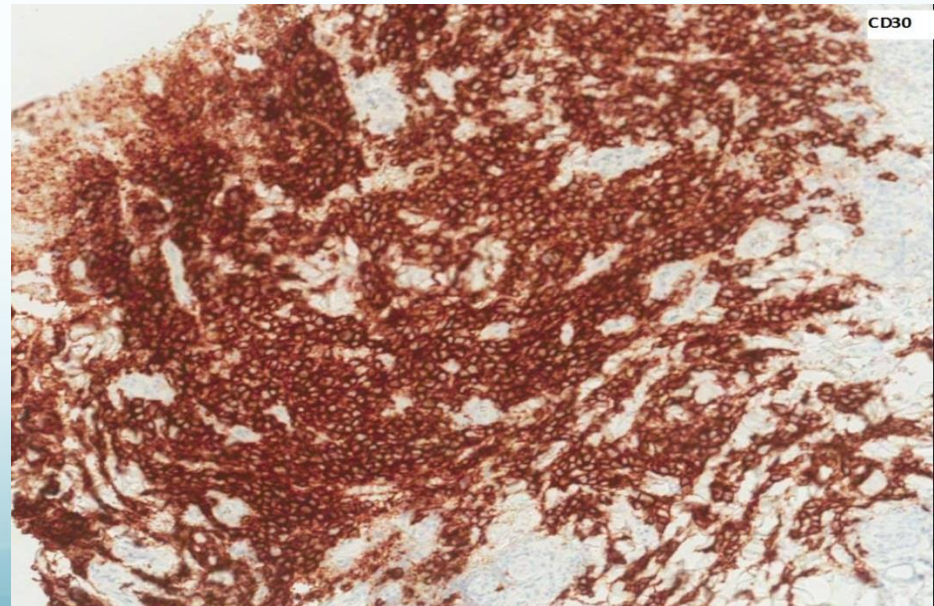
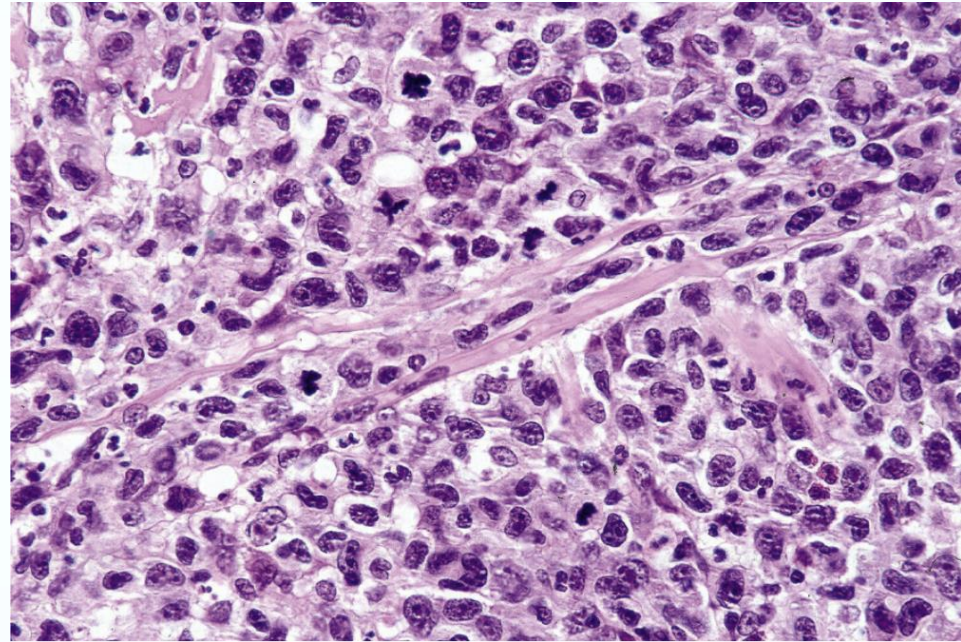


Histopathological Spectrum

- Type A
- Type B
- Type C
- Type D (epidermotropic)
- Type E (angio-invasive)
- Type F (folliculotropic)
- LyP with 6p25.3 rearrangement

Type C LyP

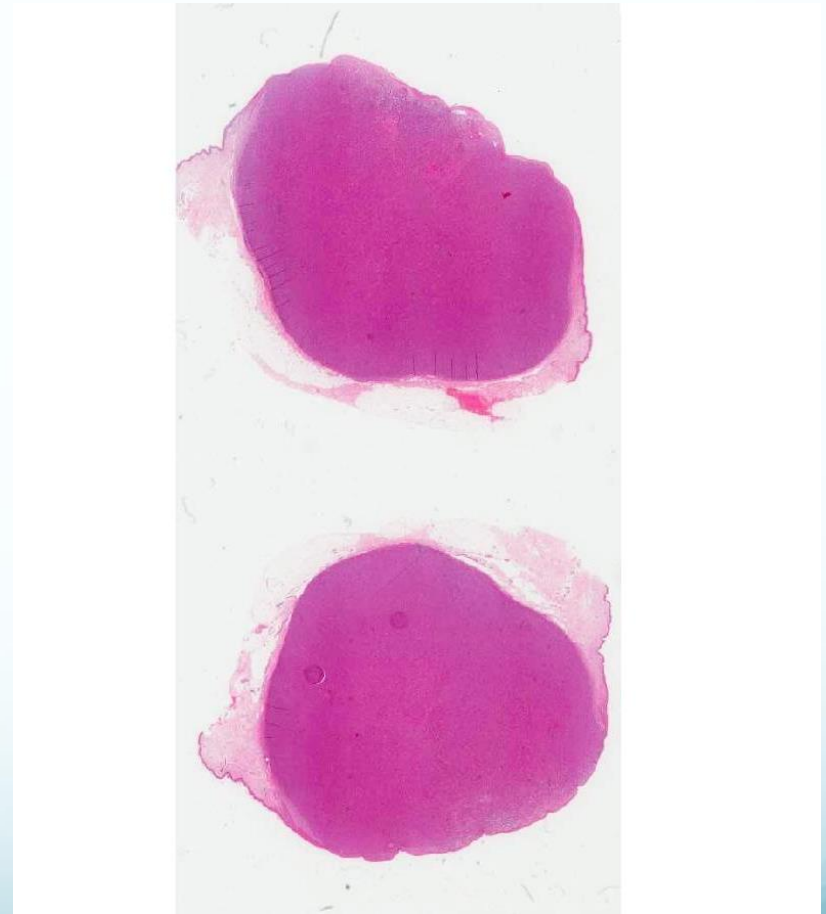
- Sheets of atypical CD30 + cells.
- Lack of polymorphic background.
- D/D: Other CD30+ T/B cell lymphoma

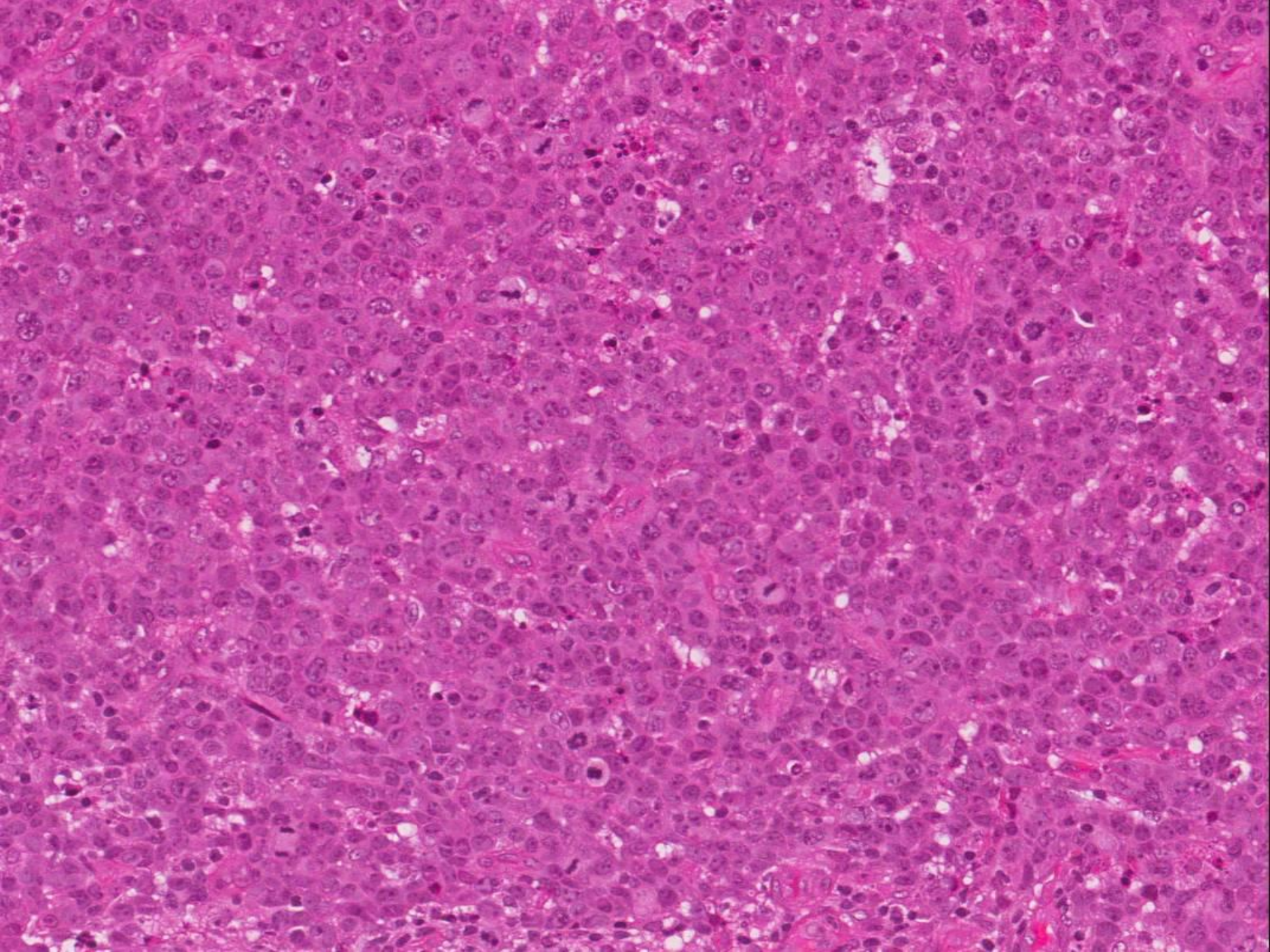


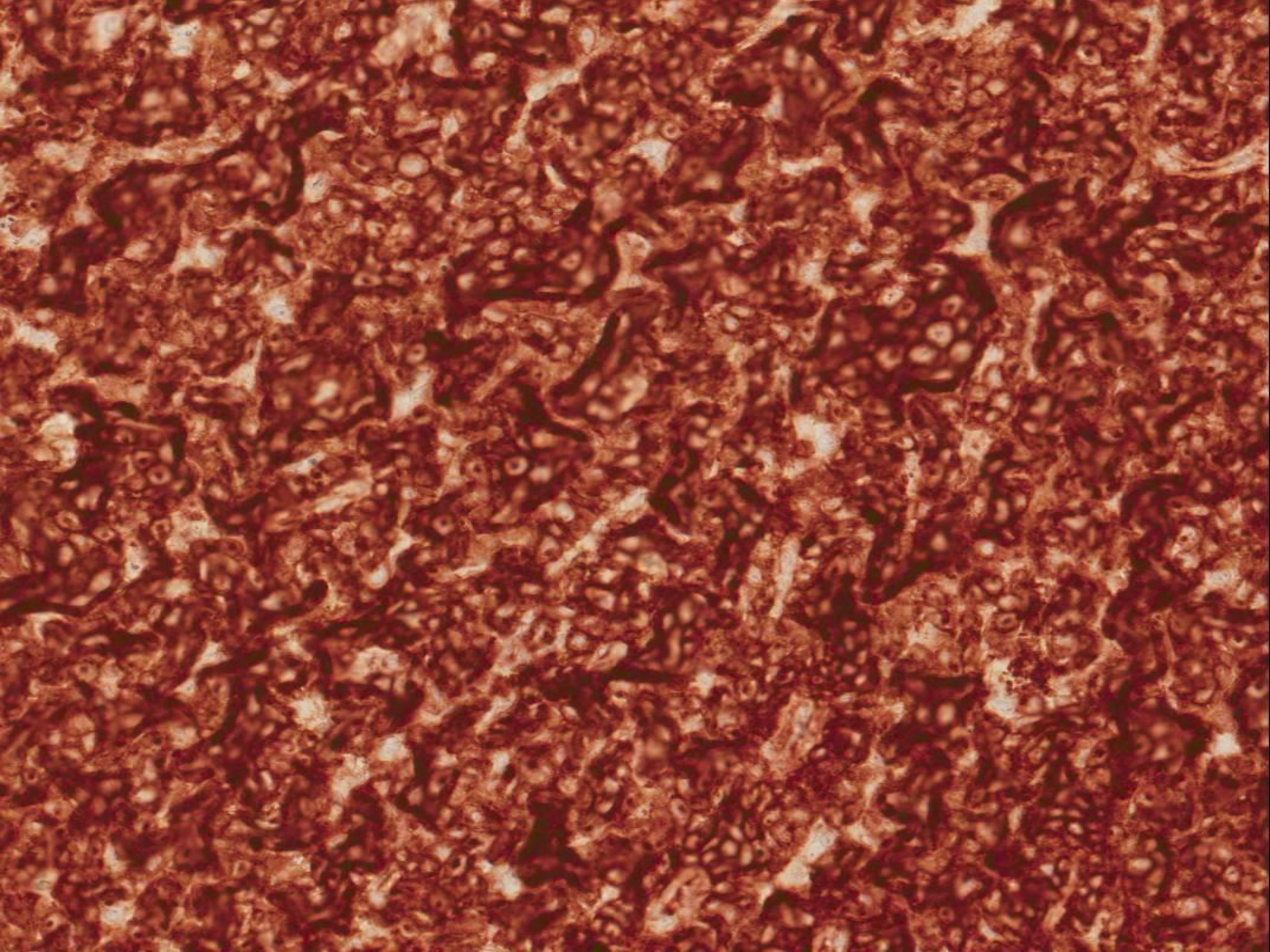
D/D of LyP Type C

- Primary Cutaneous CD30+Anaplastic T Cell Lymphoma
- Transformed Mycosis Fungoides with CD30+ cells
- Cutaneous involvement by Systemic Anaplastic T Cell Lymphoma

