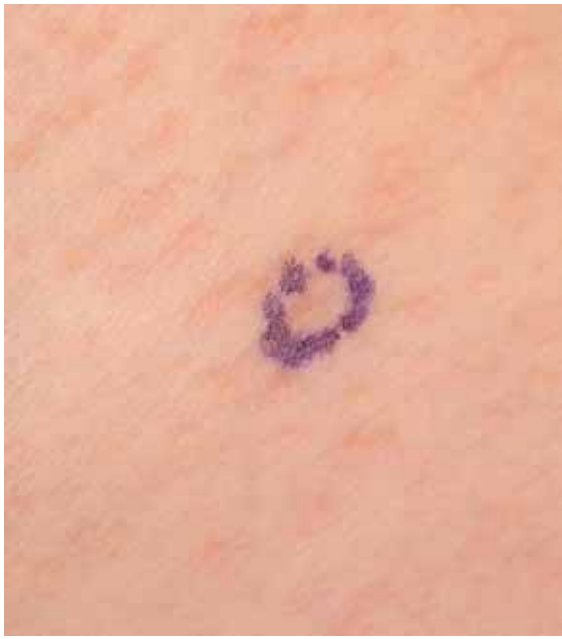
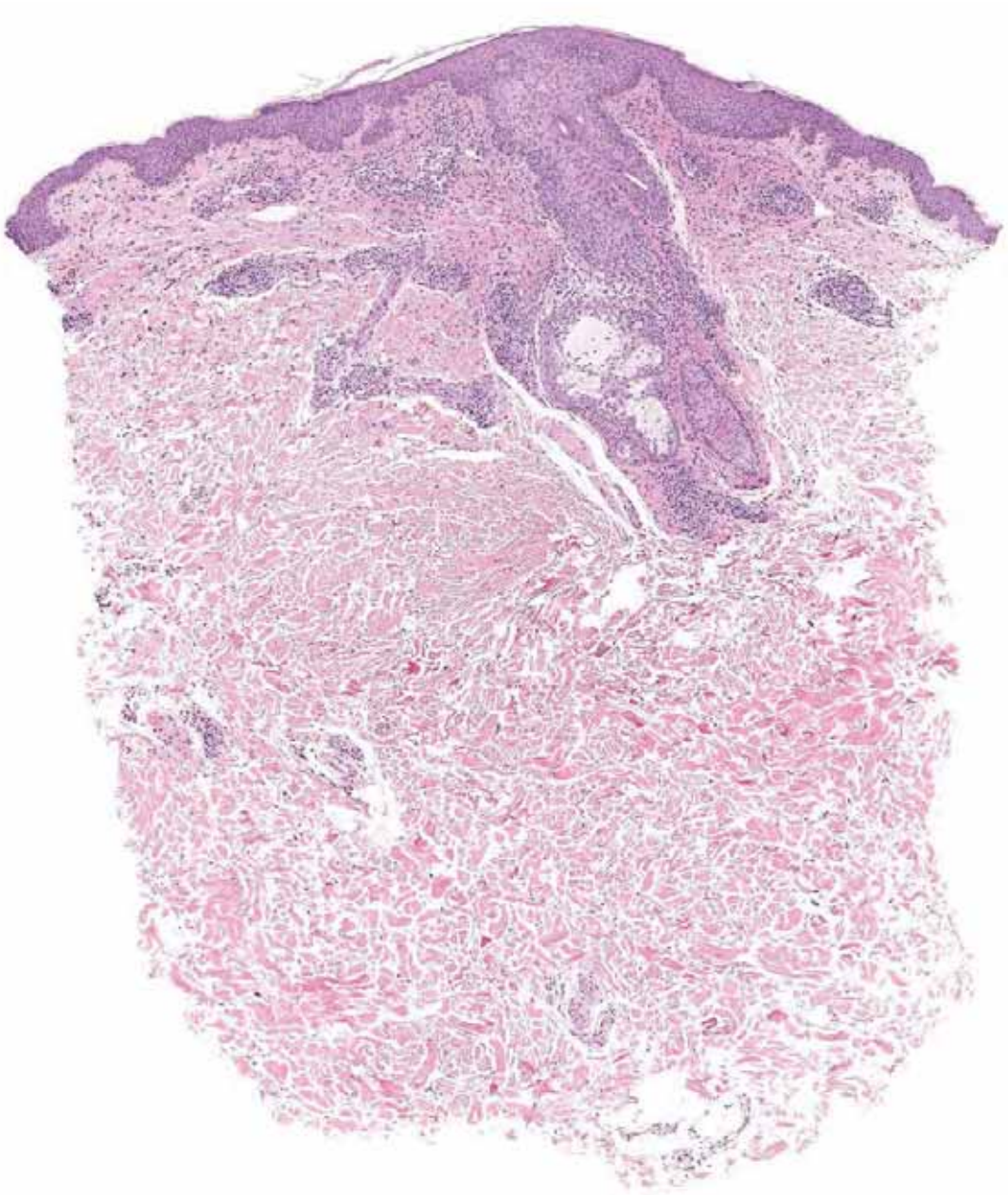

17th Summer Academy of Dermatopathology
Graz, June 30 – July 4, 2025
Adnexotropic mycosis fungoides
Lorenzo Cerroni, Europe

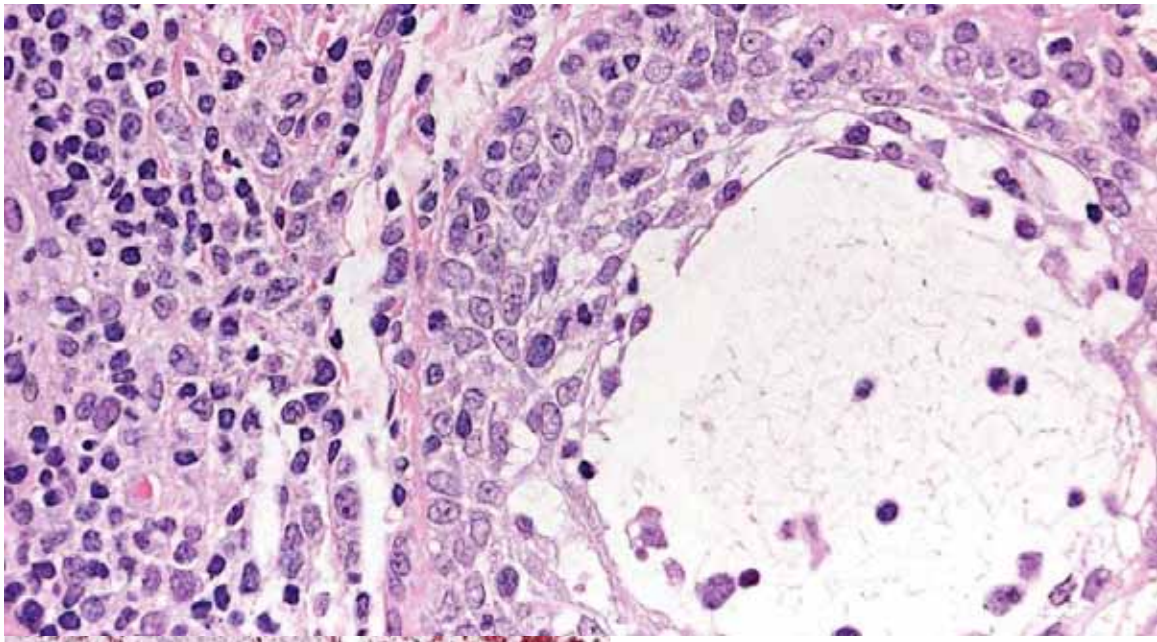


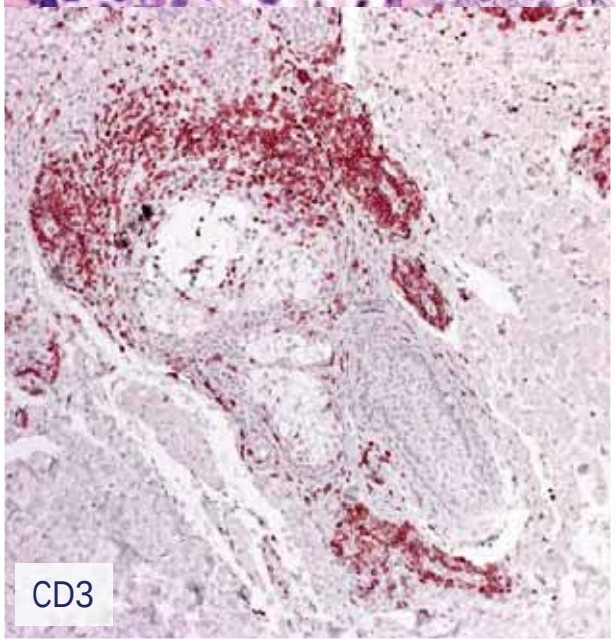
F, 25

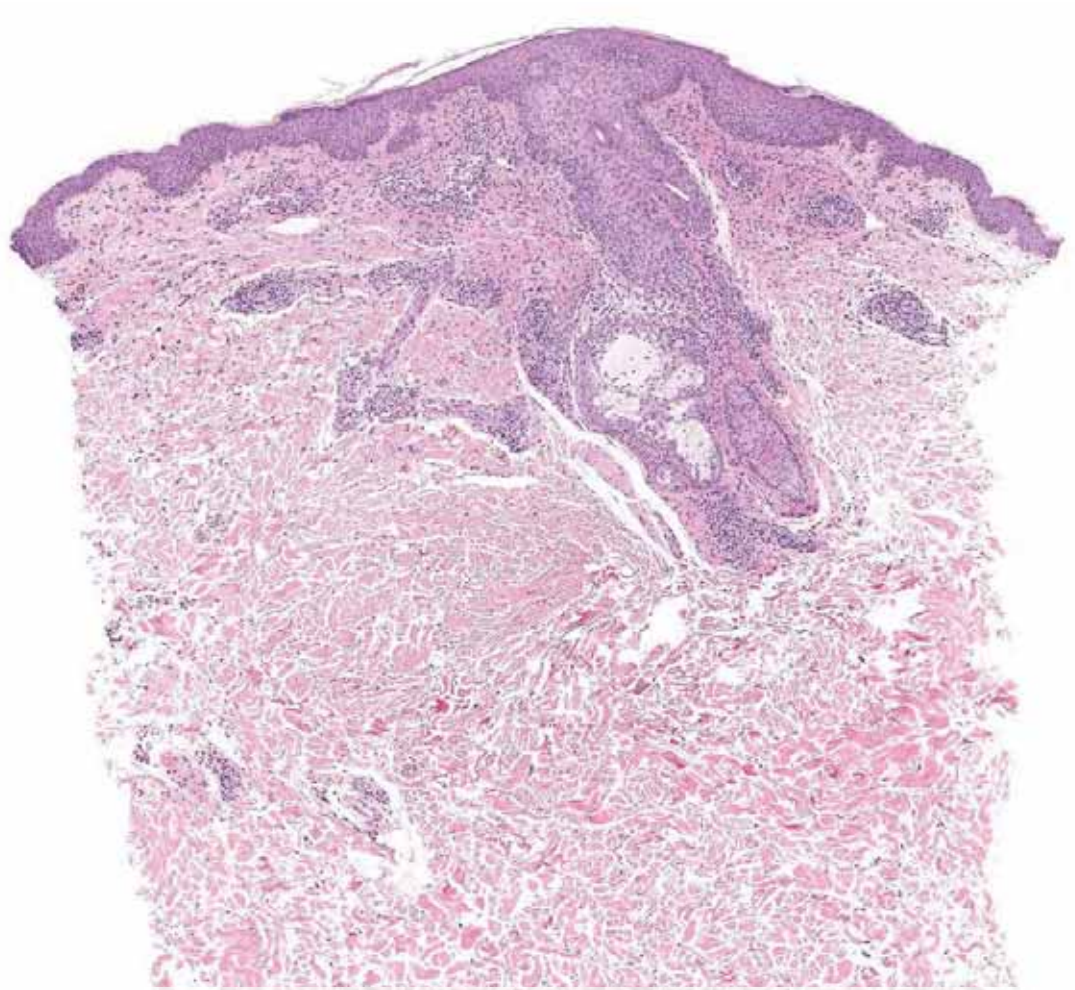
According to the patient itchy lesions on the face and neck for some days. Atopic diathesis.

A biopsy is taken.

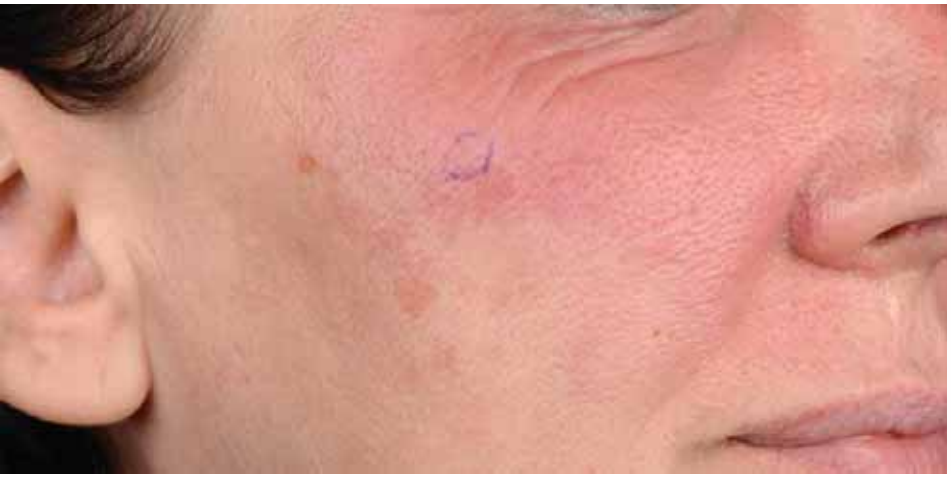




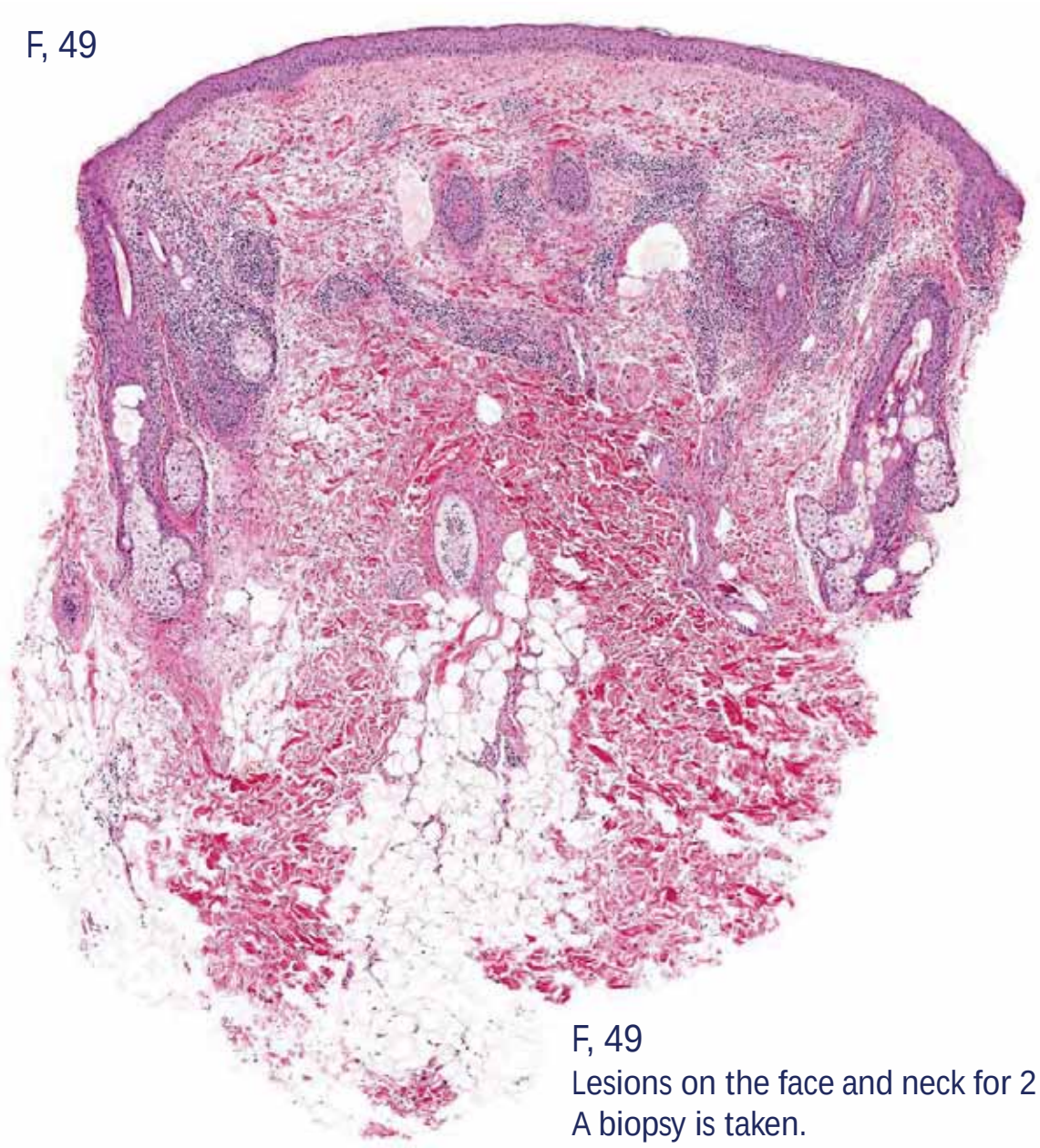

CD3



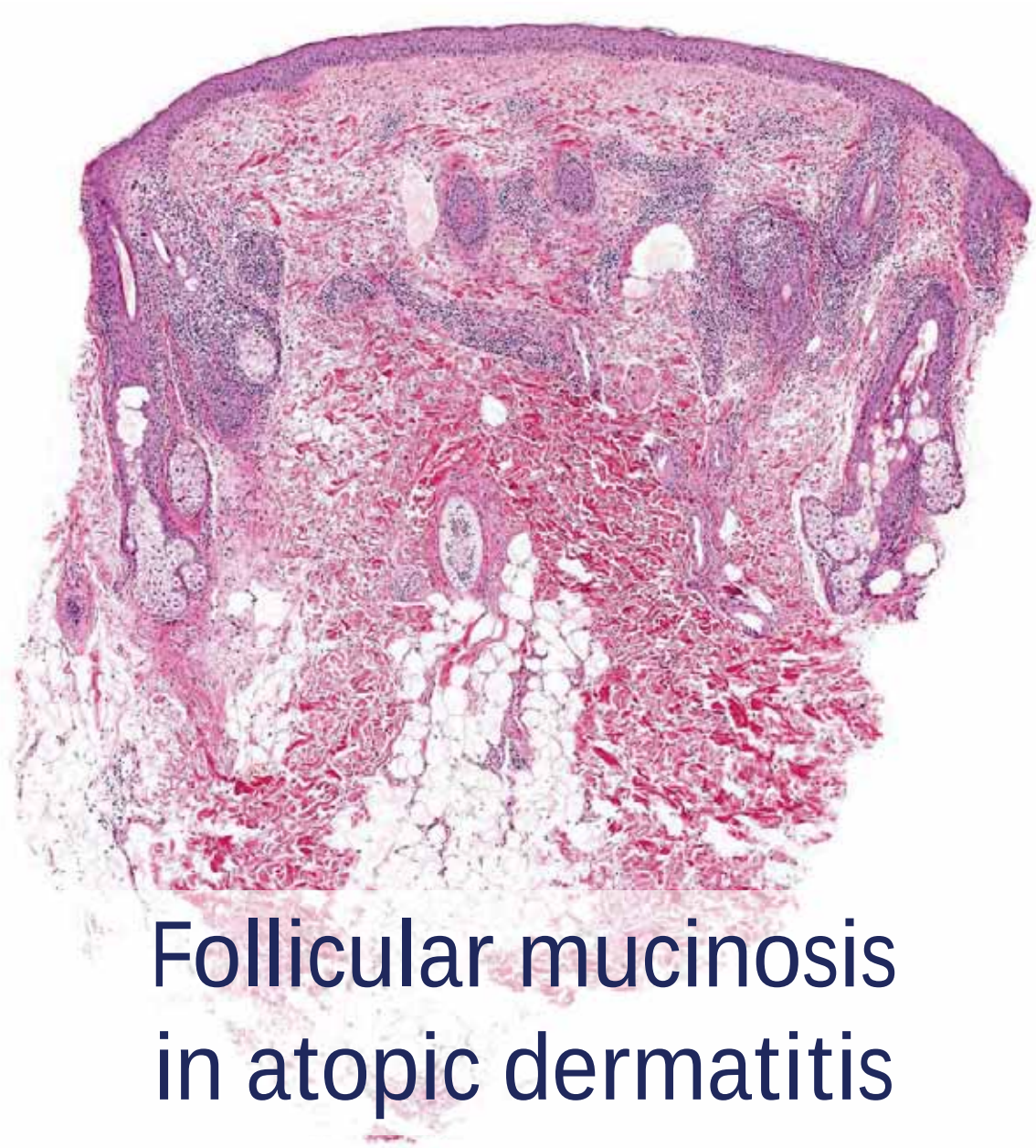
Follicular mucinosis
in atopic dermatitis



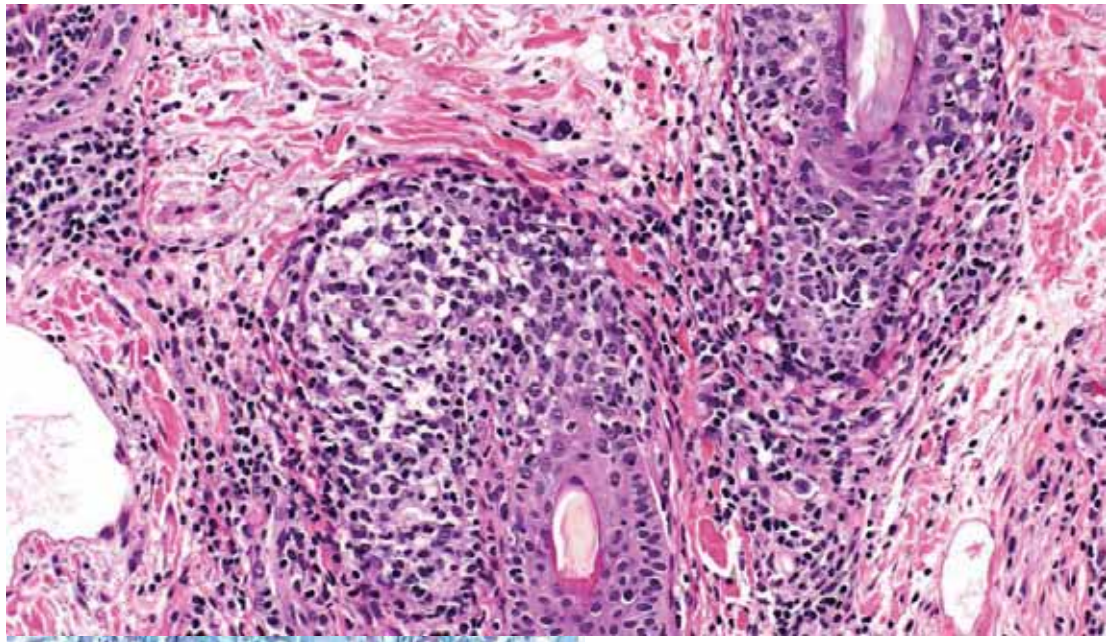
F, 49

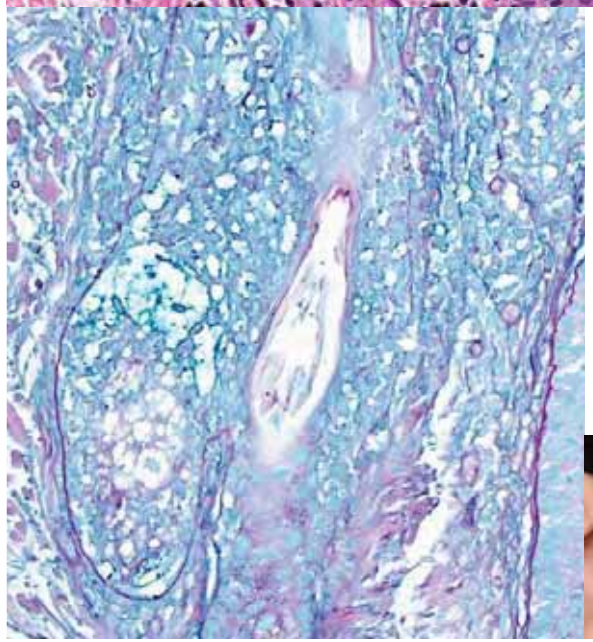


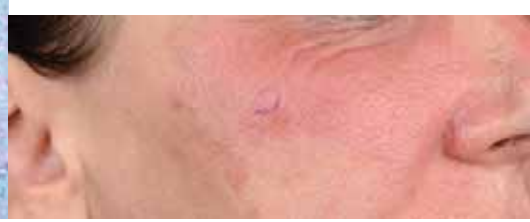
F, 49
Lesions on the face and neck for 2 months.
A biopsy is taken.



Follicular mucinosis in atopic dermatitis







Follicular Mucinosis Associated With Nonlymphoid Skin Conditions

José M. Mir-Bonafé, MD, Javier Cañueto, MD,* Emilia Fernández-López, MD,* and Ángel Santos-Briz, MD†*

Background: Follicular mucinosis coexisting with lymphoproliferative disorders has been thoroughly debated. However, it has been rarely reported in association with inflammatory disorders.

Methods: Thirteen cases have been retrieved, and those with cutaneous lymphoma or alopecia mucinosa were excluded.

Results: Follicular mucinosis was found in the setting of squamous cell carcinoma, seborrheic keratosis, simple prurigo, acne vulgaris, dextromethorphan-induced phototoxicity, polymorphous light eruption (2 cases), insect bite (2 cases), tick bite, discoid lupus erythematosus, drug-related vasculitis, and demodecidosis. Unexpectedly, our observations revealed a preponderating accumulation of mucin related to photo-exposed areas, sun-associated dermatoses, and histopathologic solar elastosis. The amount of mucin filling the follicles apparently correlated with the intensity of perifollicular inflammatory infiltrate, which was present in all cases. The concurrence of dermal interstitial mucin was found in 7 cases (54%).

Conclusions: The concurrence of interstitial dermal mucinosis or the potential role of both ultraviolet radiation and the perifollicular inflammatory infiltrates in its pathogenesis deserves further investigations. Precise recognition and understanding of this distinctive, reactive histological pattern may prevent our patients from unnecessary diagnostic and therapeutic strategies.

Key Words: follicular mucinosis, mucin, hair follicle, alopecia mucinosa, ultraviolet radiation, bone marrow transplantation

(*Am J Dermatopathol* 2014;36:705–709)

INTRODUCTION

Follicular mucinosis (FM) refers to a reactive histopathological finding characterized by the deposition of mucin within the hair follicle and/or the sebaceous glandular epithelium.[1] It was first observed in the setting of alopecia mucinosa (AM) in 1957 by Pinkus[2] in patients, which combined this microscopic finding with clinical alopecia. Since then, many authors have used both terms "AM" and "FM" indistinctively, with the resultant terminological confusion. However, in addition to AM, FM has also been described related to mycosis fungoides, folliculotropic mycosis fungoides, hematologic malignancies, and inflammatory skin conditions. Consequently, FM is currently regarded as a tissue-reaction pattern and not a condition per se or a pathognomonic finding for any disease.

The aim of this study was to add further associations and to highlight that FM may be a reactive histological pattern to a wide range of disorders with a benign outcome. Because terminology from the literature has been confusing, the appropriate understanding and recognition of this incidental finding may prevent patients from unnecessary and sometimes aggressive diagnostic and therapeutic procedures.

PATIENTS AND METHODS

All cases with histopathological findings of FM were retrospectively retrieved from January 2009 to January 2012 from the files of the Department of Dermatology, University Hospital of Salamanca, Spain. The inclusion criteria was the histopathological evidence of FM, and the exclusion criteria were the presence of alopecia or the final diagnosis of AM or primary cutaneous lymphoproliferative disorder. Clinical data included age, sex, site, and relevant medical history. All specimens were stained with Hematoxylin and Eosin, colloidal iron, and periodic acid-Schiff (PAS). Histopathologically, the following parameters were semiquantitatively graded from 1+ to 3+: (1) amount of mucin filling the follicles, (2) amount of mucin within interstitial tissue, (3) intensity of perifollicular inflammatory infiltrate, and (4) presence of solar elastosis. Finally, type of predominant inflammatory cells and other relevant histopathological findings were described. Respective treatments were noted, and all patients have been followed up to date.

RESULTS

Clinical Features

Thirteen patients (8 women and 5 men) were analyzed. FM was not previously suspected in any case. The median age of patients was 51 years (ranging from 22 to 80 years). Clinical associations included tick bite lesion (Fig. 1A), insect bite (2 patients), squamous cell carcinoma (Fig. 1B), seborrheic keratosis, dextromethorphan-induced phototoxicity (Fig. 1C), cutaneous chronic lupus erythematosus (Fig. 1D), prurigo simple, acne vulgaris, polymorphous light eruption (in 2 patients), vasculitis (Figs. 1E, F), and demodecidosis (Fig. 1G).

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The authors declare no conflicts of interest.

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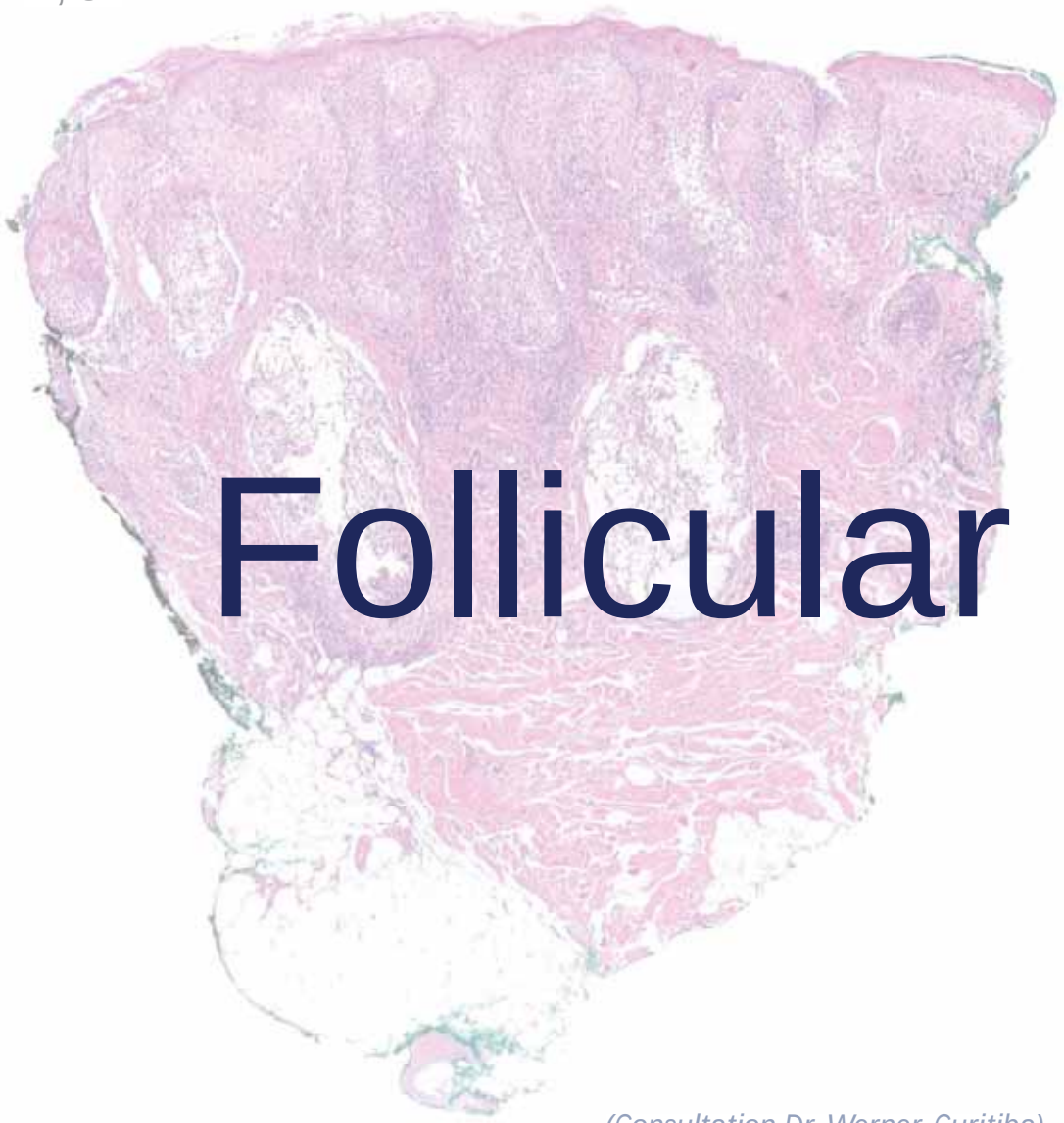
TABLE 1. Follicular Mucinosis Associated With Nonlymphoid Disorders: Histopathological Findings of 13 Cases

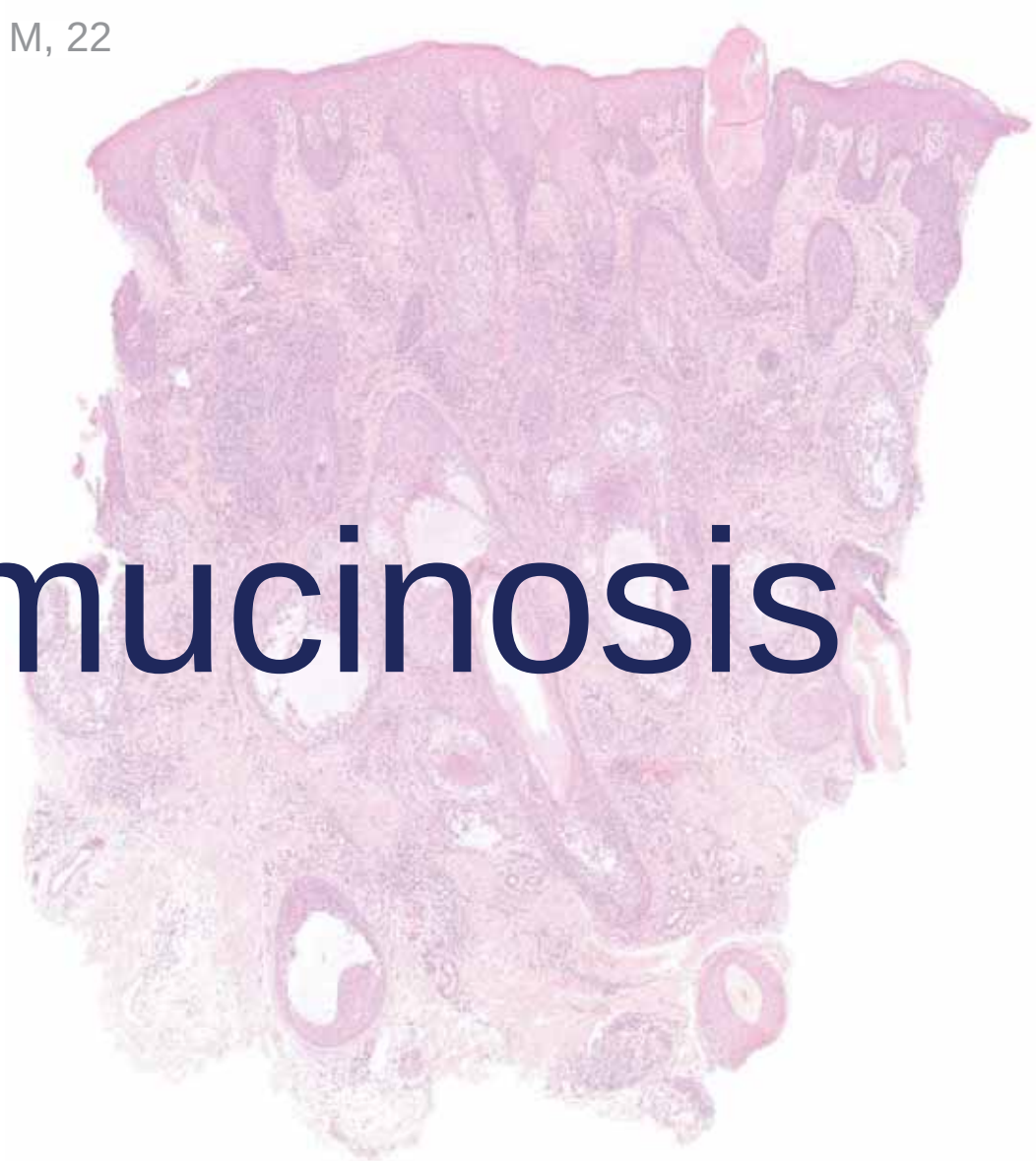
Patient Number	Associated Dermatosis	Sex-Age, yr	Follicular Mucinosis (1+ to 3+)	Dermal Interstitial Mucinosis (1+ to 3+)	Perifollicular Inflammatory Infiltrate (1+ to 3+)	Dermal Elastosis (1+ to 3+)
1	Dextromethorphan	M-65	+—	+	—+	+—+
2	SCC	M-80	+	No	—	+—+
3	SK	F-39	+	No	+	+
4	DEL	M-43	—+	—+	—+	—
5	Insect bite	M-73	+—	No	+—	No
6	Insect bite	M-57	+	+	—	No
7	Tick	F-51	+—	+	+—+	No
8	Prurigo	F-43	+	+	—	—
9	Acne vulgaris	F-22	+	No	—	No
10	PLE	F-78	+—	No	+—+	+—+
11	PLE	F-35	+—	No	—	—
12	Post-BMT Vasculitis	F-66	(a) —	+	—+	—
			(b) No	No	—+	No
13	Post-BMT demodecidosis	F-35	—+	+	—	No

12 (a) indicates biopsy from the right retroauricular area; 12 (b) indicates biopsy from the pubis.
—, mild; —+, moderate; —+—, intense; DEL, discoid lupus erythematosus; PLE, polymorphous light eruption; SCC, squamous cell carcinoma; SK, seborrheic keratosis.

M, 54



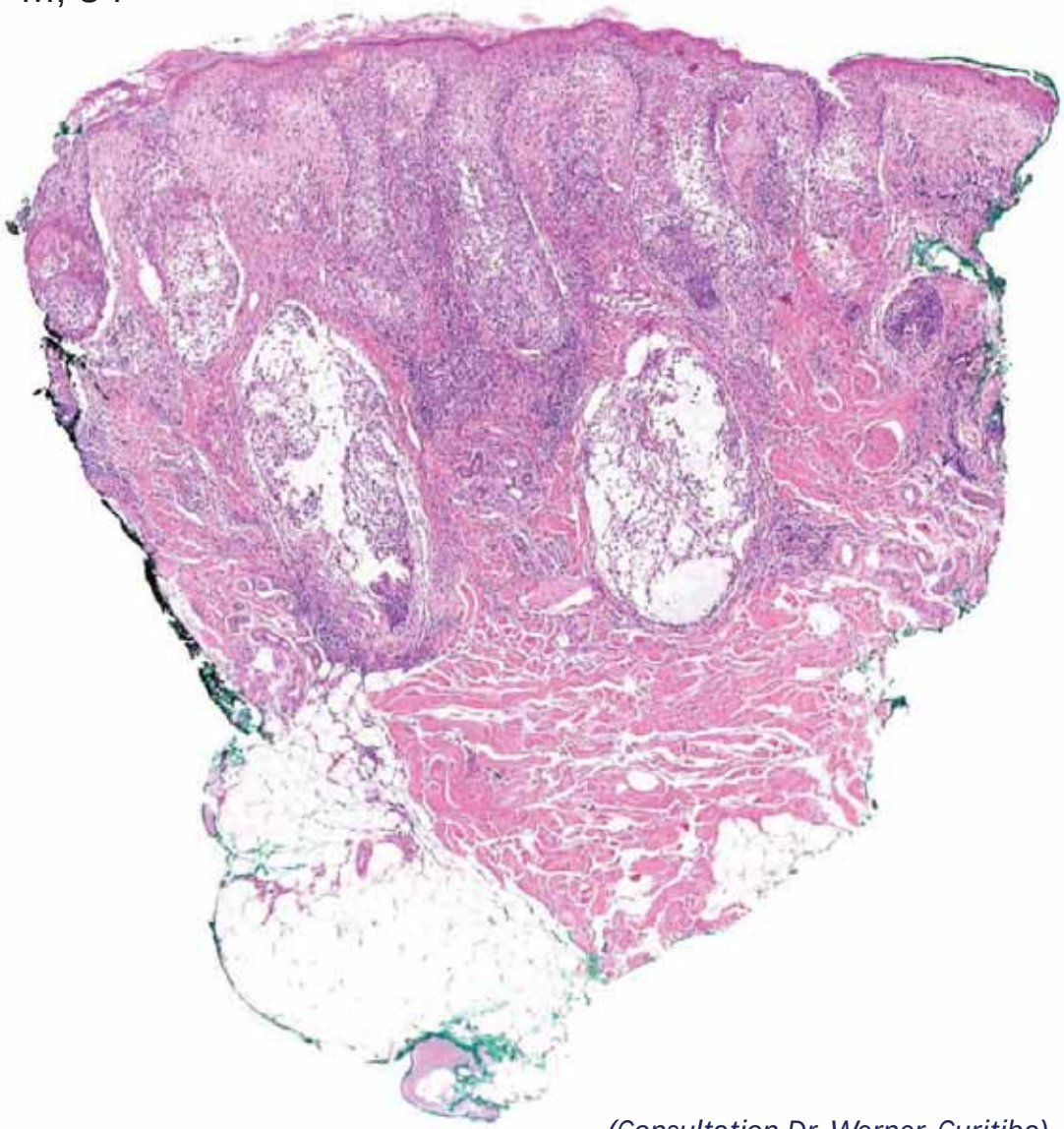
M, 22



Follicular mucinosis

(Consultation Dr. Werner, Curitiba)

M, 54



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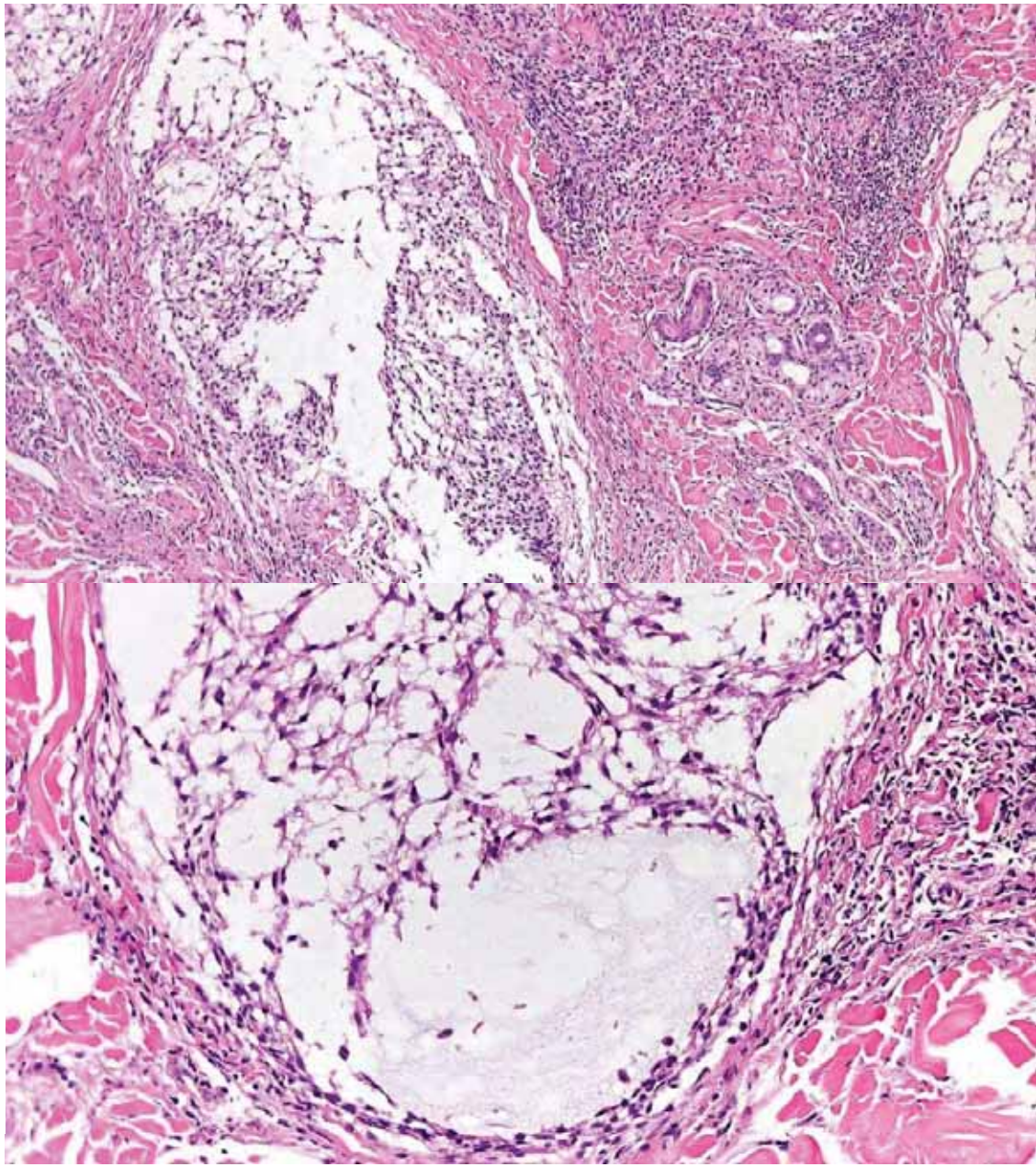
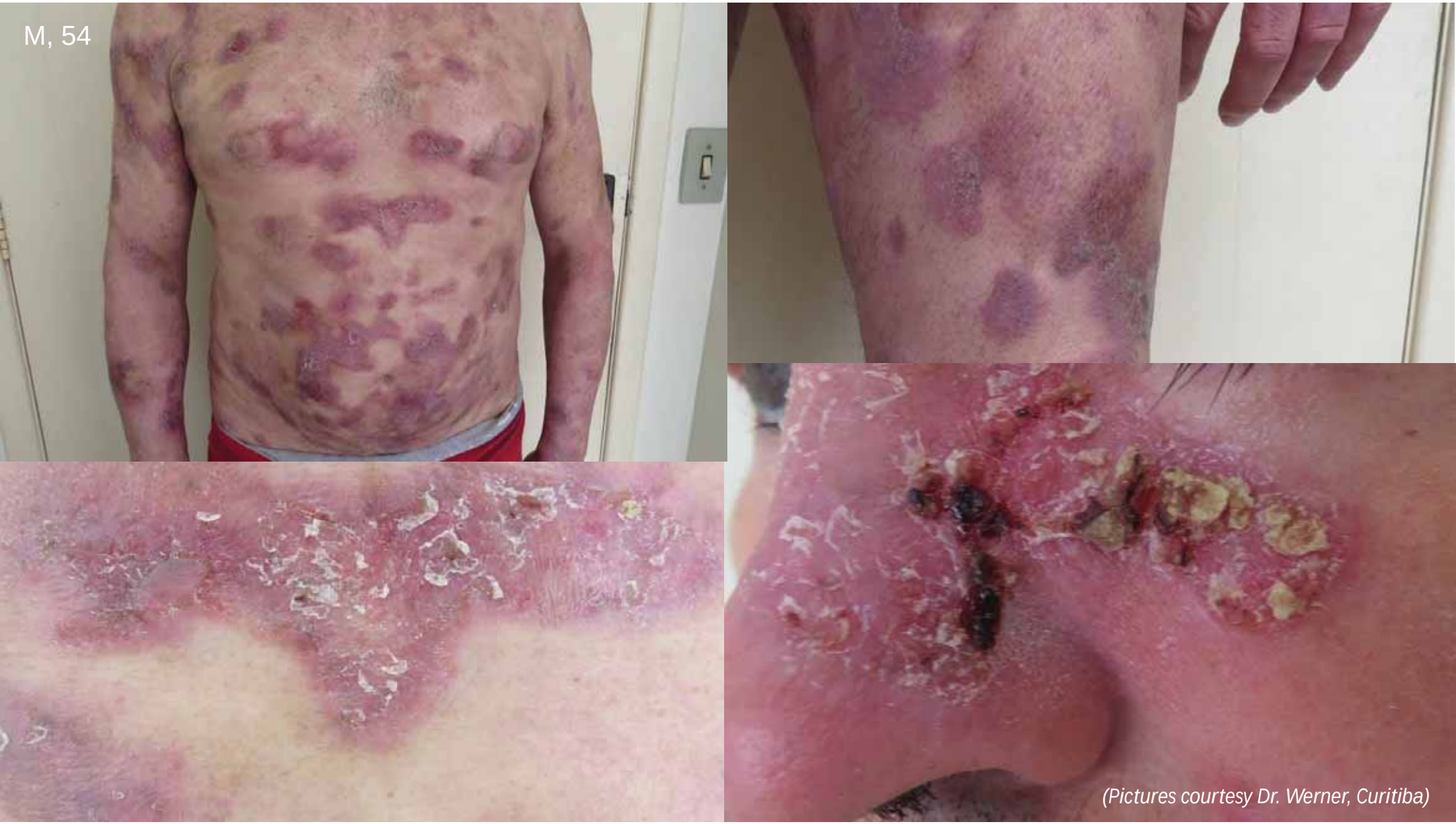
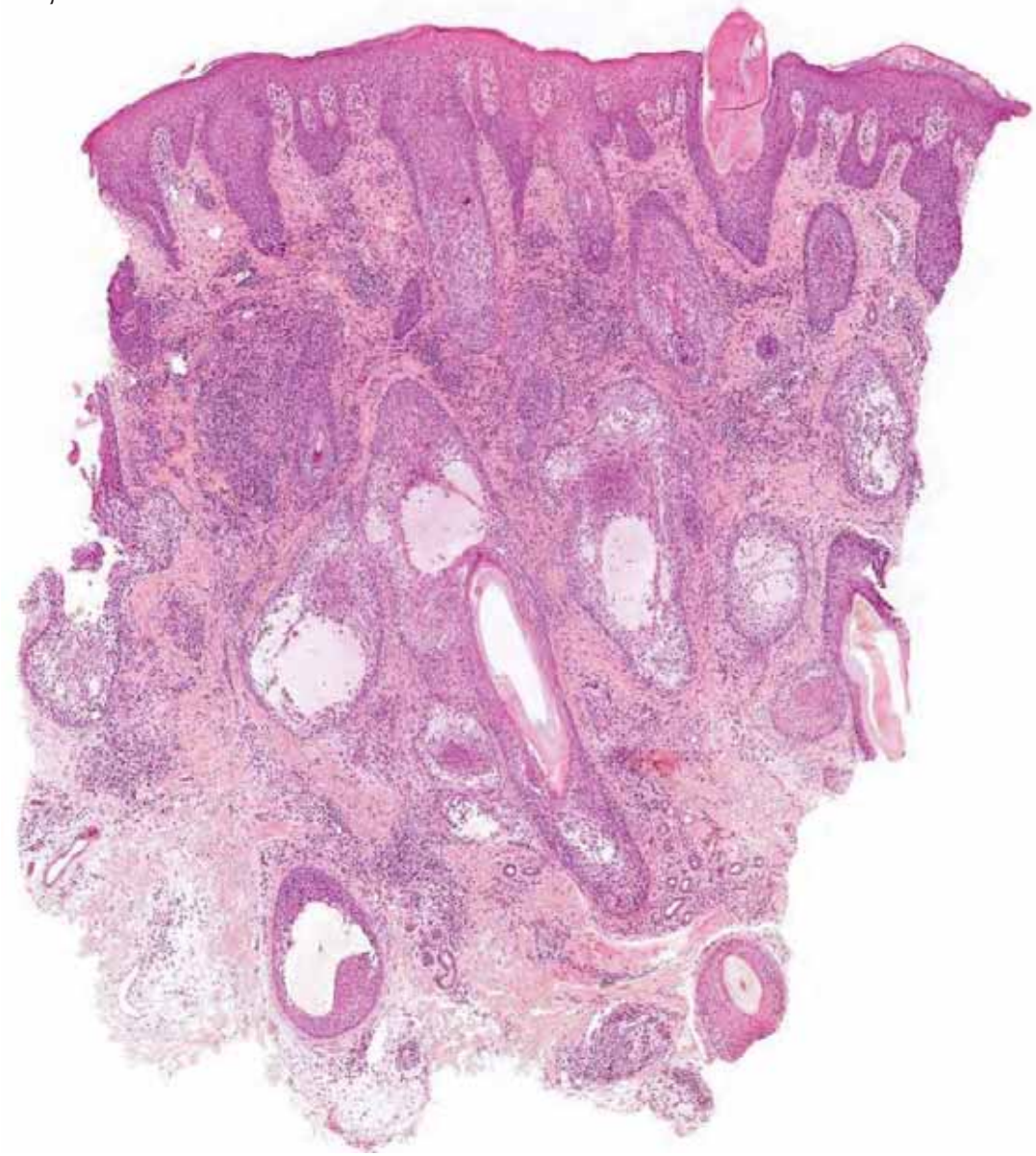
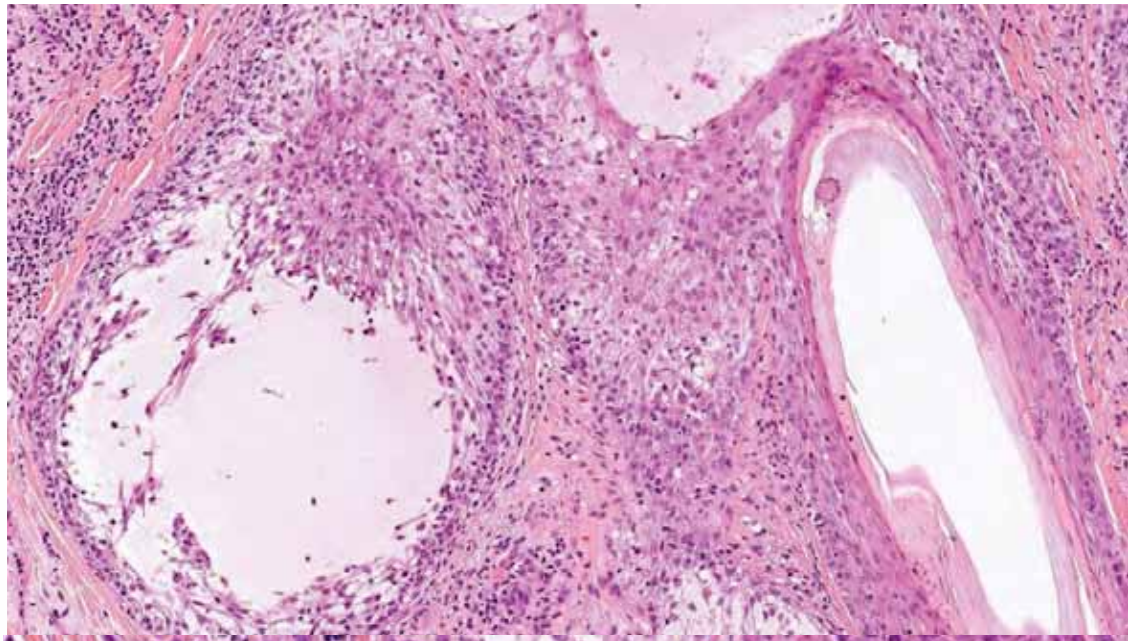
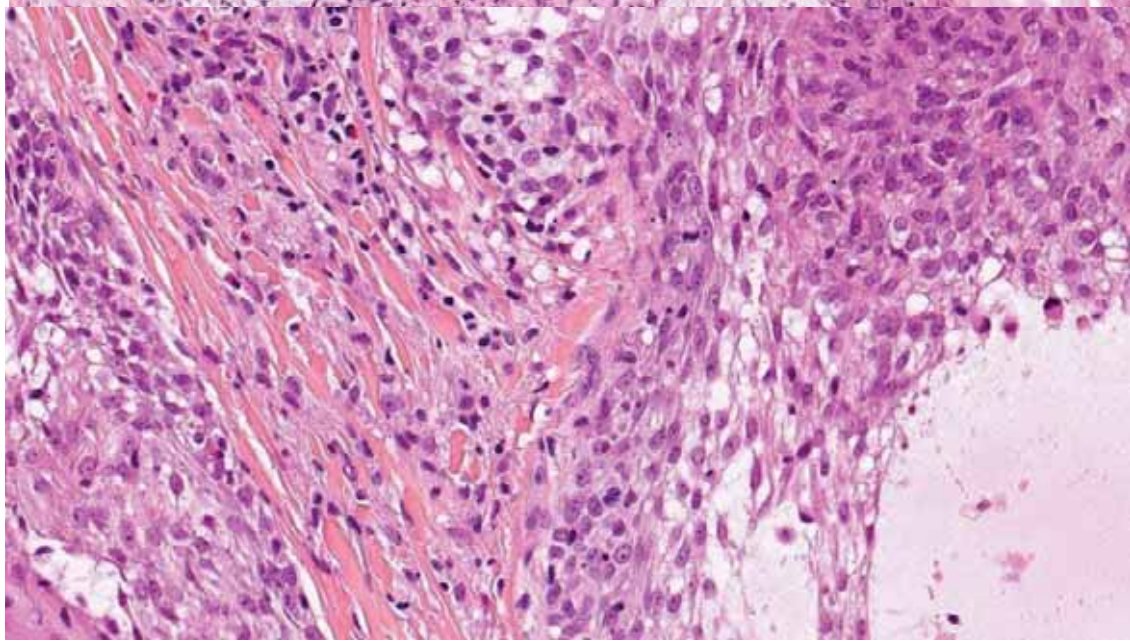



M, 54
(Pictures courtesy Dr. Werner, Curitiba)

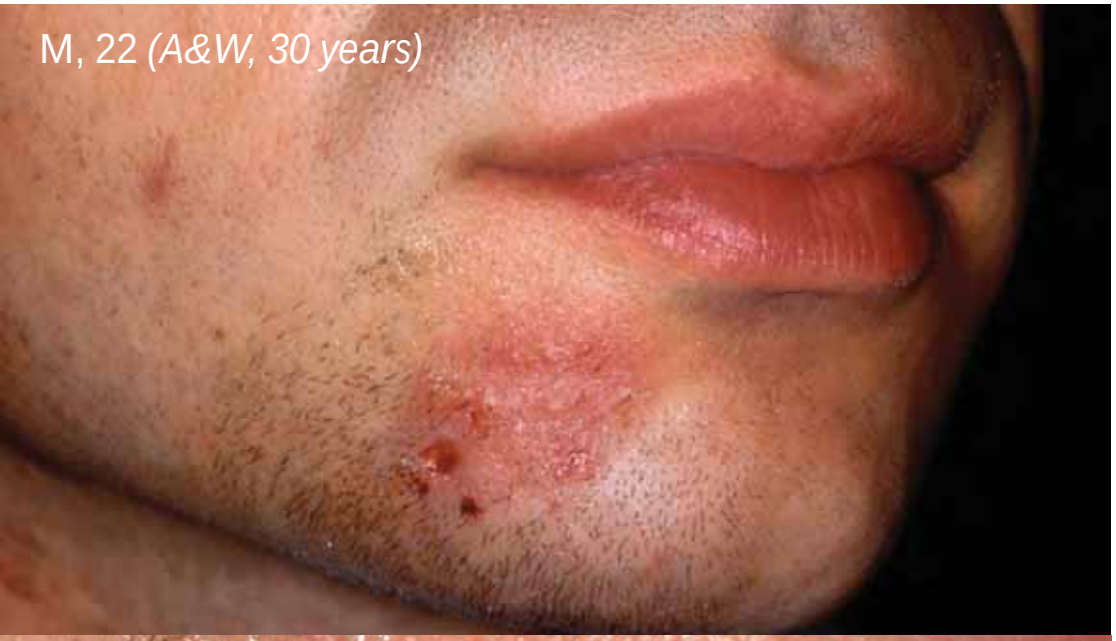
M, 22

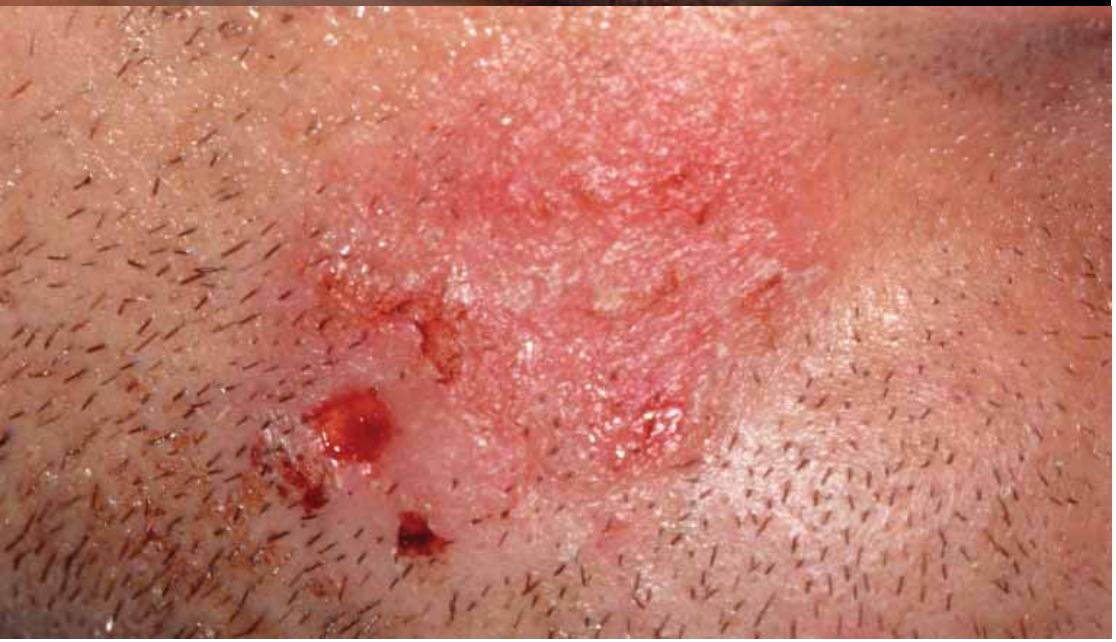


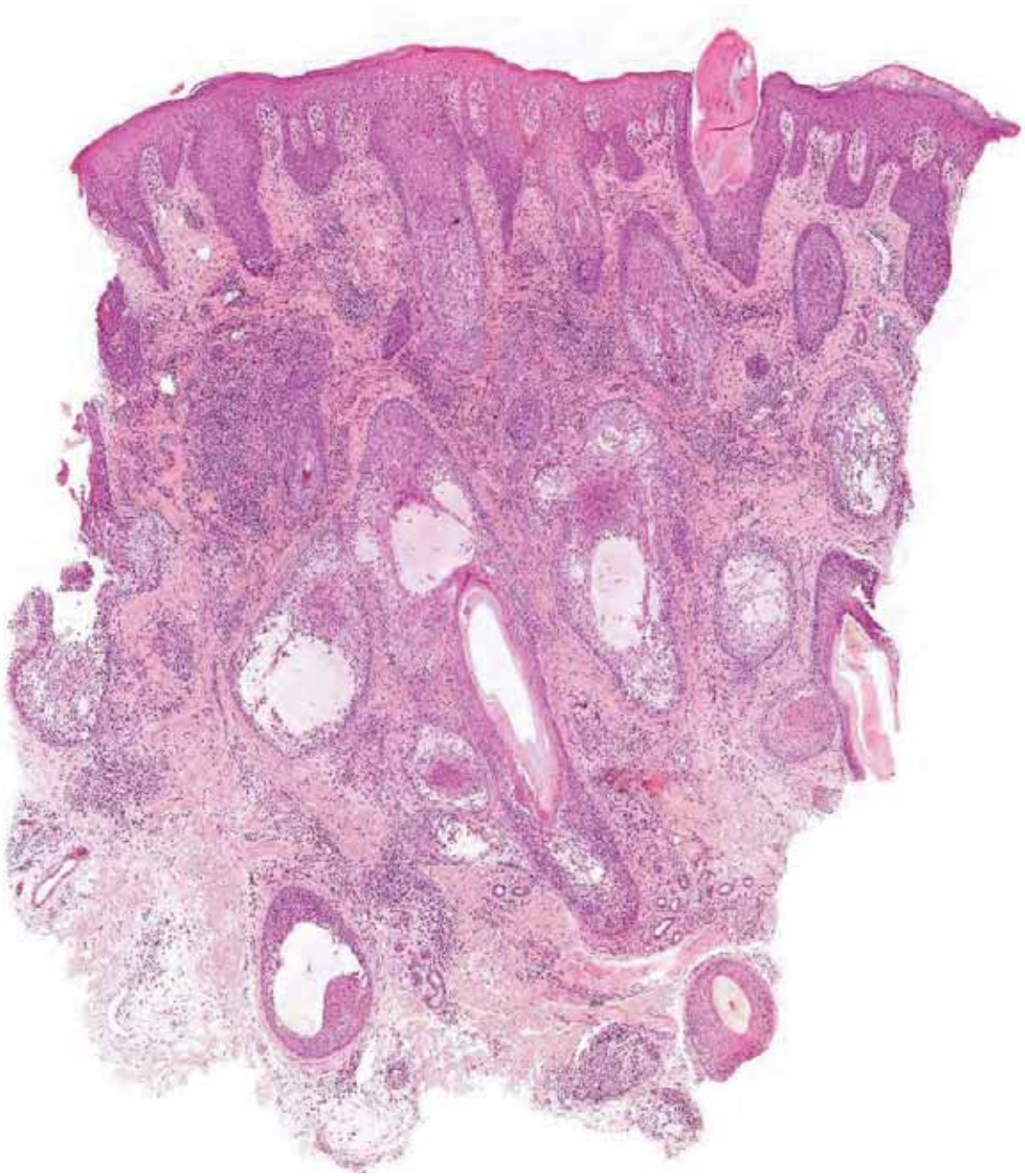




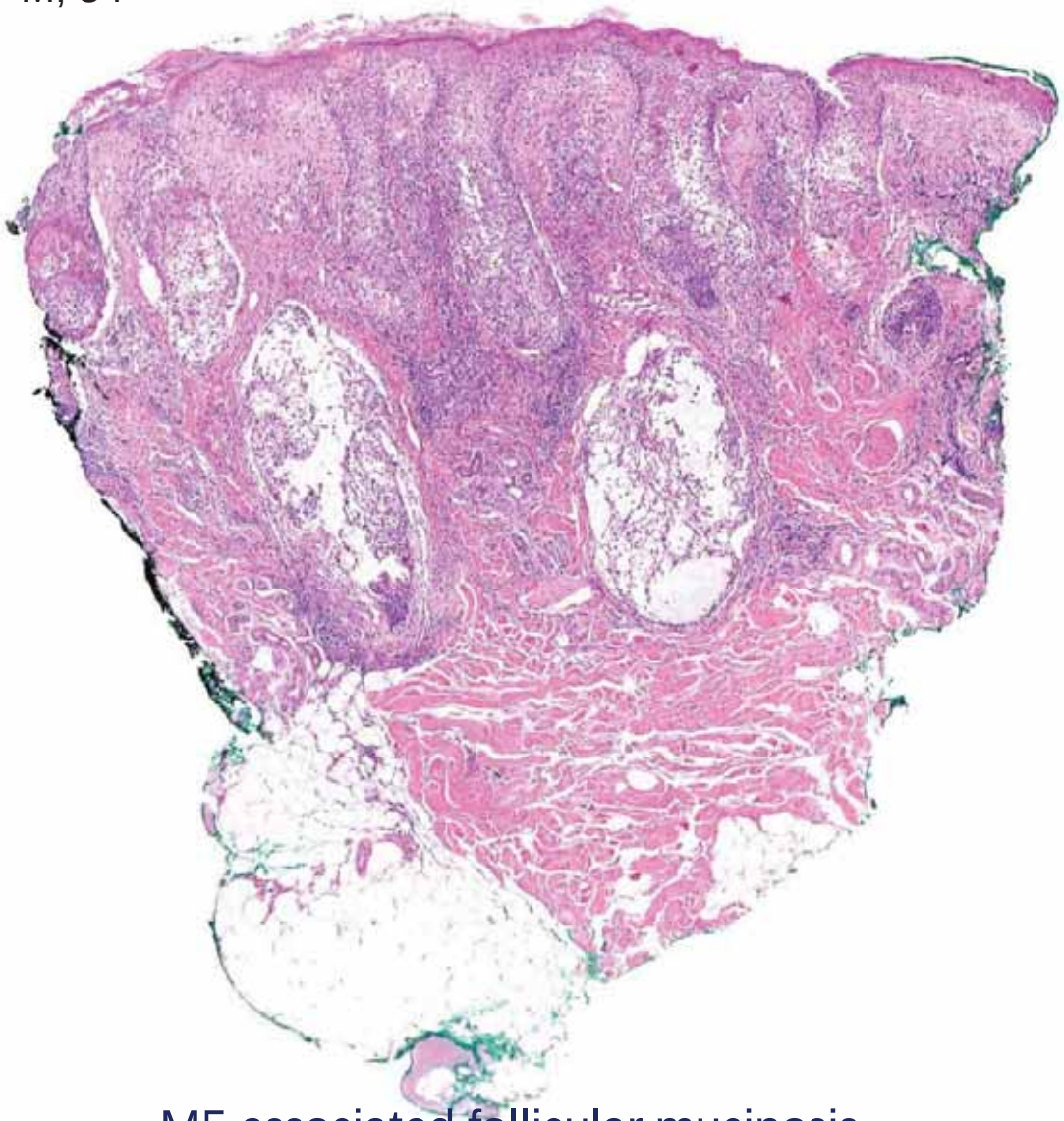
M, 22 *(A&W, 30 years)*





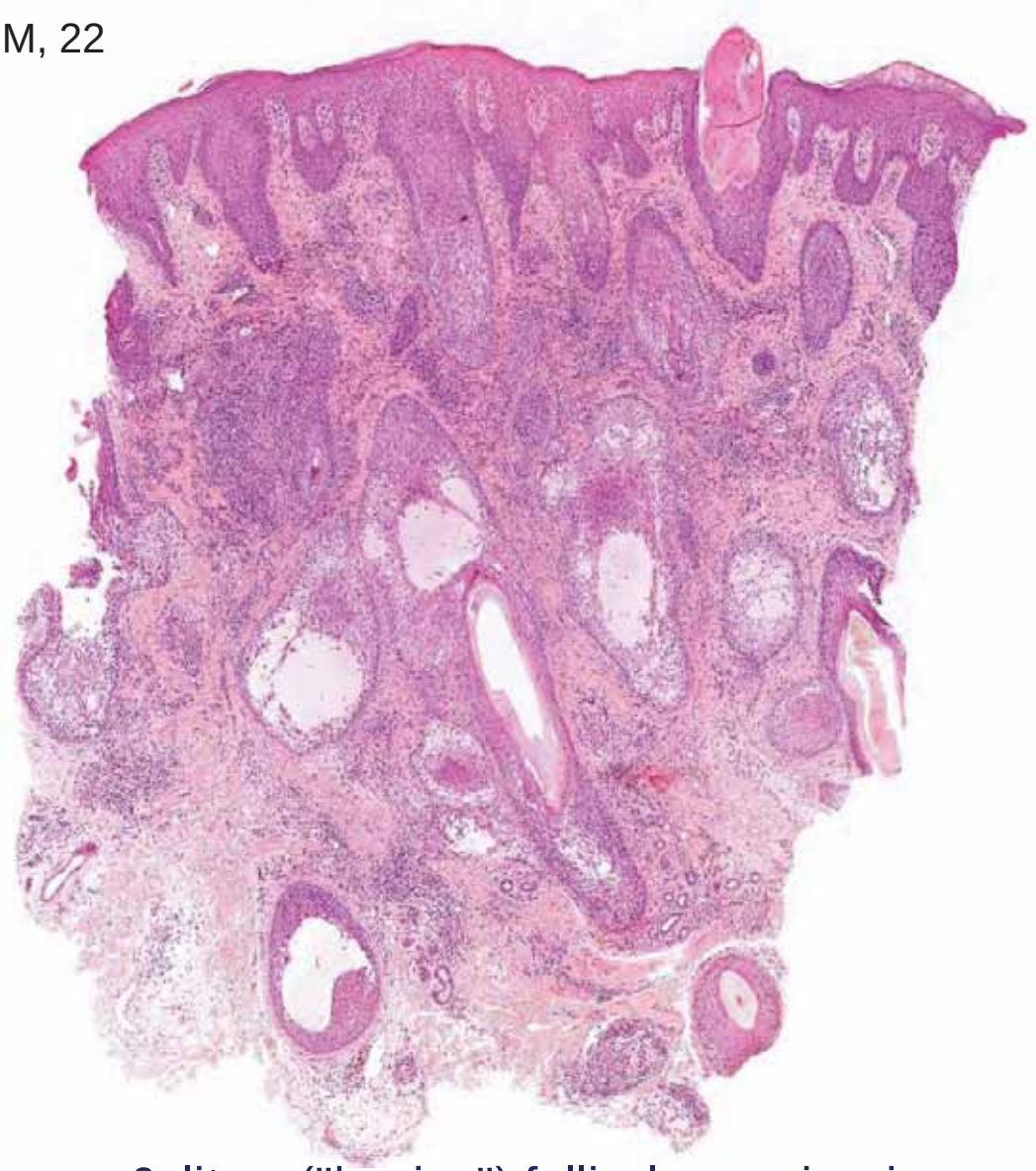


M, 54



MF-associated follicular mucinosis

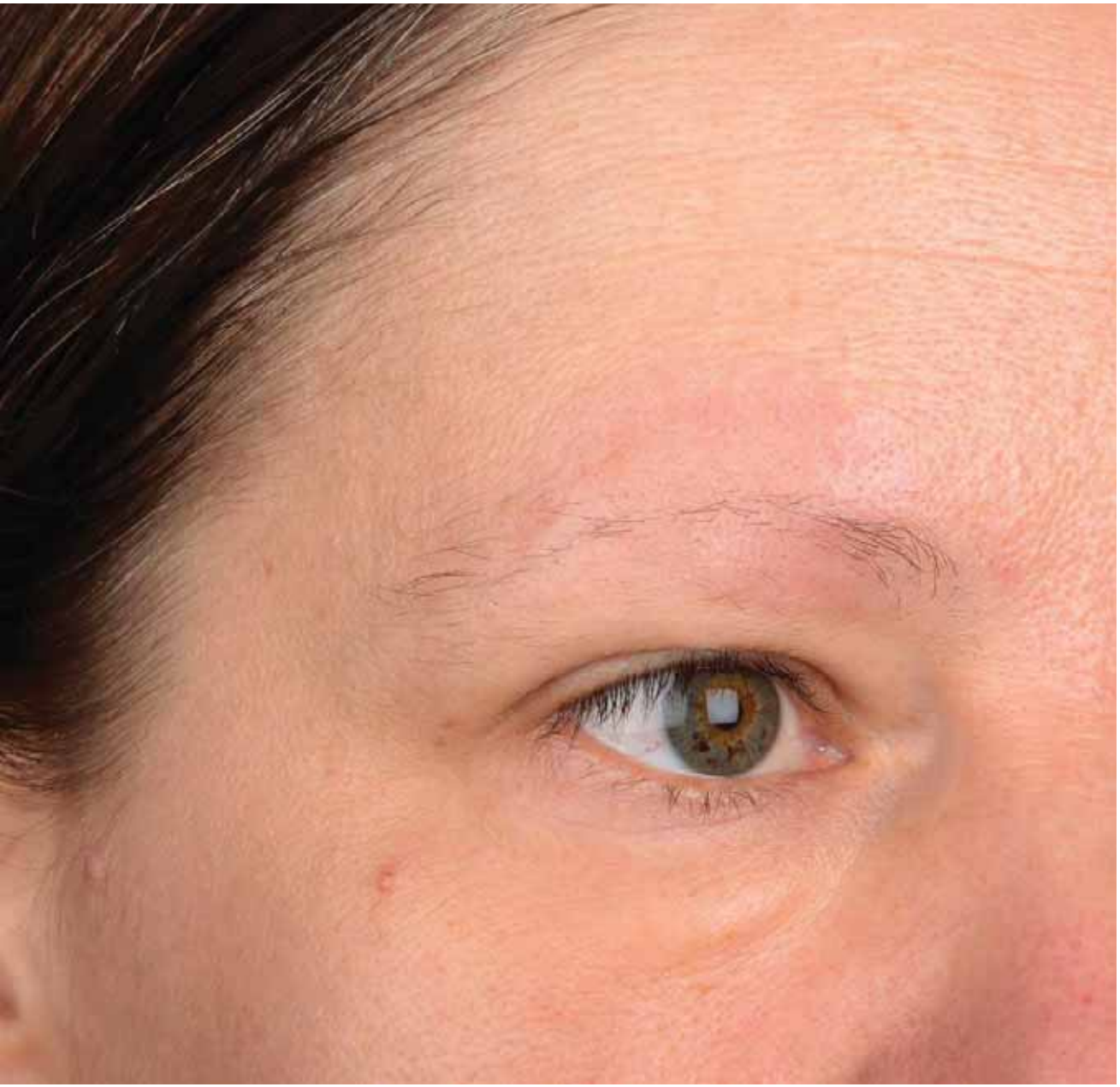
M, 22



Solitary ("benign") follicular mucinosis

"Benign" follicular mucinosis

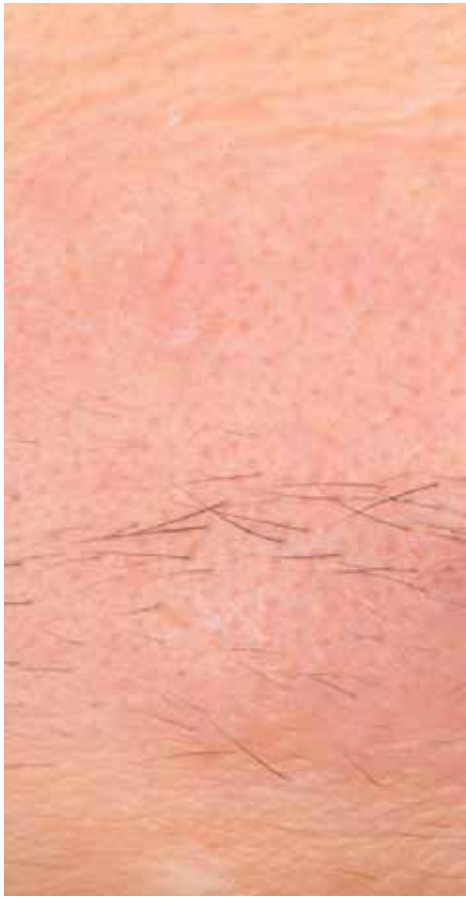
- "Benign" alopecia mucinosa presents almost exclusively as solitary lesions on the face in children or young adults
- Clinically and histopathologically indistinguishable from pilotropic MF; approx. 50% of cases monoclonal
- The exact classification of "benign" alopecia mucinosa is still a matter of debate
- Avoid overdiagnosis/overtreatment (watchful waiting advisable)

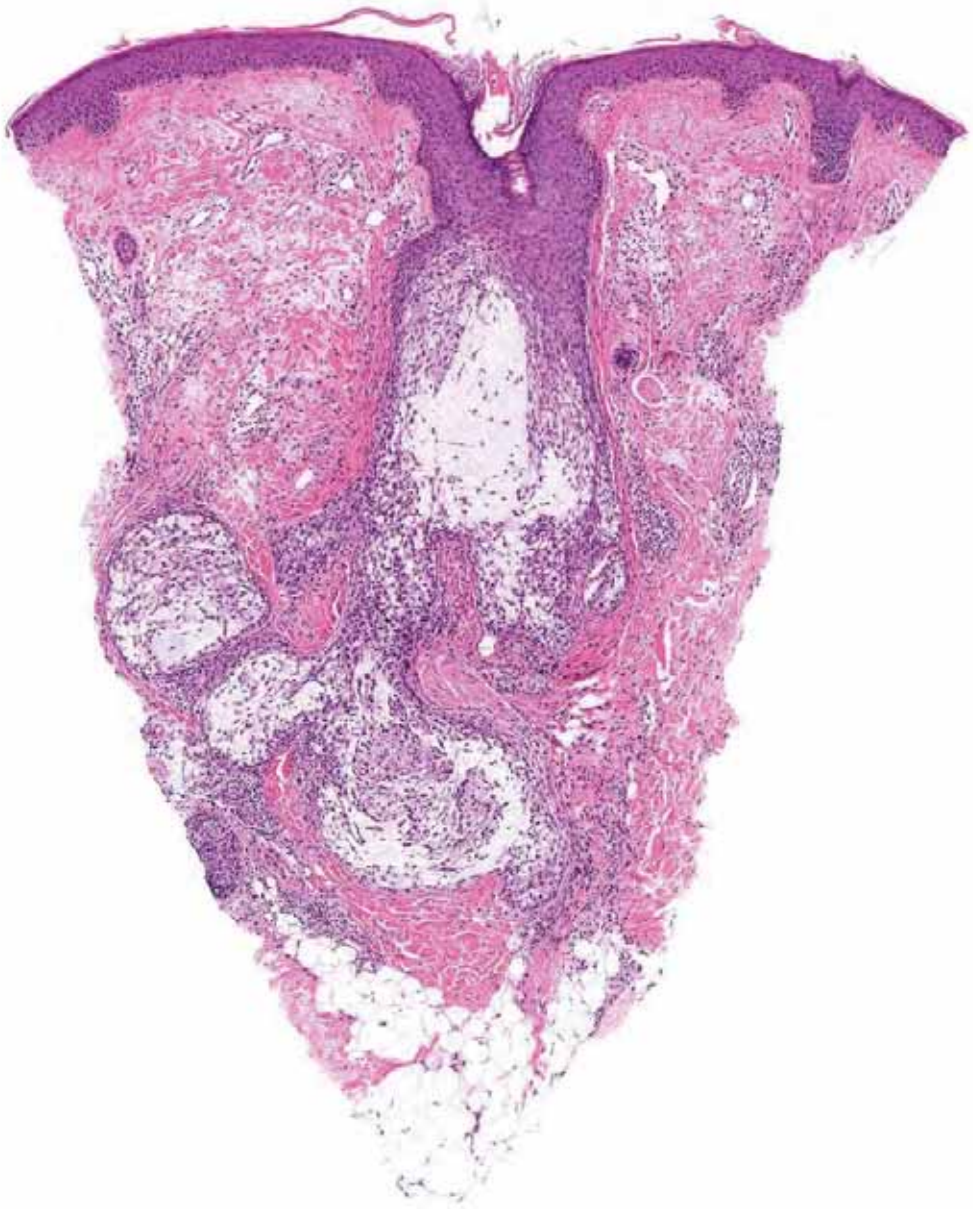


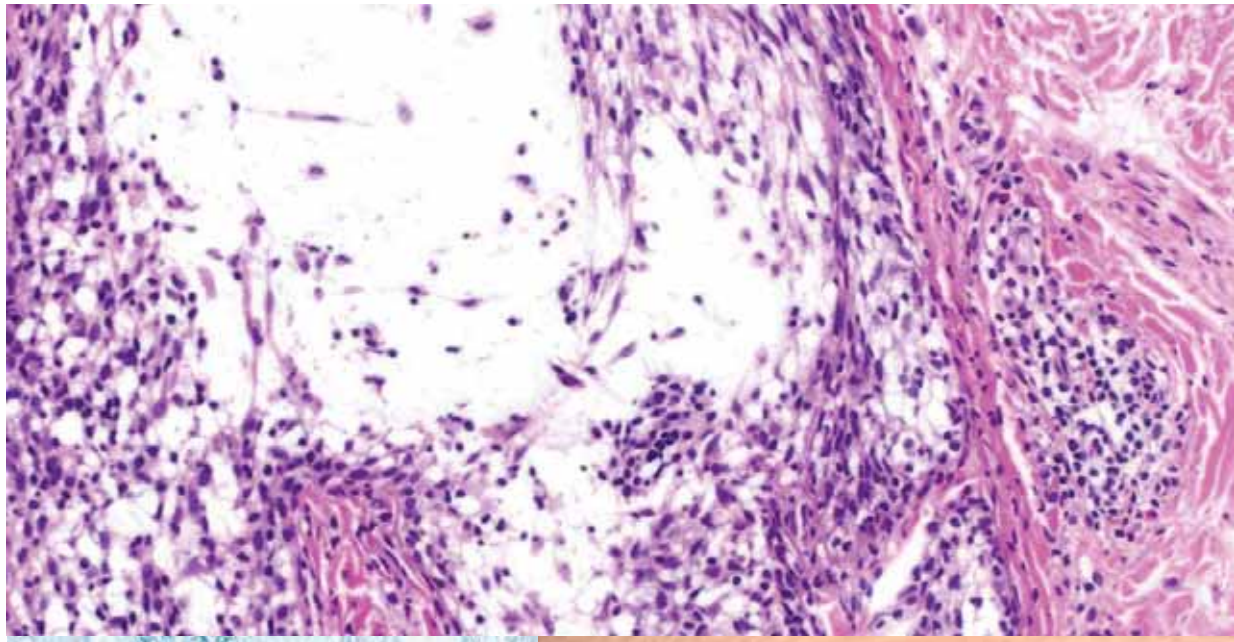
F, 41

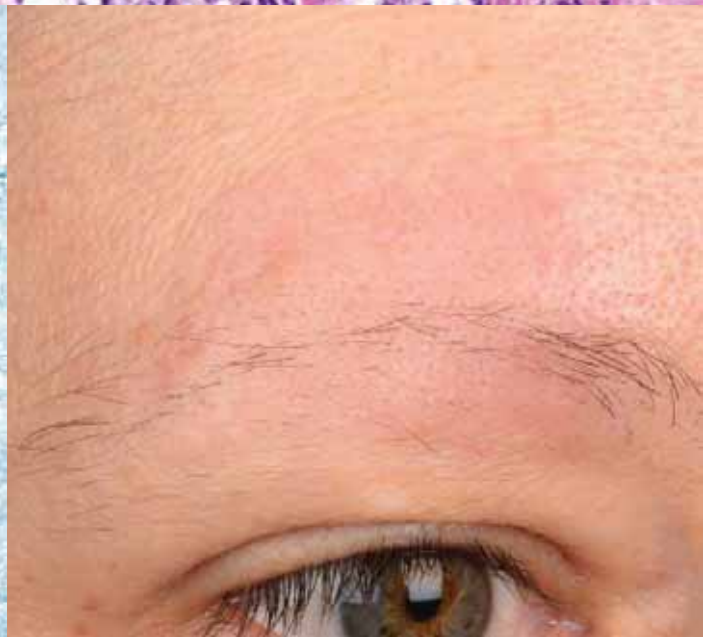
According to the patient localized alopecia on the right eyebrow for several months.

A biopsy is taken.





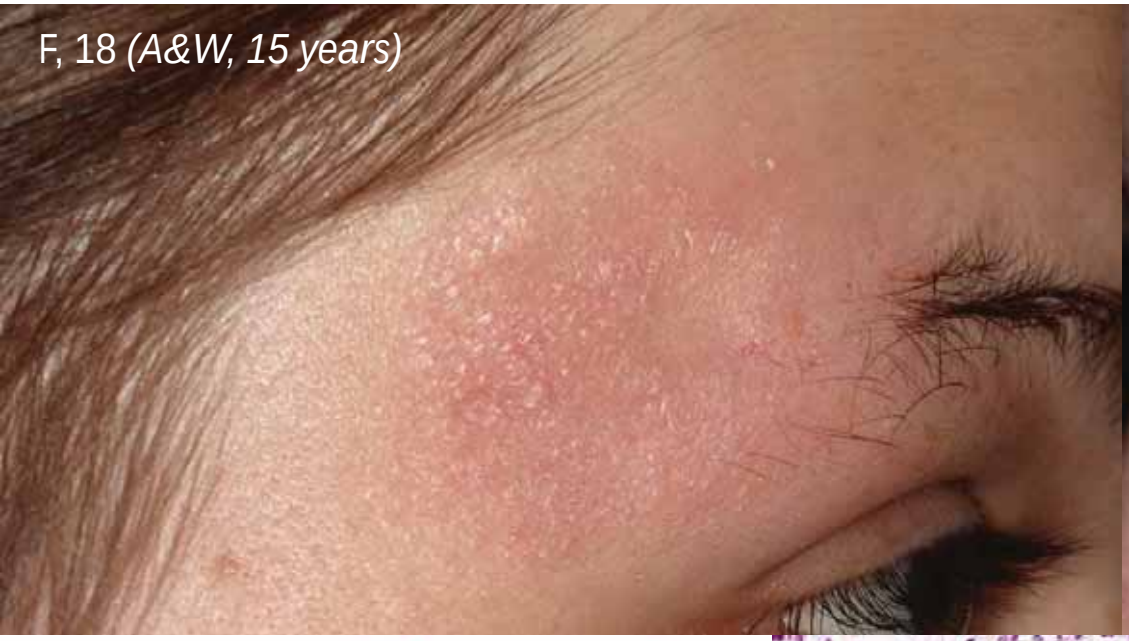


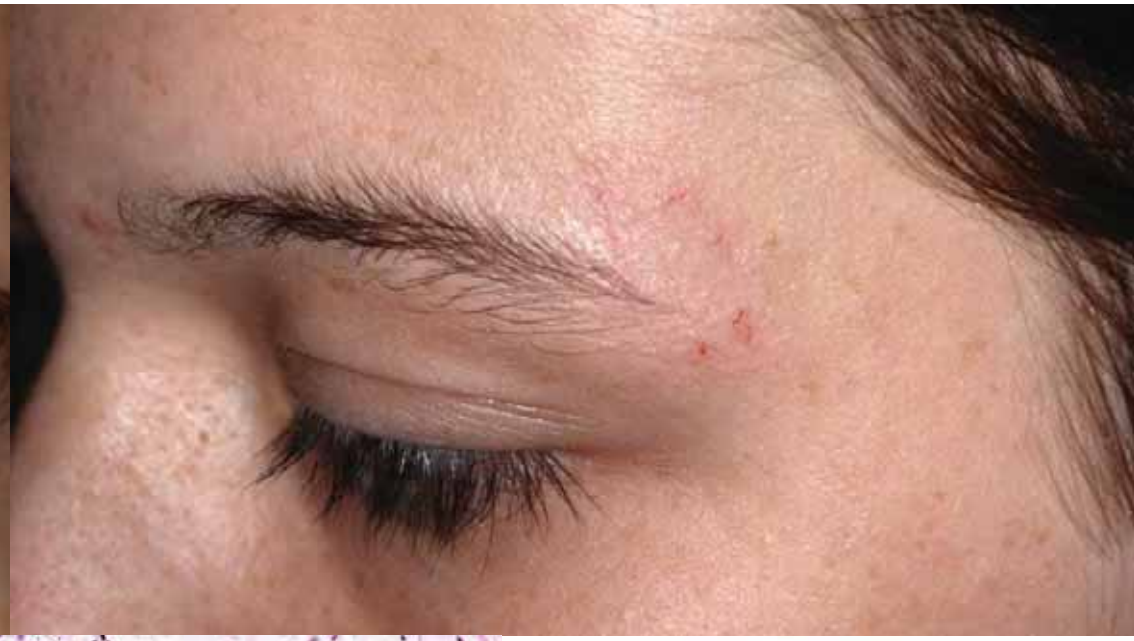


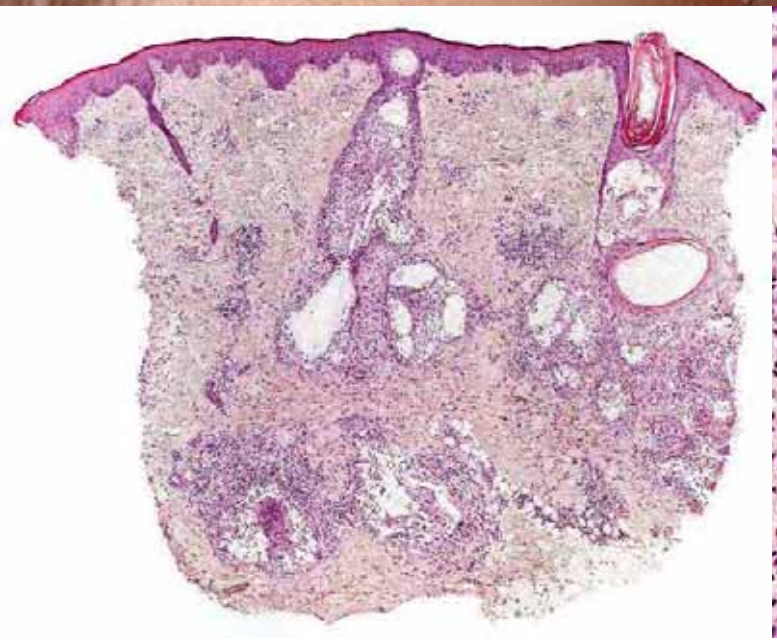
1st presentation

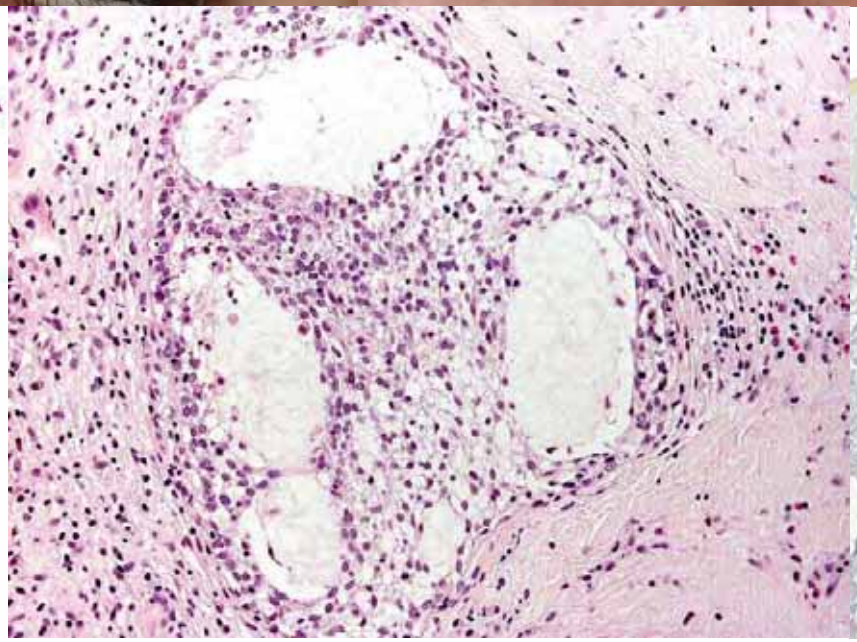
3 years later (1 month PUVA + several weeks local steroids)

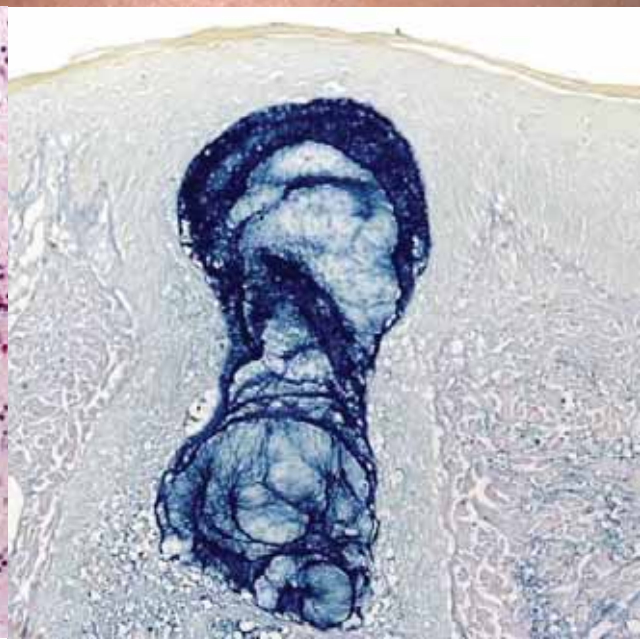
F, 18 *(A&W, 15 years)*



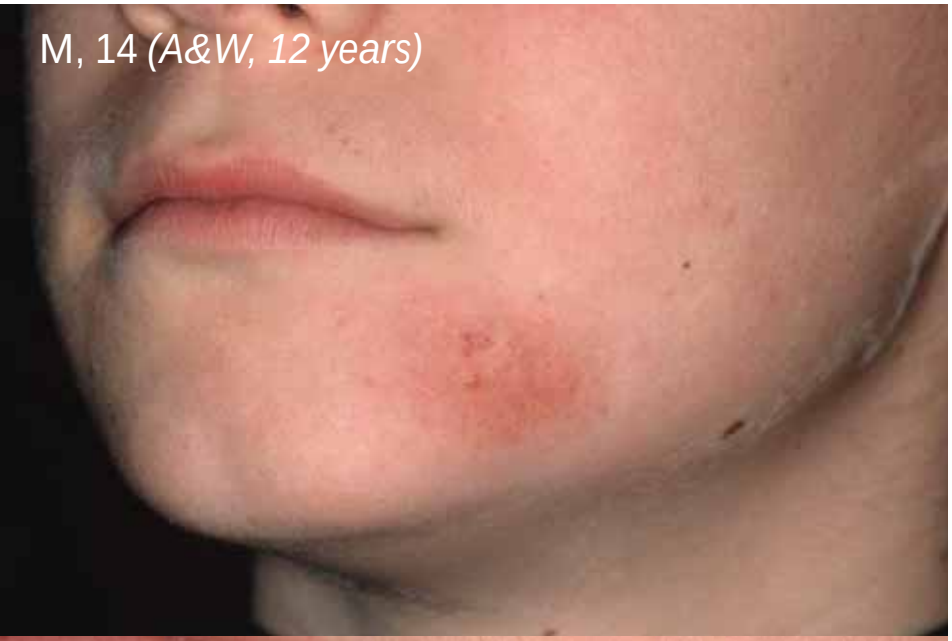


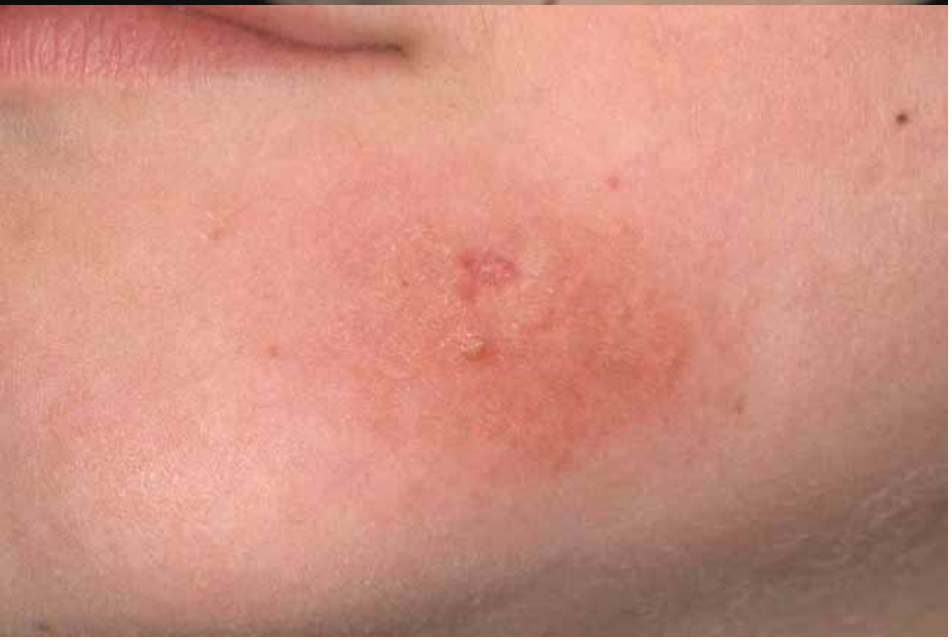


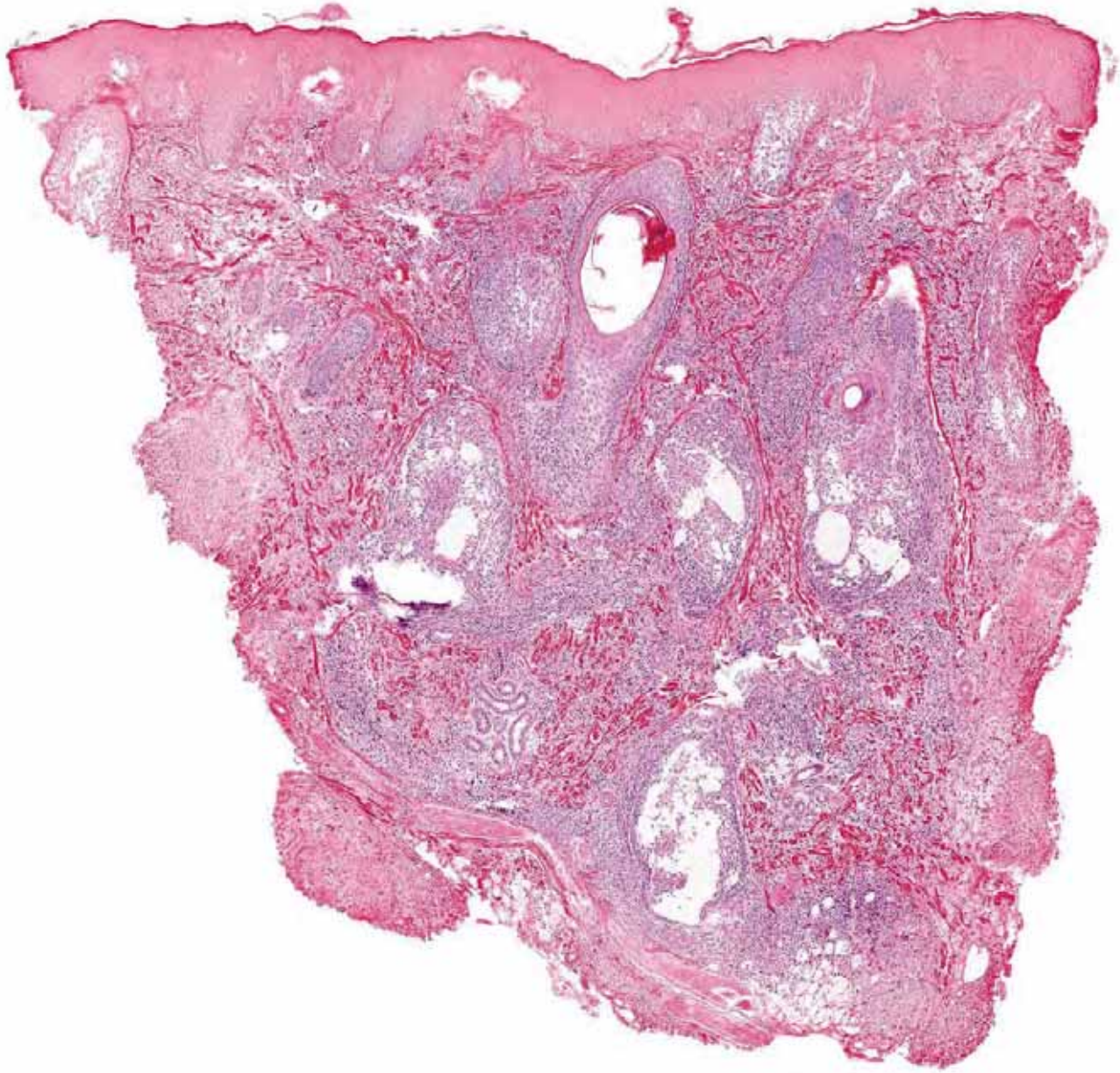




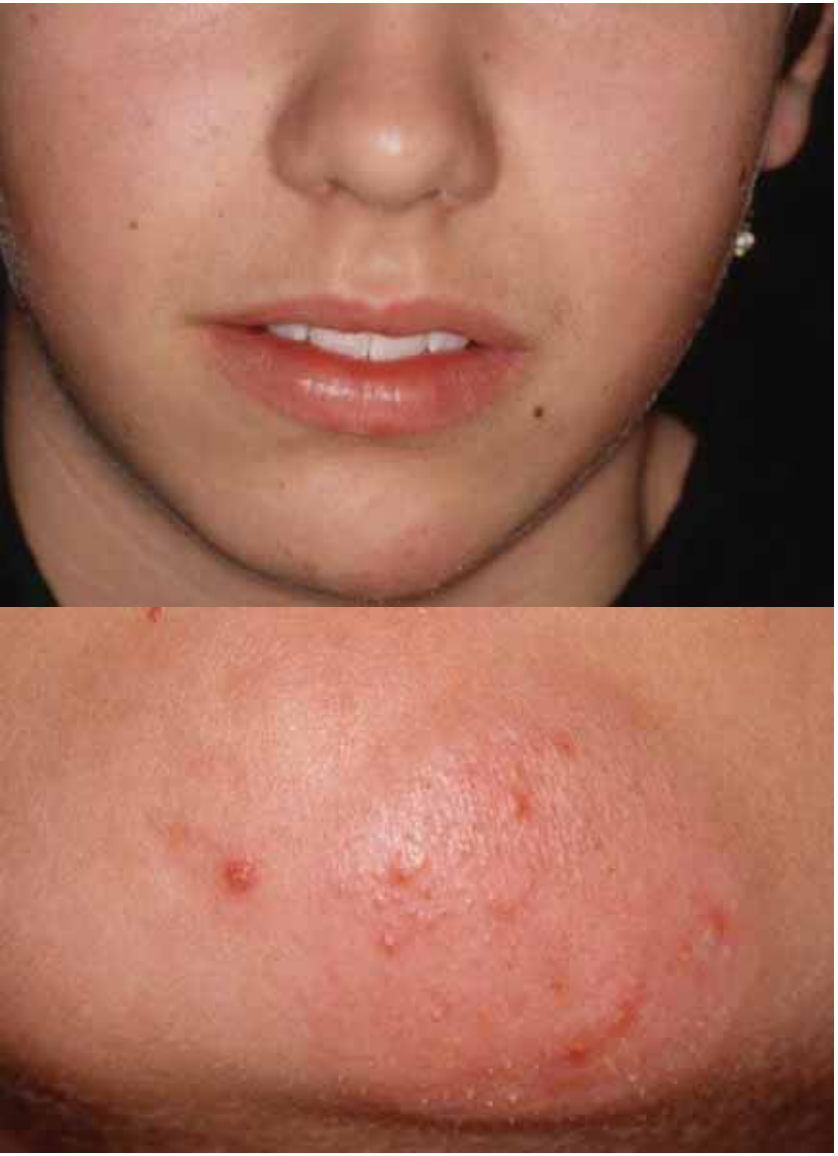
M, 14 *(A&W, 12 years)*

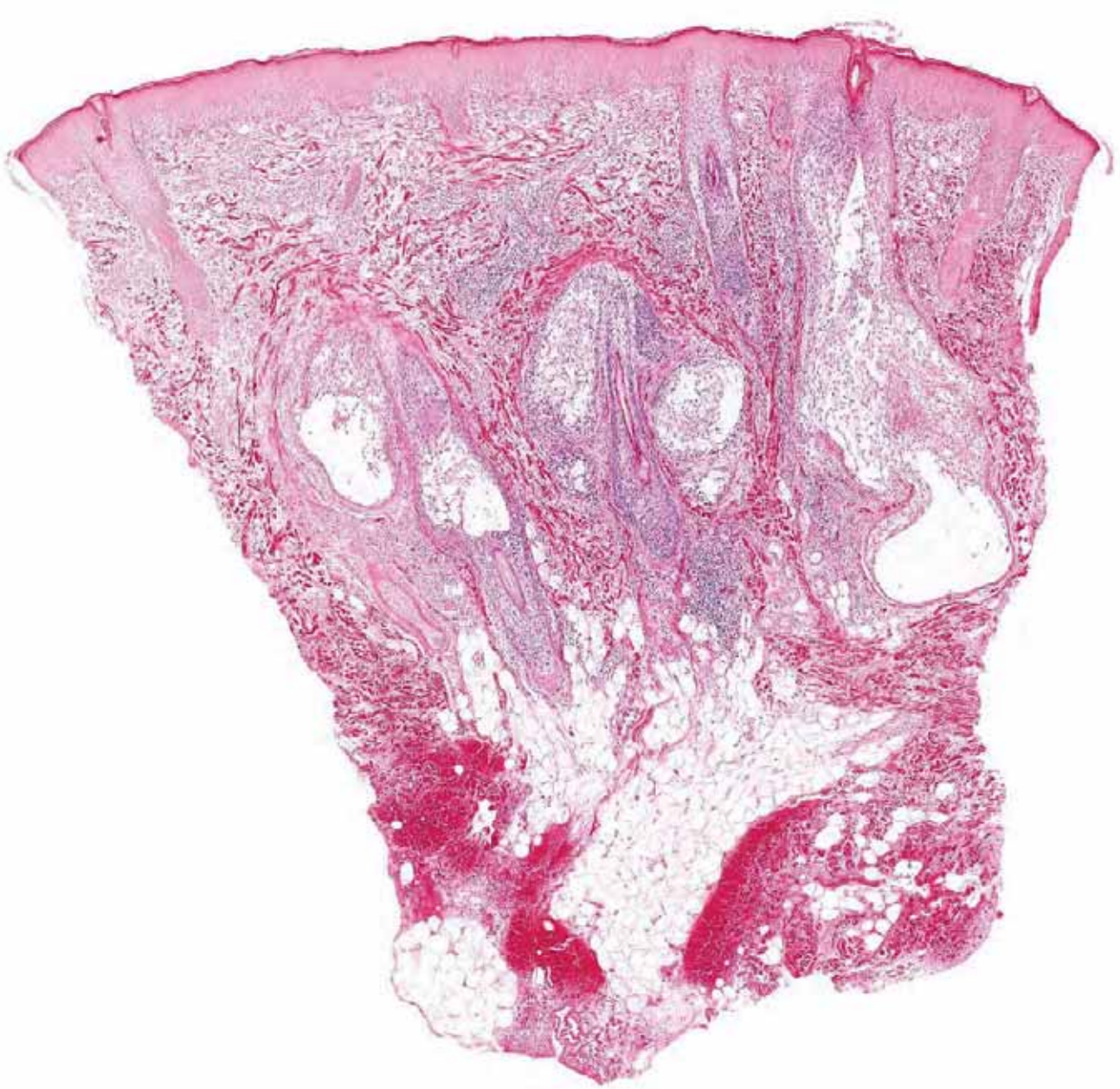




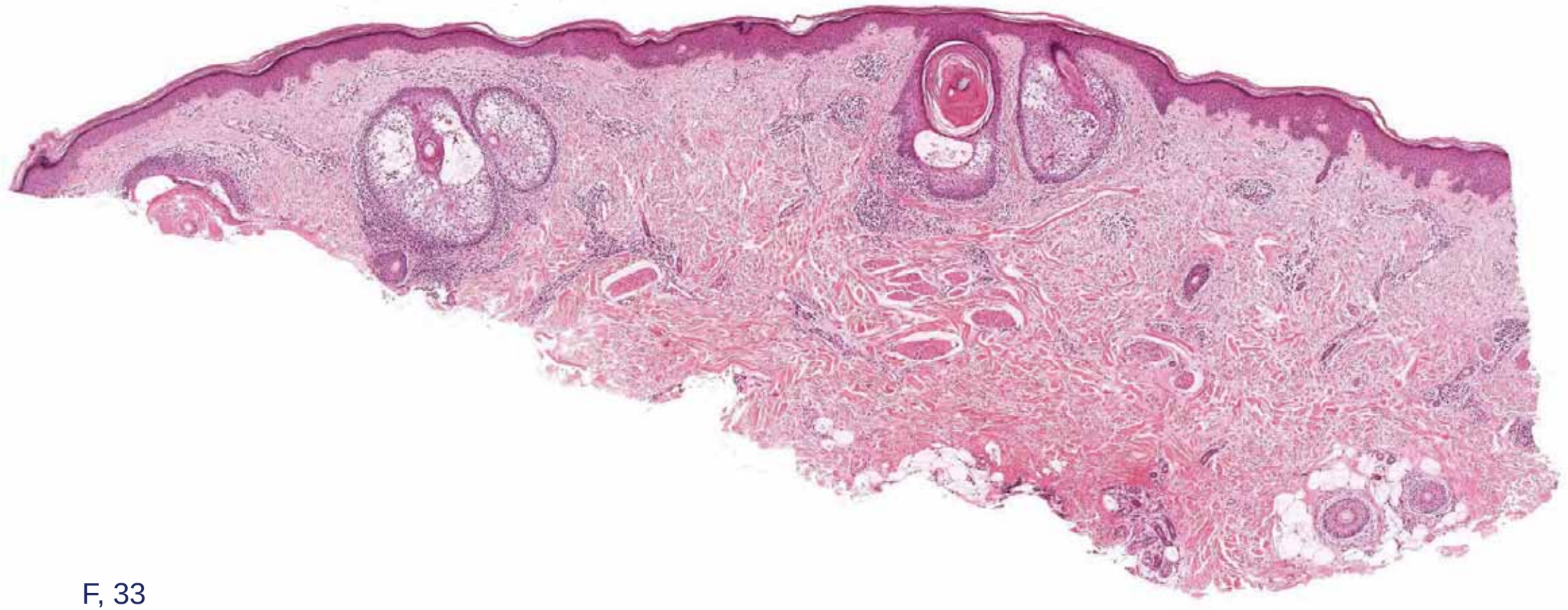


F, 13 *(A&W, 19 years)*

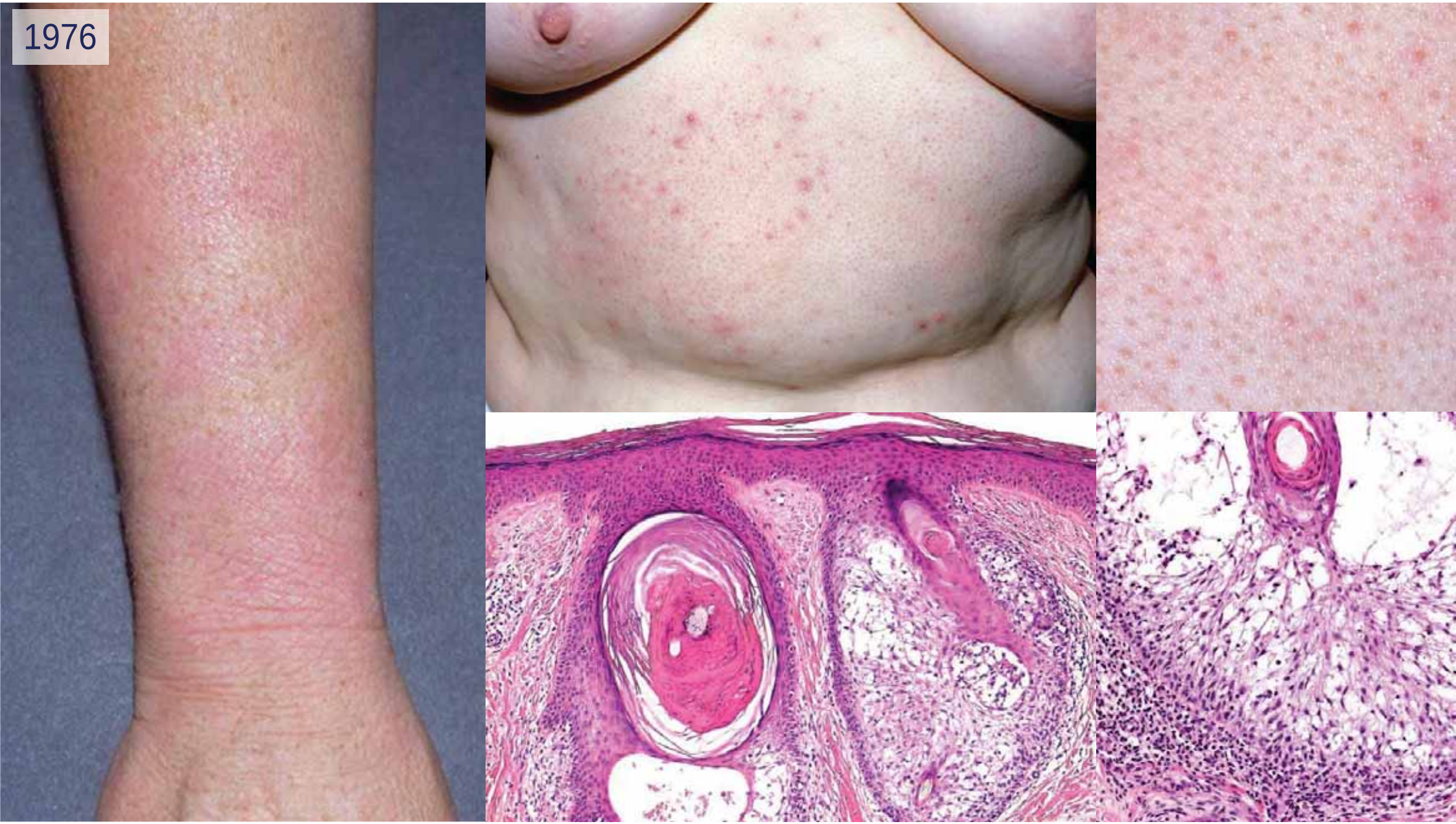




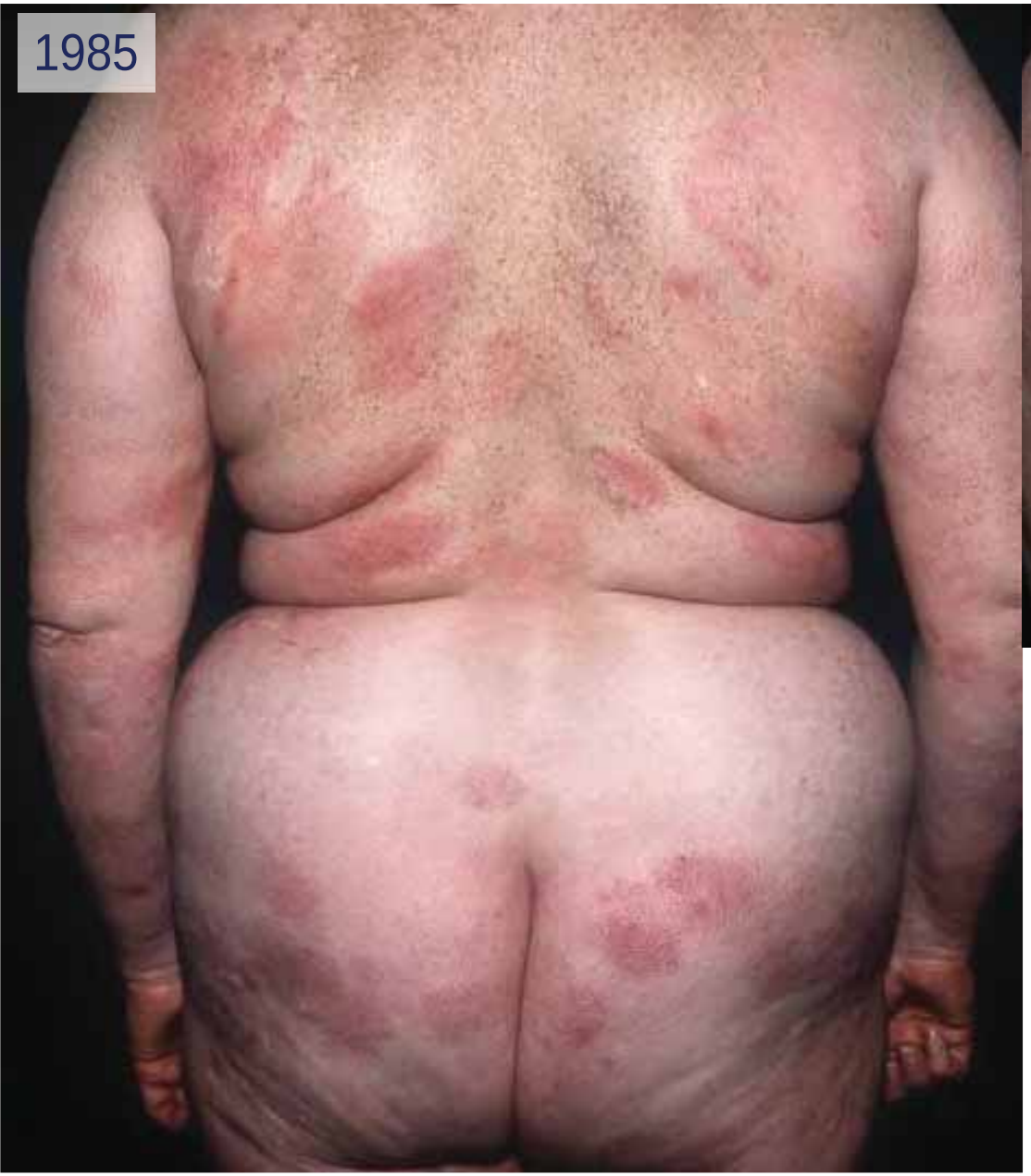
"Idiopathic" generalized follicular mucinosis ?

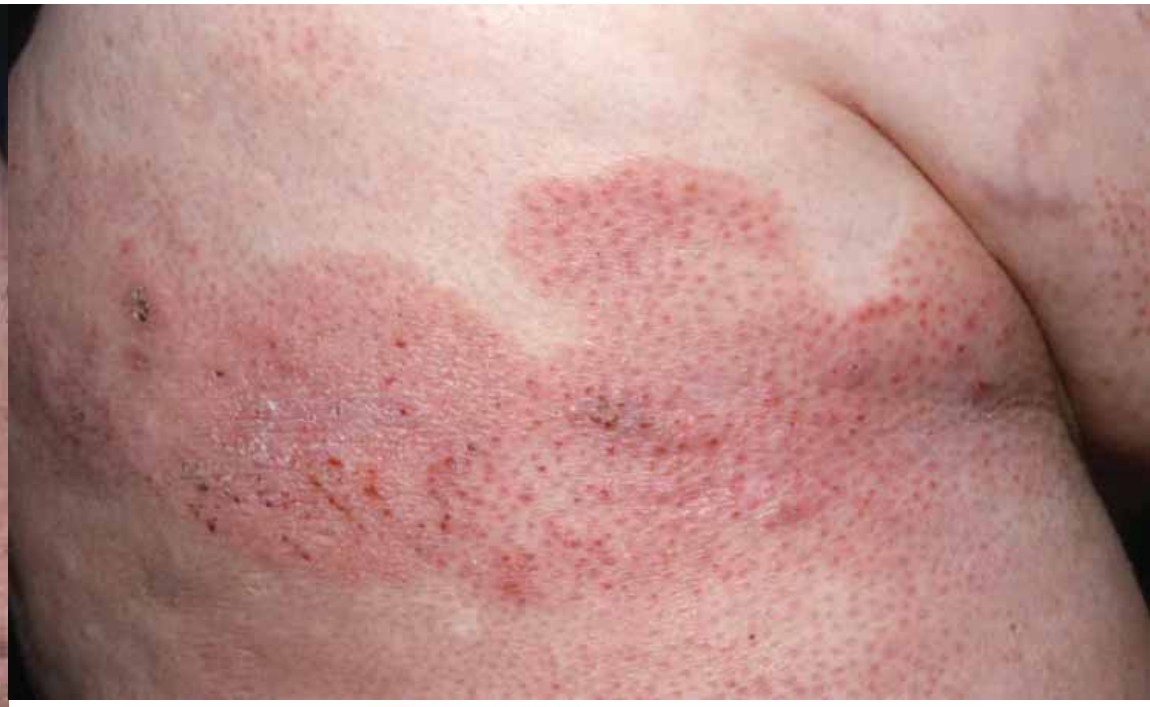


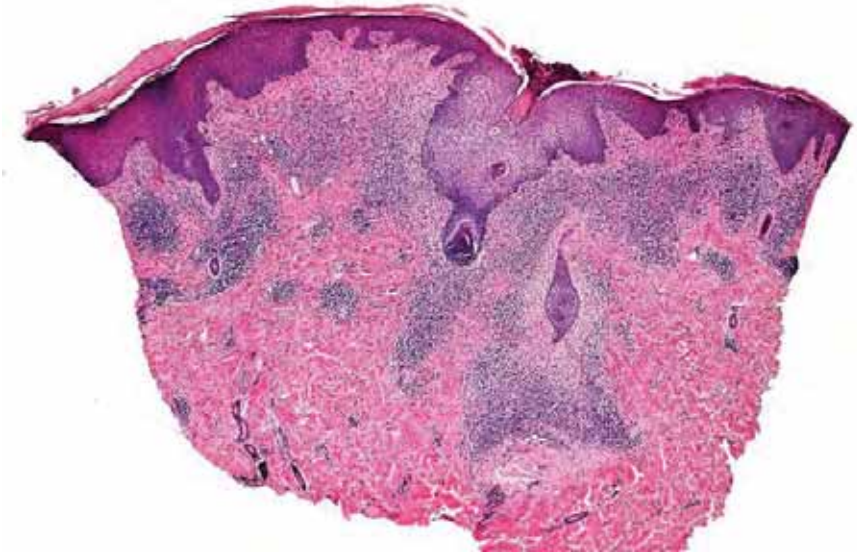
F, 33
Erythematous patches on the trunk and extremities for the last 4 years.


1976

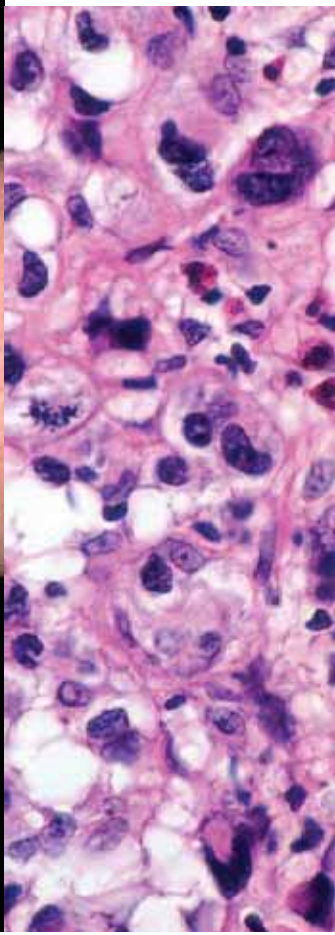
1985





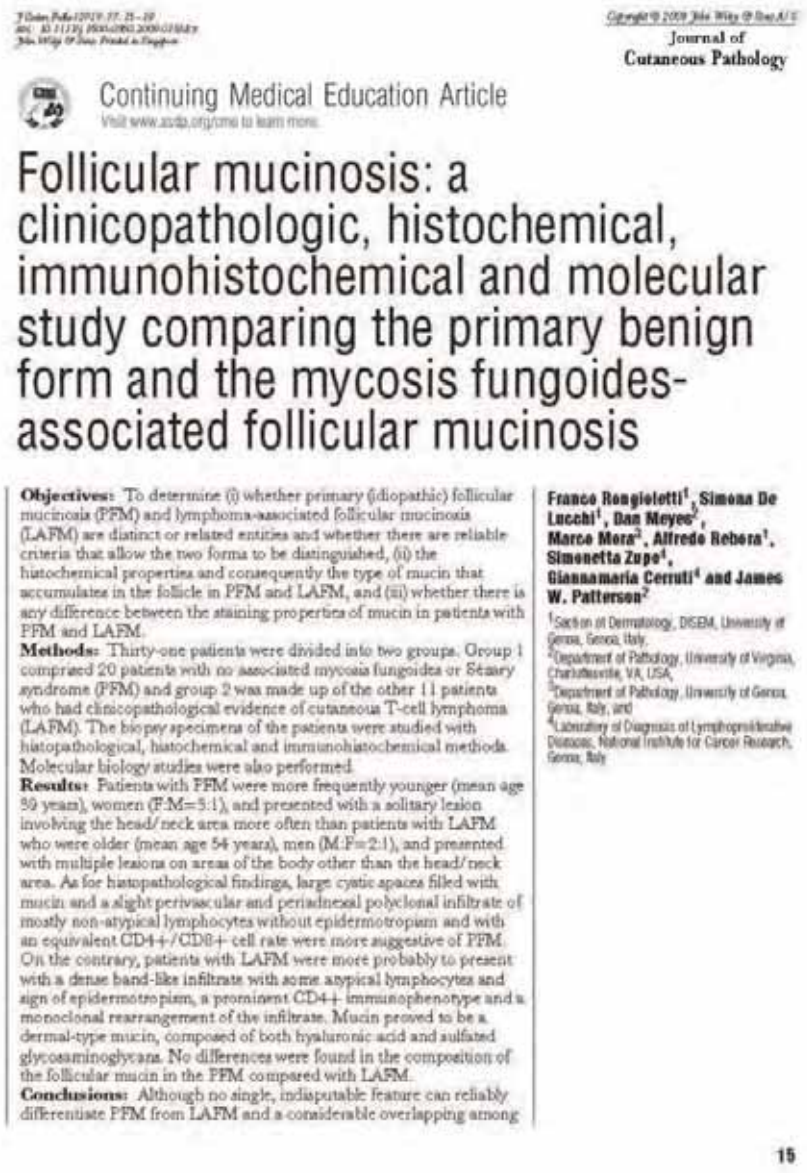


Died of MF, November 1989



"Idiopathic" generalized follicular mucinosis

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



Journal of
Cutaneous Pathology

Continuing Medical Education Article

Follicular mucinosis: a clinicopathologic, histochemical, immunohistochemical and molecular study comparing the primary benign form and the mycosis fungoides-associated follicular mucinosis

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Objectives: To determine (i) whether primary (idiopathic) follicular mucinosis (PFM) and lymphoma-associated follicular mucinosis (LAFM) are distinct or related entities and whether there are reliable criteria that allow the two forms to be distinguished, (ii) the histochemical properties and consequently the type of mucin that accumulates in the follicle in PFM and LAFM, and (iii) whether there is any difference between the staining properties of mucin in patients with PFM and LAFM.
Methods: Thirty-one patients were divided into two groups. Group 1 comprised 20 patients with no associated mycosis fungoides or Sézary syndrome (PFM) and group 2 was made up of the other 11 patients who had clinicopathological evidence of cutaneous T-cell lymphoma (LAFM). The biopsy specimens of the patients were studied with histopathological, histochemical and immunohistochemical methods. Molecular biology studies were also performed.
Results: Patients with PFM were more frequently younger (mean age 39 years), women (F:M=3:1), and presented with a solitary lesion involving the head/neck area more often than patients with LAFM who were older (mean age 54 years), men (M:F=2:1), and presented with multiple lesions on areas of the body other than the head/neck area. As for histopathological findings, large cystic spaces filled with mucin and a slight perivascular and periadnexal polyclonal infiltrate of mostly non-atypical lymphocytes without epidermotropism and with an equivalent CD4+/CD8+ cell rate were more suggestive of PFM. On the contrary, patients with LAFM were more probably to present with a dense band-like infiltrate with some atypical lymphocytes and sign of epidermotropism, a prominent CD4+ immunophenotype and a monoclonal rearrangement of the infiltrate. Mucin proved to be a dermal-type mucin, composed of both hyaluronic acid and sulfated glycosaminoglycans. No differences were found in the composition of the follicular mucin in the PFM compared with LAFM.
Conclusions: Although no single, indisputable feature can reliably differentiate PFM from LAFM and a considerable overlapping among

"Primary" follicular mucinosis (no MF or Sèzary)
n=20 (M:F = 1:3; mean age 39 years; range 12-64)
62% with solitary lesion
61% lesion(s) on the head & neck area

CTCL-associated follicular mucinosis
n=11 (M:F = 2:1; mean age 54 years; range 44-71)
100% with multiple lesions
28% lesions on the head & neck area

STUDY

Follicular Mucinosis

A Critical Reappraisal of Clinicopathologic Features and Association With Mycosis Fungoides and Sézary Syndrome

Lorenzo Cerroni, MD; Regina Fink-Puches, MD; Barbara Bäck; Helmut Kerl, MD

Context: Beginning in 1957, patients have been described with localized alopecia characterized histopathologically by mucin deposition within hair follicles (follicular mucinosis [FM]). At least 2 distinct diagnostic entities have been proposed: one occurring in children and young adults without association with other diseases ("idiopathic" FM), the other occurring in elderly patients and associated with mycosis fungoides or Sézary syndrome ("lymphoma-associated" FM).

Objective: To determine whether idiopathic and lymphoma-associated FM are distinct or related entities.

Design: Case series.

Setting: Department of Dermatology, University of Graz, Graz, Austria.

Patients: Forty-four patients with FM were divided into 2 groups. Group 1 comprised 16 patients (mean age, 37.5 years) with no associated mycosis fungoides or Sézary syndrome; group 2 was made up of the other 28 (mean age, 52.2 years), who had clinicopathologic evidence of cutaneous T-cell lymphoma.

Results: Mean age was lower in patients with idiopathic FM, but a considerable overlapping among the 2 groups was present. Location on the head and neck region was common in both groups, but most patients with lymphoma-associated FM had lesions also on other body sites. In fact, solitary lesions at presentation were common in patients with idiopathic FM (11 [68.8%] of 16 patients), but uncommon in those with lymphoma-associated FM (2 [7.1%] of 28 patients). Histopathologic findings did not allow clear-cut differentiation of the 2 groups. Finally, a monoclonal rearrangement of the T-cell receptor γ gene was demonstrated by polymerase chain reaction analysis in about 50% of tested cases from each group.

Conclusions: Criteria previously reported to differentiate idiopathic from lymphoma-associated FM proved ineffective. In analogy to localized pagetoid reticulosis (Woringer-Kolopp disease), small-plaque parapsoriasis, and so-called solitary mycosis fungoides, idiopathic FM may represent a form of localized cutaneous T-cell lymphoma.

Arch Dermatol. 2002;138:182-189

In 1957, Hermann Pinkus[1] described a group of 6 patients with localized alopecia characterized histopathologically by mucin deposition within hair follicles. In the following years, the term *follicular mucinosis* (FM) proposed by Jablonska et al[2] in 1959 slowly replaced *alopecia mucinosa*, the designation originally coined by Pinkus himself. Subsequent reports suggested that at least 2 distinct entities were encompassed under this diagnosis: one occurring in children and young adults without association with other cutaneous or extracutaneous diseases ("idiopathic" FM), the other occurring in elderly patients and associated with mycosis fungoides or Sézary syndrome ("lymphoma-associated" FM).[3-13] In addition, progression of idiopathic FM into cutaneous T-cell lymphoma (CTCL) has been well documented in several cases.[14-18]

See also pages 191 and 244

In this study, we reviewed data from a large group of patients with idiopathic and lymphoma-associated FM with respect to clinicopathologic presentation and molecular features.

RESULTS

IDIOPATHIC FM

Clinicopathologic and molecular features for patients with idiopathic FM are summarized in **Table 1**. Sixteen patients had FM without signs of CTCL or other cutaneous or extracutaneous diseases (M/F, 1.3:1;

From the Department of Dermatology, University of Graz, Austria.

Table 2. Summary of Clinicopathologic Features and Follow-up Data for Patients With Lymphoma-Associated Follicular Mucinosis

Patient No./Sex/Age, y	Location	Distribution of Lesions	Lymphoma Type	Lymphoid Infiltrate	PCR† of *TCR*γ	Follow-up (No. of mo)
17/M/36	HN	M	MF	CTCL	P	A&D (2)
18/F/36	HN	M	MF	Mild	Mo	A&D (6)
19/M/47	T	M	MF	CTCL	nd	A&D (51)
26/M/68	T, LE	M	MF	CTCL	nd	A&D (101)
21/M/51	T	M	MF	CTCL	P	A&W (82)
22/M/74	HN, T	M	MF	Dense	Mo	D-us (48)
23/M/59	HN, T	M	MF	CTCL	Mo	D (216)
24/F/39	HN	S	MF	CTCL	P	A&D (12)
25/M/48	HN, T	M	MF	Mild	nd	A&D (175)
26/M/61	T	M	MF	CTCL	Mo	A&D (6)
27/F/70	T	M	MF	Mild	P	A&W (11)
28/M/58	HN, T	M	MF	Mild	P	A&D (15)
29/M/50	HN, T, UE, LE	G	MF	CTCL	Mo	D-us (59)
30/M/56	T	G	MF	CTCL	P	A&D (54)
31/F/47	HN, T, UE	M	MF	Mild	nd	A&D (48)
32/M/48	HN, T, UE, LE	G	MF	CTCL	nd	A&D (6)
33/M/39	HN, T	M	MF	Dense	Mo	A&D (221)
34/M/80	T	M	MF	CTCL	nd	A&D (84)
35/F/55	T	M	MF	Mild	nd	D (27)
36/M/56	HN, T	M	MF	CTCL	Mo	A&D (29)
37/M/56	HN, T, UE, LE	G	MF	CTCL	nd	A&D (108)
38/M/70	T	M	MF	CTCL	nd	D (262)
39/F/39	T, UE	M	MF	Mild	P	D (204)
40/M/68	T, LE	M	MF	CTCL	Mo	A&D (6)
41/M/34	HN, T, UE, LE	G	MF	CTCL	P	D (98)
42/F/61	T, UE	M	MF	Mild	P	A&D (83)
43/F/69	ED	G	Sézary	CTCL	P	D (49)
44/M/32	ED	G	Sézary	Mild	Mo	D (19)

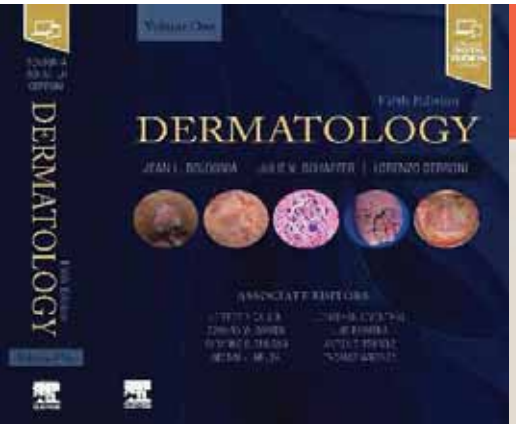
*HN indicates head and neck; T, trunk; LE, lower extremities; UE, upper extremities; ED, erythroderma; M, multiple lesions; S, solitary lesion; G, generalized lesions; MF, mycosis fungoides; CTCL, cutaneous T-cell lymphoma; P, polyclonal pattern; Mo, monoclonal pattern; nd, test not done; A&D, alive with skin disease; A&W, alive and well; D-us, dead of unrelated causes; and D, dead of disease.
†Findings of polymerase chain reaction (PCR) analysis of the T-cell receptor γ (*TCR*γ) gene rearrangement.

Table 1. Summary of Clinicopathologic Features and Follow-up Data for Patients With Idiopatic Follicular Mucinosis*

Patient No./ Sex/Age, y	Location	Distribution of Lesions	Lymphoid Infiltrate	PCR† of *TCR*γ	Follow-up (No. of mo)
1/F/54	HN	S	Dense	P	A&D (25)
2/F/20	HN	M	Dense	P	A&D (6)
3/M/16	HN	S	Mild	nd	A&D (12)
4/M/48	HN	S	Dense	Mo	A&W (215)
5/M/61	HN	M	Dense	P	A&W (225)
6/M/53	HN	S	Mild	Mo	A&D (19)
7/M/21	HN	S	Mild	Mo	A&W (242)
8/M/22	HN	S	Mild	P	A&W (111)
9/F/61	HN	S	Mild	nd	A&D (5)
10/M/27	HN	S	Dense	Mo	A&W (29)
11/F/35	T	M	Mild	P	A&D (6)
12/F/18	HN	S	Mild	Mo	A&W (52)
13/F/13	HN	S	Mild	nd	A&D (14)
14/F/50	HN	M	Dense	Mo	A&D (12)
15/M/58	HN	S	Mild	nd	A&W (166)
16/M/45	HN	M	Mild	nd	A&D (6)

*HN indicates head and neck; T, trunk; S, solitary lesion; M, multiple lesions; P, polyclonal pattern; nd, test not done; Mo, monoclonal pattern; A&D, alive with skin disease; and A&W, alive and well.
†Findings of polymerase chain reaction (PCR) analysis of T-cell receptor γ (*TCR*γ) gene rearrangement.

"Criteria previously reported to differentiate idiopathic from lymphoma-associated FM proved ineffective. (...) idiopathic FM may represent a form of localized cutaneous T-cell lymphoma."



Mucinoses 46

Franco Rongioletti

Primary follicular mucinosis is an idiopathic benign form of the disease, apparently not linked to lymphoma. Clinically, it presents as an acute or subacute eruption in *children and young adults* and is characterized by one or several pink plaques, often composed of grouped follicular papules. There may be associated scale, and lesions are limited to the face and scalp and are associated with alopecia. Papulonodules, annular plaques, folliculitis, follicular spines, and acneiform eruptions have also been described. **A second type of follicular mucinosis, characterized by: (1) a more generalized distribution (extremities, trunk and face;** (2) larger and more numerous plaques; (3) a chronic clinical course; and (4) occurrence in a slightly older age group, **is probably best regarded as a secondary follicular mucinosis associated with atopic dermatitis or cutaneous T cell lymphoma**, rather than a primary condition. (...)

The differentiation between primary follicular mucinosis and mycosis fungoides-associated follicular mucinosis is very difficult, and there is no single reliable criterion. Although the existence of a primary form of follicular mucinosis has been questioned by some authors (who consider it as an “indolent” localized form of cutaneous T cell lymphoma), features in favor of a primary form are the young age of the patient, a solitary plaque or limited number of lesions in the head and neck region, spontaneous resolution, and the absence histologically of epidermotropism and atypical lymphocytes. Detection of clonal T cell gene rearrangements does not seem to help differentiate the two types.

Pediatric Dermatology Vol. 30 No. 2 192–198, 2013

Pediatric Follicular Mucinosis: Presentation, Histopathology, Molecular Genetics, Treatment, and Outcomes over an 11-Year Period at the Mayo Clinic

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Department of Dermatology, Mayo Clinic, Rochester, Minnesota

Abstract: Follicular mucinosis (FM) and folliculotropic mycosis fungoides (MF) are rare in children, and data regarding long-term outcomes are limited. We sought to describe clinical and histopathologic findings of children with FM with and without MF, as well as treatments administered and clinical outcomes. We conducted a retrospective chart review of patients younger than 22 years (at time of diagnosis) with a biopsy demonstrating FM who were seen in the Dermatology Department at the Mayo Clinic from September 1, 1999, to September 1, 2010. Eleven patients (six male, five female) ages 11 to 19 years at the time of diagnosis met the inclusion criteria. Follow-up data were available for 10 patients, with a mean duration of 4.9 years. The head, neck, and extremities were the most common sites of involvement, and lesions were follicular-based papules (18%), scaly alopecic patches and plaques (45%), or a combination of the two (36%). Overall, three patients were confirmed to have MF. T-cell receptor gene rearrangement demonstrated clonality in two cases and was equivocal in one case. Treatments included topical corticosteroids, topical retinoids, oral minocycline, and, in patients with MF, ultraviolet light and topical bexarotene. Lesions resolved completely in seven patients, partially in one, and not at all in two (no follow-up data on one patient). Of the three patients with MF, two had complete resolution, and one has intermittent flares. To our knowledge, no patients developed other lymphoproliferative disorders. FM in children is rare. A histopathologic diagnosis of FM does not equate to folliculotropic MF in all cases. Most patients responded to treatment with topical steroids, topical retinoids, or phototherapy. In our series of patients, the disease ran a benign course.

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[1]Both authors contributed equally to the manuscript.

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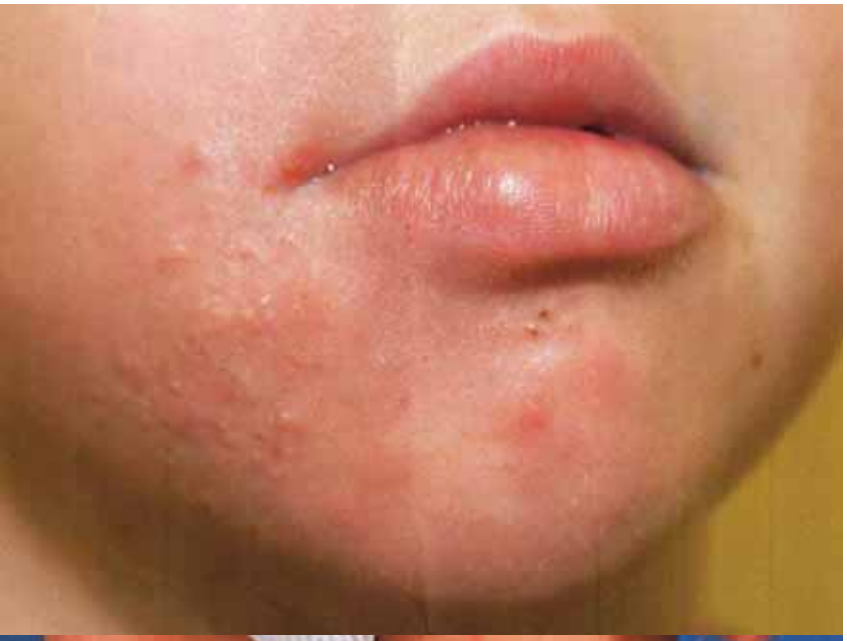
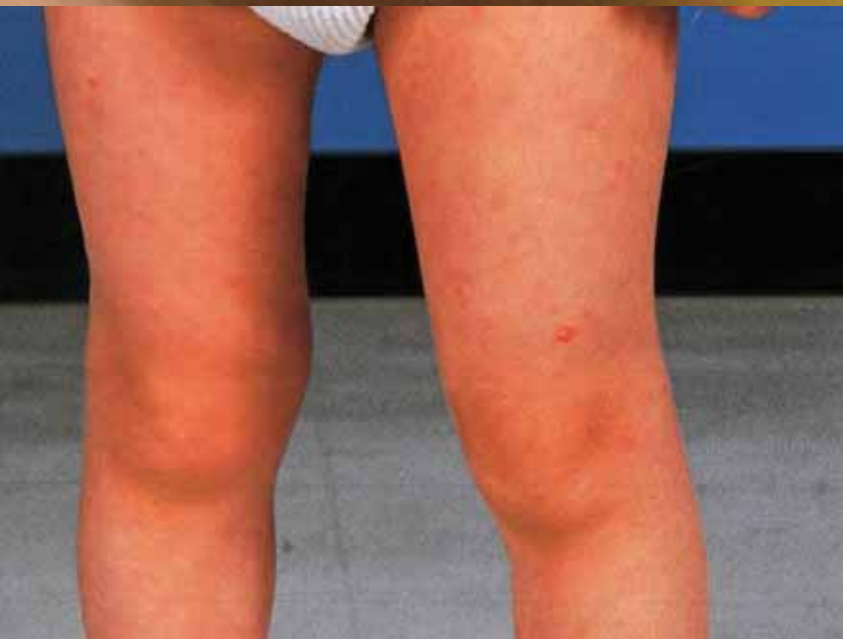
11 patients (age: 11-19)
10 patients with follow-up data
Mean follow-up: 4,9 years (median: 4,5)
3 patients developed MF (30%)





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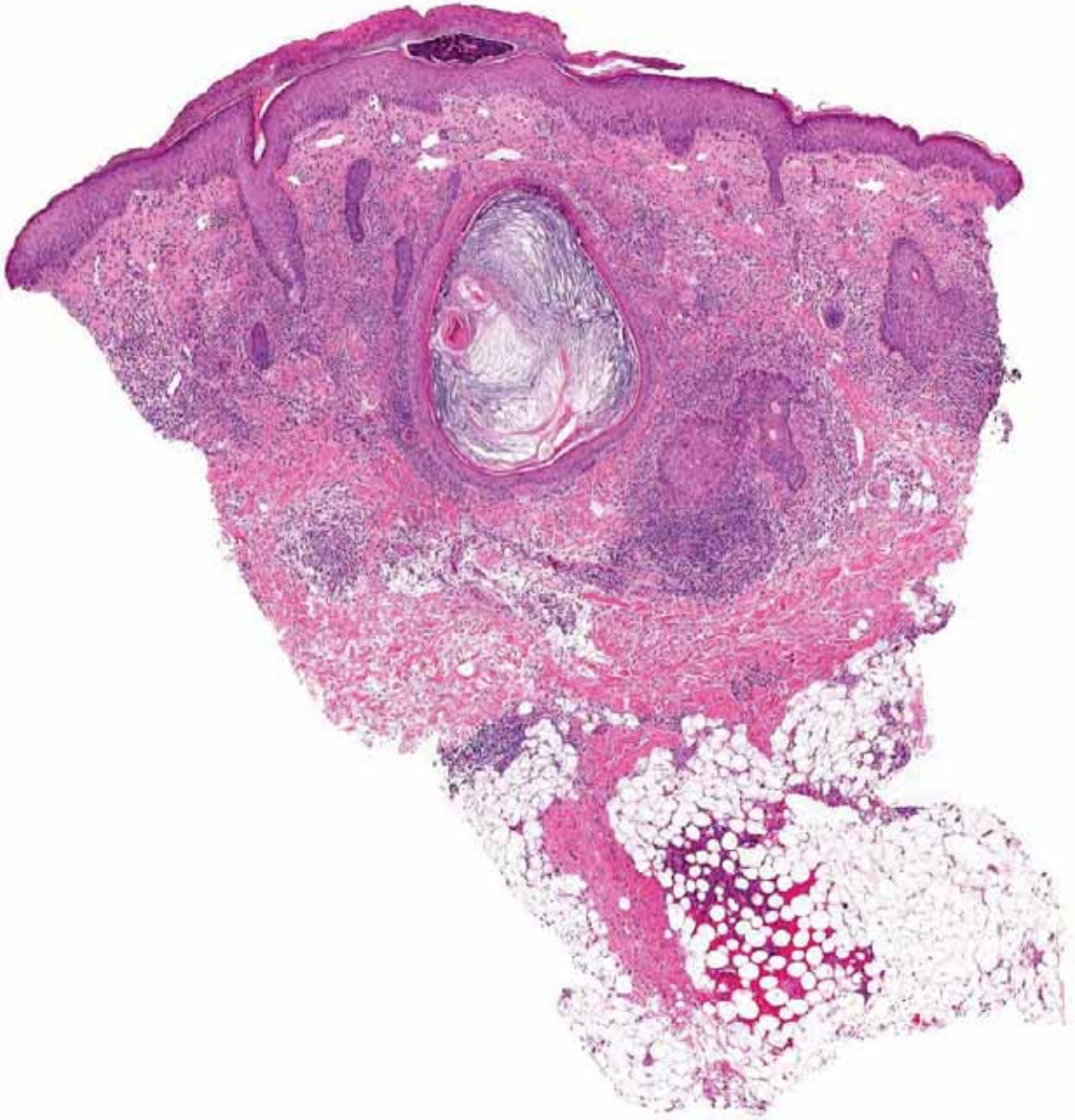

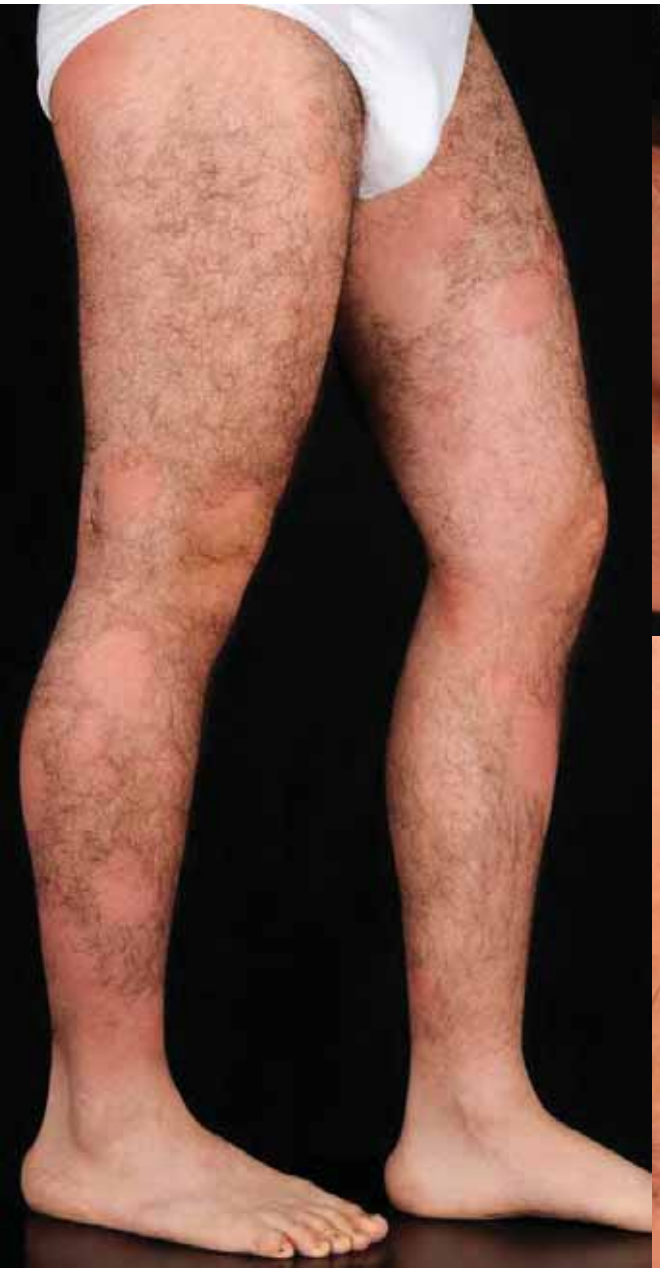

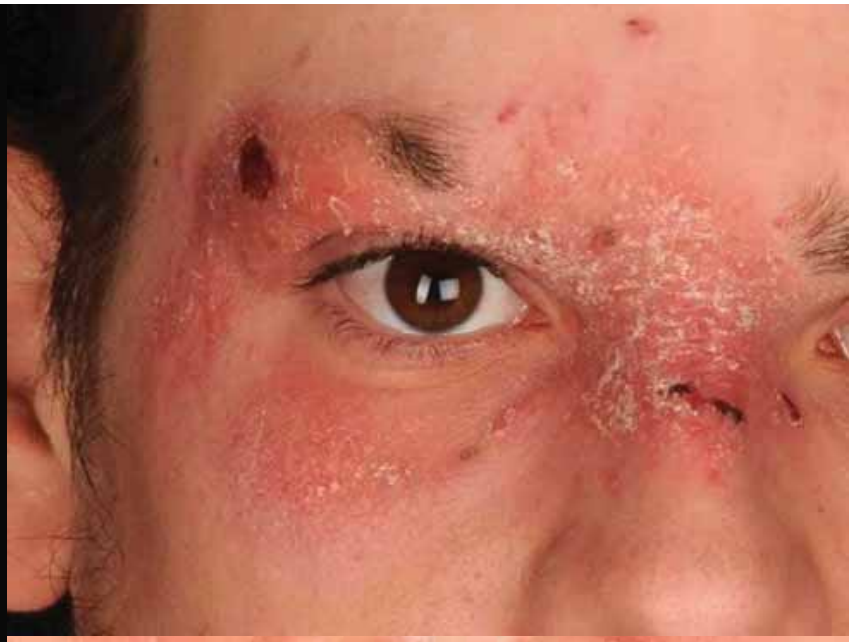

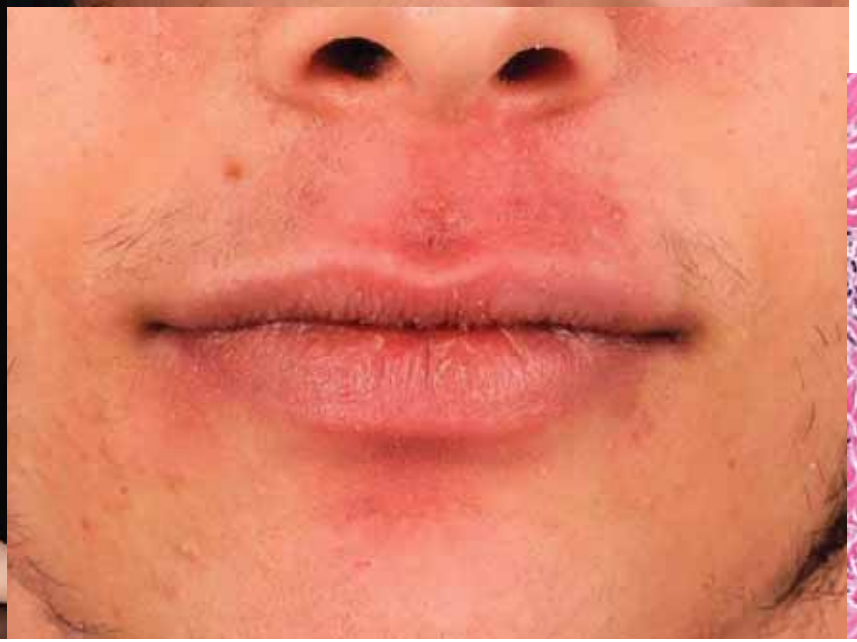

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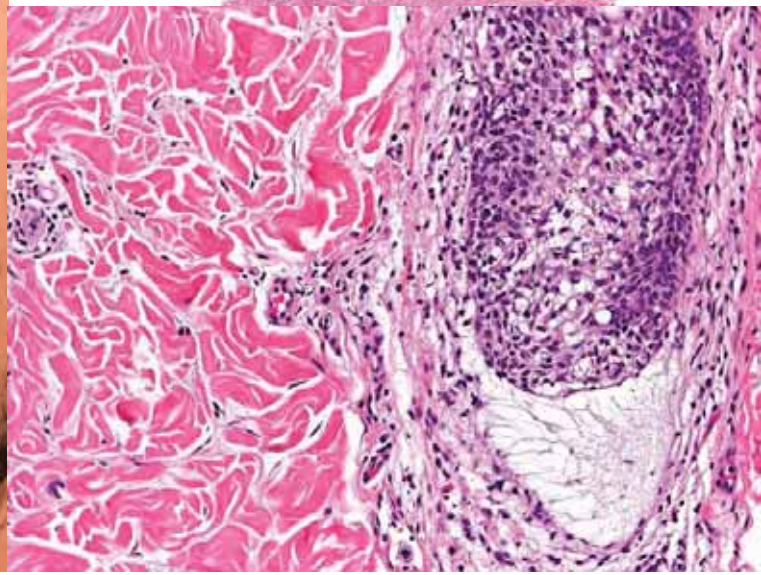

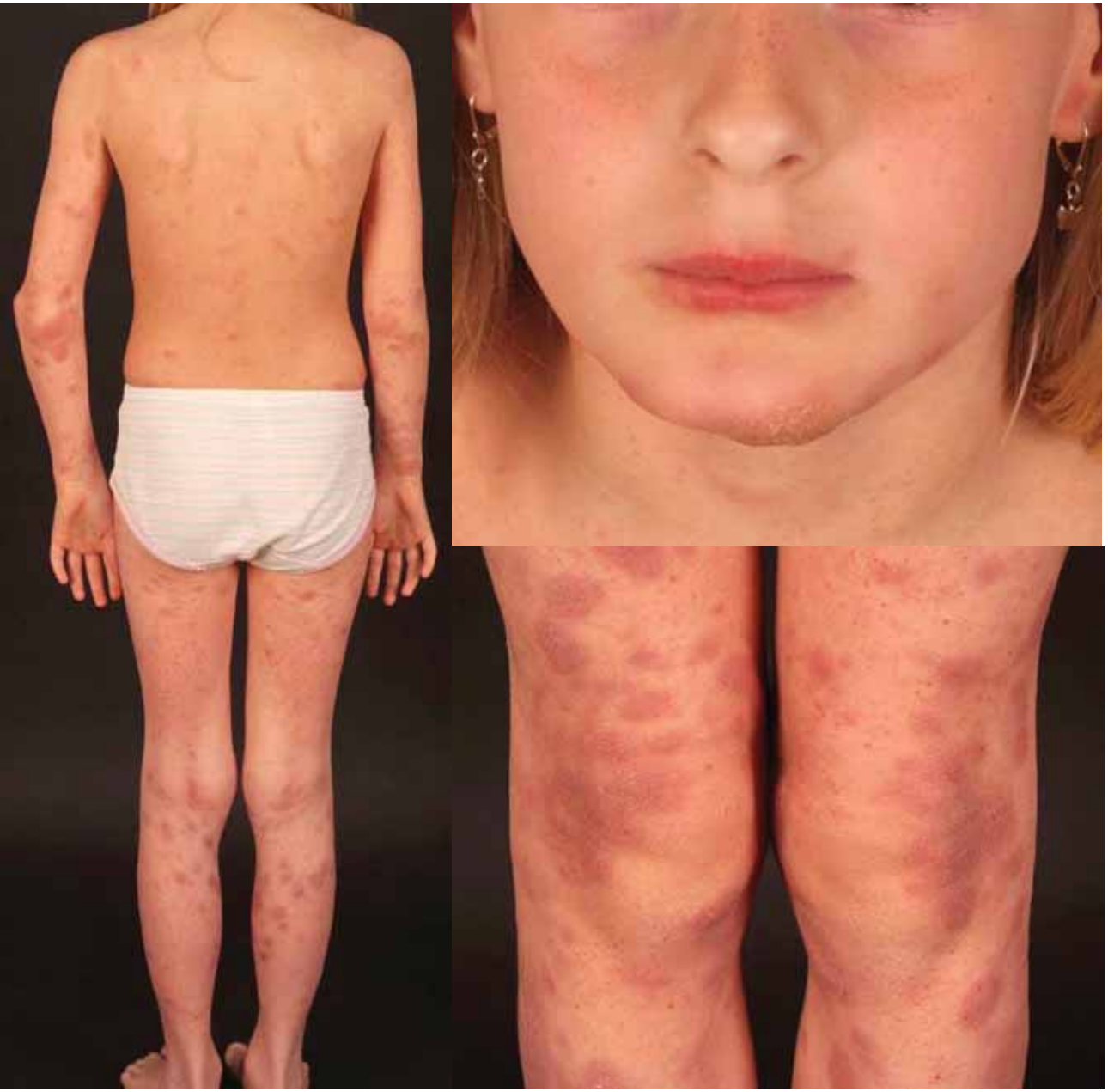

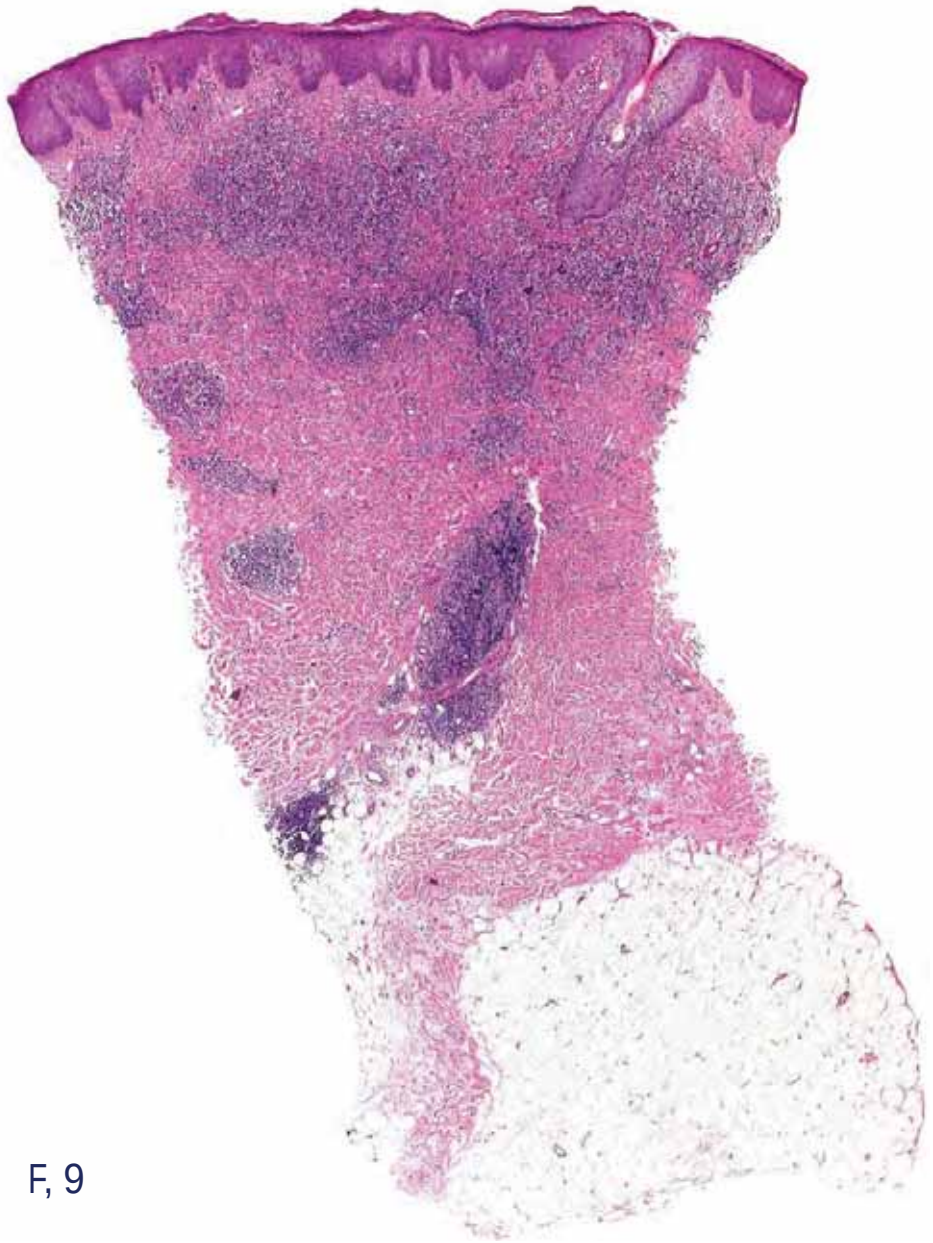

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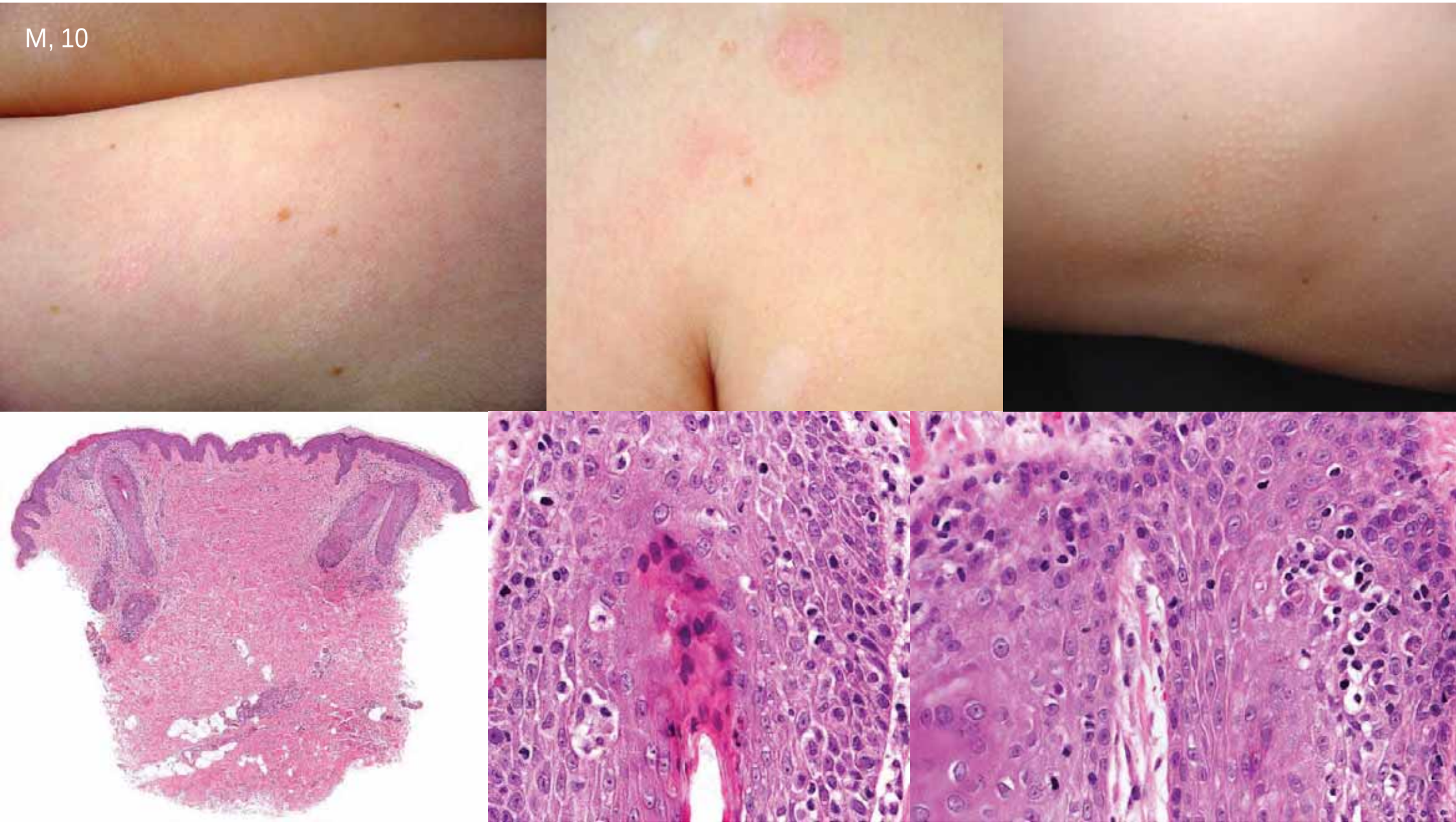
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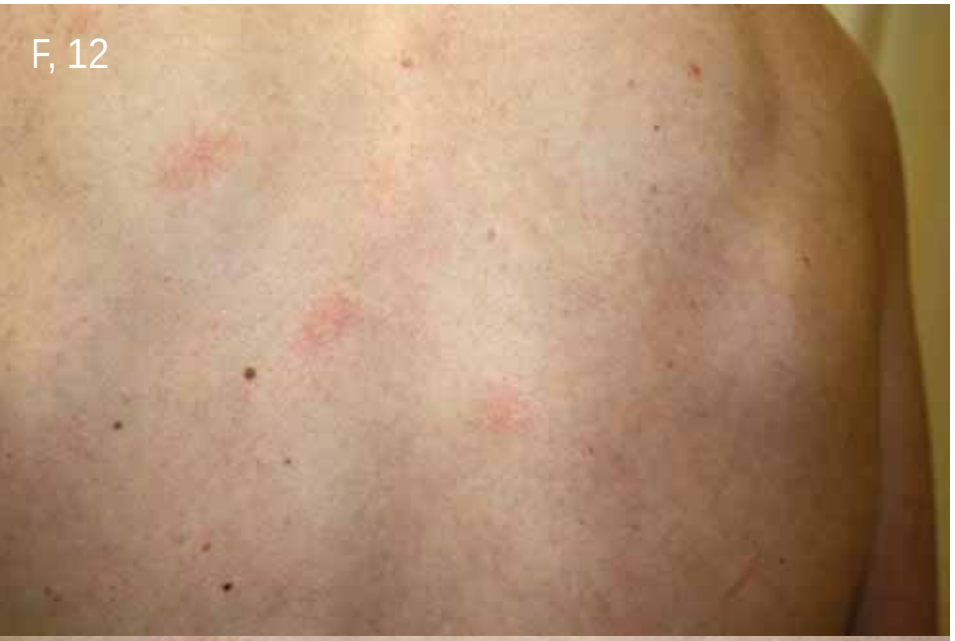
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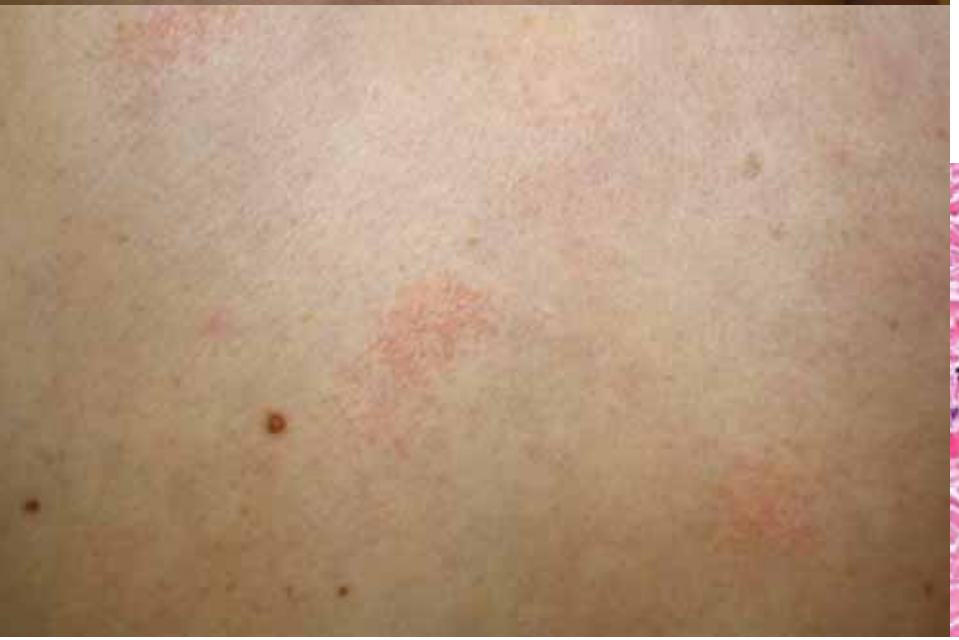

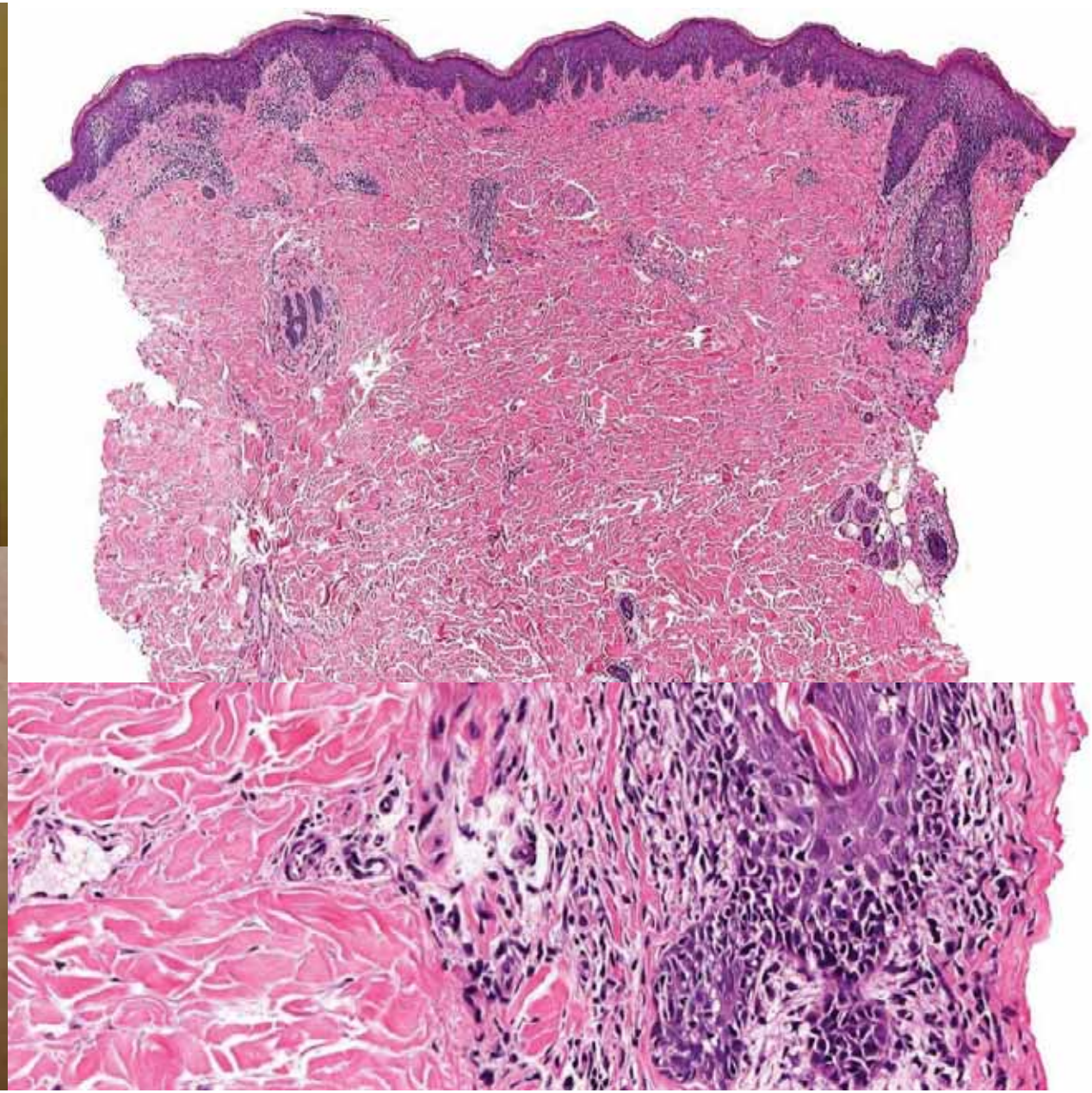

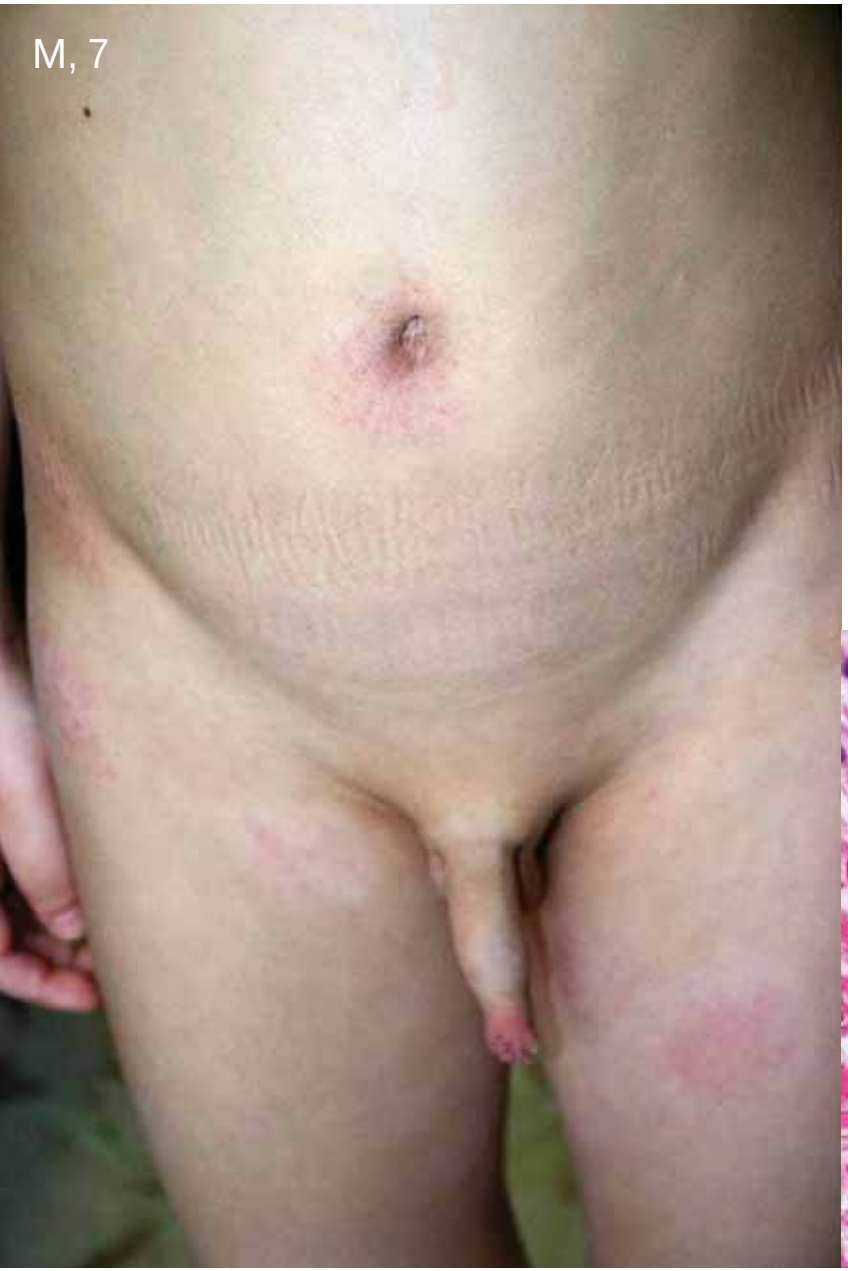
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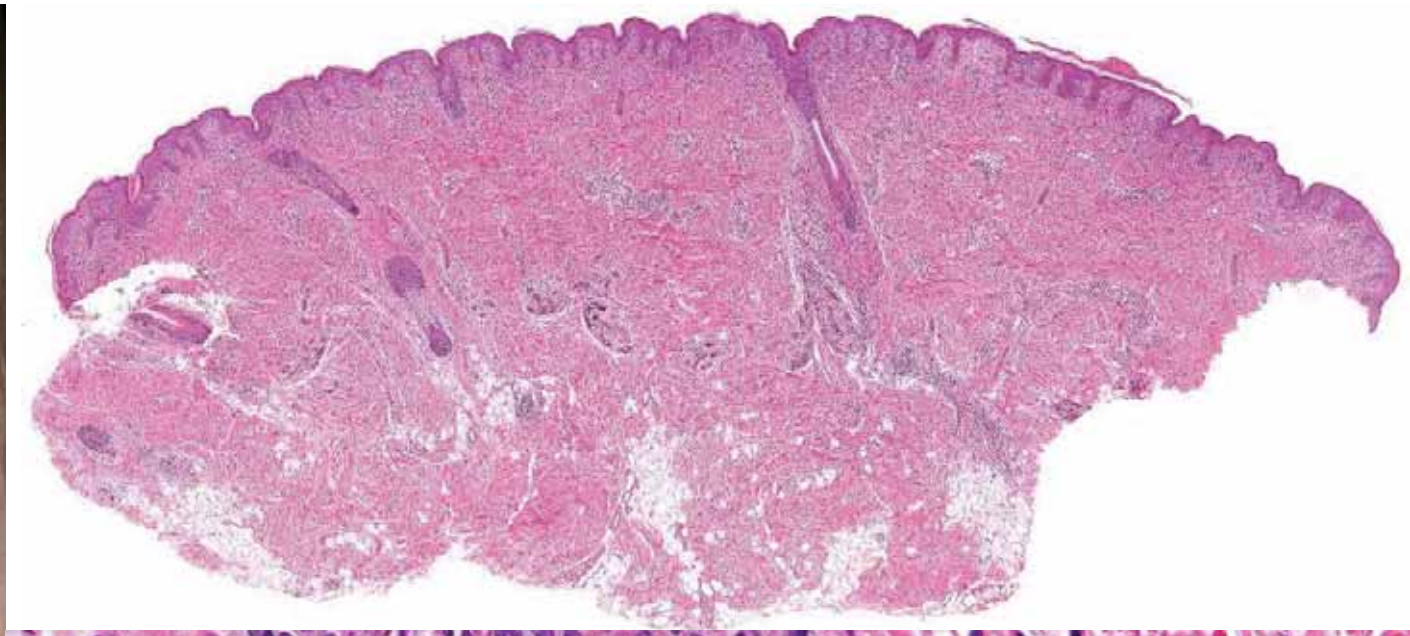
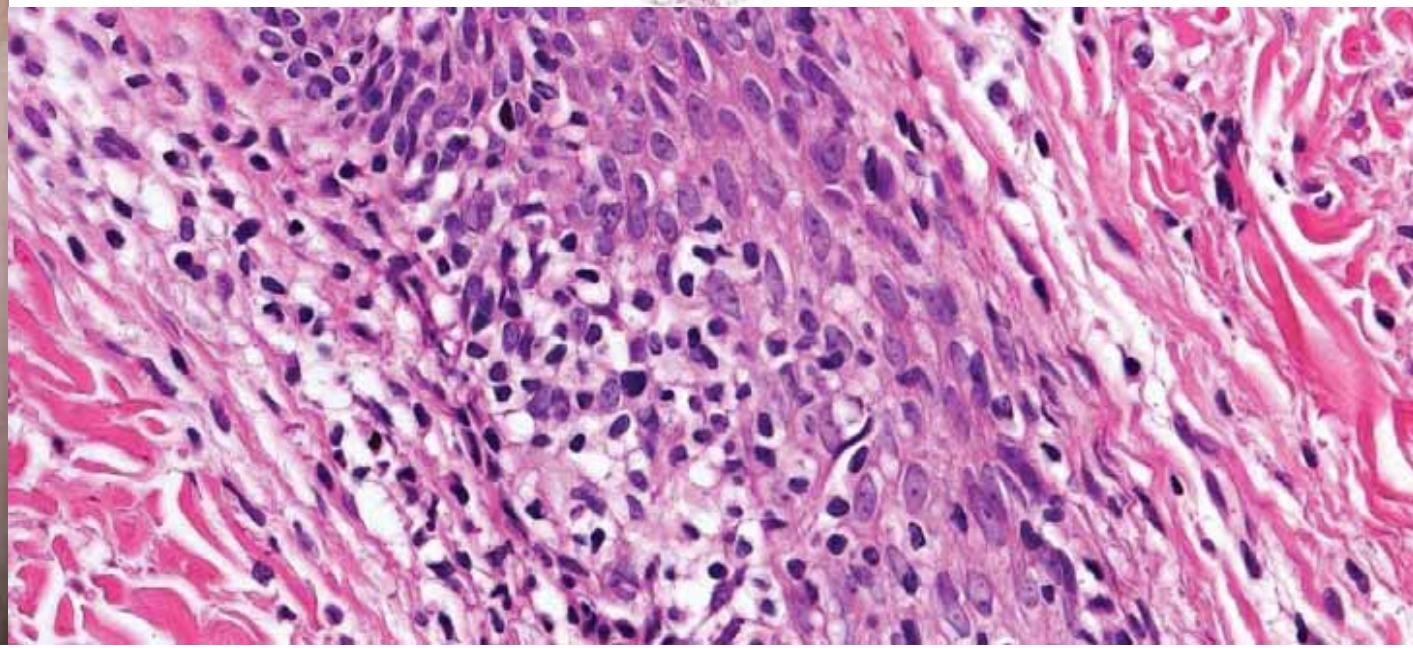




Pediatric follicular mucinosis & mycosis fungoides

- Solitary/localized lesions are localized mostly on the face and have a benign course; by contrast, generalized "idiopathic" follicular mucinosis in children is a variant of early MF *(my opinion)*
- Significance of multiple facial lesions not well understood
- Children and adolescents may present with the benign or "generalized idiopathic" forms, or may show inequivocable signs of MF associated with follicular mucinosis
- Besides presentation as a solitary lesion, no reliable clinicopathologic criteria exist to distinguish "benign" follicular mucinosis from the MF-associated form

CONTRARY VIEW ON BEHALF OF PATIENTS

Alopecia mucinosa is mycosis fungoides

ALMUT BÖER, M.D. & A. BERNARD ACKERMAN, M.D.

A MONOGRAPH FROM Ardor Scribendi

FROM *DERMATOPATHOLOGY: PRACTICAL AND CONCEPTUAL*

A. Bernard Ackerman, Editor

Alopecia Mucinosa is Mycosis Fungoides

Almut Böer, MD, Ying Guo, MD,† and A. Bernard Ackerman, MD†*

Abstract: Confusion abounds regarding the terms "follicular mucinosis" and "alopecia mucinosa," not only concerning definition and essential character, but of relationships between themselves on one hand and between themselves and mycosis fungoides on the other. We address here those issues in methodical fashion, first in historical perspective by review, scrupulously and critically, of what has been said in the many articles devoted to the subject; we next tell how the terms "alopecia mucinosa" and "follicular mucinosis" came to be and how they are employed currently; we then set forth our own observations pertinent to clinical, histopathologic, and biologic aspects of the condition called, conventionally, "alopecia mucinosa," those observations based on our own findings in sections of tissue cut from 54 biopsy specimens taken from 45 patients, all of them having been signed out previously as "follicular mucinosis;" we proceed to forge clinico-pathologic correlation of lesions in 14 of those 45 patients, utilizing assessments, by examination grossly and microscopically, of attributes in the very same lesion. Last, we propose a concept, and s

mucinosis is referred to as alopecia mucinosa . . . An attempt to assess the malignant potential of follicular mucinosis reveals the enigmatic nature of this and other cutaneous T-cell dyscrasias that are not clearly malignant. CTCL may be present before the development of alopecia mucinosa or may be diagnosed for the first time on the histologic examination of a biopsy specimen of alopecia mucinosa. There seems to be no reliable clinical finding for determining which patient with alopecia mucinosa will also have CTCL.

Heald PW, Edelson RL. In: Fitzpatrick TB, Eisen AZ, Wolff K, et al., eds. *Dermatology in General Practice*. 4th ed; 1993.[1]

■ Alopecia mucinosa (follicular mucinosis) . . . this condition is now classified into two types: a primary (idiopathic) type and a secondary (symptomatic) variety. When these types can be distinguished, the primary form, which may lead to perma-

TABLE 2. Explanation and Definition of Terms

Conventional Terminology	
Alopecia mucinosa	Designation introduced in 1957 by Herman Pinkus for a condition typified clinically by discrete follicular papules within plaques that were alopecic and characterized histopathologically by mucin housed in infundibular, follicular, and sebaceous epithelium.
Follicular mucinosis ("Mucinosis follicularis")	Term proposed in 1959 by Jablonska et al as a synonym for what Pinkus had called alopecia mucinosa. Others have asserted that it should be employed only as a description of a particular finding histopathologically.
Our Terminology	
Epithelial mucinosis	Term introduced by us to designate findings histopathologically of deposits of mucin in infundibular, follicular, and sebaceous epithelium. It may be encountered in a host of conditions.
Mycosis fungoides with epithelial mucinosis	Designation introduced by us for a specific expression of mycosis fungoides fulfilling criteria for mycosis fungoides, clinically and histopathologically, in addition to deposits of mucin being present in infundibular, follicular, and sebaceous epithelium.

Alopecia Mucinosa

Inflammatory Plaques with Alopecia Characterized by Root-Sheath Mucinosis

HERMANN PINKUS, M.D., Monroe, Mich.
With the cooperation of Warren L. Macaulay, M.D.; Herbert Z. Lund, M.D.; James R. Delaney, M.D.; Harold E. Anderson, M.D., and Joseph M. Hitch, M.D.

The cases forming the subject of this paper were collected over a period of seven years. They are presented here with the expectation that similar cases have been seen by others. It is hoped that discussion may be stimulated and more may be learned about the nature of the disease process and the peculiar histologic changes forming its basis.

Report of Cases

CASE 1.—The first of these cases came to my attention in August, 1950, in the form of a biopsy sent in by Dr. Warren L. Macaulay of Fargo, N. D. He wrote that the specimen came from a red, scaly, and slightly elevated plaque just above the medial part of the right eyebrow of a 29-year-old white man. There was some loss of hair where the lesion encroached on the eyebrow. The plaque had been present for about seven weeks and had enlarged gradually. Examination for fungi had been negative, and there was no improvement during three weeks when an ointment containing sulfur and salicylic acid was applied. The lesion resembled an eczematous plaque, but was somewhat more infiltrated. On biopsy, the tissue seemed gelatinous, and sarcoid, lymphoblastoma, or deep mycotic infection were considered postoperatively. The histologic changes to be described later were unusual and no definite diagnosis could be offered.

CASE 2.—A similar picture was seen in sections which Dr. Herbert Z. Lund of Greensboro, N. C., sent me in February, 1954, with the following information: "This is an 11-year-old girl who has a slight general increase in the development of hair on the extremities. There are localized areas which are completely hairless, chiefly on the arms. This has been present for six or eight months. The hair follicles in these areas are accentuated but do not appear grossly to contain keratin plugs or to be surrounded by an inflammatory reaction."

CASE 3.—A few months later, a specimen was received from Dr. James R. Delaney of Detroit. The biopsy specimen was from the scalp of a 64-year-old white man whose general health appeared good. About seven weeks previously his attention had been called to two areas of alopecia, one in the suboccipital area, the other just posterior to the vertex. These were asymptomatic. On examination, Dr. Delaney observed two palpable tumors that felt almost like lipomas, being moderately elevated and erythematous. A few slightly dilated follicles were noted, but there was no macroscopic plugging of follicular ostia. There was some very fine scaliness. Blood count and sedimentation rate were normal. No definite clinical diagnosis was offered.