Primary Cutaneous CD30+ Anaplastic T cell lymphoma



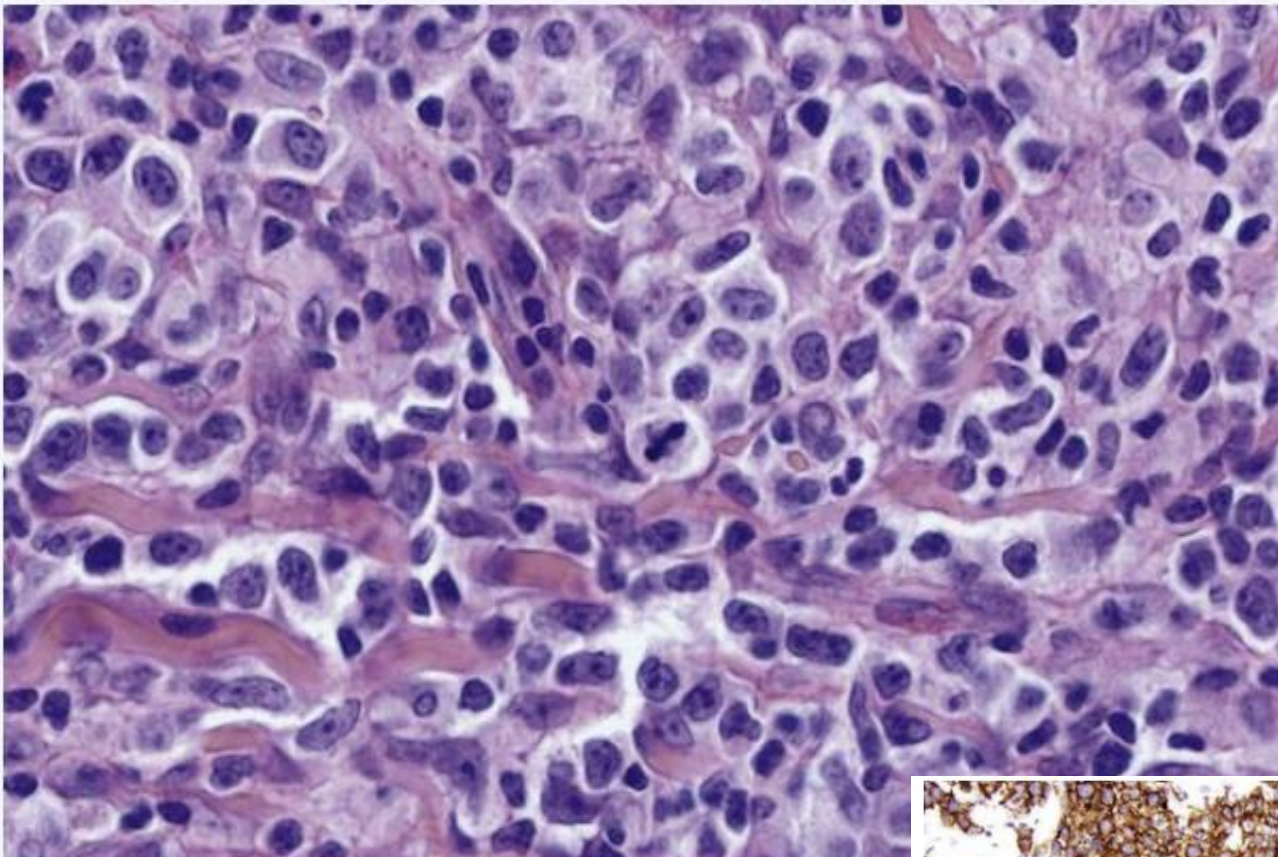




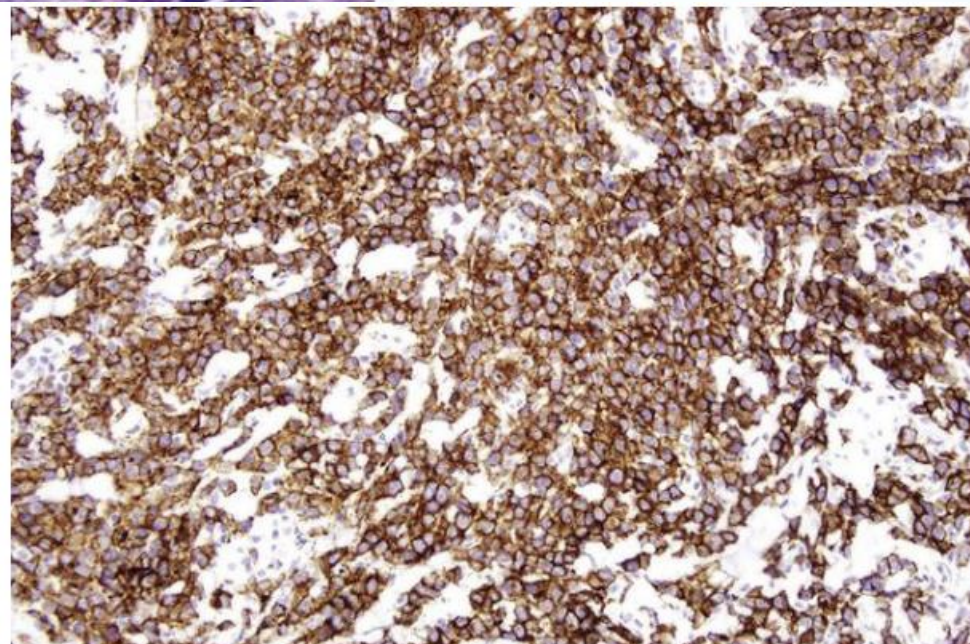
Transformed Mycosis Fungoides



c/o McKee's textbook



Transformed MF:
sheets of large
blasts



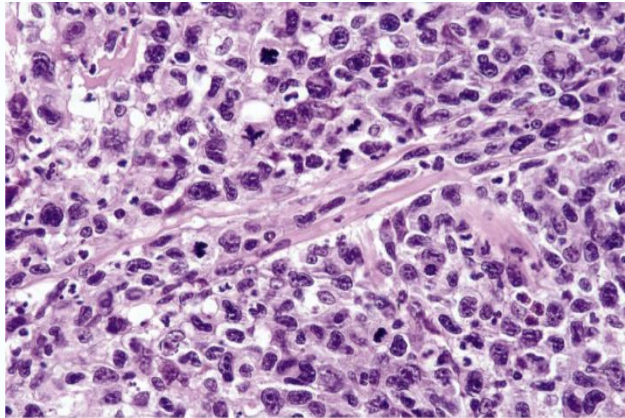
CD30

Cutaneous Involvement by Systemic Anaplastic T cell lymphoma



CD30+
Alk1 usually +
EMA usually +

D/D of Type C LyP



CD3+, CD30+, CD4+, CD8-



LyP



Cutaneous involvement by systemic ALCL



Primary cutaneous ALCL



Transformed MF

Histopathological Spectrum

- Type A
- Type B
- Type C
- Type D (epidermotropic)
- Type E (angio-invasive)
- Type F (folliculotropic)
- LyP with 6p25.3 rearrangement

LyP Type D

ORIGINAL ARTICLE

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,*‡ Zsolt Argenyi, MD,§ Regina Fink-Puches,*
Amelia Lissia, MD,|| Mario Magaña, MD,¶ Luis Requena, MD,#
Ingrid Simonitsch, MD,** and Lorenzo Cerroni, MD**

Abstract: Lymphomatoid papulosis (LyP) is a recurrent, self-healing eruption belonging to the spectrum of cutaneous CD30+ lymphoproliferative disorders. Three main histologic subtypes of LyP are recognized: type A (histiocytic), type B (mycosis fungoides—(MF)-like), and type C (anaplastic large cell lymphoma-like). We reviewed 26 biopsies from 9 patients (M:F = 6:3, median age: 29; mean age 27.2; age range 10 to 38) who presented with clinical features typical of LyP but with histopathologic aspects that resembled primary cutaneous aggressive epidermotropic CD8+ cytotoxic T-cell lymphoma. In all but 1 case atypical lymphoid cells showed expression of CD30, and in 8 of 9 cases a T-cell cytotoxic phenotype could be observed (βF1+, CD3+, CD4–, CD8+). Expression of at least 1 cytotoxic marker (TIA-1, granzyme B) was observed in all cases. Polymerase chain reaction analysis of the T-cell receptor genes revealed a monoclonal rearrangement in 2 of 5 cases. Follow-up data were available for 8 patients (6

Key Words: lymphomatoid papulosis, primary cutaneous aggressive epidermotropic CD8+ cytotoxic T-cell lymphoma, mycosis fungoides, cytotoxic lymphoma, cutaneous T-cell lymphoma

(*Am J Surg Pathol* 2010;34:1168–1175)

Lymphomatoid papulosis (LyP) is defined as a chronic, recurrent, self-healing eruption of papules and small nodules, characterized by a waxing and waning course and by histopathologic features of a cutaneous T-cell lymphoma^{6,21}; 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 classification of tumors of hematopoietic and lymphoid tissues.^{21,31} Histopathologically, 2 subtypes

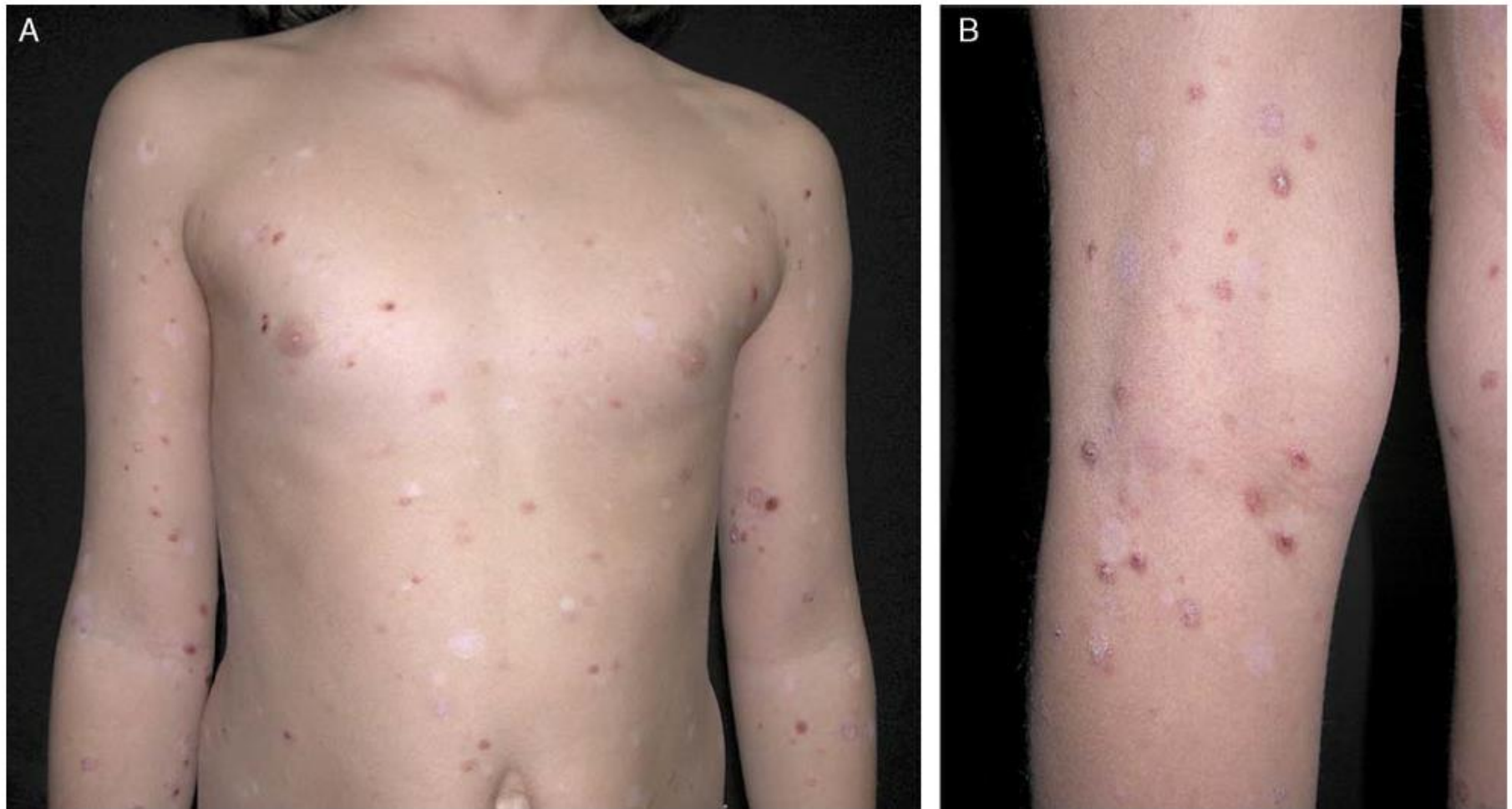


FIGURE 1. Generalized, partly necrotic papules and small nodules on the trunk (A) and leg (B). Note several hypopigmented, partly scarring areas related to regressed lesions (Case 8).