CASE 4.—The next specimen was sent in May, 1955, by Dr. Harold E. Anderson of Battle Creek, Mich. This was from an erythematous scaly lesion with dilated follicles measuring about 3 cm. in diameter and situated on the left cheek of a 30-year-old white woman. Duration was five months. The lesion had been diagnosed tentatively as discoid lupus erythematosus and had shown slight improvement under chloroquine therapy. After the biopsy had been read, Dr. Anderson made it possible for me to see this patient. Figure 1 is the reproduction of a color photograph taken on May 21, 1955. It shows a slightly erythematous plaque with somewhat irregular and indistinctly elevated border occupying the left side of the upper lip and adjoining part of the cheek. There was firm, somewhat uneven palpable infiltration. The follicular openings were empty and somewhat patulous. There was a superficial crusted fissure where the plaque reached the nasal fold. Otherwise the surface was dry. There was no visible scale, perhaps because petrolatum had been applied by the patient. Diascopy revealed a few yellowish brown spots in the peripheral zone.

CASE 5.—A 10-year-old white girl was first seen on Oct. 6, 1956, with a slightly infiltrated, sharply defined, and mildly scaly plaque on her chin.

Received for publication May 22, 1957.

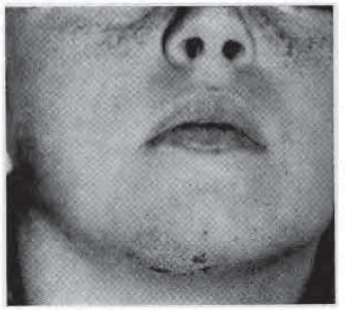
From the Department of Dermatology, Wayne State University College of Medicine, Detroit.

Read before the 77th Annual Meeting of the American Dermatological Association, Inc., Belleair, Fla., April 13, 1957.

6 cases (2M, 4F)
Age: 8, 10, 11, 29, 30, 64
Location:
Scalp
Eyebrow
Cheek
Chin, Cheek
Head & Neck, Chest
Generalized

Fig. 1 (Case 4).—Biopsy scar visible at lower lateral border of the lesion.

Fig. 2 (Case 5).—Two plaques on chin and right cheek. Crusting due to irritation by antifungal ointment.



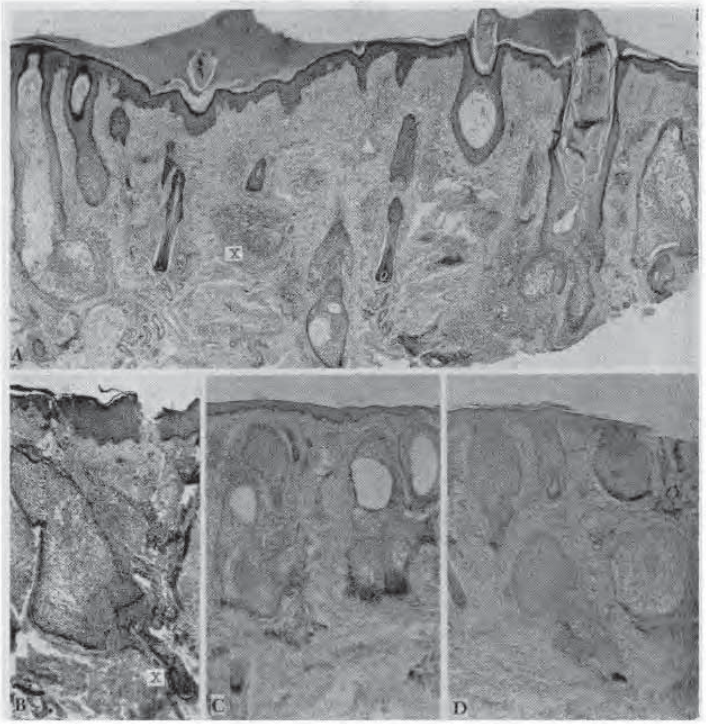


Fig. 3.—Low-power photographs of sections from Cases 1-4, stained with hematoxylin and eosin. *A* (Case 1), note that not all follicles are affected. "X" marks area of inflammatory infiltrate around free mucin in the corium. *B* (Case 2), sebaceous gland and middle portion of root sheath affected. Lower part of follicle fairly normal with growing hair ("X"). *C* (Case 3), edema of outer root sheath and cysts. *D* (Case 4), edematous follicles resemble nests of basal-cell epithelioma.

Alopecia Mucinosa

Inflammatory Plaques with Alopecia Characterized by Root-Sheath Mucinosis

HERMANN PINKUS, M.D., Monroe, Mich.
With the cooperation of Warren L. Macaulay, M.D.; Herbert Z. Lund, M.D.; James R. Delaney, M.D.; Harold E. Anderson, M.D., and Joseph M. Hitch, M.D.

The cases forming the subject of this paper were collected over a period of seven years. They are presented here with the expectation that similar cases have been seen by others. It is hoped that discussion may be stimulated and more may be learned about the nature of the disease process and the peculiar histologic changes forming its basis.

Report of Cases

CASE 1.—The first of these cases came to my attention in August, 1950, in the form of a biopsy sent in by Dr. Warren L. Macaulay of Fargo, N. D. He wrote that the specimen came from a red, scaly, and slightly elevated plaque just above the medial part of the right eyebrow of a 29-year-old white man. There was some loss of hair where the lesion encroached on the eyebrow. The plaque had been present for about seven weeks and had enlarged gradually. Examination for fungi had been negative, and there was no improvement during three weeks when an ointment containing sulfur and salicylic acid was applied. The lesion resembled an eczematous plaque, but was somewhat more infiltrated. On biopsy, the tissue seemed gelatinous, and sarcoid, lymphoblastoma, or deep mycotic infection were considered postoperatively. The histologic changes to be described later were unusual and no definite diagnosis could be offered.

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1st description ??

Dermatologische Wochenschrift

Bd. 136 1957 / Heft 48

Aus der Hautklinik der Johannes-Gutenberg-Universität Mainz
(Direktor: Prof. Dr. E. Keining)

Mucophanerosis intrafollicularis et sebaglandularis

Von
O. BRAUN-FALCO

Mit 13 Abbildungen

Herrn Prof. E. Keining-Mainz zum 65. Geburtstag gewidmet

Während das Verhalten saurer, mesenchymaler Mukopolysaccharide, die einen wesentlichen Anteil der mesenchymalen Interzellularsubstanzen ausmachen, in der Haut unter normalen und pathologischen Bedingungen von vielen Autoren in den letzten Jahren bearbeitet wurde, ist über Vorkommen und Bedeutung epithelialer Mukopolysaccharide in der Haut kaum etwas bekannt geworden. Zwar wissen wir, daß bestimmte epitheliale Hauttumoren oft muzinöses Material enthalten, normalerweise aber finden sich Metachromasie gebende anionische Polysaccharide lediglich im unteren Drittel des wachsenden Haarfollikels, und zwar in den äußeren Zellagen der äußeren Wurzelscheide. MONTAGNA, CHASE und MELNAGNO glauben, daß es sich dabei um Chondroitinsulfat B handelt. Es ist daher verständlich, wenn das Vorkommen muzinösen Materials in epithelialen Hautanteilen bei nicht tumorösen Hautaffektionen mit besonderem Interesse studiert wird. PINKUS (1.) berichtete anläßlich des XI. Internationalen Dermatologen-Kongresses in Stockholm 1957 unter dem Titel „Polysaccharide thesaurismosis in the external root sheath with clinical picture of inflammatory alopecia" über einige Fälle von entzündlich plattenartig infiltrierten Herden mit Alopezie, bei denen sich histologisch als hervorstechendstes Merkmal eine mukoide Metaplasie der äußeren Wurzelscheide im oberen Follikelsegment nachweisen ließ. In einer weiteren Studie faßt PINKUS (2.) seine Beobachtungen unter dem Titel „Alopecia mucinosa: Inflammatory plaques with Alopecia characterized by root sheath mucinosis" zusammen. Wir selbst (5.) haben in einer Diskussionsbemerkung zum Vortrag von PINKUS bereits unter Demonstration entsprechenden Bildmaterials zum Ausdruck gebracht, daß wir in den letzten Jahren gleichartige histologische Veränderungen bei einer Reihe diagnostisch völlig verschiedenartiger Hautprozesse gesehen haben. Im folgenden seien unsere bisherigen Beobachtungen zusammengestellt.

Fall 1: 53j. Mann. Beruf: Tierpfleger. Seit 8 bis 10 Tagen Rötung an der Nasenspitze, die stark juckte.

Befund: An der Nasenspitze findet sich ein wenig charakteristischer nicht ganz pfennigstückgroßer, entzündlich geröteter, scharf begrenzter, leicht infiltrierter Herd, der kaum über das Hautniveau erhaben ist und eine geringe, ziemlich fest anhaftende Schuppung aufweist. Beim Abziehen der Schuppen mit der Pinzette zeigen sich an der Unterseite der Schuppen andeutungsweise follikuläre Hornzapfen. Pilzpräparat negativ.

Zunächst wurde [illegible]

Clinica Dermosifilopatica della R. Università di Torino.

Über einen Fall universeller Alopecia areata in Verbindung mit Mycosis fungoides.

Von

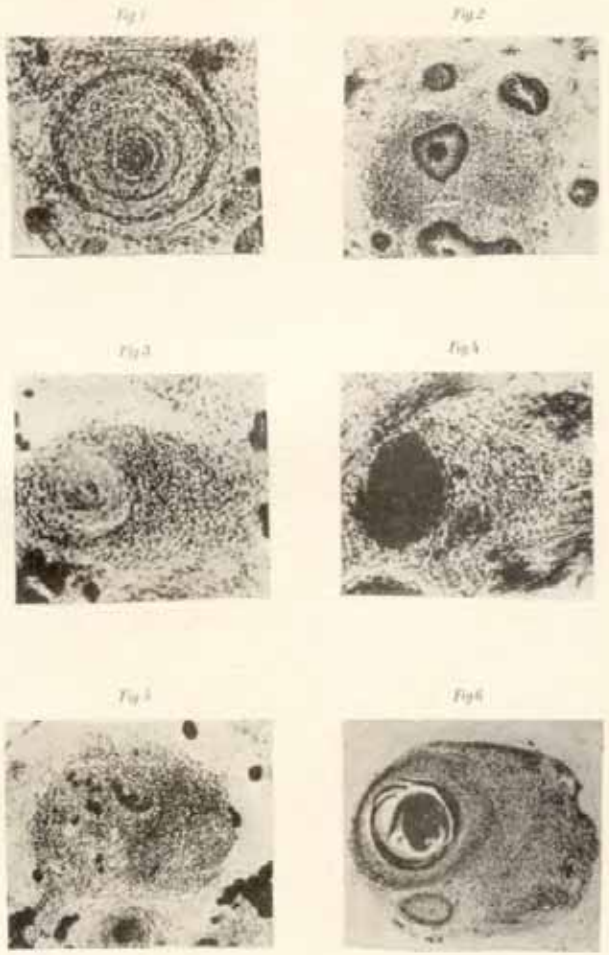
Professor Dr. **Sebastiano Giovannini.**

(Hiezu Taf. I u. II.)

Unter den vielen und mannigfaltigen Hautaffektionen, die in Verbindung mit Alopecia areata einhergehen, gelang es mir bis jetzt nicht, die Mycosis fungoides erwähnt zu finden. Bei dieser Krankheit ist wohl von Besnier und Hallopeau (1), Breda (2), Wolters (3), Hallopeau und Weil (4), Augagneur (5) und anderen der Ausfall der Kopf- und Körperhaare, bald begrenzt, bald sehr ausgebreitet, bemerkt worden, aber dabei handelte es sich um Fälle, in denen die Alopecie gewöhnlich in Hautpartien auftrat, die von mykotischen Erscheinungen, wie erythematösen und ekzematösen Läsionen, Verdickungen, Abschuppungen etc. schon ergriffen waren, und es fehlt die Angabe, ob Merkmale der Areata vorkamen. Aus diesem Grunde erscheint mir folgender Fall von typischer, allgemeiner Alopecia areata, von prämykotischen Läsionen gefolgt, wert veröffentlicht zu werden, umsomehr als er nicht gewöhnliche Einzelnheiten darbot.

Krankengeschichte. Patientin G., Bäuerin, in der Umgebung von Vercelli wohnhaft, ist 1880 geboren. Von ihrer Familie ist nichts bemerkenswertes zu erwähnen. Patientin wurde im 3. Lebensjahre, als sie so schwach war, daß sie noch nicht gehen konnte, vom typhösen Fieber befallen, welches 3 Monate andauerte und erst nach einem Jahre gelang es ihr, sich gänzlich von demselben zu erholen. Beinahe zwei

Giovannini: Alopecia areata in Verbindung mit Mycosis fungoides.



Giovannini: Alopecia areata in Verbindung mit Mycosis fungoides.

Giovannini S, Arch Derm Syphil 1906, 78, 1-20

C. Kreibich, Arch. f. Dermatologie u. Syphilis. 1926;150:243-248

(Aus der Deutschen dermatologischen Klinik in Prag. — Vorstand: Prof. *C. Kreibich*.)

Mucin bei Hauterkrankung.

Von

C. Kreibich.

Mit 2 Textabbildungen.

(Eingegangen am 22. Dezember 1925.)

K. Josef, 20 Jahre alt. Vor 9 Monaten Beginn der Erkrankung an der Beugefläche des rechten Oberschenkels, Hinaufziehen zur rechten Glutäalhälfte, Übergreifen auf die linke Gesäßhälfte; allmählich kamen ähnliche Herde an den Oberarmen, Unterschenkeln, im Gesicht und Hals hinzu. Ein Herd mit Carbolwasser behandelt, Reizung mehrerer Herde nach Art eines Ekzems.

Status praesens: Groß, schlank mit guter Muskulatur. Hauterkrankung in mehreren Herden. Das Wesen derselben ist am besten wiedergegeben in zwei symmetrischen Herden in der Glutäalgegend. Die Herde sind besonders nach oben von einer deutlich blassen, anämischen Zone begrenzt. Dann beginnt vielleicht mit einer leichten Niveauerhebung der eigentliche Herd mit einer gelblichroten Farbe, die in allen Herden festgehalten ist. Sich selbst überlassen zeigen die Stellen eine feinblätterige Schuppung, und zwar besteht hier meist ein Unterschied zwischen Mitte und Rand, am Rand ist die Schuppe an der Oberfläche festhaftender, drückt vielleicht hier sogar etwas auf die Unterlage, wodurch die Haut knitterig aussieht, wodurch leichte Atrophie vorgetäuscht wird; im Zentrum der Armherde ist die Schuppe leichter abhebbar, löst sich im Bad auch tatsächlich ab, wodurch die Farbe mehr rötlich zum Vorschein kommt und an den Oberarmherden ganz leicht cyanotisch ist. Deutliche Atrophie ist im Zentrum nicht zu sehen, obwohl zu vermuten ist, daß die Haut daselbst etwas in ihrem Gewebe verändert ist. In der unteren Hälfte der Oberarmherde treten die Follikel deutlich hervor und werden durch Arrectorenkontraktion noch prominenter als buckelige Erhebungen, aus deren Mitte bei forciertem Drucke ein trockener Comedo auszudrücken ist. Letzteres Symptom ist in der Glutäalgegend viel deutlicher. Hier ist das Zentrum der Herde durchaus mit solchen Comedonen besetzt, so daß beim Überstreichen von oben nach unten, nicht aber von unten nach oben, das Gefühl des Reibeisens besteht. Hier lassen sich die Hornpfröpfe leichter auspressen, und es folgt ein Tropfen einer klaren klebrigen Flüssigkeit. Durch Sekundärinfektion hier und da Folliculitis und Furunkel, was aber mit dem Wesen der Erkrankung nichts zu tun hat.

Alle Herde liegen im Niveau der Haut, zeigen keine Härte, Infiltration usw. Glutäalherde nach innen vom anämischen Saum eine minimale weiche Elevation. Daß die Follikelbetonung im Prozeß nicht durch die Gesäßgegend allein bedingt war, geht daraus hervor, daß die Oberarmherde an je einer umschriebenen Stelle über dem Biceps das gleiche Symptom aufwiesen. Auch ein etwa handtellergroßer Herd über dem Adamsapfel zeigt in der Mitte etwas follikuläre Keratose. Dieser Herd, ein Fleck am Nacken und ein Streifen im rechten Oberarmherd zeigten

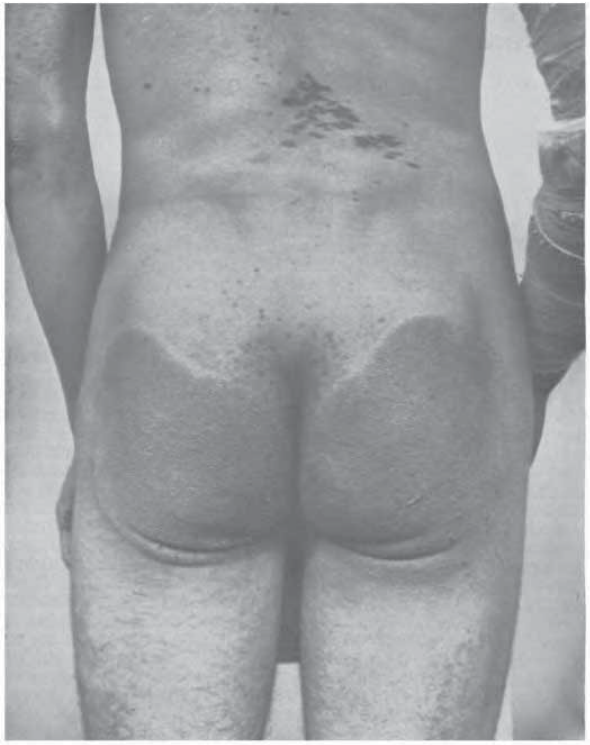


Abb. 1.

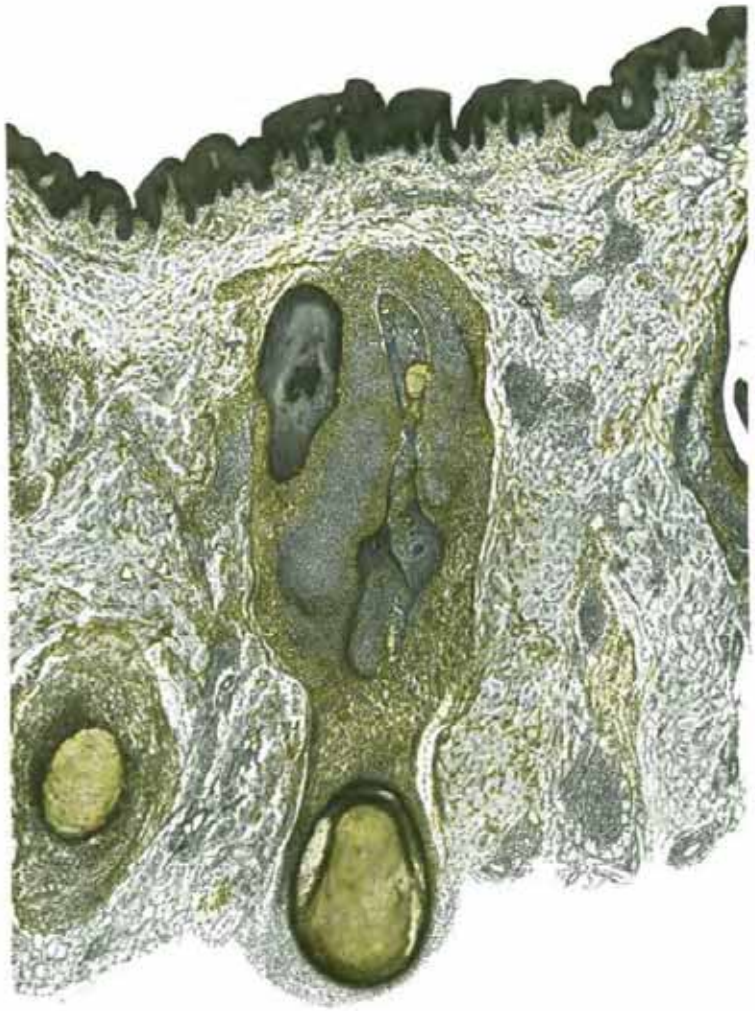


Abb. 2.

"Es kann natürlich nach beiden obigen Fallen nicht verallgemeinert werden, dab die *Brocqsche* Krankheit immer ein "Myxerythem" ist, aber es ist die Anregung geboten, daraufhin zu untersuchen."

Aus der Hautklinik der königl. ung. Pázmány-Péter-Universität in Budapest (Direktor: ö. o. Prof. Dr. Ludwig Nékám) und Dermatologischen Abteilung der Graf-Apponyi-Albert-Poliklinik in Budapest (Vorstand: Prof. Dr. Ludwig Török)

Ein ungewöhnlicher, sich durch entzündliches Follikularödem auszeichnender Hautausschlag

Klinischer Teil:
Dr. E. Lehner, Oberarzt

Histologischer Teil:
Dr. L. Szodoray, Assistent der Hautklinik

Mit 7 Abbildungen

Der 20jährige Mann meldete sich in der Poliklinik und gab an, daß sein Ausschlag ungefähr vor 2 Monaten plötzlich entstanden sei. Am Rücken von der Skapularlinie bis zur Kreuzgegend symmetrische, heller- bis pengögroße, runde oder ovale, mit den Spaltlinien der Haut parallel gelagerte Herde. Sie sind hell, beinahe weiß, flach erhaben, scharf abgegrenzt und beim Betasten prall-elastisch. Die Oberfläche ist infolge einer Follikularkeratose rauh und schuppend. Das pralle Ödem behält nicht den Fingereindruck. Ähnliche oder kleinere und weniger pralle Herde befinden sich symmetrisch auf der Brust, im Gesicht, in den Nasolabialfalten, besonders links und in der Umgebung der linken Ohrmuschel. An den Streckseiten der Oberarme, in der Glutäal- und Kniegegend symmetrisch gelegene, bohnen- bis pengögroße, nicht ödematöse, mattrote, wenig schuppende, entzündlich erythematöse Flecken. Mäßige Infiltrate (Abb. 1)

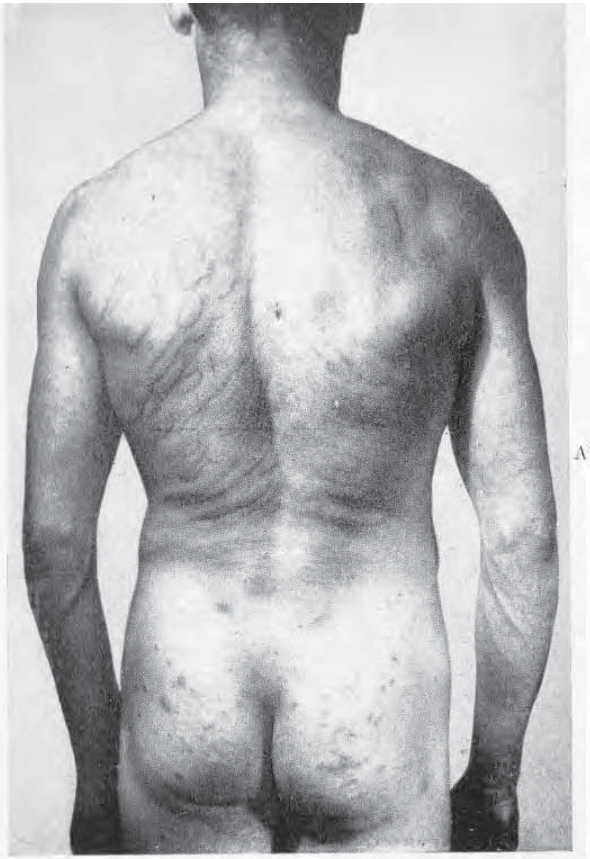


Abb. 1.
Klinisches Bild der Hauterscheinungen am Rücken, am Höhepunkt der Entwicklung

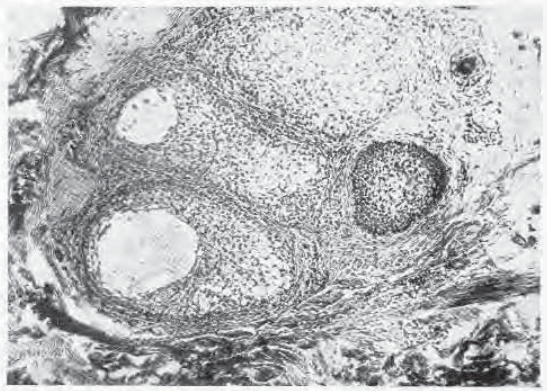


Abb. 5. Querschnitt einer Follikelgruppe. Ödem und Zystenbildung

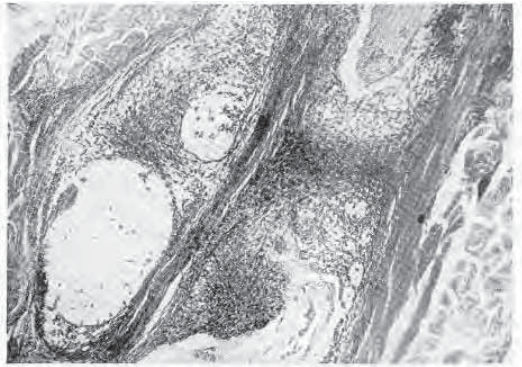


Abb. 3. Multiple Vesikel in der Wurzelscheide.
Die Schichten sind nicht mehr unterscheidbar. Vergrößerung 400fach

Lehner E & Szodoray L.
Derm Wochenschr 1939;108:678-685

JAMA Dermatology | Original Investigation

Clinical Staging and Prognostic Factors in Folliculotropic Mycosis Fungoides

Suzanne van Santen, MD; Rachel E. J. Baatsch, MD, PhD; Remco van Doorn, MD, PhD; Barbara Horváth, MD, PhD; Marjolein S. Bruijn, MD, PhD; Cornelus J. G. Sanders, MD; Jacco C. de Pooter, MD; Michelle M. van Rossum, MD, PhD; Ellen R. M. de Haas, MD, PhD; Joep C. J. M. Vermeer, MD, PhD; Marcel W. Bekkenk, MD, PhD; Maarten H. Vermeer, MD, PhD; Rein Willemze, MD, PhD

IMPORTANCE Large case series suggest that patients with folliculotropic mycosis fungoides (FMF) have a worse prognosis than patients with classic mycosis fungoides (MF). However, recent studies described a subgroup of patients with FMF with a more favorable prognosis. Distinction between indolent and aggressive FMF may have important therapeutic consequences but is hampered by the inability of the current tumor-node-metastasis-blood (TNMB) staging system to classify patients with FMF in a clinically meaningful way.

OBJECTIVE To differentiate between indolent and aggressive FMF using clinicopathological criteria and to define prognostic factors in patients with FMF.

DESIGN, SETTING, AND PARTICIPANTS In this prospective cohort study, we followed 203 patients with FMF, included in the Dutch Cutaneous Lymphoma Registry between October 1985 and May 2014 at a tertiary referral center hosting the Dutch Cutaneous Lymphoma Registry. Overall, 220 patients with FMF had been registered, but 17 patients with incomplete follow-up data or a history of classic MF were excluded.

MAIN OUTCOMES AND MEASURES Main outcomes included clinical and histological characteristics, disease progression, and survival. Prognostic factors were investigated using Cox proportional hazard regression analysis. Distinction between early plaque-stage FMF and advanced plaque-stage FMF was made by a blinded review of skin biopsy specimens from patients presenting with plaques.

RESULTS In a cohort of 147 men and 56 women (median [range] age, 59 [15-93] years), patients with histologically early plaque-stage FMF had a very similar overall survival (OS) rate to patients with only patches and/or follicular papules (10-year OS, 77% vs 80%), while the survival rate of patients with histologically advanced plaque-stage FMF was almost identical to that of patients presenting with tumors (10-year OS, 25% vs 27%). Subsequently, 3 clinical subgroups with significantly different survival data were distinguished: early skin-limited FMF (group A; n = 84; 5-year and 10-year OS, 92% and 72%); advanced skin-limited FMF (group B; n = 102; 5-year and 10-year OS, 55% and 28%); and FMF presenting with extracutaneous disease (group C; n = 17; 5-year and 10-year OS, 23% and 2%). Age at diagnosis, large cell transformation and secondary bacterial infection were independent risk factors for disease progression and/or poor survival.

CONCLUSIONS AND RELEVANCE The results of this study provide useful criteria to differentiate between indolent and aggressive FMF and confirm the existence of a subgroup of FMF with a favorable prognosis.

Supplemental content at jamadermatology.com

Author Affiliations: Author affiliations are listed at the end of this article.

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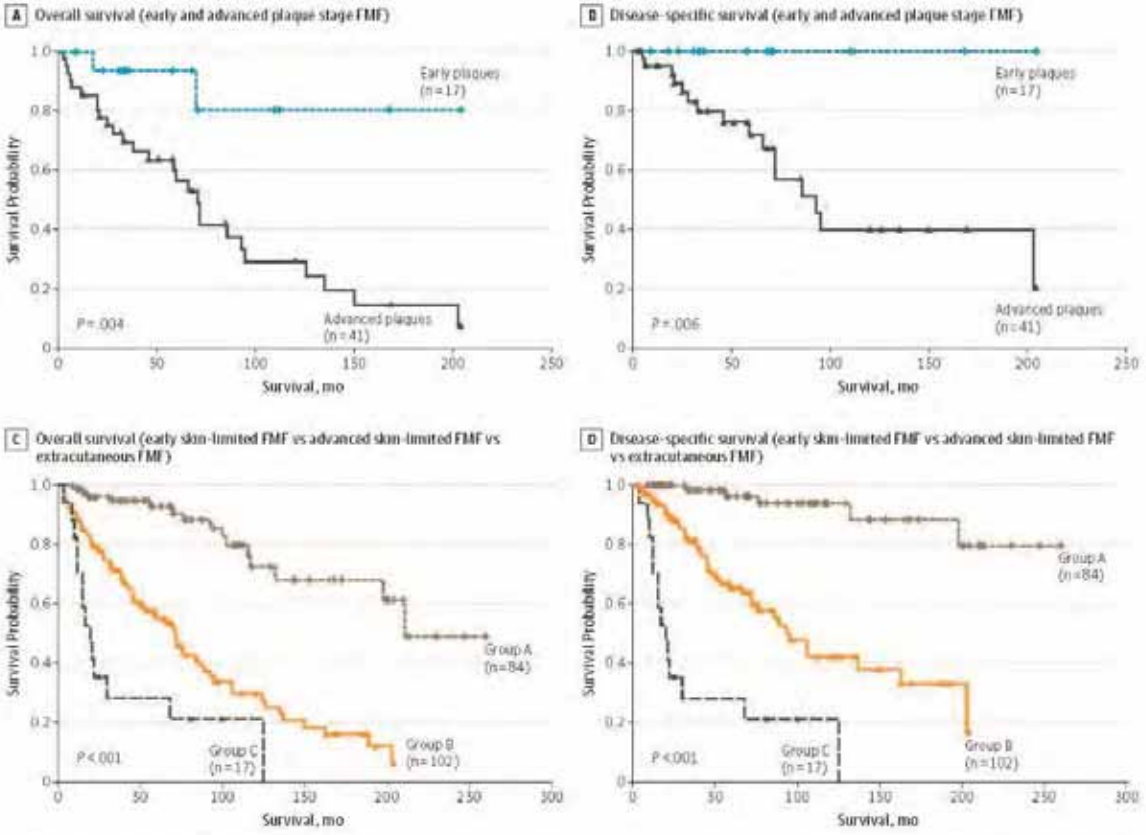
JAMA Dermatol. 2016;152(9):981-1000. doi:10.1001/jamadermatol.2016.1957
Published online June 15, 2016.

Figure 3. OS and DSS of Patients With FMF



A and B, OS and DSS of patients with early and advanced plaque-stage FMF. C and D, OS and DSS of patients with early skin-limited FMF (group A), advanced skin-limited FMF (group B), and FMF presenting with extracutaneous disease (group C). DSS indicates disease-specific survival; FMF, folliculotropic mycosis fungoides; OS, overall survival.

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ORIGINAL ARTICLE

WILEY

Plaque stage folliculotropic mycosis fungoides: histopathologic features and prognostic factors in a series of 40 patients

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Abstract

Background: Folliculotropic mycosis fungoides (FMF) is a distinct variant of mycosis fungoides. Recent studies recognized indolent and aggressive subgroups of FMF, but there is controversy how patients presenting with plaques should be classified. The present study describes the histopathologic features of 40 FMF plaques. The aim of the study was to identify risk factors for disease progression and poor outcome in this group.

Methods: Clinical, histopathological, and immunophenotypical data from 40 patients with plaque stage FMF were reviewed and analysed for risk factors for disease progression and survival.

Results: After a median follow up of 80 months, disease progression occurred in 20 of 40 patients. Percentage of atypical cells, cell size, percentage of Ki-67+ cells, and co-existent interfollicular epidermotropism, but not the extent of perifollicular infiltrates, were associated with disease progression and reduced survival, while extensive follicular mucinosis was associated with increased survival.

Conclusions: This study underlines that FMF patients presenting with plaques represent a heterogeneous group and that a subgroup of these patients may have an indolent clinical course. It further shows that histological examination is a valuable tool to differentiate between indolent and aggressive disease.

KEYWORDS
folliculotropic mycosis fungoides, histopathology, prognosis, risk factor

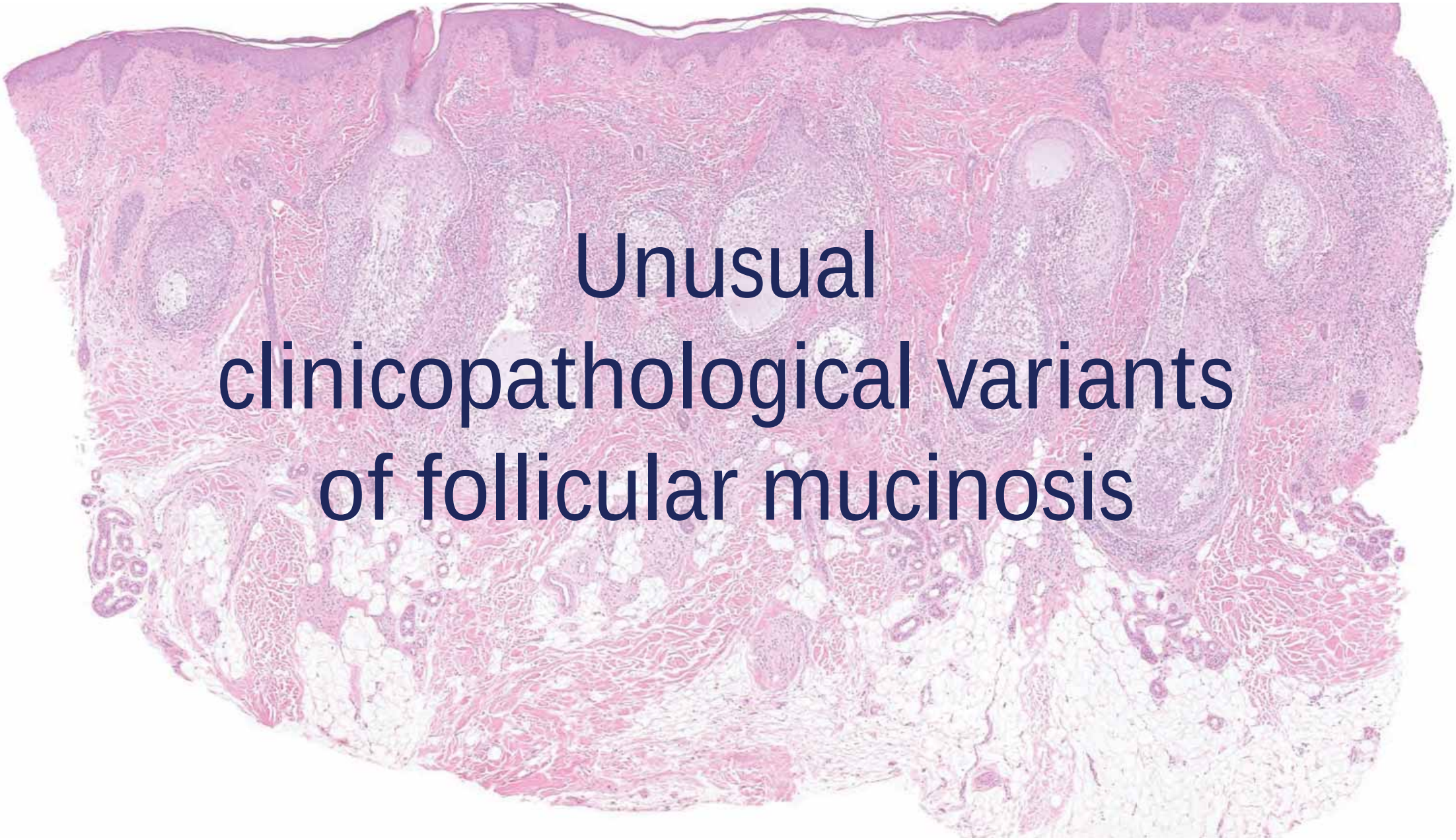
1 INTRODUCTION

Folliculotropic mycosis fungoides (FMF) is recognized as a distinct variant of mycosis fungoides (MF). FMF is histopathologically characterized by the presence of folliculotropic infiltrates consisting of atypical, T-cells, that often spare the epidermis.[1–3] Clinically, skin lesions are preferentially located in the head and neck region and are frequently accompanied by focal alopecia, and may include (grouped) follicular papules, acneiform and cystic lesions, plaques and tumors and in some patients keratosis pilaris-like skin lesions, which are located preferentially on the extremities or trunk.[1,3,4–11] Previous studies emphasized that FMF patients have a worse prognosis when compared to classic MF patients and should be treated more aggressively.[1,2] However, more recent studies reported that not all patients with FMF have an unfavorable prognosis and suggested that distinction should be made between an indolent (early stage) and an aggressive group (advanced stage) of FMF.[4,7,11] Patients presenting with only follicle-based papules, acneiform, or keratosis pilaris-like lesions have early stage disease (stages IA-IIA), run an indolent clinical course and have an excellent prognosis, while patients presenting with

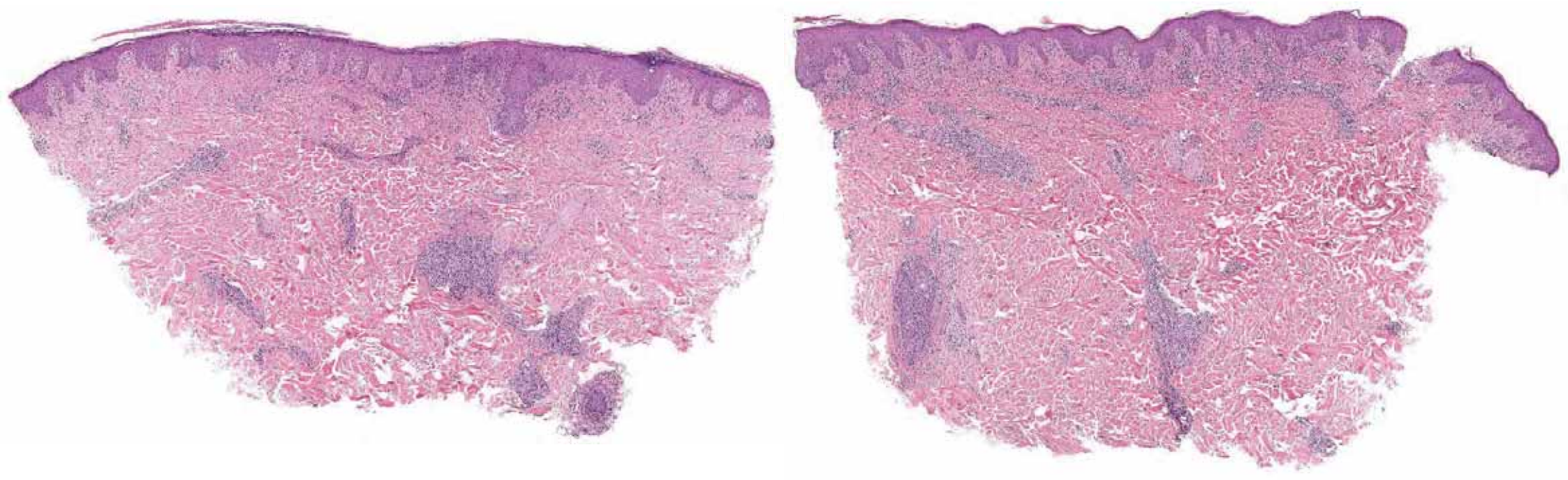
TABLE 3 Univariate and multivariate analysis of relevant histopathologic features in plaque stage folliculotropic mycosis fungoides

		DSS				OS				PFS			
	N	Univariate analysis		Multivariate analysis		Univariate analysis		Multivariate analysis		Univariate analysis		Multivariate analysis	
	40	HR (95%CI)	P-value	HR (95%CI)	P-value	HR (95%CI)	P-value	HR (95%CI)	P-value	HR (95%CI)	P-value	HR (95%CI)	P-value
Age at diagnosis			0.004		0.11		0.001		0.34		0.001		0.10
<60 years	26	1				1				1			
>60 years	14	4.7 (1.6-13.4)				5.2 (2.0-13.4)				5.8 (2.1-15.8)			
Extent of infiltrate			0.79		-		0.69		-		0.51		-
Minimal perifollicular	4												
Prominent perifollicular	14												
Extensive perifollicular/confluent	18												
Completely diffuse	4												
Follicular atypia			0.50		-		0.12		-		0.07		-
Mild	6										Ref		
Moderate	17										0.36		
Extensive	17										0.06		
Follicular mucinosis			0.04		0.81		0.009		0.96		0.02		0.75
No or focal spots	20	1				1				1			
Moderate (confluent/diffuse)	20	0.30 (0.10-0.91)				0.25 (0.9-0.71)				0.31 (0.12-0.81)			
Interfollicular epidermotropism			0.003		0.33		0.007		0.56		0.005		0.34
Absent	26	1				1				1			
Present	12	4.9 (1.7-13.8)				3.5 (1.4-8.7)				3.6 (1.5-8.8)			
Percentage atypical cells			0.005		0.28		0.005		0.48		0.004		0.60
<25%	19	1				1				1			
>25%	21	8.6 (1.9-38.8)				5.0 (1.6-11.2)				4.2 (1.5-11.7)			
Cell size			0.008		0.23		0.006		0.37		<0.001		0.63
Small-medium	33	1				1				1		1	
Medium-large	7	4.4 (1.5-13.0)				4.0 (1.5-10.7)				9.5 (3.2-27.6)		4.5 (1.8-16.3)	
Percentage of blast cells			0.58		-		0.08		-		0.01		0.95
<10%	34									1			
>10%	6									3.7 (1.3-11.2)			
Percentage of Ki-67+ cells			<0.001		0.62		<0.001		0.83		<0.001		0.27
<10%	29	1		1		1		1		1			
>10%	11	7.7 (2.7-22.3)		5.3 (1.3-21.2)		7.3 (2.7-19.7)		4.2 (1.2-14.7)		5.3 (2.1-13.6)			

Note: Bold and underlined values were considered significant, as p<0.05 was considered significant.
Abbreviations: CI, confidence interval; DSS, disease-specific survival; HR, hazard ratio; NI, number; OS, overall survival; PFS, progression-free survival.



Unusual clinicopathological variants of follicular mucinosis



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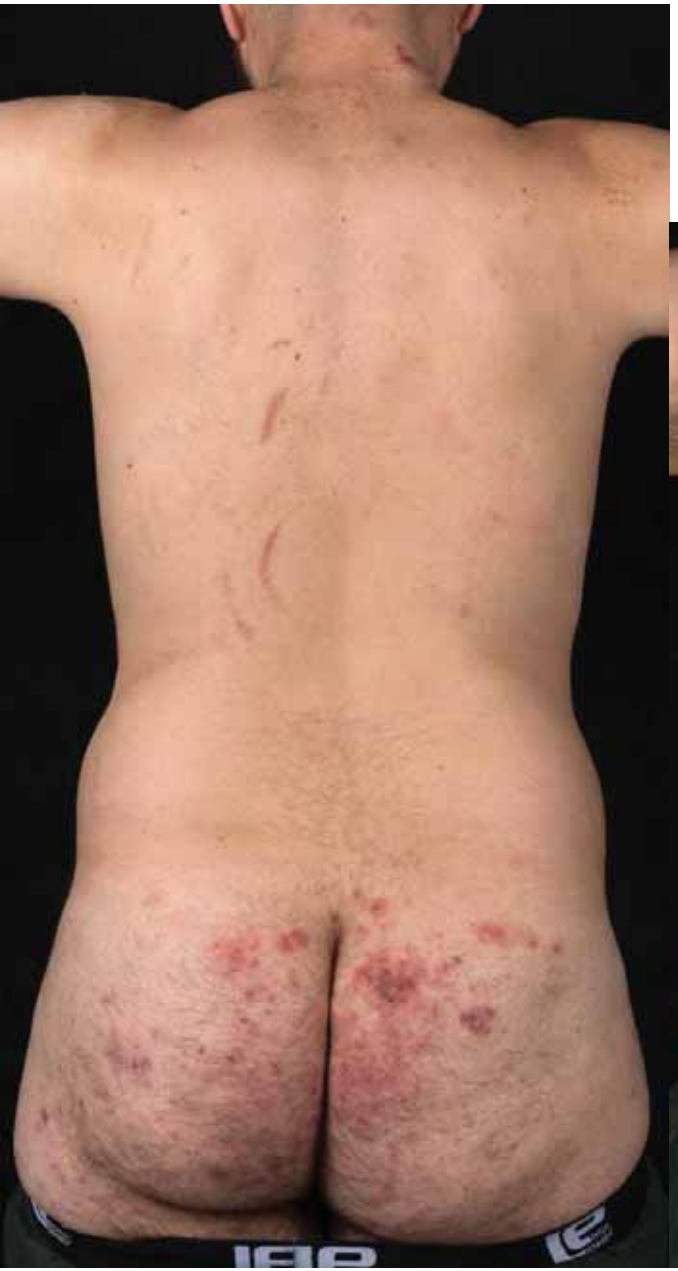
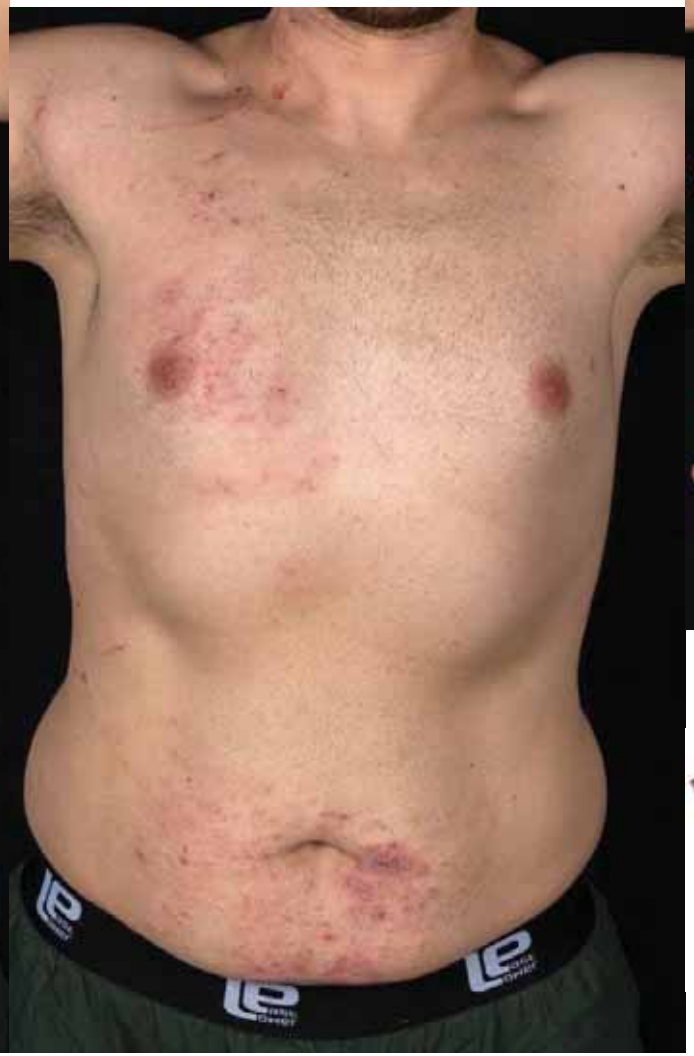
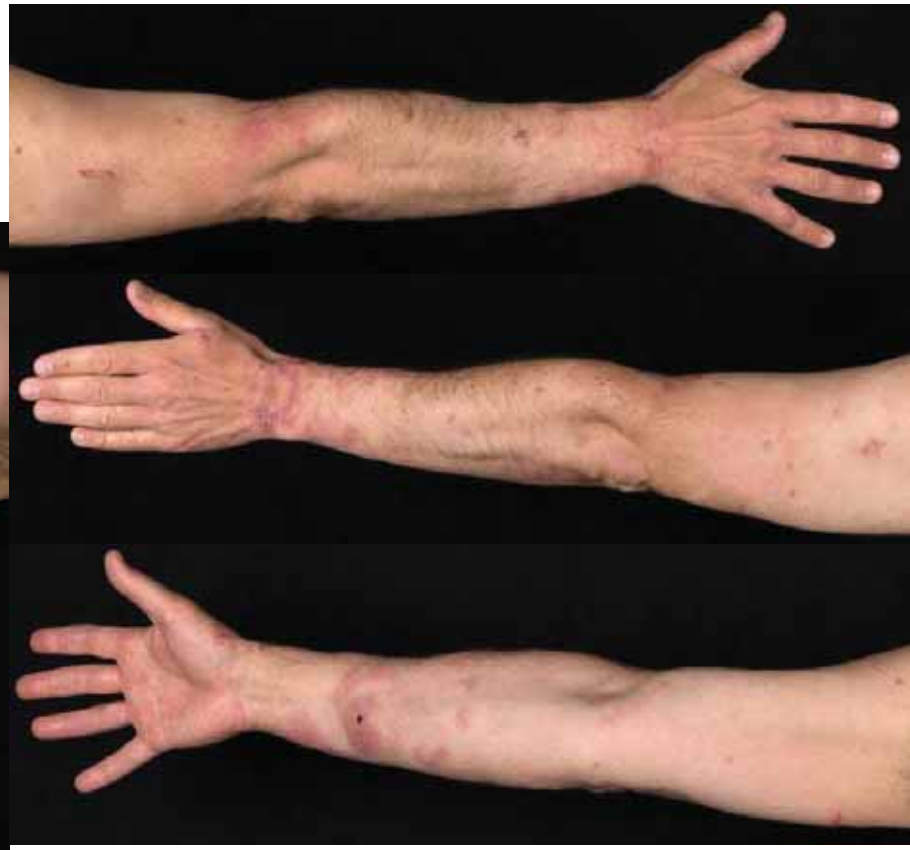
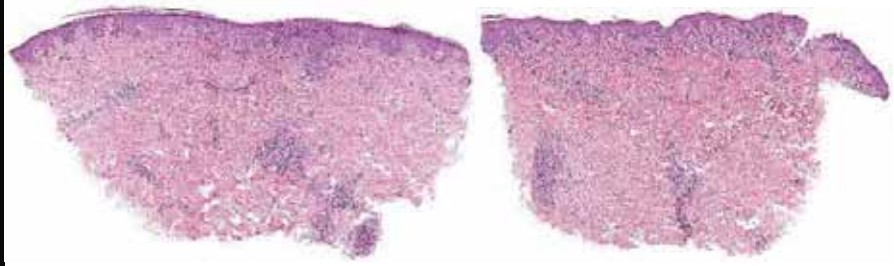
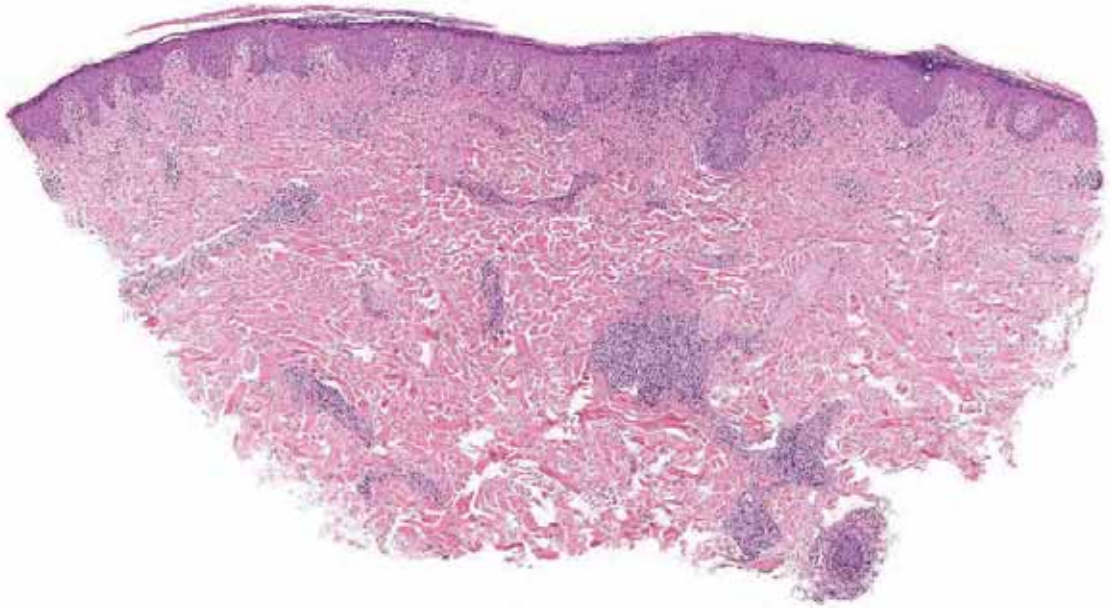
According to the patient skin lesions for approximately 4 years, mostly asymptomatic (?). Improvement under the sun. Previous treatments with doxycycline, UVB 311nm, tacrolimus ointment and local steroids without improvement; at present 3x guselkumab (last time 3 months before presentation).
Two biopsies are taken (right lower arm, abdomen).

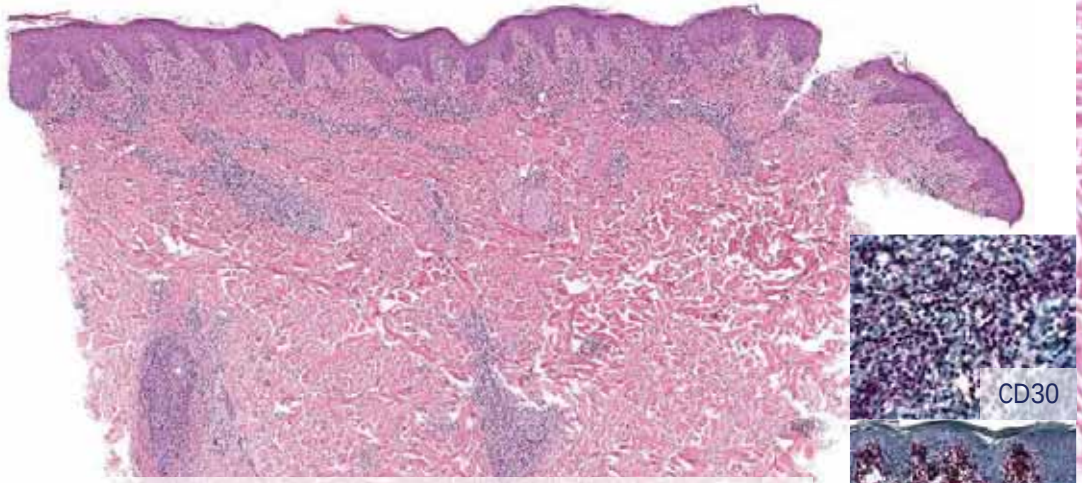


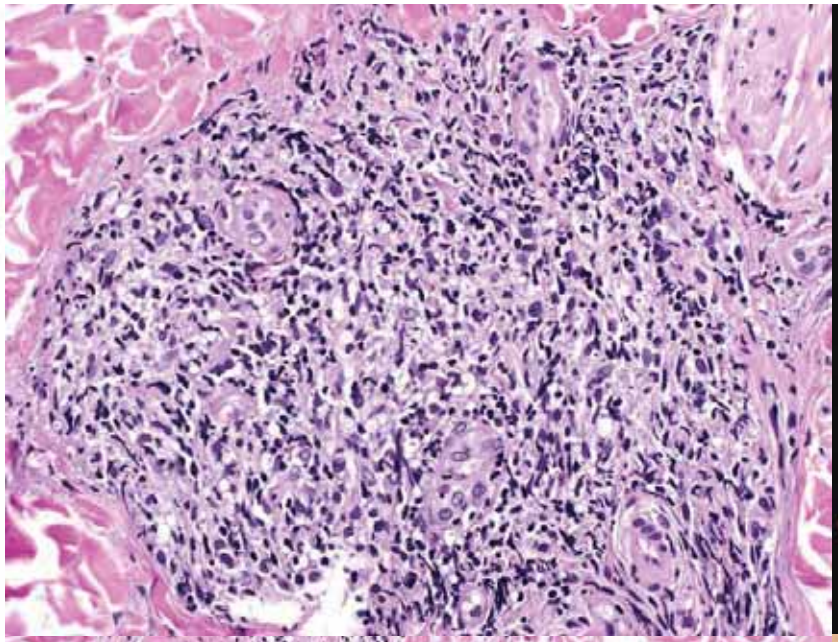


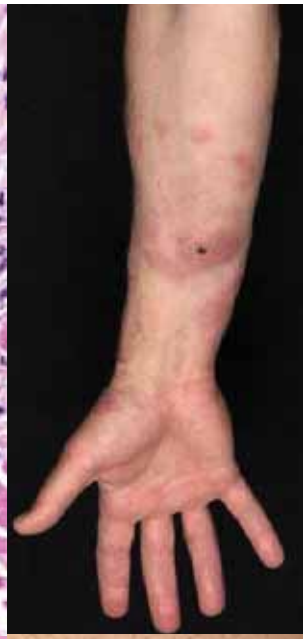


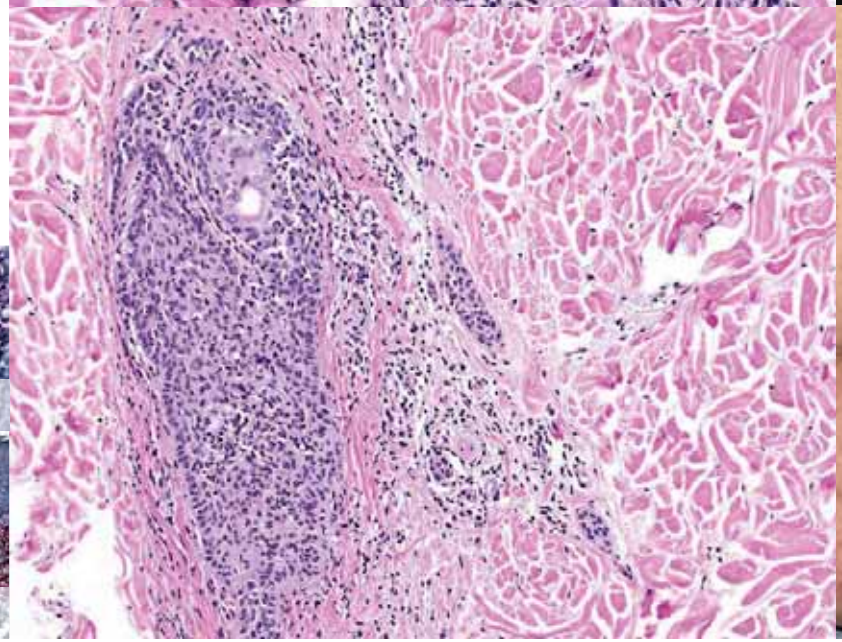


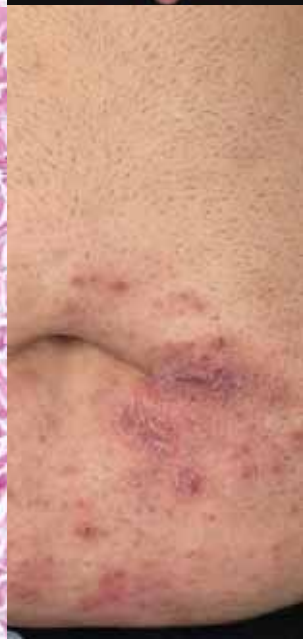




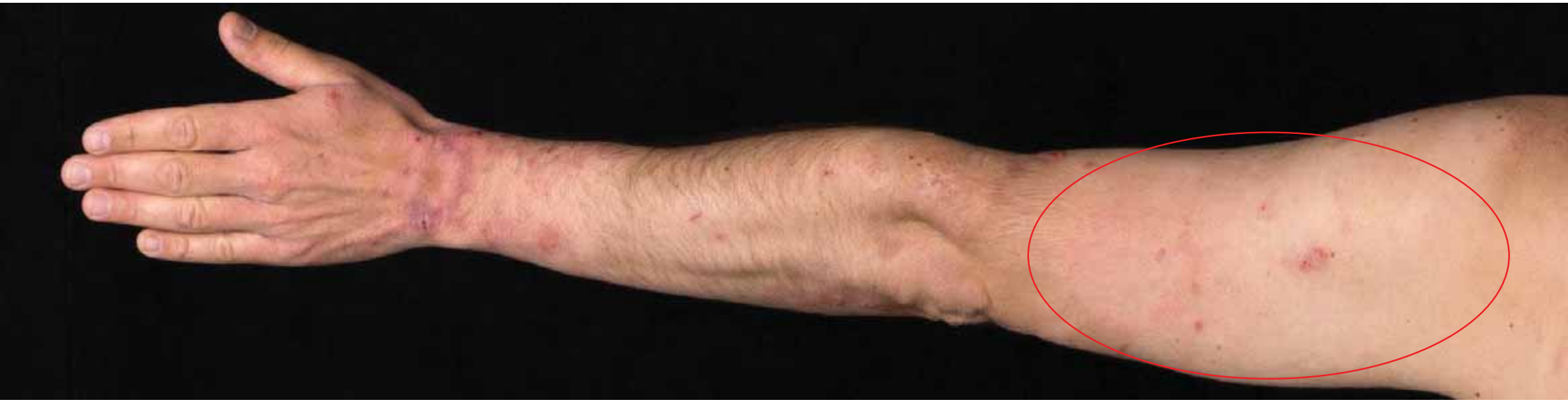




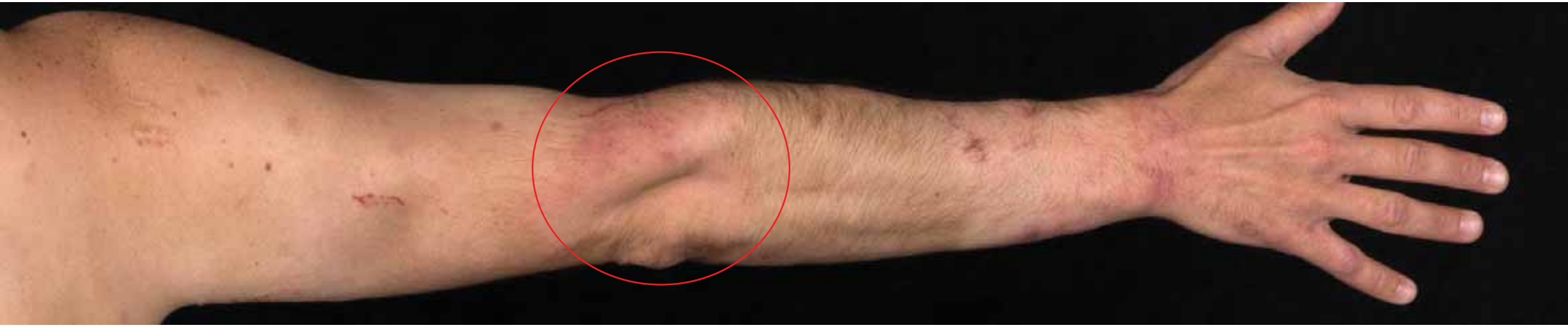




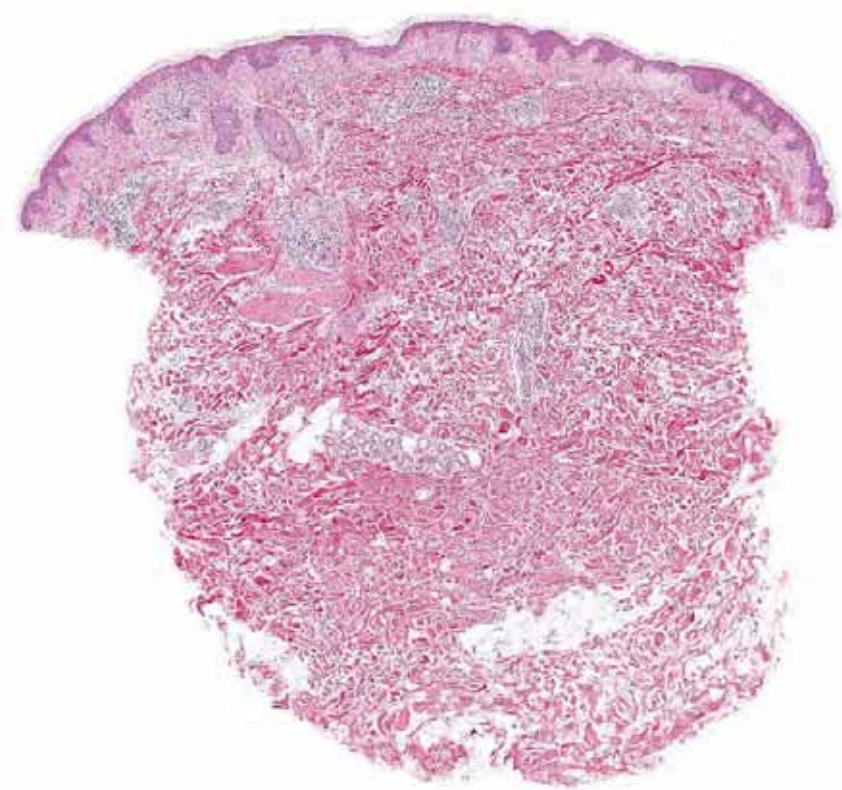
Adnexotropic MF

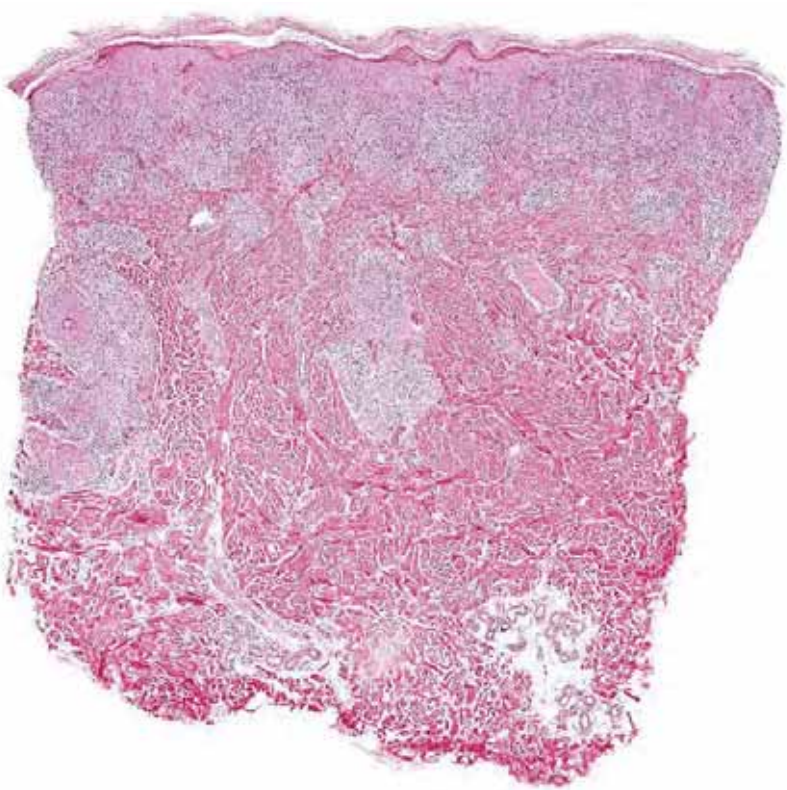


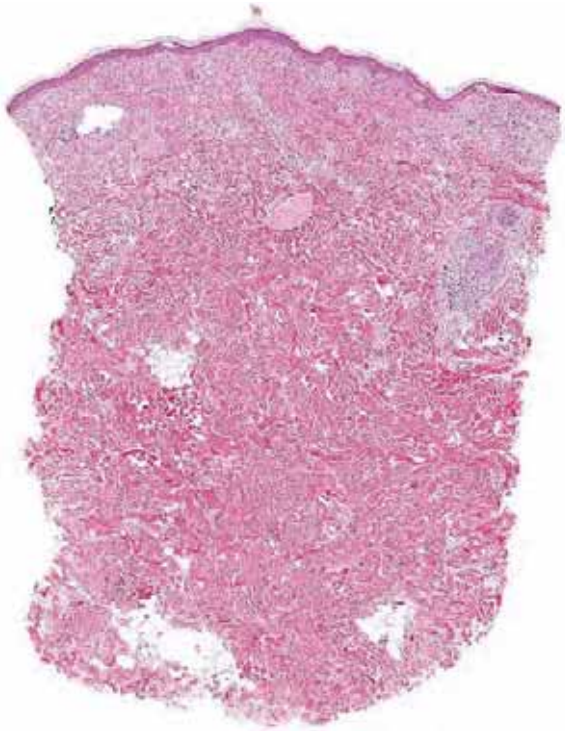
Partly hypopigmented, partly erythematous lesions

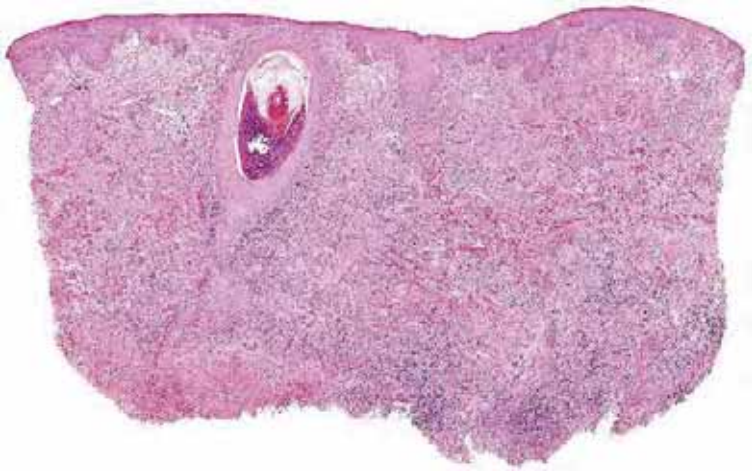


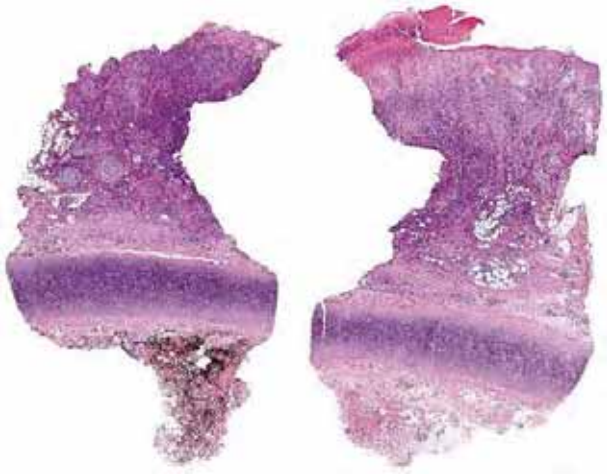
Focal alopecia











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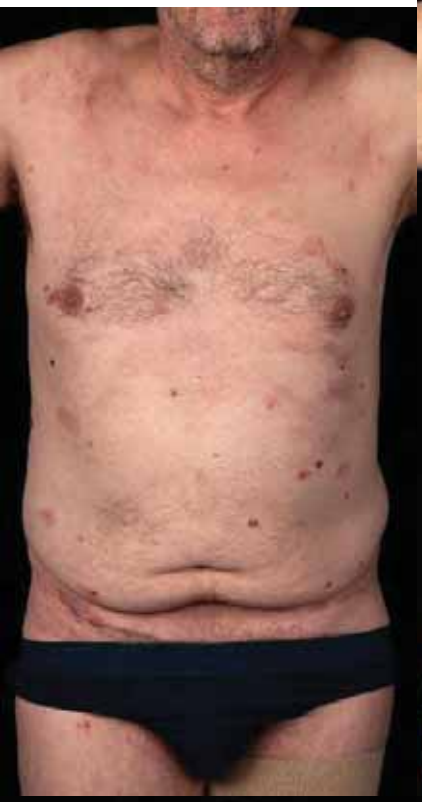
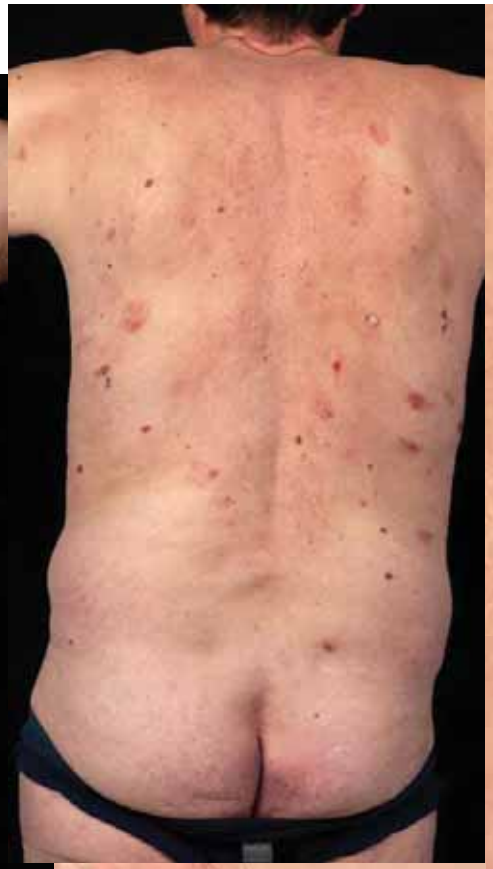
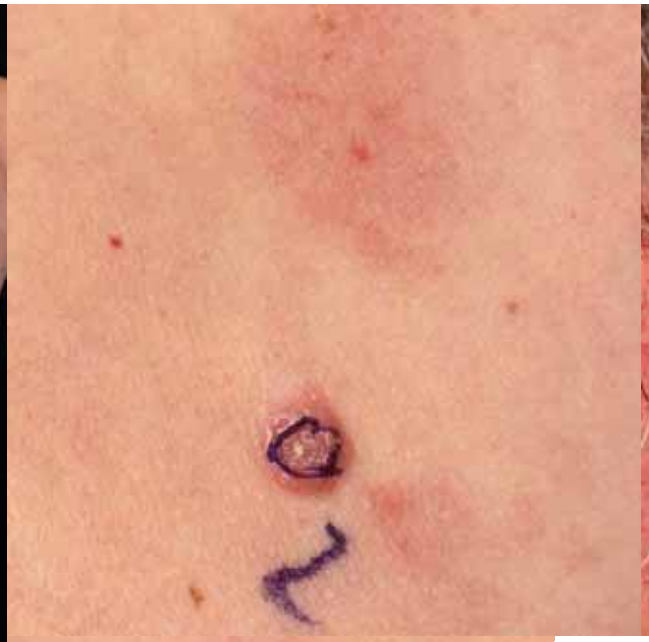
History of solitary CD30+ cutaneous lymphoproliferative disorder of the lower lip 9 years before presentation (CR after biopsy).

Itchy skin lesions starting after a holiday in Brazil 6 months previously (no mention of skin lesions in a visit 9 months before for a venous thrombosis of the left leg). Ear lesions for 3 weeks.

Four biopsies are taken from the scalp, left breast, left flank and right back. A fifth biopsy from the external ear canal had been taken one day previously by an otorhinolaryngologist.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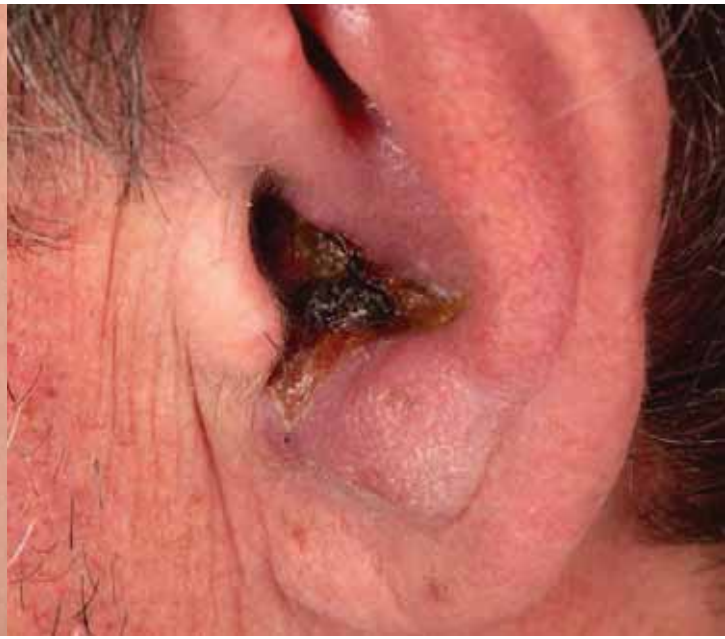

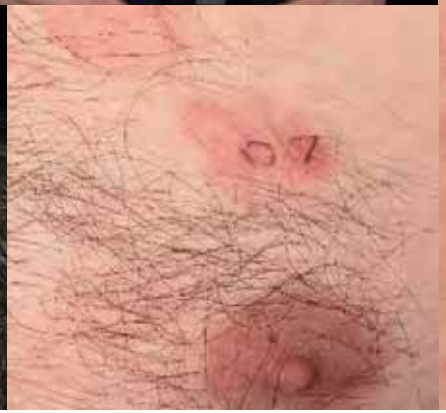
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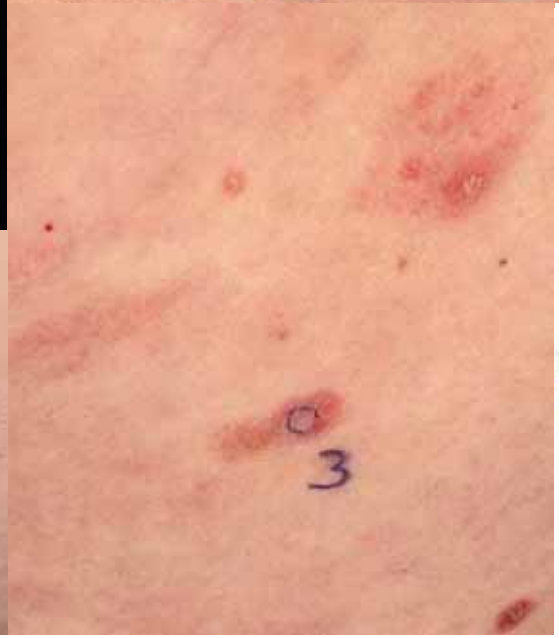
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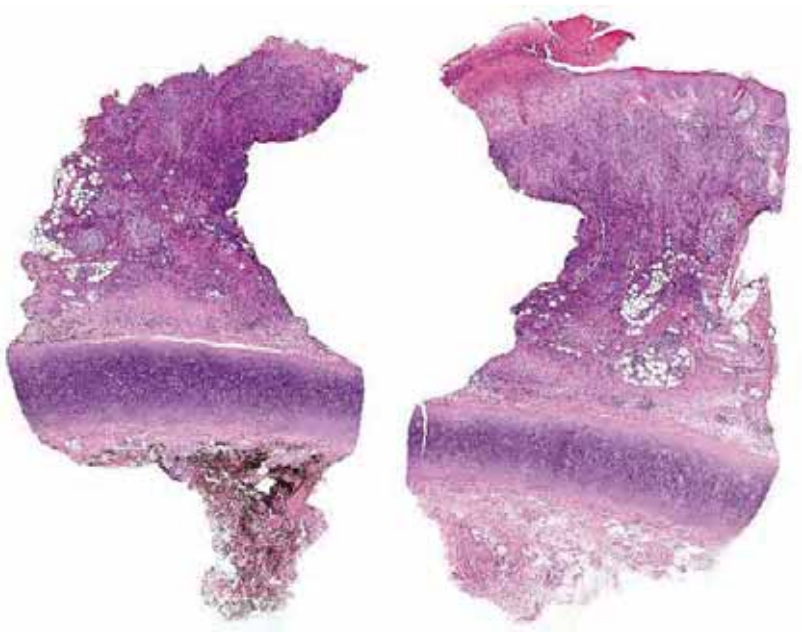

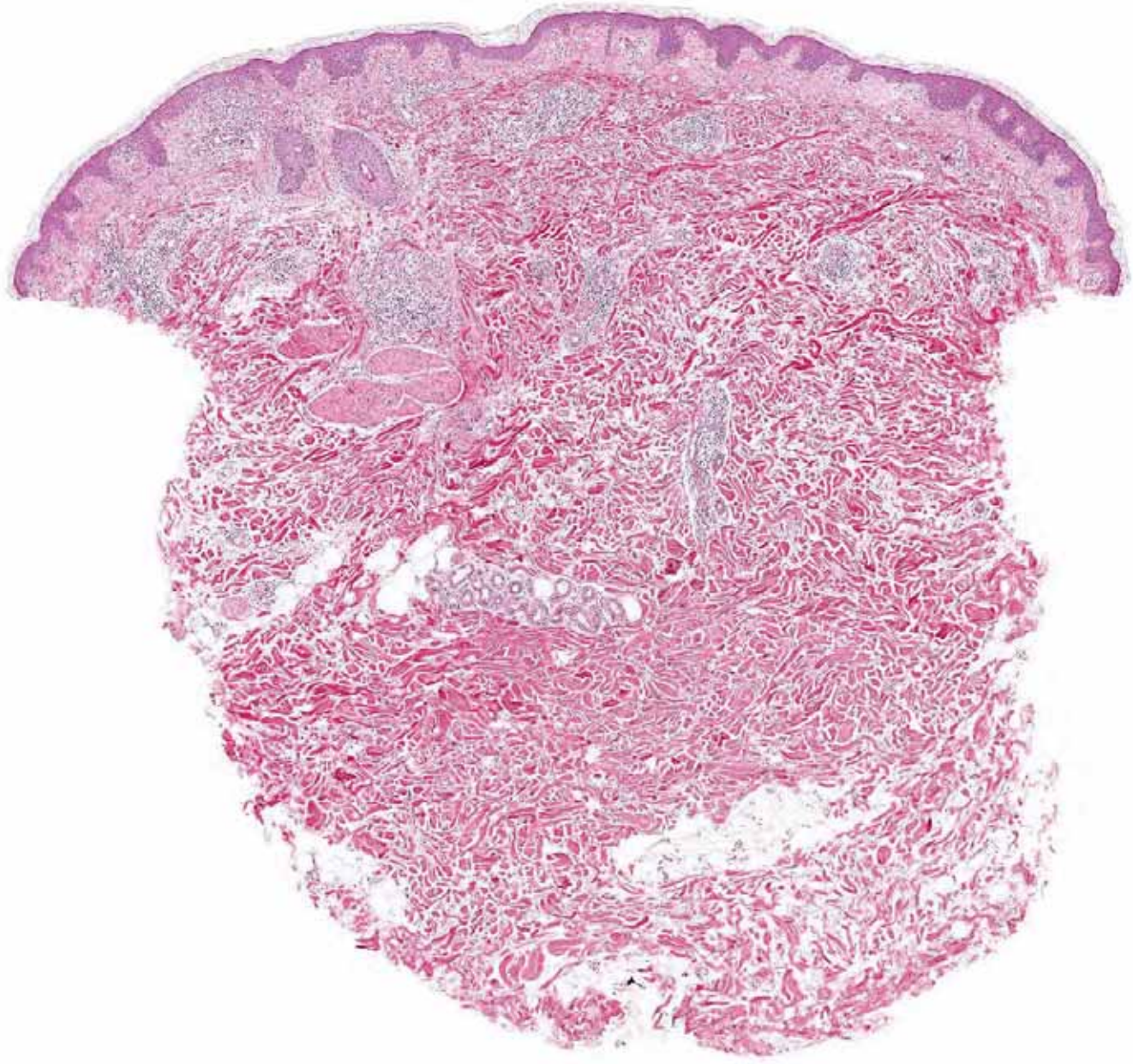

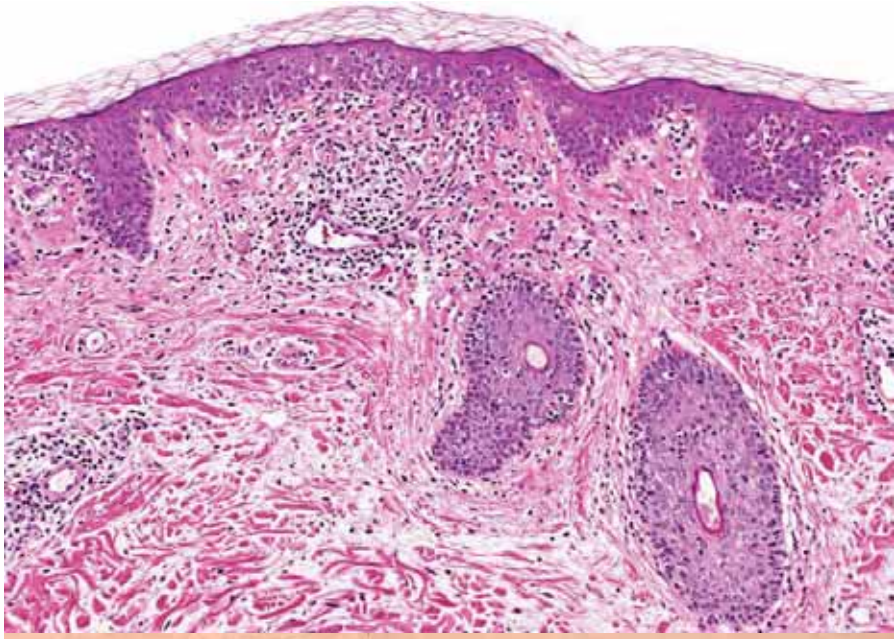

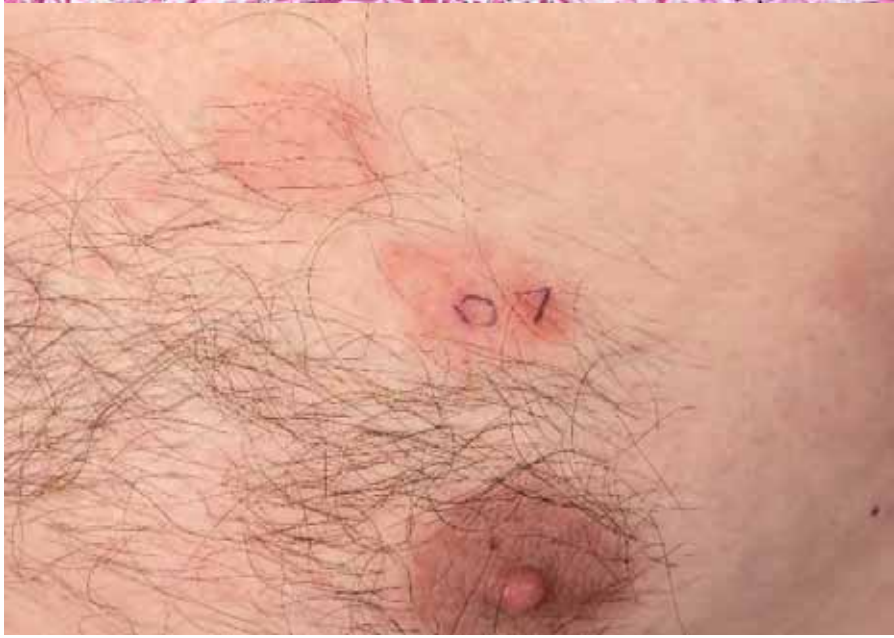

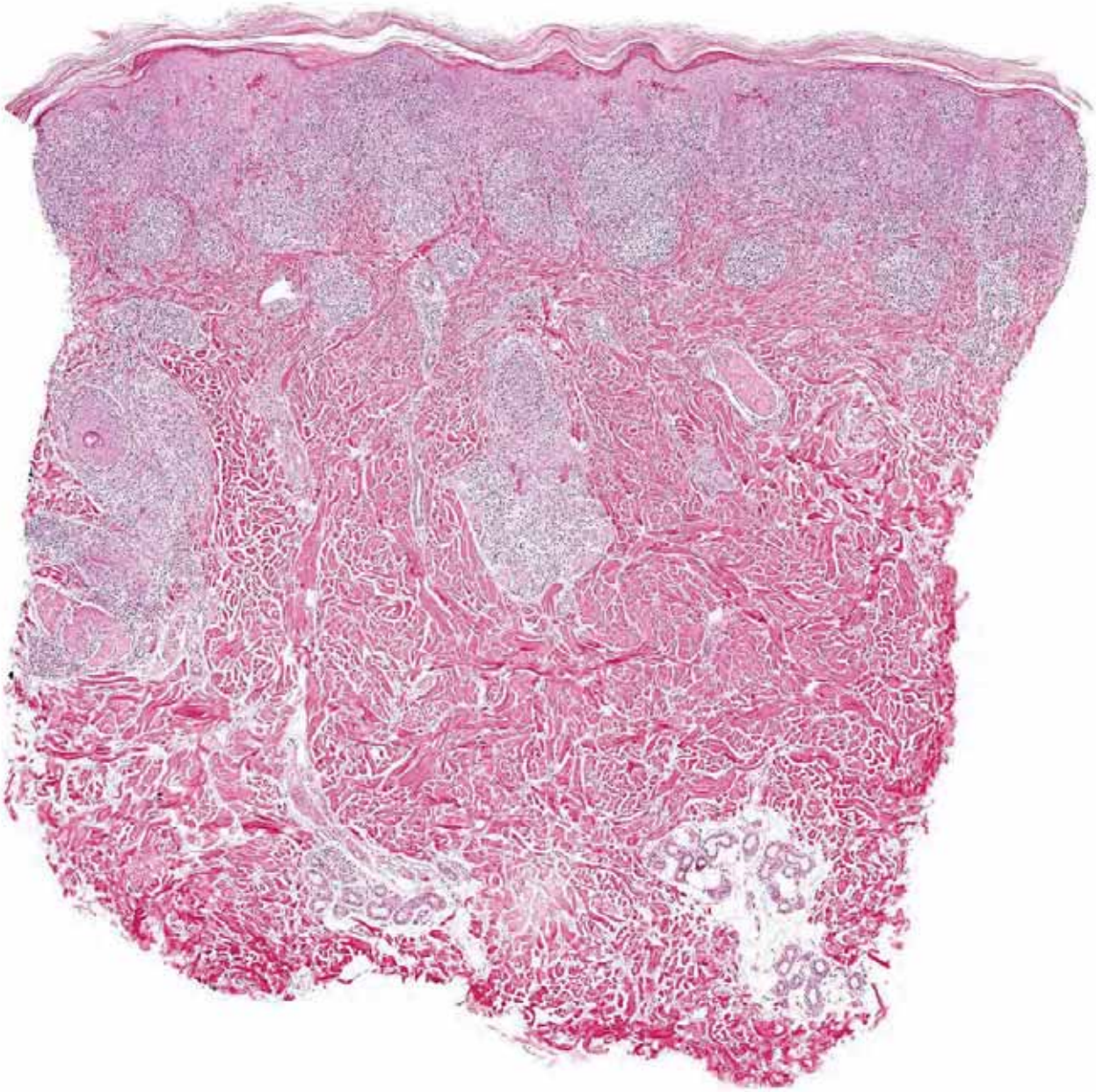

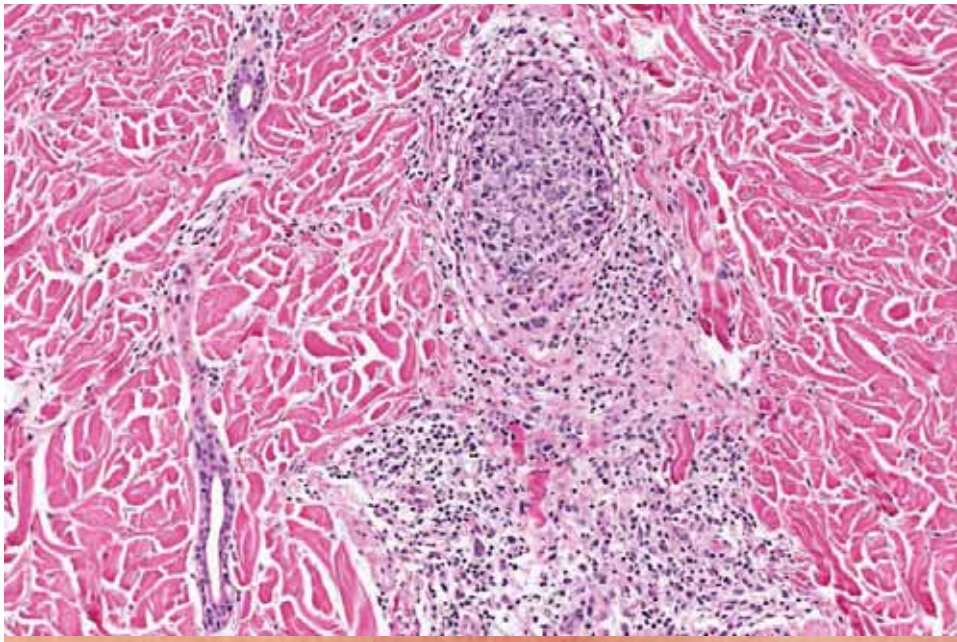

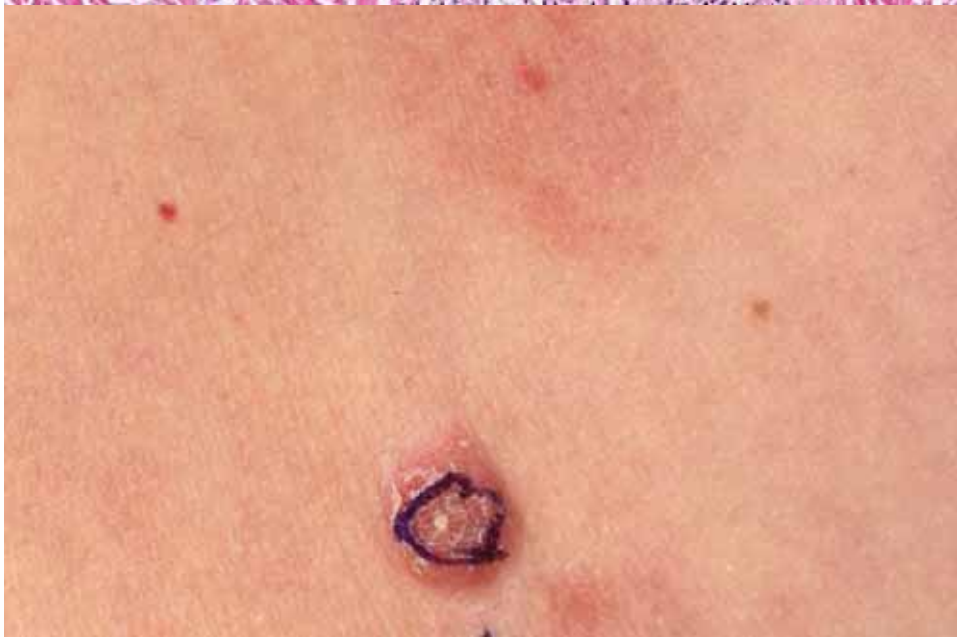

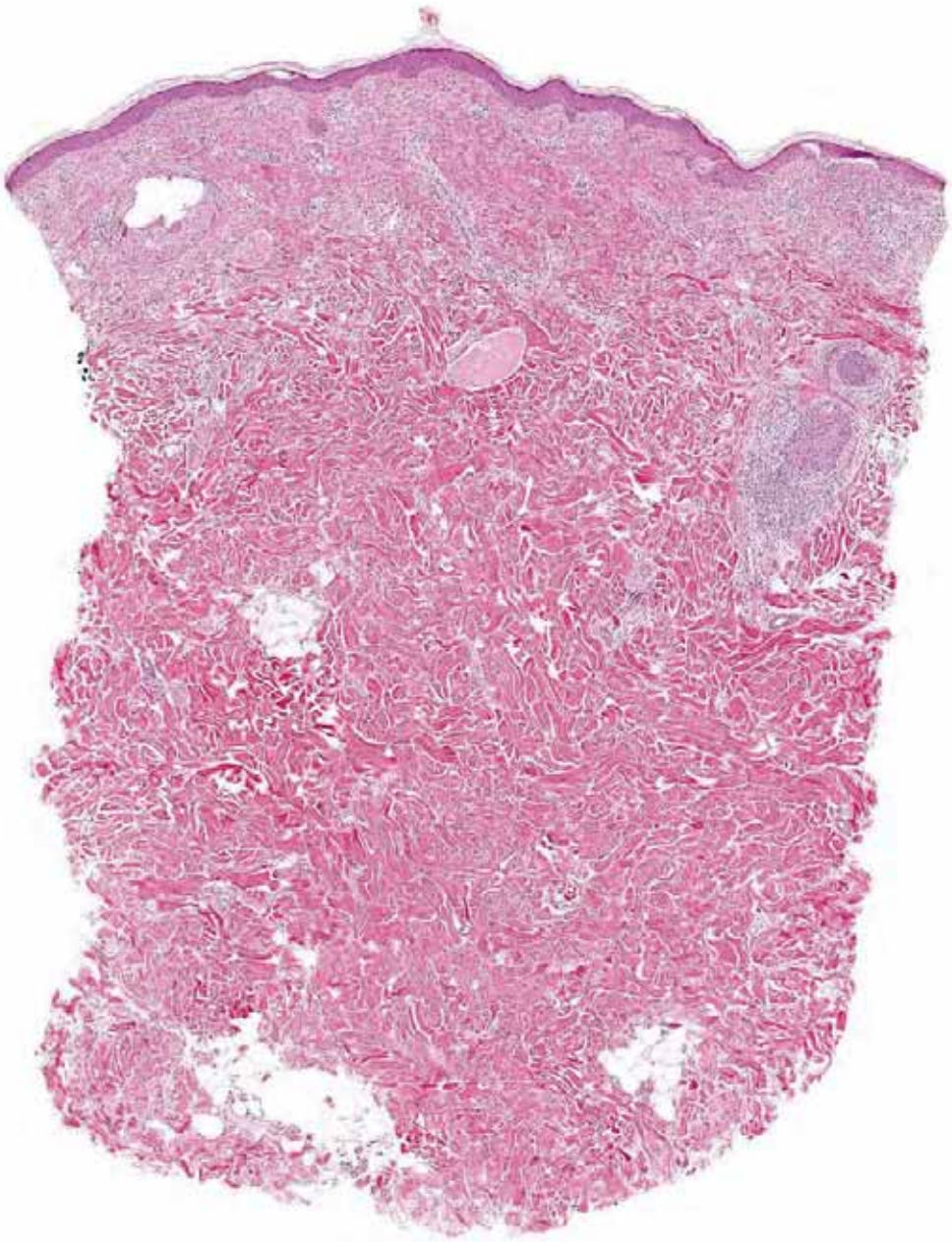

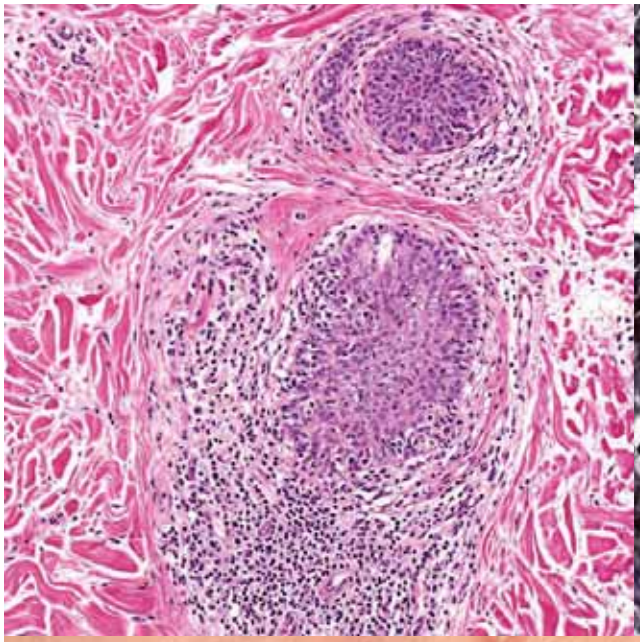

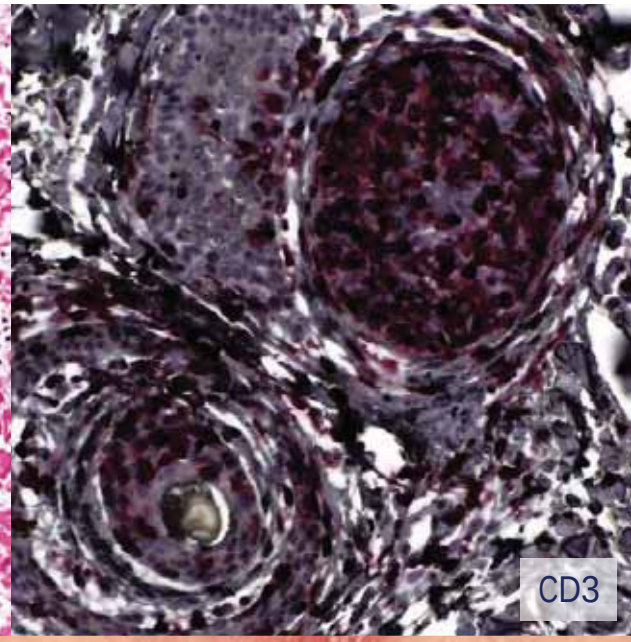
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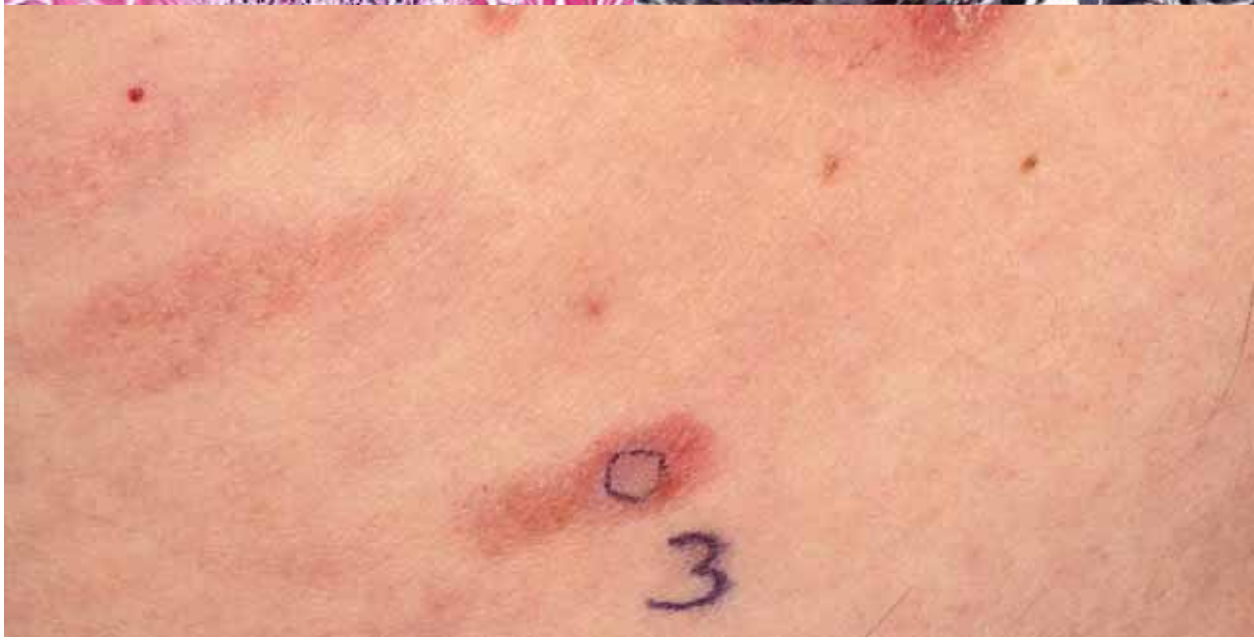
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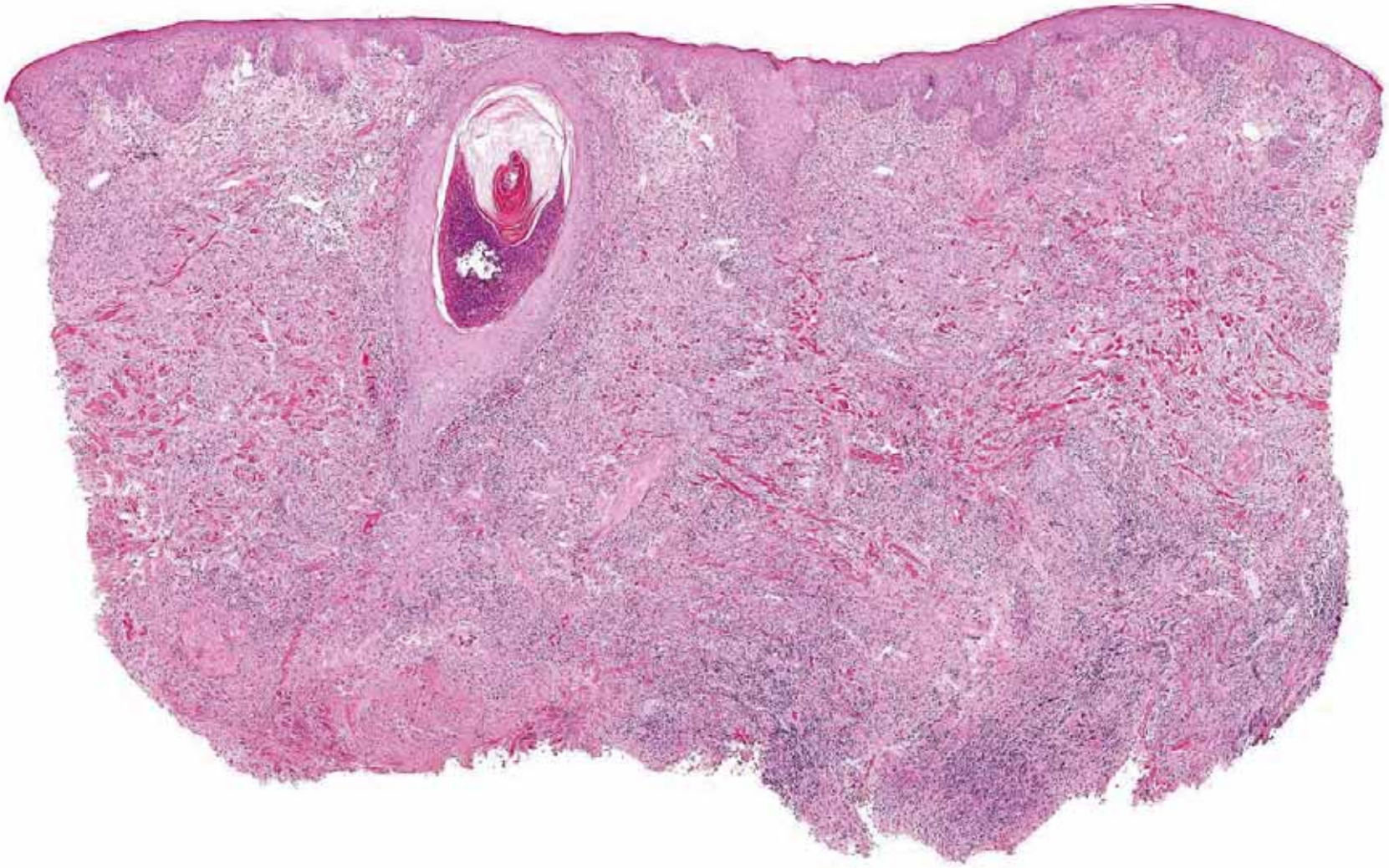

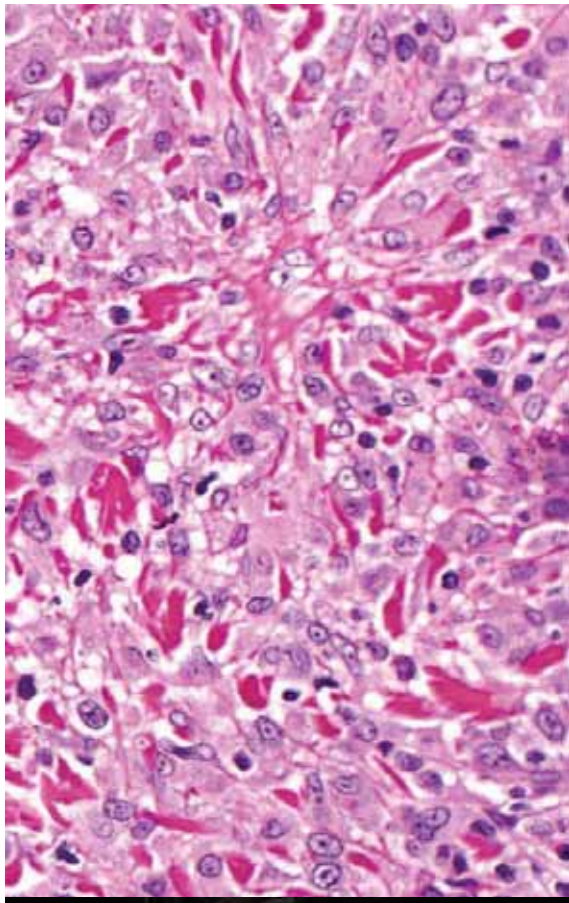

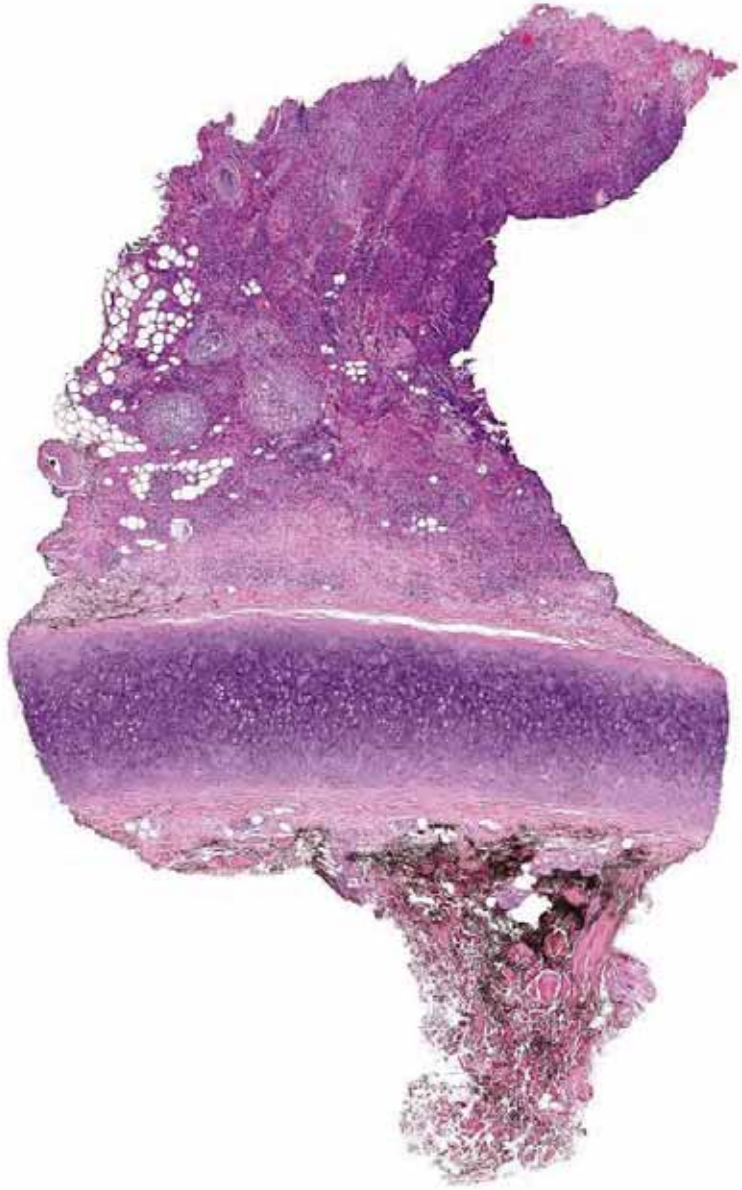

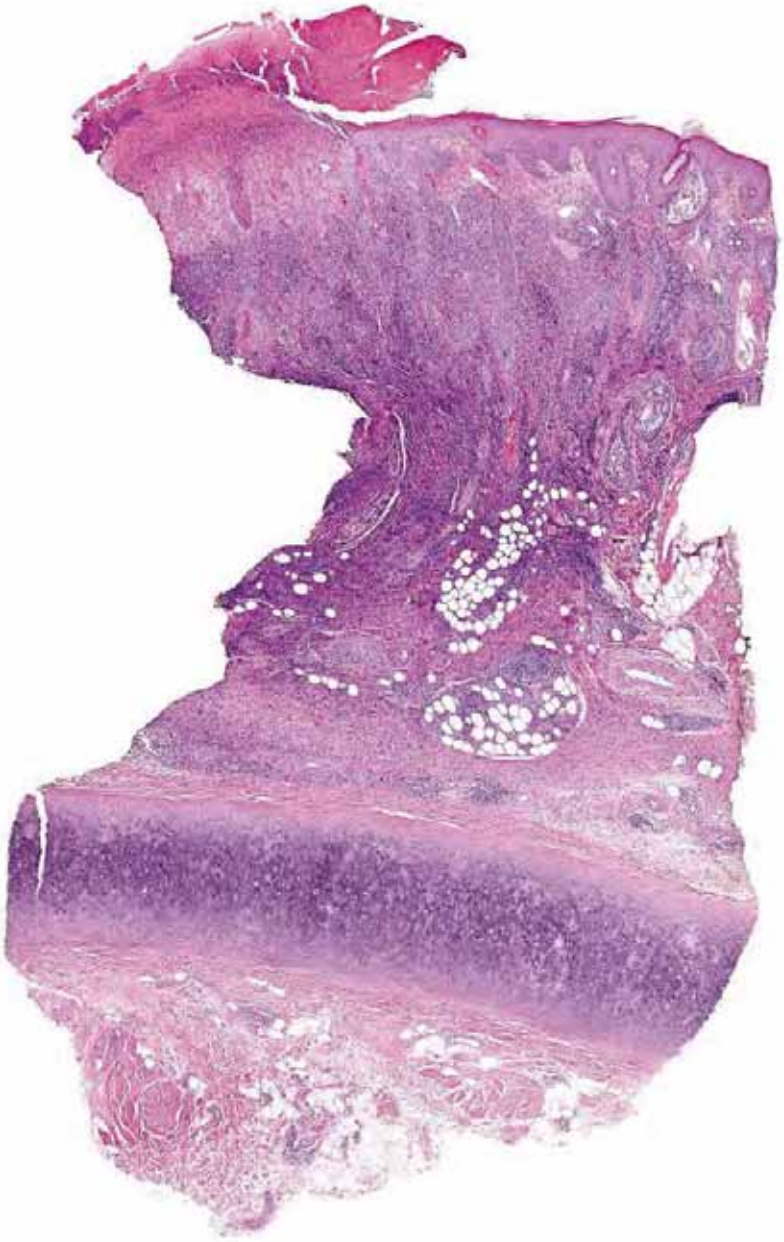

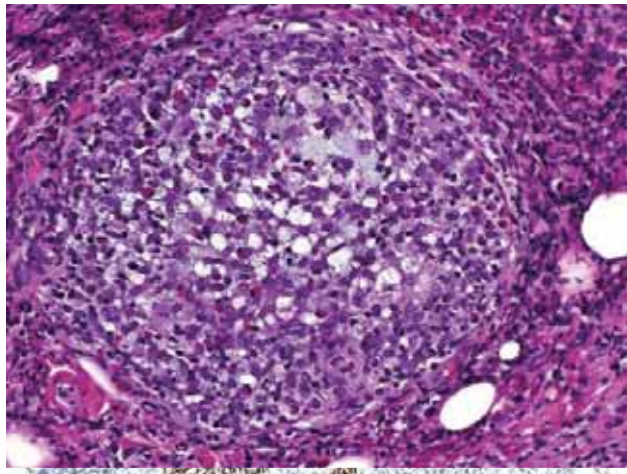

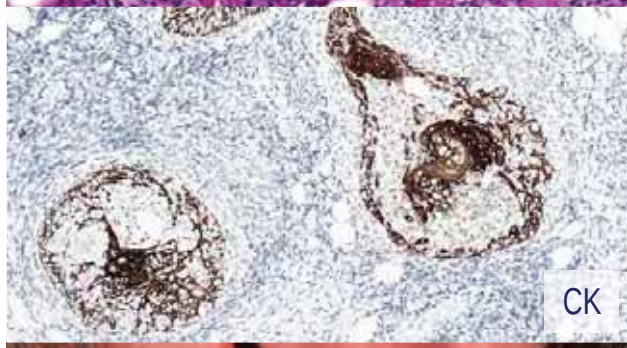
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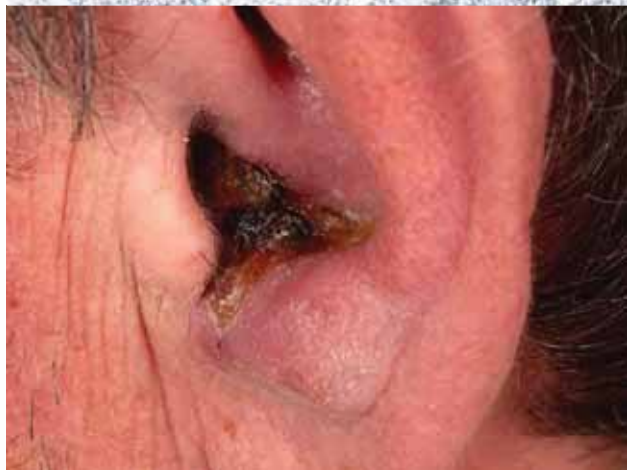
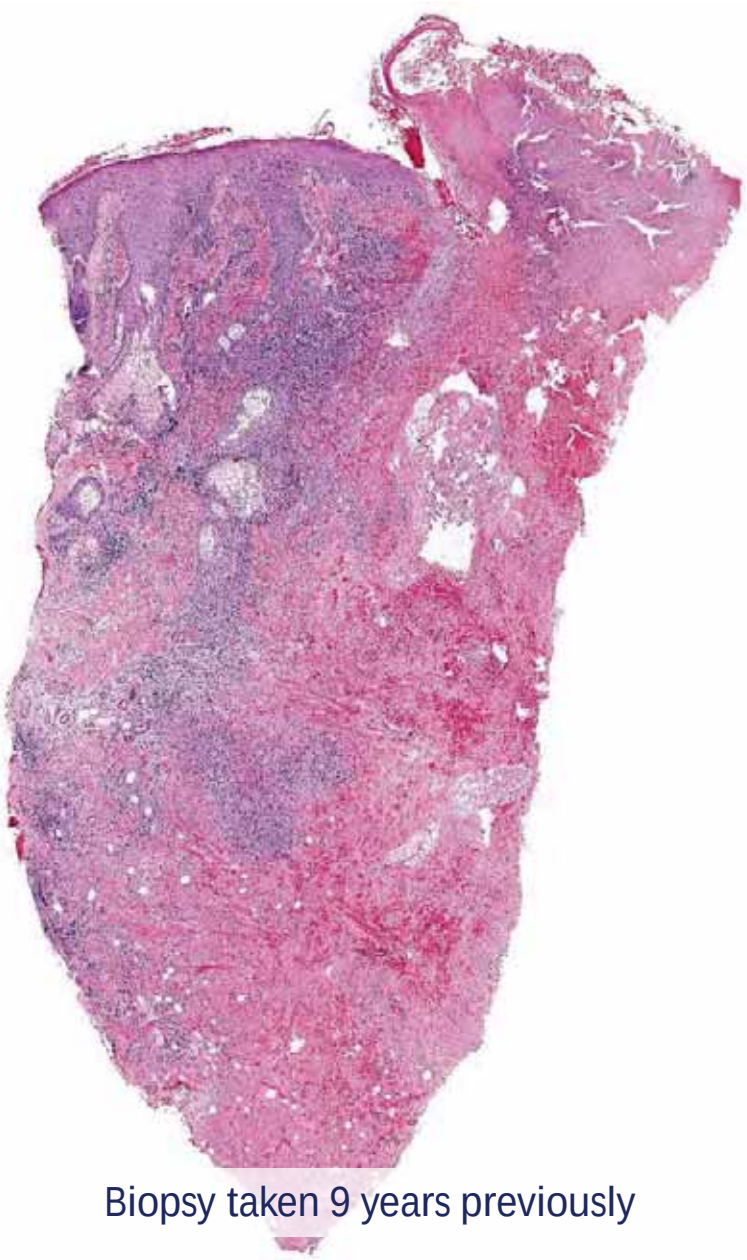
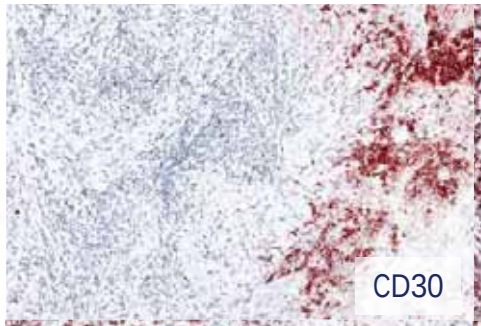
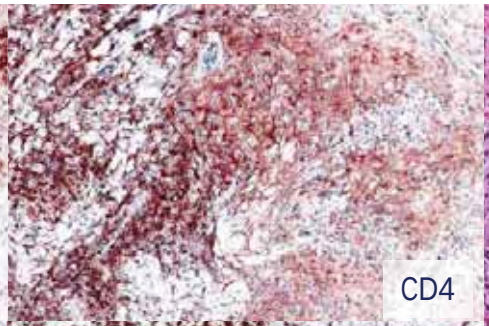


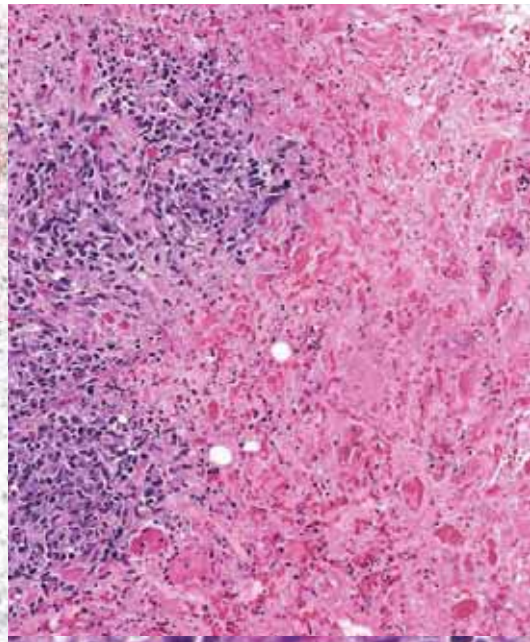
Adnexotropic mycosis fungoides

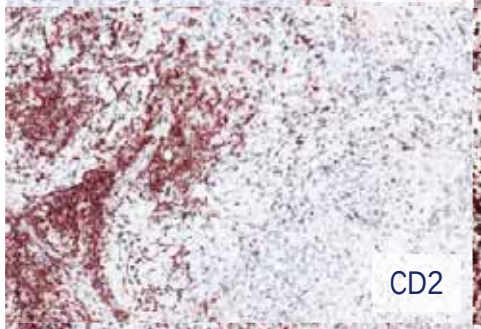


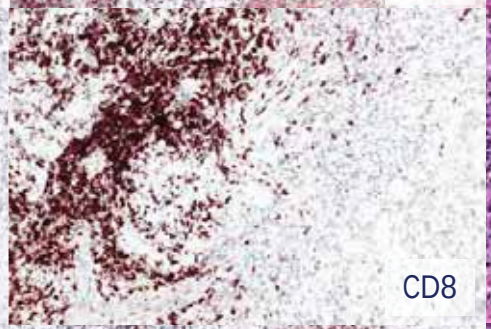
Biopsy taken 9 years previously

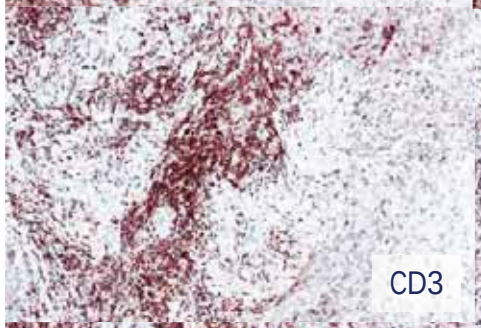


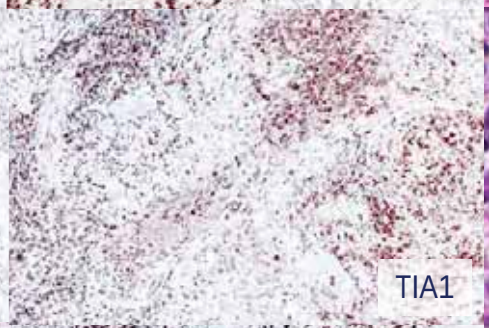


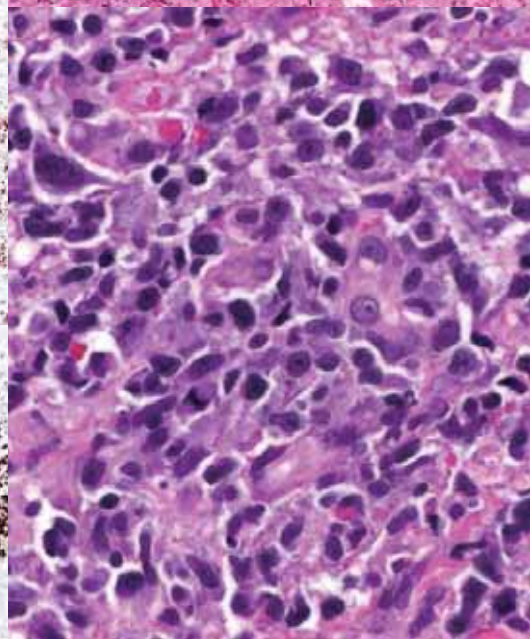


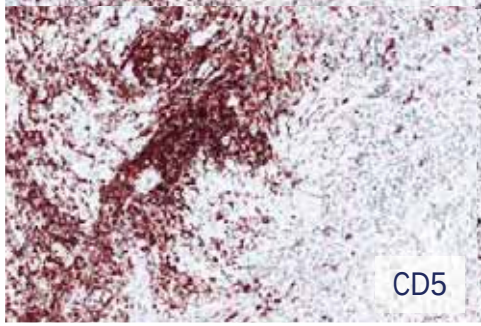


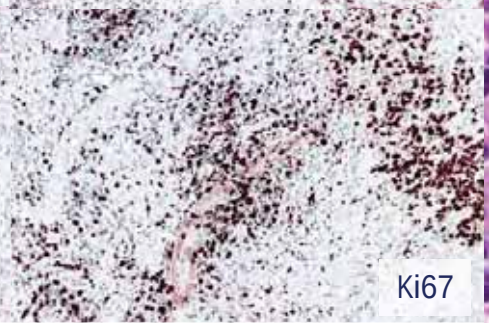


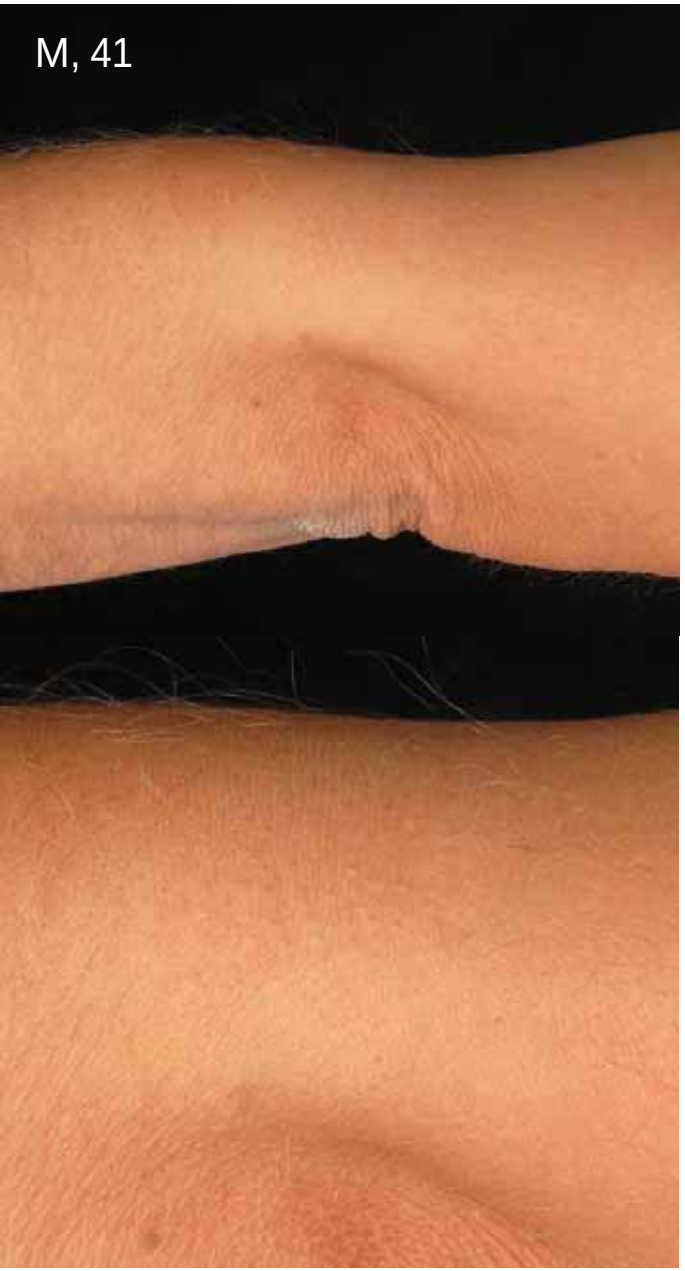


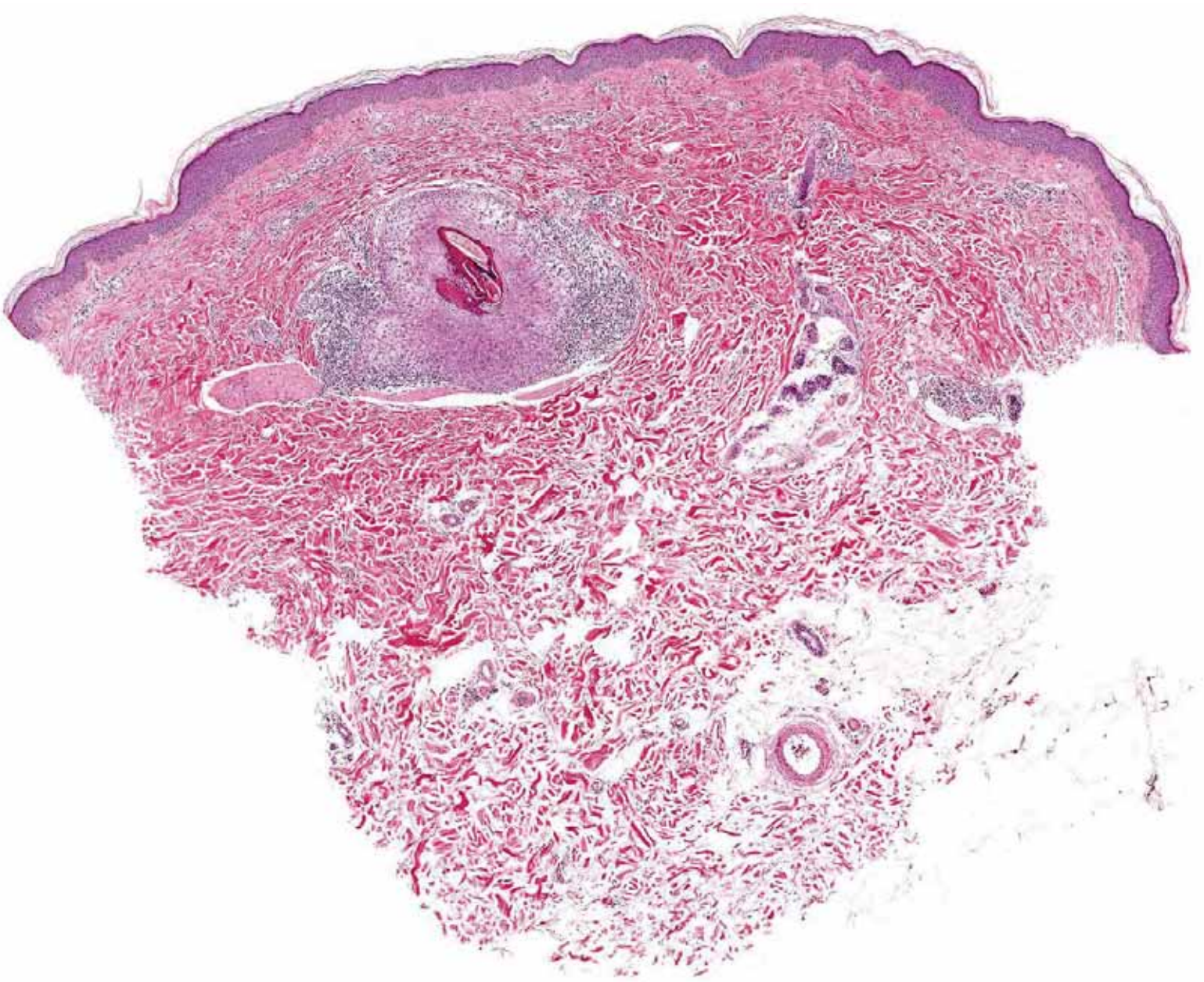


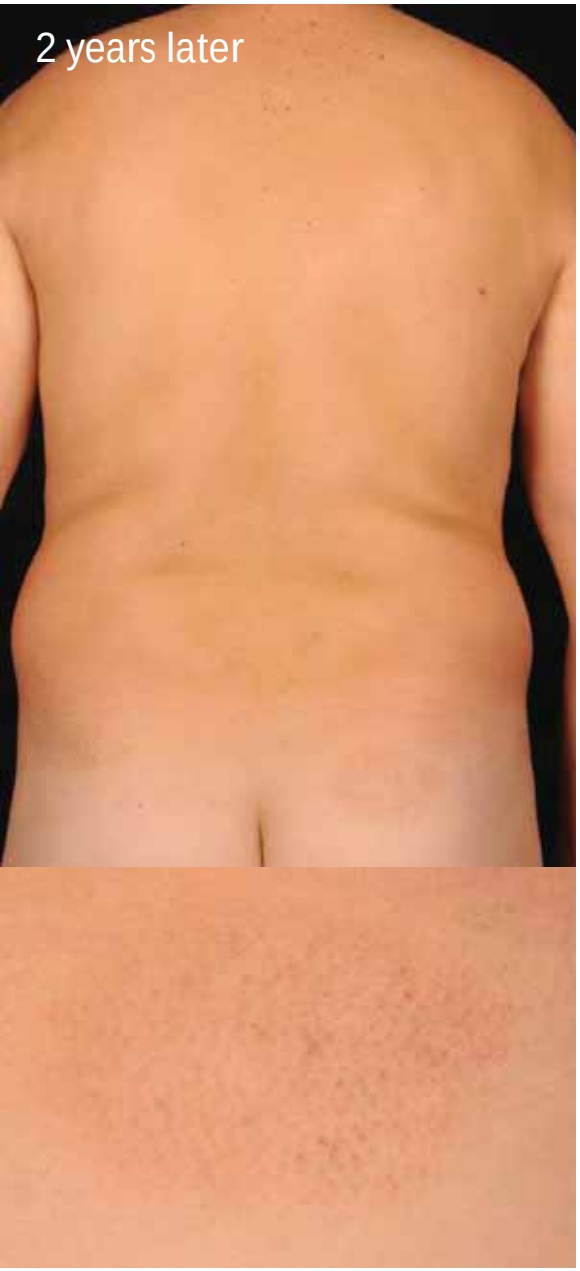







M, 41

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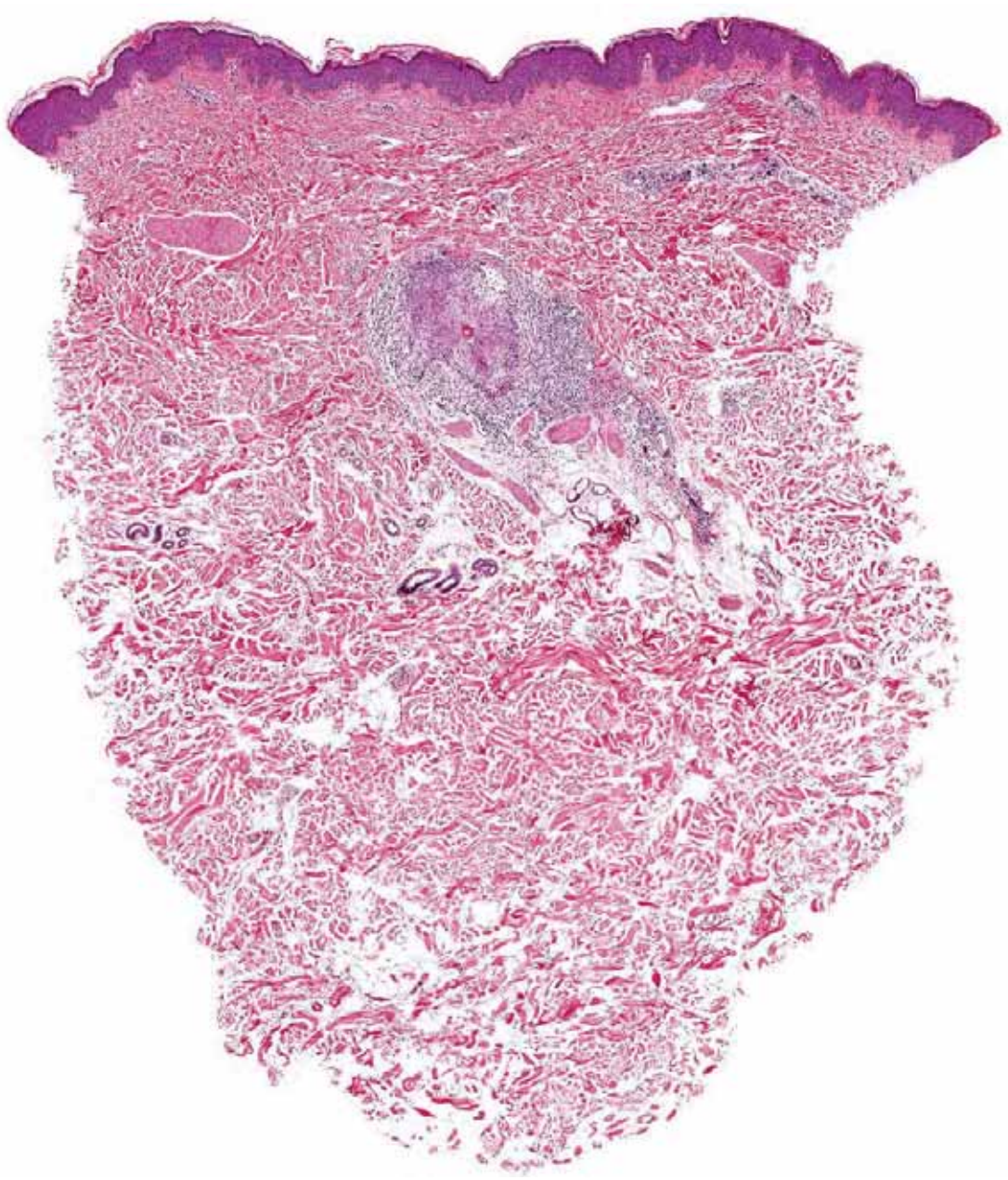
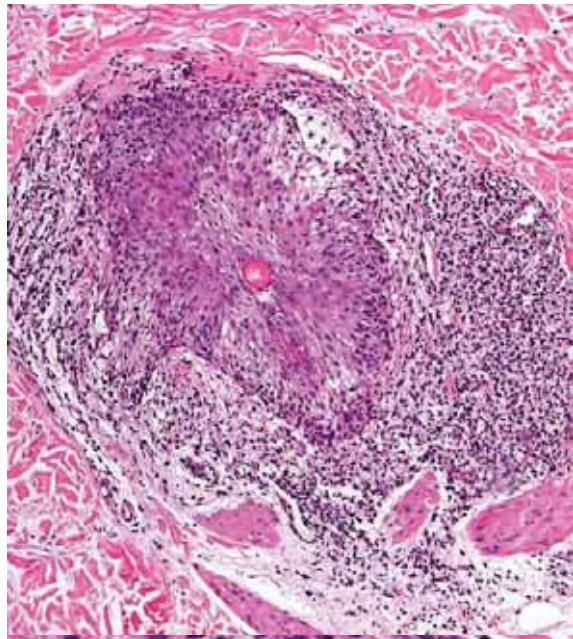
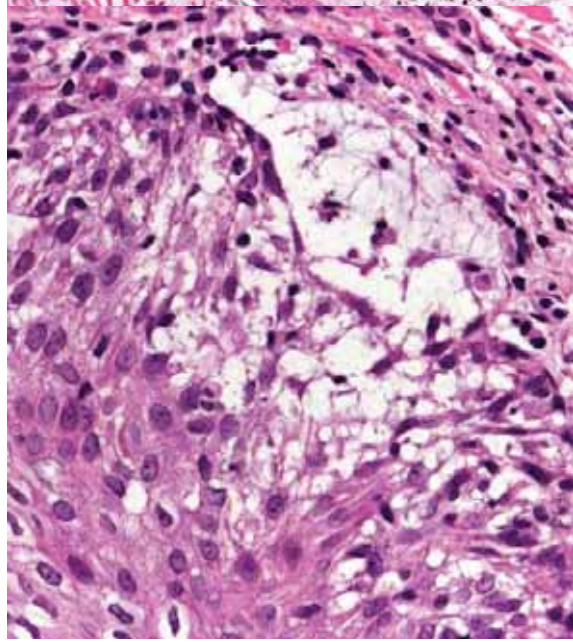
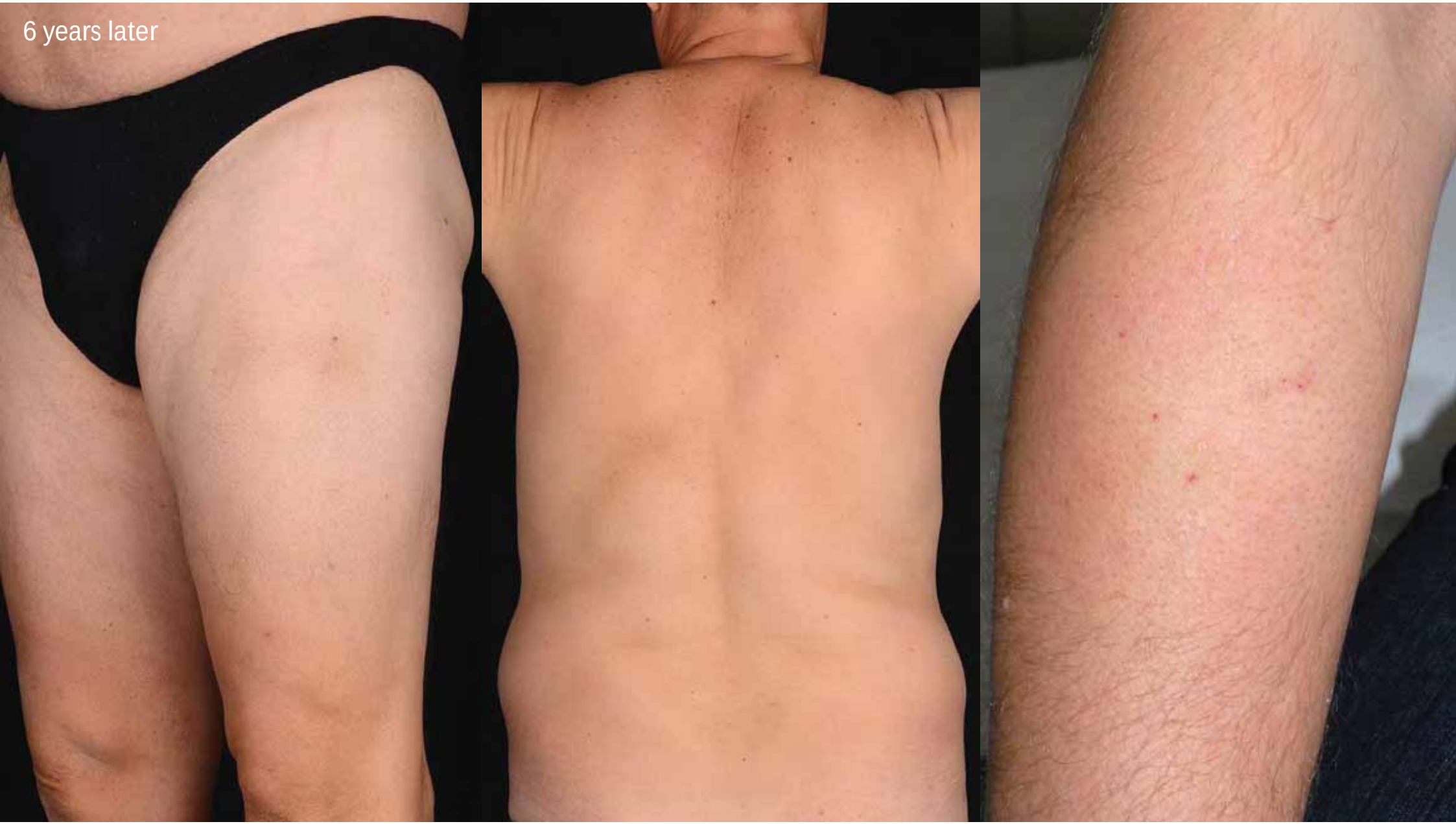
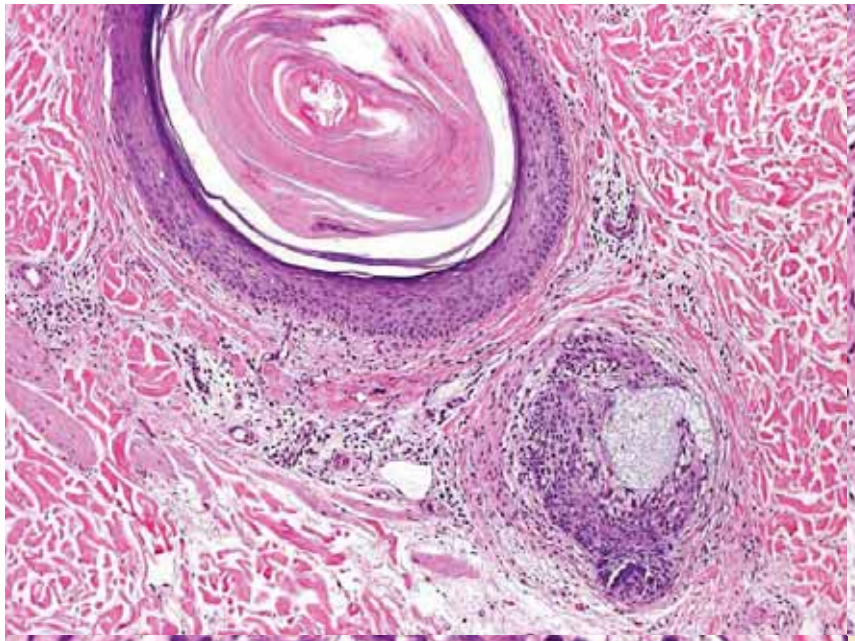
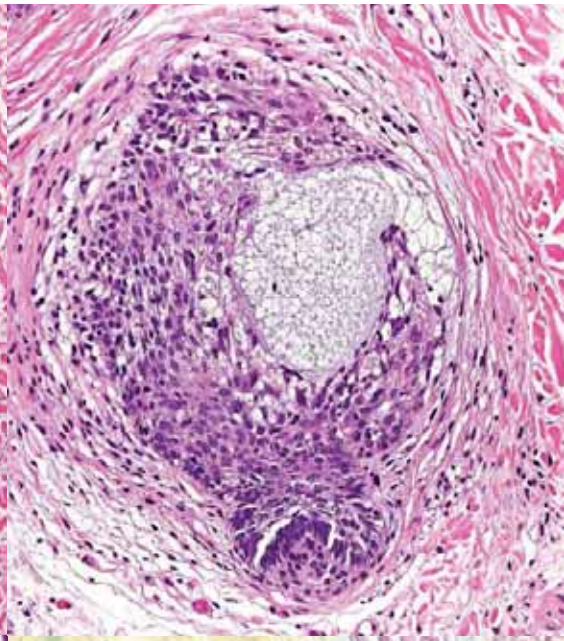


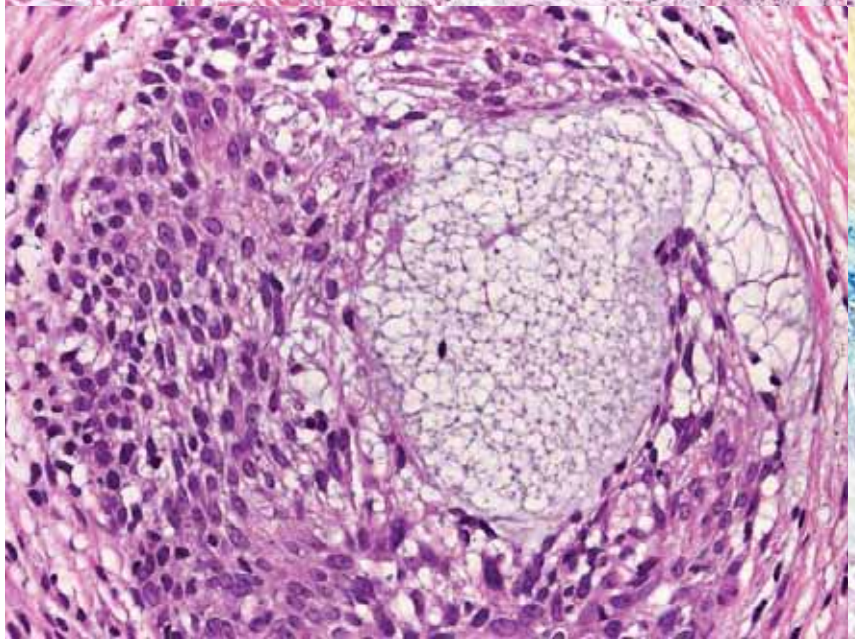


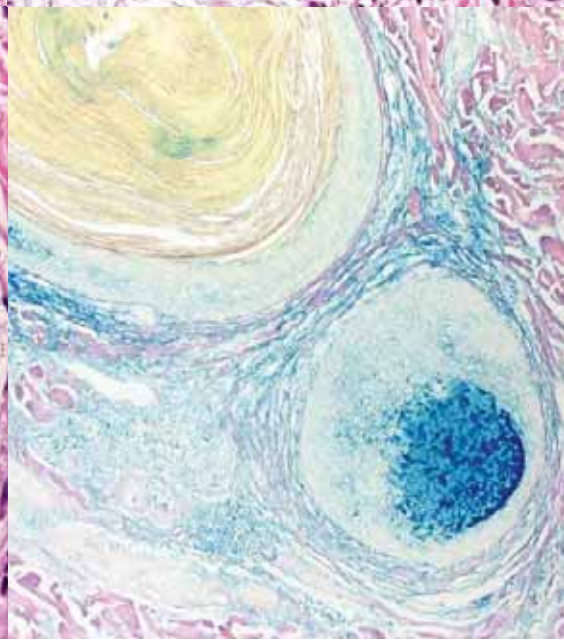


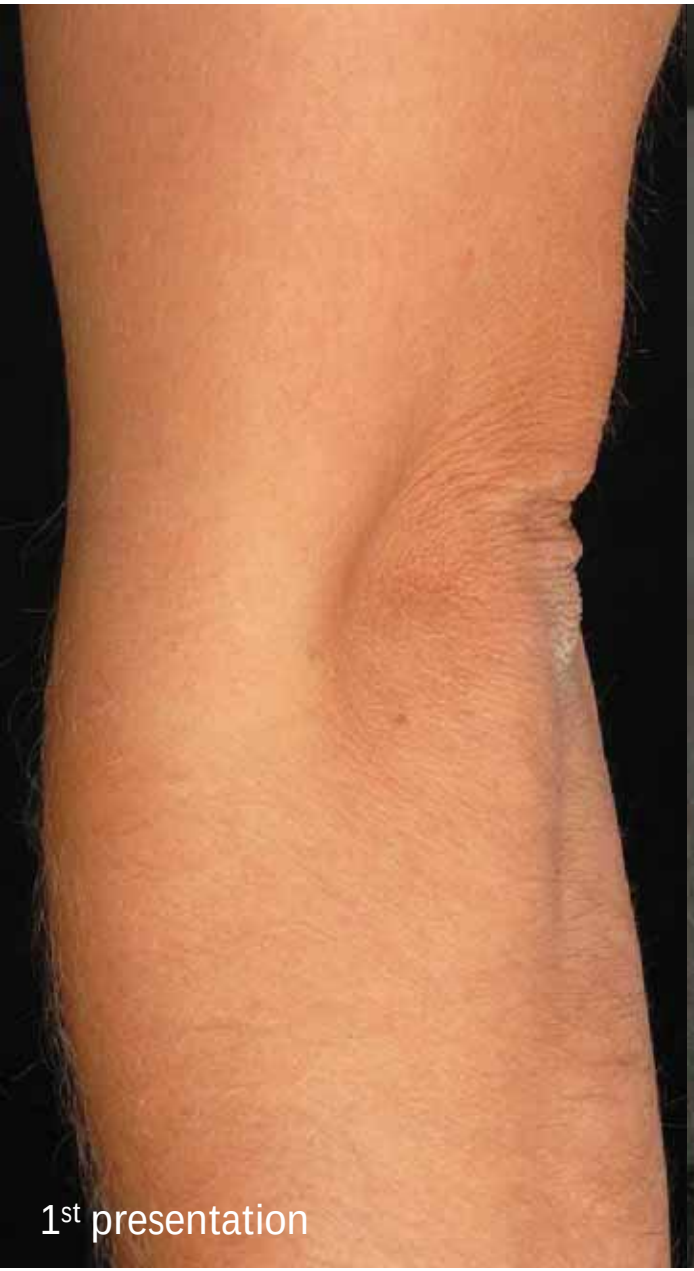

6 years later



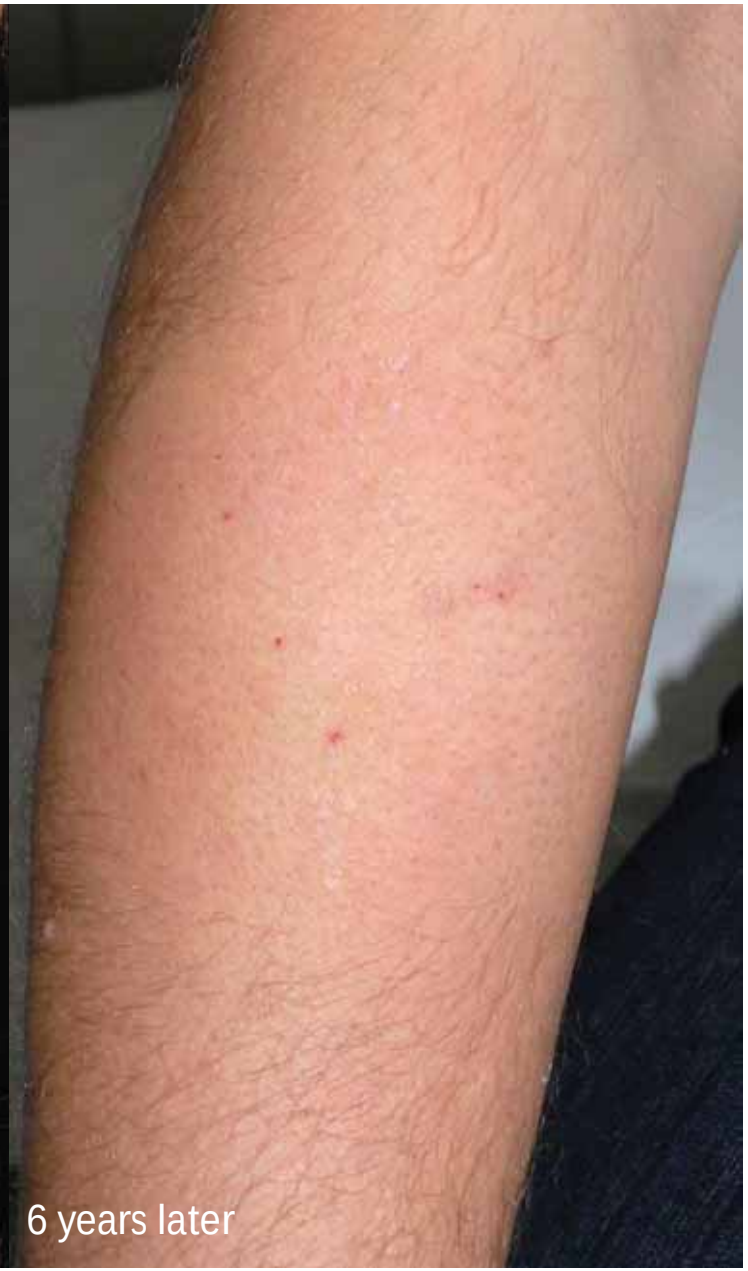




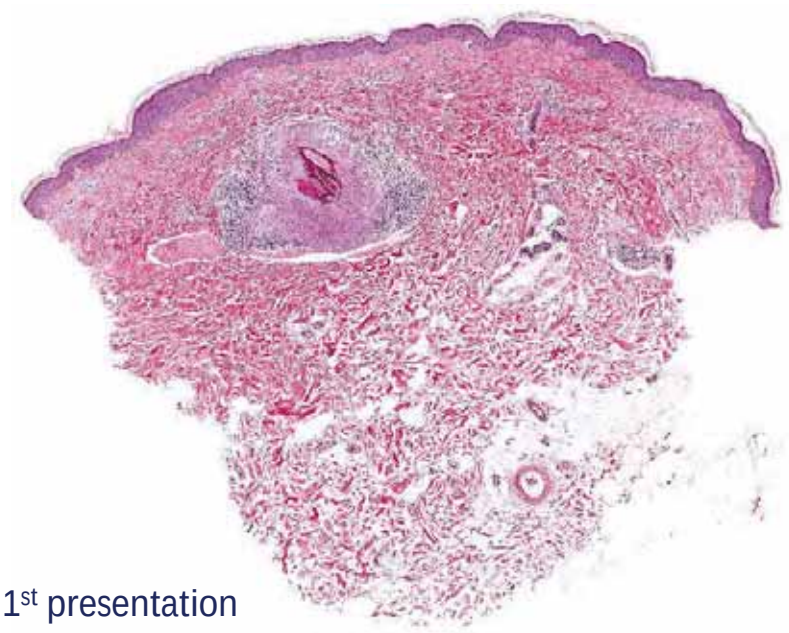




1st presentation



6 years later

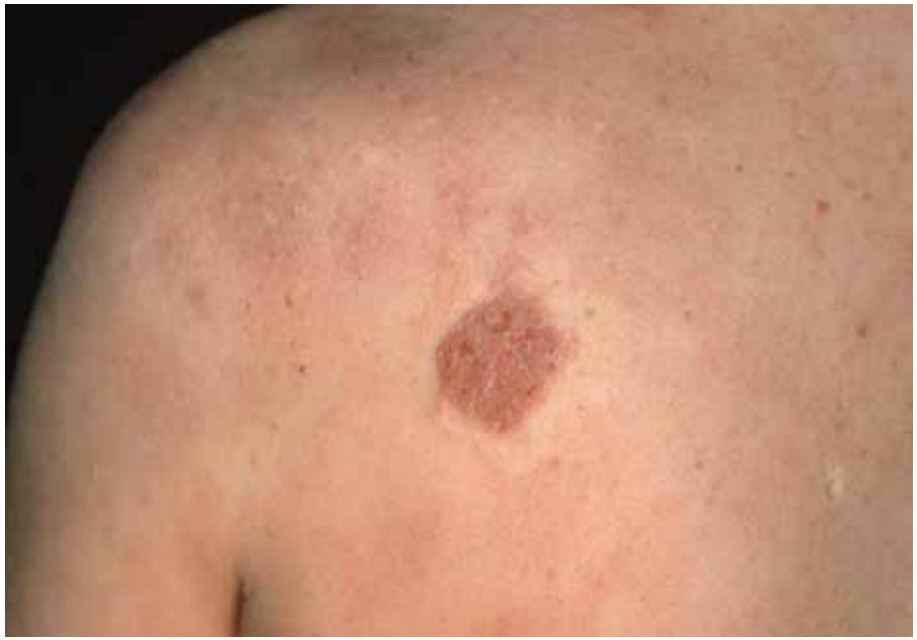


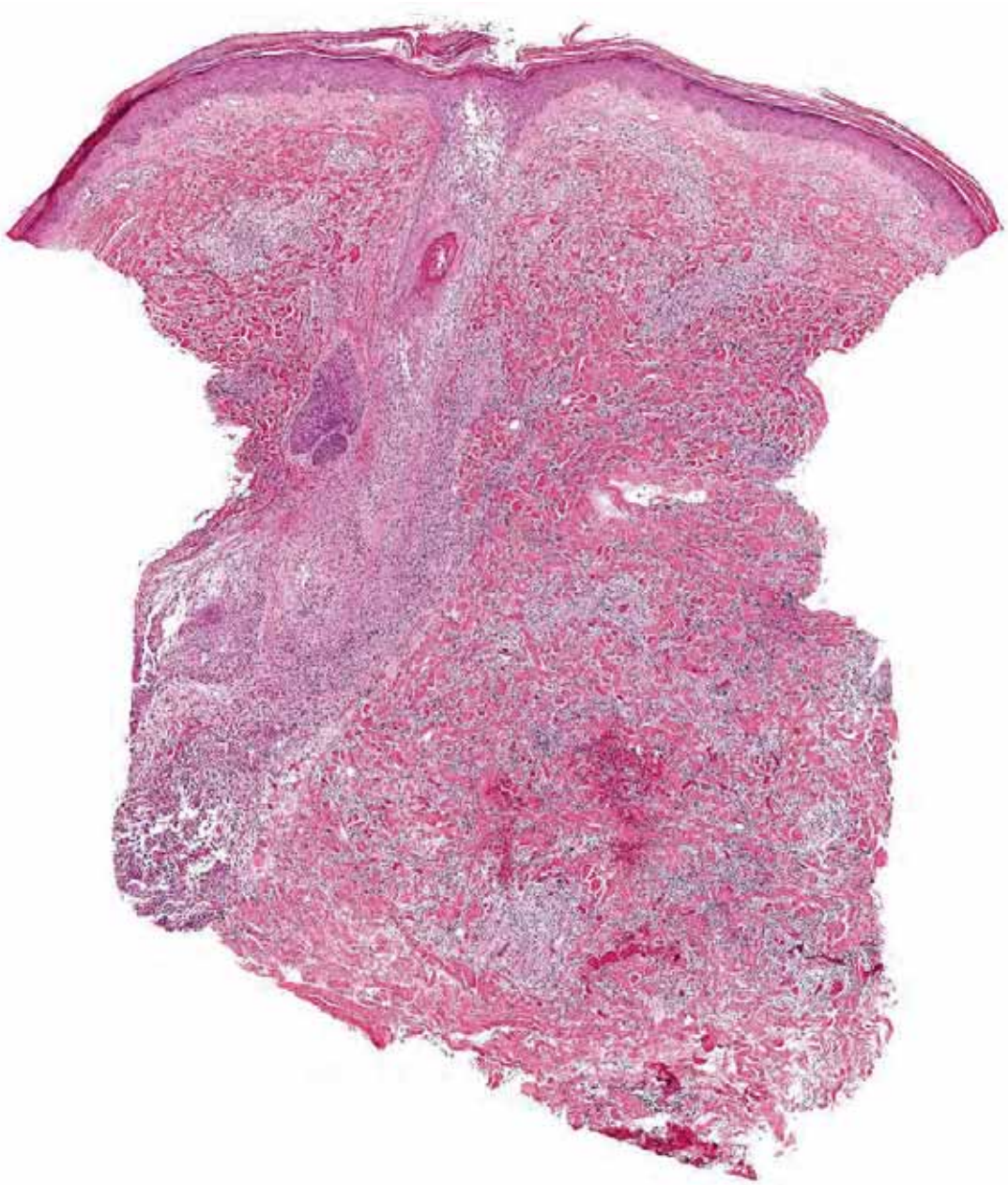
1st presentation

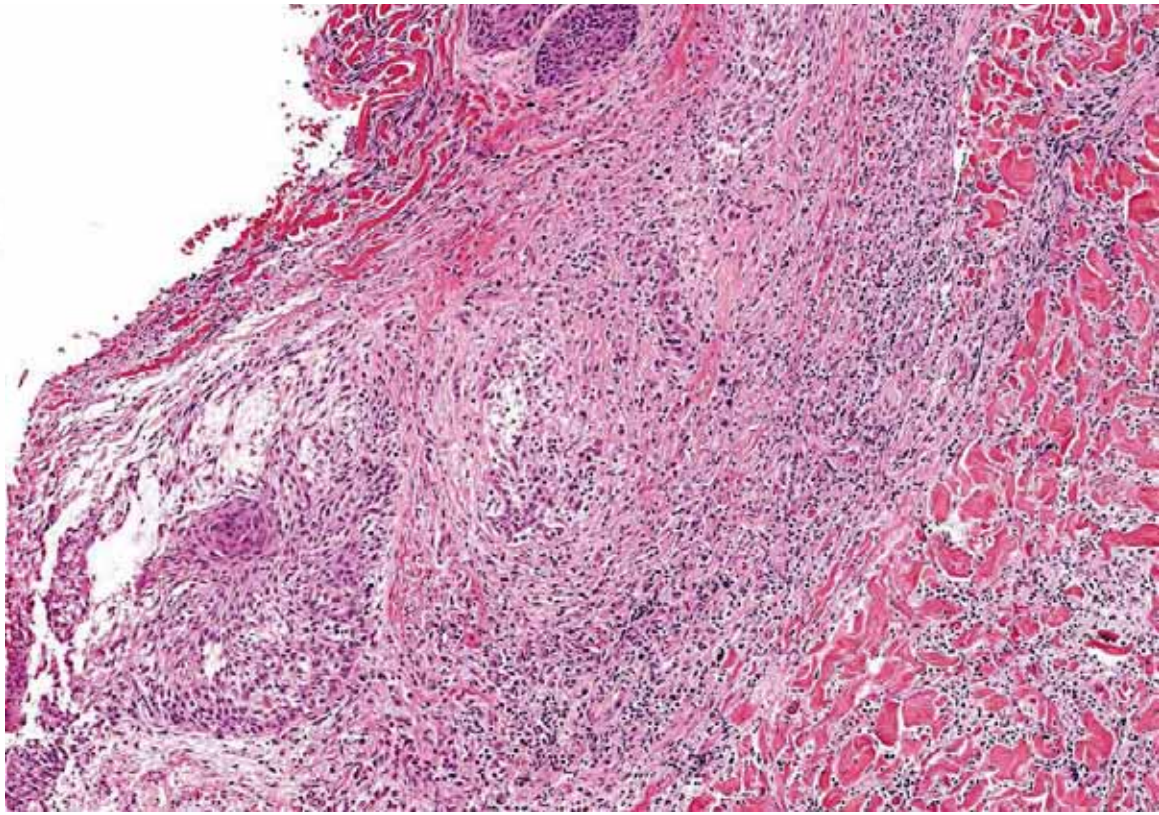
6 years later

M, 41

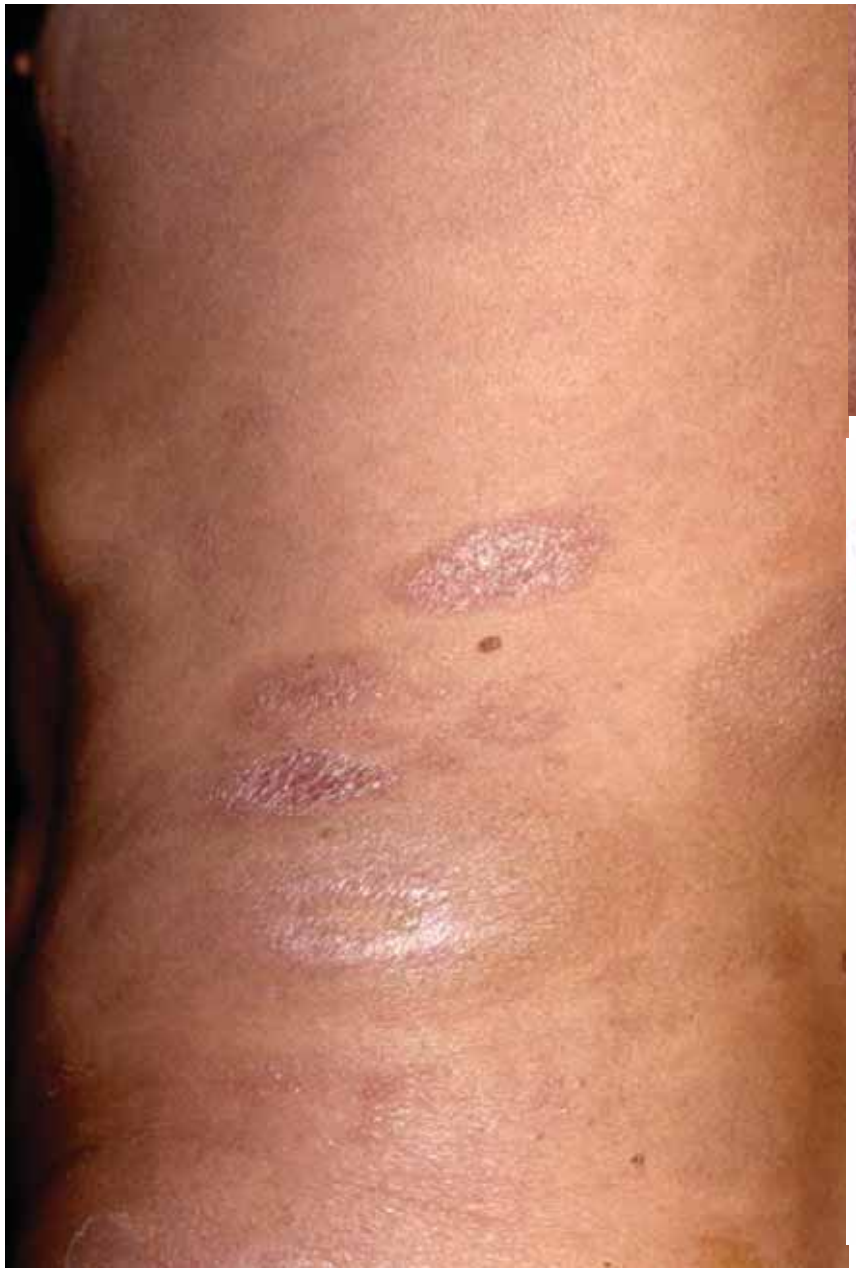
Itchy lesions with alopecia of the face for >2 years; itchy eczematous lesions with partial impetiginization on the trunk and extremities for some months.