full color
online

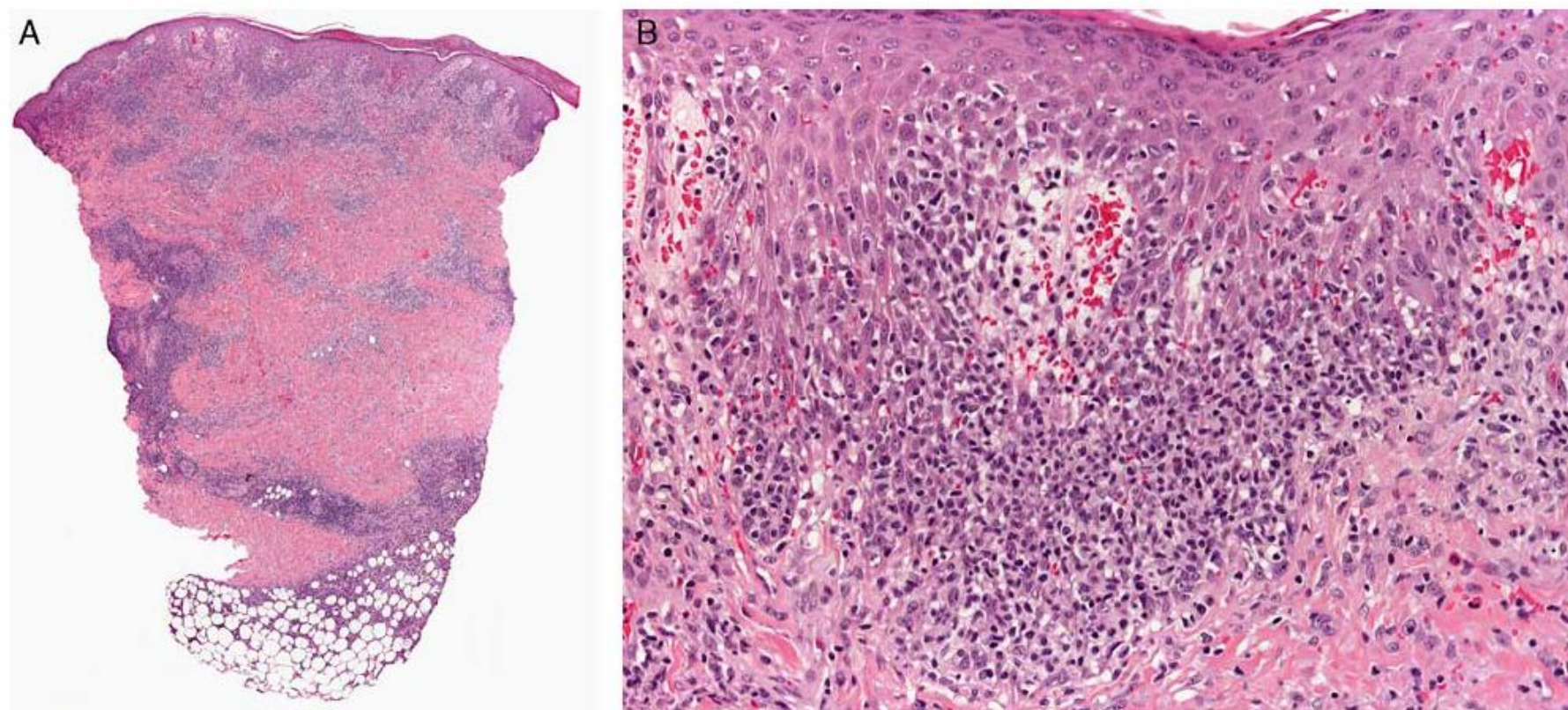


FIGURE 4. Histopathologic features of case 2. A, Dense lymphoid infiltrates involving the entire dermis and subcutaneous fat. B, Note prominent epidermotropism with epidermal hyperplasia. [full color](#)
[online](#)

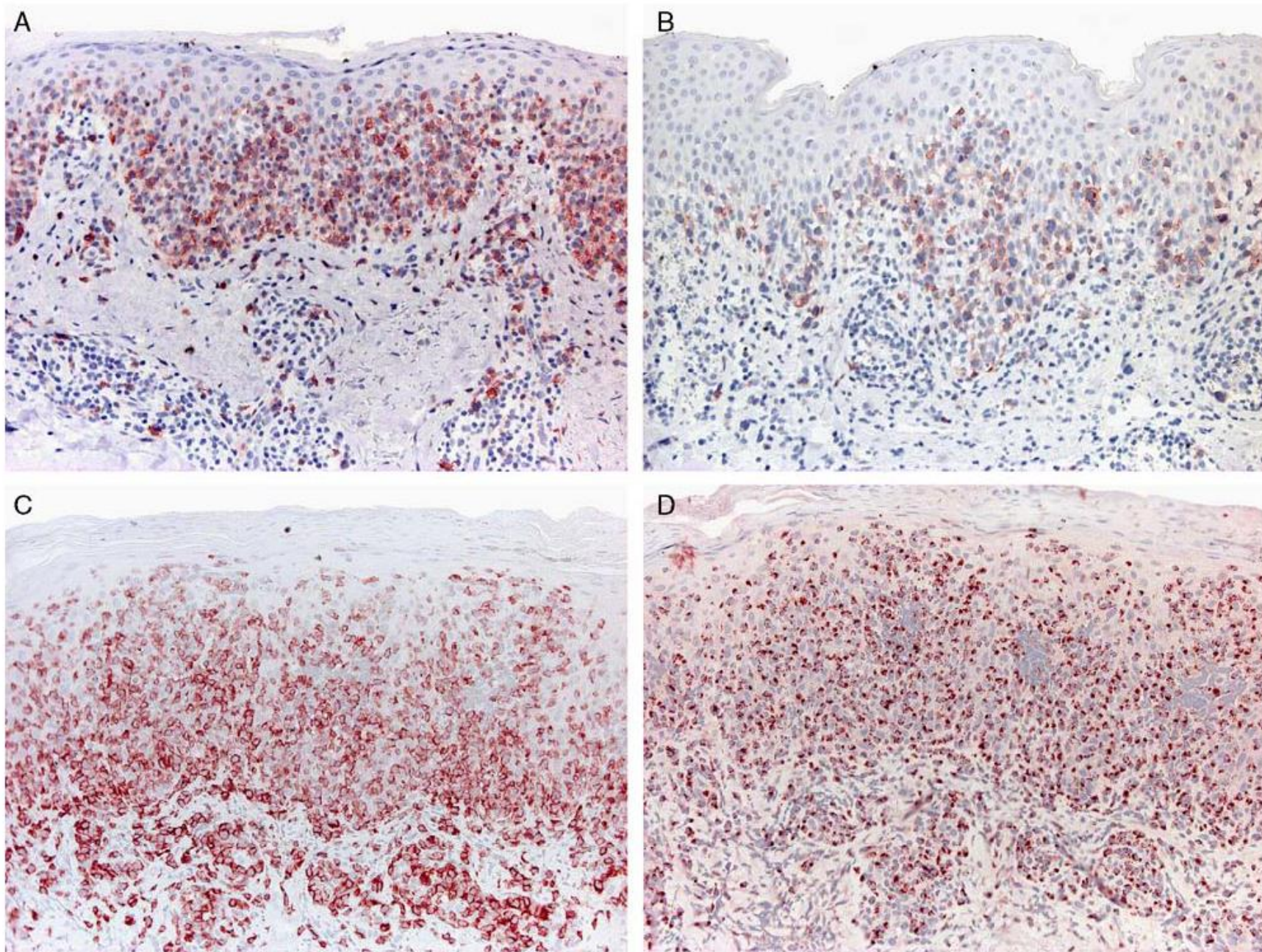


FIGURE 6. Different expression of CD30 and other phenotypic features. A, Strong expression of CD30 (case 6); (B) weak expression of CD30 (case 9); (C) strong expression of CD8 and of (D) granzyme B (both stainings: case 6). [full color online](#)

Histological D/D

- Primary Cutaneous CD8+ aggressive epidermotropic CD+ T cell Lymphoma
- Pagetoid Reticulosis
- CD8+ Mycosis Fungoides

Histopathological Spectrum

- Type A
- Type B
- Type C
- Type D (epidermotropic)
- Type E (angio-invasive)
- Type F (folliculotropic)
- LyP with 6p25.3 rearrangement



**Expanding
clinical
spectrum**

Case 7

59/F presented with
a area of ulceration
with haemorrhagic
crust (eschar like) on
chin

?cellulitis

?pyoderma
gangrenosum

?atypical infection



Punch bx from ulcer

- Histo report: Extensive ulceration with eosinophil rich dermal infiltrate consistent with eosinophilic cellulitis
- Investigations: Raised eosinophil count
- Imaging: Lung nodules

?Churg Strauss Vasculitis

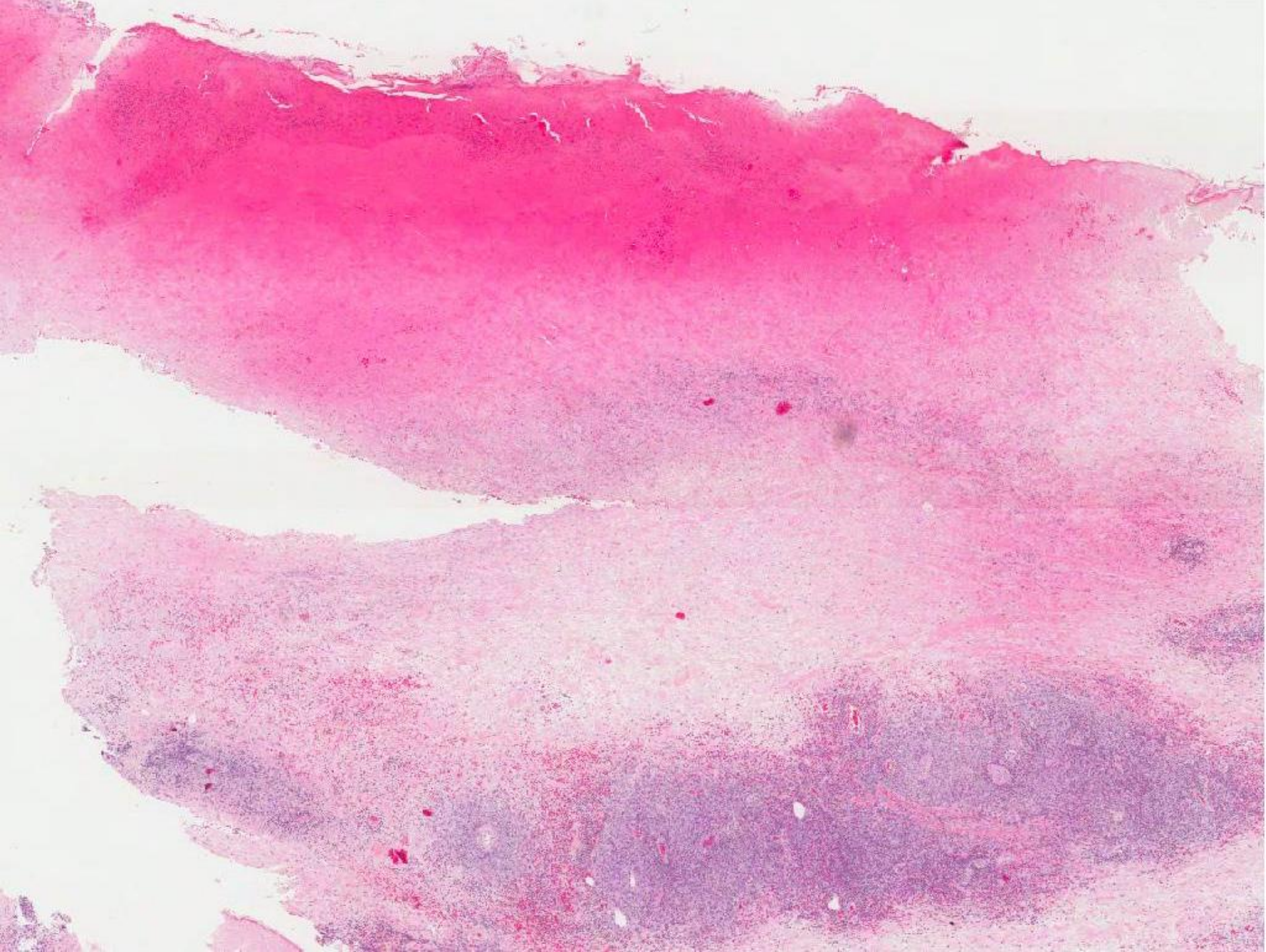
- Referred to respiratory team
- In the meantime, treated with prednisolone and the ulcer rapidly healed with scarring