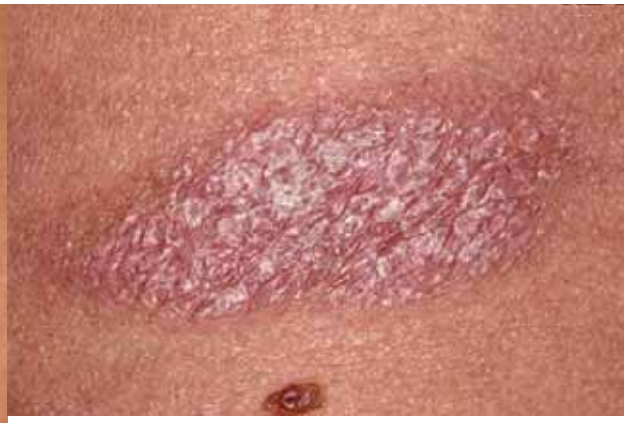


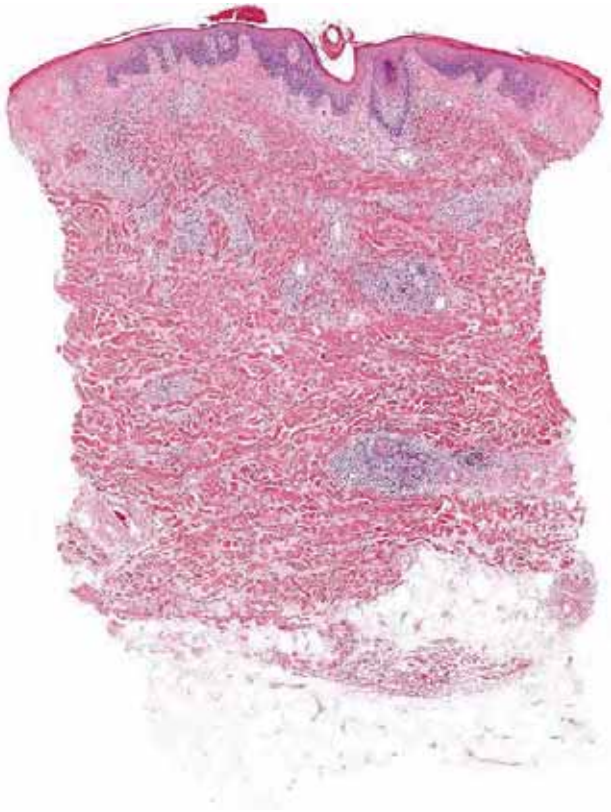


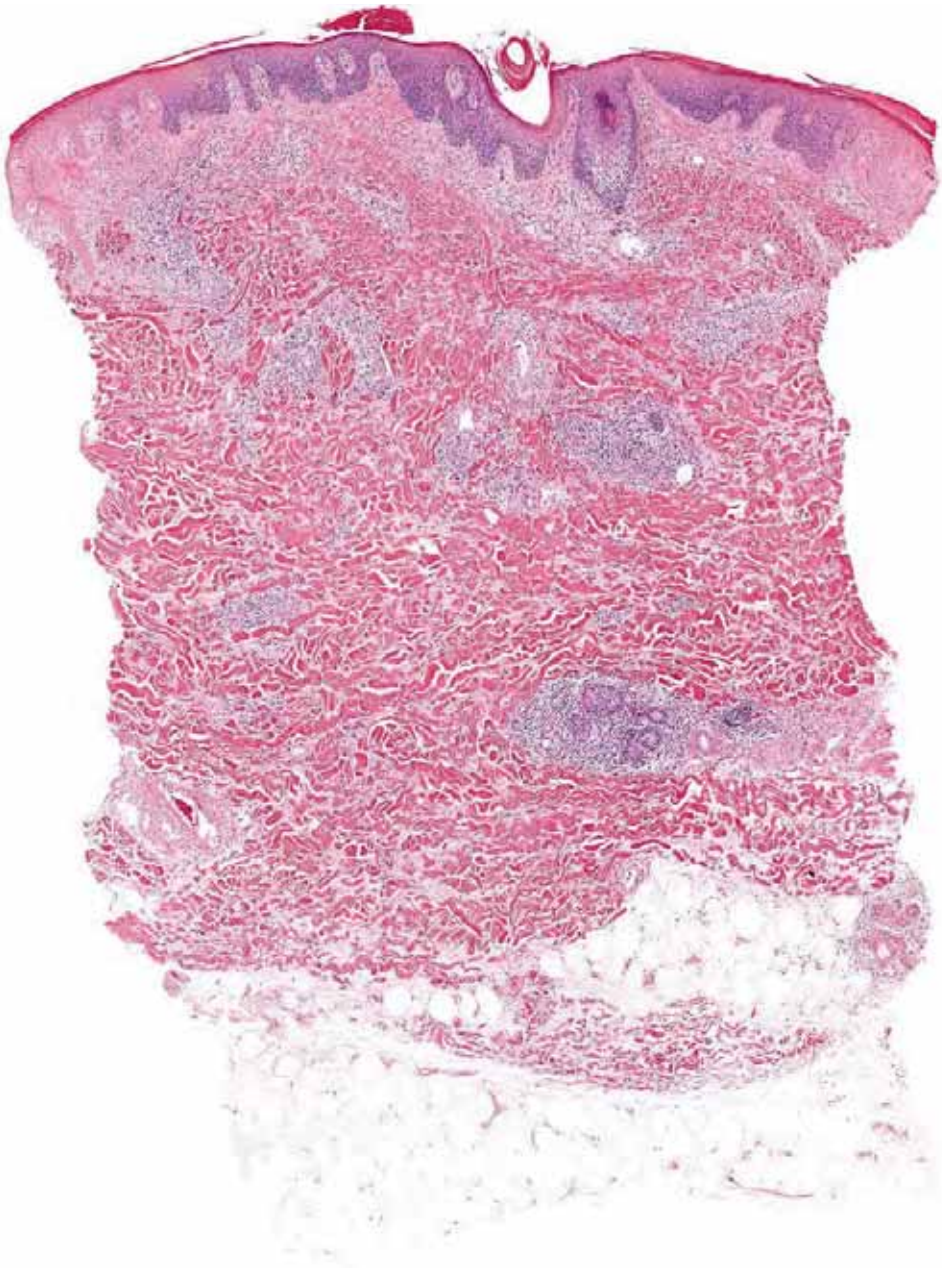


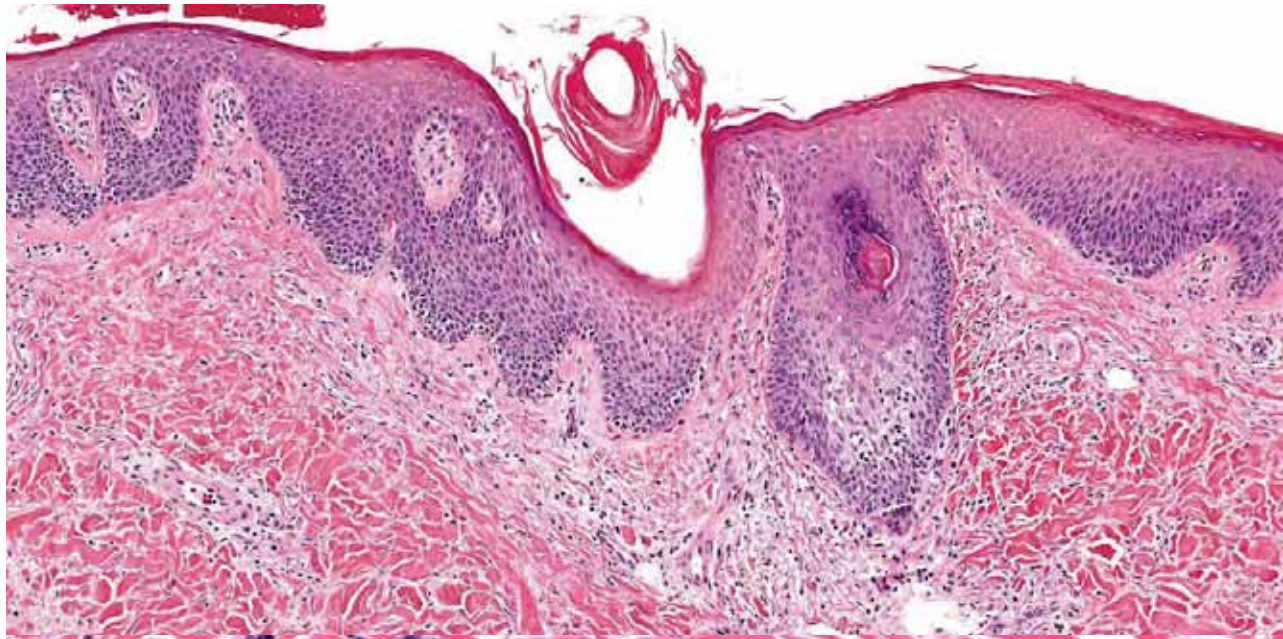
3 months later

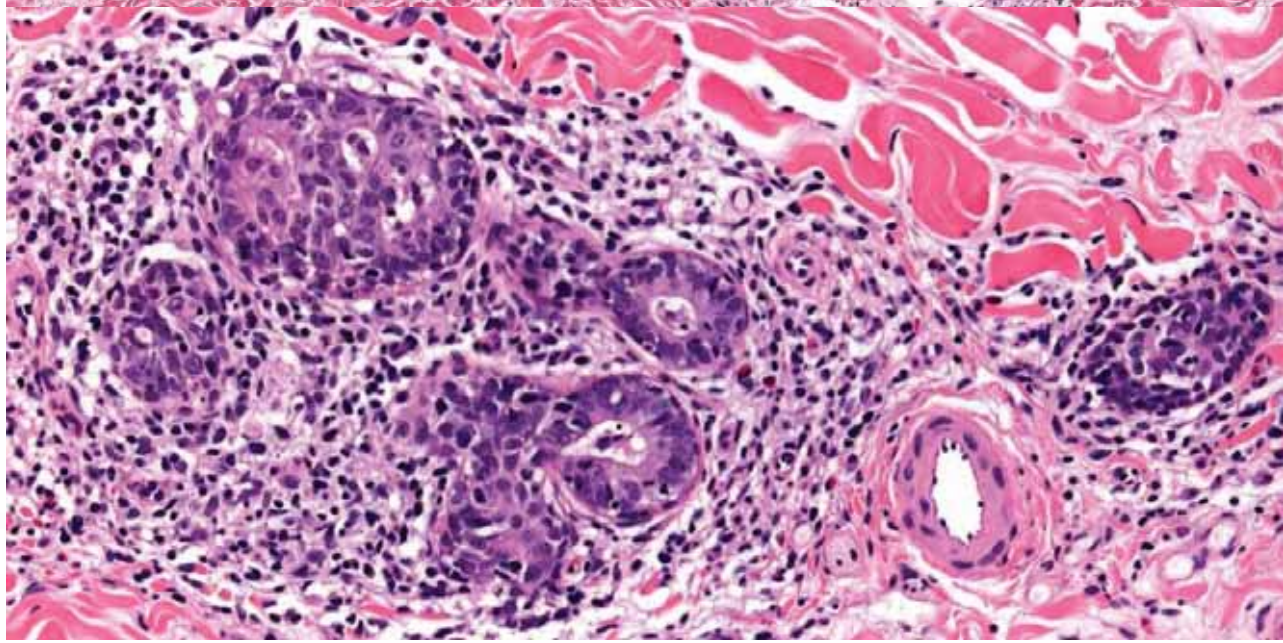


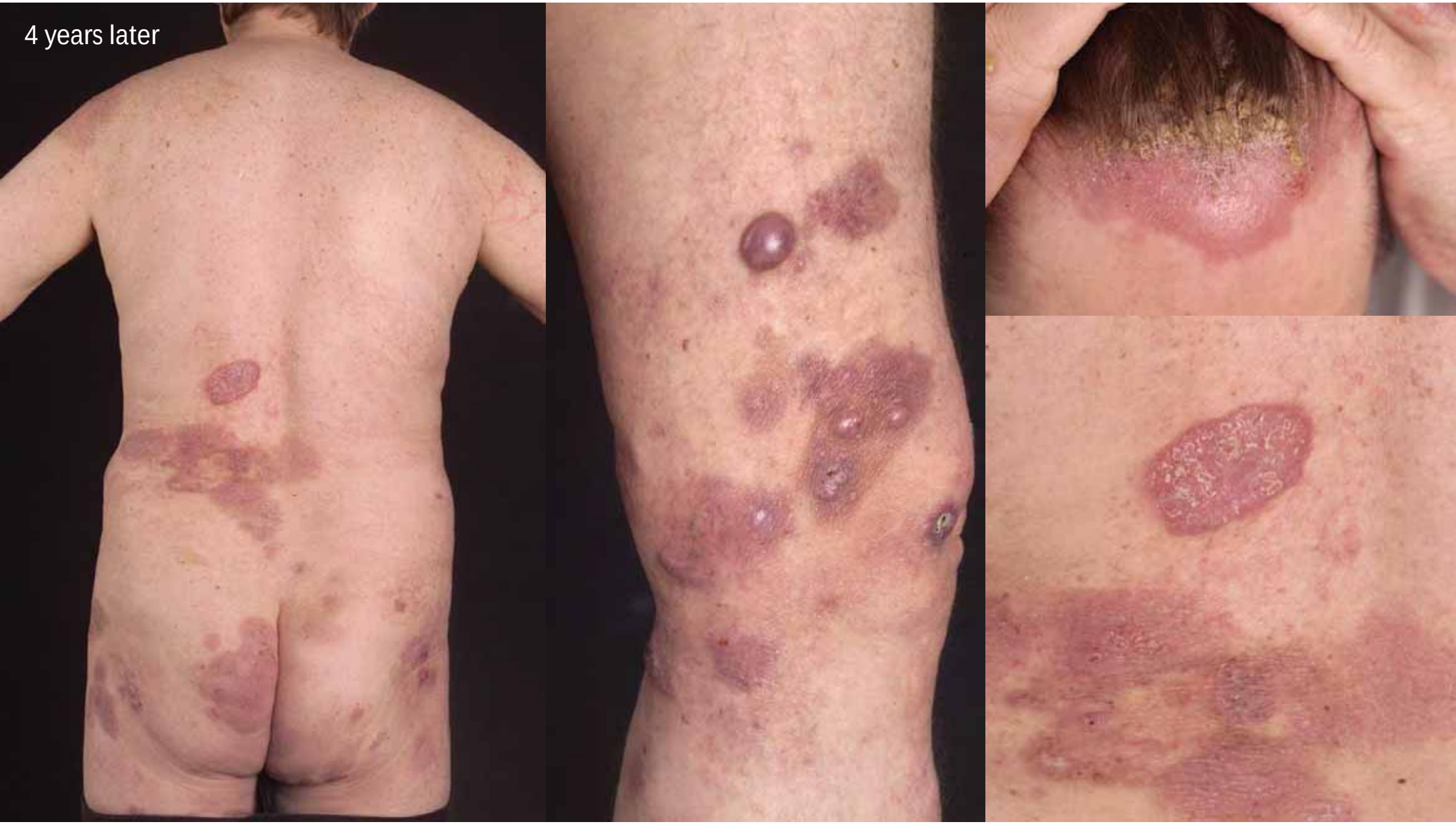


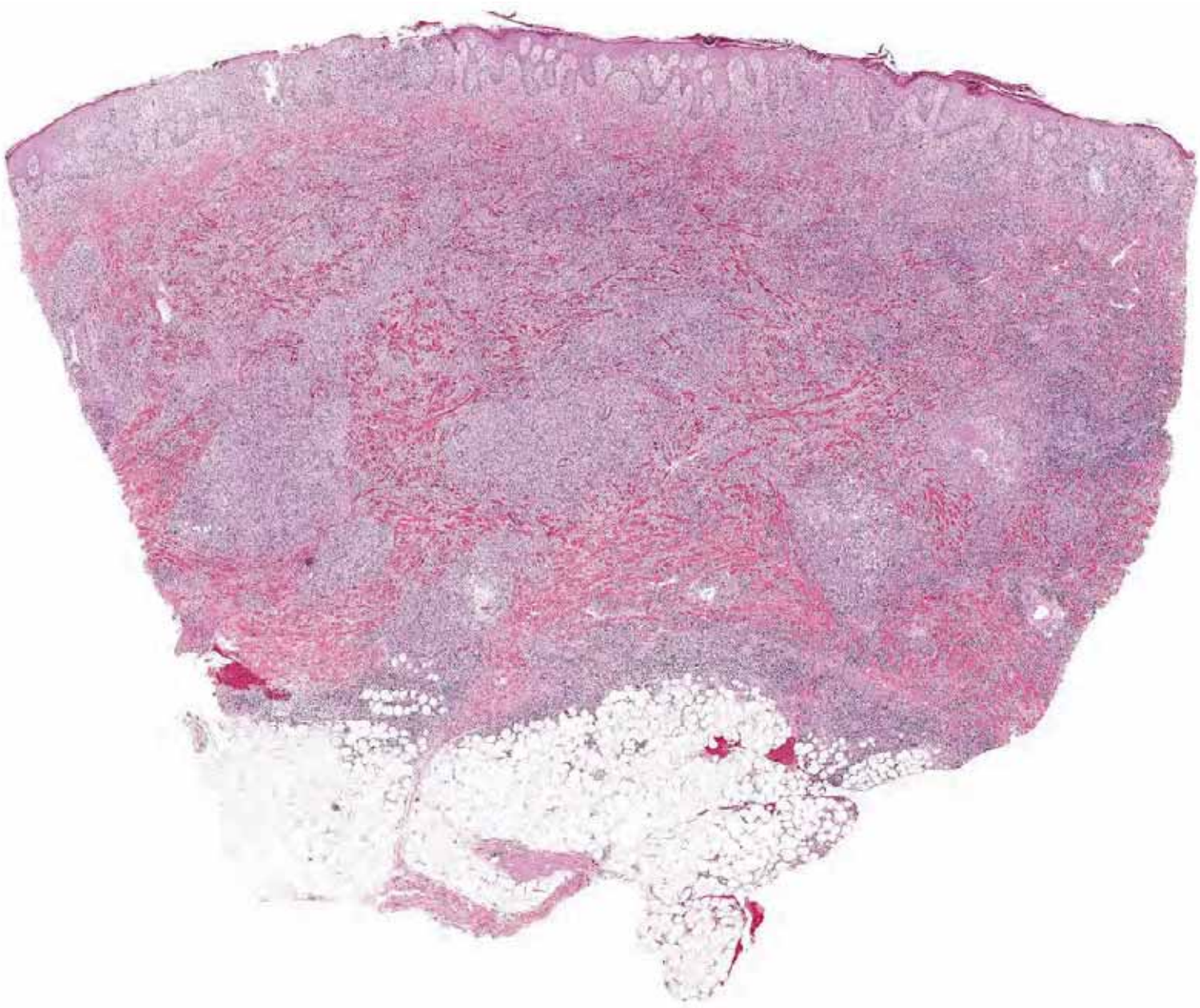


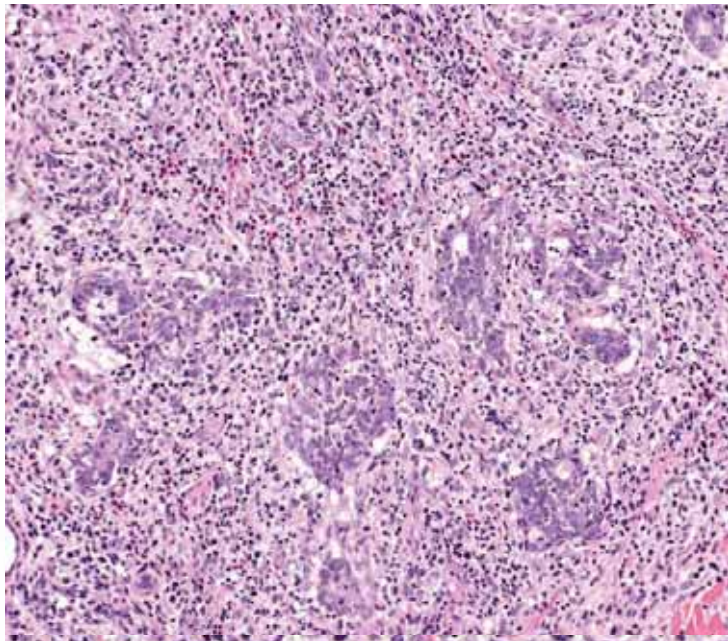


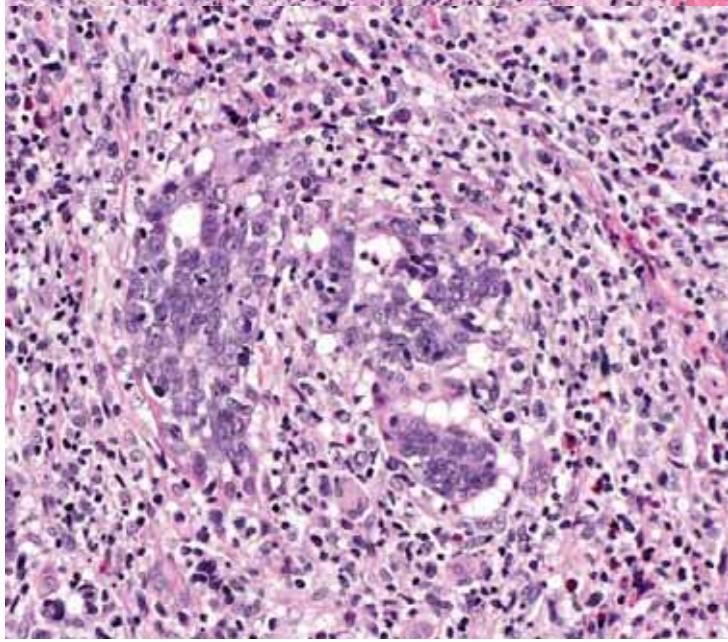


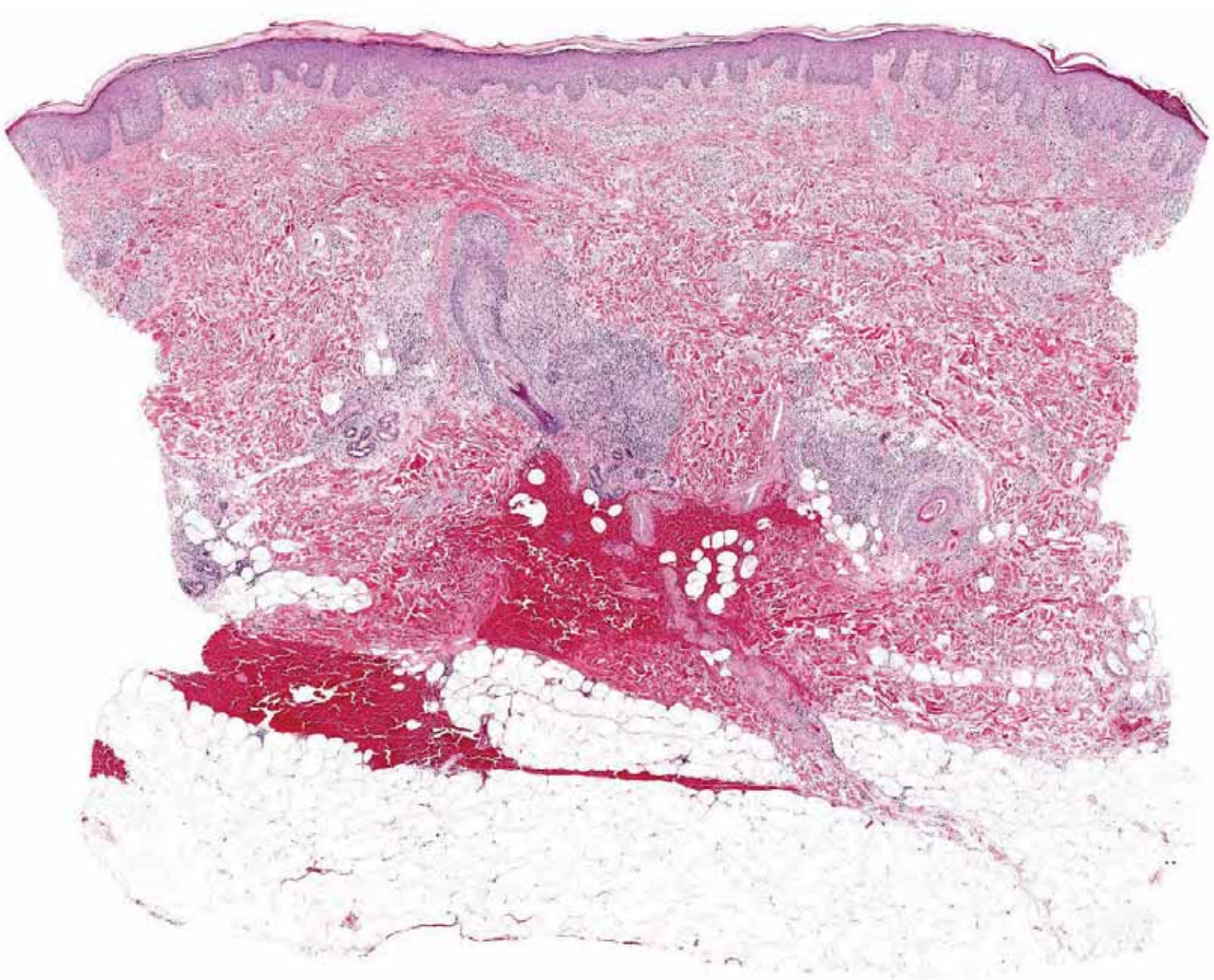


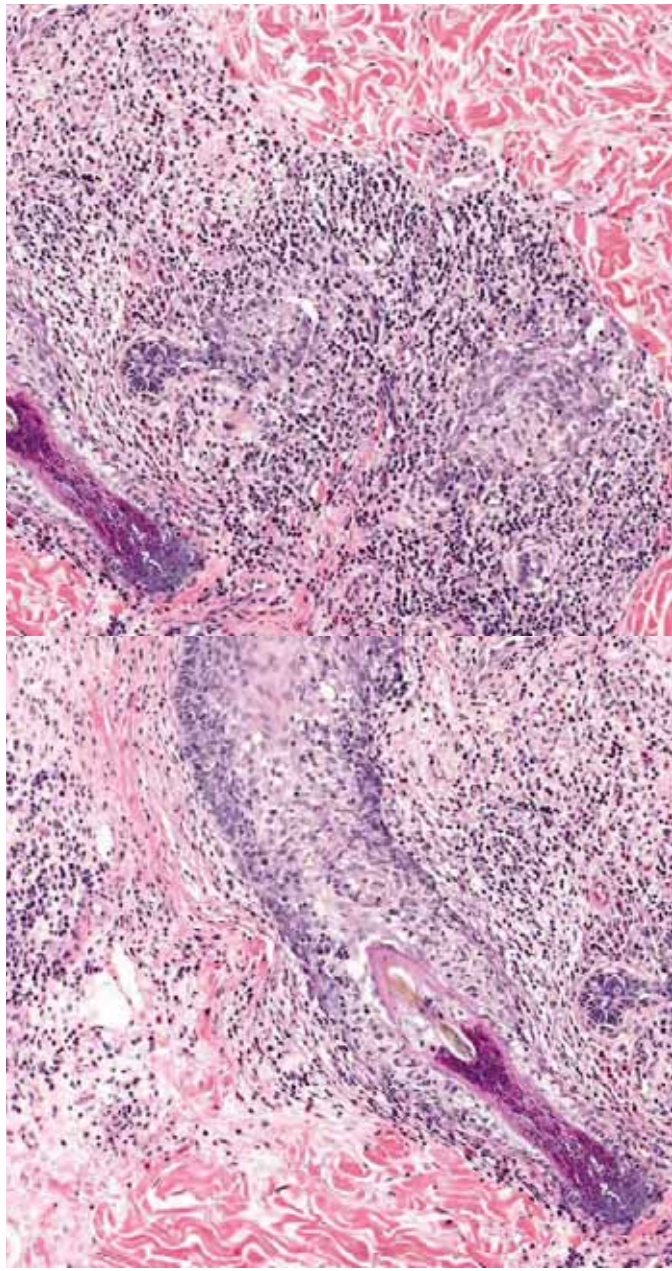

4 years later

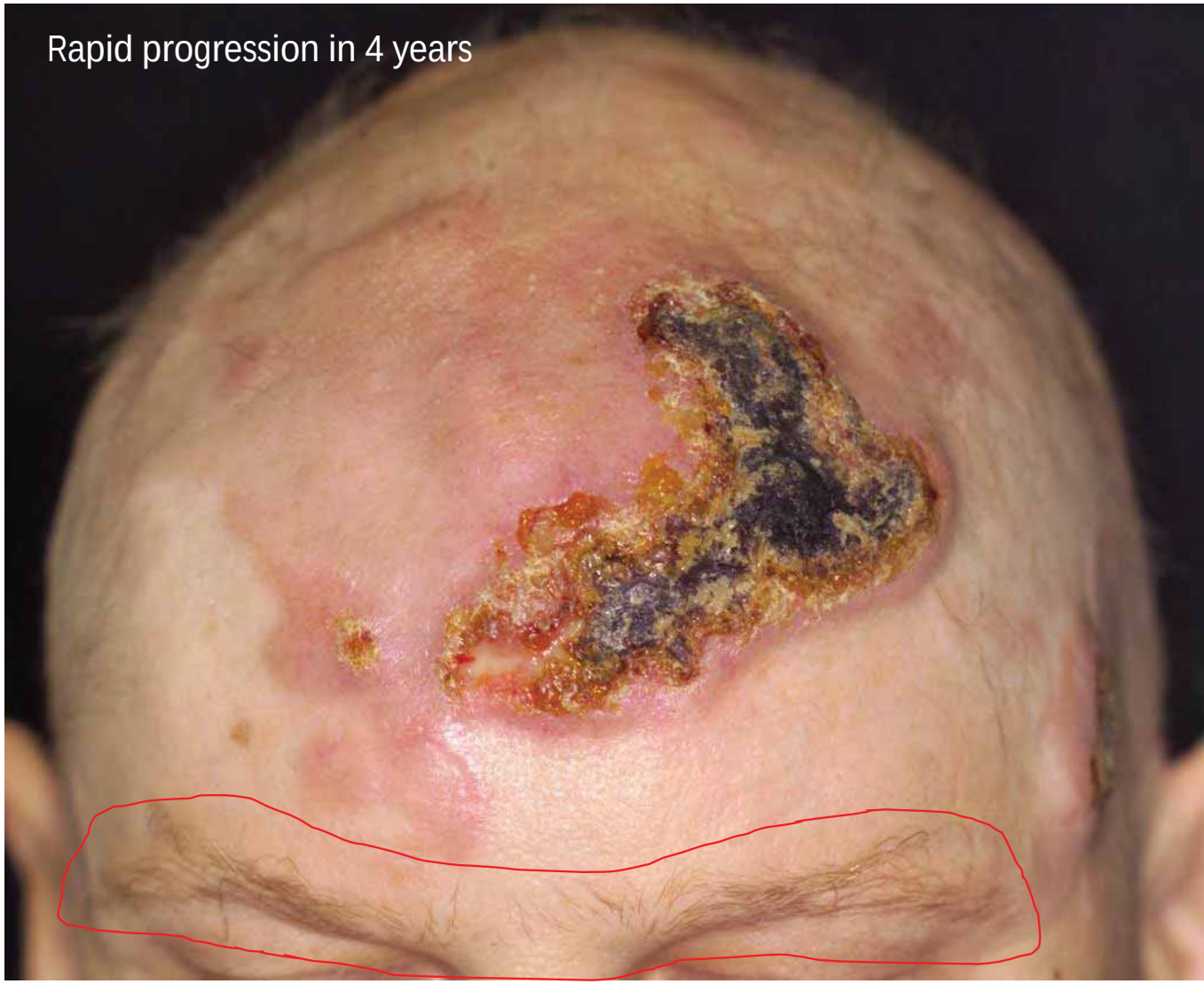


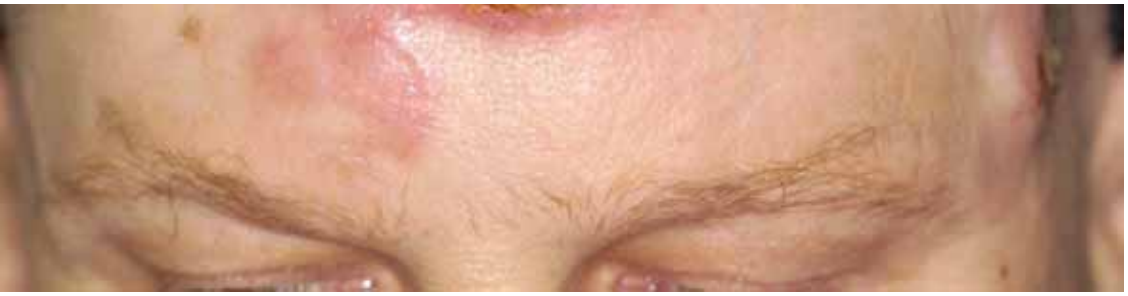




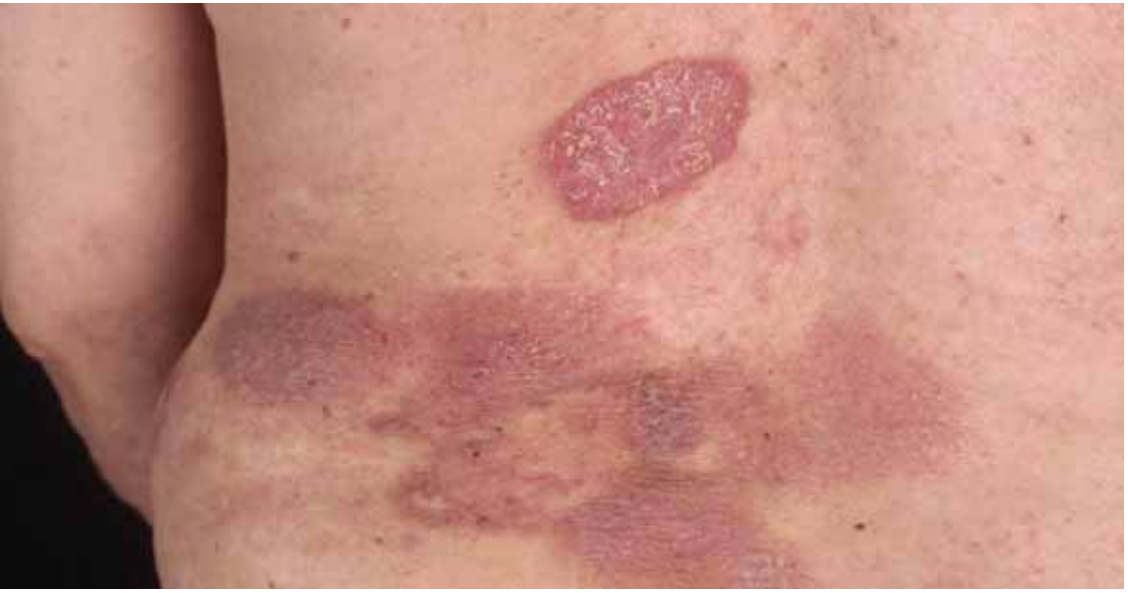




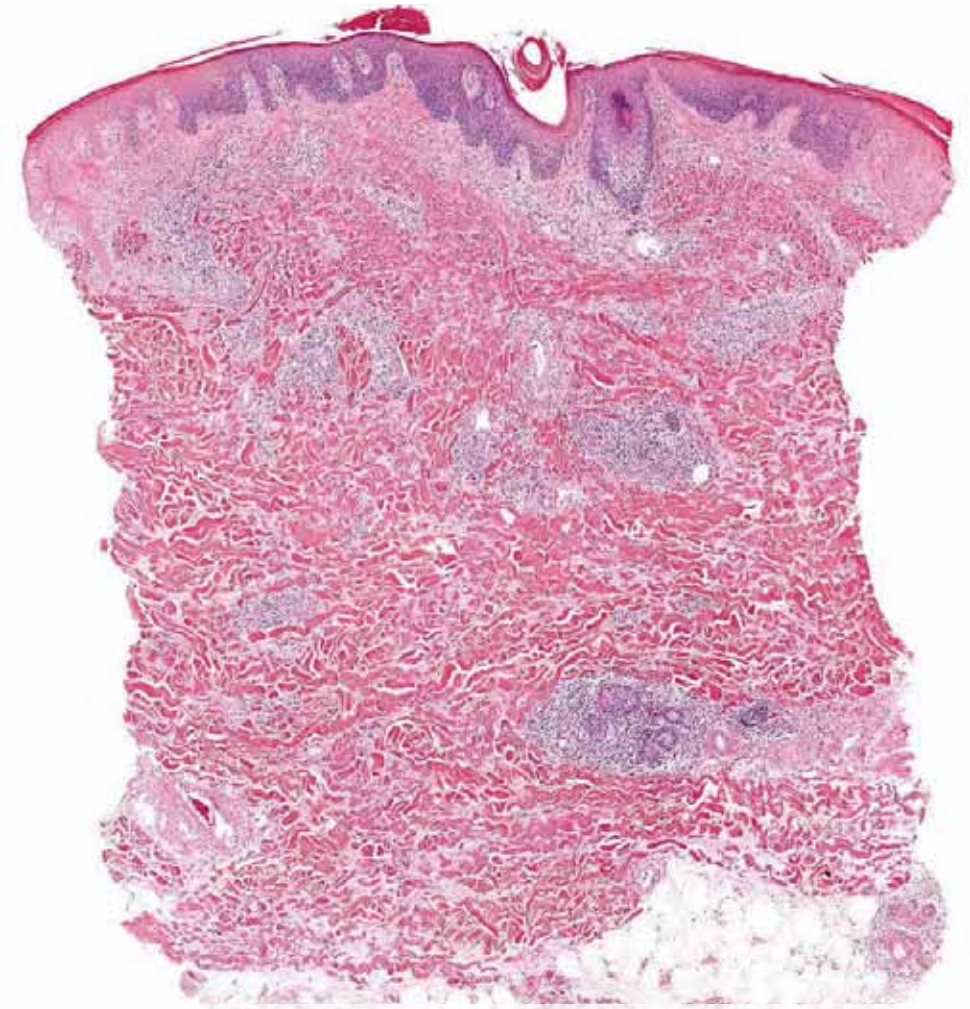

Rapid progression in 4 years



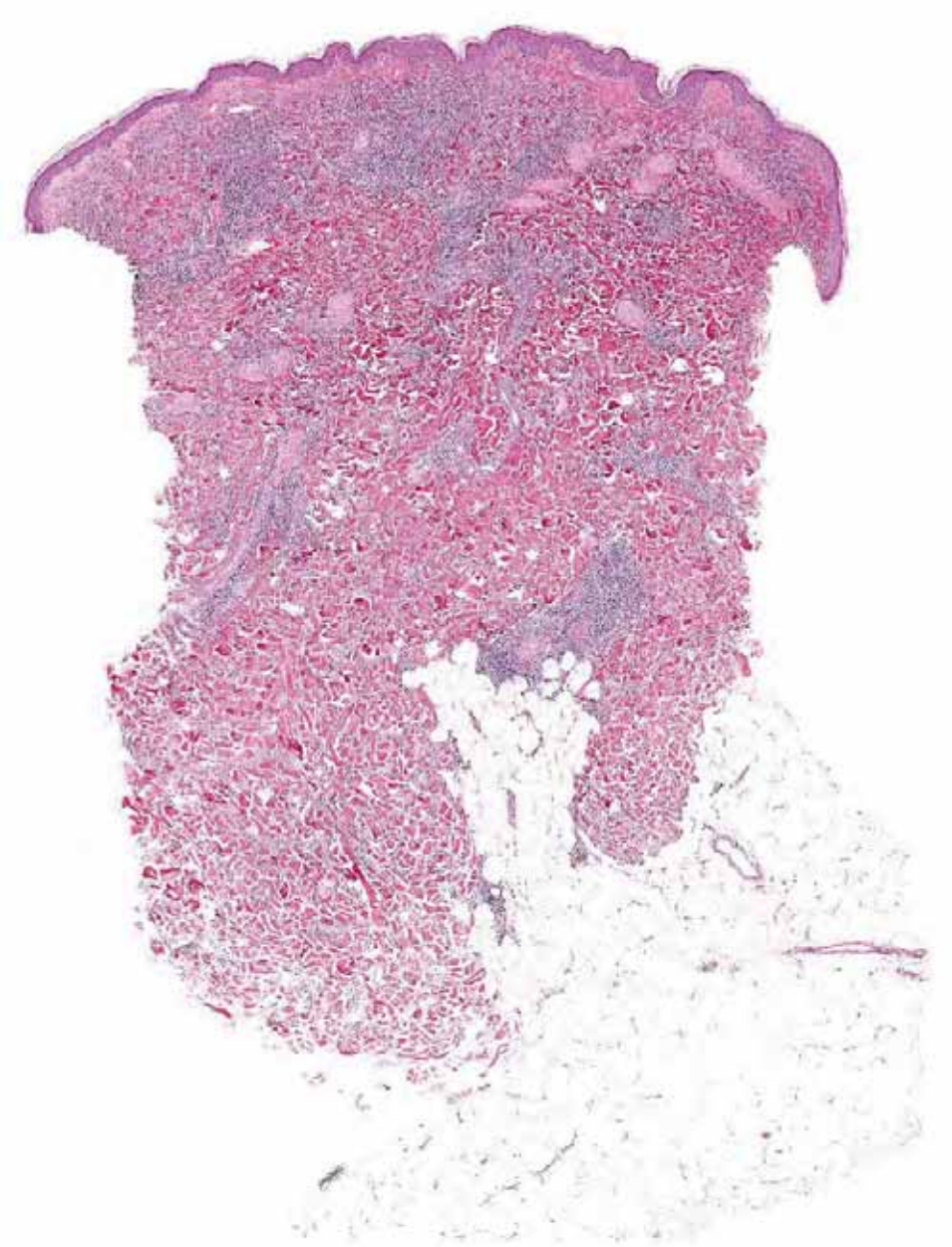
Alopecia in pilotropic MF is reversible



Pilotropic MF may present also "conventional" lesions of MF

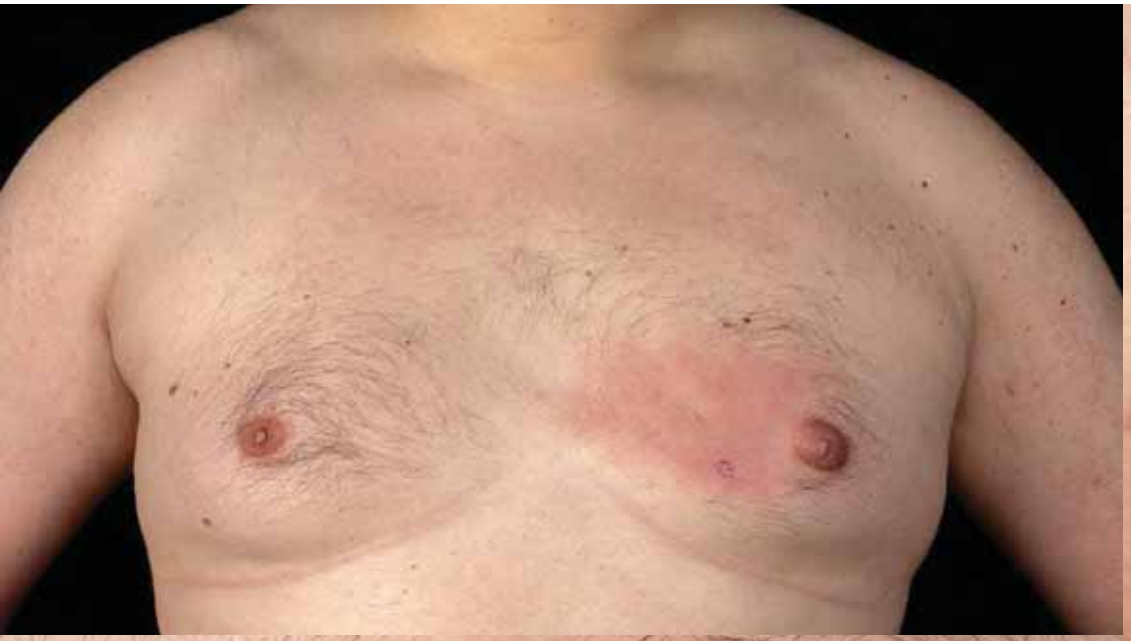
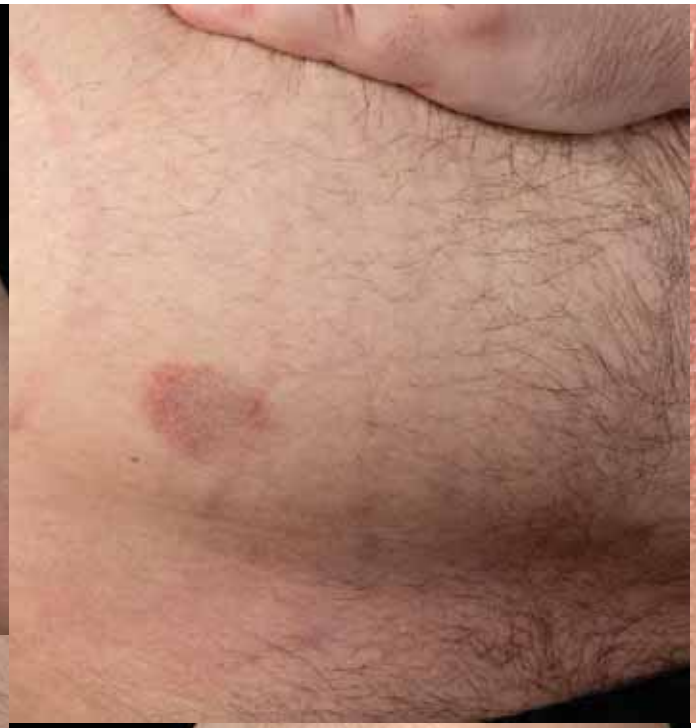


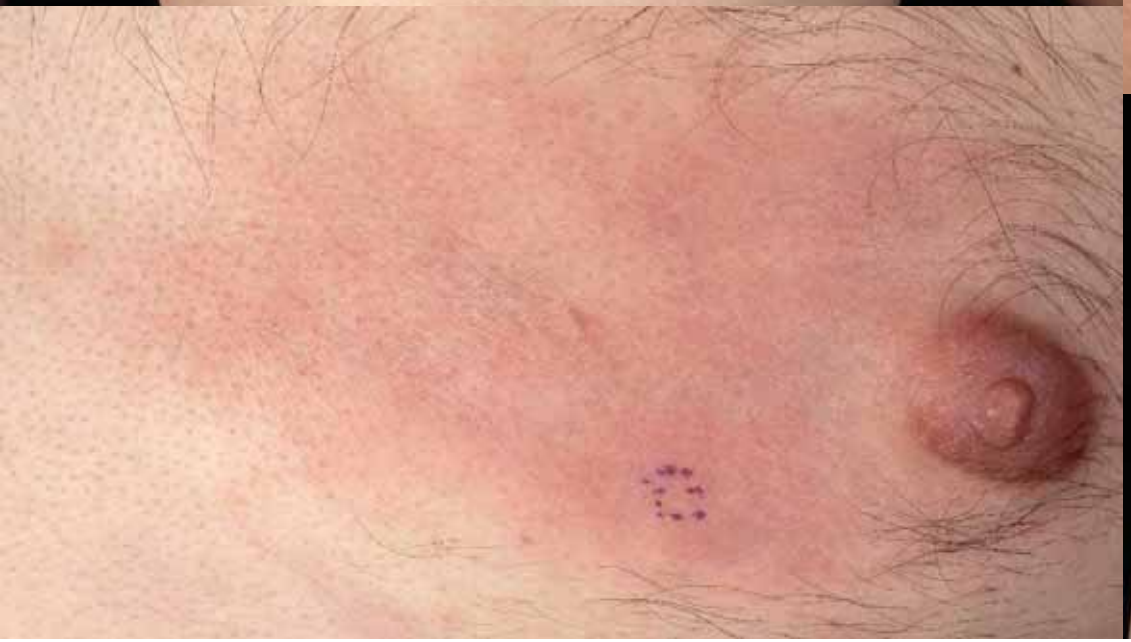
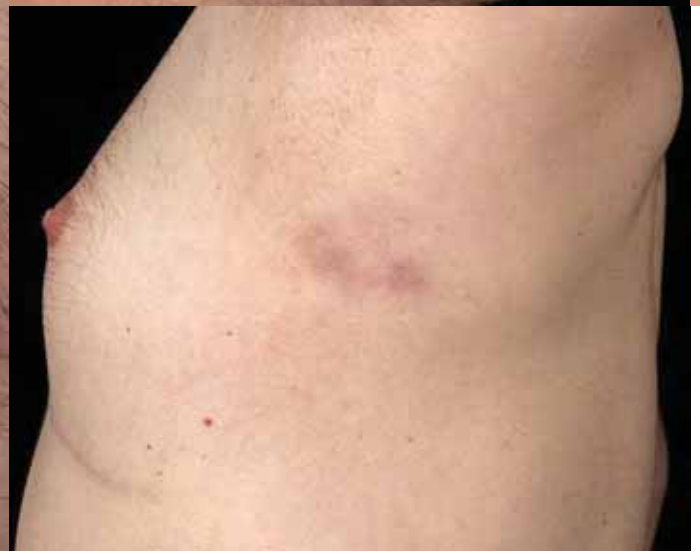
"Pilotropic" MF is commonly syringotropic as well (and pilotropism may be minimal or absent in some biopsies)

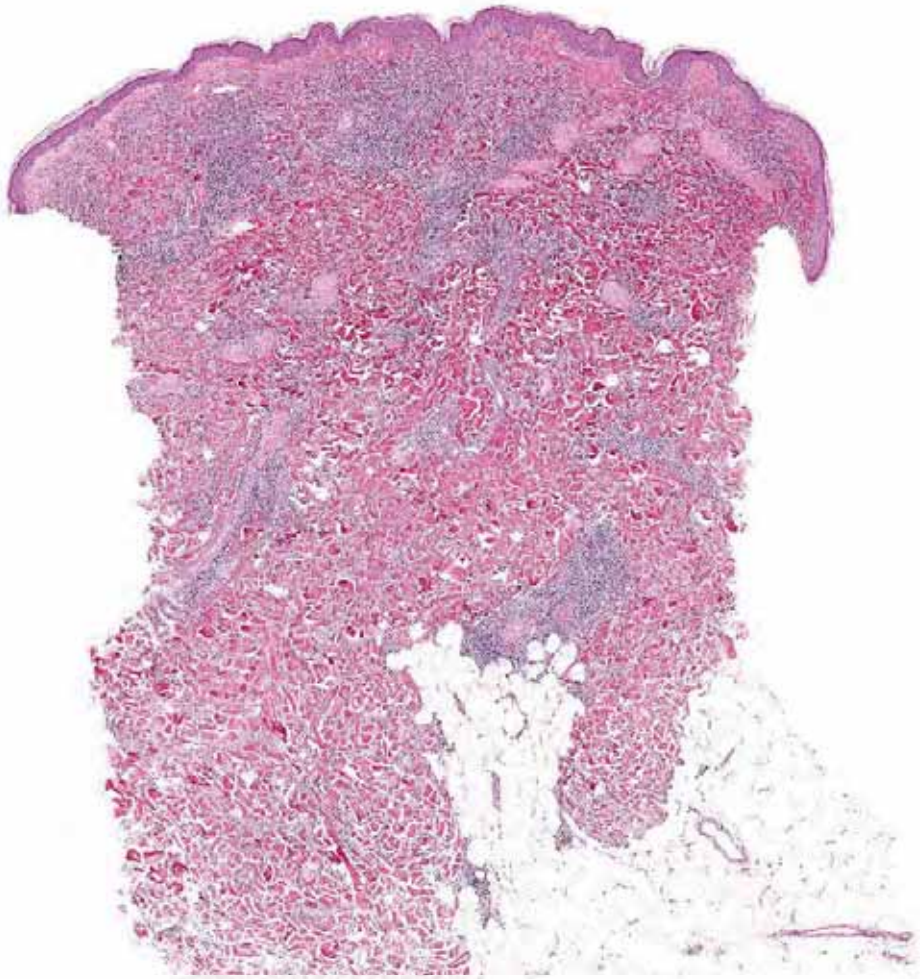


M, 32

According to the patient asymptomatic skin lesions starting on the breast 7-8 months before observation.

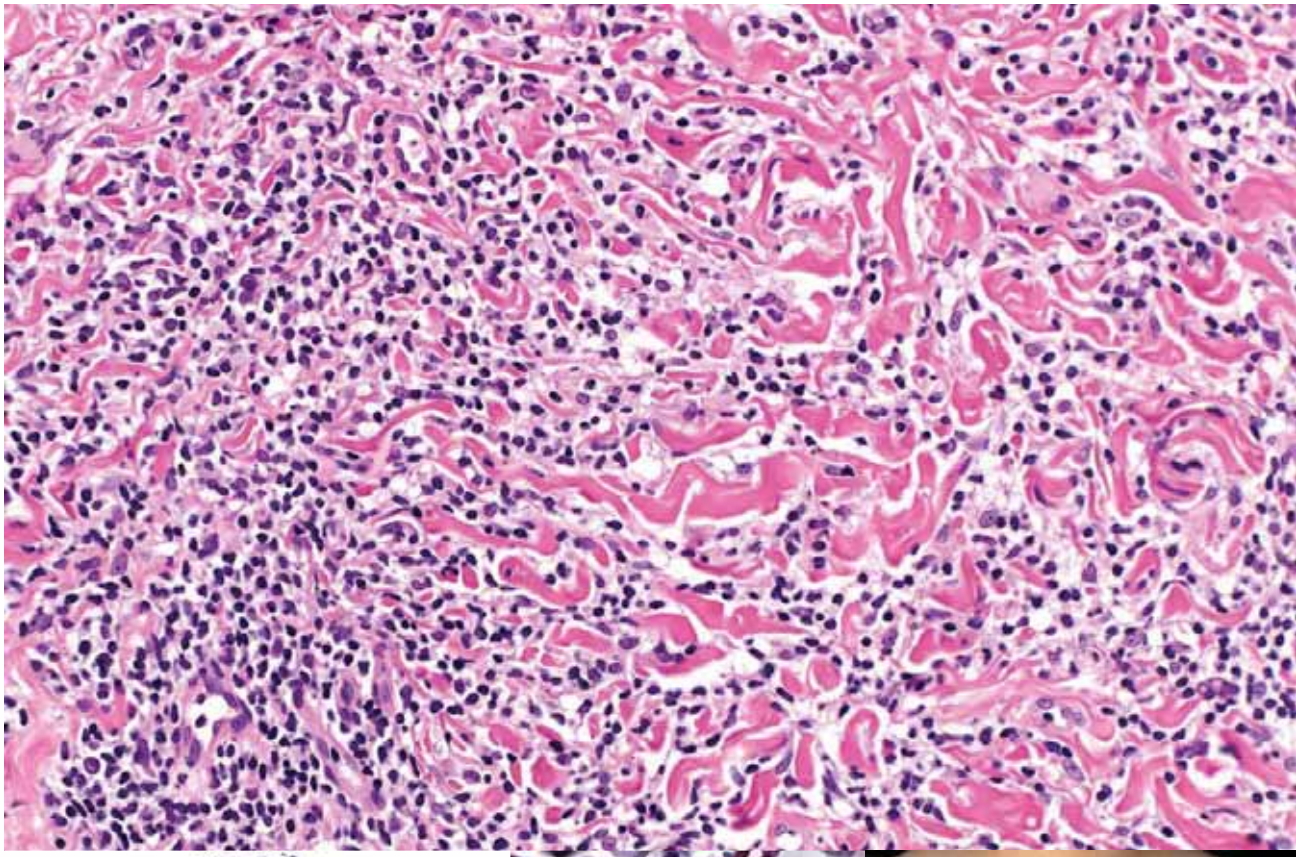



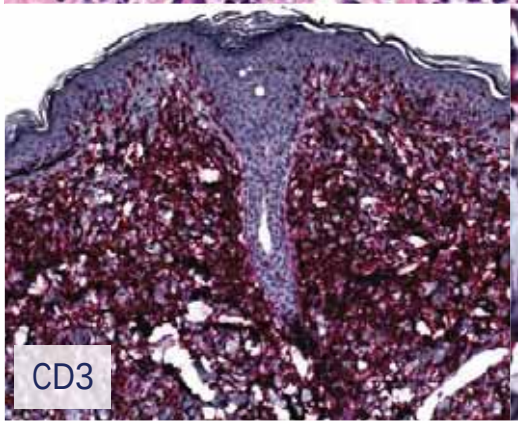



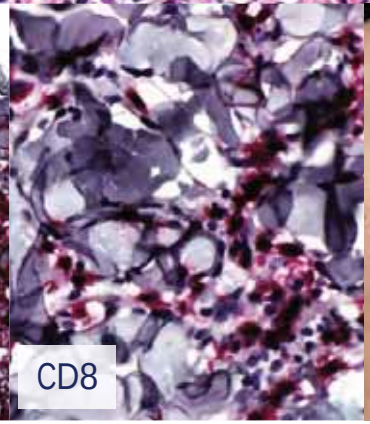



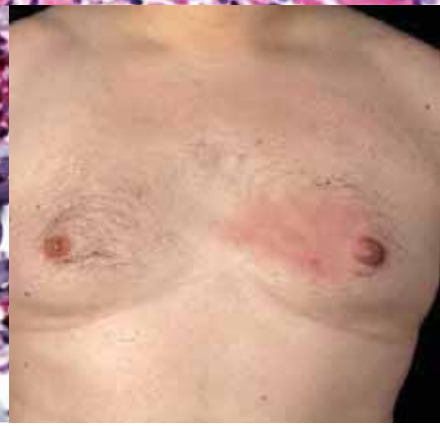
Mycosis fungoides

interstitial; clinically pilotropic

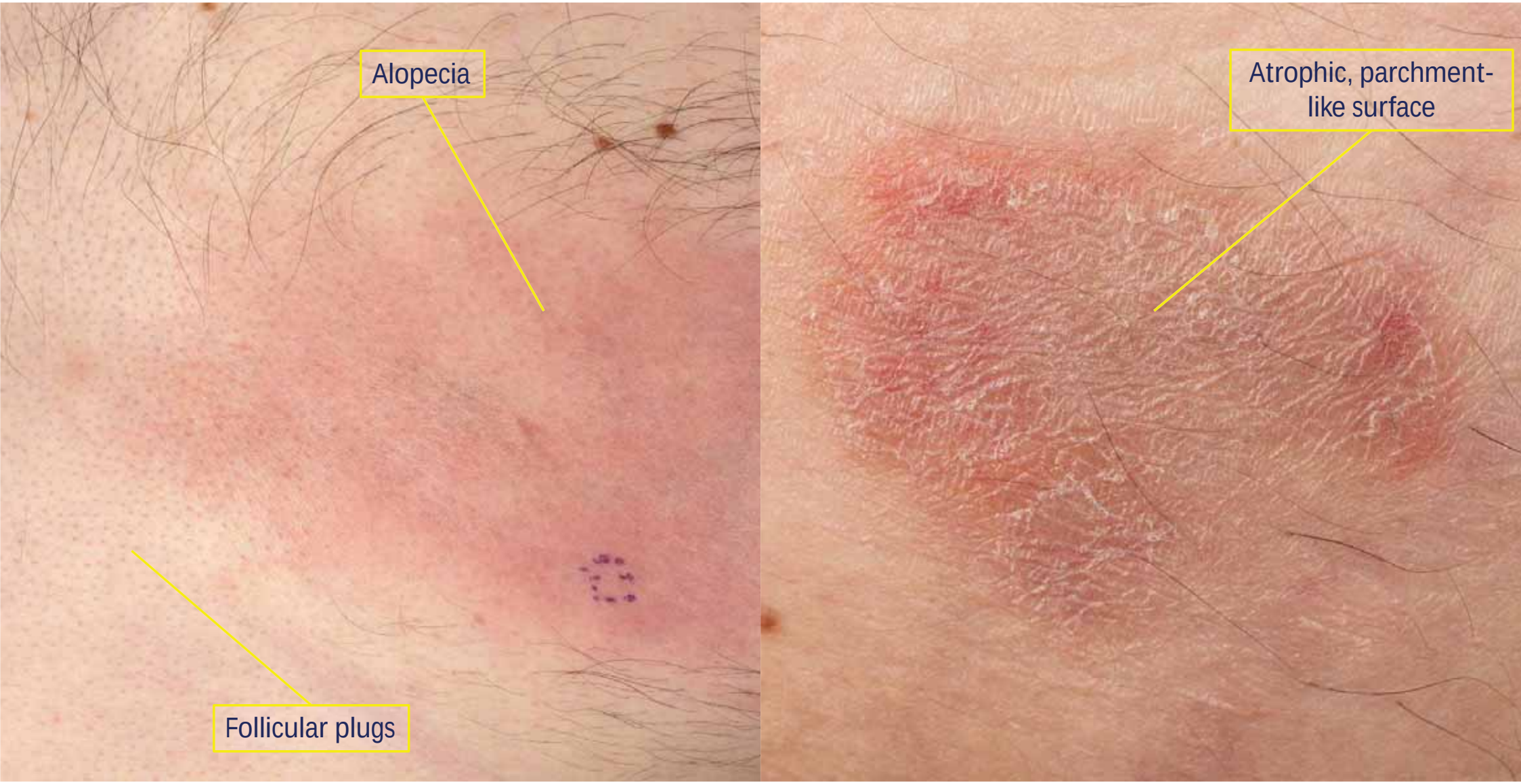


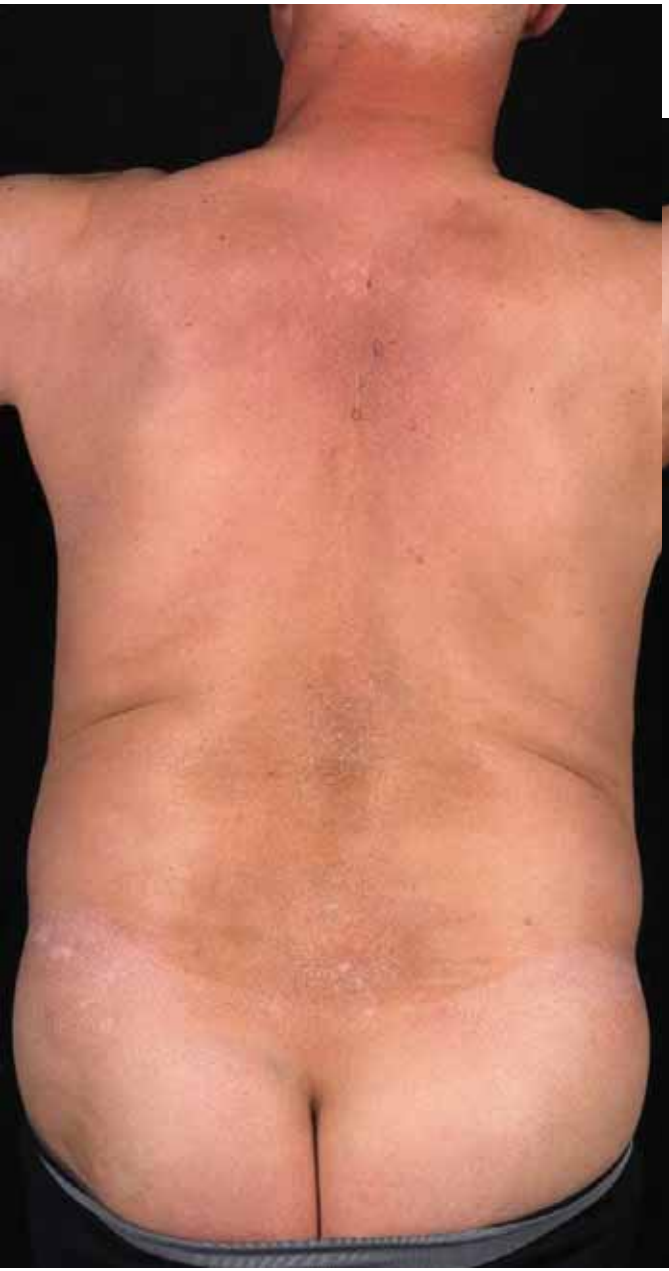


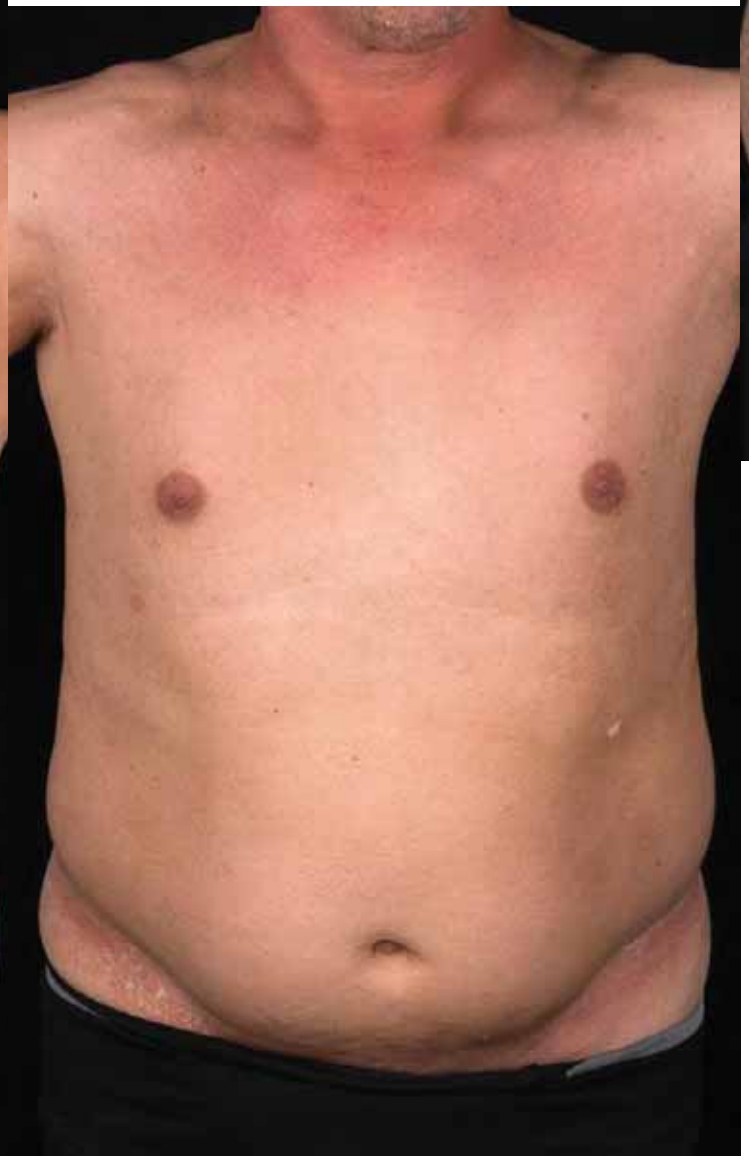


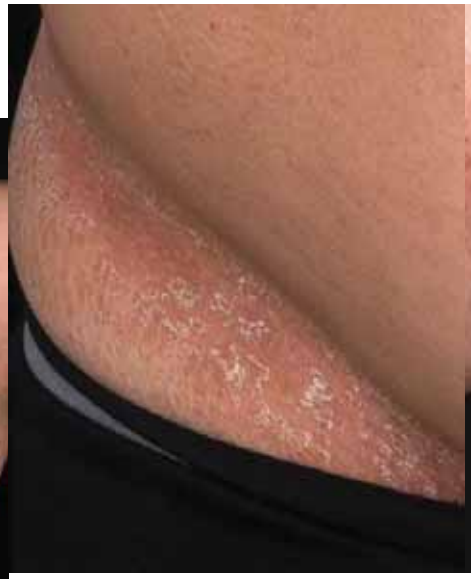


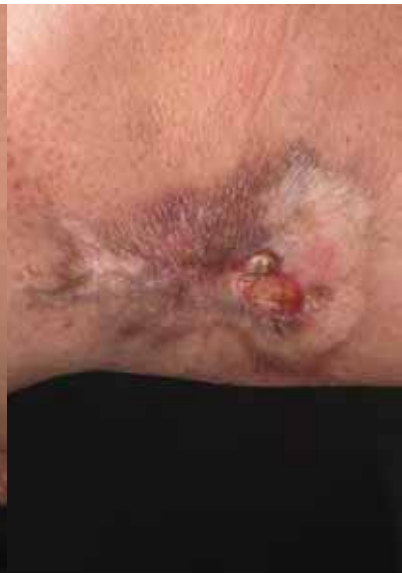
Clinical clues











M, 47

Patient comes from a neighboring country.

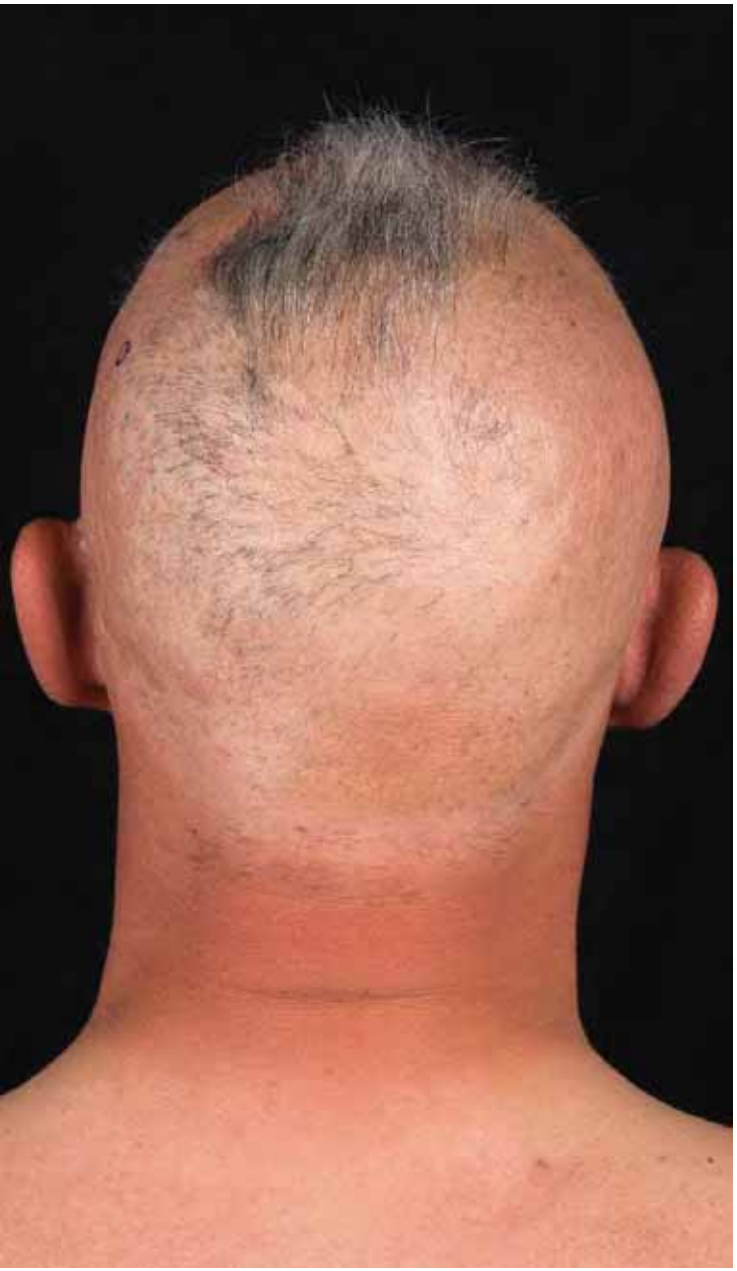
History of surgical excision of a lesion on the lateral aspect of the right knee with prolongued wound healing, reported as "tumoral T-cell proliferation, probably MF".

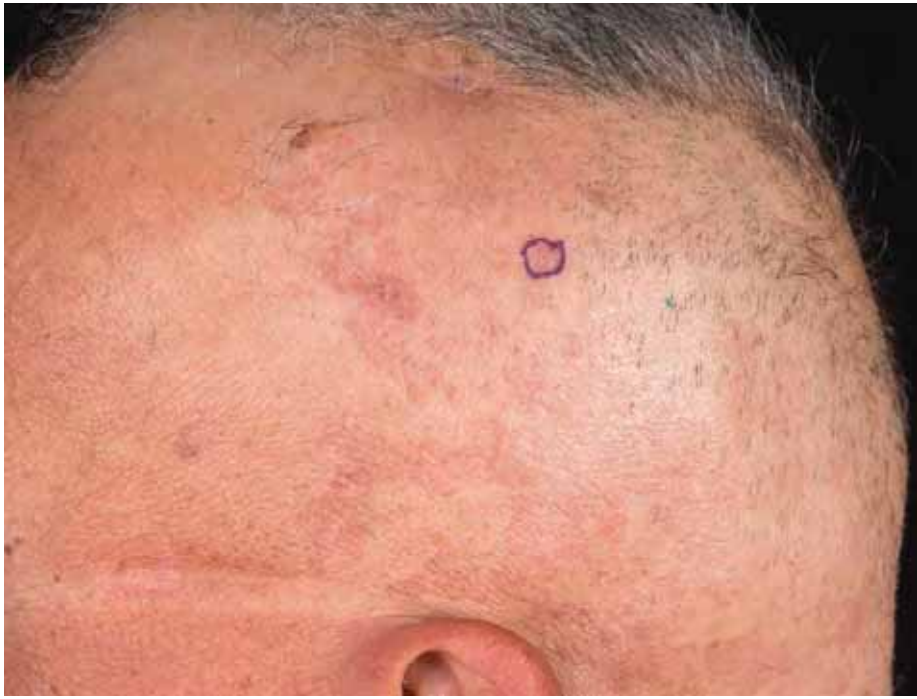
Subsequently alopecia and onset of lesions on the right sole. In the last 3 months ichthyosiform skin lesions on the legs.

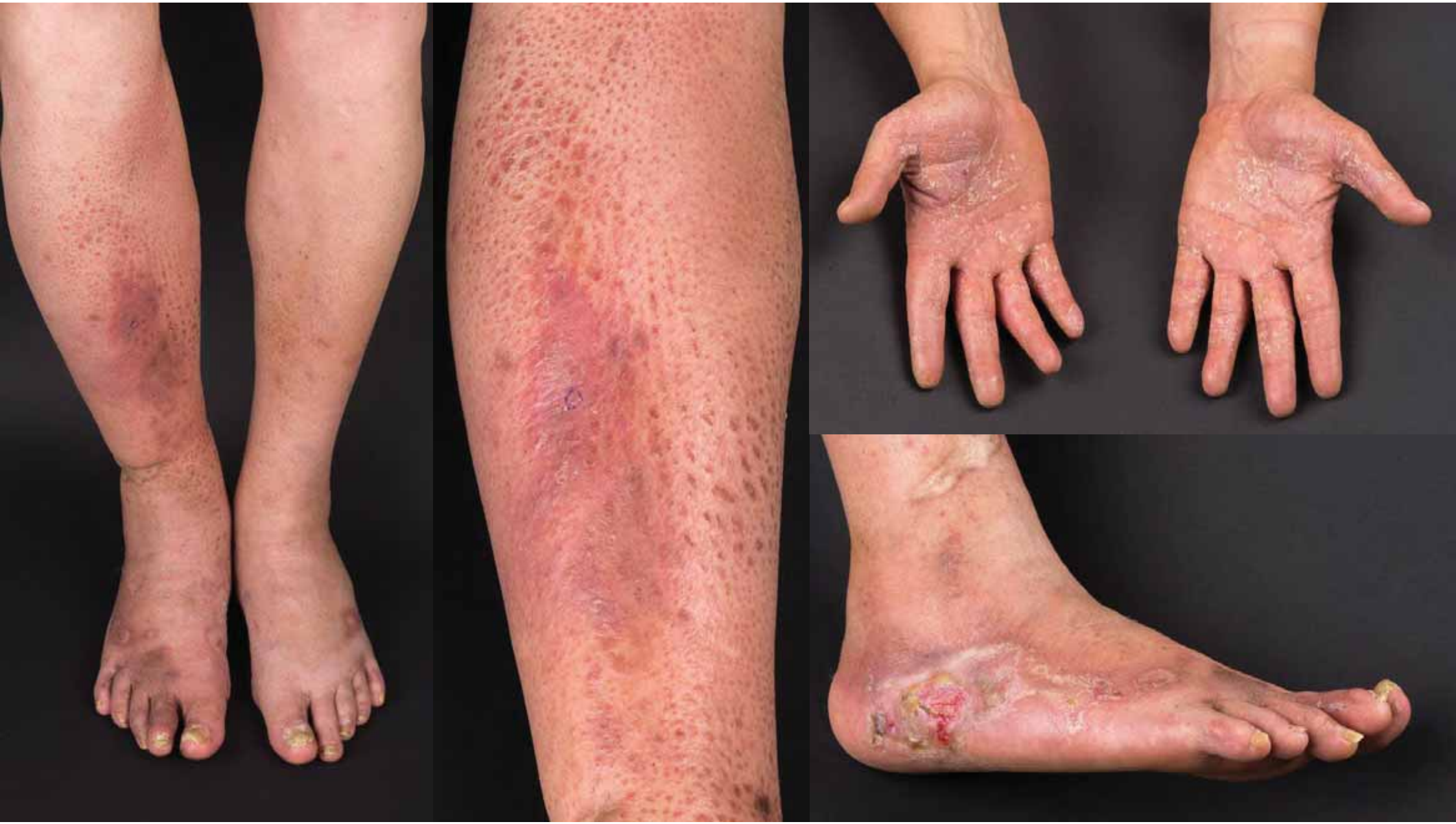
Scaly lesions on the palms since years.

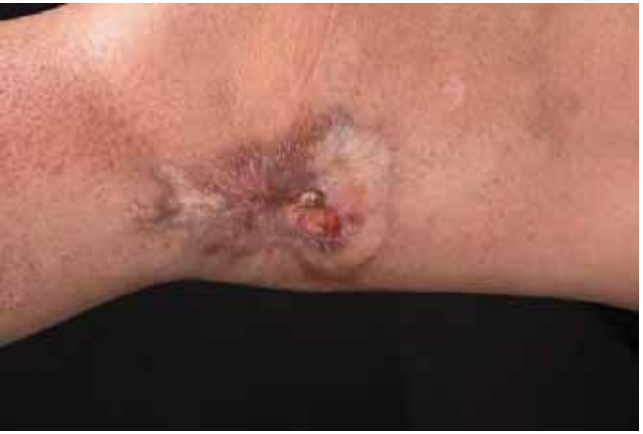
At present treated with acitretin; previously MTX, PUVA without improvement.

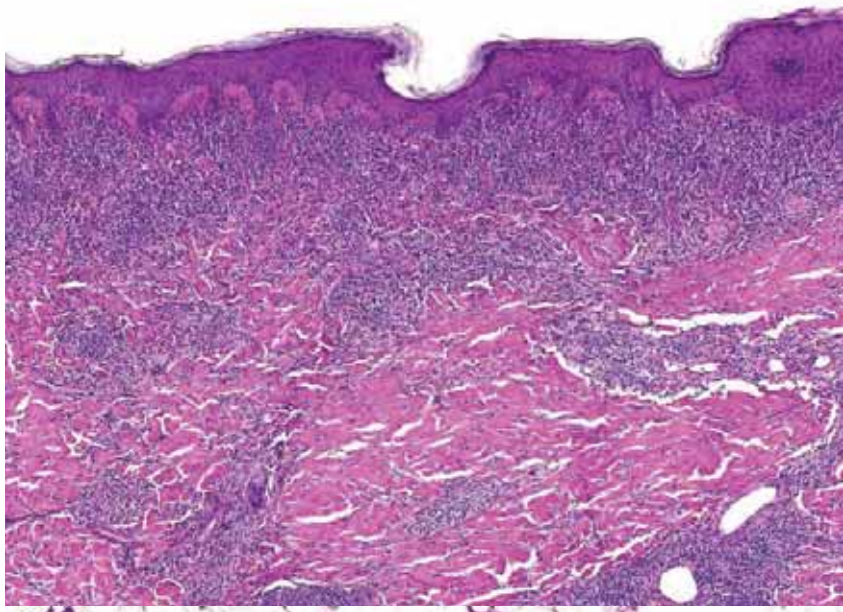
Two biopsies are taken (scalp, leg).

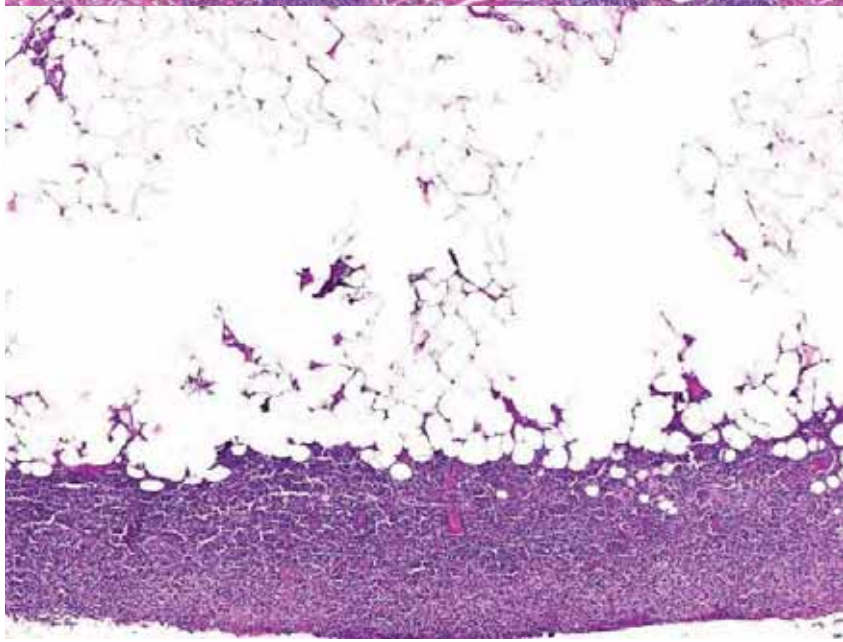




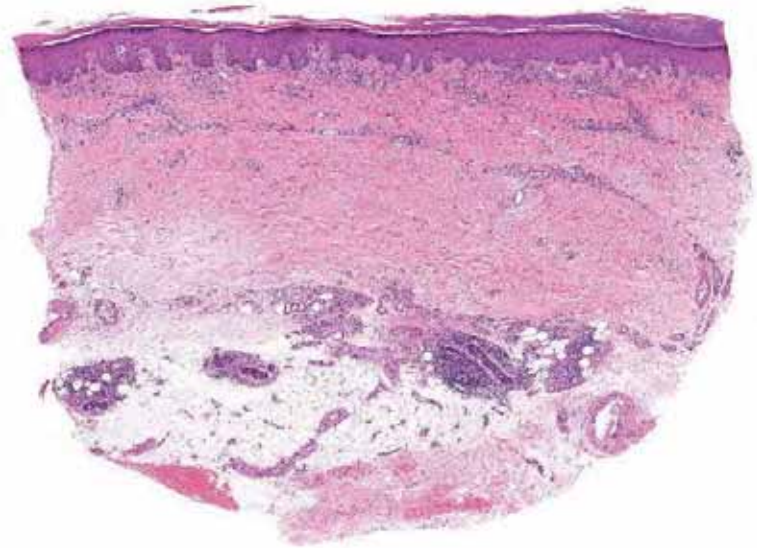
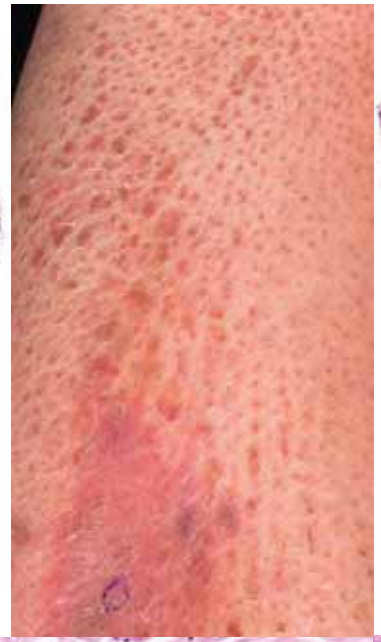
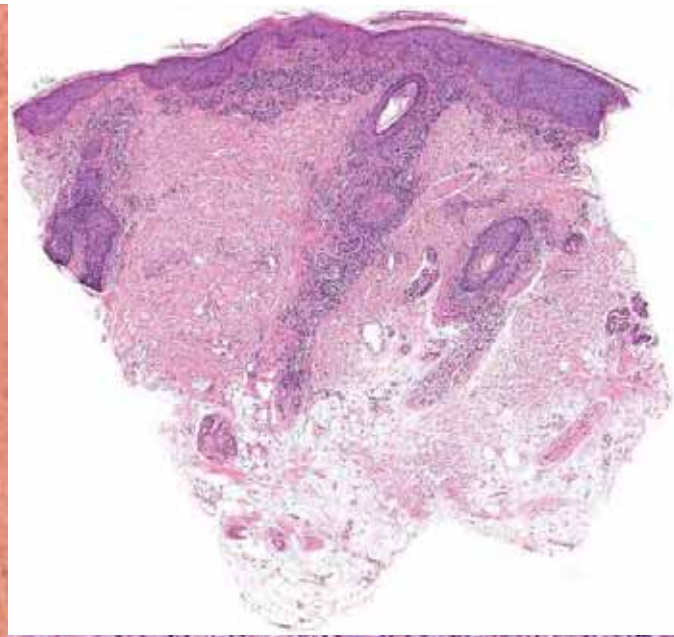
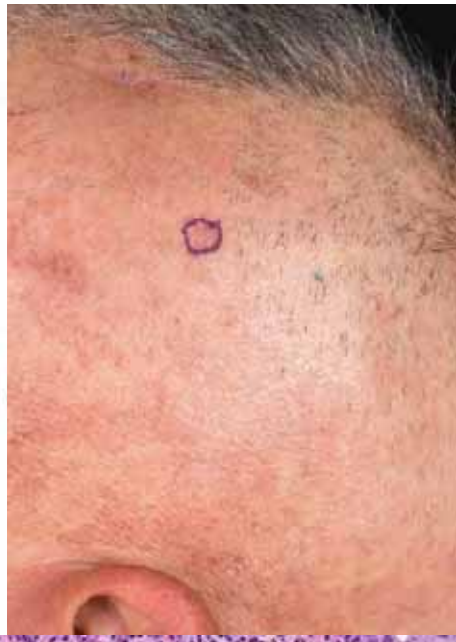
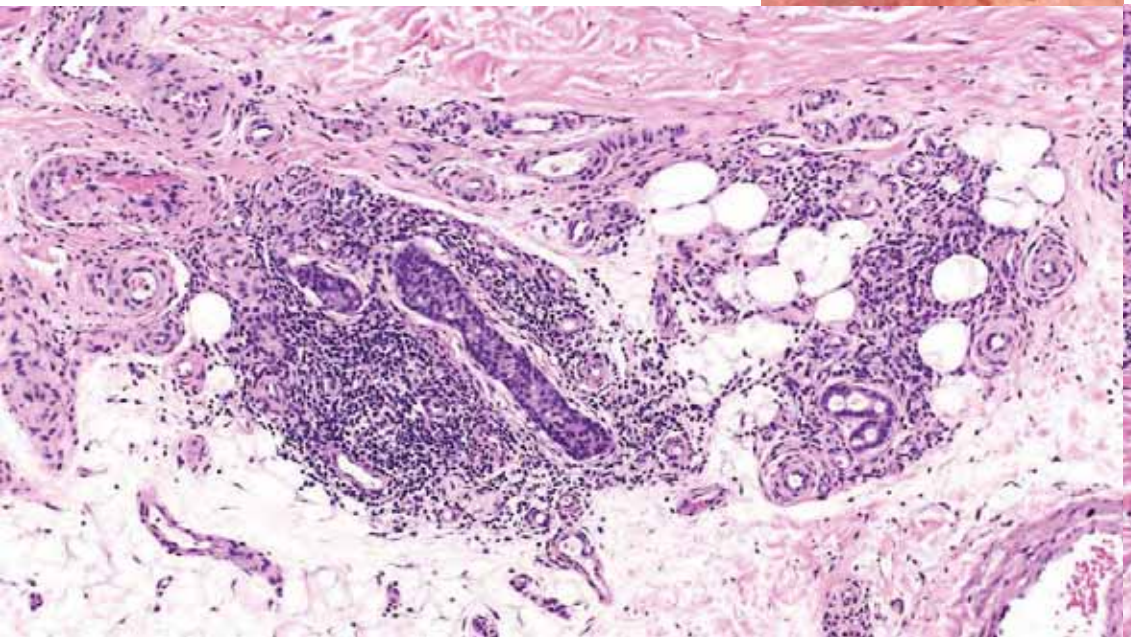
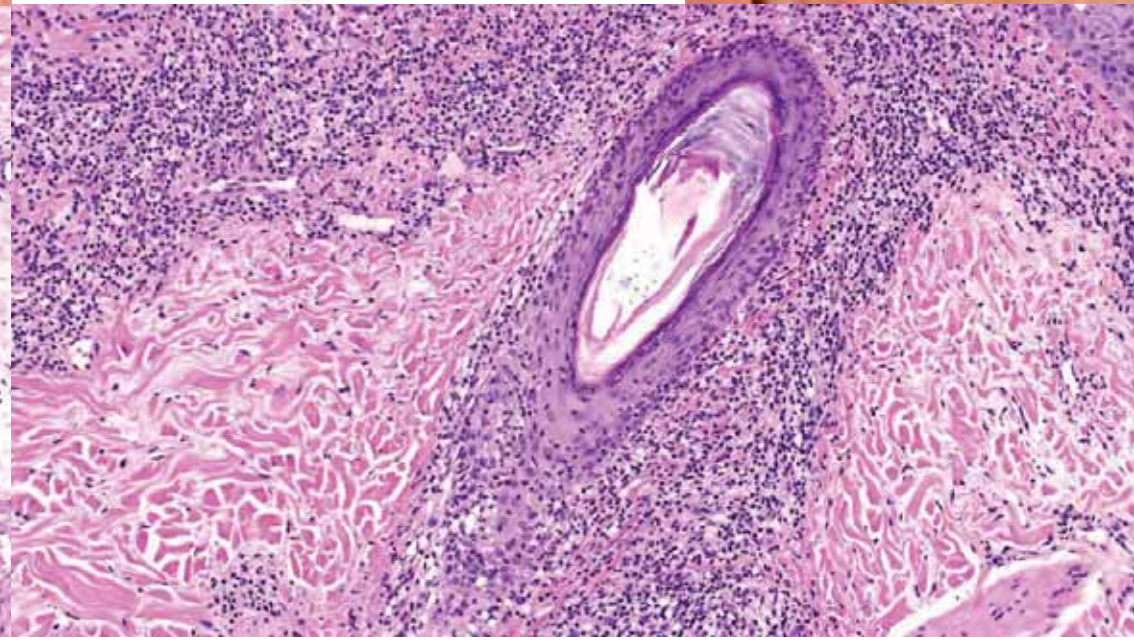


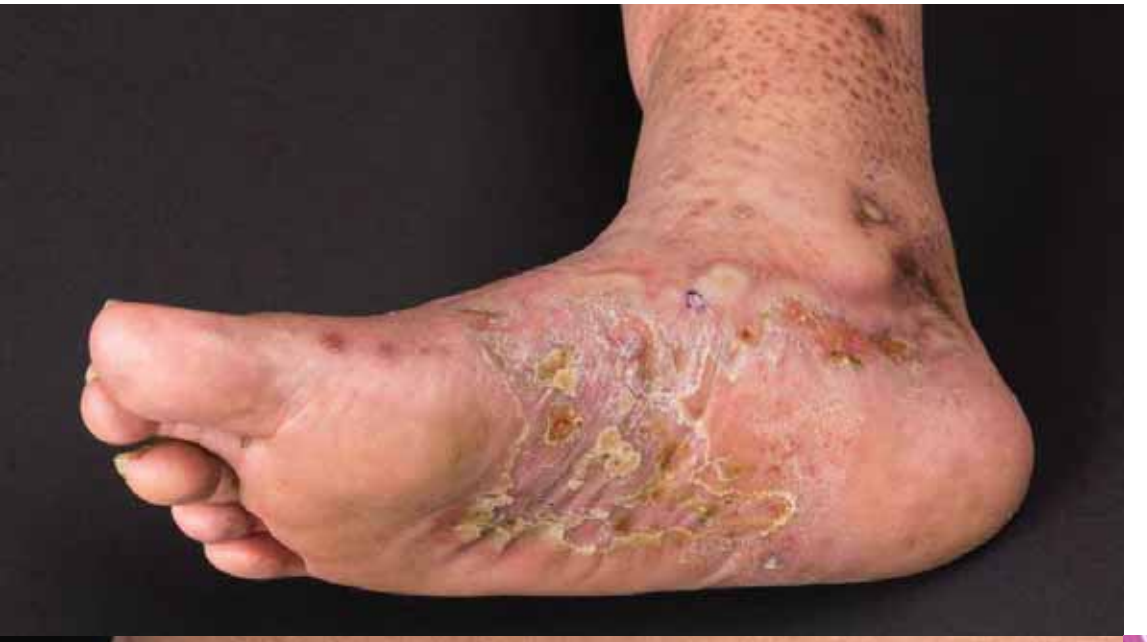


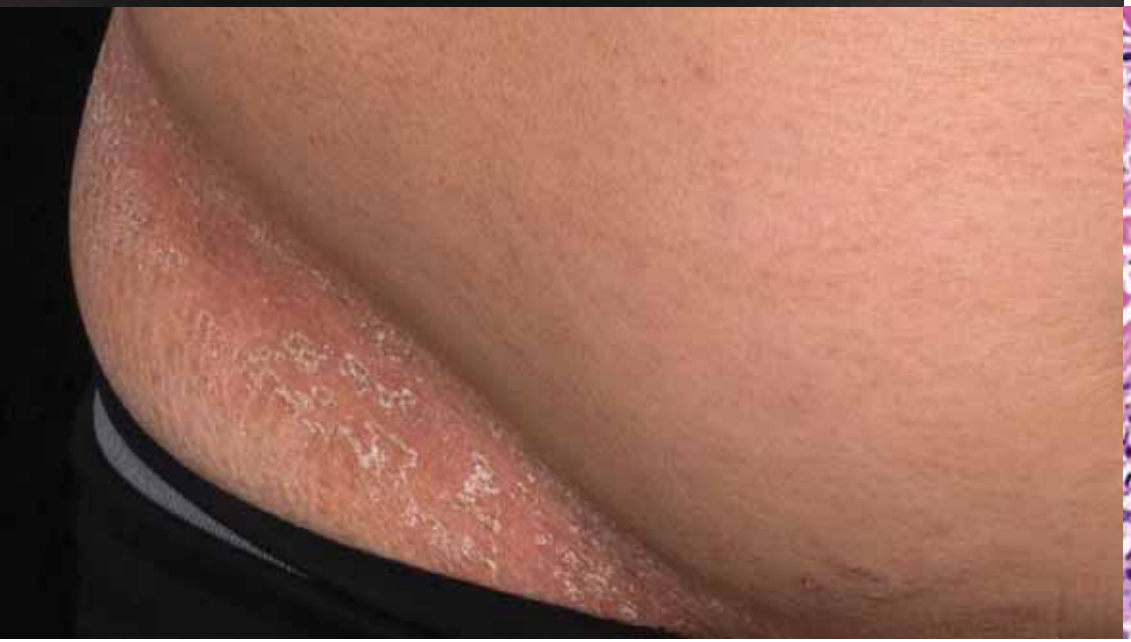


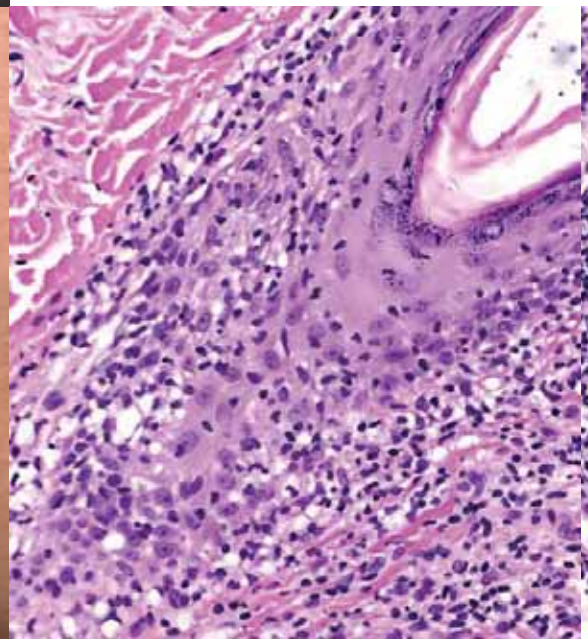


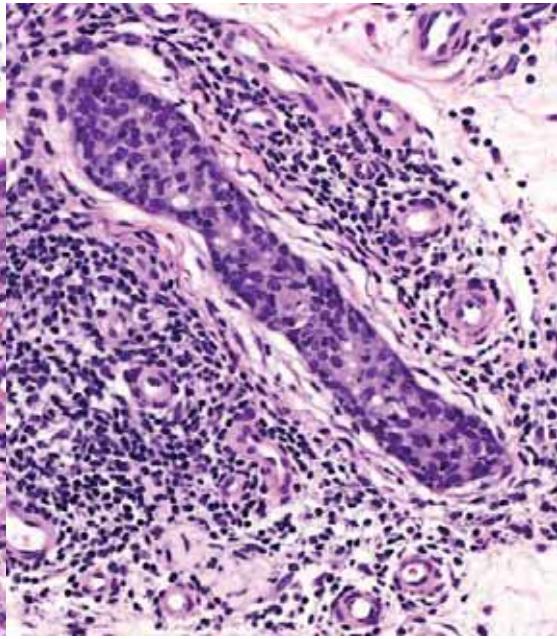
Original biopsy

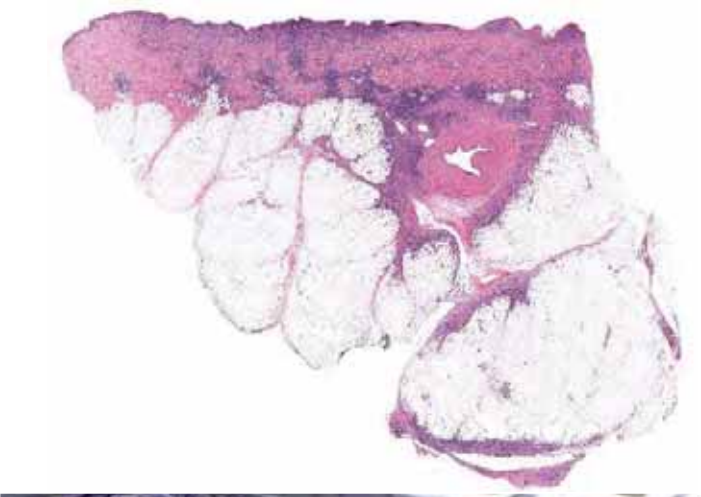


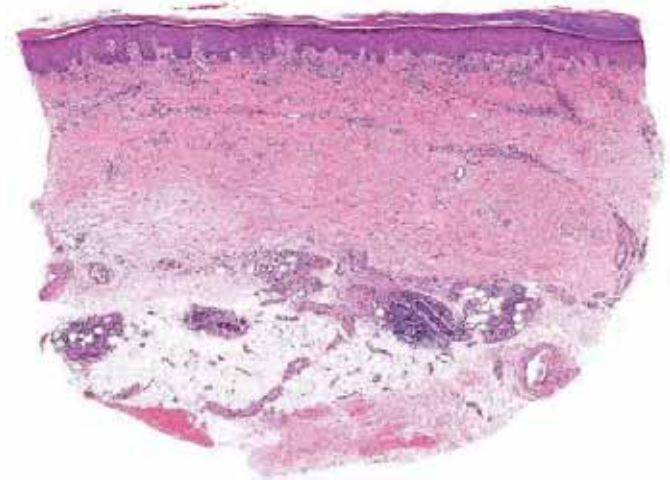


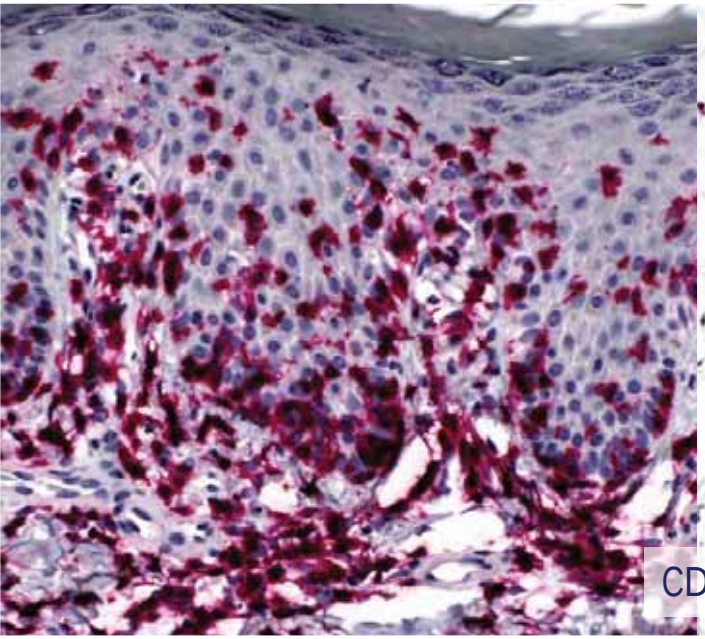




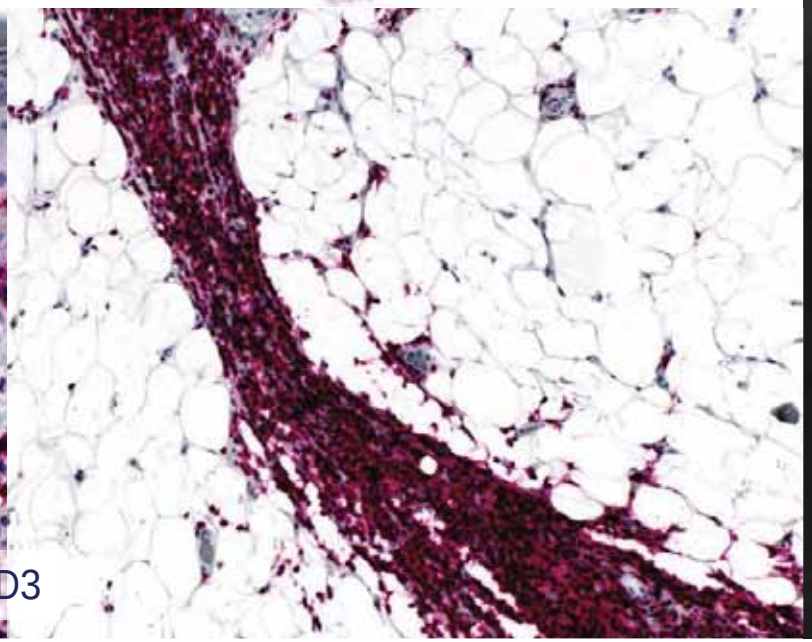
Adnexotropic mycosis fungoides

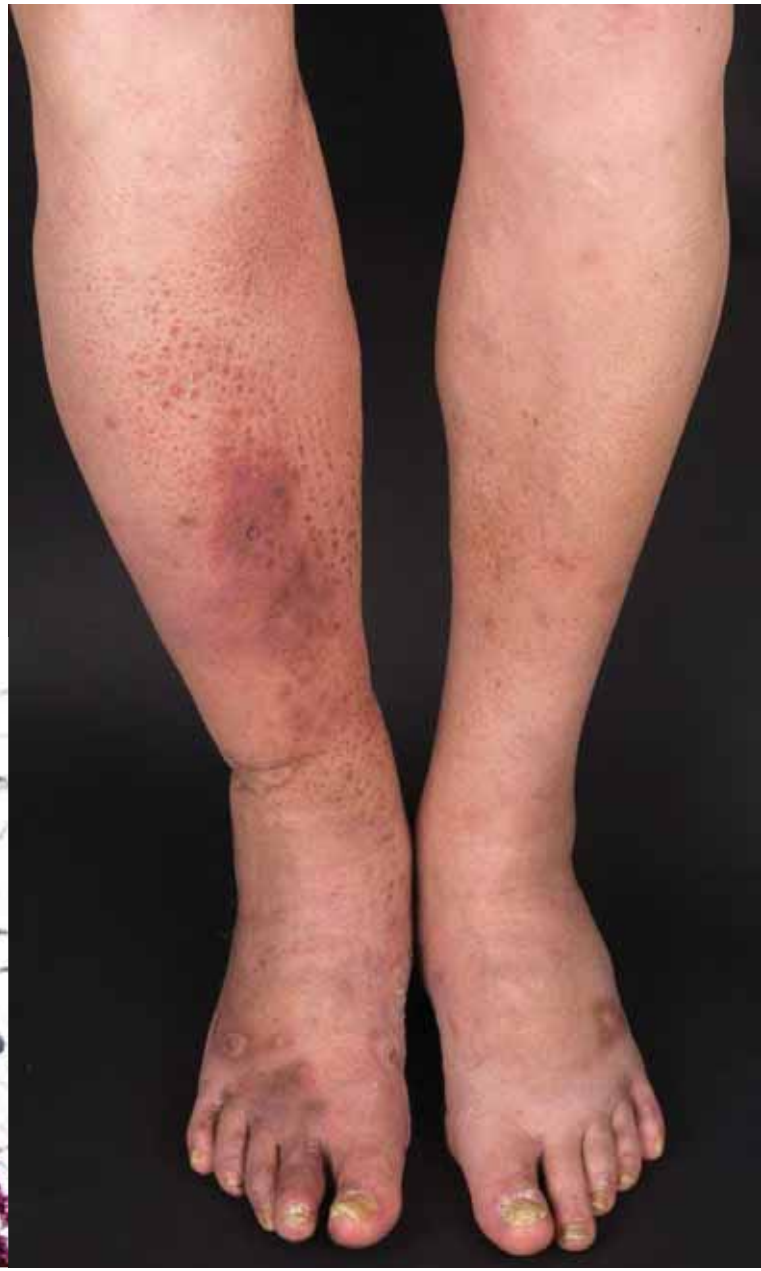




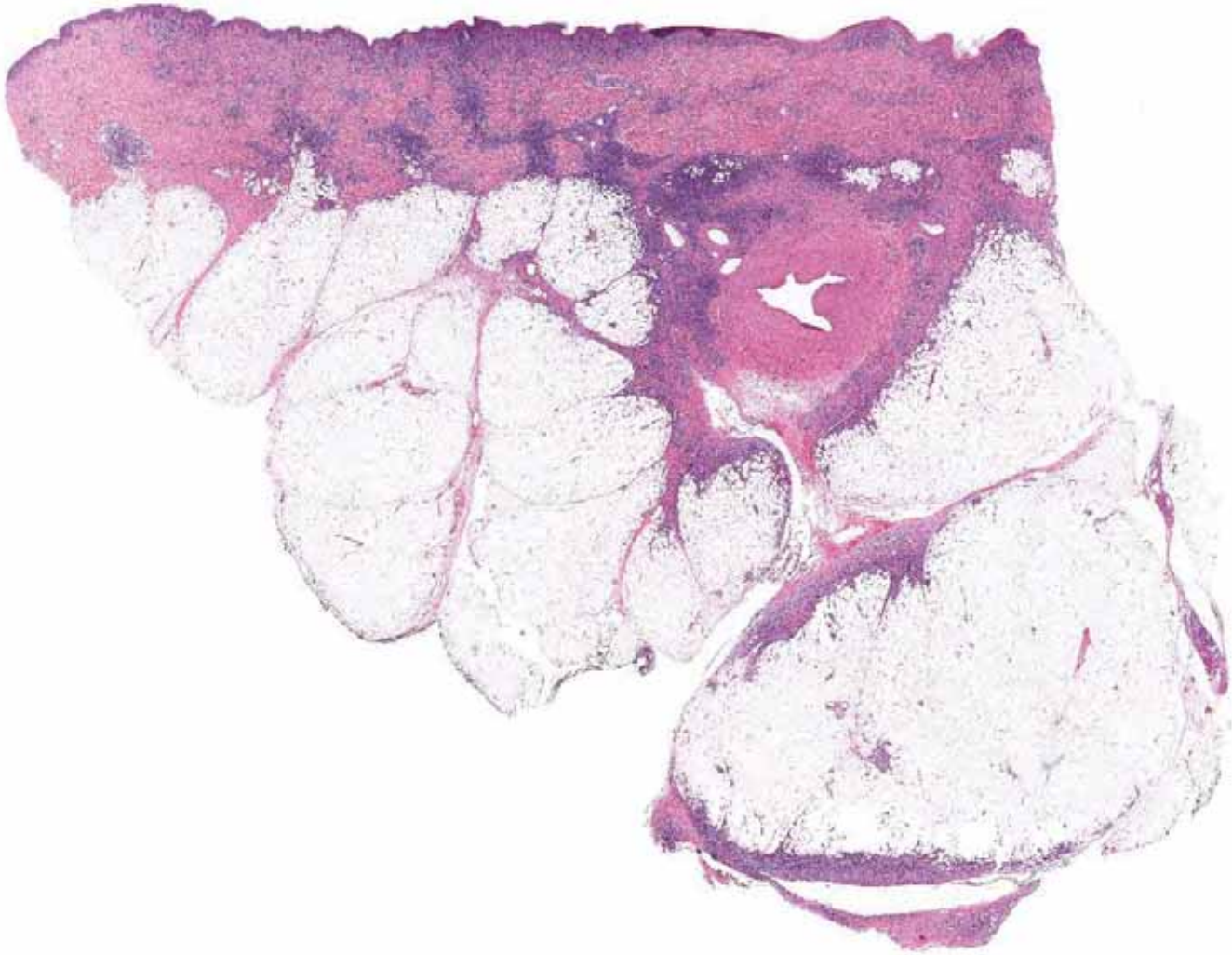


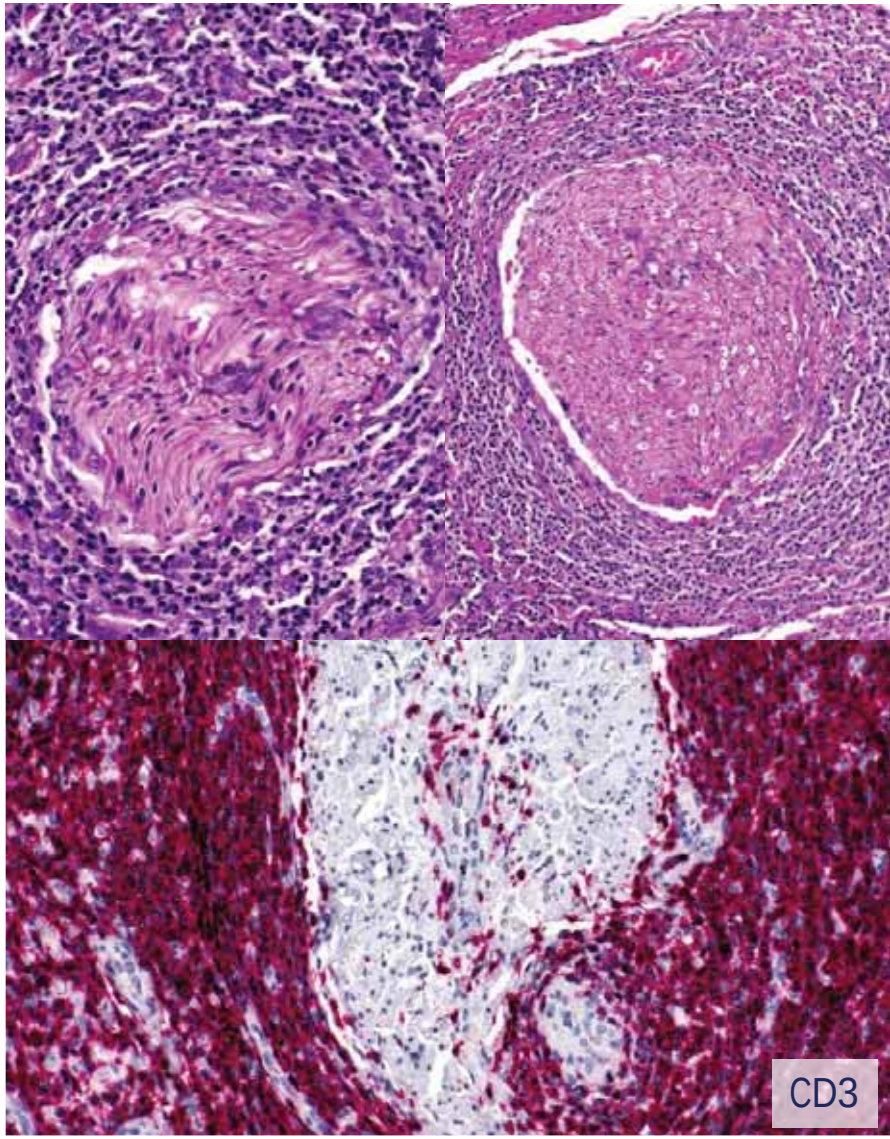
CD3





Adnexotropic & neurotropic mycosis fungoides





CASE OF THE MONTH

ABSTRACT: Occasional cases of peripheral neuropathy have been reported in classic mycosis fungoides. A rare variant of mycosis fungoides is the granulomatous form. We describe the occurrence of myopathy and peripheral neuropathy in a young woman who had skin lesions since the age of 12 years. At the age of 20 years they were diagnosed as granulomatous mycosis fungoides. The skin lesions resolved with interferon therapy and radiation. She then presented with cardiac and pulmonary symptoms and signs that were initially thought to be due to sarcoidosis or systemic vasculitis. A nerve and muscle biopsy showed granulomatous mycosis fungoides. To our knowledge, involvement of muscle and nerve by granulomatous mycosis fungoides has not been reported previously. Early reports suggested a favorable prognosis for the granulomatous subtype of mycosis fungoides. Based on a literature review and the course in our case, however, granulomatous mycosis fungoides seems to be an indicator of aggressive disease and ultimately a poor prognosis.

Muscle Nerve **36**: 860–865, 2007

MUSCLE AND NERVE INVOLVEMENT IN GRANULOMATOUS MYCOSIS FUNGOIDES

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Neoplastic infiltration of nerve is an uncommon cause of neuropathy, essentially confined to hematological malignancy, including lymphoma, leukemia, and myeloma.[...] The lymphoma is almost invariably of the non-Hodgkin's type, and 75% of cases are B-cell malignancies.[14] Although there are a few reports of peripheral neuropathy in classic mycosis fungoides,[...] there are no reports of muscle and nerve involvement in granulomatous mycosis fungoides, which is a rare variant of mycosis fungoides. We describe the muscle, nerve, and skin pathology in a case having clinical evidence of systemic involvement with granulomatous mycosis fungoides.

CASE REPORT

A 25-year-old woman, originally from Jamaica, first came to medical attention at the age of 12 years, with skin lesions in the form of elevated scaling erythema. Several skin biopsies were done and diagnosed as xanthogranuloma. The skin biopsy done in 2003, when she was 20 years of age, was diagnosed as granulomatous mycosis fungoides. In August 2003, she was treated with interferon, psoralen with ultraviolet A photochemotherapy, and radiation from the knees to her ankles as well as from her elbows to her wrists. She also had interferon and Accutane treatment between October 2003 and November 2004. There was no recurrence of the skin lesions. In November 2004, she developed congestive heart failure with biventricular dilation and cardiomegaly. She then developed progressive shortness of breath and was diagnosed with hypoxic respiratory disease that required continuous oxygen use. The computed tomography lung scans showed bilateral ground-glass opacities, interlobular septal thickening, and upper-lobe architectural distortion, which were initially thought to be due to heart failure, but a diagnosis of sarcoidosis was also considered. An open lung biopsy was regarded as too risky, given her low pulmonary reserve and pulmonary hypertension.

She was referred for neuromuscular evaluation in April 2005. At this time, she reported first noting weakness of the third digit of her right hand approximately 7 years earlier, but this was not disabling and

Abbreviations: [illegible]
Key words: [illegible]
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Published online [illegible] in Wiley InterScience (www.interscience.wiley.com). DOI [illegible]

British Journal of Dermatology 1998; 139, 299–301.

Peripheral nervous system involvement in a patient with large T-cell lymphoma arising from a pre-existing mycosis fungoides

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Summary A 29-year-old man was examined for disseminated erythematous scaling patches and plaques and reddish, partially ulcerated nodules. Histological examination showed a dense, diffuse, epidermotropic infiltrate located in the entire dermis to the subcutaneous tissue, composed mainly of large pleomorphic T lymphocytes. Immunohistochemistry revealed positivity of neoplastic cells for T-cell-associated markers, negativity for CD30 antigen and for B-cell markers. Polymerase chain reaction analysis detected a clonal amplification of T-cell receptor γ. Based on clinicopathological and molecular findings, the diagnosis of large T-cell lymphoma (LCL) arising from a pre-existing mycosis fungoides was made. Seven months after primary diagnosis, meningeal and peripheral nervous system involvement developed with no other evidence of systemic disease. Despite chemotherapy and radiation therapy, the patient died 3 months after the diagnosis of nervous system involvement. In patients with cutaneous LCL, mild neurological symptoms may precede the complete diagnostic picture by some weeks. A rapid and fatal progression characterizes the clinical course of the disease.

Mycosis fungoides (MF), the most common malignant T-cell lymphoma of the skin, is clinically characterized by a typical evolution from patches to plaques and eventually nodules. The disease has a slow progression and a 5-year-survival rate of about 80%.[1] The most common extracutaneous sites include lymph nodes followed by lung, spleen, liver, kidney, thyroid, pancreas, bone, breast and central nervous system (CNS).[2] In the advanced stages, MF may evolve to a large T-cell lymphoma (LCL) which is associated with a more aggressive biological behaviour and poor prognosis.[3] We describe a 29-year-old man with LCL arising from a pre-existing MF followed by rapid and fatal meningeal and peripheral nervous system complications with no other evidence of visceral involvement.

Case report

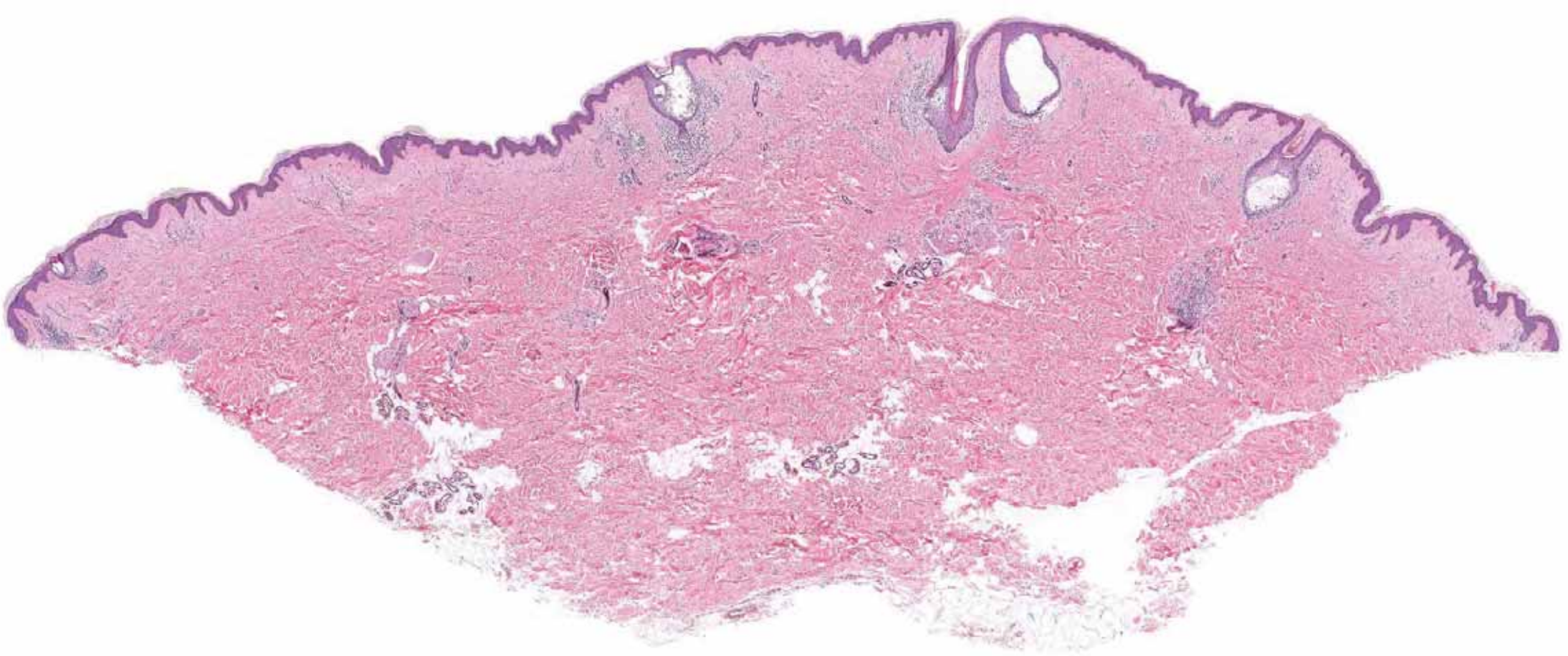
A 29-year-old man was examined for disseminated erythematous scaling patches and plaques and reddish-violaceous, partially ulcerated nodules (Fig. 1a). The lesions varied from 1·5 to 4 cm in diameter and were asymptomatic. In addition, hypopigmented macules were present on the upper and lower extremities. Physical examination failed to reveal any lymph node involvement. The patient's medical history was remarkable for erythematous scaling lesions on the buttocks for 10 years and self-healing nodular lesions on the lower extremities for 3 years. Histological examination of skin biopsy specimens from nodular lesions showed a dense, diffuse infiltrate throughout the dermis and subcutis, composed mainly of large pleomorphic lymphocytes and immunoblasts. Atypical mitoses were frequent. Focal areas of epidermotropism could be also observed (Fig. 1b,c). Histology from a plaque lesion showed an epidermotropic infiltrate located in the superficial and middle dermis, composed of small cells with cerebriform nuclei admixed with large pleomorphic cells.

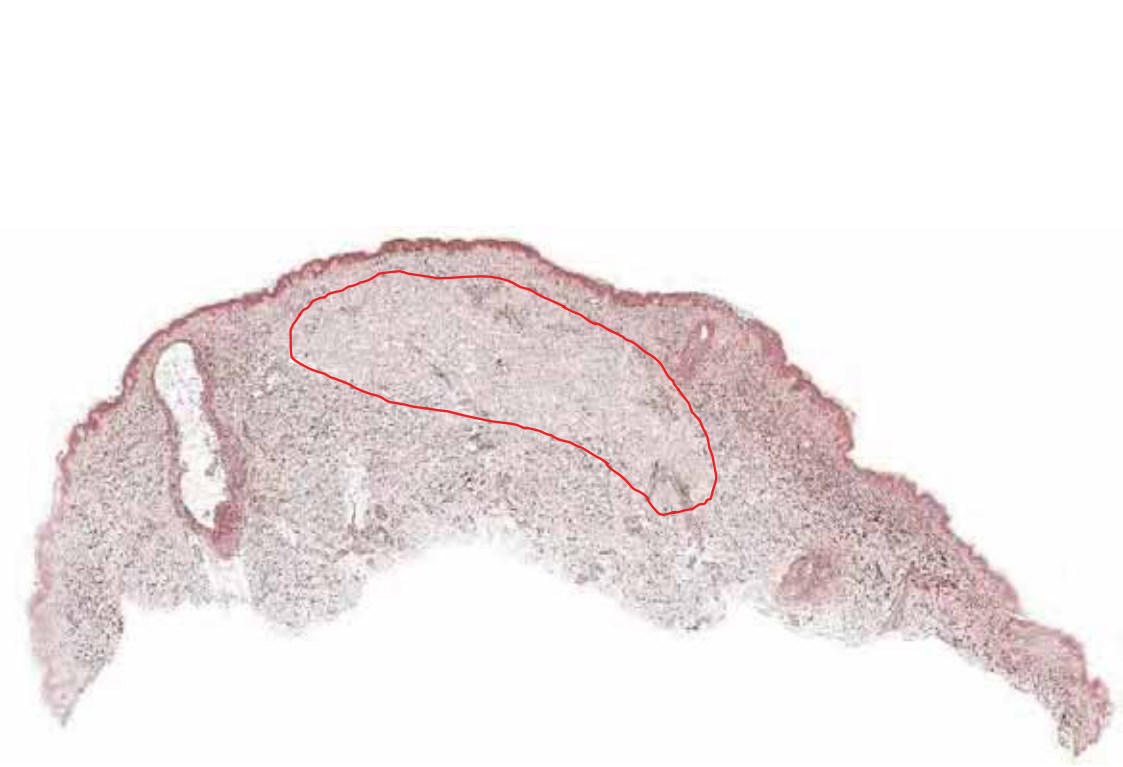
Immunohistochemical studies revealed reactivity of neoplastic cells for leucocyte common antigen, UCHL-1 (CD45RO), MT1, Mib-1 and negativity for CD8 and CD30 as well as for B-cell associated antigens. The patient was seronegative for anti-Epstein–Barr virus, human immunodeficiency viruses type 1 and 2, human T-cell leukaemia virus type 1, *Borrelia burgdorferi* and

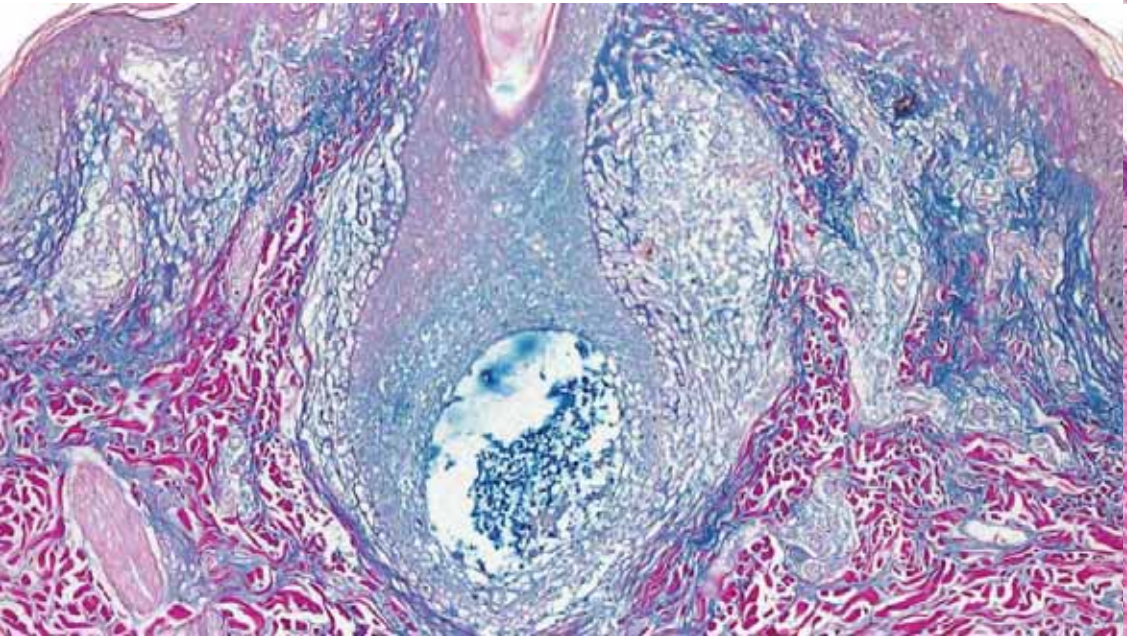
Correspondence: Ketty Peris, MD. E-mail: chimenti@caspur.it

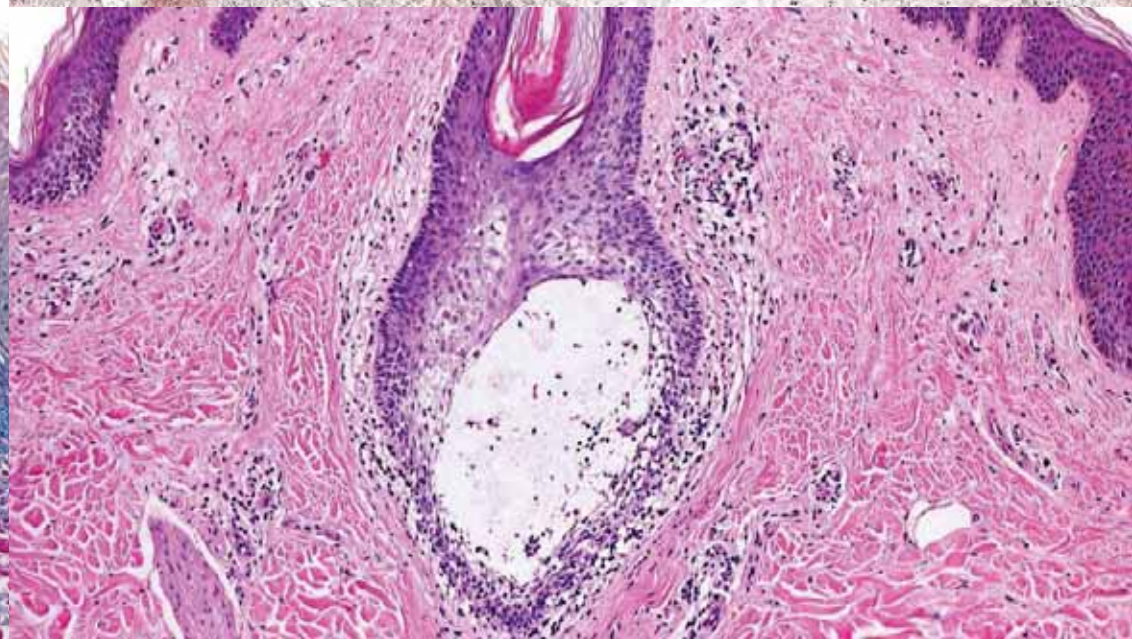
F, 47

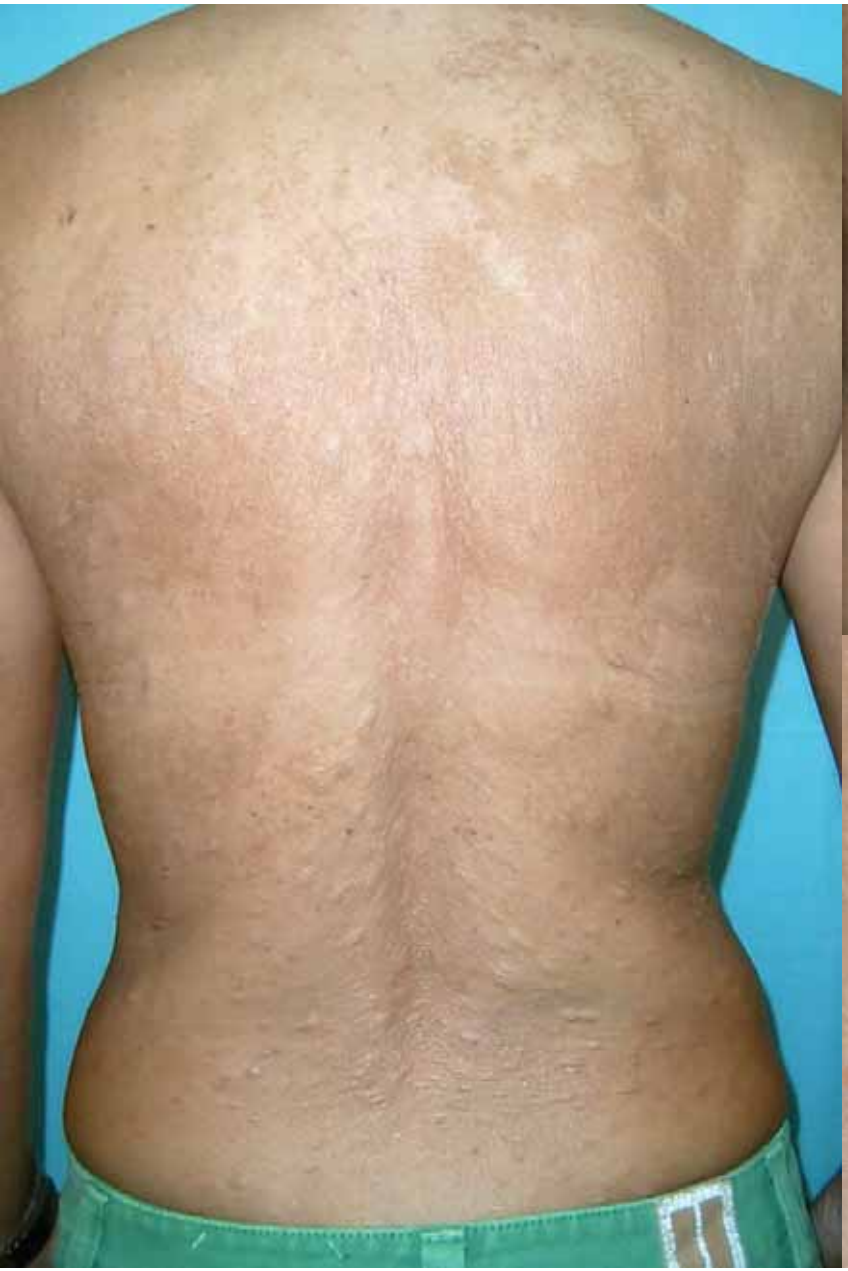
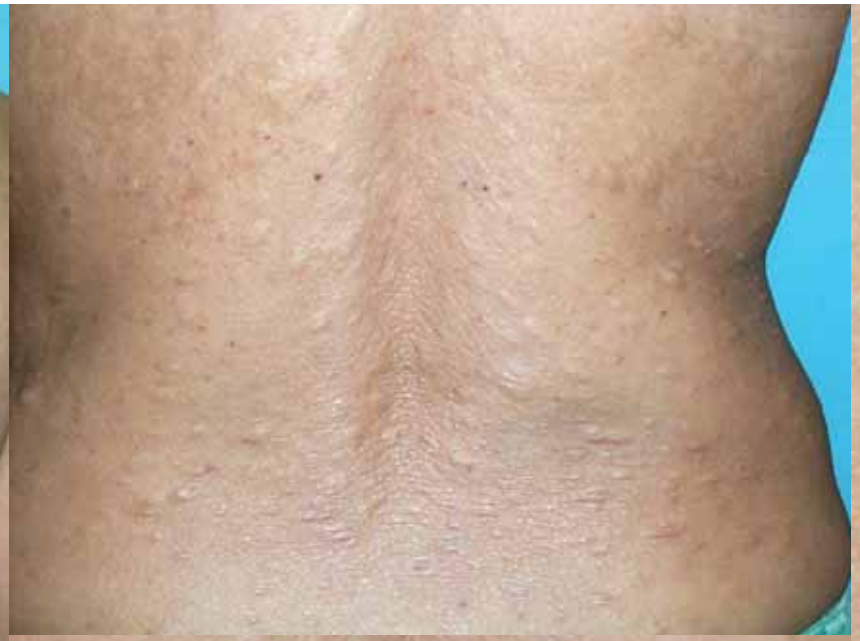
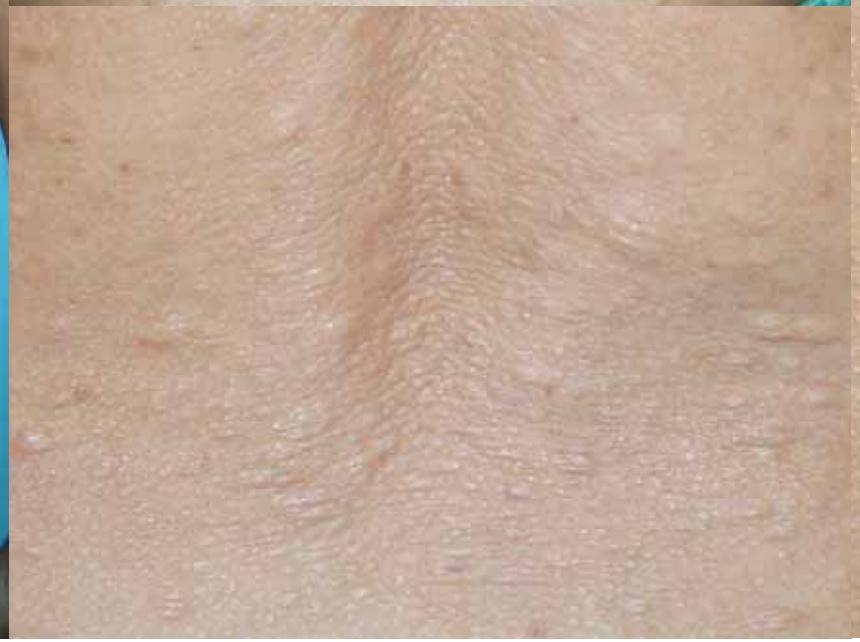
Asymptomatic papular lesions on the trunk for a few years.

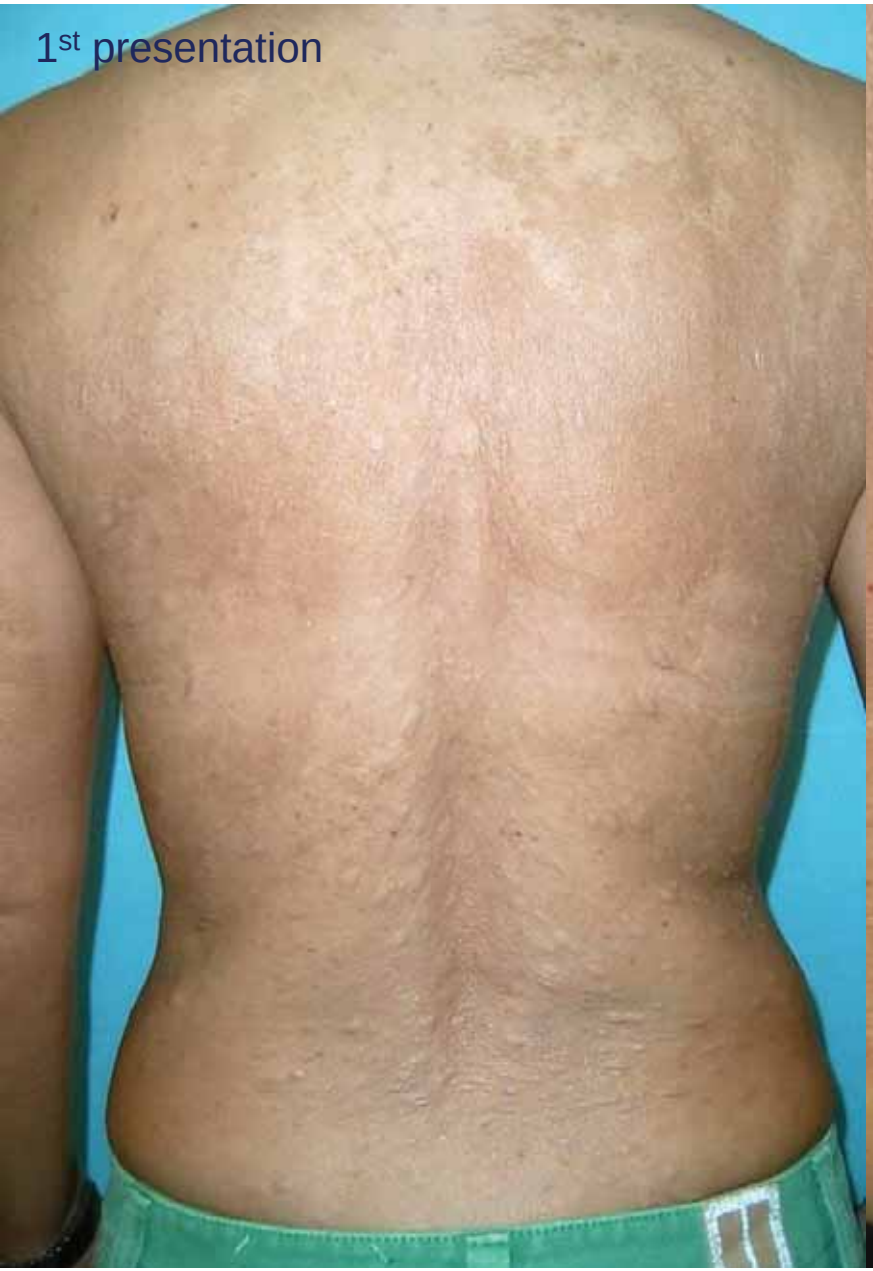






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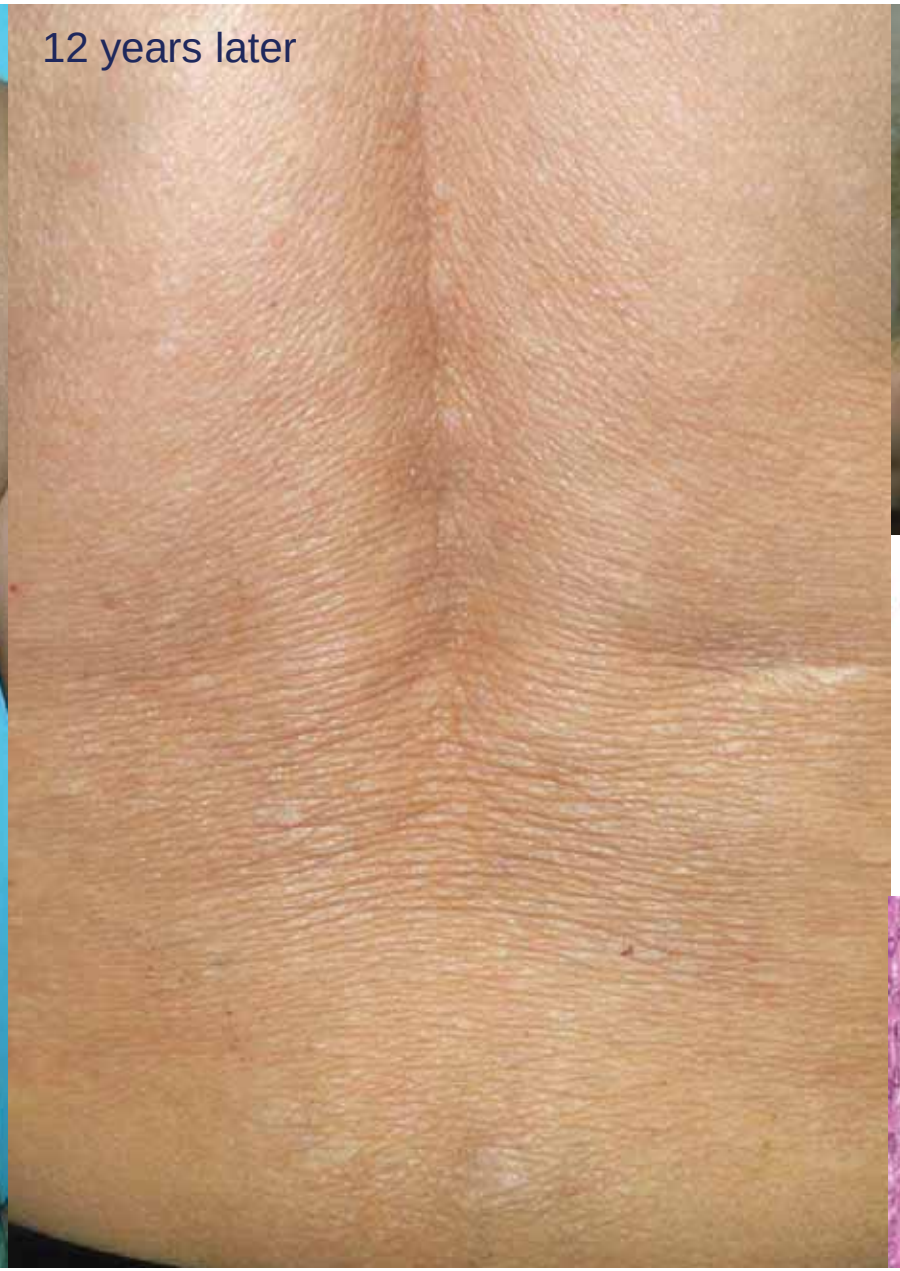
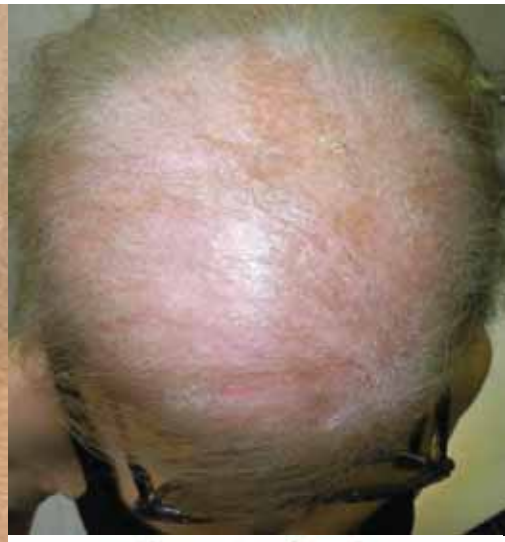
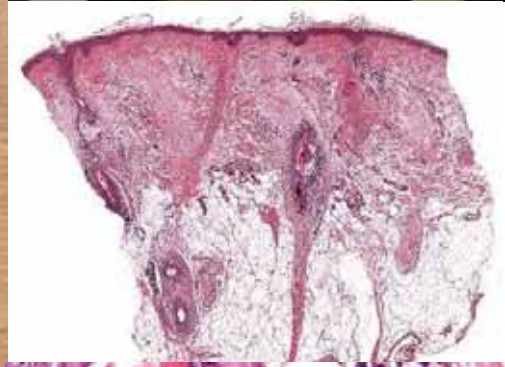
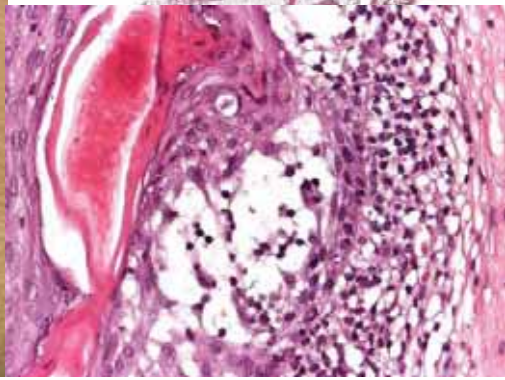

12 years later







Anetodermic follicular mucinosis

- Rare cases of anetodermic MF have been described (MF with secondary anetoderma)
- Anetoderma in follicular mucinosis exceedingly rare
- Follicular mucinosis with secondary anetoderma or anetoderma related to other conditions and with "non-specific" follicular mucinosis? The distribution of the lesions and the finding of follicular mucinosis in different biopsies point to a primary follicular mucinosis; the follow-up with similar lesions 12 years later confirms the diagnosis

CASE REPORT

DOI 10.1111/j.1365-2133.2007.08293.x

Anetodermic mycosis fungoides: a new clinicopathological variant of mycosis fungoides

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Summary

Mycosis fungoides is the most common type of primary cutaneous T-cell lymphoma. Several rare clinicopathological variants of mycosis fungoides have been described. Patients with these variants often also have classic mycosis fungoides at other sites of the body. Anetoderma is a cutaneous disorder in which multiple, oval lesions or atrophic plaques with wrinkled surface develop progressively due to loss of the dermal elastic tissue. Primary anetoderma occurs when there is no underlying associated disease and it arises on clinically normal skin, whereas secondary anetoderma appears in the same site as a previous specific skin lesion. There is a large list of heterogeneous dermatoses associated with secondary anetoderma. Two patients developed areas of secondary anetoderma on plaque stage lesions of mycosis fungoides. The lesions consisted of exophytic nodular lesions, with very soft consistency on palpation, scattered over the hyperpigmented plaques in one patient and violaceous infiltrated plaques with overlying epidermal atrophy and mild scale in the other. Histopathological study demonstrated that the cells involving the dermis were mainly T-helper lymphocytes, with few histiocytes and some multinucleate giant cells engulfing distorted elastic fibres. Elastic tissue stain demonstrated that elastic fibres were almost completely absent in the dermis of the anetodermic lesions. Anetodermic mycosis fungoides should be added to the list of clinicopathological variants of mycosis fungoides and mycosis fungoides should also be considered as a possible disease causing secondary anetoderma. Anetodermic mycosis fungoides shows clinical and histopathological features different from those of granulomatous slack skin.

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15 April 2007

Key words
anetoderma, elastic tissue anomalies, mycosis fungoides

Conflicts of interest
None declared.

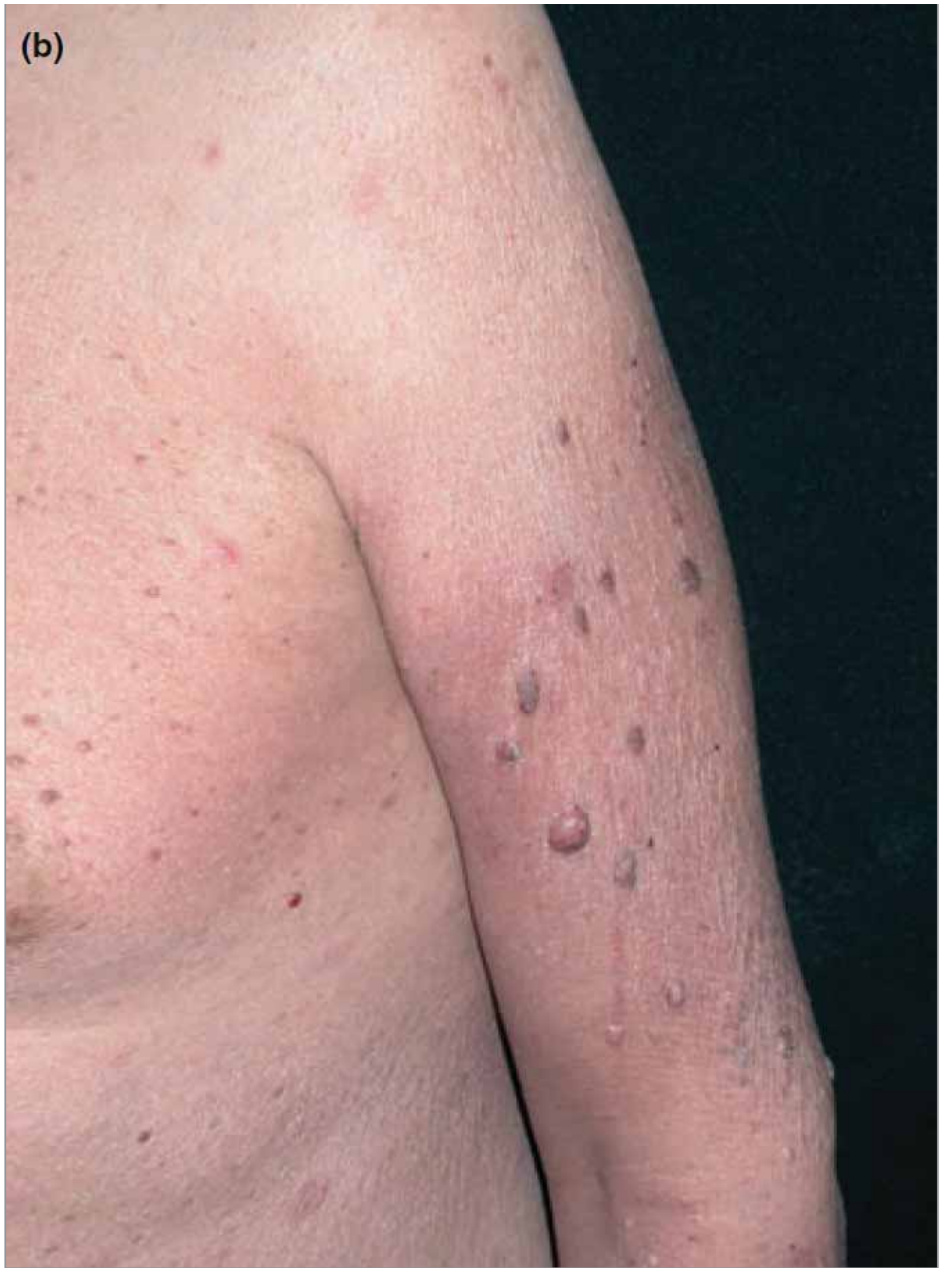
Mycosis fungoides is the most common type of primary cutaneous T-cell lymphoma. Traditionally, it is divided into three clinical phases: patch, plaque and tumour stages and the clinical course is usually protracted over years and decades. Several clinicopathological variants of mycosis fungoides have been described[1] (Table 1). Patients with these variants often also have classic mycosis fungoides at other sites of the body and, although in the past some of them were considered as distinct entities, they are now interpreted as just clinicopathological variants of mycosis fungoides with little or no prognostic significance.

We describe here two patients with anetodermic mycosis fungoides. This variant of mycosis fungoides was not included in the recent World Health Organization–European Organization for Research and Treatment of Cancer classification for cutaneous lymphomas[2] and, to our knowledge, there has been no previous description of this clinicopathological variant. Therefore, anetodermic mycosis fungoides should be added to the list of clinicopathological variants of mycosis fungoides and mycosis fungoides should also be considered as a possible cause of secondary anetoderma.

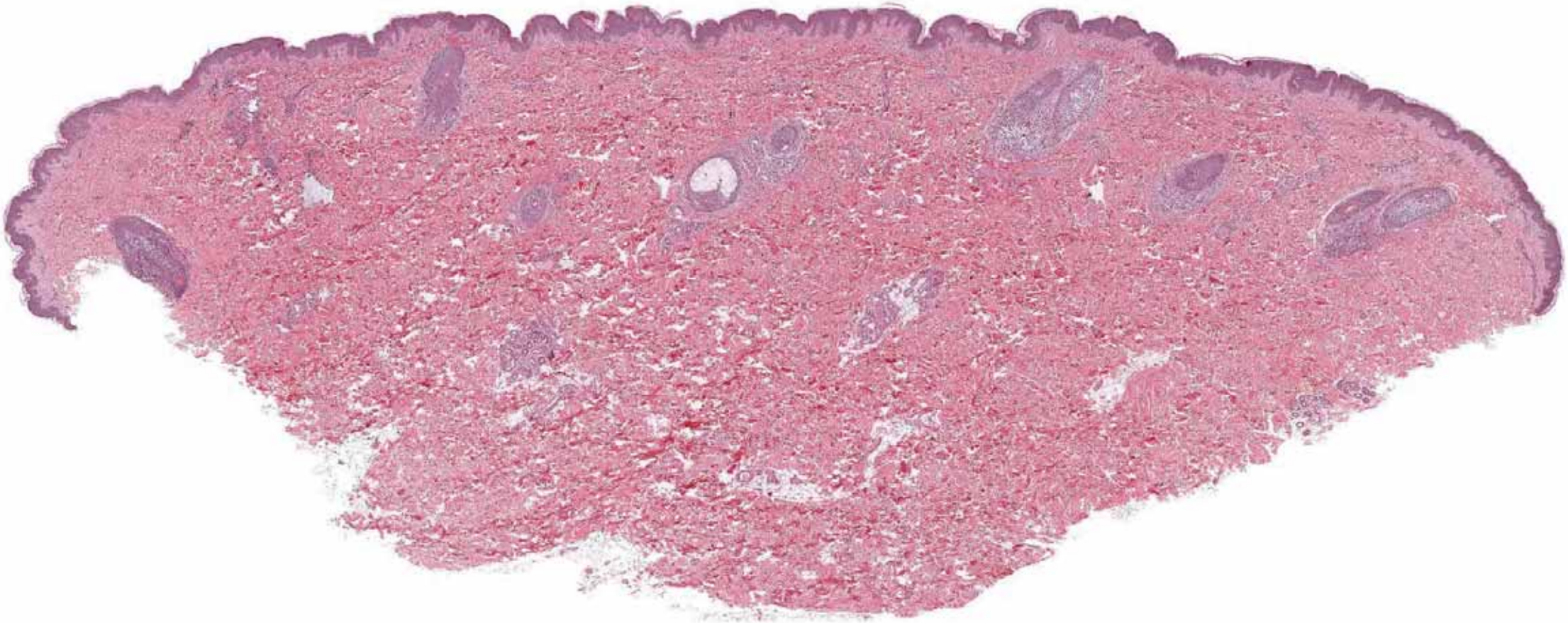
Case reports

Patient 1

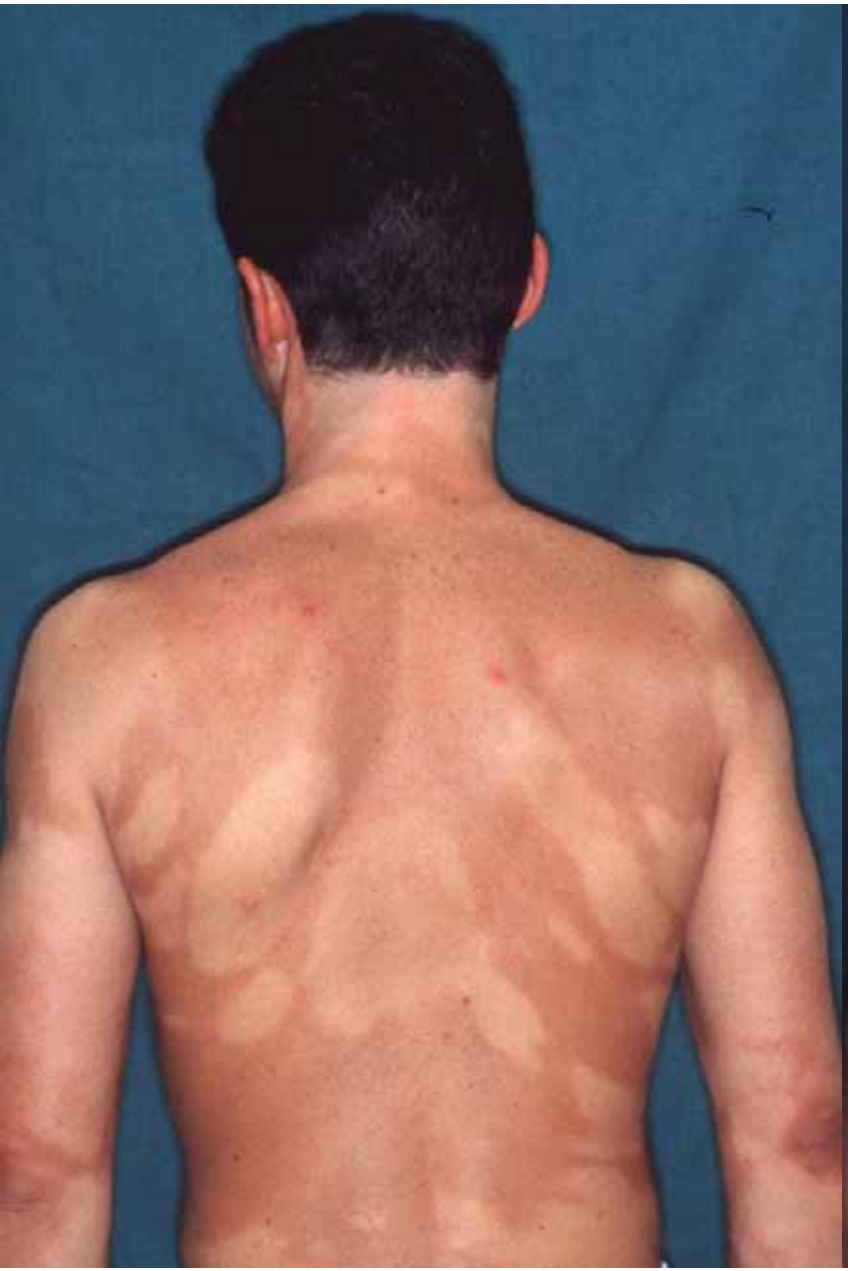
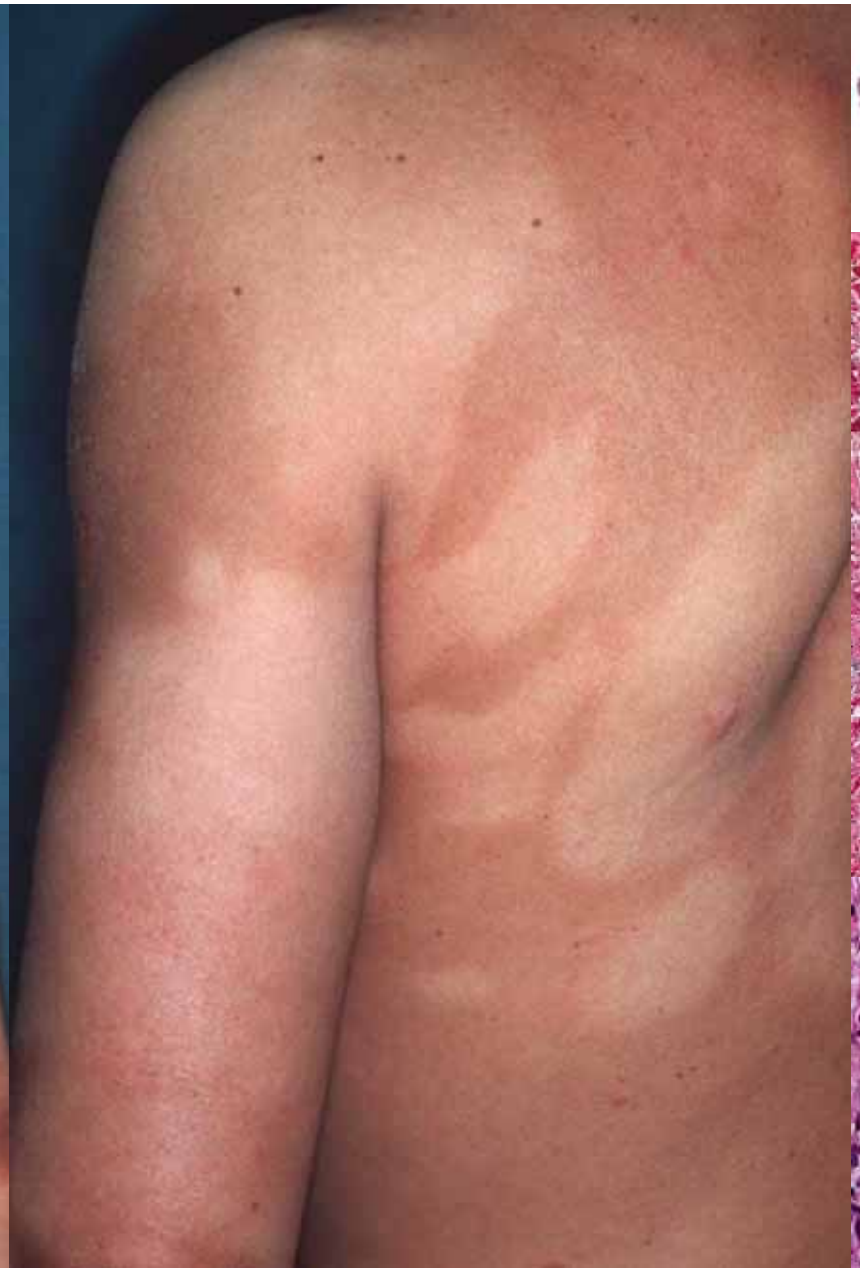
A 65-year-old man, with a history of alcohol abuse and psoriasis, was admitted to the hospital for inpatient treatment of an extensive cutaneous eruption that had been present for 5 years. Skin examination at the time of hospital admission revealed generalized cutaneous hyperpigmentation and scaling of the upper and lower extremities, back, abdomen (Fig. 1a), buttocks and face. There was prominent hyperpigmentation around the eyes and large scales with ichthyosiform

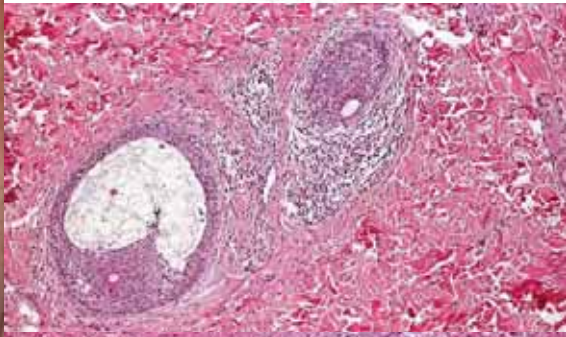
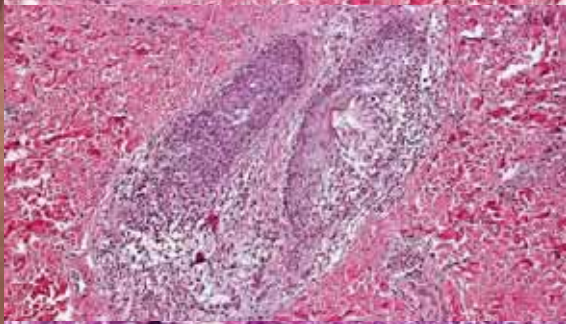
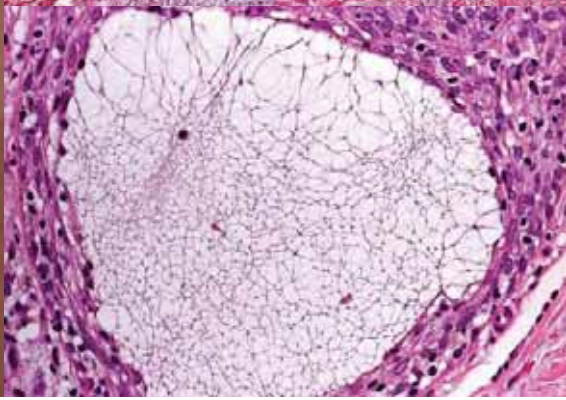


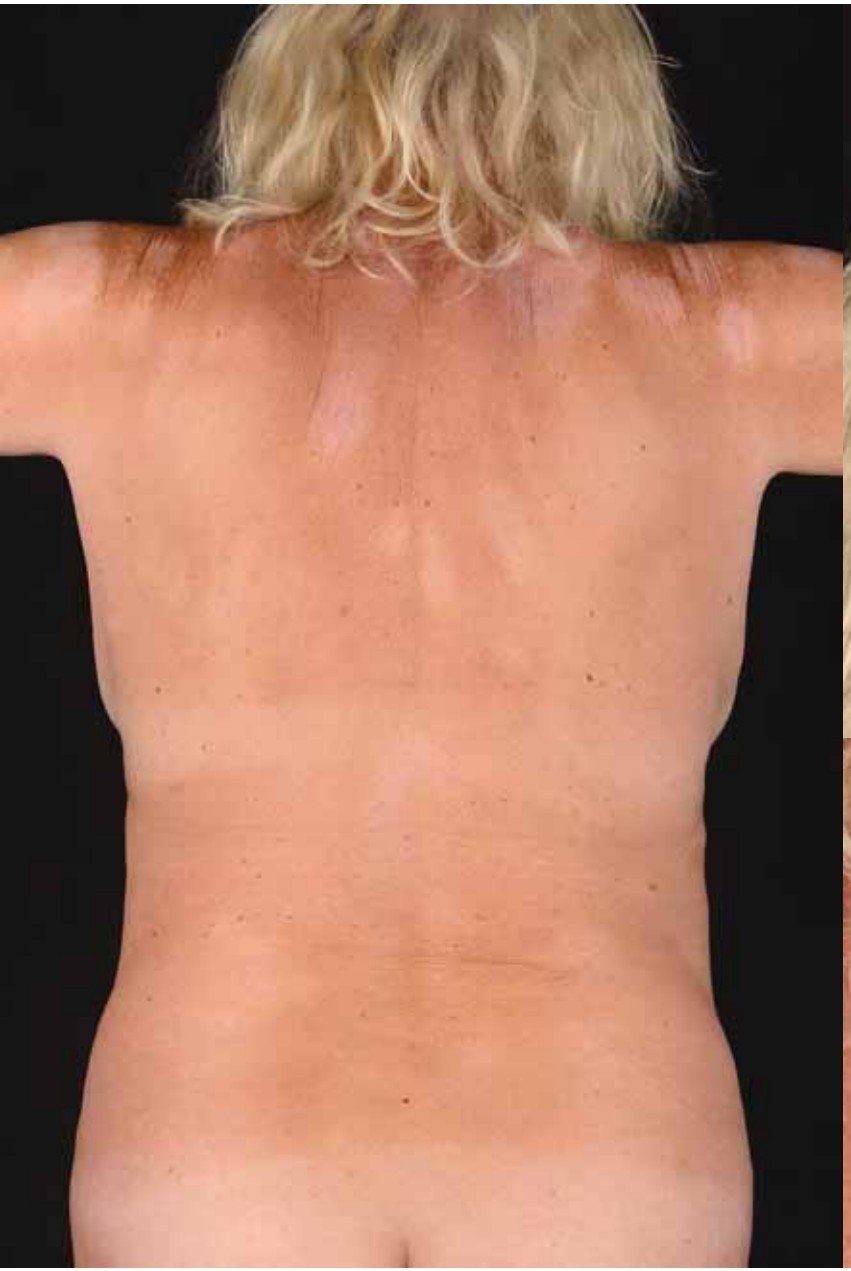
M, 25
Generalized hypopigmented lesions on the trunk and upper extremities for some months.

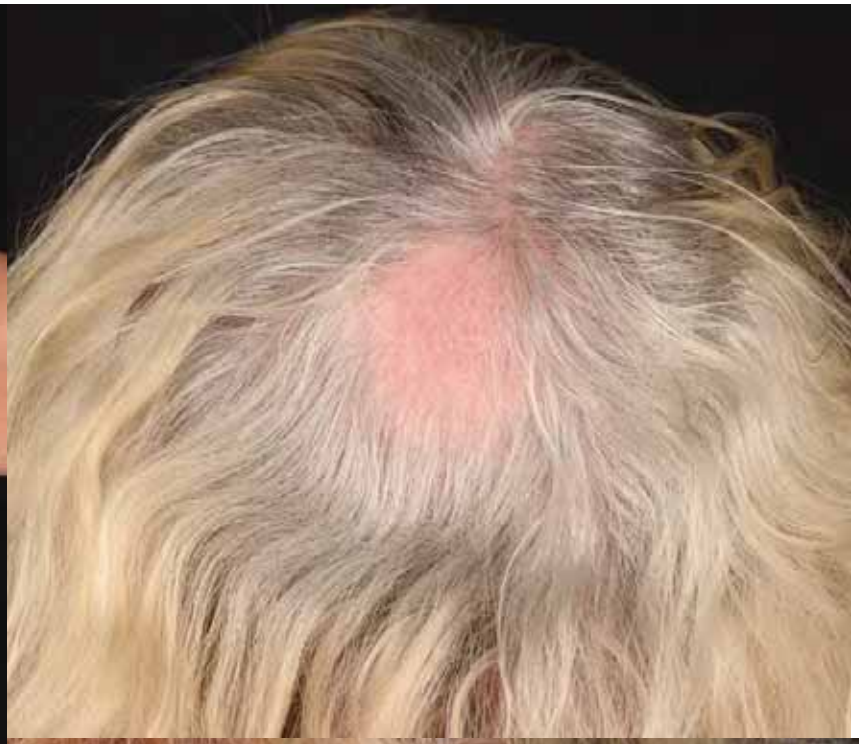


(Consultation Dr. Luca Muscardin, Roma)

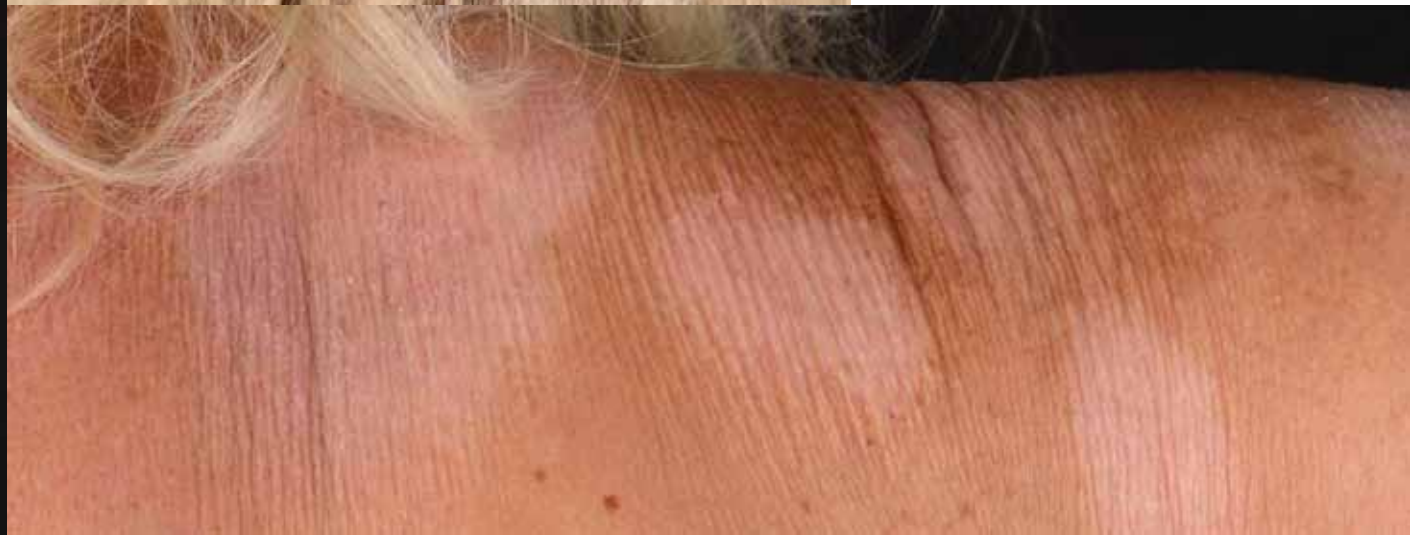


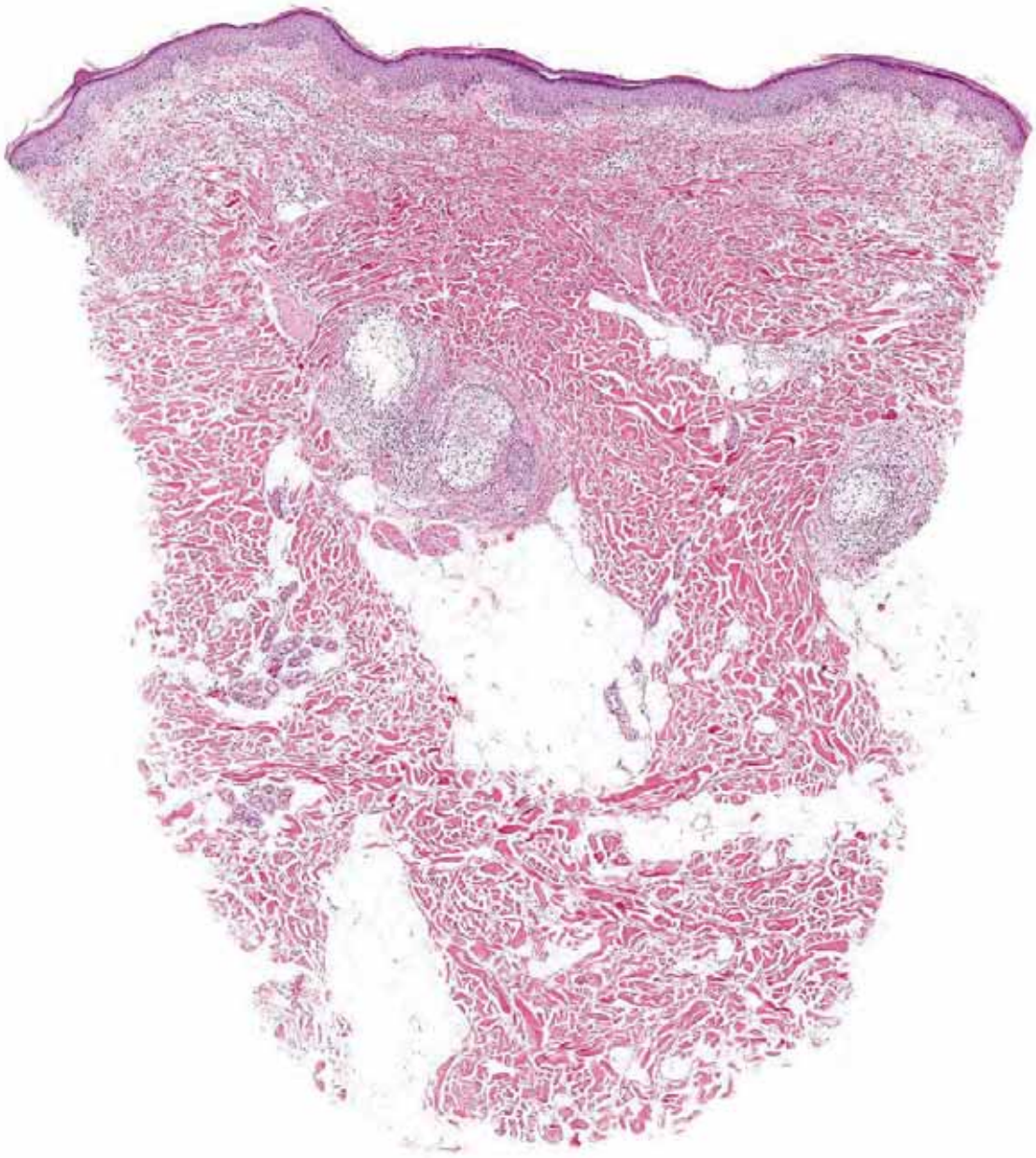


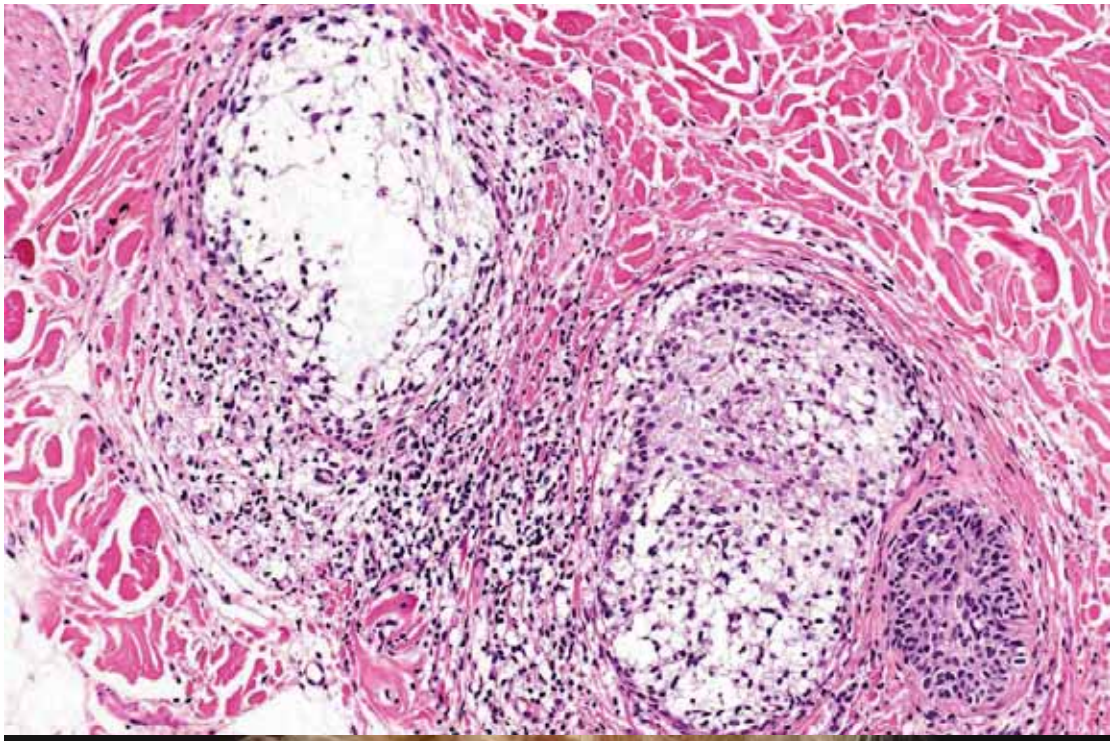
F, 58

According to the patient hair loss "for a long time". Generalized lesions on the back and upper extremities for 1 week. Allergic rhinitis. An external biopsy taken a few weeks before presentation was reported as follicular mucinosis.

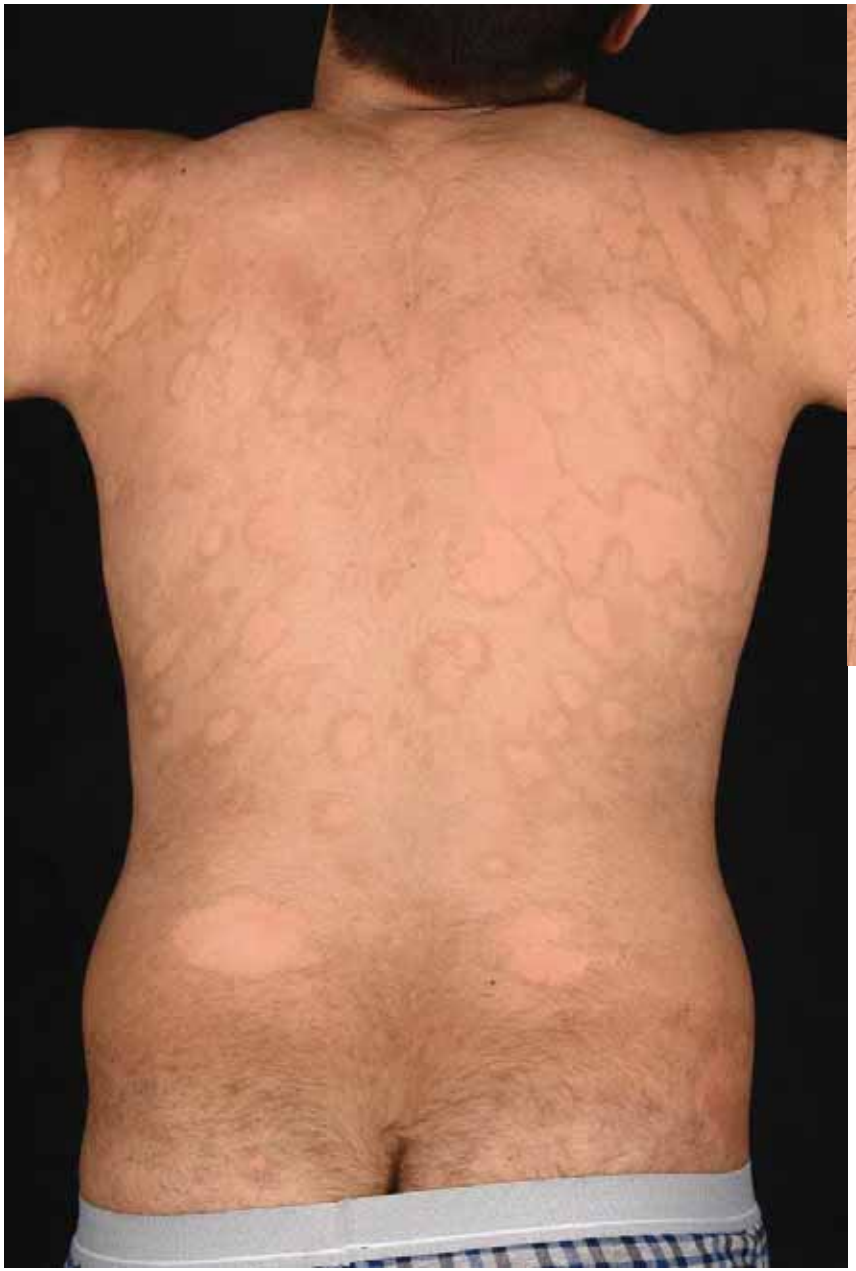
A new biopsy is taken.







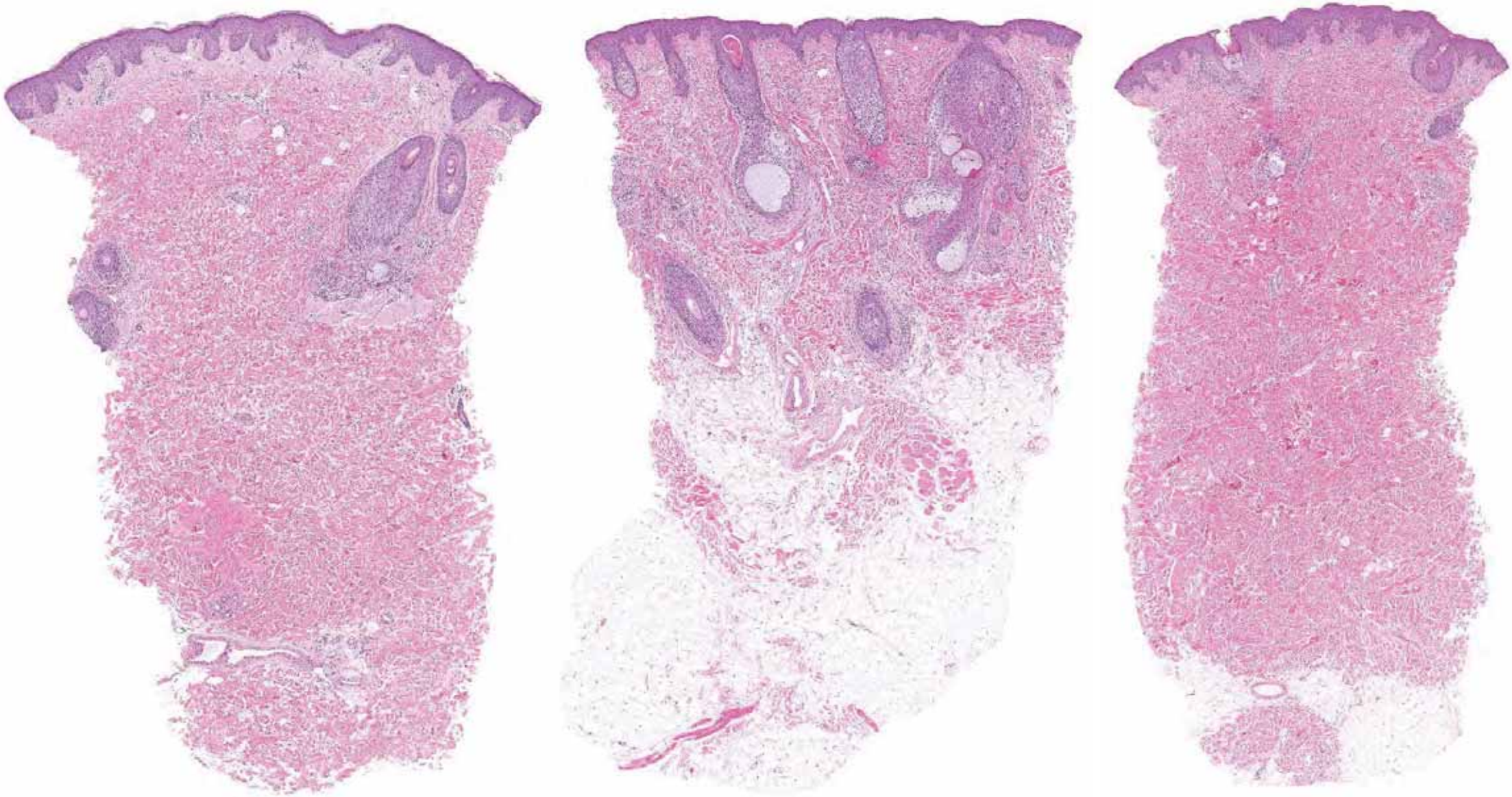
Complete regrowth of hairs on the scalp and resolution of lesions on the trunk and upper extremities following 1 year of PUVA treatment. No new lesions (follow-up: 2 months)

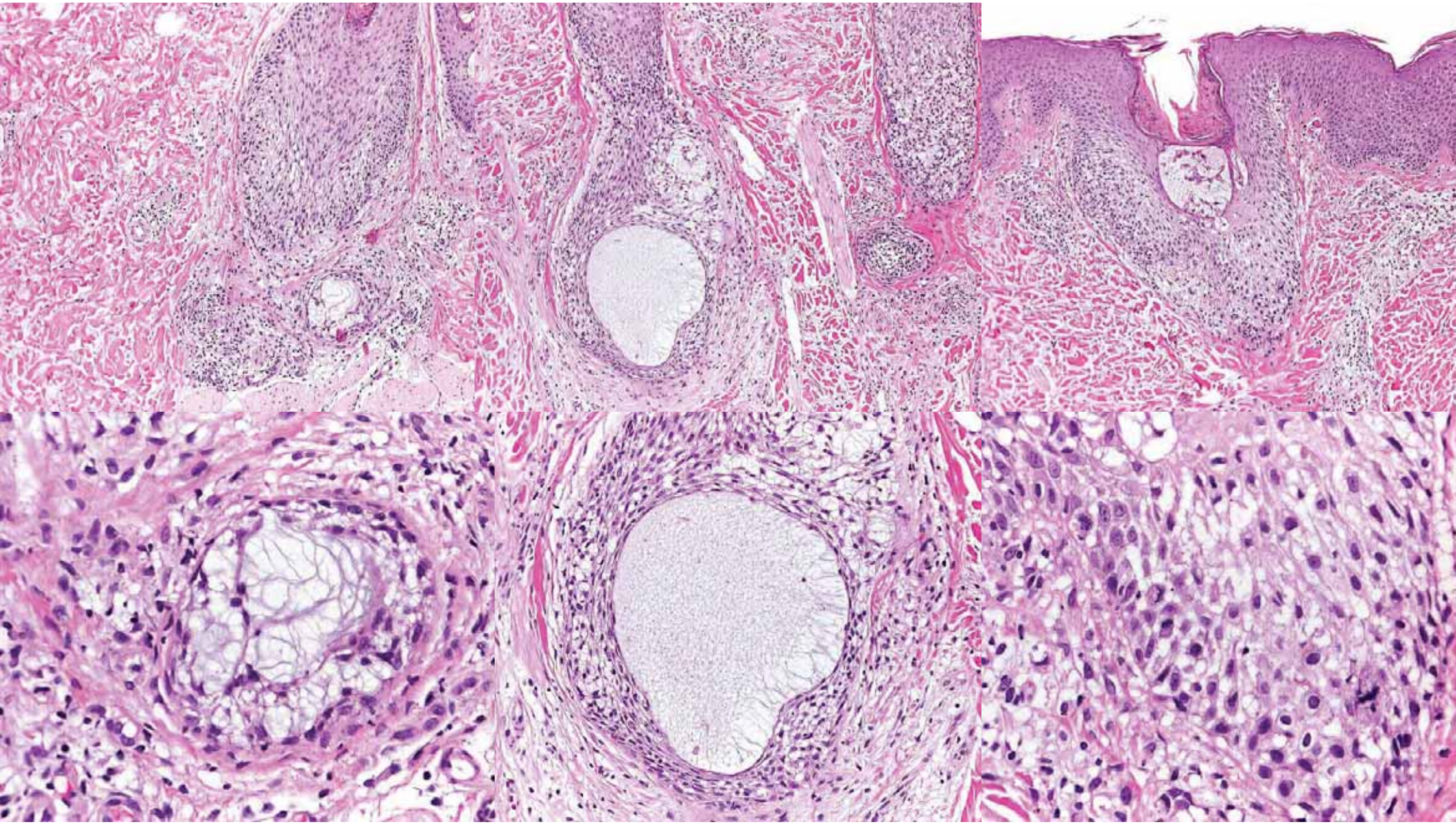


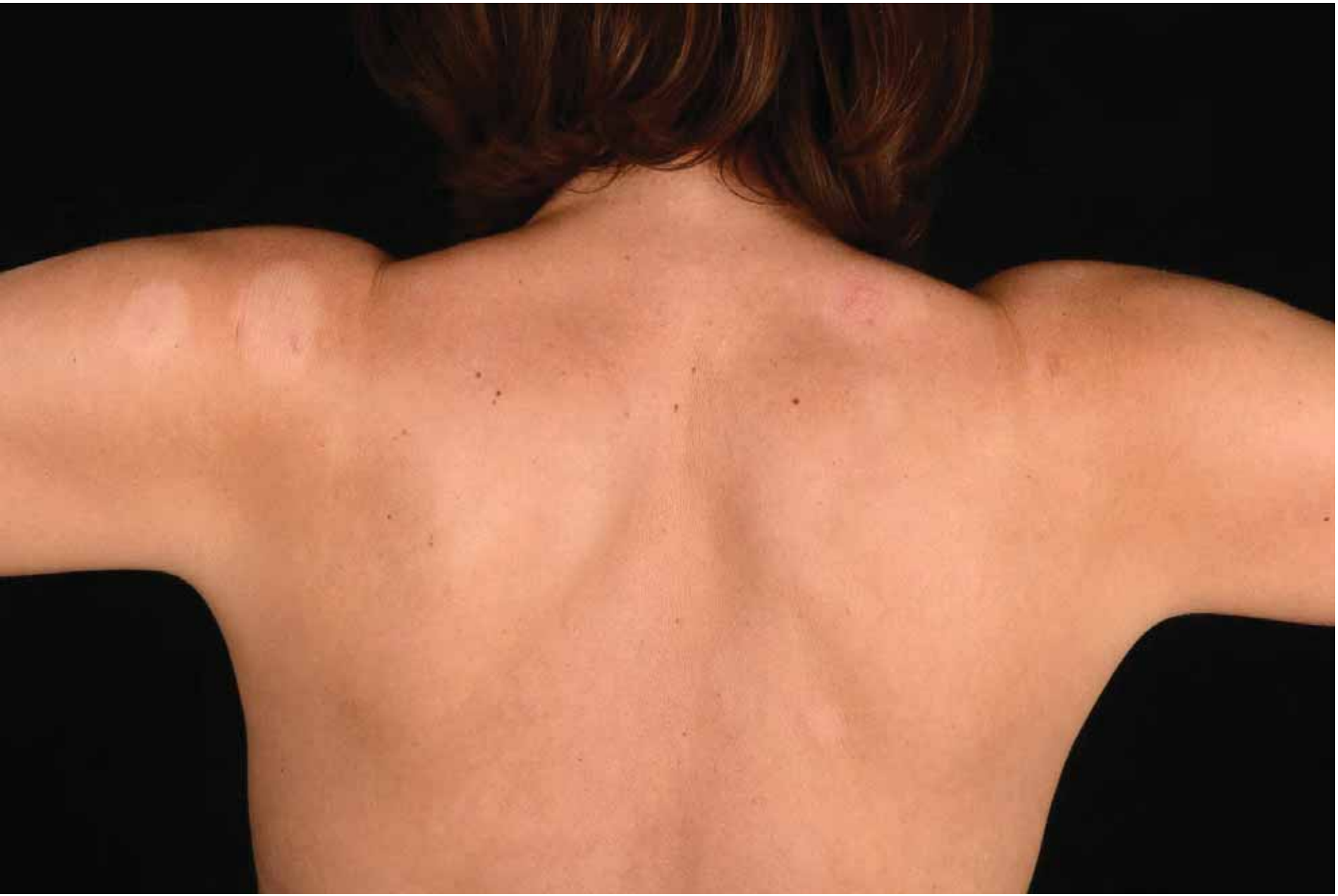
M, 14

According to the patient partly erythematous, partly hypopigmented lesions on the face, trunk and upper extremities for 6 months.

A biopsy is taken.



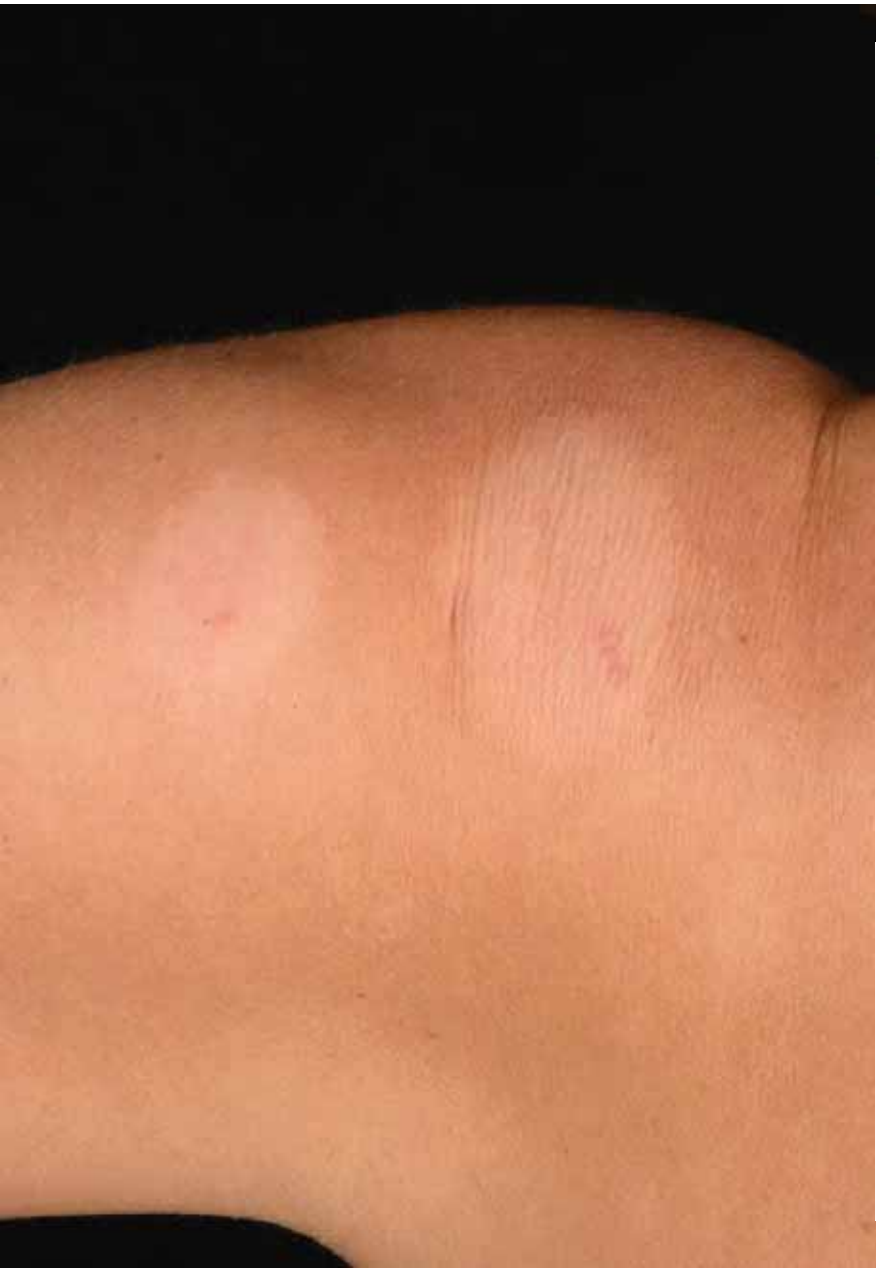


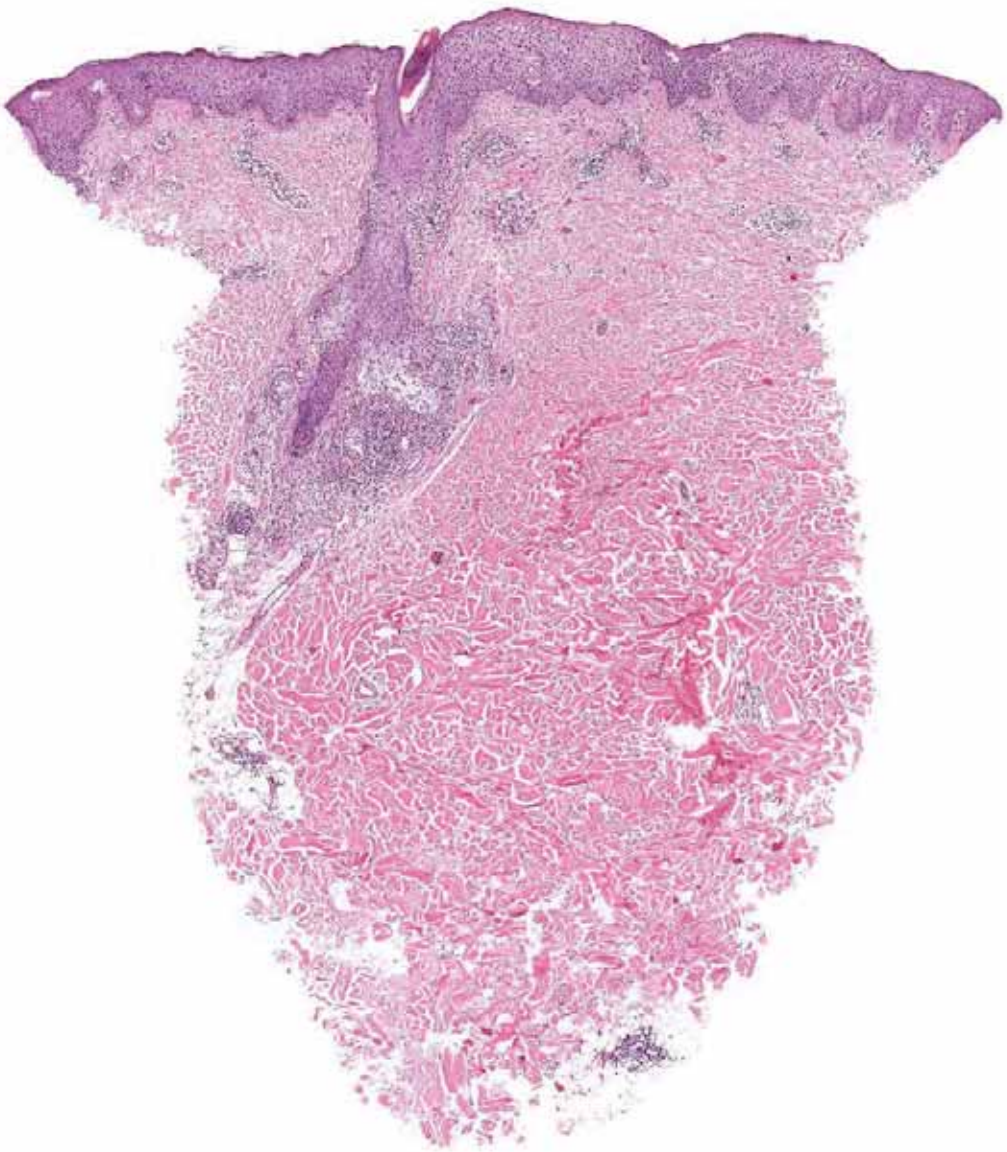


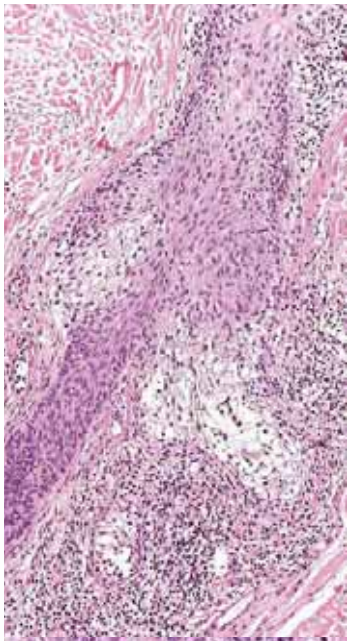
F, 41

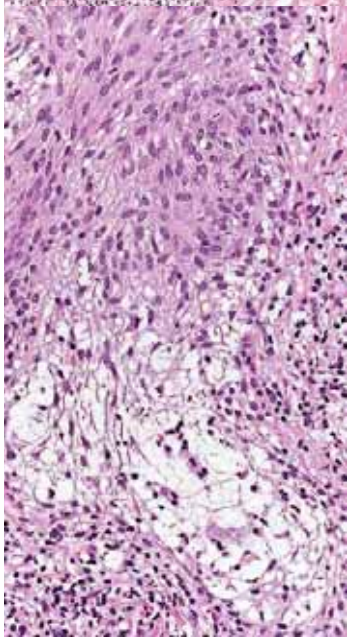
Skin lesions on the trunk and upper extremities for approximately 9 months. No improvement with local steroids and local tacrolimus.

A biopsy is taken.

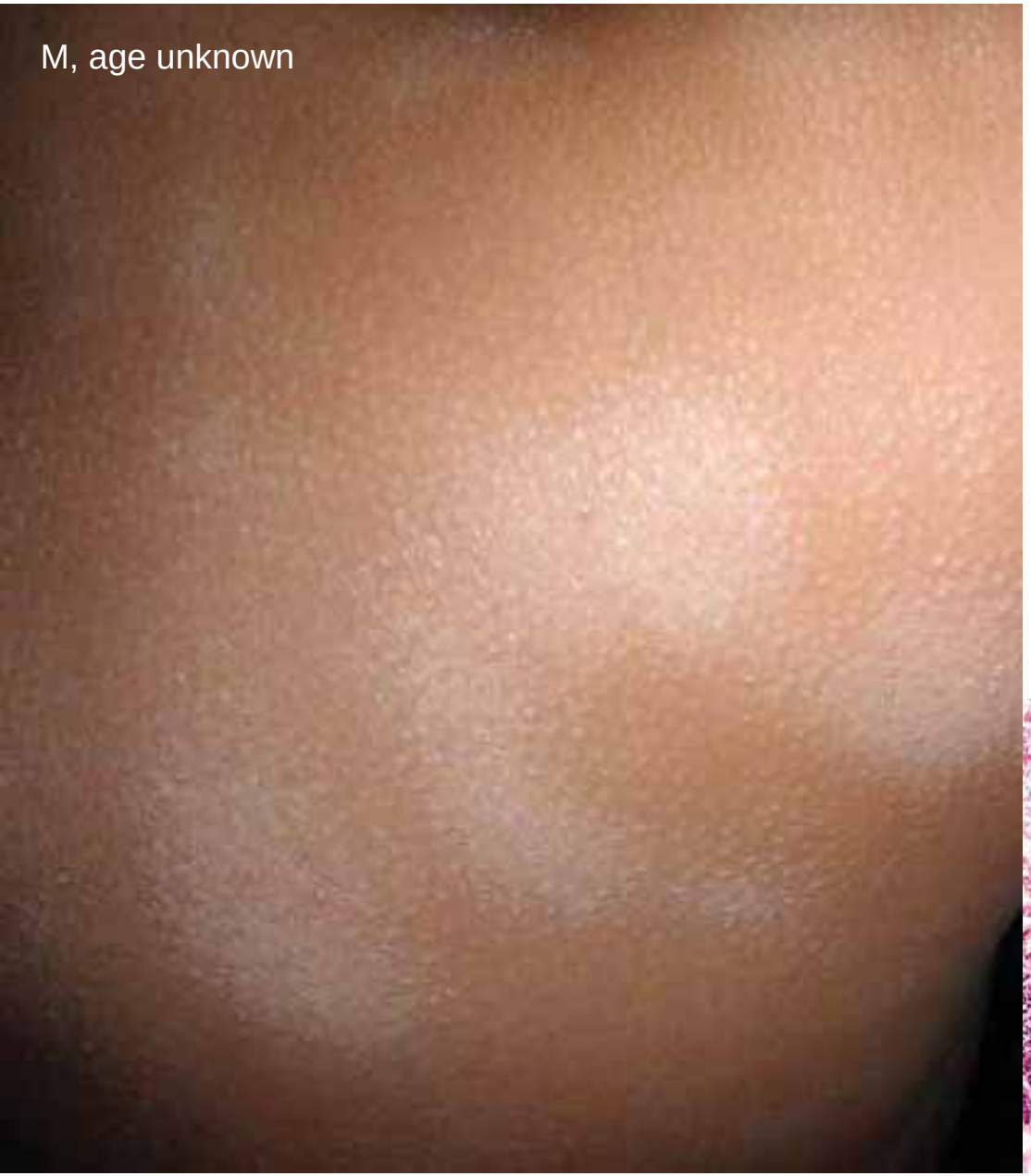


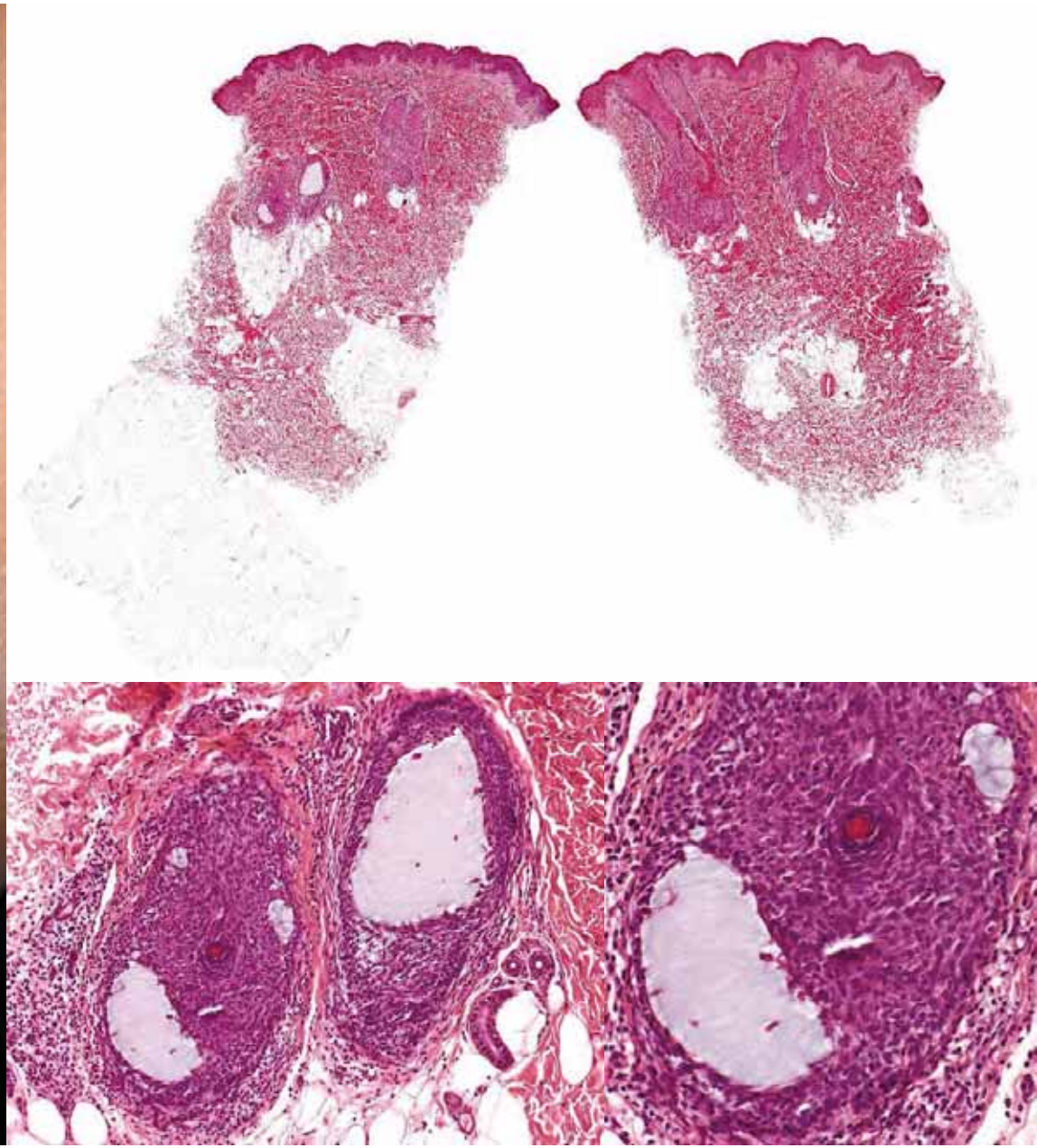






M, age unknown





Skin colored & hypopigmented follicular mucinosis

- Lesions of generalized follicular mucinosis may be characterized by the lack of an erythematous component, or may be hypopigmented
- This clinical presentation may be compared conceptually to hypopigmented mycosis fungoides; association to clear-cut MF yet unclear
- Histopathologically no differences with conventional follicular mucinosis

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CASE REPORT

Uncommon presentation of mycosis fungoides: Eyelid margin involvement

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ABSTRACT

Mycosis fungoides is a cutaneous T-cell lymphoma that has been rarely reported to involve ocular structures. A 33-year-old woman who had received therapy for mycosis fungoides on the trunk for 11 years, presented to our clinic with new plaques and tumors on her eyebrows and eyelid margin, and alopecia of her eyelashes and eyebrow. The histopathological examinations supported the diagnosis of mycosis fungoides. There was no intraocular involvement with tumor. The mycosis fungoides was of stage II B, and the patient was referred to medical oncology and radiation oncology clinics for treatment. She was placed on a radiotherapy schedule. The involvement of mycosis fungoides in the ocular area is rare in the published work. The importance of eye involvement is being seen in advanced cases, and there is a possible association between mycosis fungoides and poor prognosis by being an indicator of systemic involvement.

Key words: ectropion, eyebrow, eyelid neoplasm, facial neoplasm, mycosis fungoides

INTRODUCTION

Mycosis fungoides (MF) is a low-grade cutaneous T-cell lymphoma (CTCL) that has a slow progression.[1] Generalized systemic disease occurs in the late-stage disease and infrequently involves ocular structures.[2,3] We report a case of MF without any systemic involvement although presenting with eyelid margin involvement.