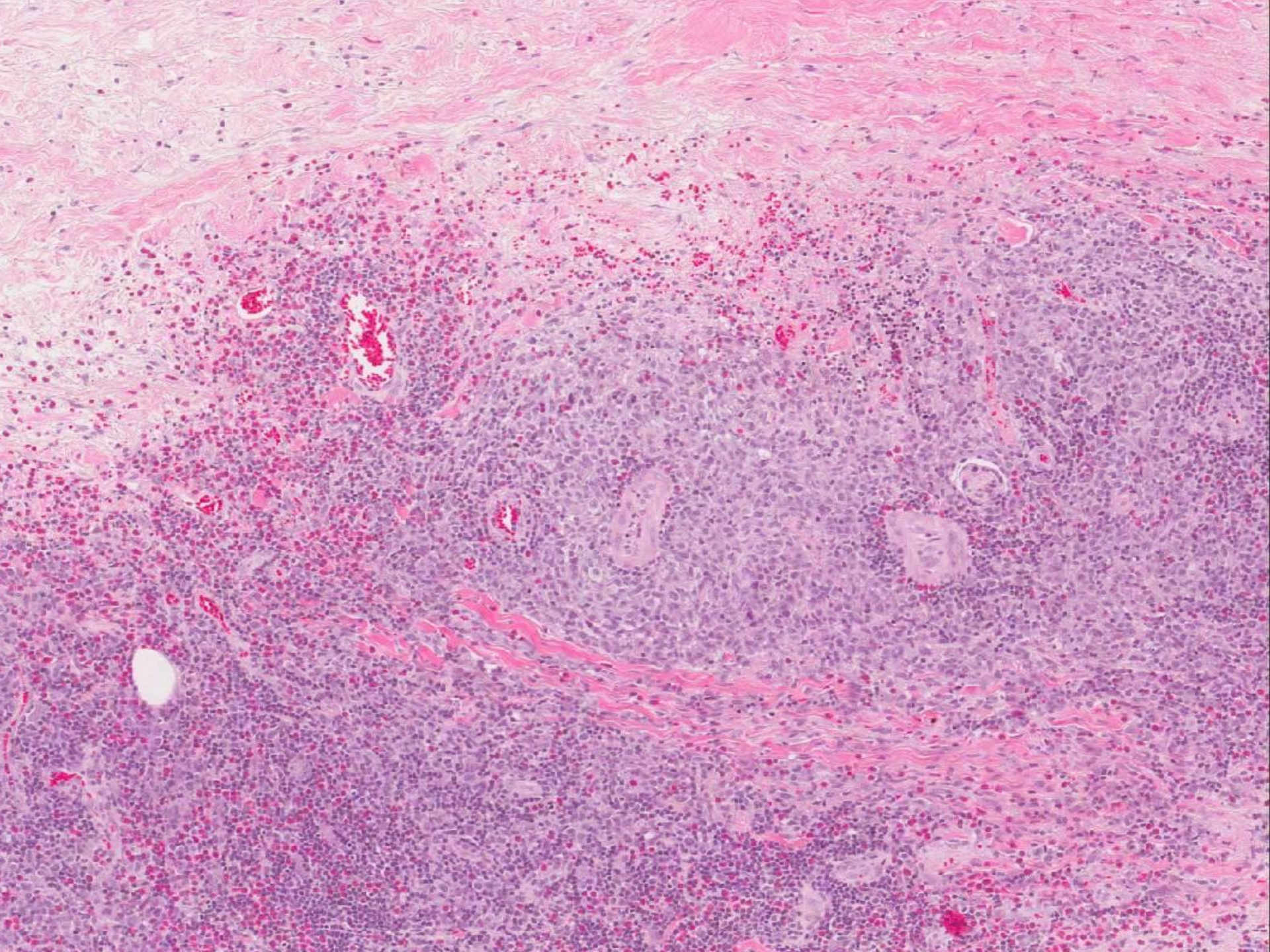


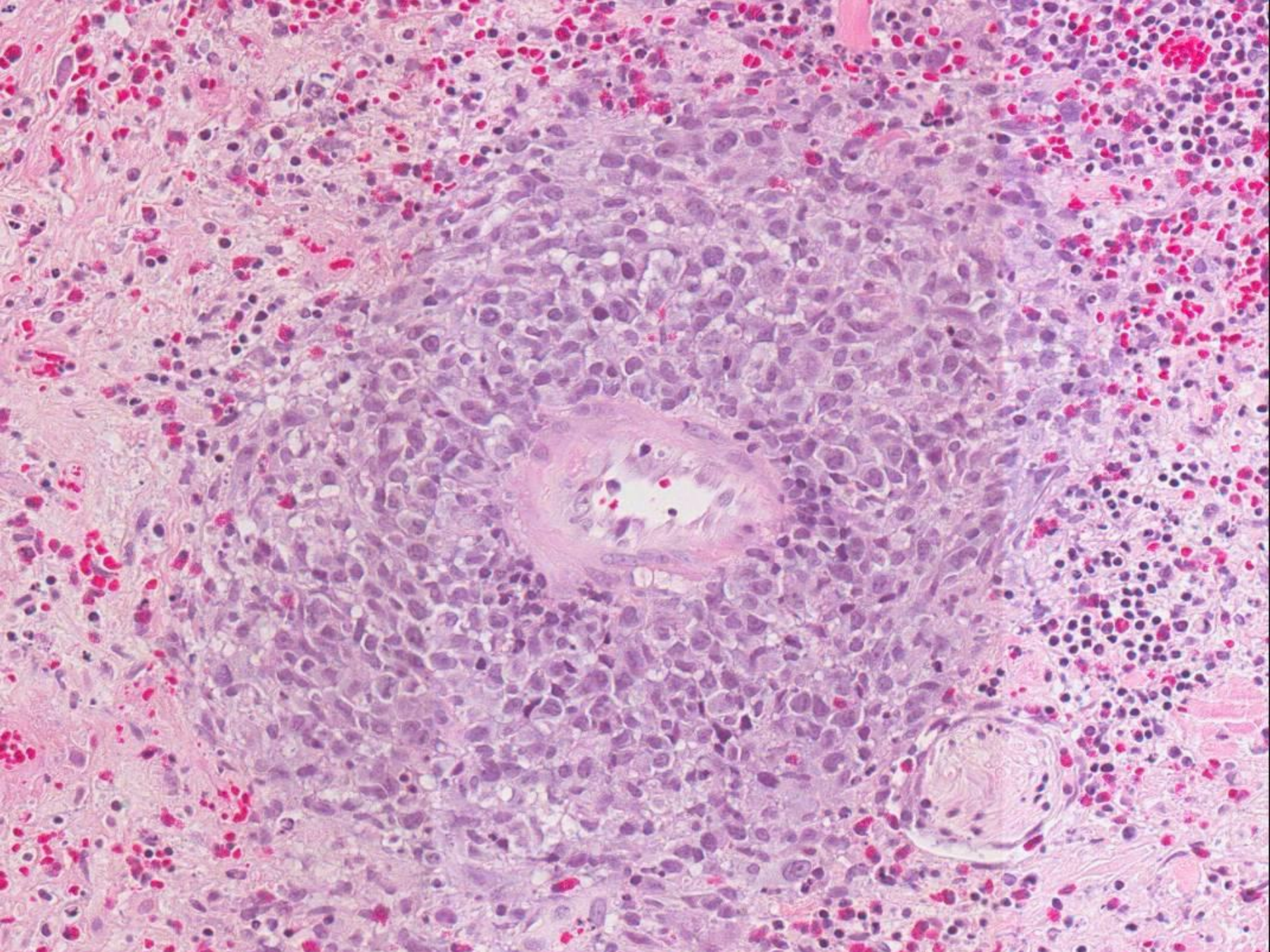
2 new similar lesions developed on her breast

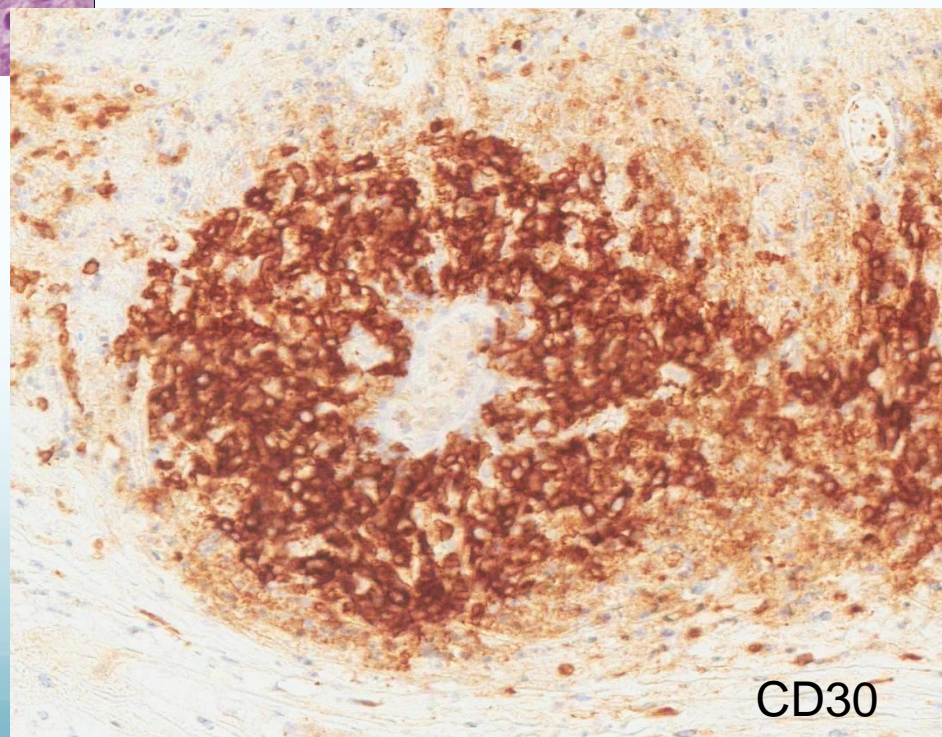
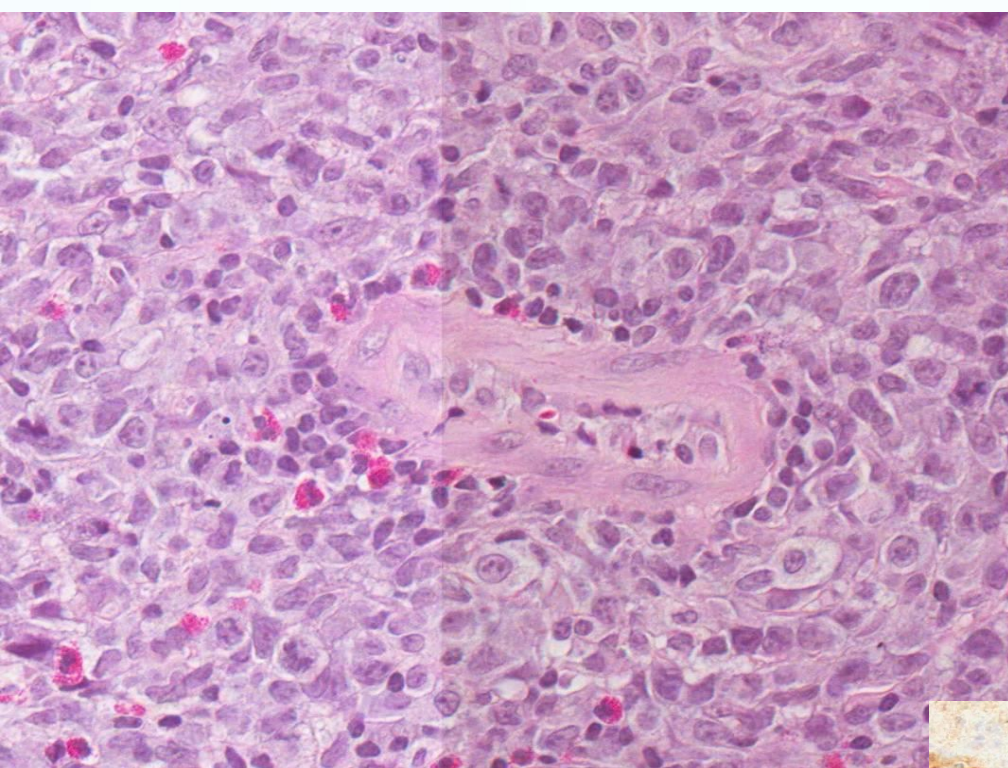
2nd Bx
Histo report:
High grade T Cell
Lymphoma and
referred to us.











More History

- No Lymphadenopathy or systemic symptoms
- Lesions on the breast were also healing rapidly
- Previous history of similar lesion in 2009, which healed spontaneously

Angioinvasive lymphomatoid papulosis: a new variant simulating aggressive lymphomas.

Kempf W¹, Kazakov DV, Schärer L, Rütten A, Mentzel T, Paredes BE, Palmedo G, Panizzon RG, Kutzner H.

- Type E LyP
- Oligolesional papules rapidly ulcerate to form large 1-4cm eschar like lesions
- Clinical d/d- pyoderma gangrenosum, ulcerative herpes, vasculitis
- Histo- Angiocentric and angiodestructive infiltrate