CASE REPORT

A 33-year-old woman presented with plaques and tumoral lesions on the nose, eyelids, cheeks, arms and shoulders. She had a diagnosis of MF on her trunk and shoulder dating from 11 years before, and had received various treatments such as topical corticosteroids, psoralen plus ultraviolet A (PUVA) therapy, systemic chemotherapy and radiotherapy. The lesions on her brows appeared 6 years previously, whereas the tumors on her right eyelid margins and alopecia on her eyelashes occurred during the last months. The physical examination revealed no pathology. On dermatological examination, infiltrative plaques and tumoral lesions were found at the superior and inferior margins of the right eyelid and the right side of the glabella, cheeks, neck and upper arms (Fig. 1). She also had ectropion and madarosis. Alopecia was observed of the right eyelashes and partially of the left eyebrow. In histopathological examinations of the lesions sited at the arm, nose and eyelid margin, findings of a tumoral stage of MF were revealed (Figs 2,3). Only a slight epidermotropism could be observed, as the tumor was at tumoral stage (Fig. 4). There was infiltration of hair follicles with atypical lymphocytes, and areas of mucinous degeneration were noted (Figs 3,5).

Blood and serum analysis, chest radiography and computed tomography were normal. No intraocular involvement with MF was detected. The MF was staged as II B, and referred to the Medical Oncology

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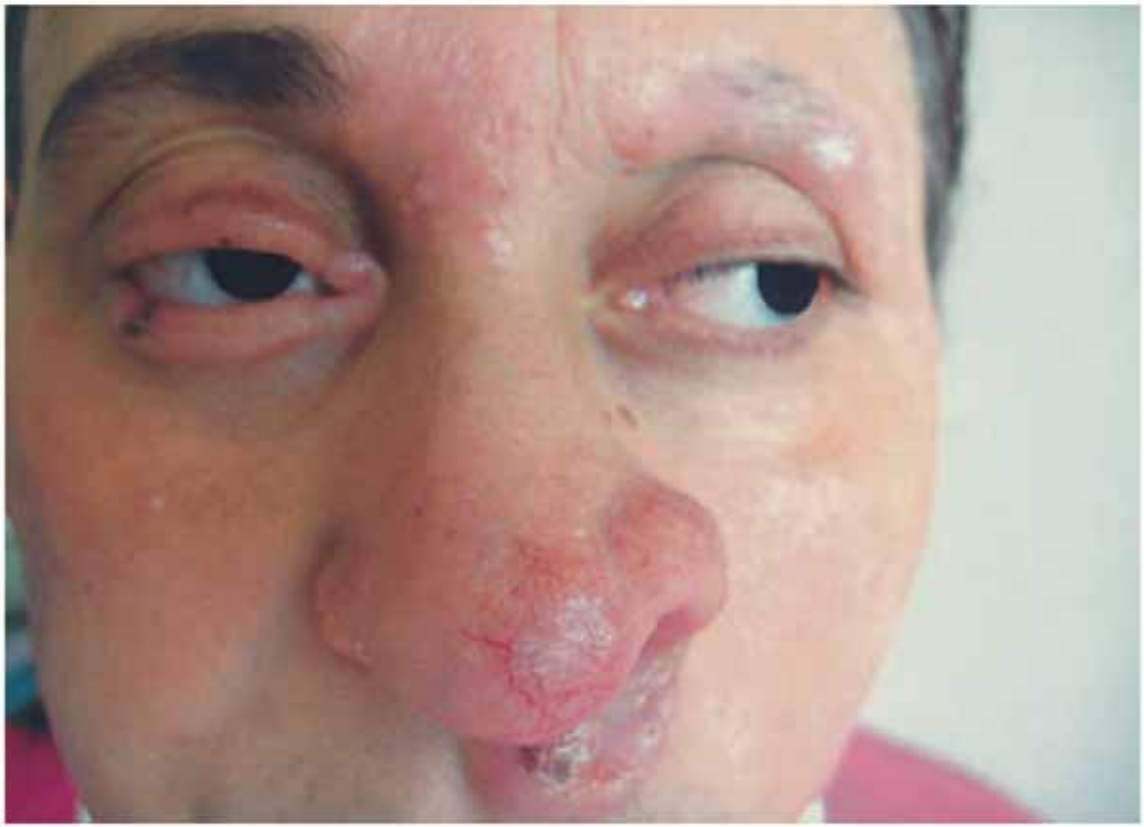
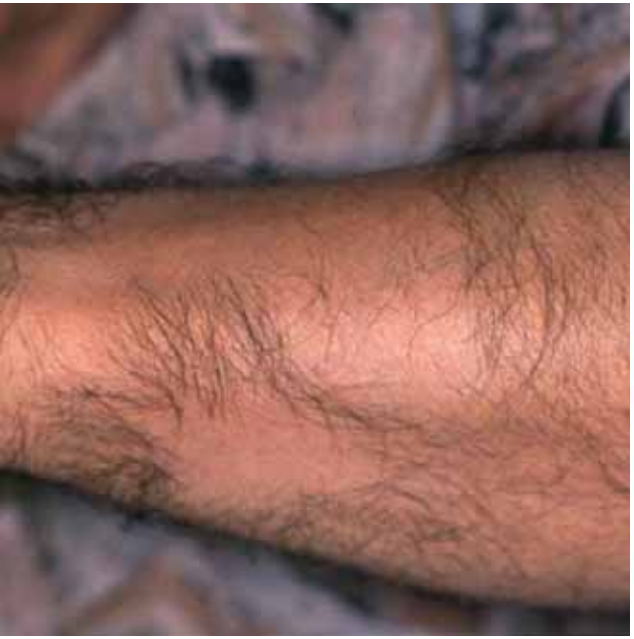
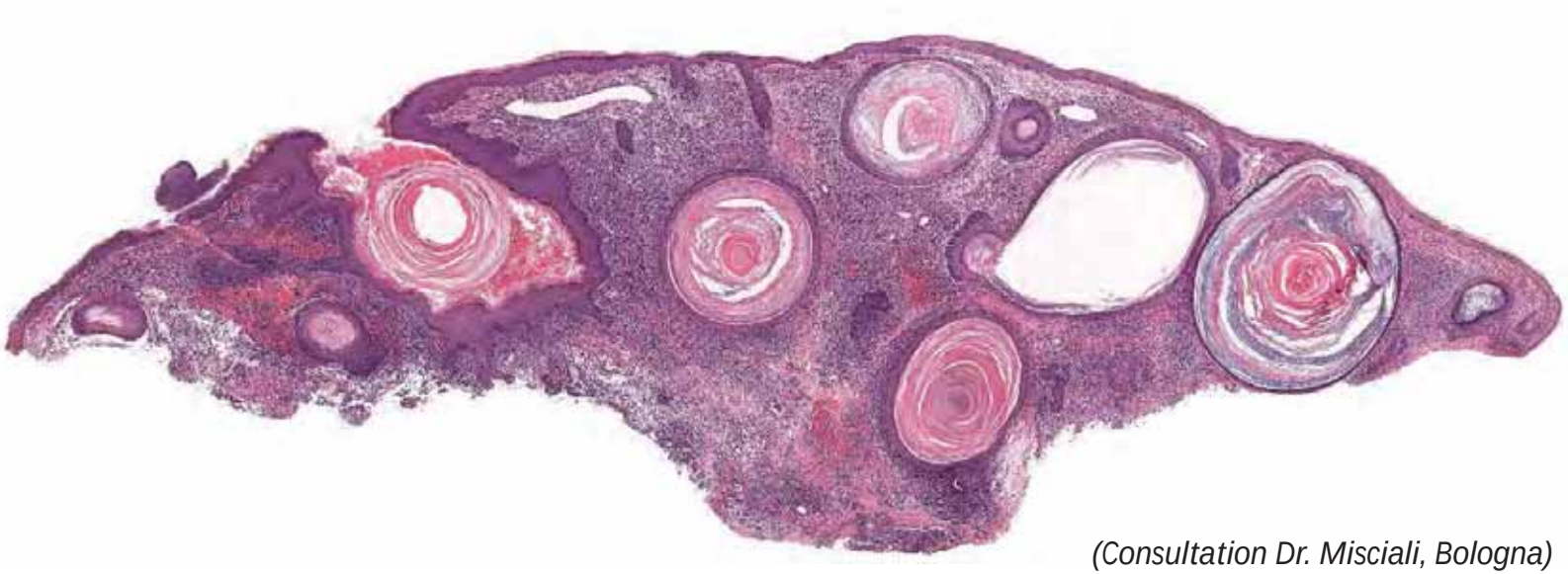
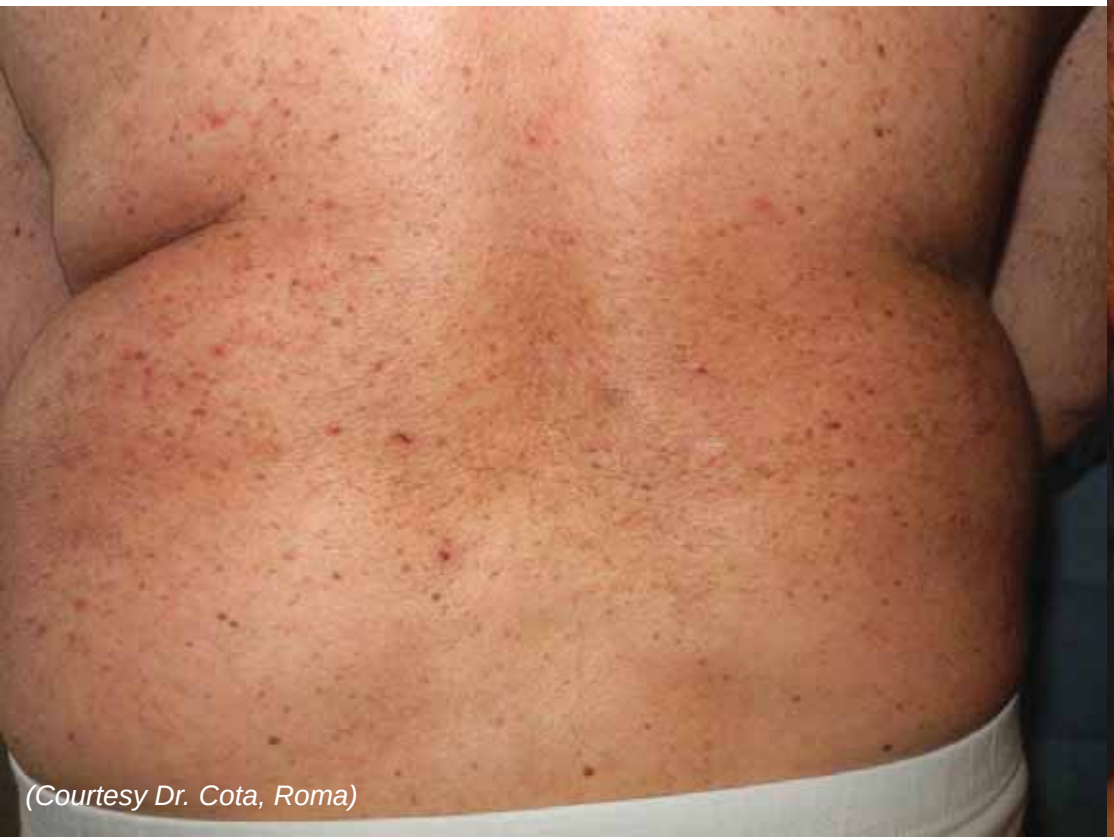






(Consultation Dr. Misciali, Bologna)



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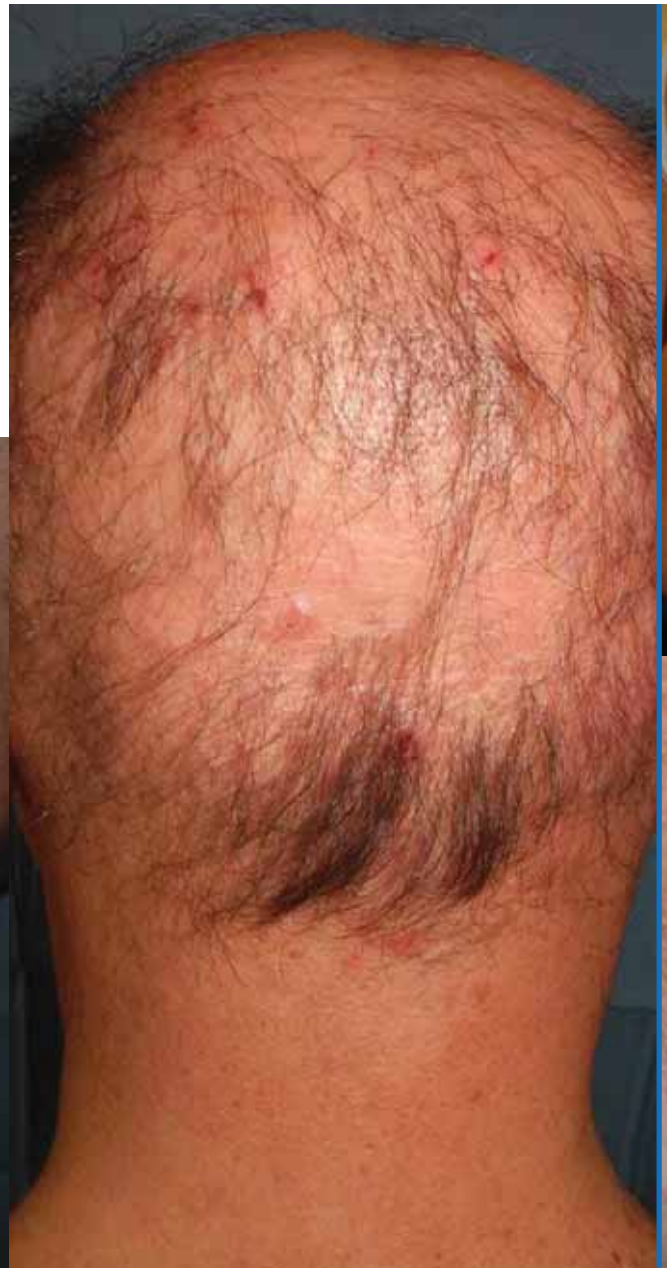
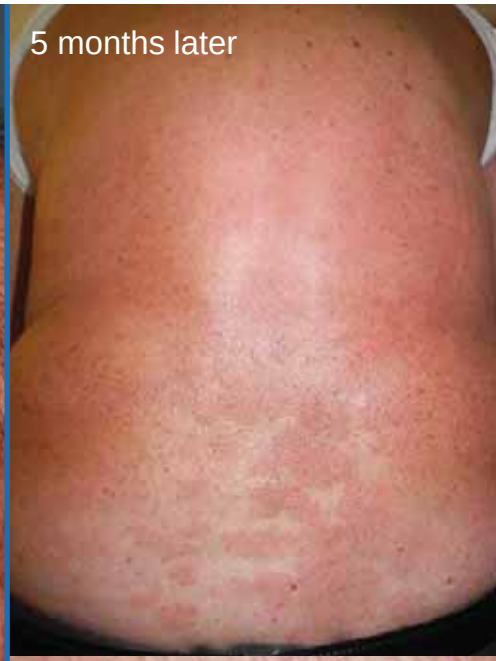
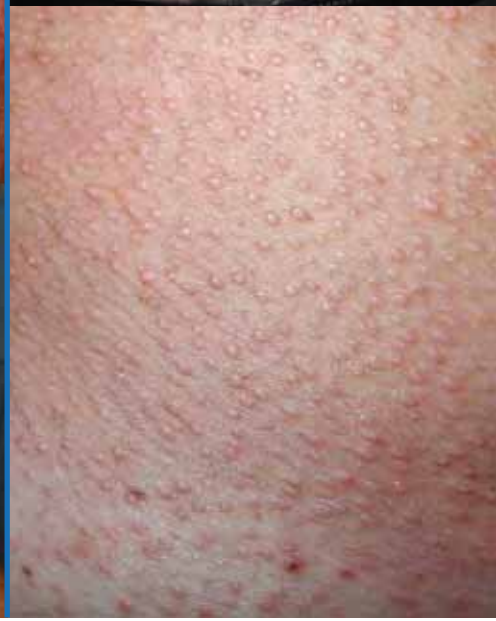
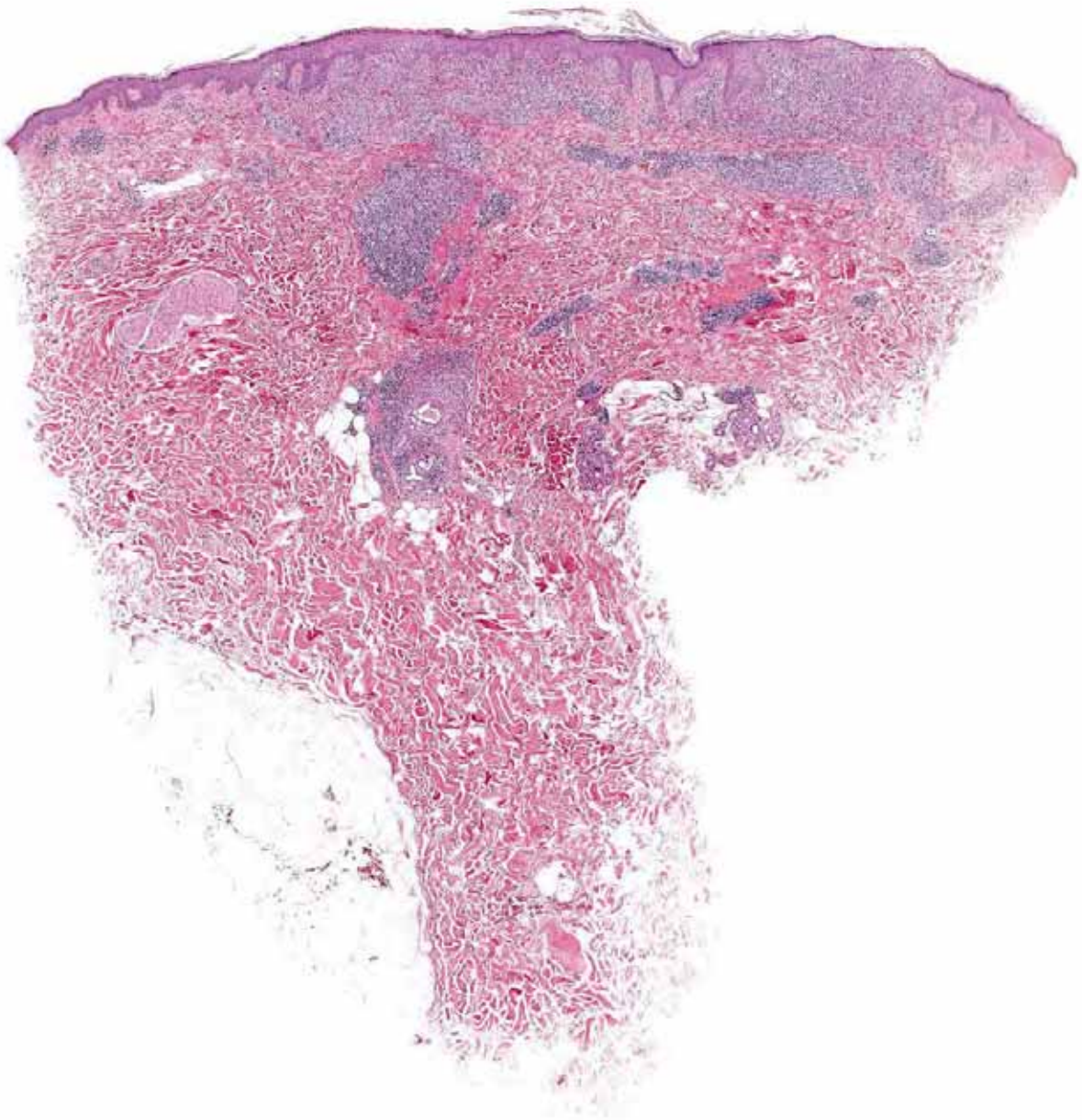
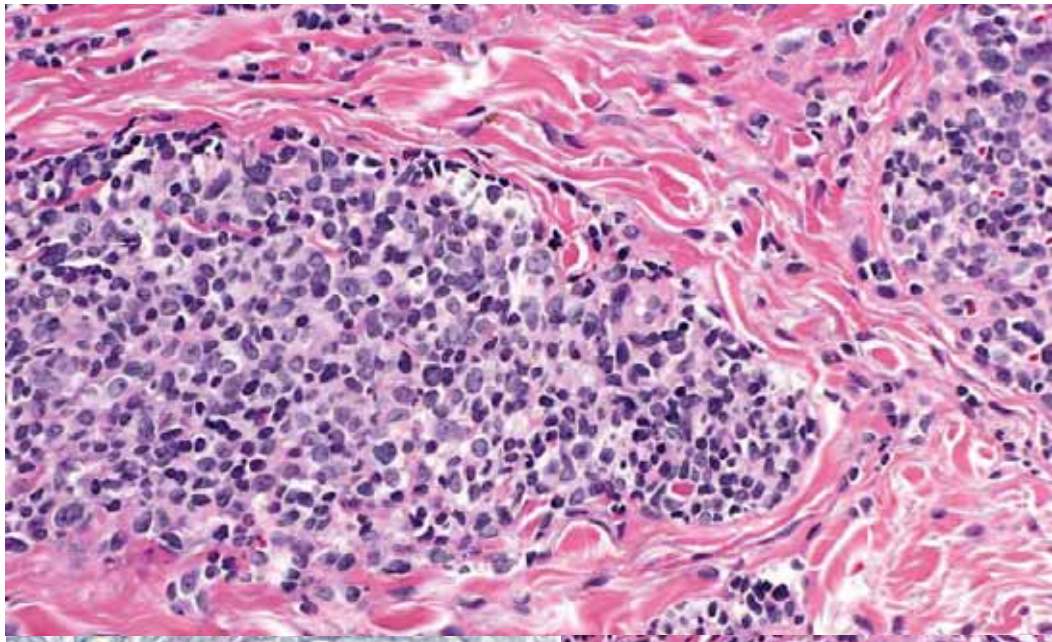


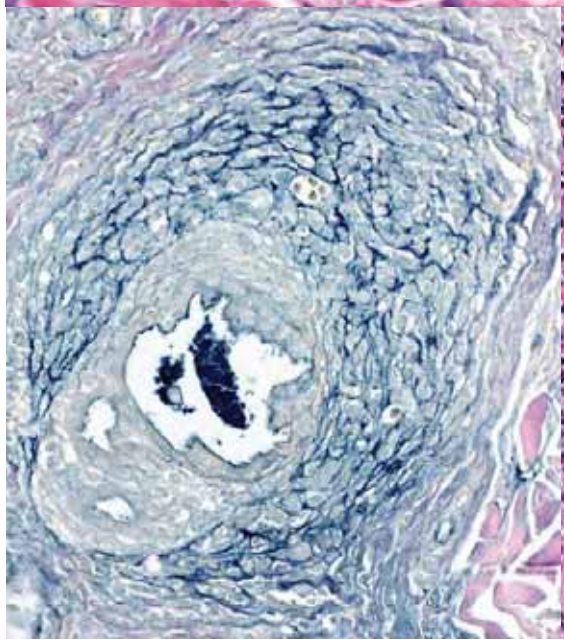


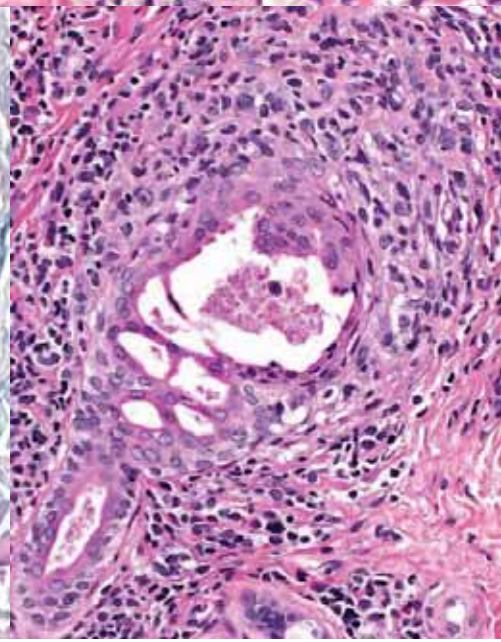
5 months later



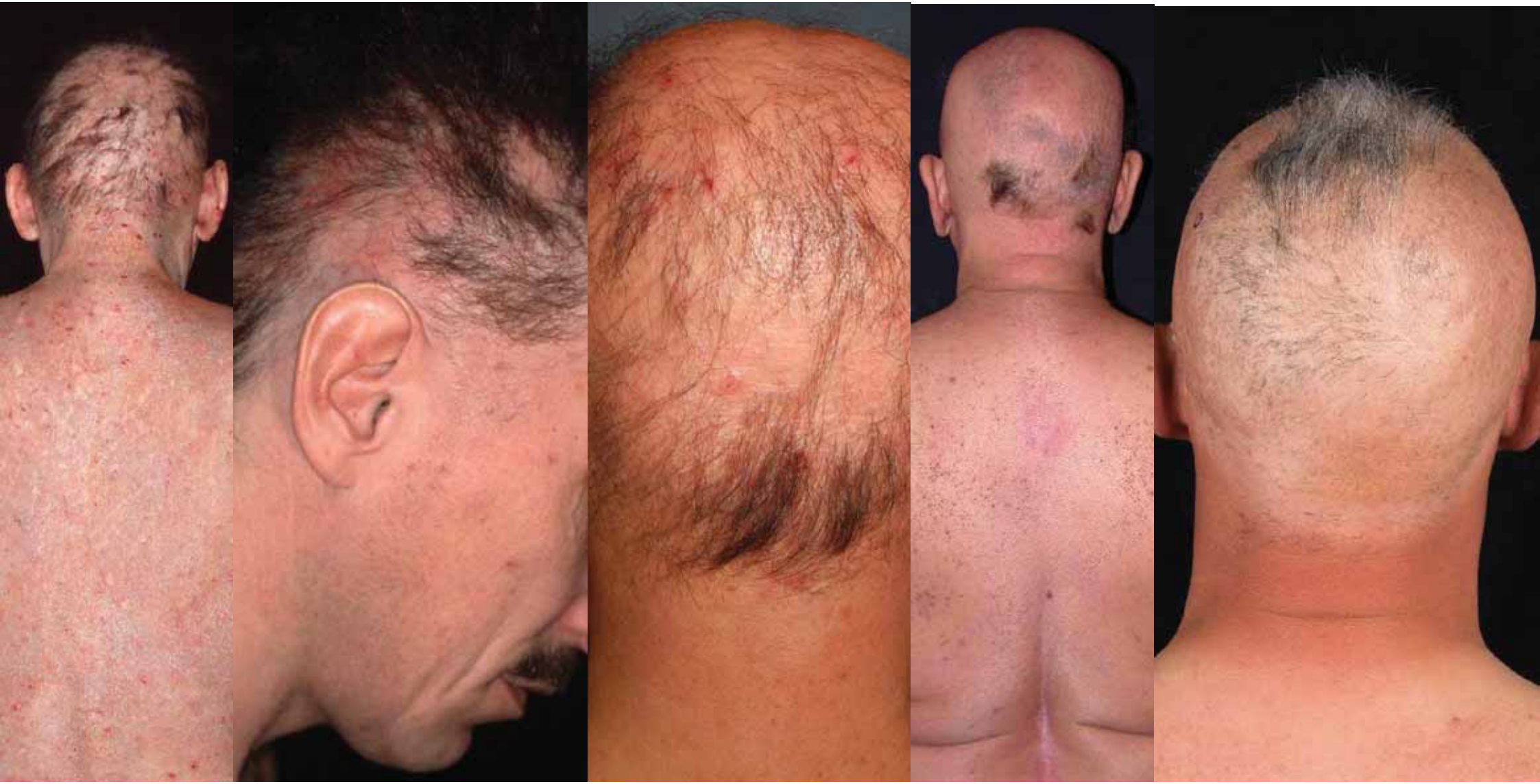


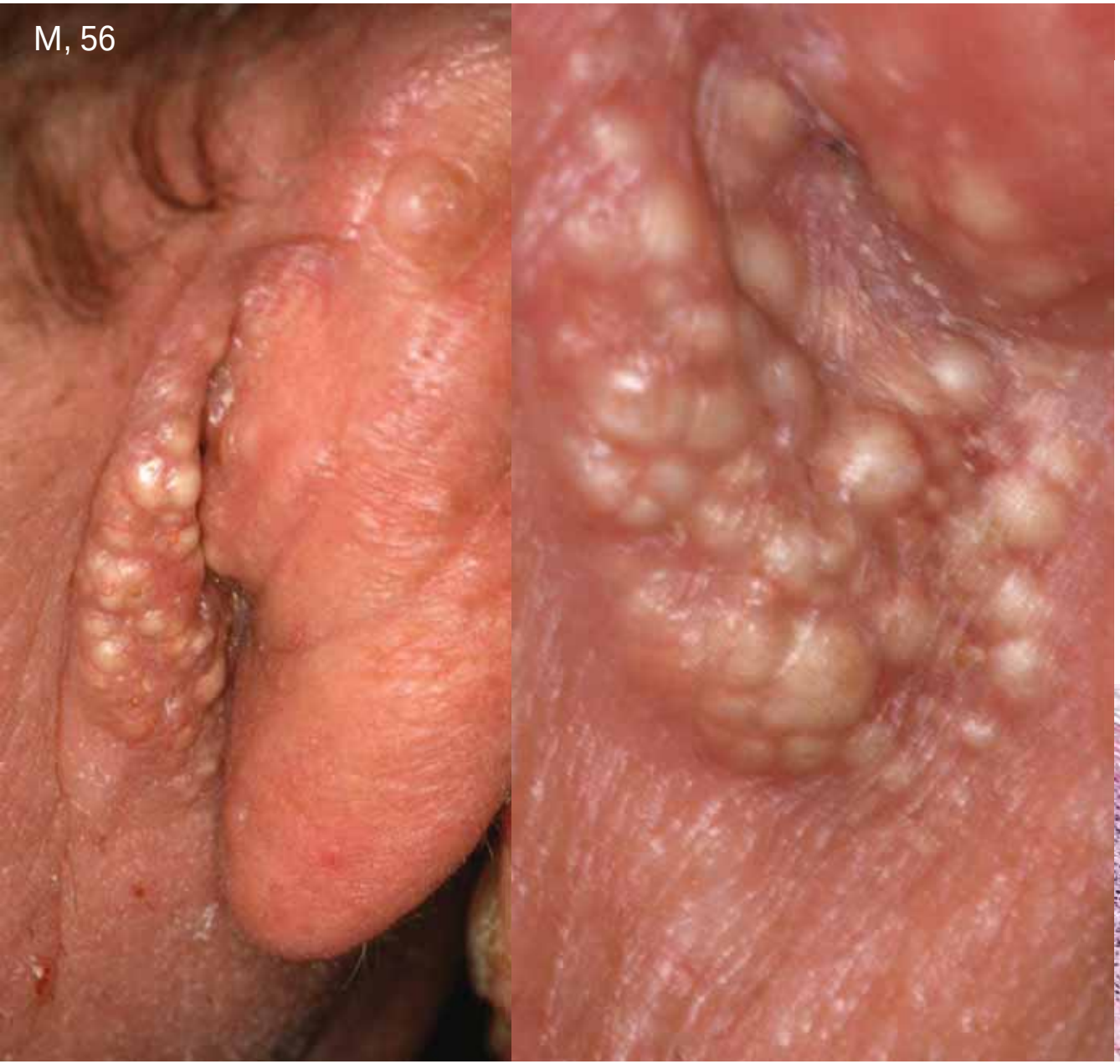




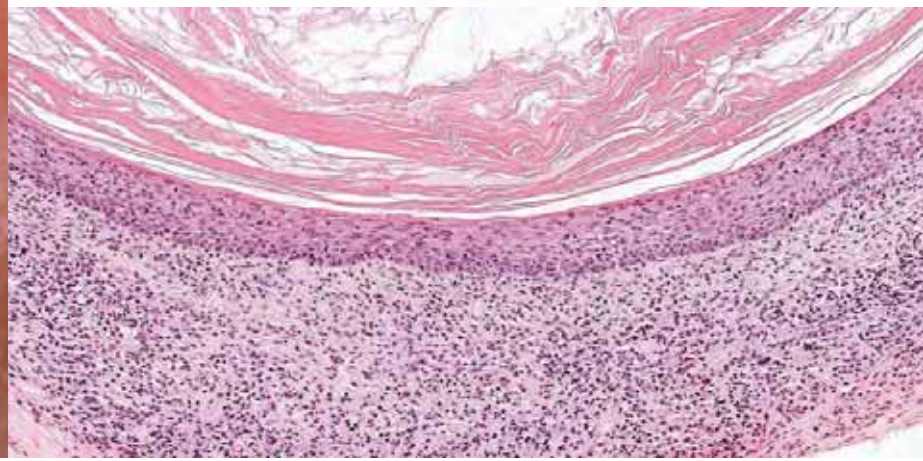


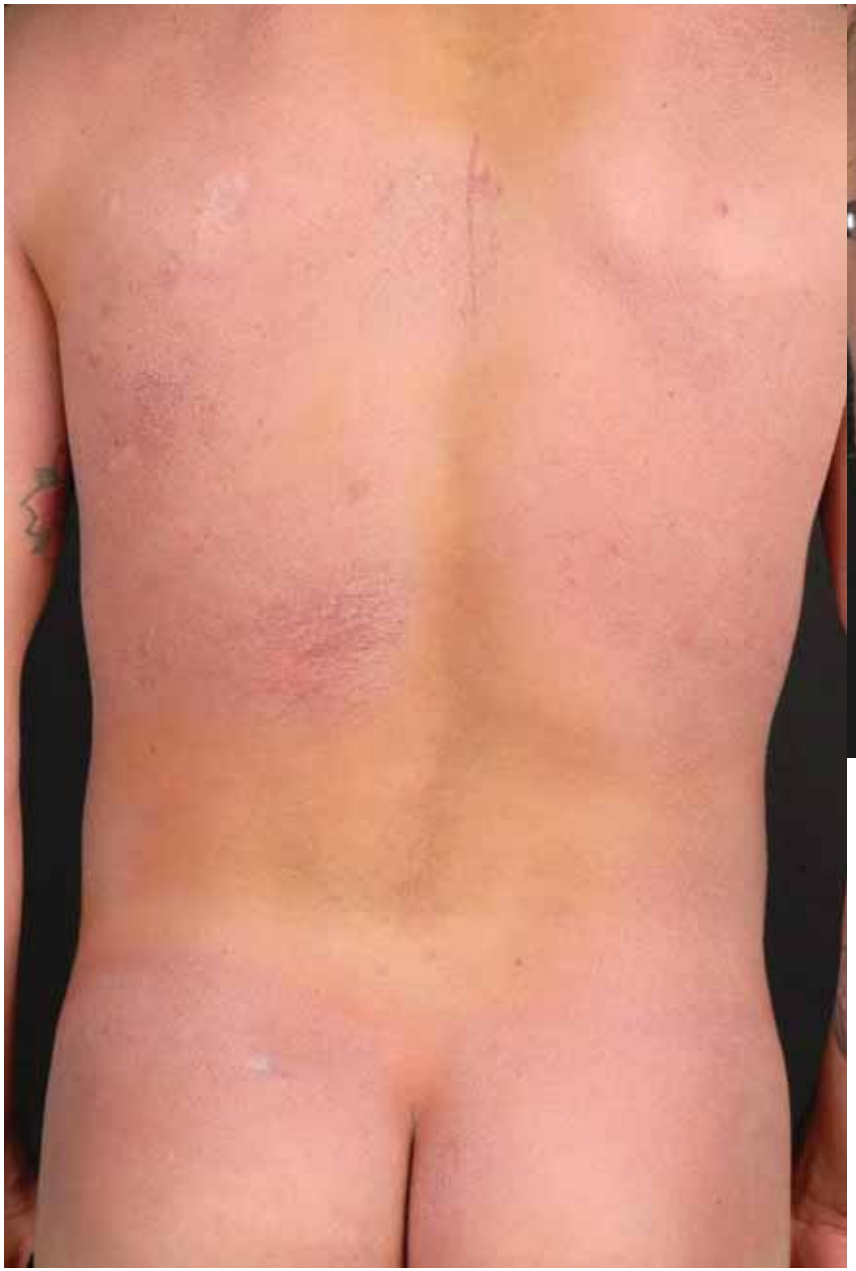
Patchy, irregular alopecia in adnexotropic mycosis fungoides

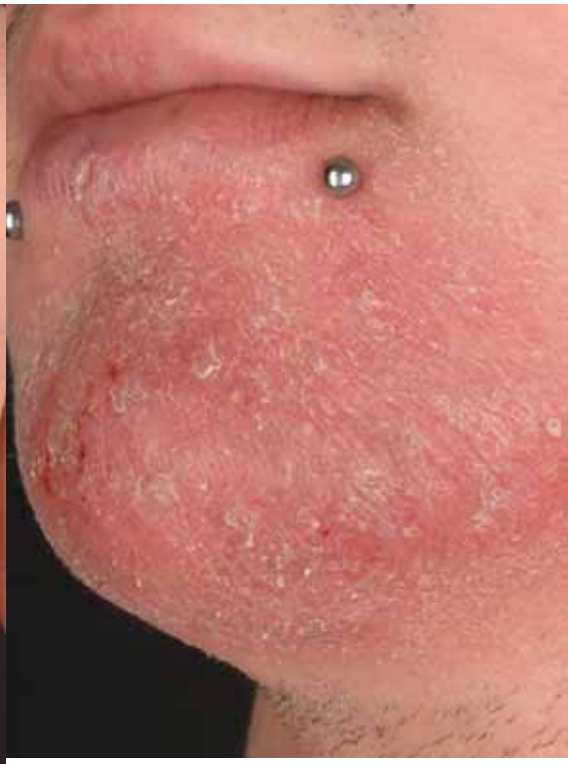




"Milia en plaque" in mycosis fungoides with cysts and comedones



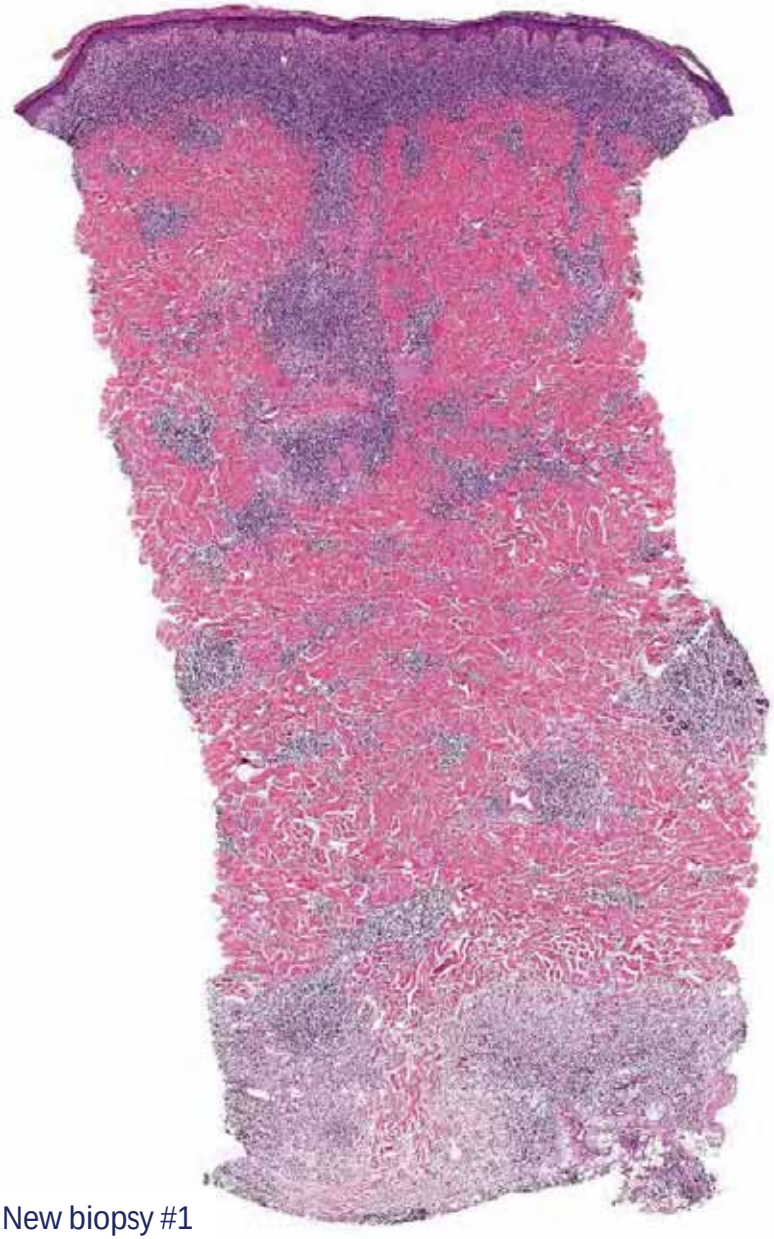




M, 19

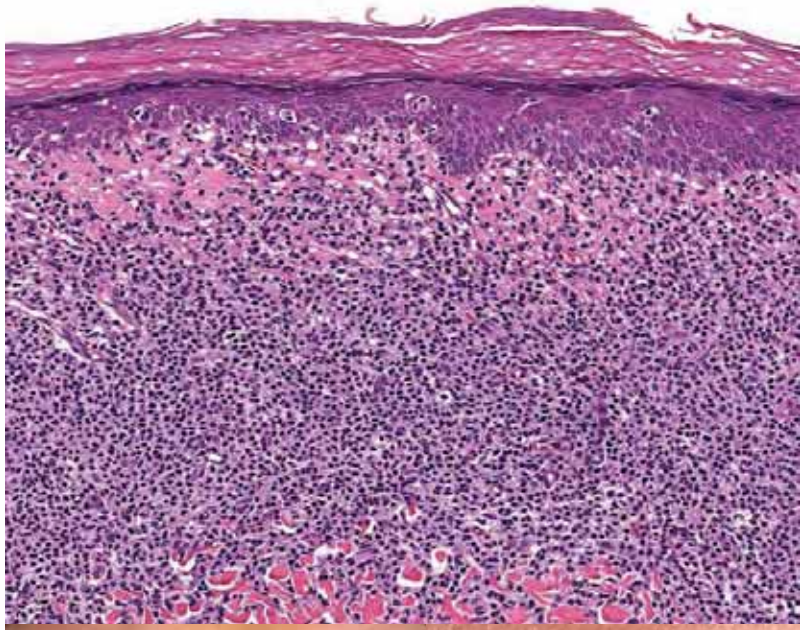
According to the patient lesion on the chin for 5 years, followed one year later by lesions on the trunk and extremities. Three previous external biopsies had been interpreted as pseudolymphoma.

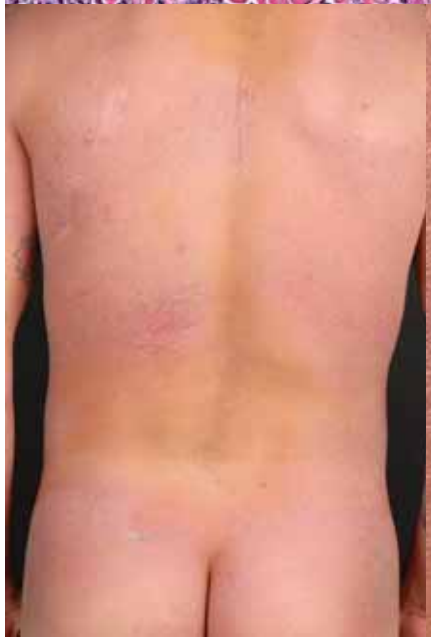
Two new biopsies are taken (back, left upper arm); the old biopsies are reviewed.

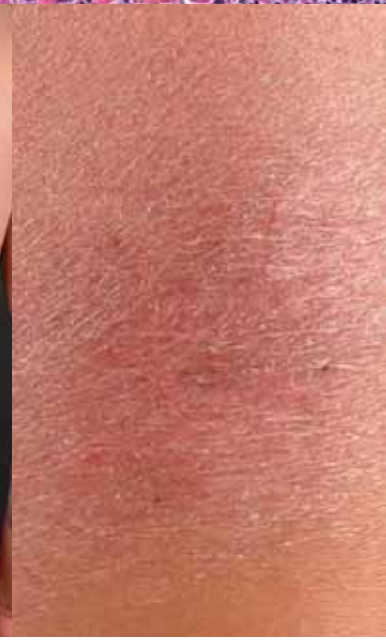


New biopsy #1

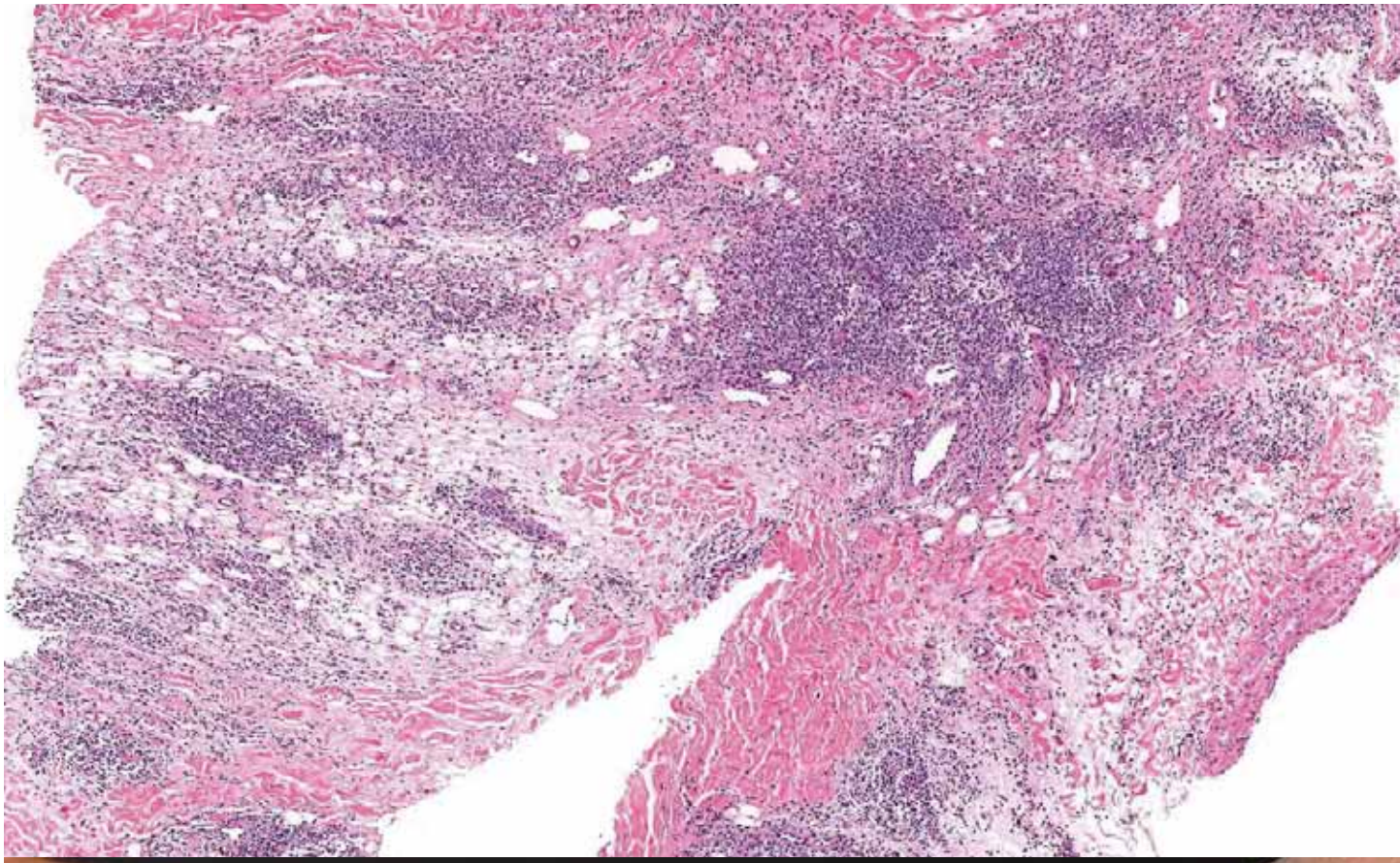
CD3

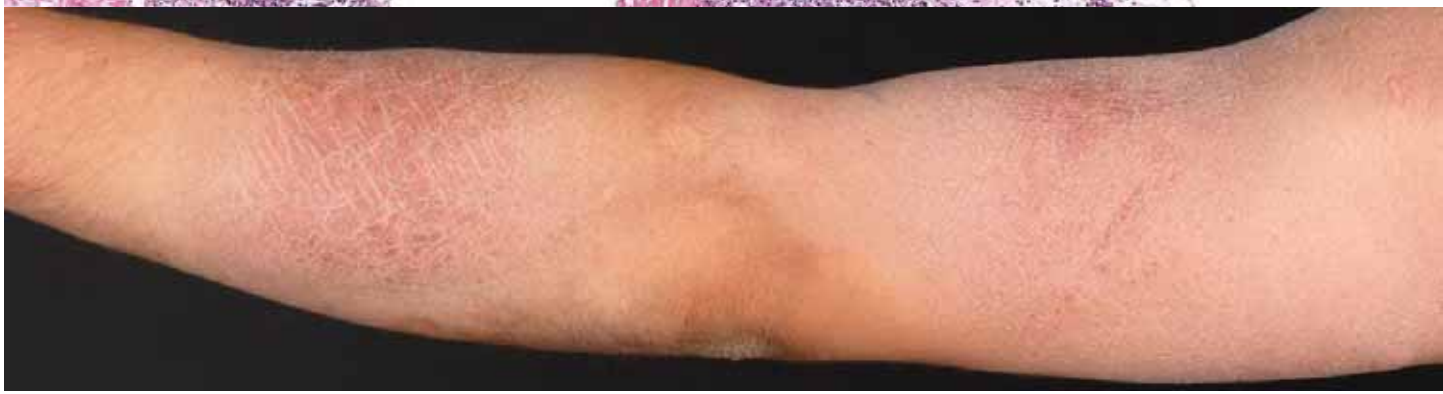


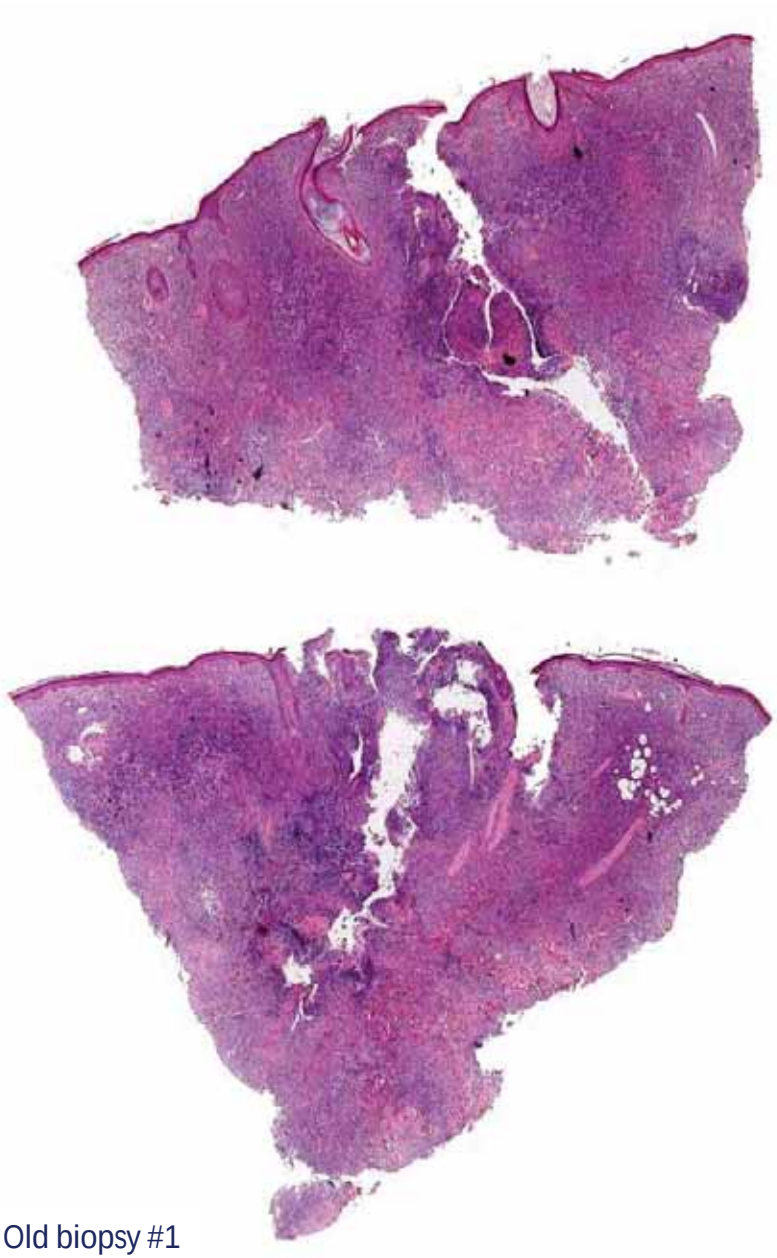




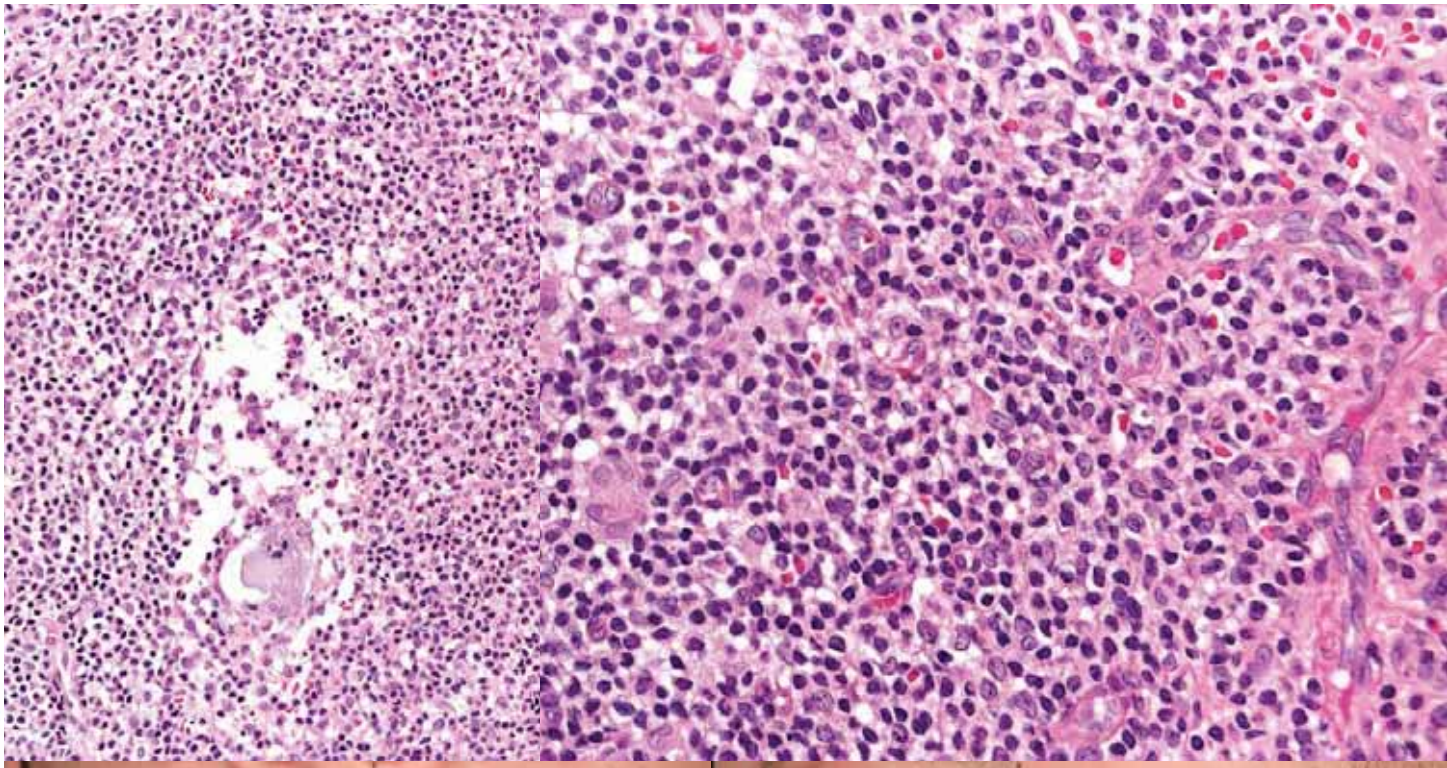
New biopsy #2

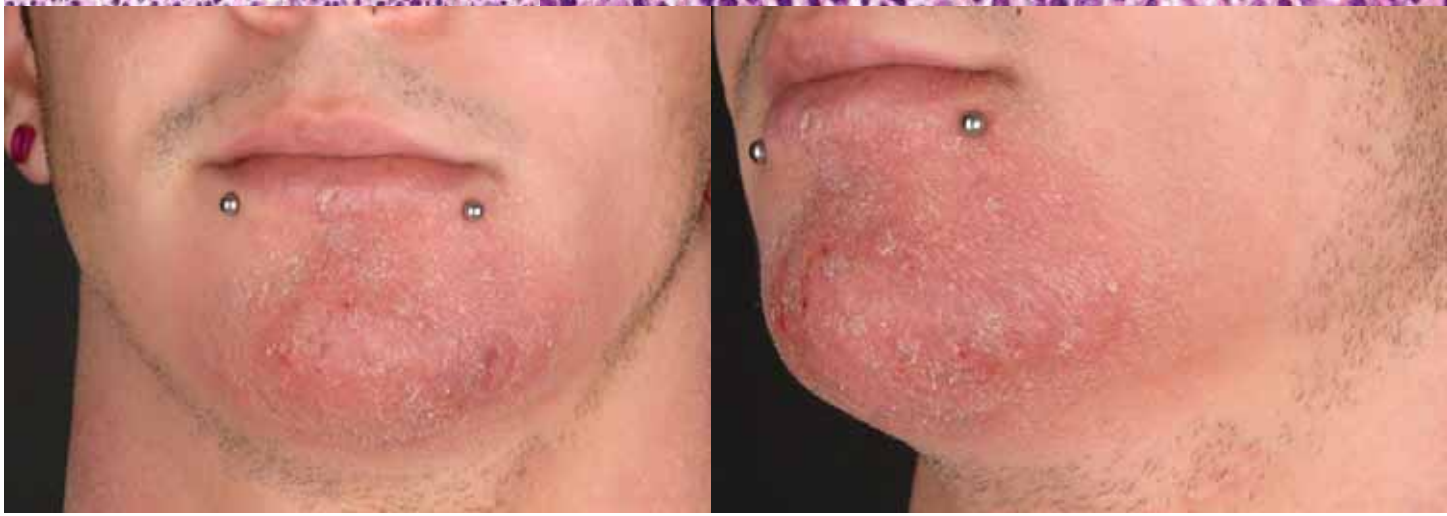


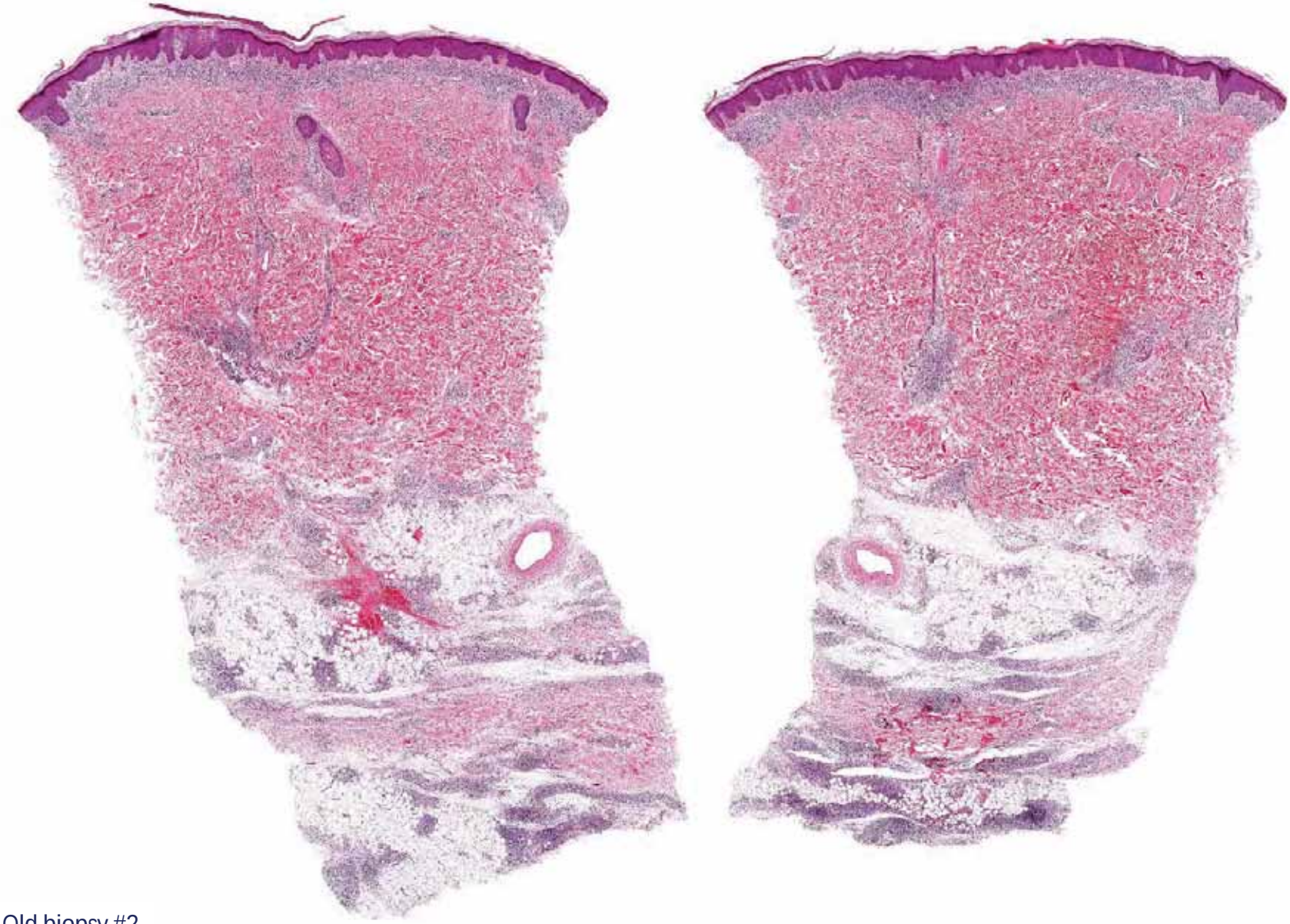


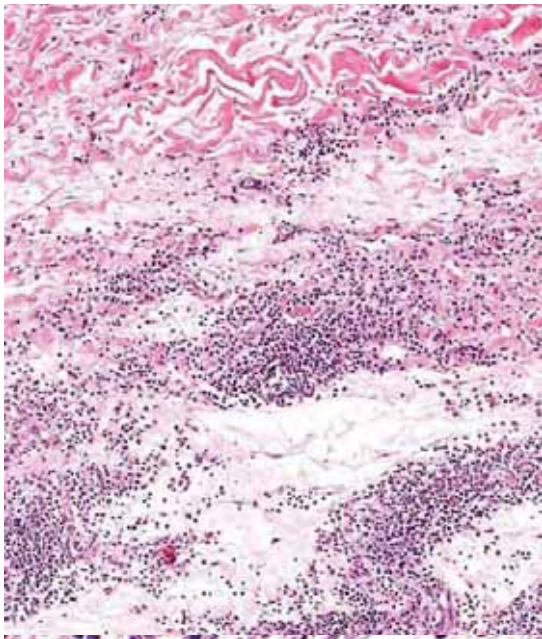


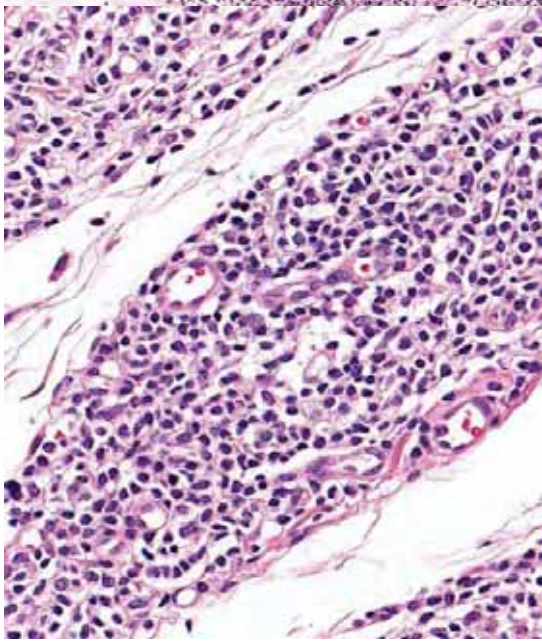
Old biopsy #1



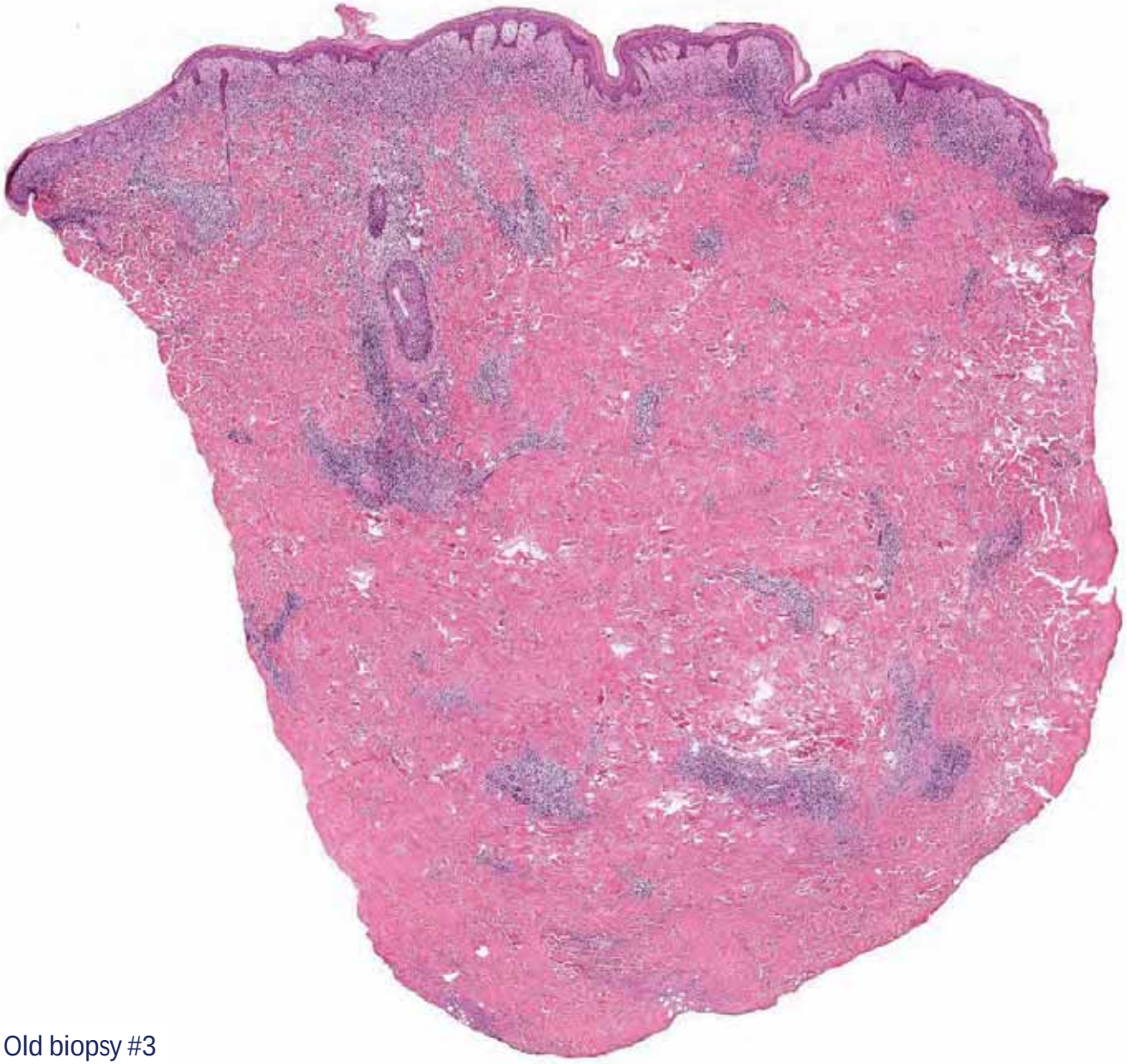




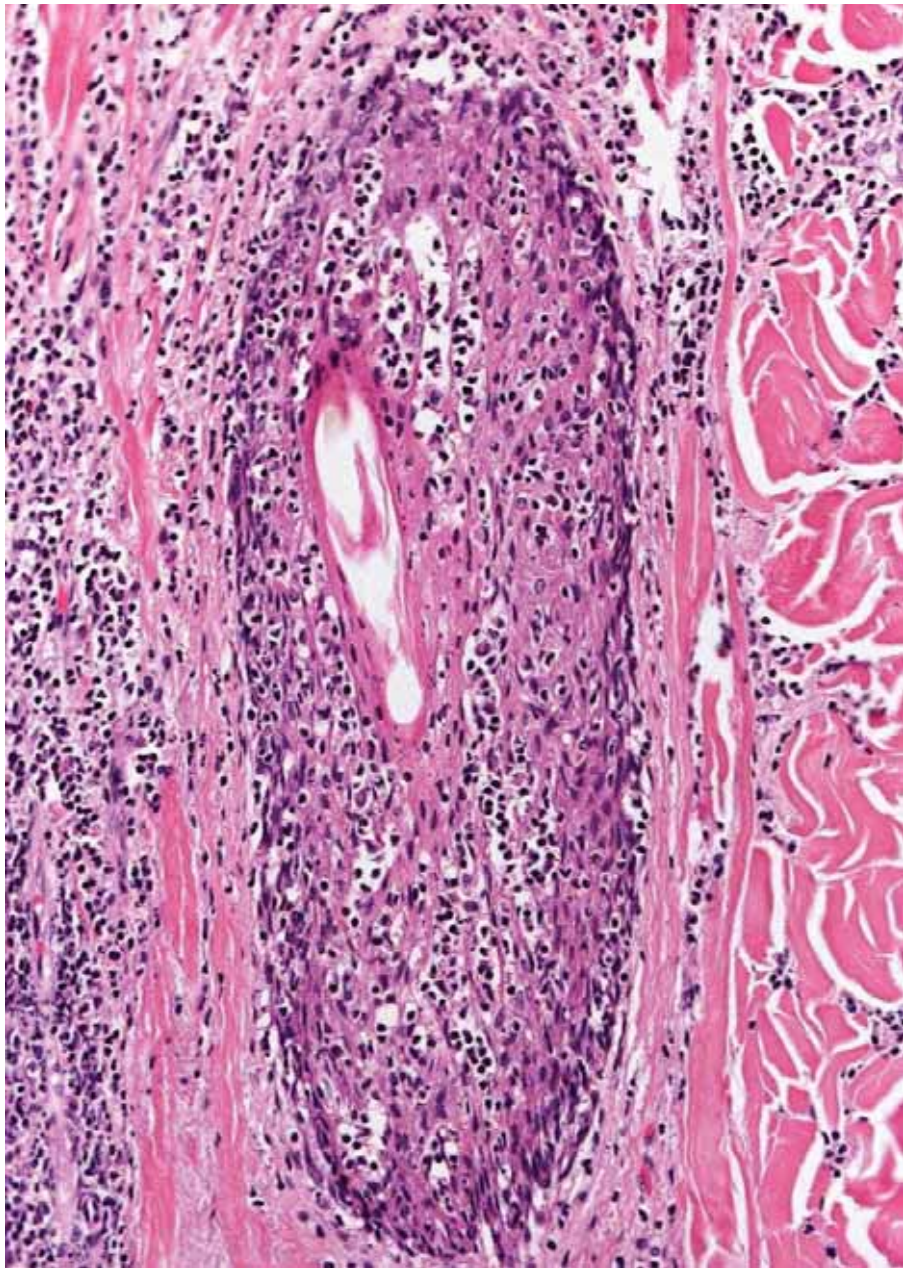


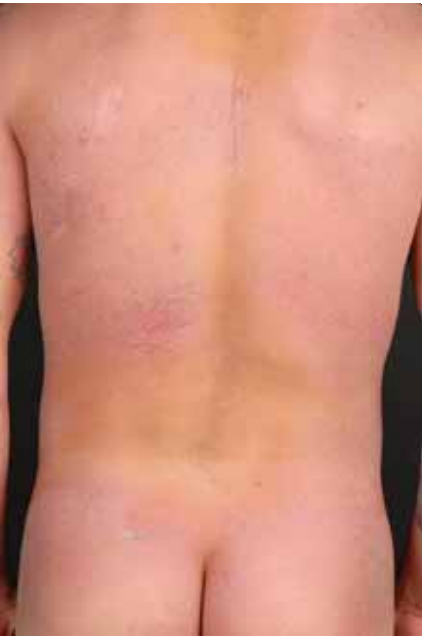


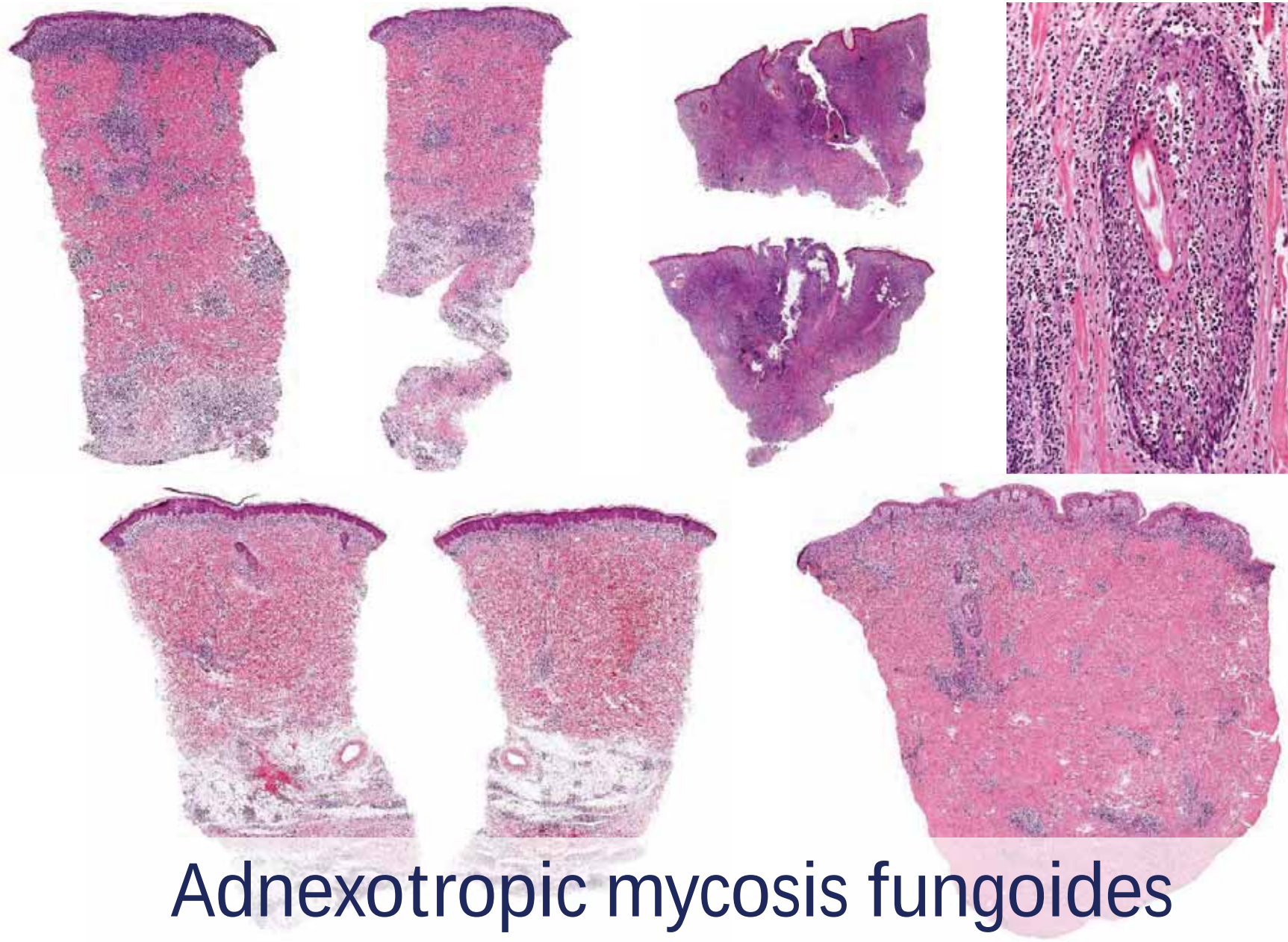
Old biopsy #2



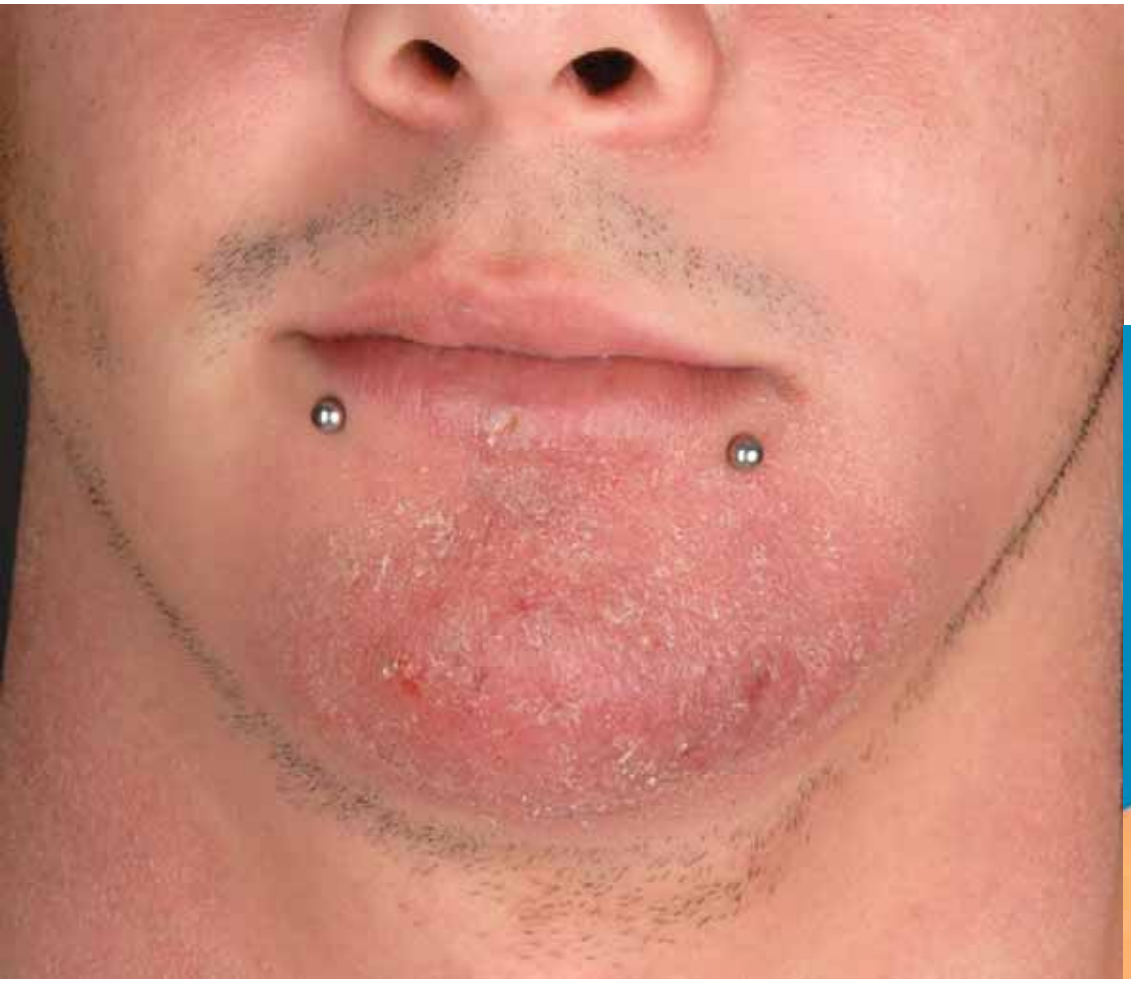
Old biopsy #3



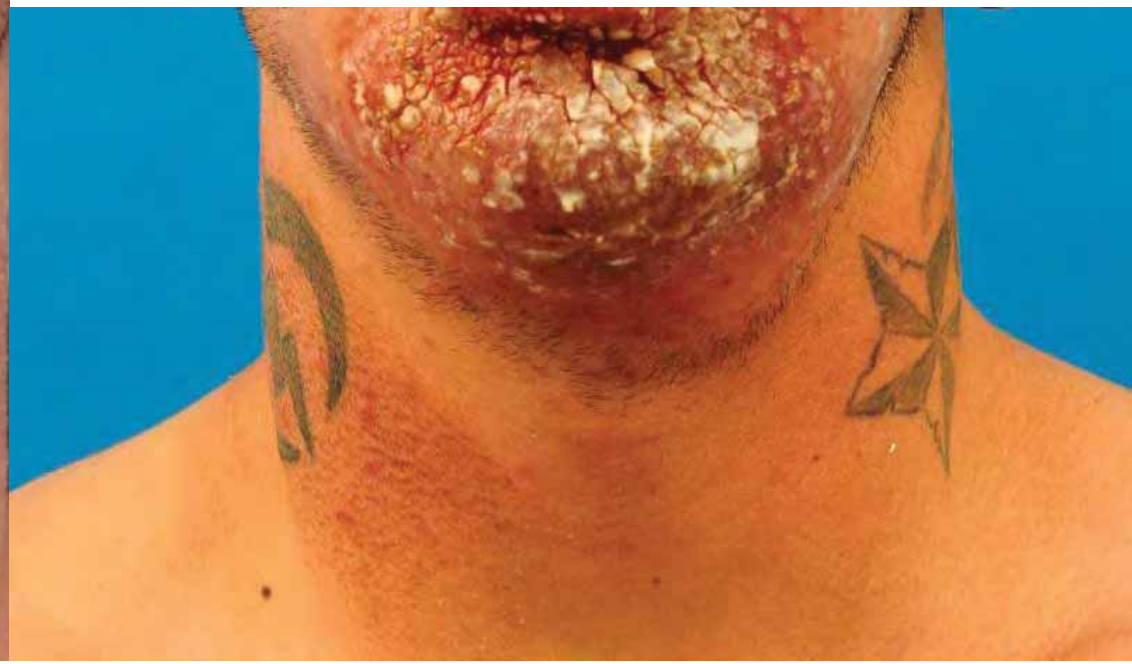




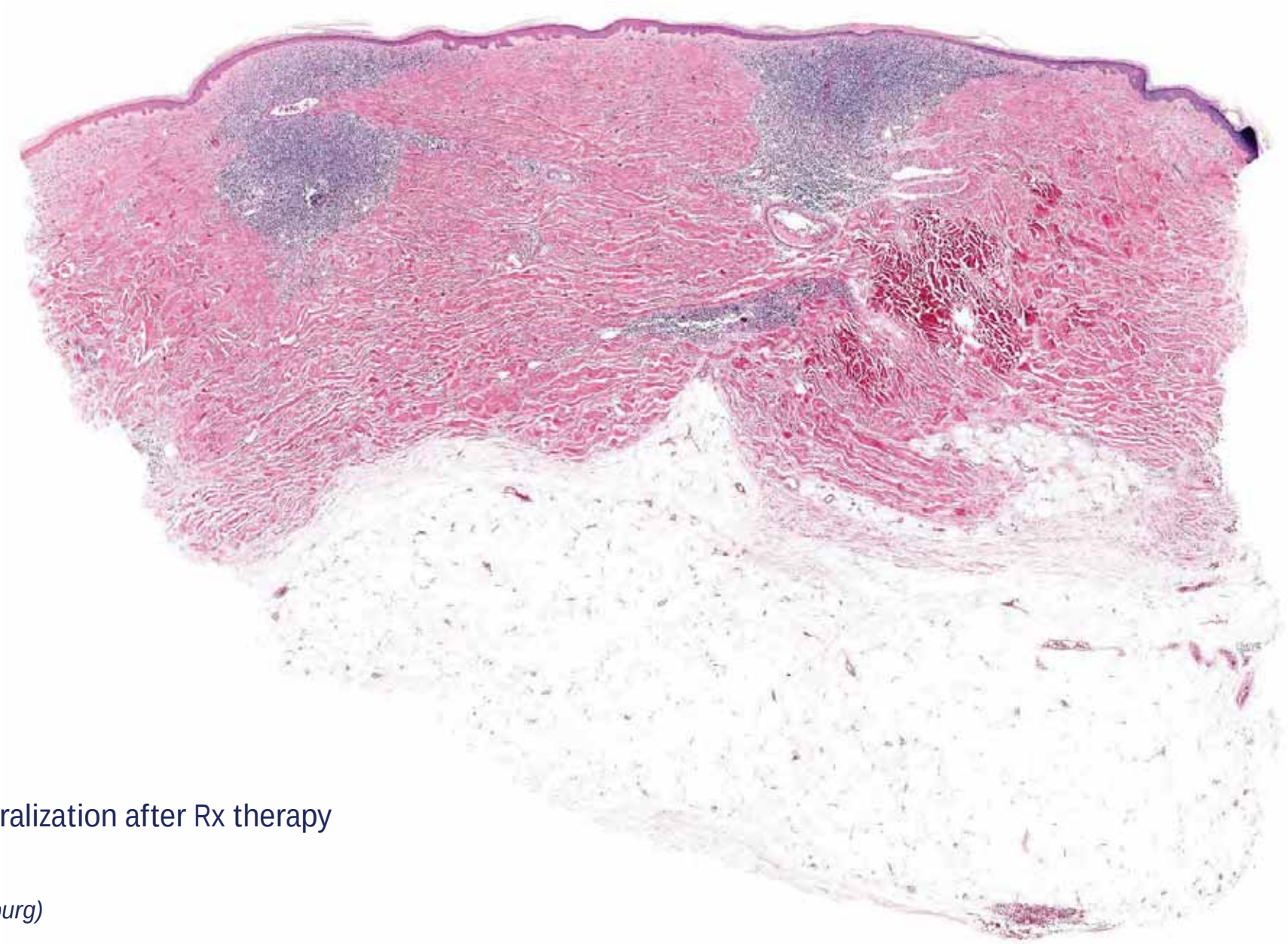
Adnexotropic mycosis fungoides



1st presentation

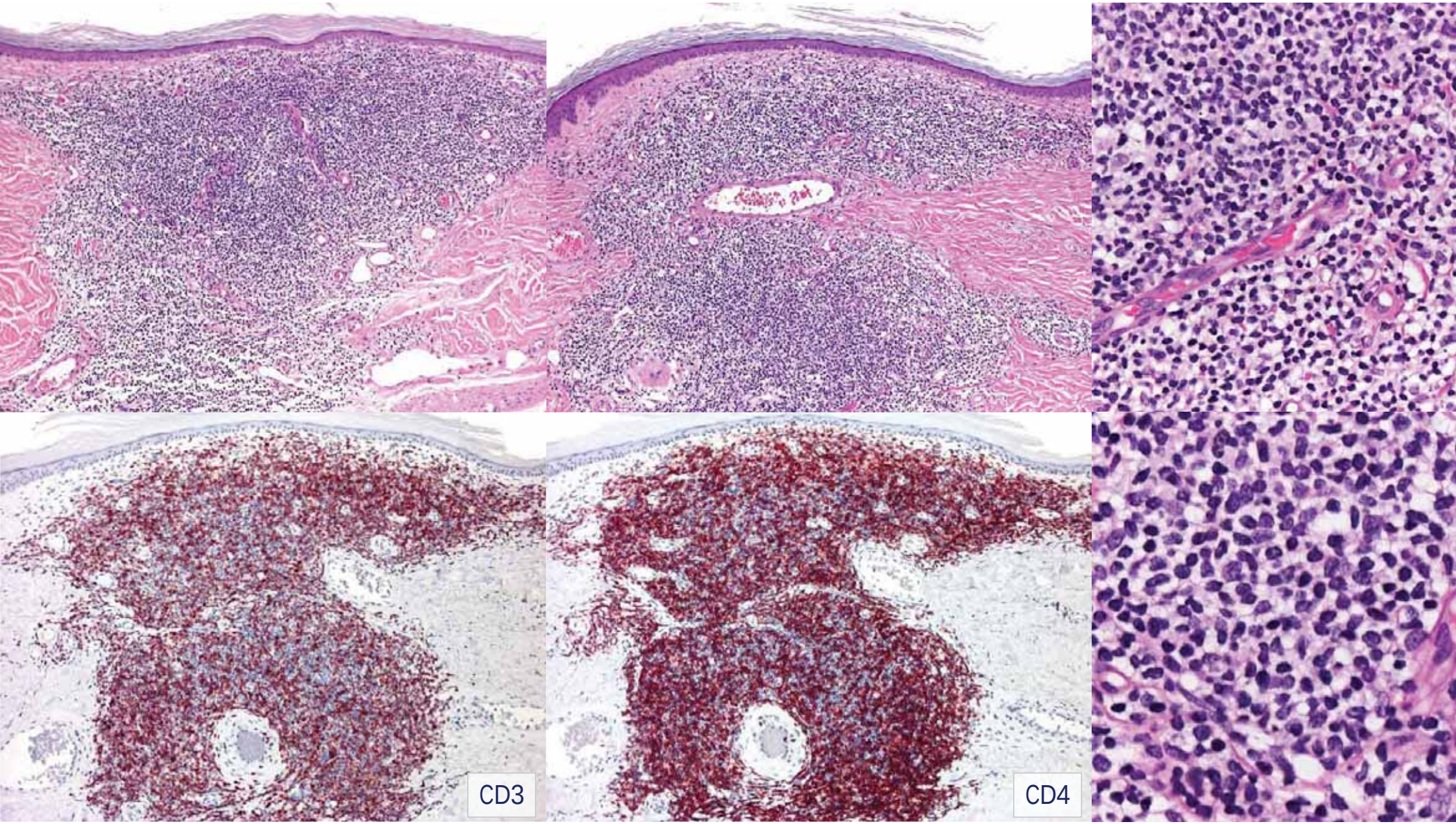


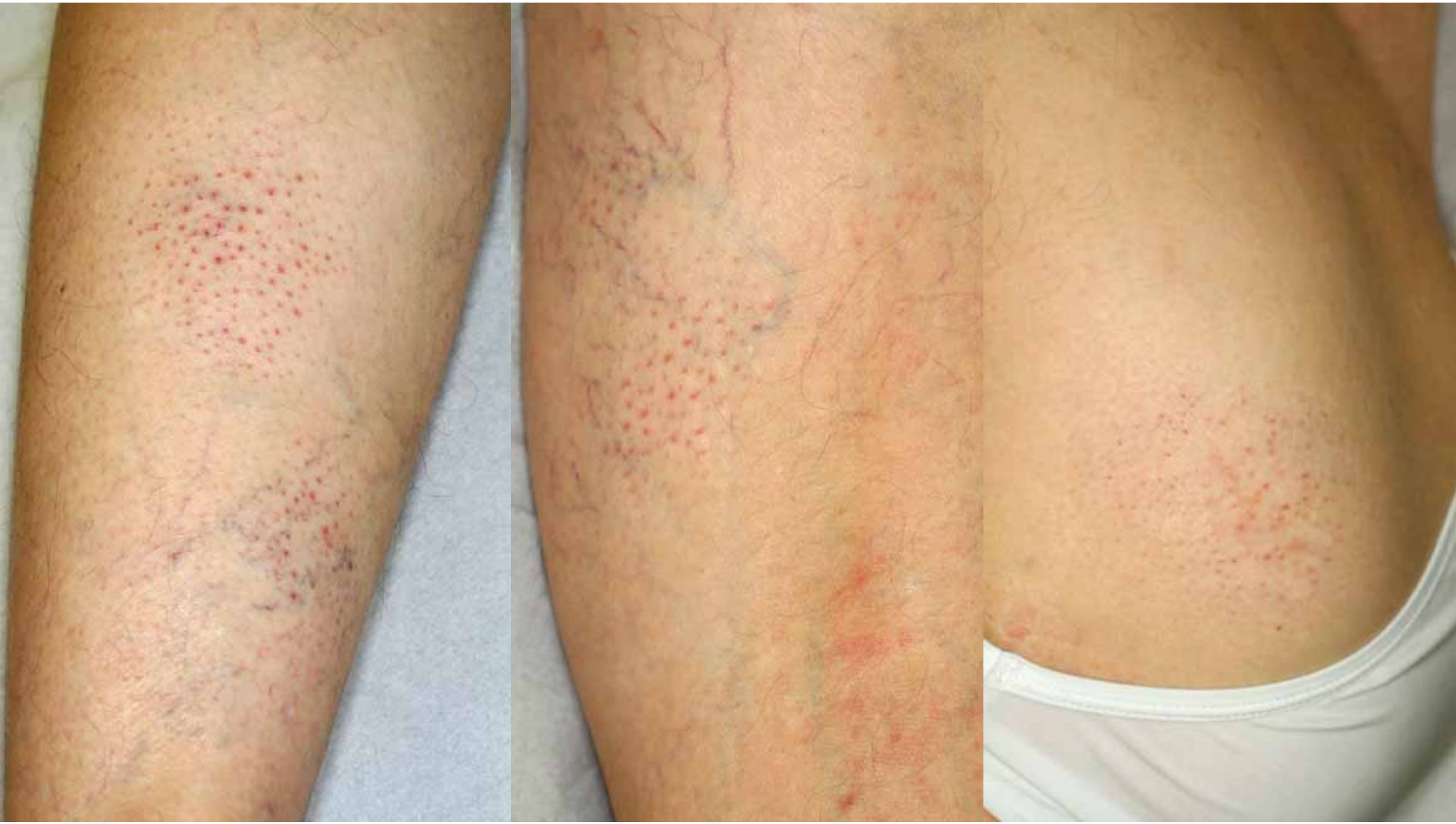
3 years later

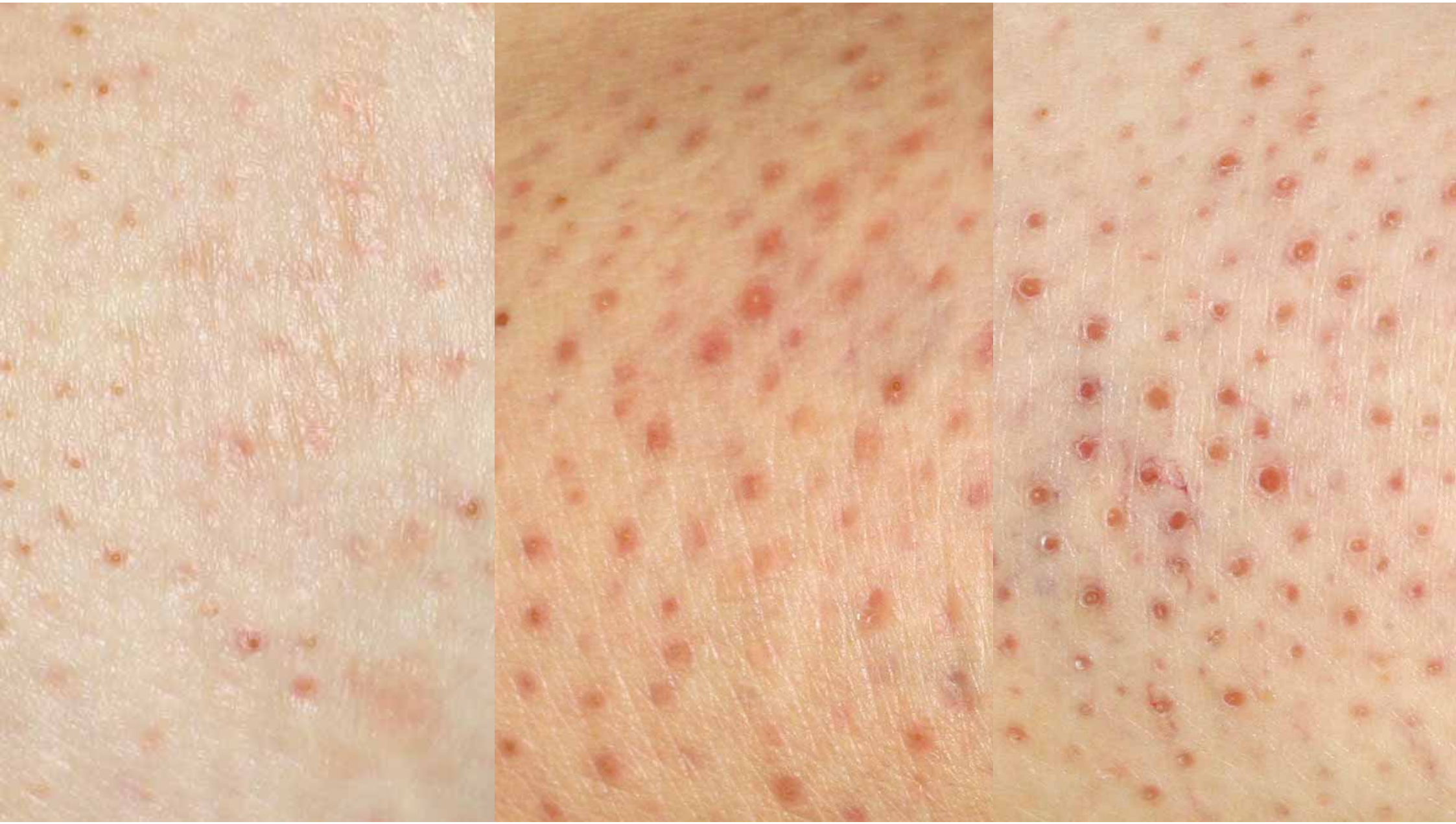


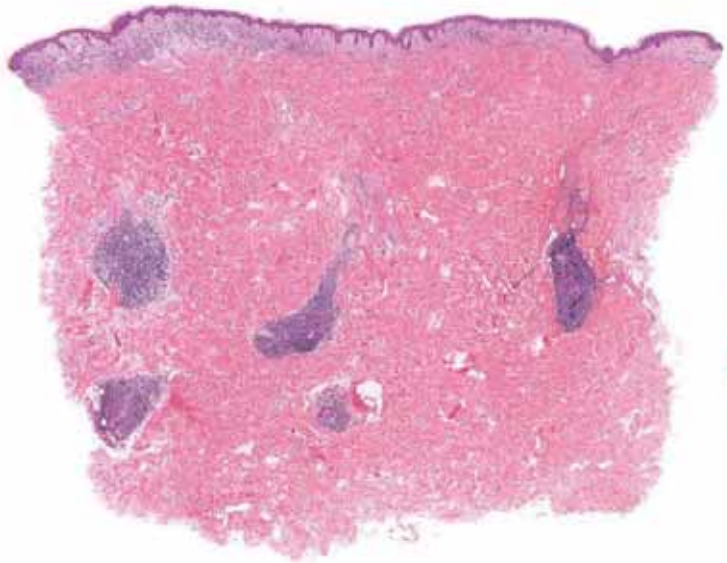
M, 58
Rapid relapse and generalization after Rx therapy
of a solitary MF lesion