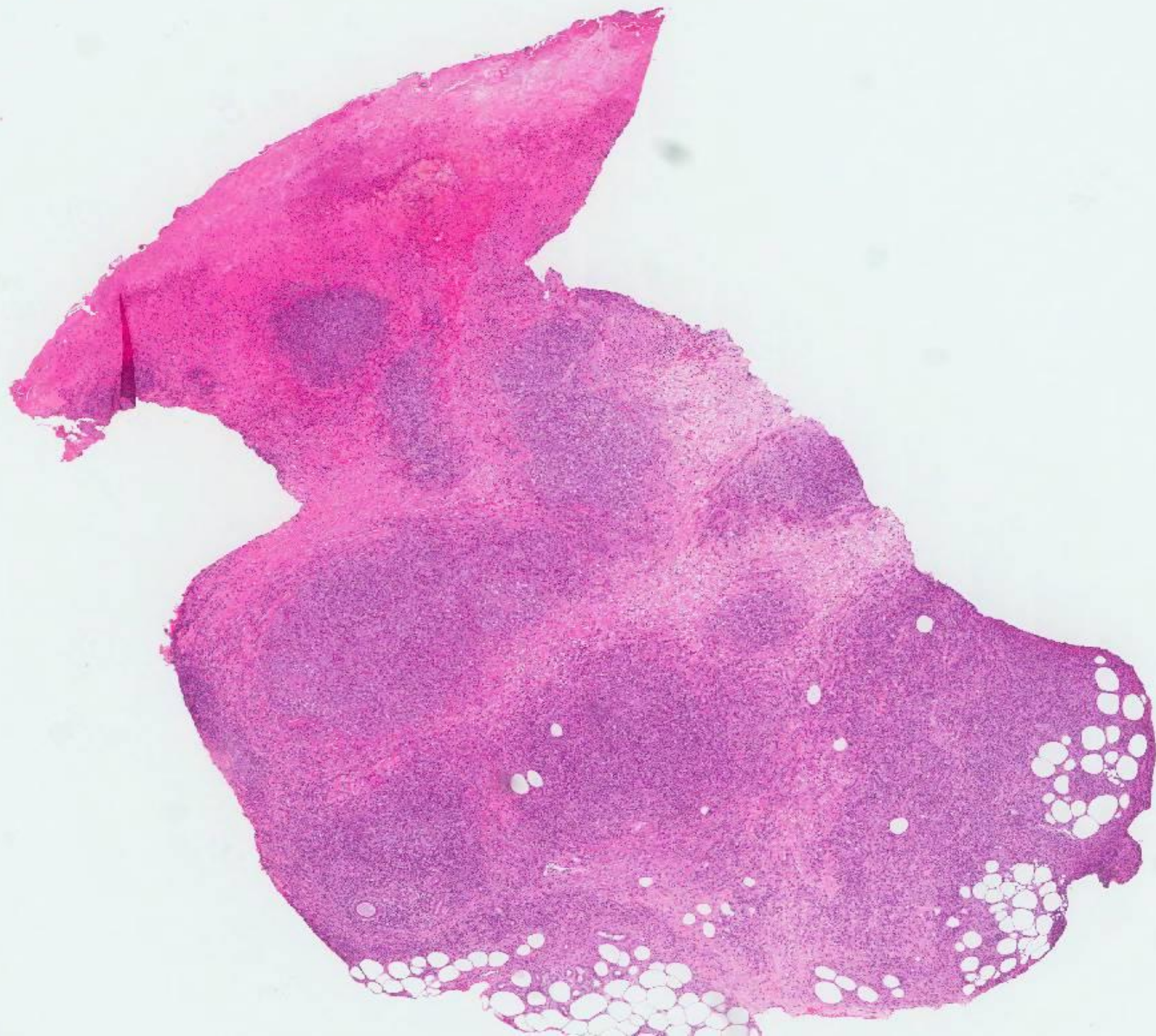
Histological D/D of angiocentric T cell lymphoid proliferation

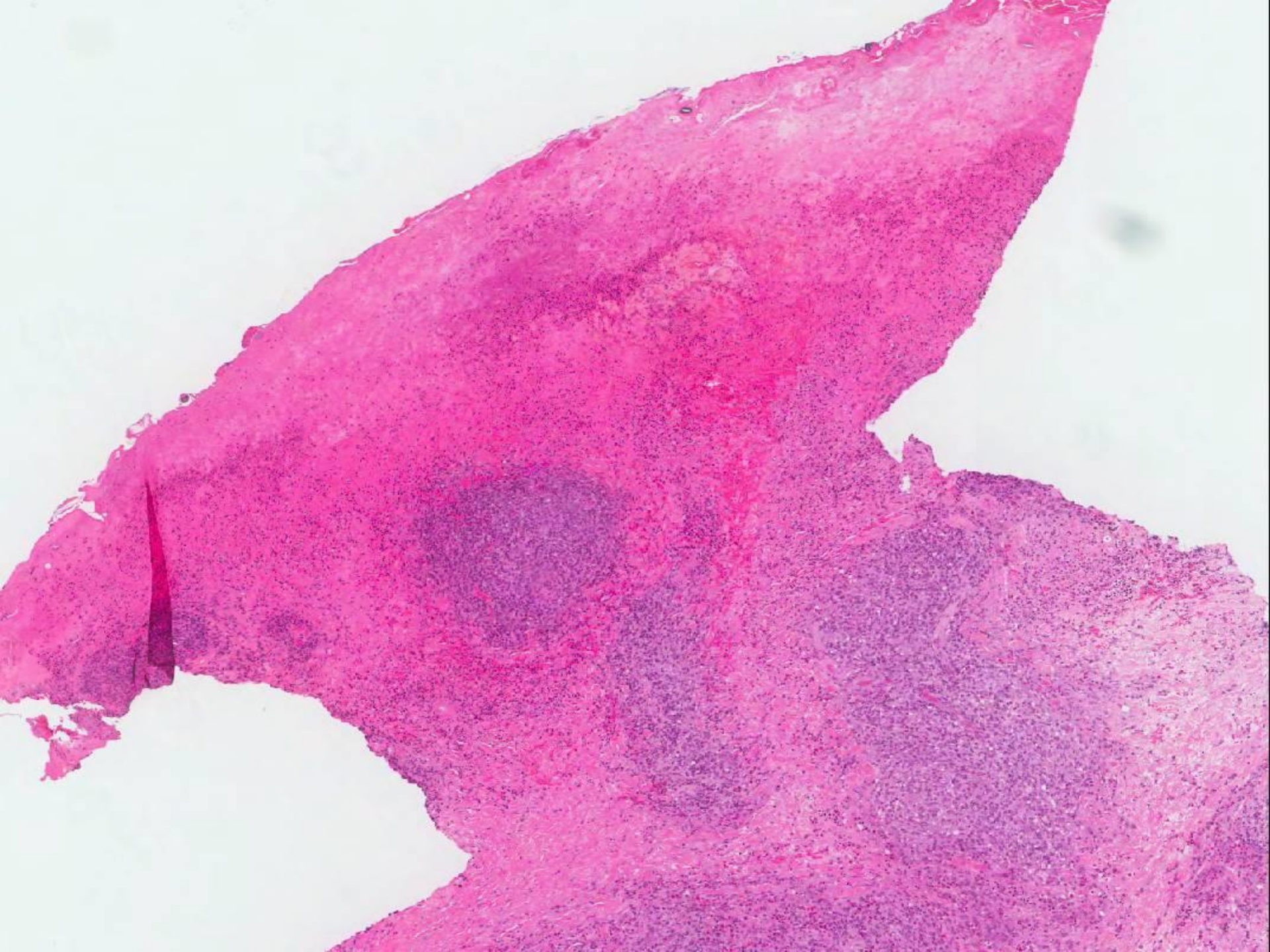
- Extranodal T/NK cell lymphoma, nasal type
- Gamma/Delta T cell lymphoma

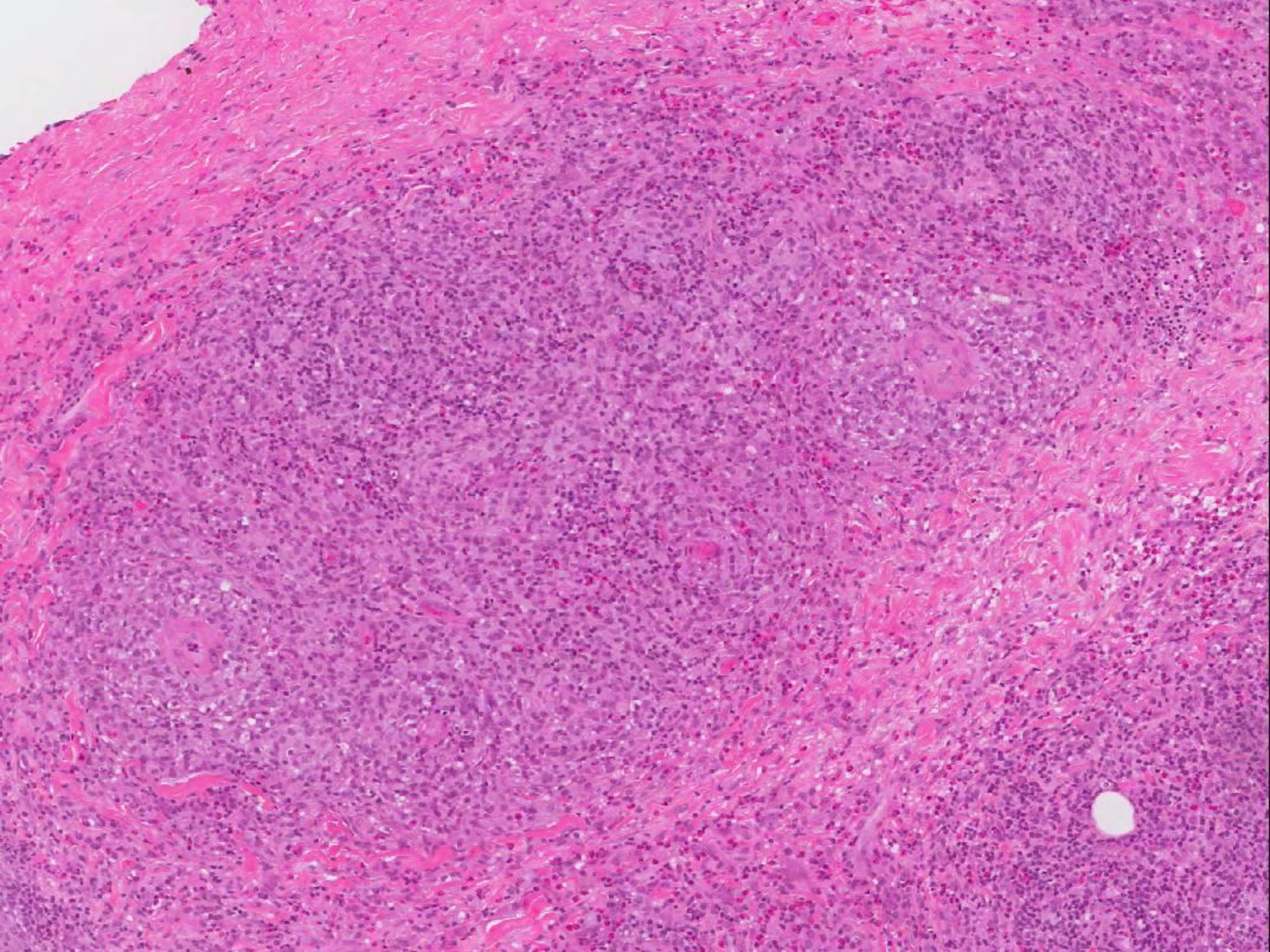


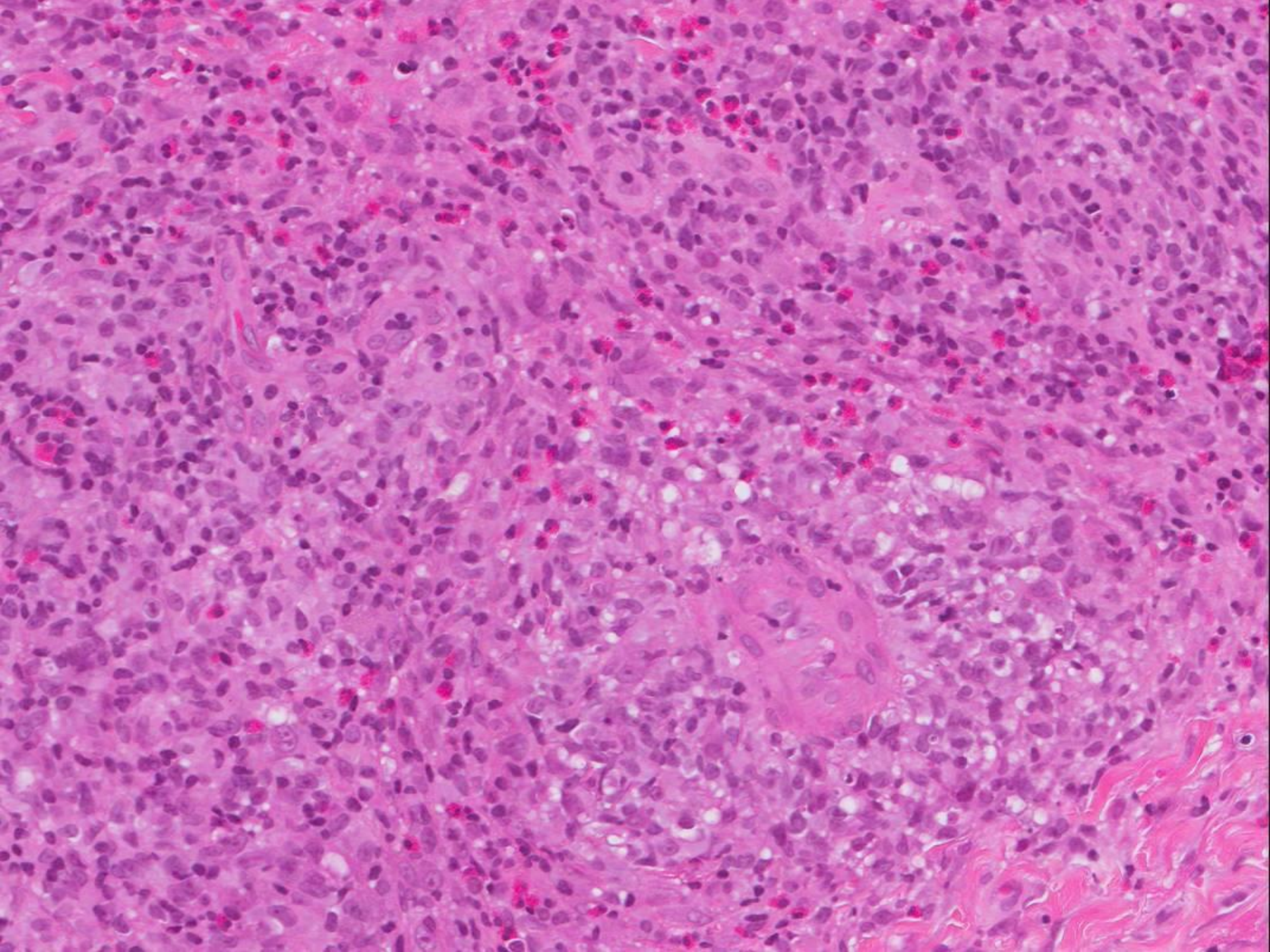
Case 8

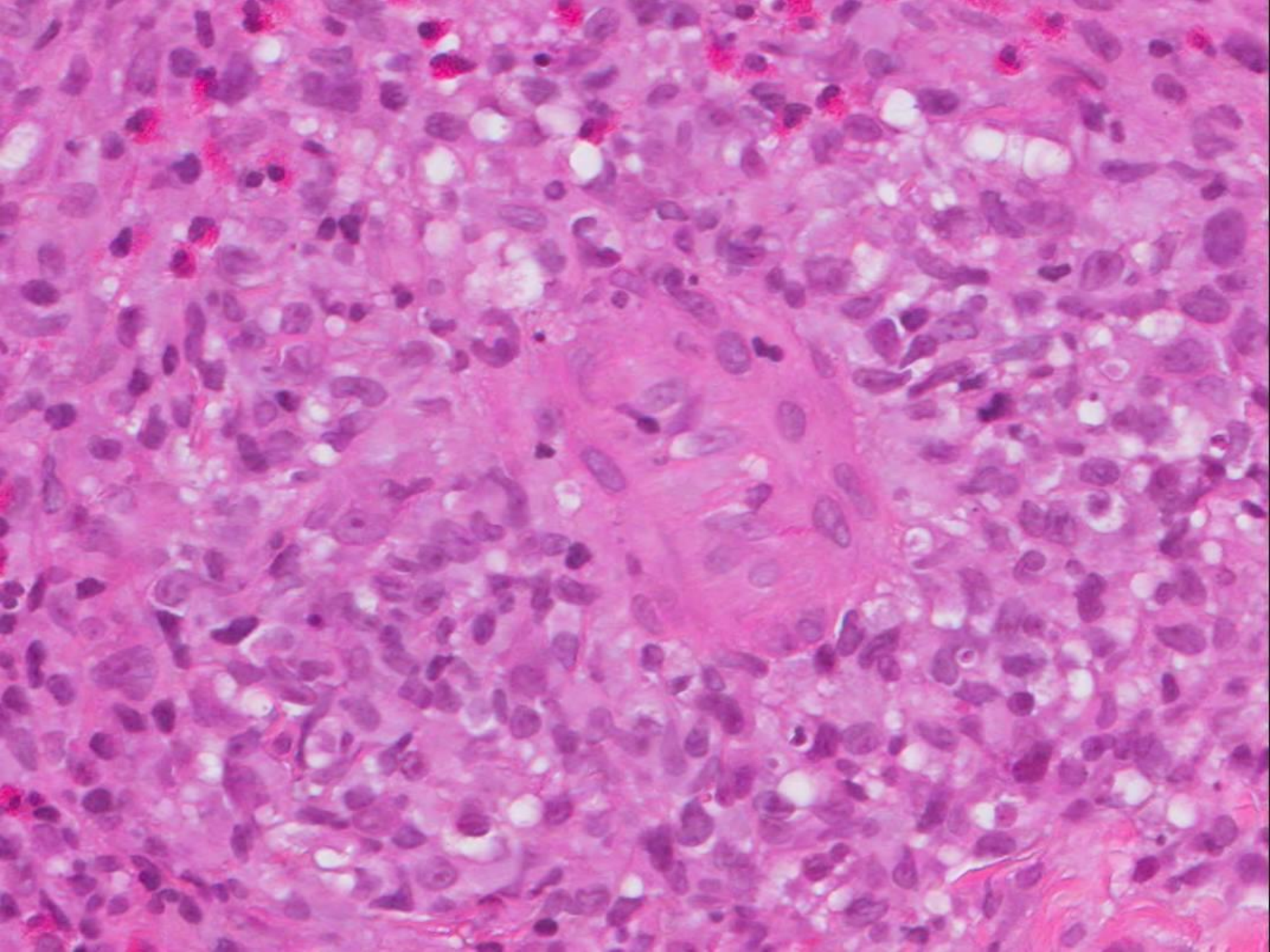
- 51/F
- Scabbed eroded solitary plaque left axilla
- ?pyoderma gangrenosum ?infective



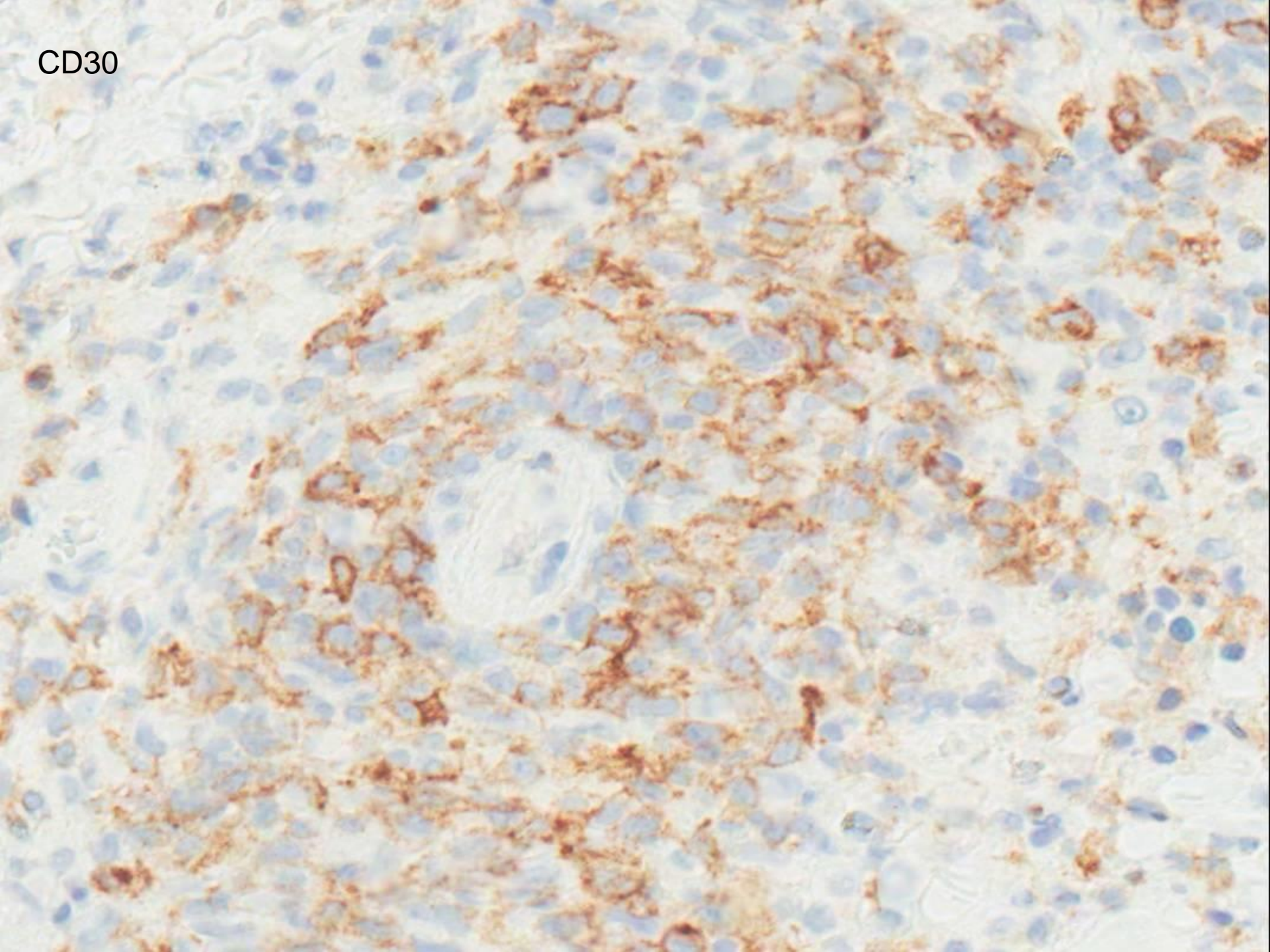








CD30



Histopathological Spectrum

- Type A
- Type B
- Type C
- Type D (epidermotropic)
- Type E (angio-invasive)
- Type F (folliculotropic)
- LyP with 6p25.3 rearrangement

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

Werner Kempf, MD,^a Dmitry V. Kazakov, MD, PhD,^b Hans-Peter Baumgartner, MD,^c and Heinz Kutzner, MD^d
Zürich and Zug, Switzerland; Pilsen and Prague, Czech Republic; and Friedrichshafen, Germany

Background: Follicular lymphomatoid papulosis (LyP) describes a variant of LyP with perifollicular infiltrates and some degree of folliculotropism of CD30⁺ atypical lymphocytes. So far, only a few cases of follicular LyP have been described.

Objective: Our goal was to study the clinicopathologic features of follicular LyP in a series of 11 cases (9 male, 2 female; age range 7-78 years, mean age 50 years).

Methods: In all, 113 cases of LyP were reviewed to select cases showing follicular involvement. Histology was correlated with the clinical data to exclude cases of CD30⁺ anaplastic large-cell lymphoma or folliculotropic mycosis fungoides.

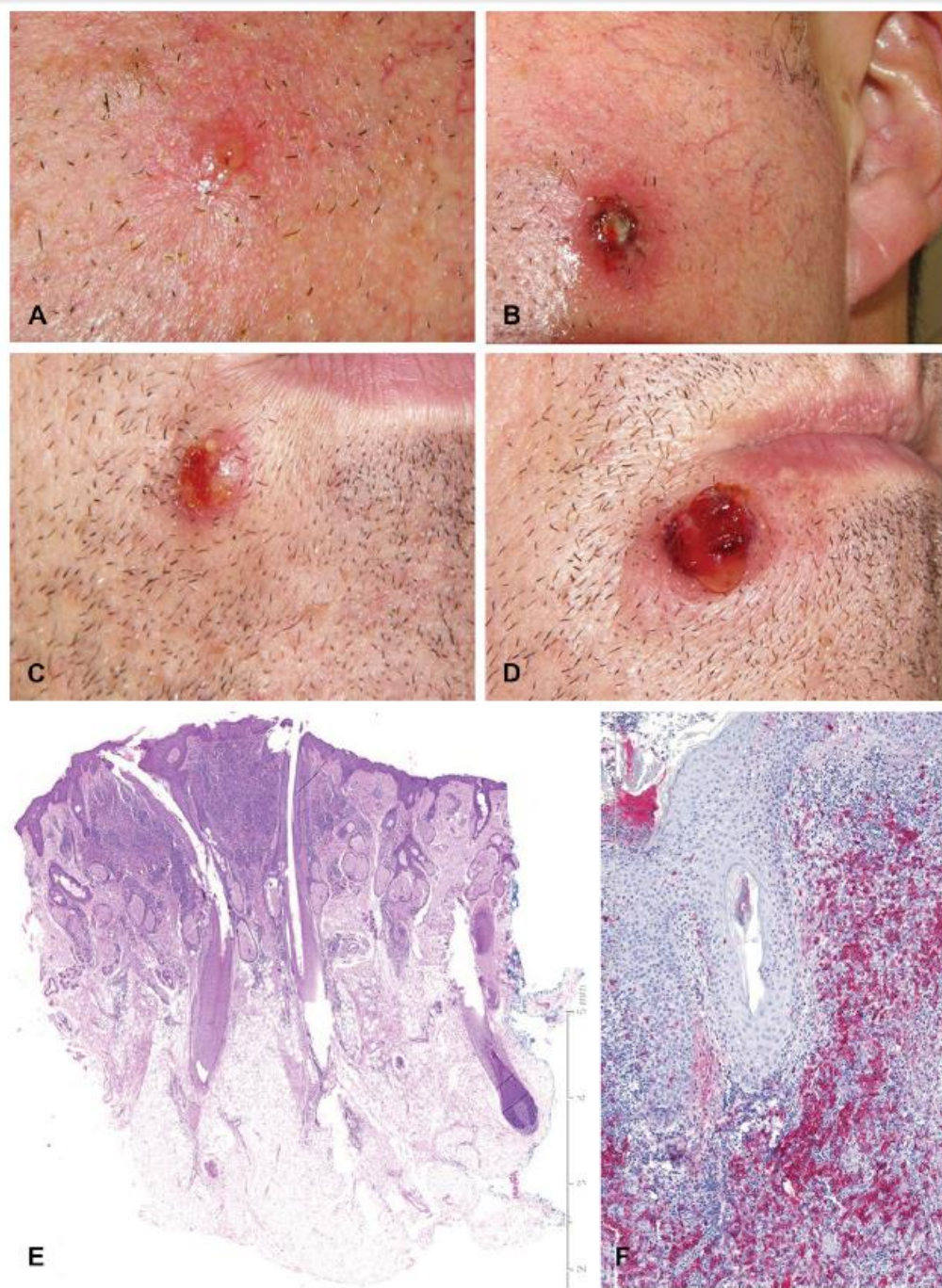


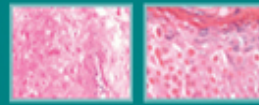
Fig 2. Follicular lymphomatoid papulosis (LyP). Lesions were localized to face (regional LyP) (A to D). Pustules are present (A and C). Histopathologically, there is perifollicular infiltrate



PDF



Info



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CASE REPORT

Follicular lymphomatoid papulosis with follicular mucinosis: a clinicopathologic study of 3 cases with literature review and conceptual reappraisal

Emilie Dore , Brian L. Swick, Brian K. Link, Grant K. Ghahramani, Vincent Liu

First published: 16 January 2017 [Full publication history](#)

DOI: 10.1111/cup.12871 [View/save citation](#)

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Abstract

Lymphomatoid papulosis (LyP), characterized by recurring, waxing and waning, cutaneous papulonodules, is increasingly recognized to represent a heterogeneous collection of pathologically dissimilar subtypes. Recently, a follicular LyP variant was proposed, featuring folliculotropism.



[View issue TOC](#)
Volume 44, Issue 4
April 2017
Pages 360–366

Histopathological Spectrum

- Type A
- Type B
- Type C
- Type D (epidermotropic)
- Type E (angio-invasive)
- Type F (folliculotropic)
- LyP with 6p25.3 rearrangement

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

Karai, Laszlo J. MD^{*,†}; Kadin, Marshall E. MD^{*}; Hsi, Eric D. MD[§]; Sluzevich, Jason C. MD^{//}; Ketterling, Rhett P. MD[§]; Knudson, Ryan A. BS[§]; Feldman, Andrew L. MD[§]

- Older adults
- Localised lesions (clinical d/d benign inflamm dermatosis/ low grade epithelial tm)
- Histo-

Biphasic pattern

Epidermotropic small cerebriform lymphocytes (CD30+)

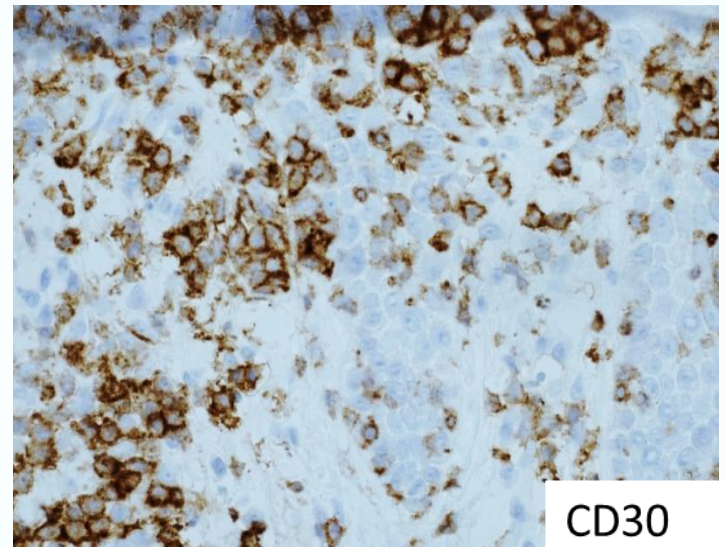
Dermal component-large transformed CD30+ lymphocytes

- Initial histo imp: Transformed MF
- Diagnosis by CPC

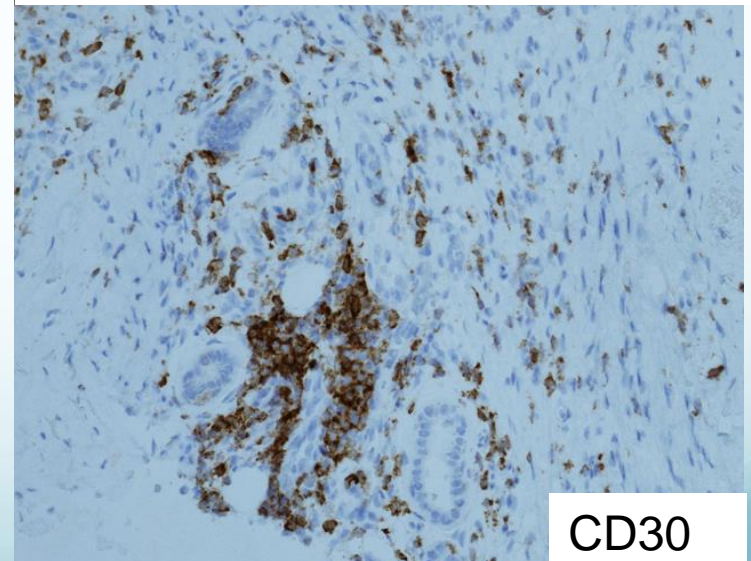
Case 9

- Referred case from Wales
- 74/M single dome shaped papule on back
- Outside histo report-non specific with d/d of drug reaction, lupus, reticular erythematous mucinosis
- Does not fit clinically





Superficial epidermotropic infiltrate



Deep infiltrate

More History

- First lesion resolved spontaneously and another similar lesion appeared in its vicinity
- Patient came for bx 2 weeks later, 2nd lesion was also showing signs of regression.

Histopathological Spectrum

- Type A
- Type B
- Type C
- Type D (epidermotropic)
- Type E (angio-invasive)
- Type F (folliculotropic)
- LyP with 6p25.3 rearrangement

Why is LyP included in the WHO-EORTC
Classification of Cutaneous Lymphomas?

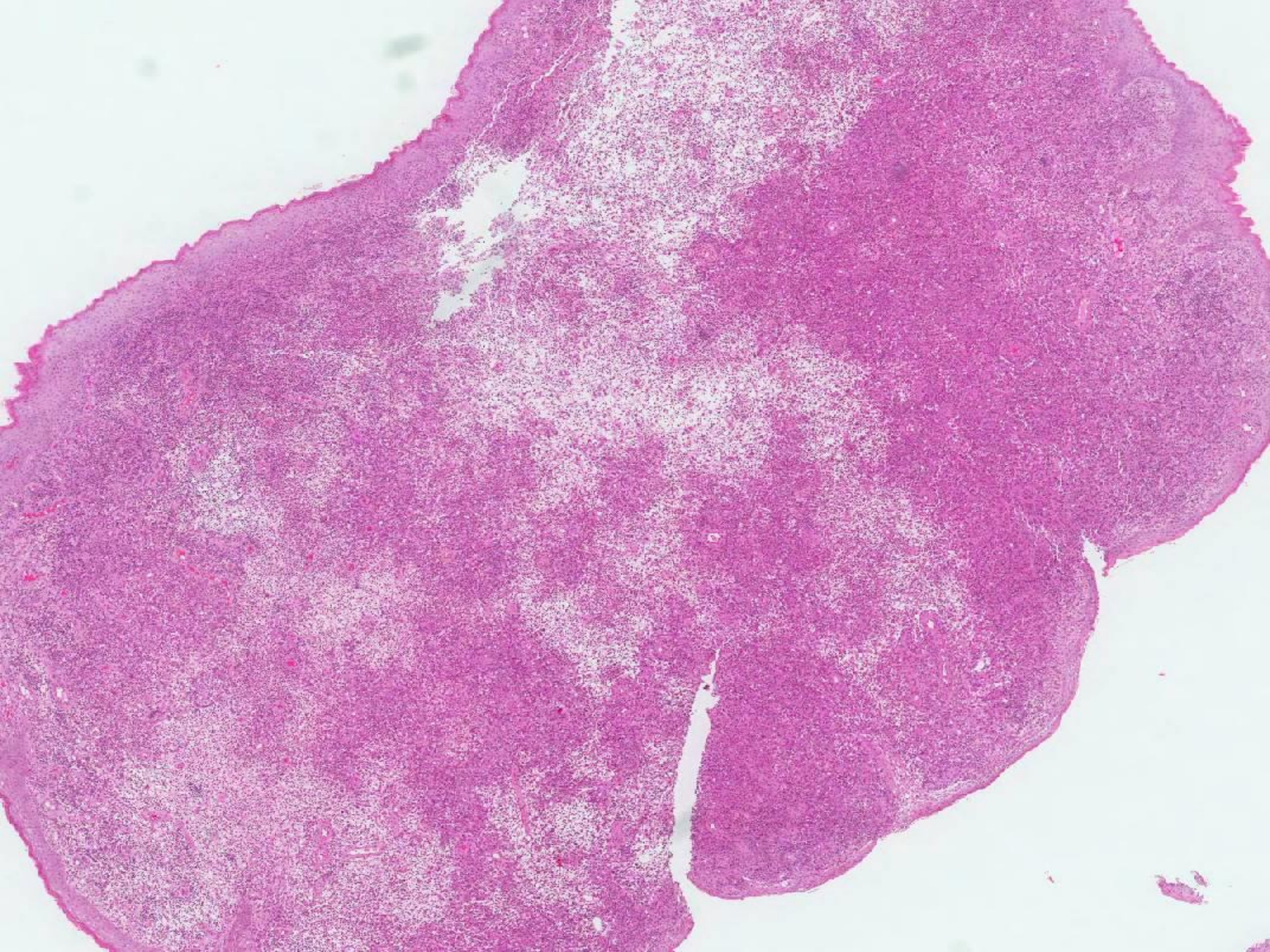
Case 1

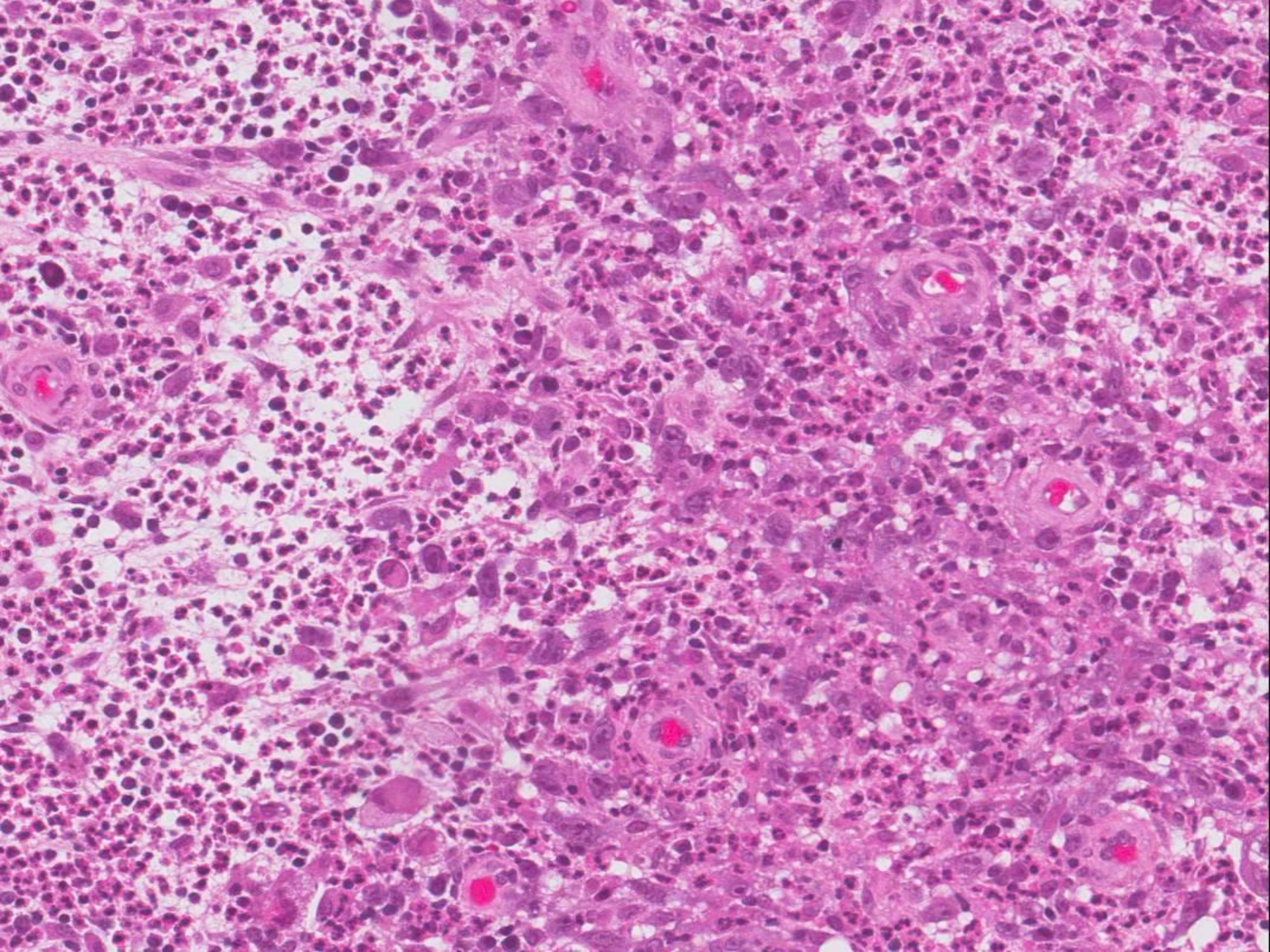
- 70/F widespread papular rash, initially thought to be scabies and later diagnosed as LyP.

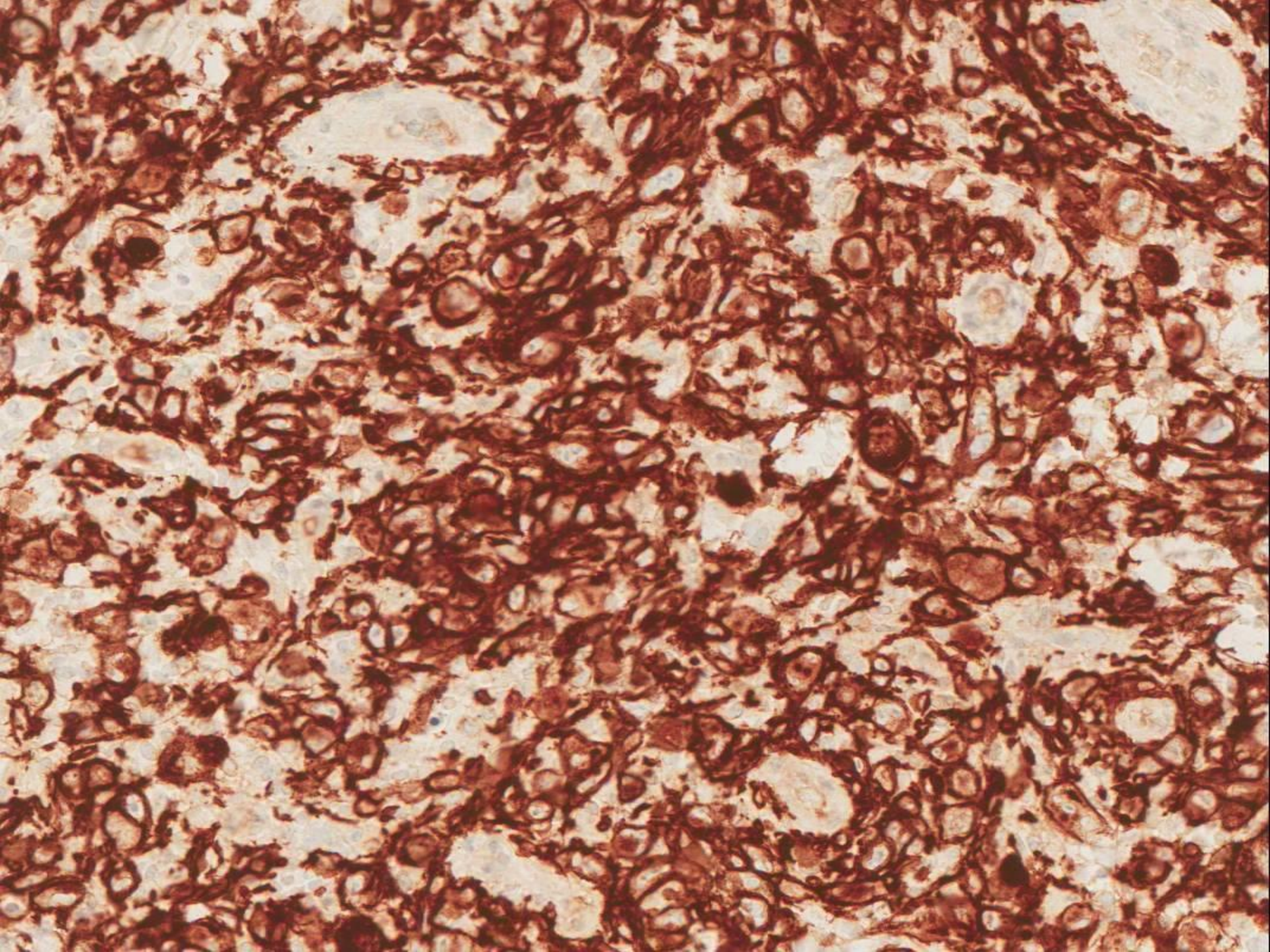


Developed a 5cm tumour nodule on forearm,
no sign of regression









Diagnosis

?LyP type C

? Primary Cutaneous CD30+ anaplastic T cell lymphoma
in association with LyP

?LyP type C

Primary Cutaneous CD30+ anaplastic T cell lymphoma in association with LyP

(Large size and lack of spontaneous regression)

Why is LyP classified as Cutaneous Lymphoma?

1. 5-20% show association with a second malignant lymphoma (either preceding, concomitant, subsequent)
2. 40-100% of LyP skin lesions show monoclonal rearrangement of TCR genes.
3. ??

Case Study 10

- 68/M
- Widespread telangiectatic/purpuric rash
- Trunk, upper and lower limbs
- Mildly itchy

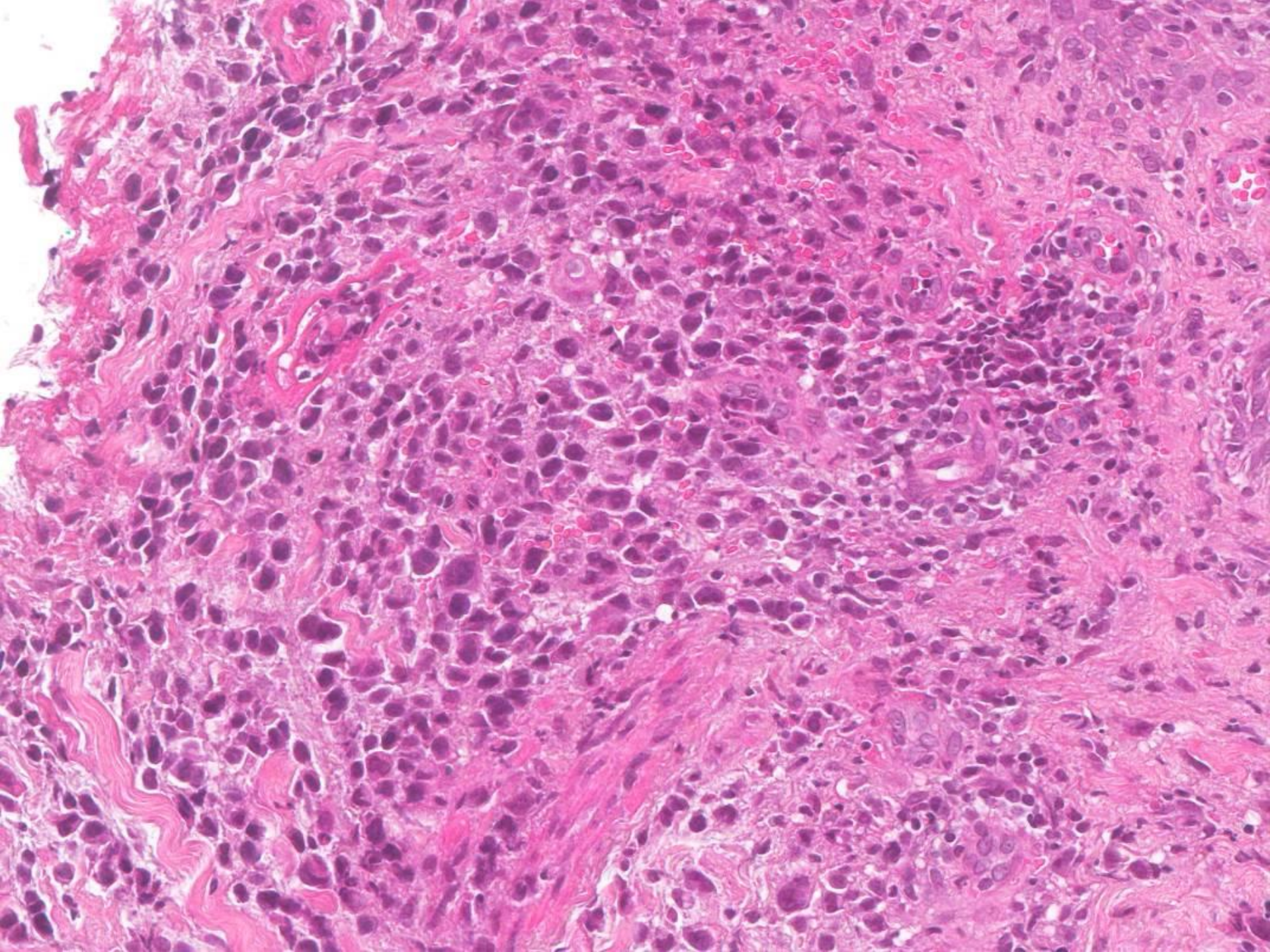


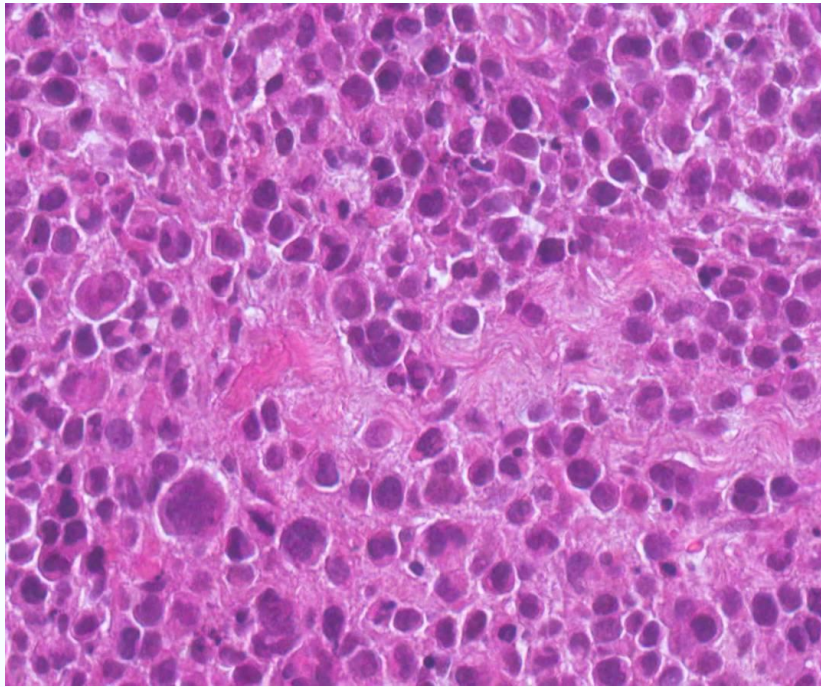
Clinical D/D:
1. Telangiectatic MF
2. Urticaria pigmentosa
3. Atypical PPD

CPC diagnosis

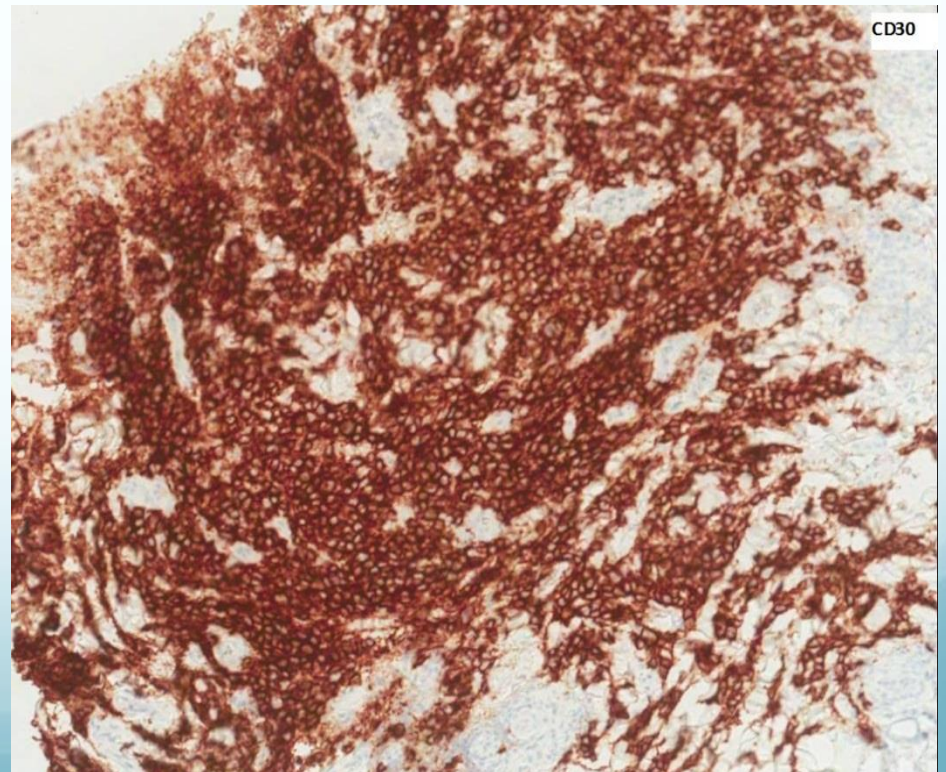
Purpuric/Telangiectatic Mycosis Fungoides





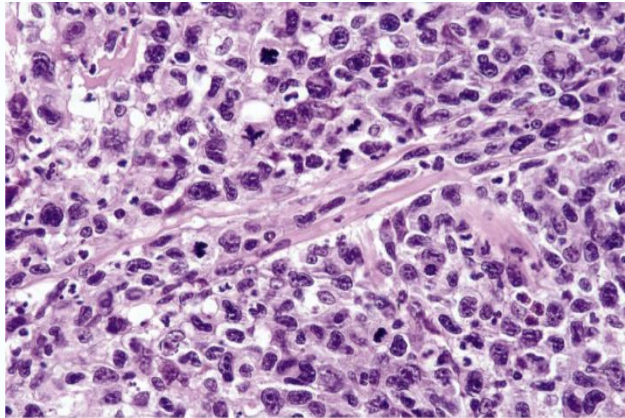


Sheets of large atypical cells



CD30

D/D of Type C LyP



CD3+, CD30+, CD4+, CD8-



LyP



Cutaneous involvement by systemic ALCL



Transformed MF



Primary cutaneous ALCL

Histological D/D

- Transformed MF
- LyP Type C on a background of MF
- Primary Cutaneous ALCL **x**
- Systemic ALCL involving skin **x**

Clonality analysis

- TCRPCR- monoclonal T cell expansion
- Same T cell clone as previous Mycosis Fungoides (same size and distribution of monoclonal peaks)

J Am Acad Dermatol. 2003 Oct;49(4):620-3.

Lymphomatoid papulosis associated with mycosis fungoides: a study of 21 patients including analyses for clonality.

- *7 patients assessed for clonality.*
- *All 7 showed identical clone in MF and LyP lesions.*

Few lesions started healing spontaneously

FINAL DIAGNOSIS:

Lymphomatoid Type C on a background of purpuric MF

Why is LyP classified as Cutaneous Lymphoma?

1. 5-20% show association with a second malignant lymphoma (either preceding, concomitant, subsequent)
2. 40-100% of LyP skin lesions show monoclonal rearrangement of TCR genes.
3. Same clone detected in LyP and second lymphoma
?Different clinical manifestation of a unique T cell clonal proliferation

SUMMARY

- Clinical and Pathological spectrum continues to expand with new variants described
- Awareness of spectrum essential as many of the subtypes can easily be mistaken for much more aggressive lymphomas
- Close Clinico-pathological correlation essential

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- Dr Richard Azurdia,
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- Dr Rob Lister
- Dr Su Enn Low
- Dr Naveen Sharma
- Dr Nitin Khirwadkar
- Dr Magda Mikhail
- Dr Geetha Menon

Visit us....Dermpath team,
Royal Liverpool University Hospital
arti.bakshi@rlbuht.nhs.uk



A photograph of a modern glass skyscraper at dusk. The building's glass facade reflects the colorful sky, which is filled with soft, pinkish-orange clouds. The building is illuminated from within, with some windows glowing. In the foreground, there is a street with a traffic light showing a red light. A few people are visible walking on the sidewalk. The overall scene is a city street at twilight.

THANK YOU