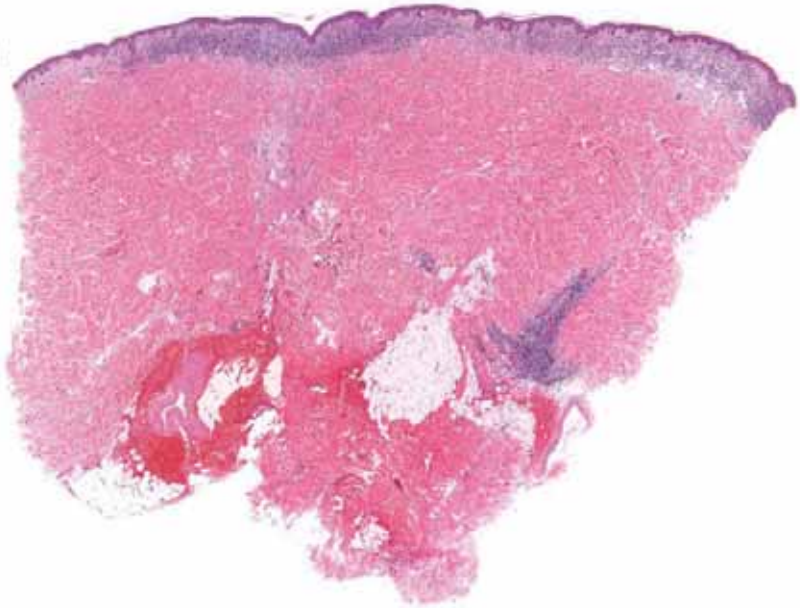
(Consultation Dr. Laimer, Salzburg)

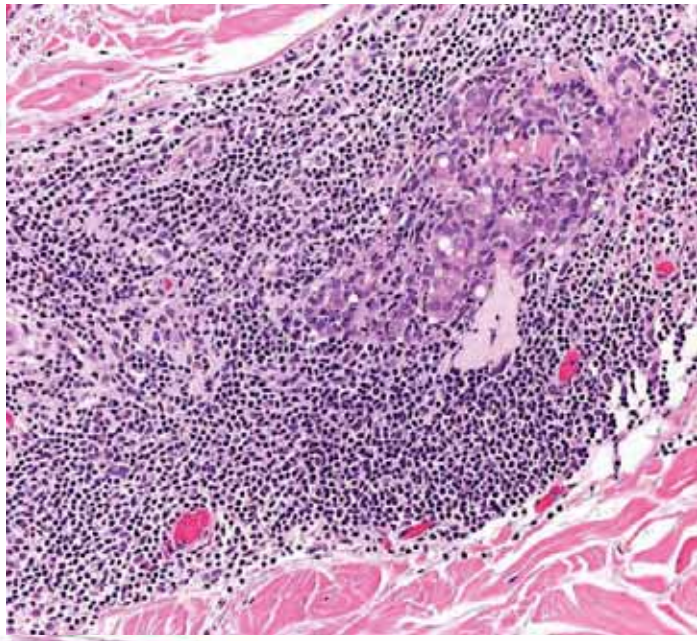

CD3
CD4

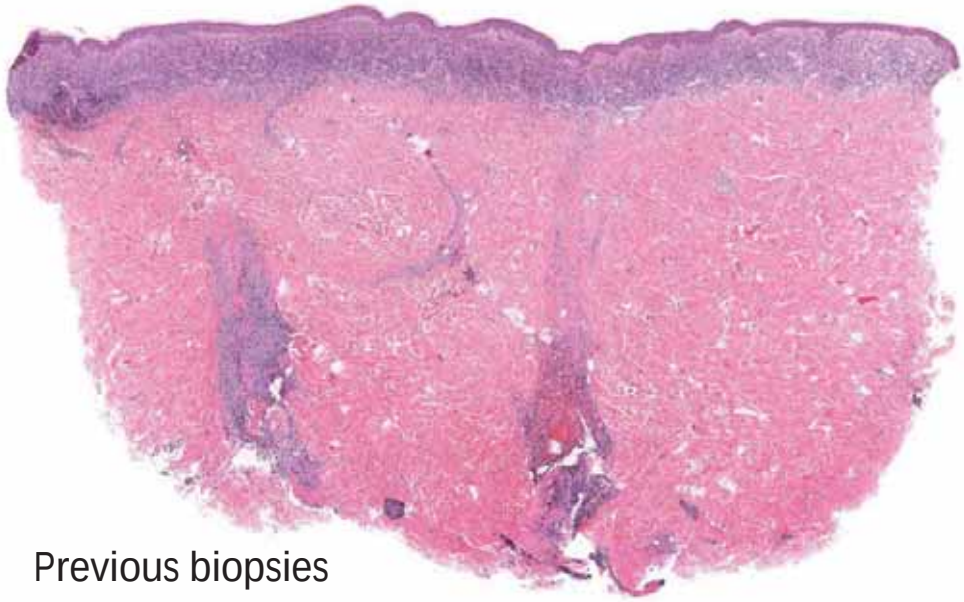




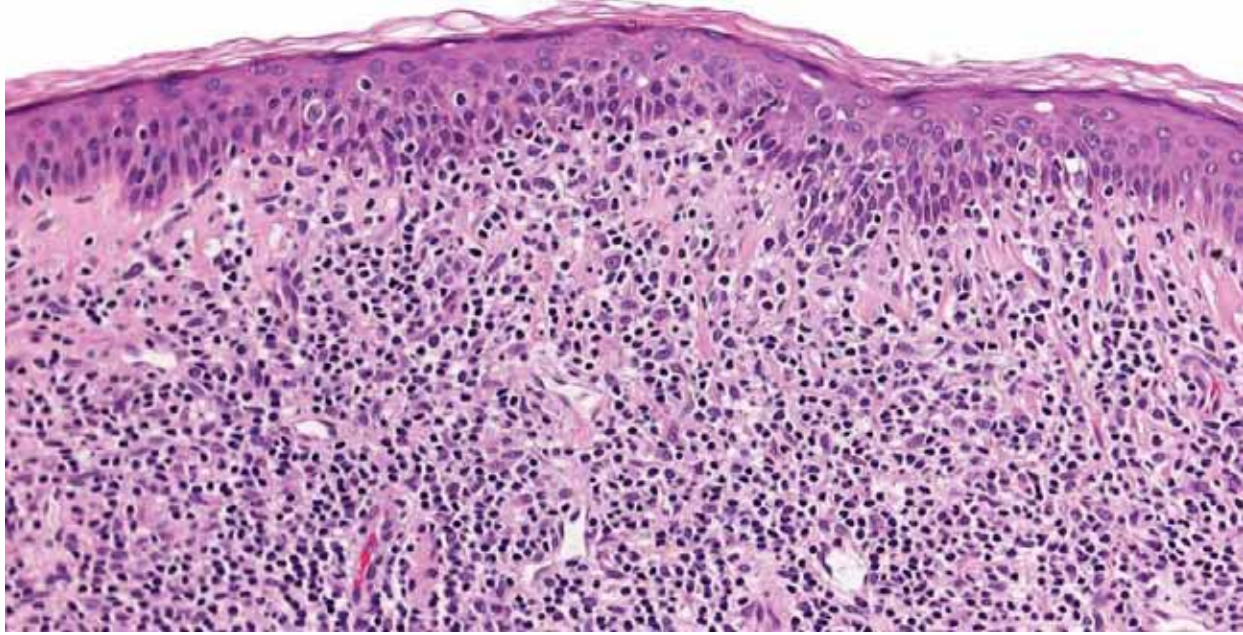


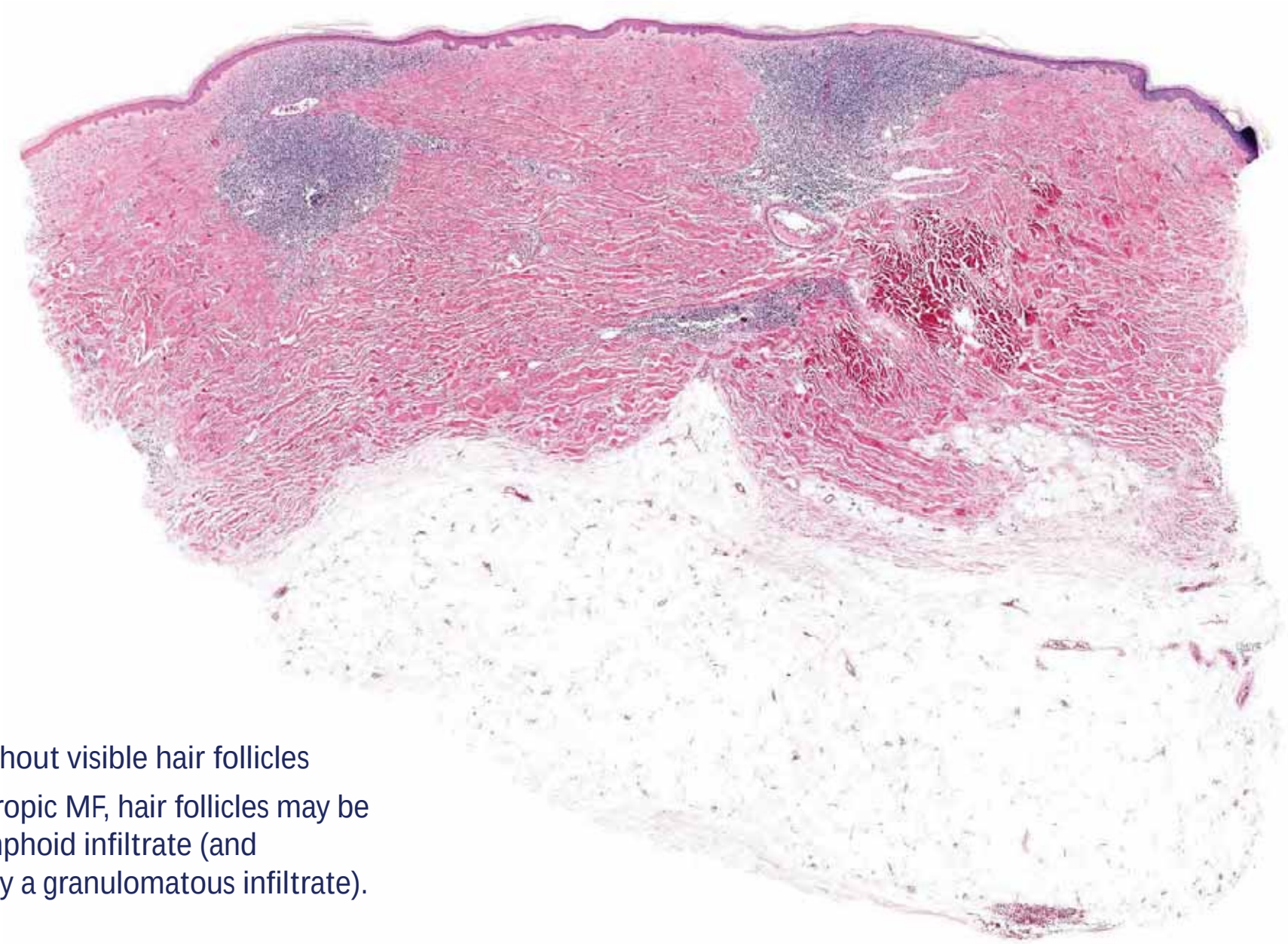






Previous biopsies





Pilotropic MF without visible hair follicles

In some cases of pilotropic MF, hair follicles may be "wiped off" by the lymphoid infiltrate (and sometimes replaced by a granulomatous infiltrate).

Acneiform Presentations of Folliculotropic Mycosis Fungoides

Huma Shamim, MBBS, Christie Riemer, MD,† Roger Wenig, MD,‡ Olayemi Sokumbi, MD,§ Gabriel Sciallis, MD,¶ Marian McEvoy, MD,‖ Daniel Mischke, MD,** and Nneka Comfere, MD††*

Background: Folliculotropic mycosis fungoides (FMF) is a variant of cutaneous T-cell lymphoma that has clinical overlap with a variety of inflammatory follicular unit disorders. However, we describe distinctive presentations of FMF with acneiform features that can be diagnostically challenging, leading to diagnostic delay.

Objective: To highlight the importance of histopathologic and immunohistochemical evaluation for diagnostic confirmation of presumed inflammatory follicular unit based disorders that are unusual in presentation or unresponsive to standard therapies.

Methods: A cross-sectional retrospective study of 5 consecutive patients with a histopathologic diagnosis of FMF was conducted. The clinical, histopathologic, immunophenotypic, and molecular genetic features of cases are presented.

Results: We describe 5 patients with clinical and histopathologic presentations of FMF masquerading as hidradenitis suppurativa, furunculosis, or acne vulgaris (age range 34–66 years, 4:1 female to male). Clinical morphologies included open and closed comedones, inflammatory pustules, papules and nodules, follicular papules with keratotic plugging, cysts, and scarring involving the face, trunk, and intertriginous areas. All patients failed to respond to standard therapies, including topical and oral antibiotics, topical and oral retinoids, or topical corticosteroids, before receiving the diagnosis of FMF. Lesional skin biopsies showed a perifollicular CD4-positive T-lymphocytic infiltrate with pilotropism, mucinous deposition, foreign-body granulomatous inflammation, acute inflammation, and follicular epithelial necrosis. None had concurrent systemic cutaneous fungoides.

Limitations: Small retrospective cohort study.

Conclusion: We present these cases to expand the clinical and histopathologic spectrum of FMF that may strikingly resemble acneiform disorders and to highlight the importance of diagnostic reconsideration with histopathologic evaluation.

Key Words: folliculotropic mycosis fungoides, subtleman T-cell lymphoma, acneiform lesions

(*Am J Dermatopathol* 2021;43:85–92)

LEARNING OBJECTIVES

After participating in this activity, physicians should be better able to:

1. Identify diagnostic histopathologic and immunohistochemical features of folliculotropic mycosis fungoides.
2. Distinguish the varied acneiform clinical presentations of folliculotropic mycosis fungoides.

INTRODUCTION

Folliculotropic mycosis fungoides (FMF) is a rare variant of cutaneous T-cell lymphoma that shares clinical features with a variety of inflammatory follicular unit disorders, including acne vulgaris, acne comedonicus, discoid lupus, scarring alopecia, and keratosis pilaris.[1,2] Patients often present with predominant involvement of the head and neck region, significant pruritus, and alopecia.[2] Typical lesional morphologies include open and closed comedones, inflammatory pustules, papules and nodules, and follicular papules with hyperkeratotic plugging, cysts, and scarring. The mean age at presentation ranges from 46 to 59 years, with a male-to-female ratio of 2.5:1.[3] Histopathologic features include perifollicular CD4-predominant atypical T lymphocytes with associated pilotropism, syringotropism, follicular mucinosis, mixed granulomatous, and acute inflammation. Diagnosis may be challenging especially in early stages of the disease, often leading to diagnostic delay (mean time to diagnosis: 5 years), and delays in management resulting in advanced stages of the disease when the diagnosis is eventually rendered.

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Study concept and design (N. Comfere, Data collection (C. Riemer and H. Shamim); Data analysis and interpretation (N. Comfere, C. Riemer and H. Shamim); Drafting of the manuscript (H. Shamim, C. Riemer, and N. Comfere); Critical revisions and final approval: All authors.

All authors, faculty, and staff in a position to control the content of this CME activity and their spouse/life partners (if any) have disclosed that they have no financial relationships with, or financial interests in, any commercial organizations relevant to this educational activity.

Correspondence: Nneka Comfere, MD, Department of Dermatology and Laboratory Medicine and Pathology, 200 First Street SW, Rochester, MN 55905 (e-mail: Comfere.Nneka@mayo.edu).

FIGURE 1. Clinical image of patient 1: Indurated papules and plaques with postinflammatory hyperpigmentation involving the face.

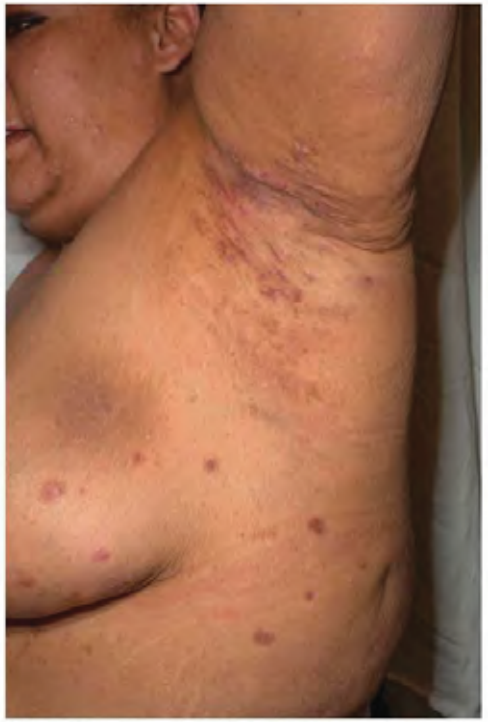


FIGURE 2. Clinical image of patient 2: Double-barreled comedones and scars on the breast and axilla. Firm, skin colored papules involving the face.

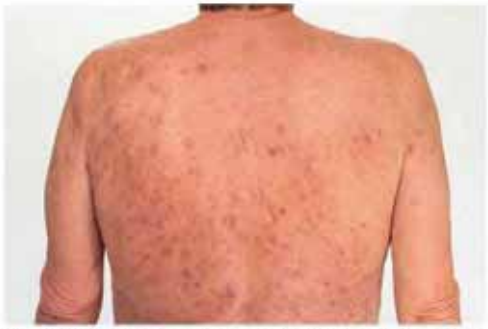
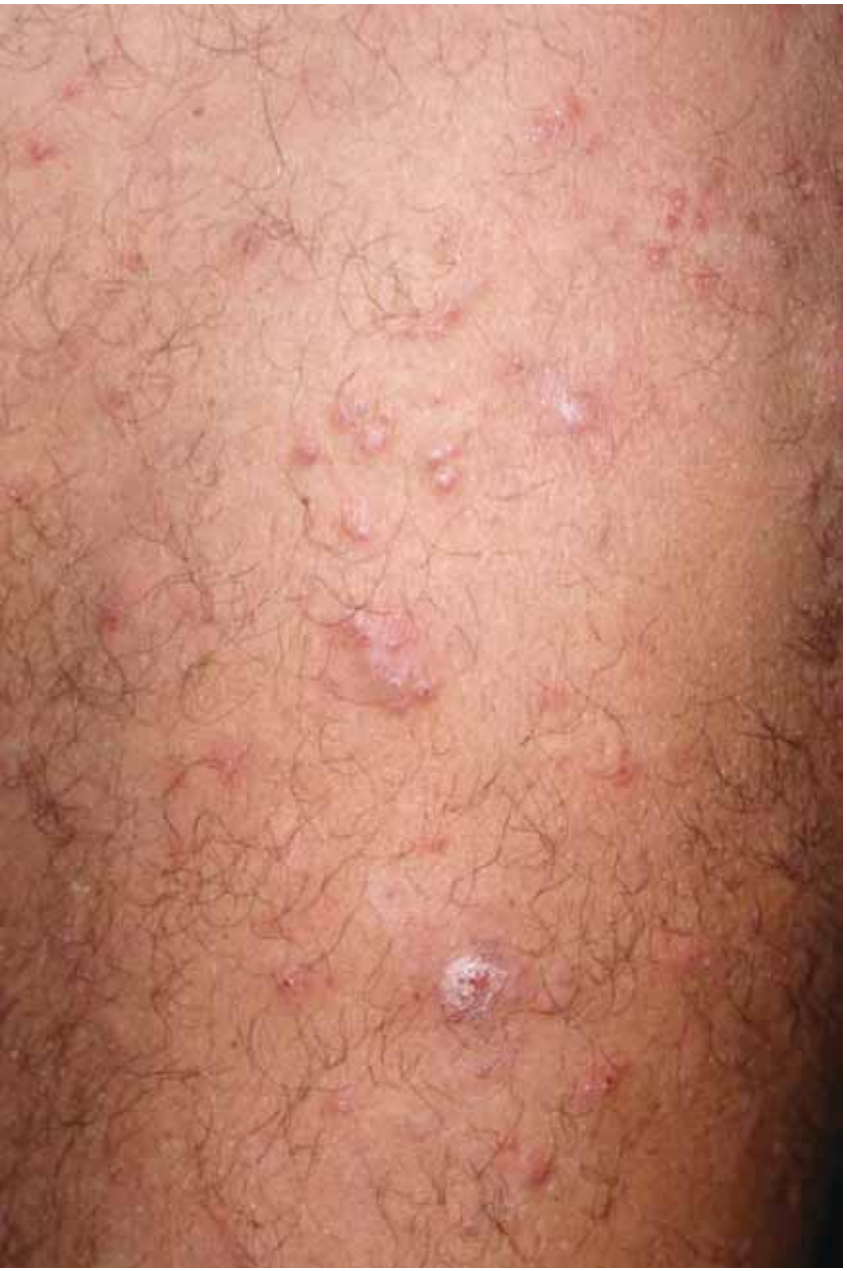
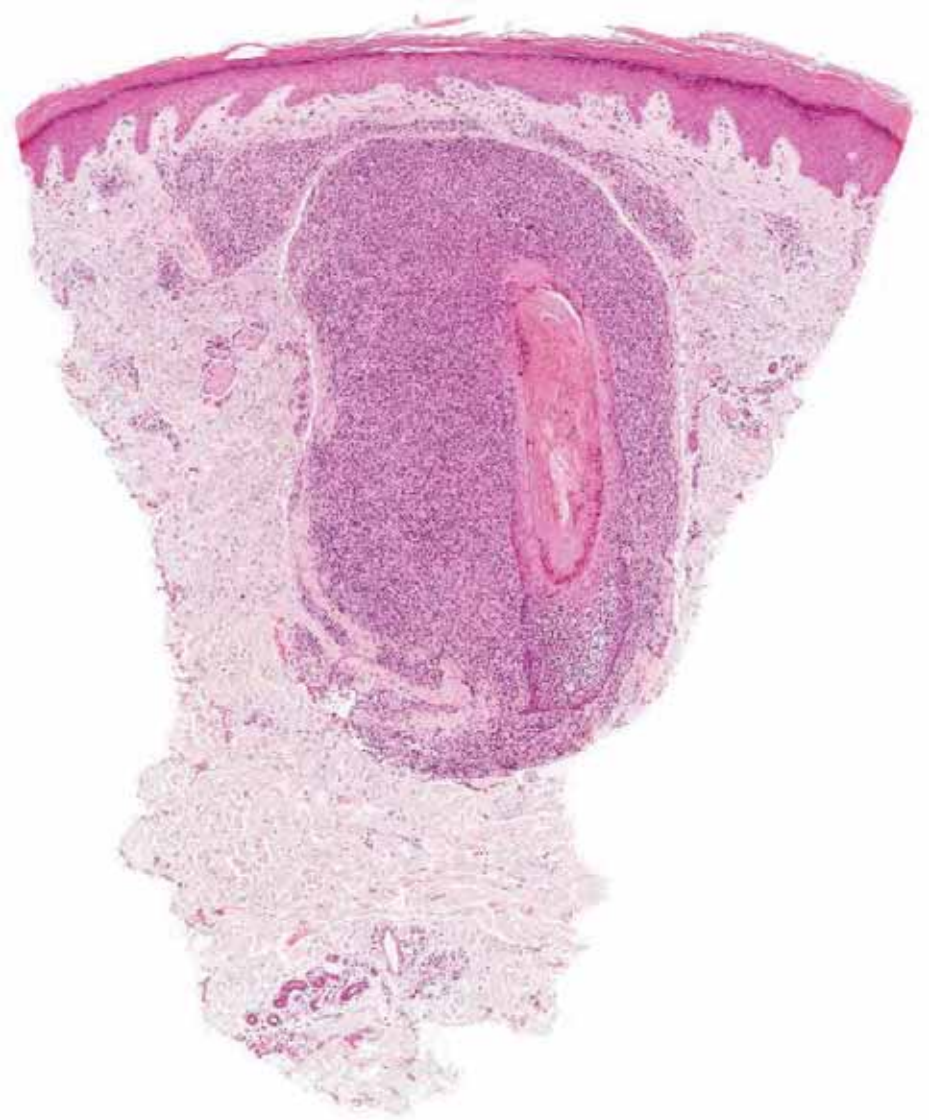
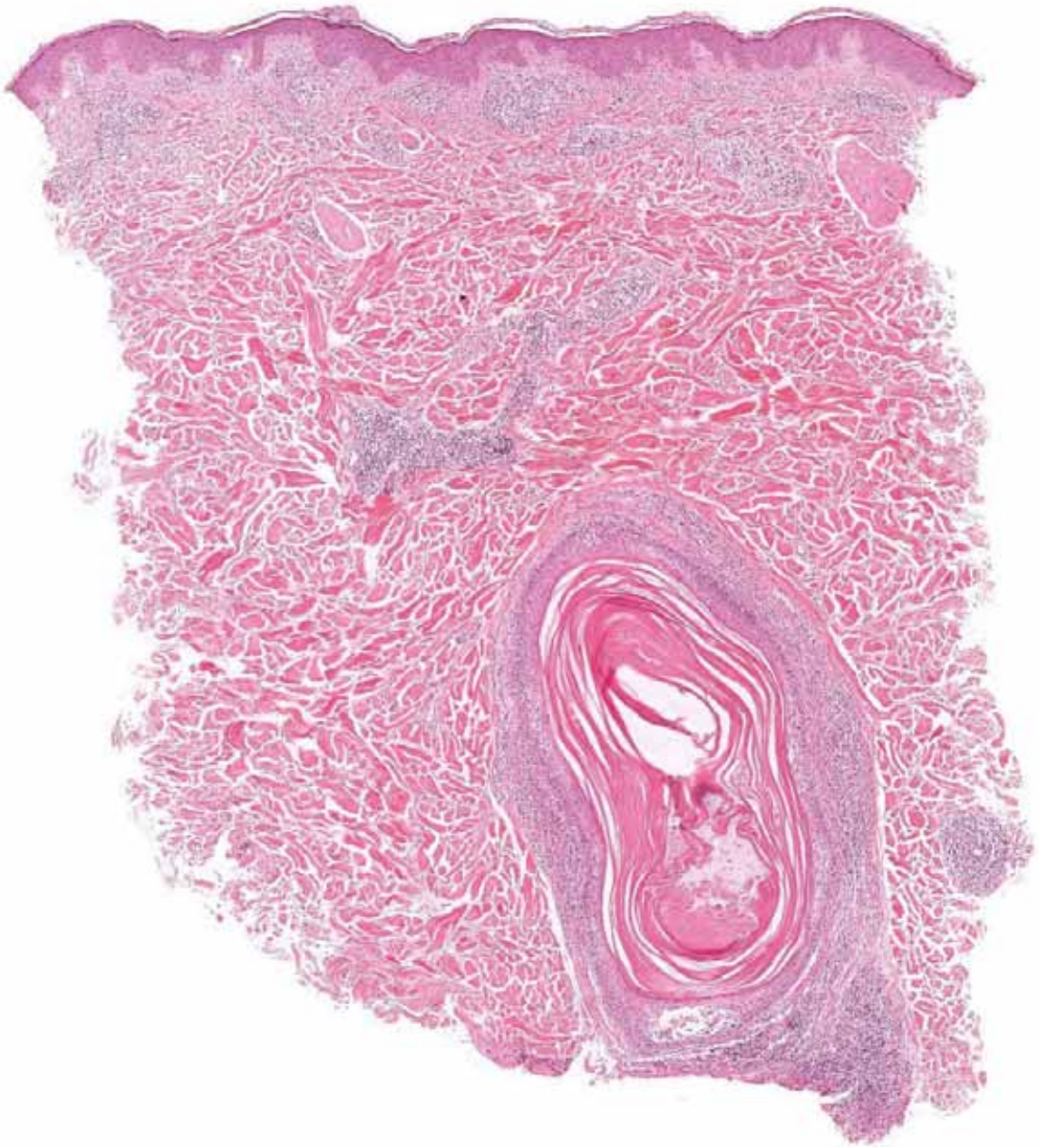


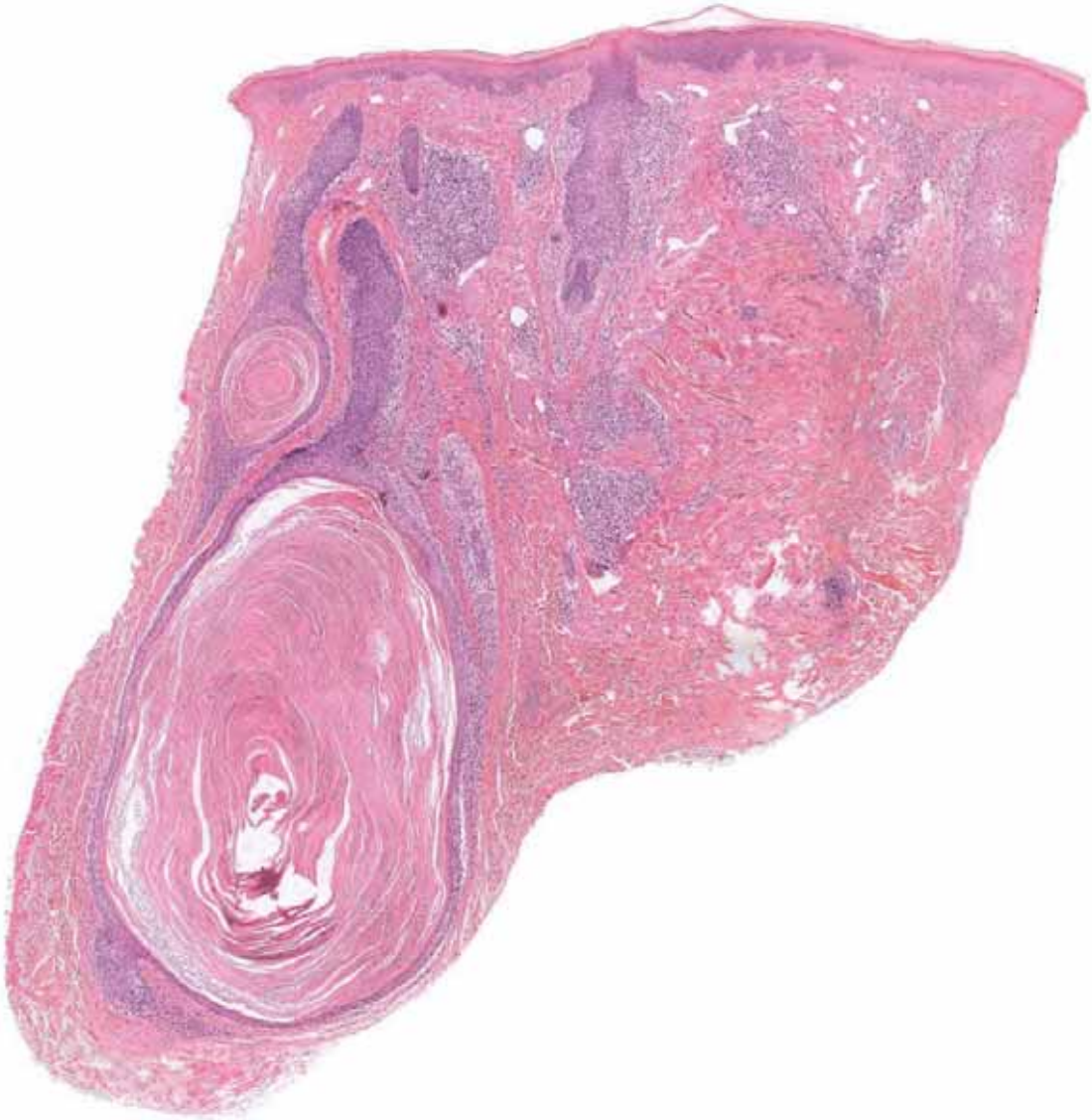
FIGURE 3. Clinical image of patient 3: Comedones and inflamed cysts on the trunk.

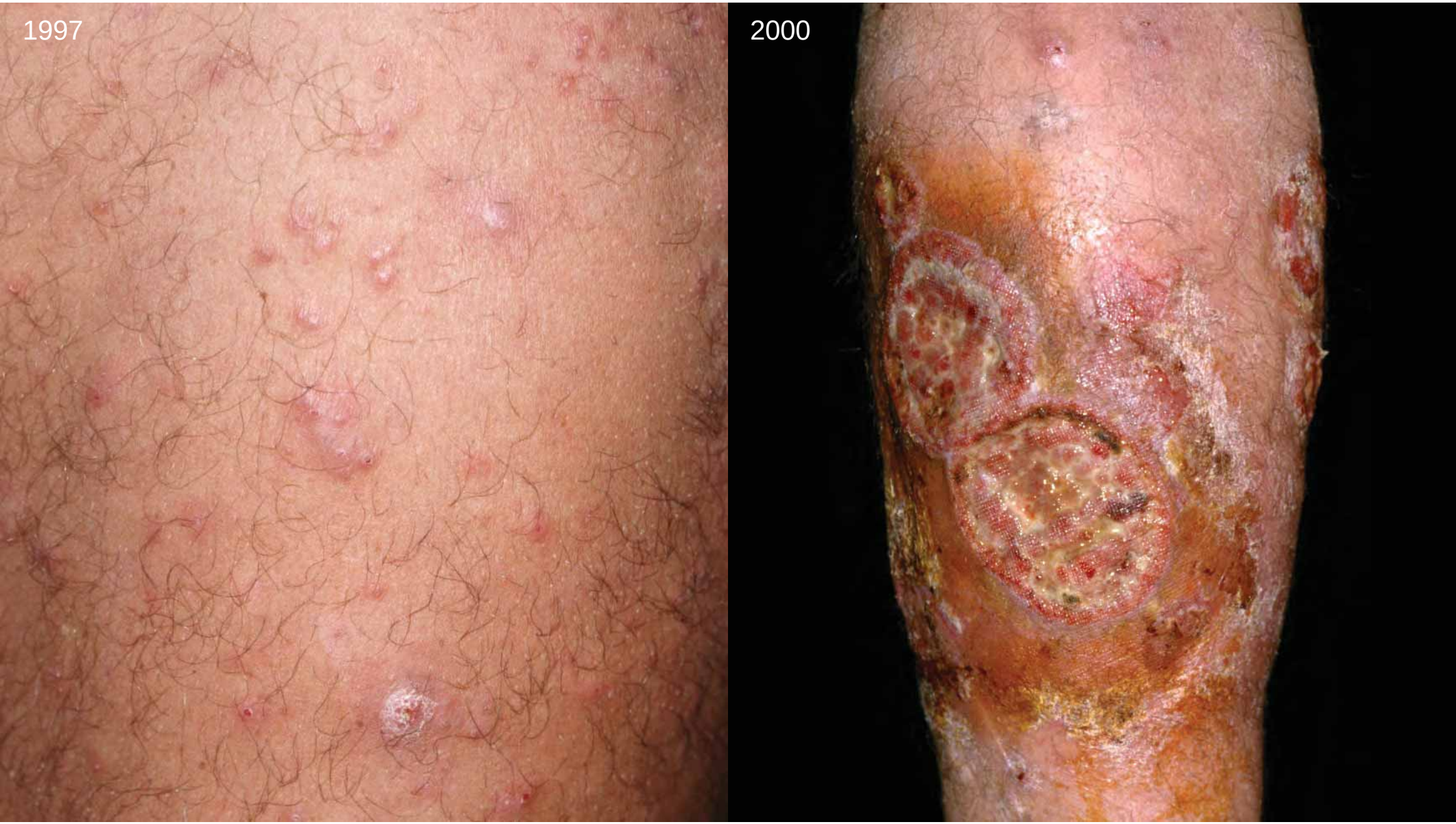


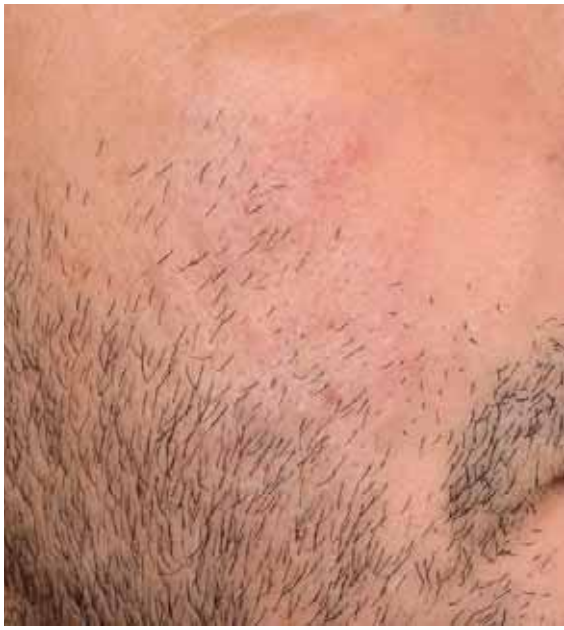
Acneiform pilotropic mycosis fungoides







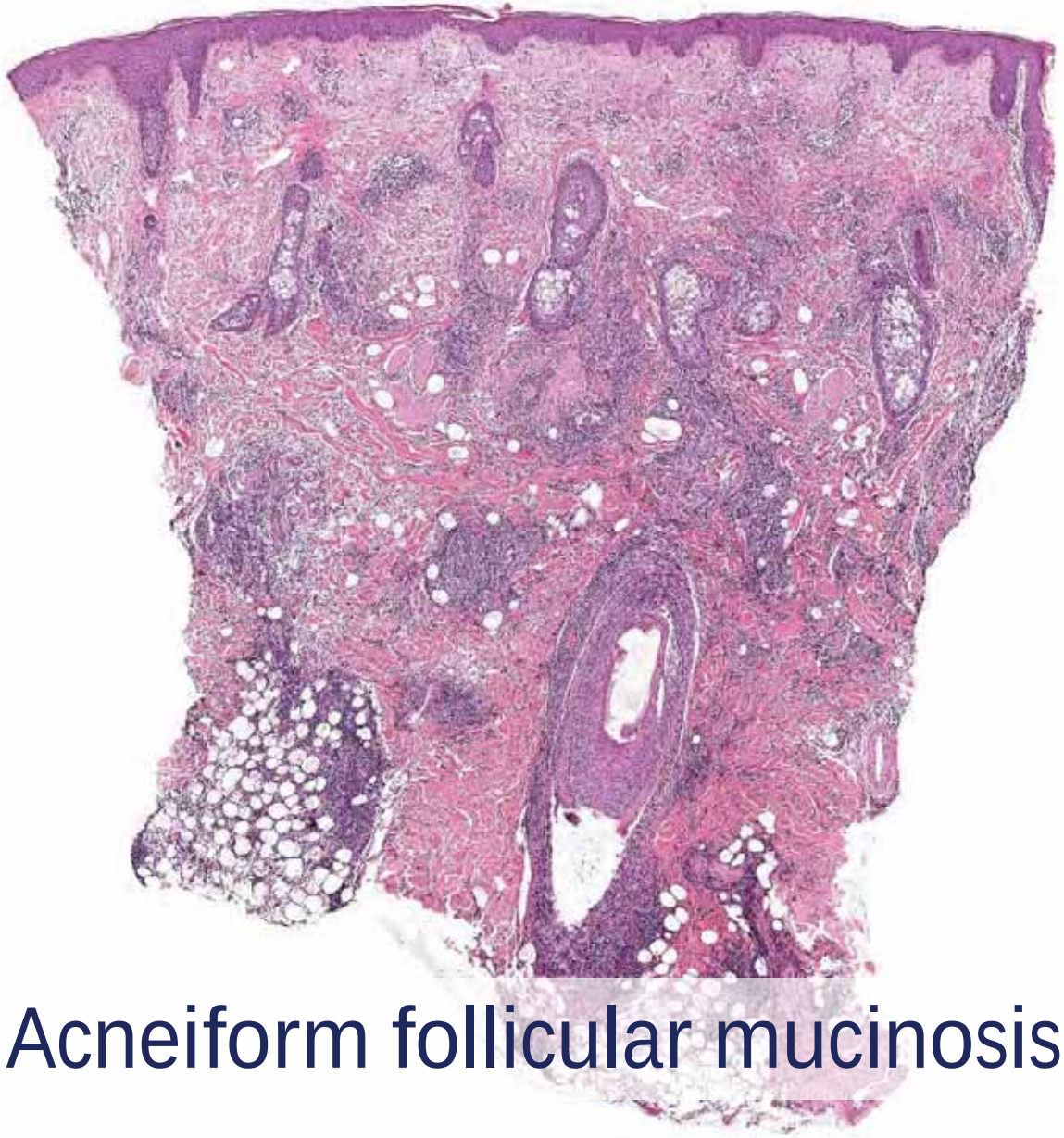

1997
2000

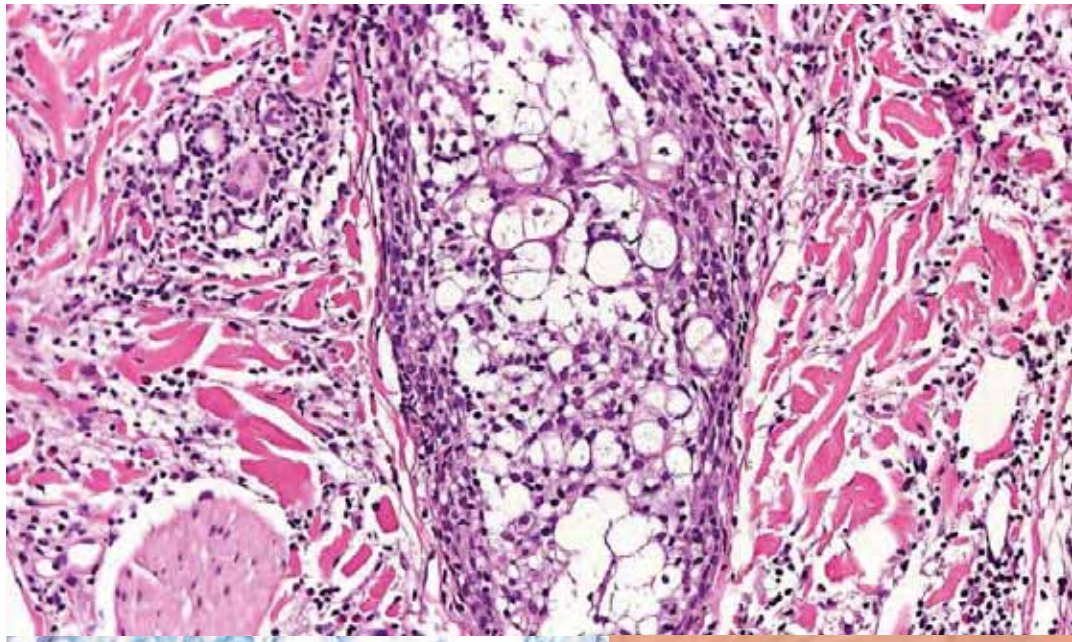


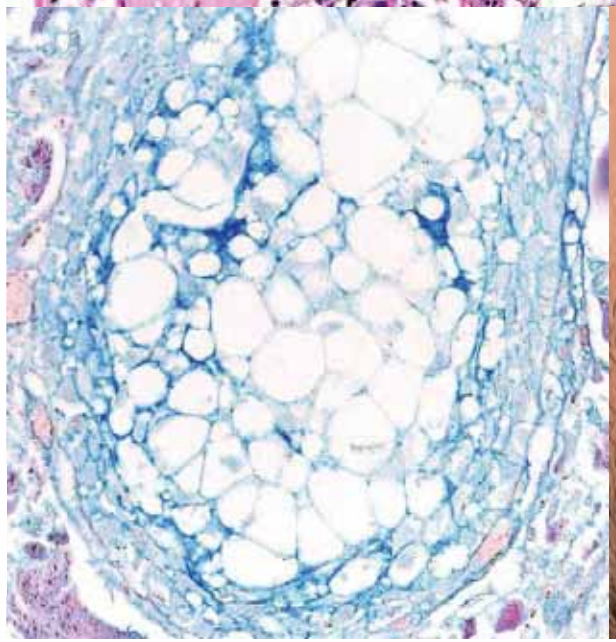
M, 39

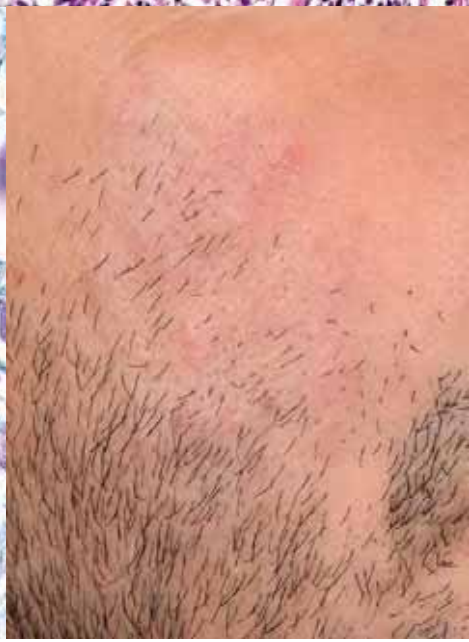
According to the patient lesions on the face for approximately 2 weeks. No improvement with oral antibiotics.

A biopsy is taken.







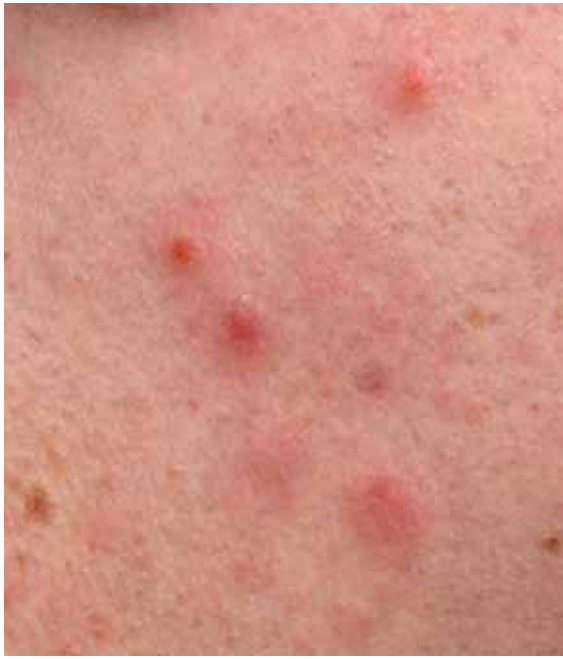


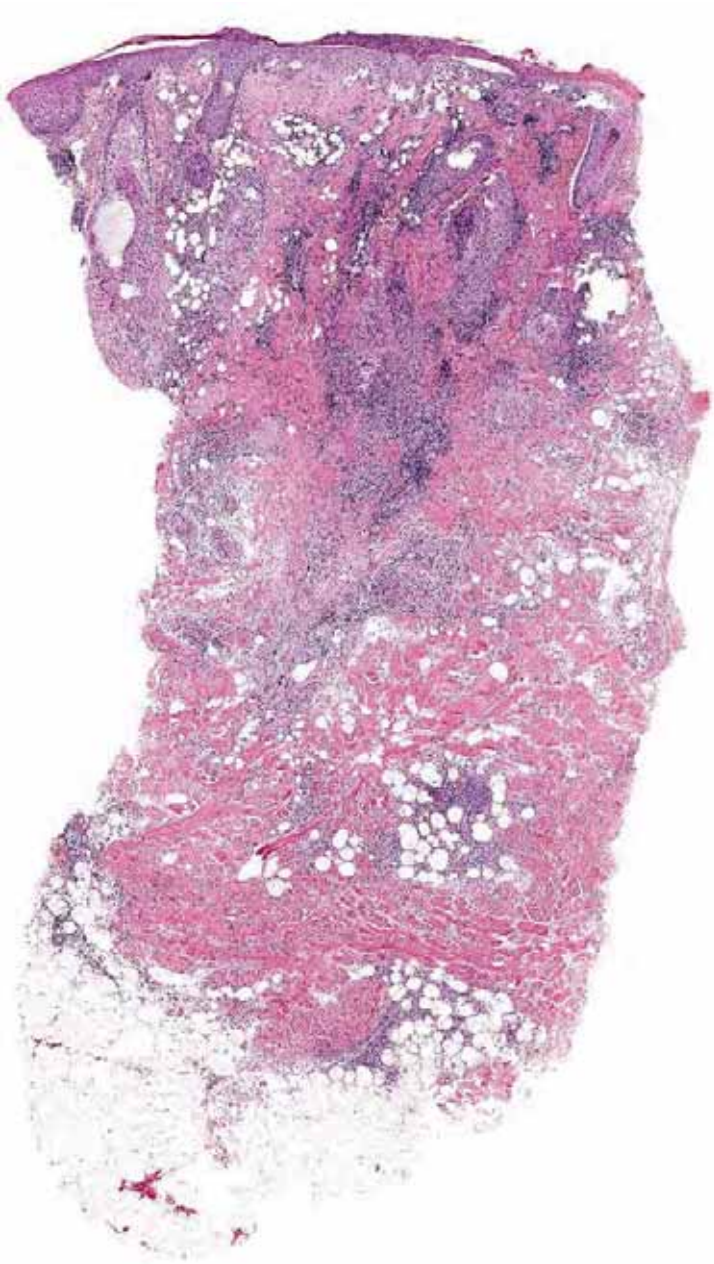
Acneiform follicular mucinosis

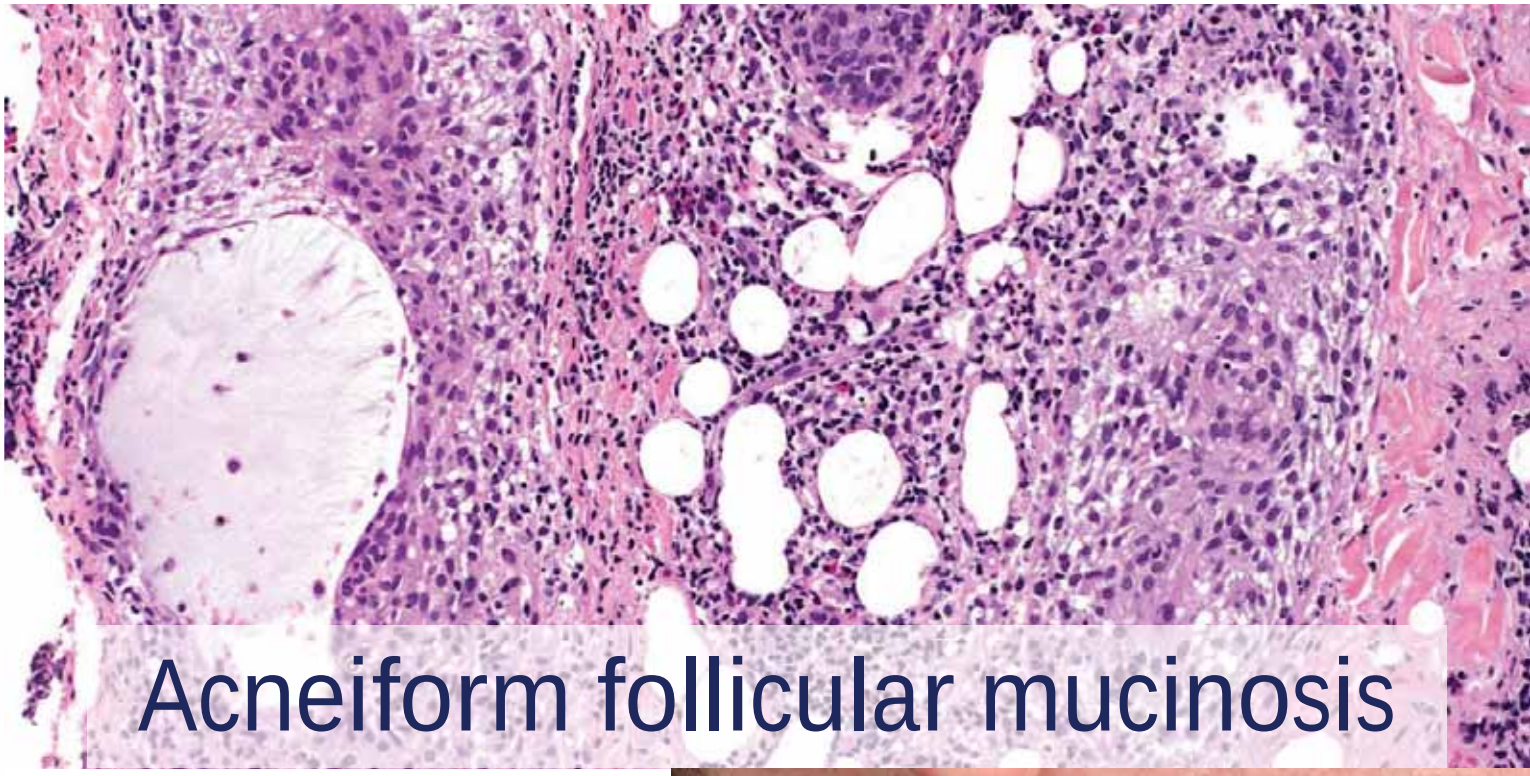
M, 28

According to the patient slightly itchy lesions on the face for approximately 1 year.

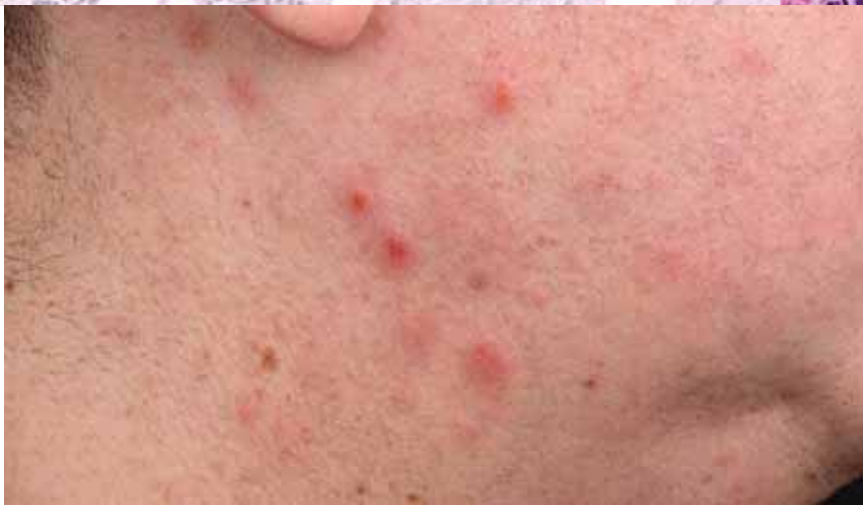
A biopsy is taken.



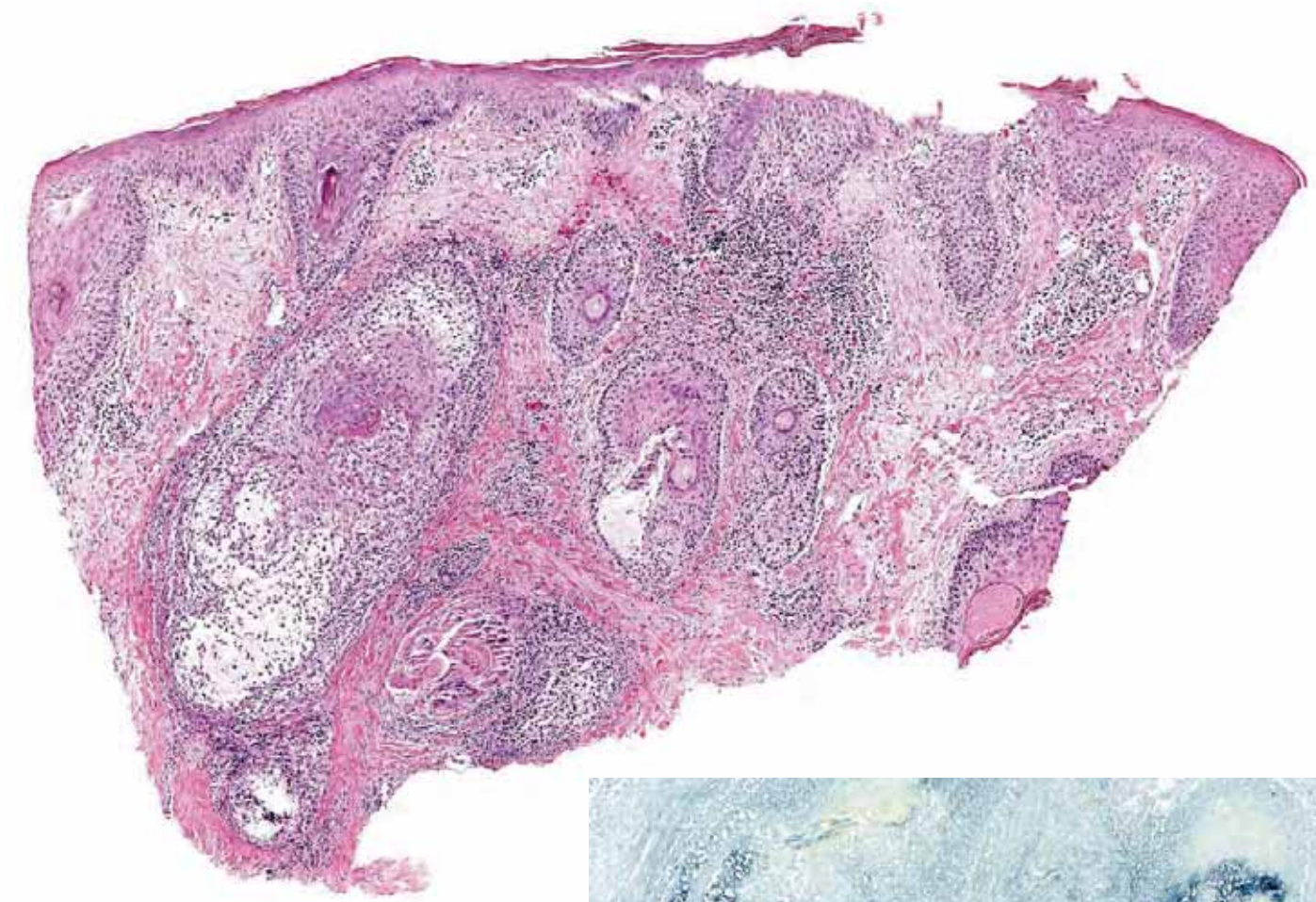


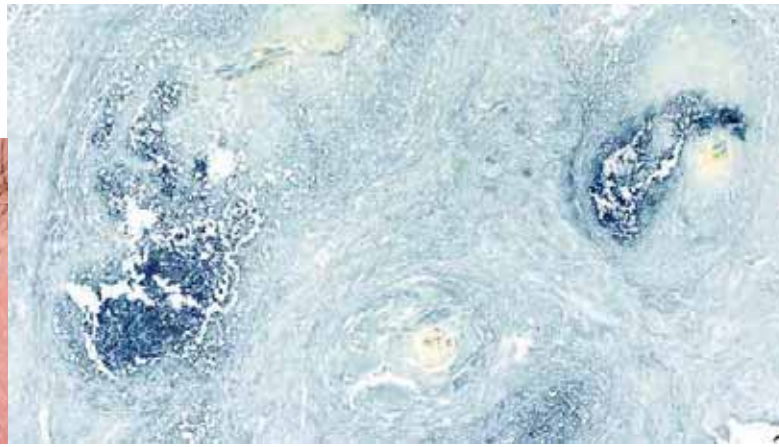


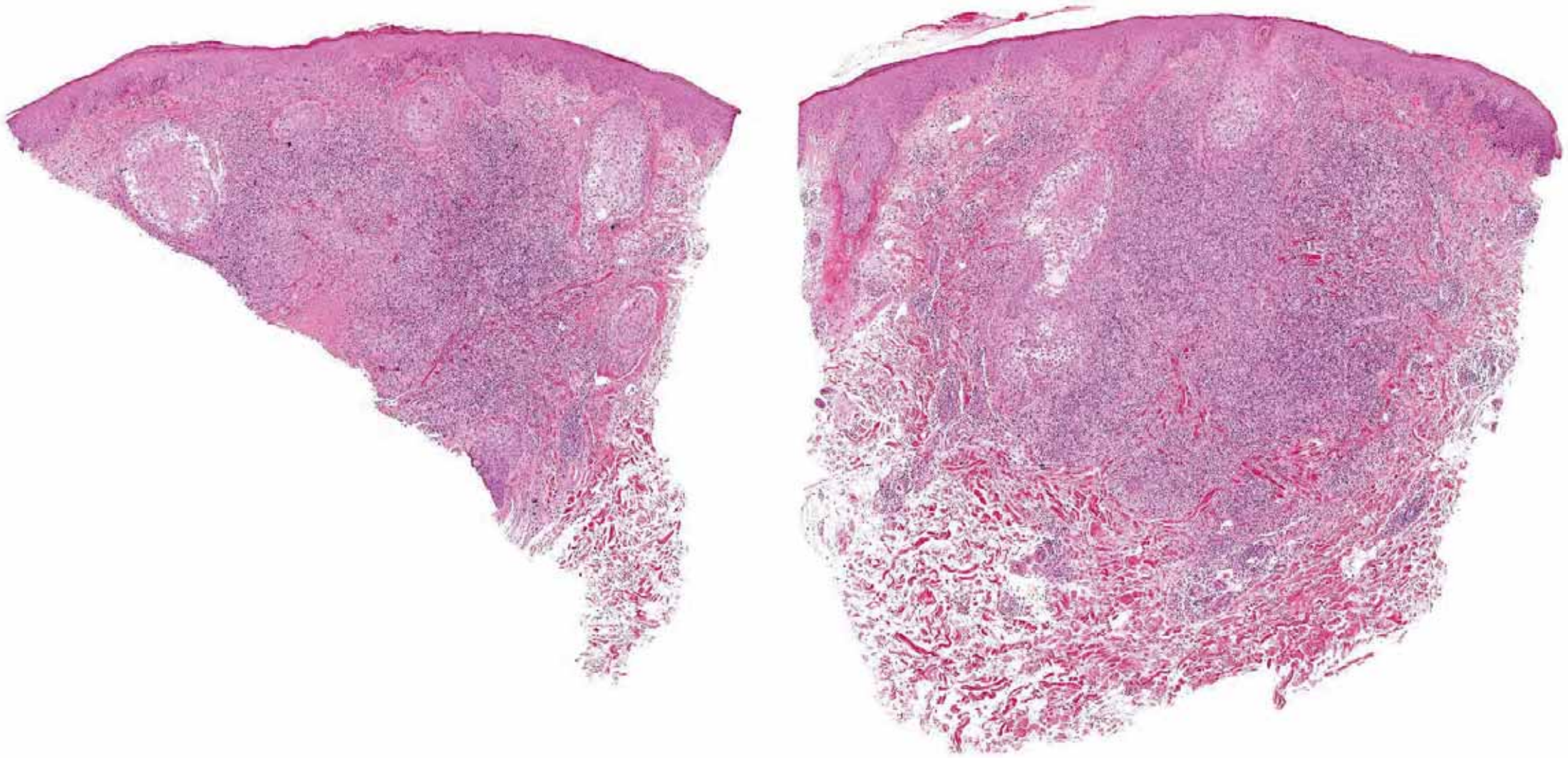
Acneiform follicular mucinosis



3 months later



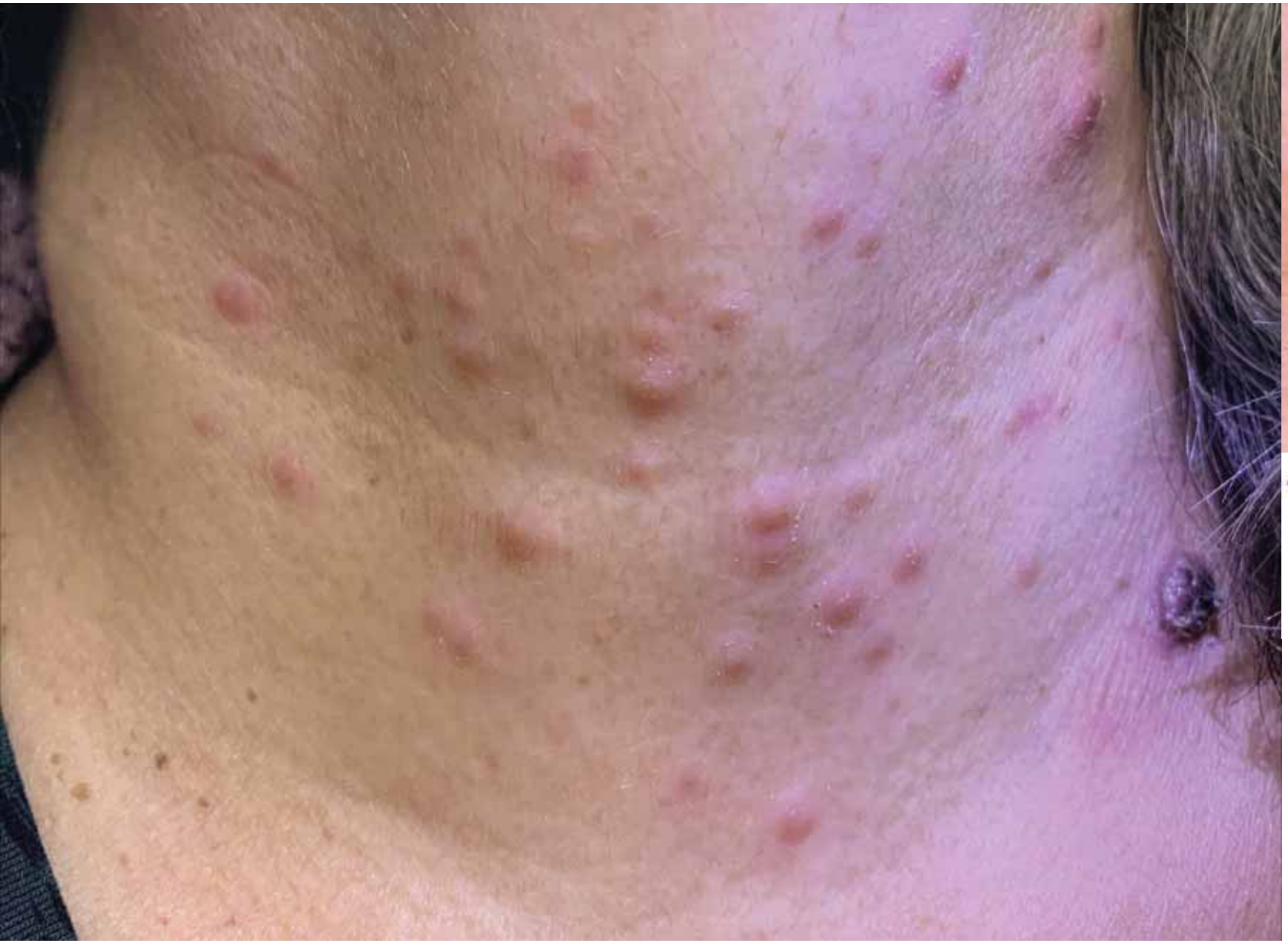


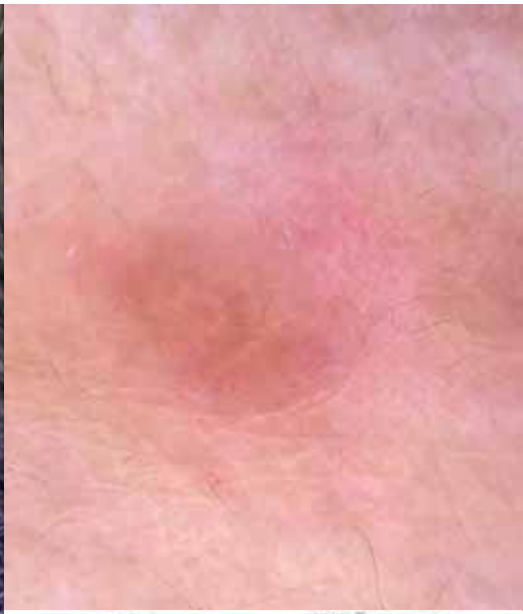


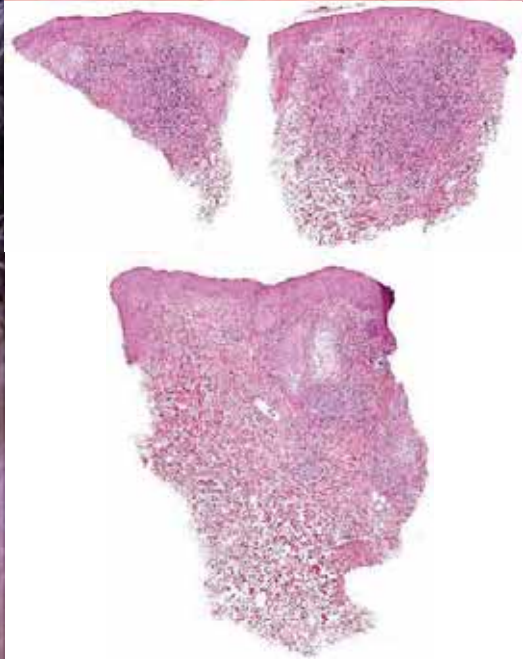
F, 56

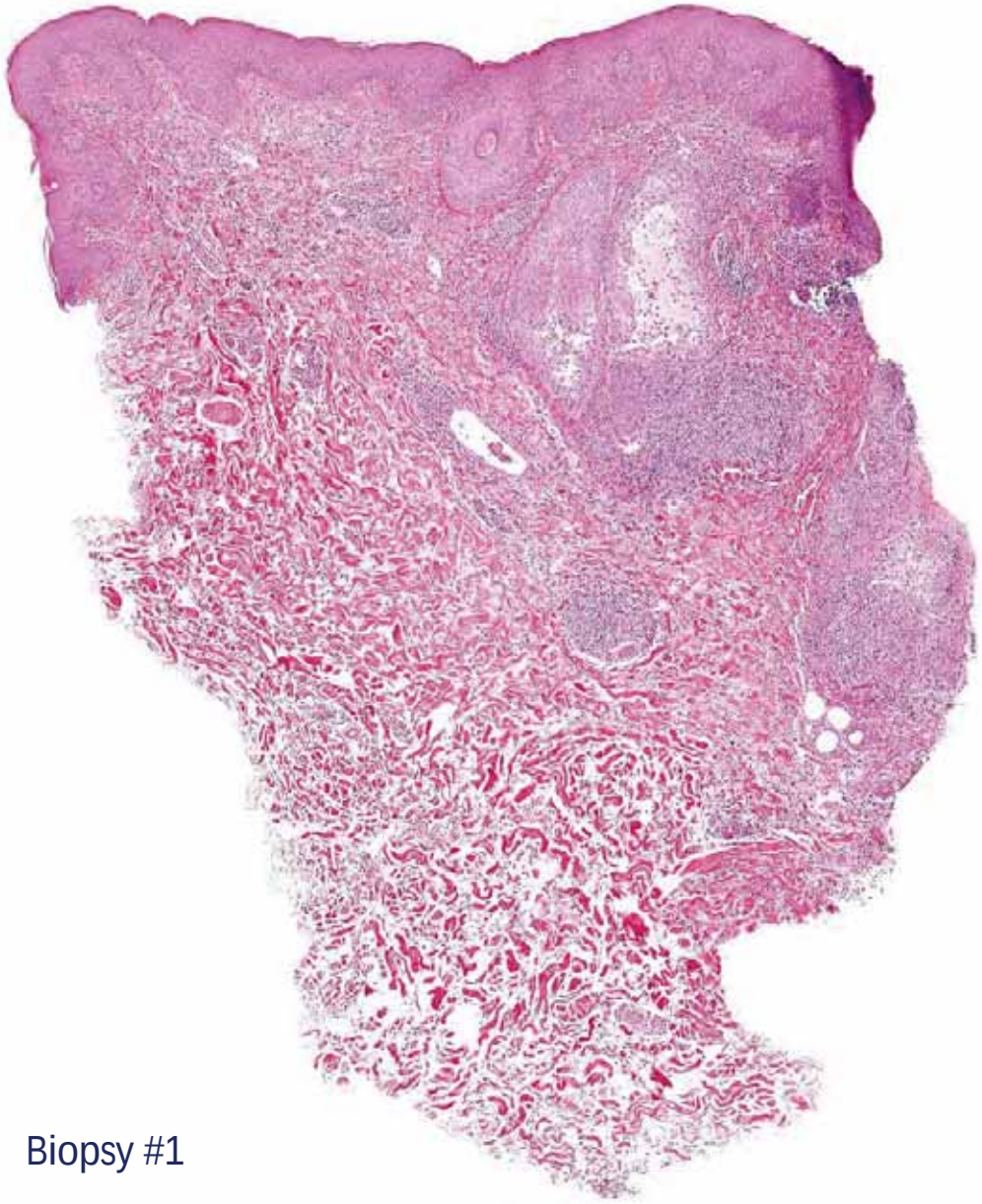
According to the patient erythematous, itchy papules on the neck for 10 months. No other complaints.

Consultation Dr. Thai Yen Ly (Halifax, Canada)

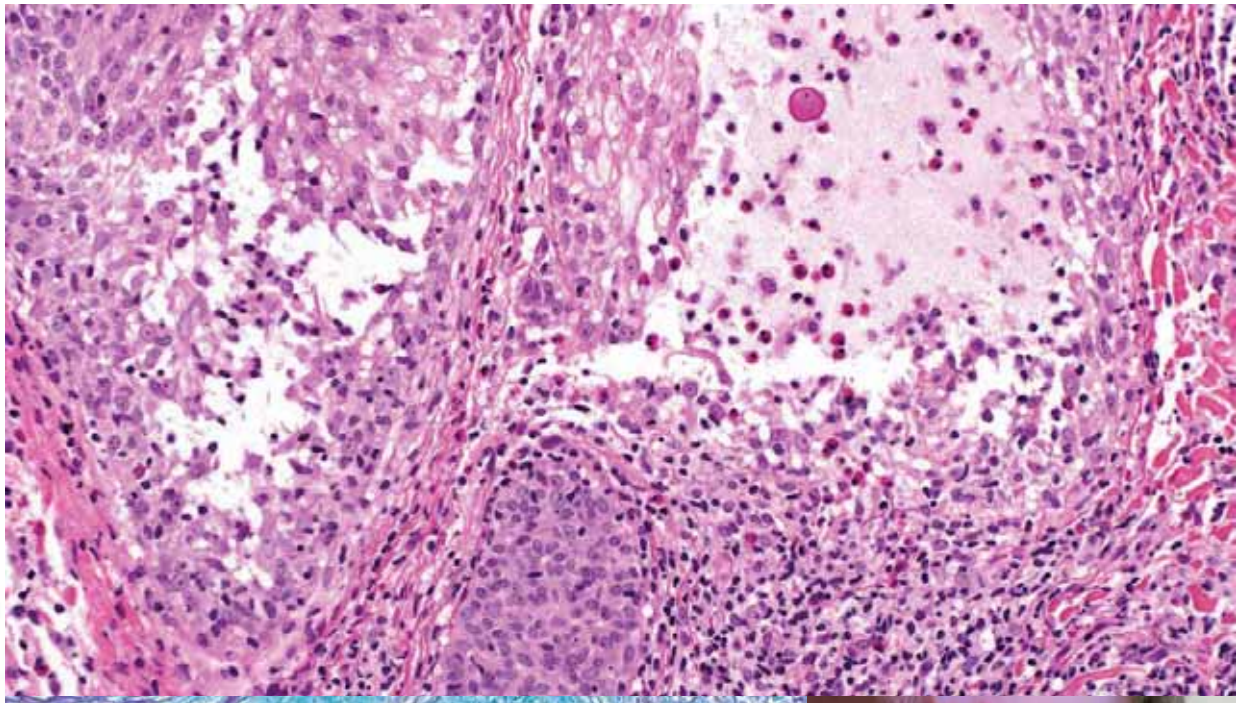


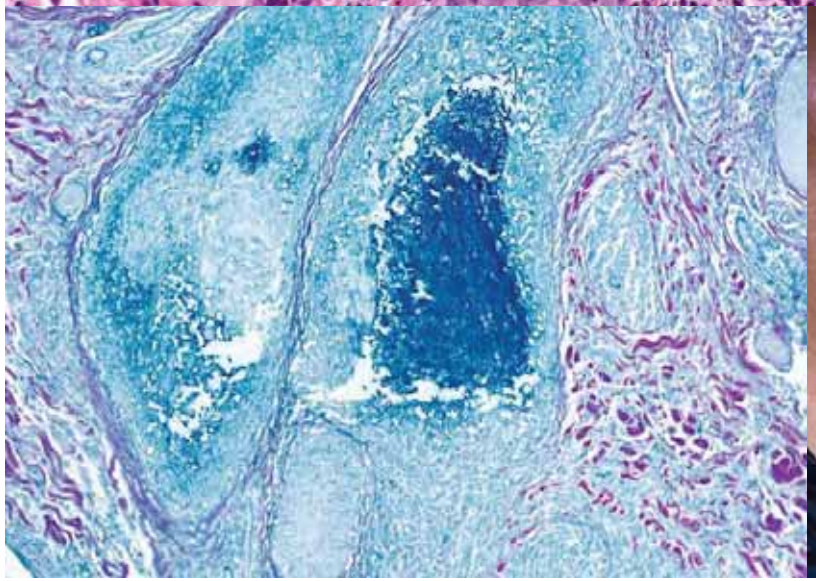


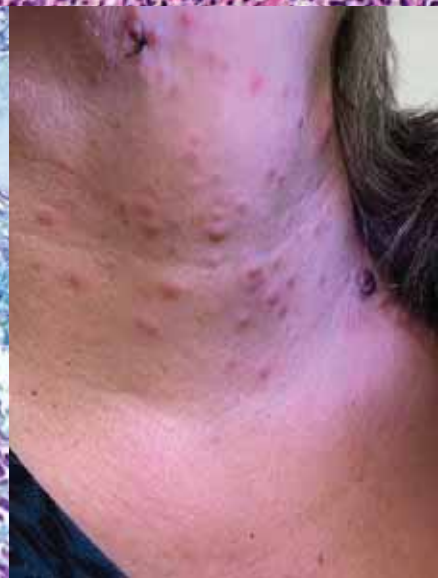


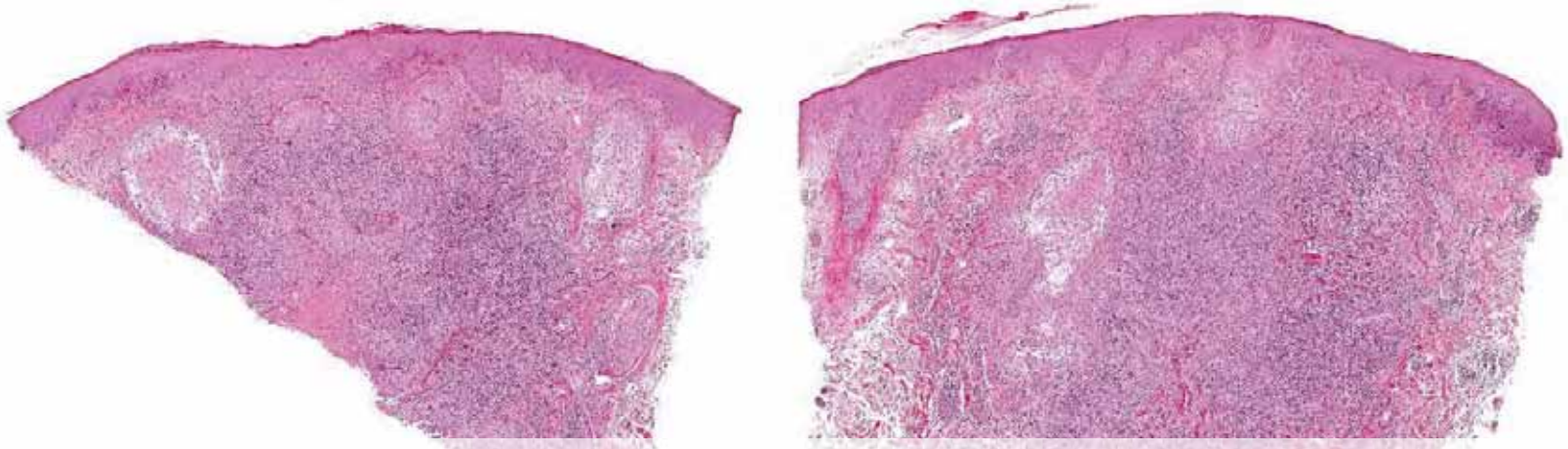


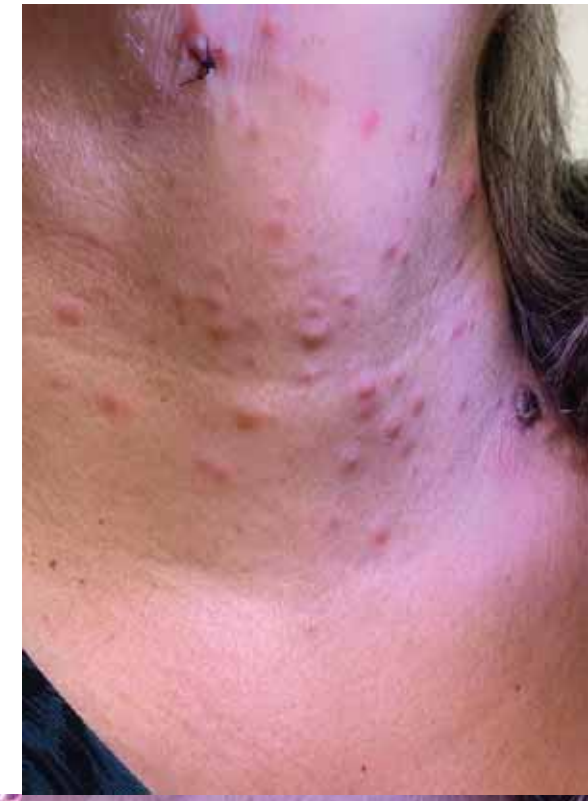
Biopsy #1





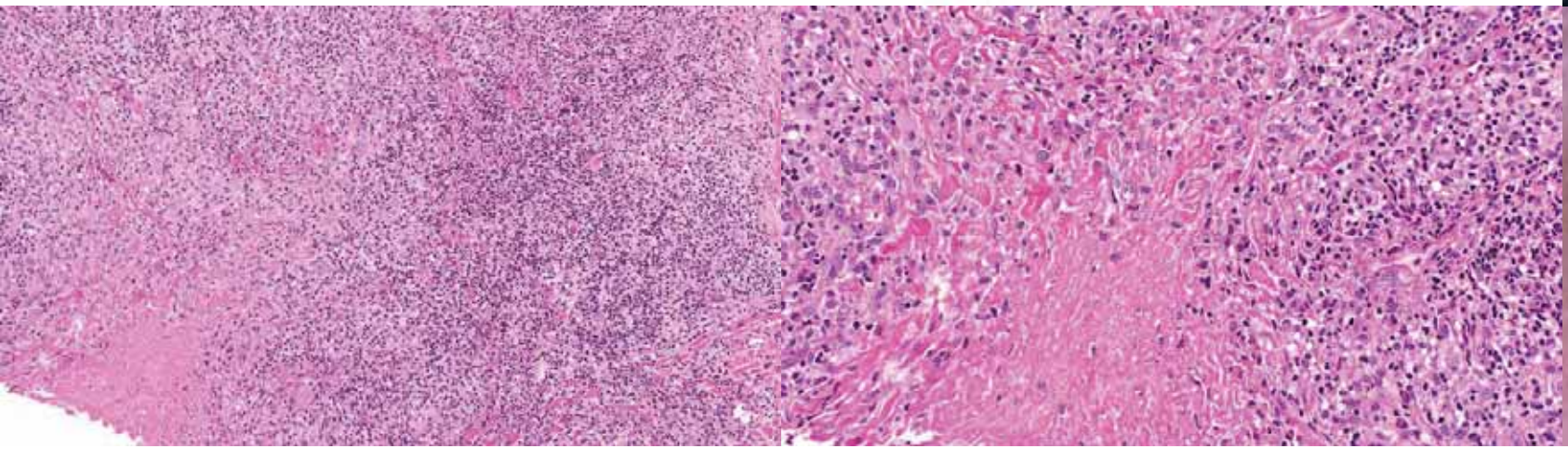


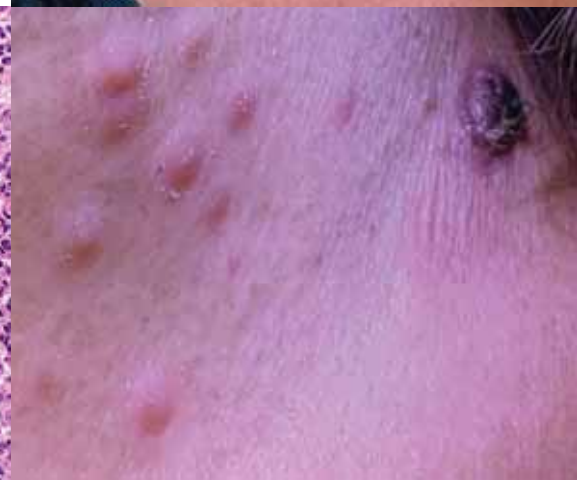


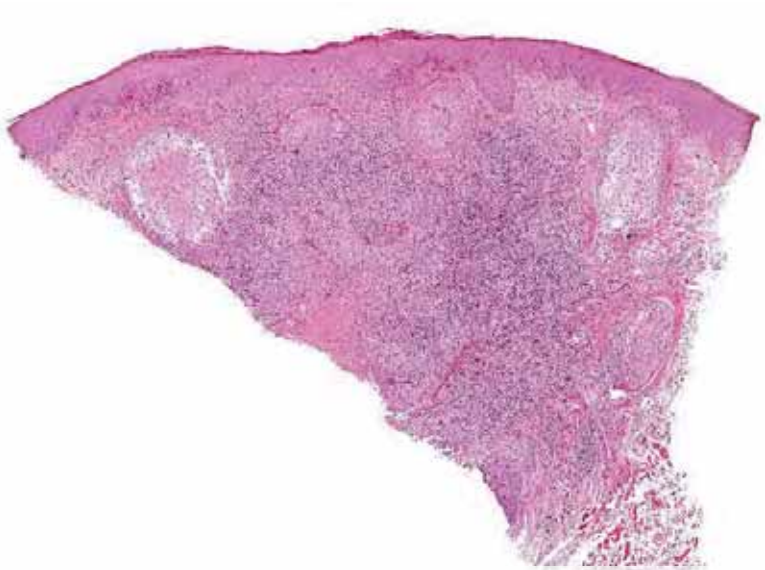


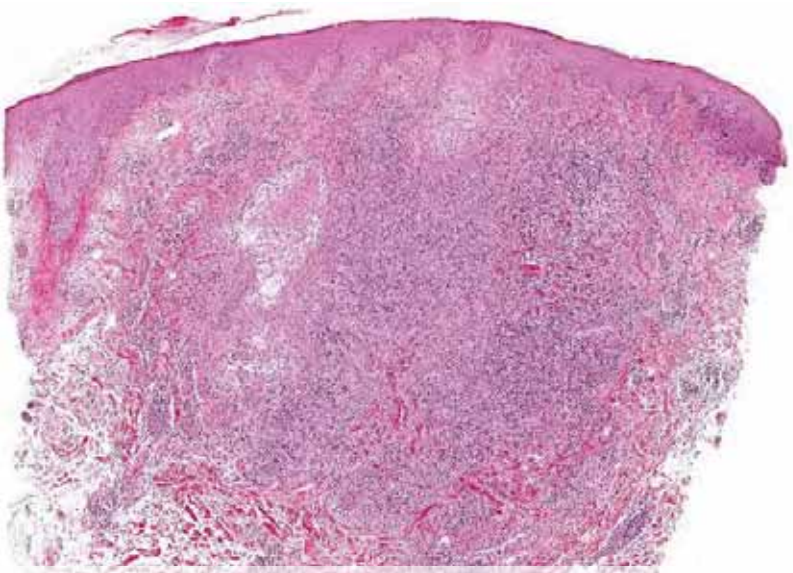
Acneiform follicular mucinosis & lupus miliaris disseminatus faciei

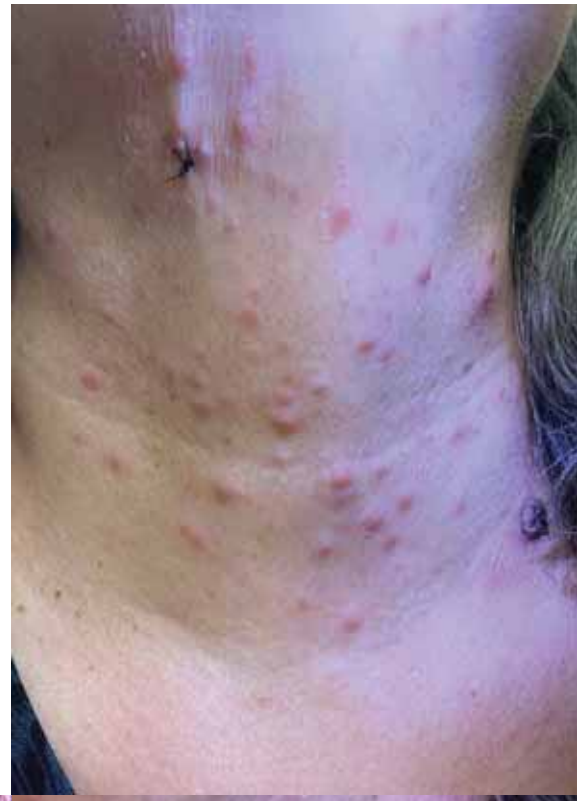
Biopsy #2



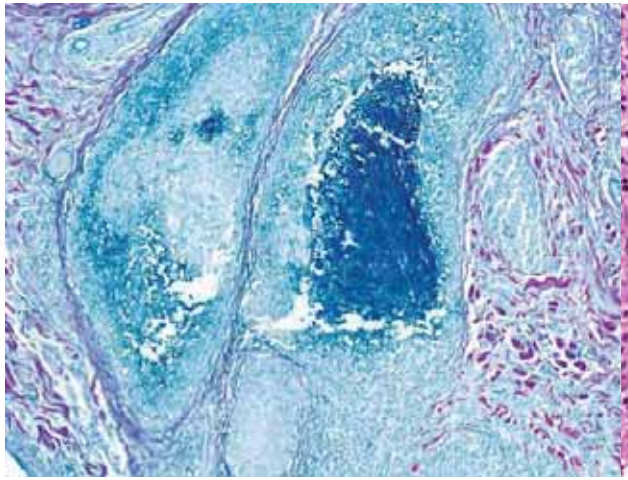


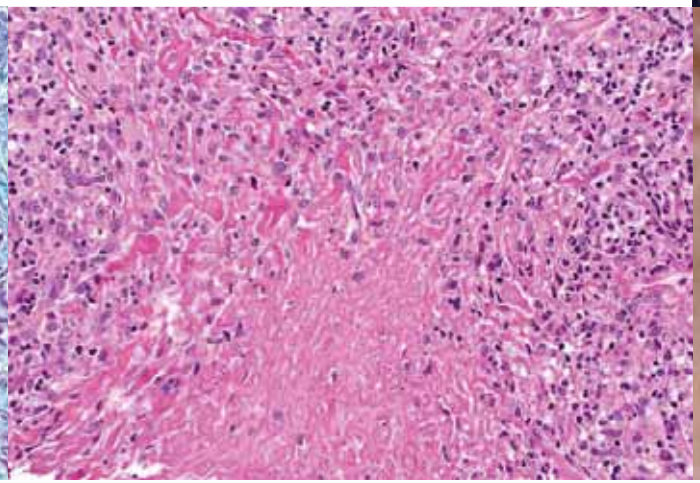


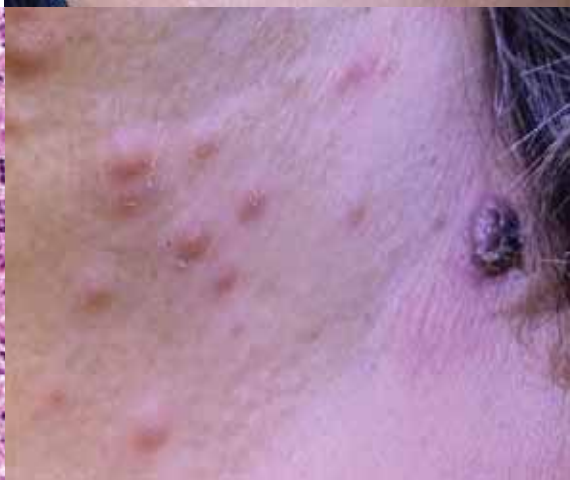




Acneiform follicular mucinosis with focal lupus miliaris disseminatus faciei-like reaction







British Journal of Dermatology (1992) 127, 54–56

Mycosis fungoides with a widespread follicular eruption, comedones and cysts

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The Skin Hospital, Chapel Street, Salford M3 7QF, U.K.

Accepted for publication 30 December 1991

Summary We describe a patient with a rare variant of mycosis fungoides (MF) presenting as a widespread follicular eruption with cysts and comedones.

The association of epidermal cysts and MF has been reported previously.[1–3] We present a case in which MF was associated with comedones, cysts and a widespread follicular eruption. A similar clinical presentation has been described in a patient with follicular mucinosis,[4] but there was no evidence of follicular mucinosis in our patient.

Case report

A 61-year-old man presented with an 18-year history of dry scaly skin, initially over the buttocks, but gradually spreading to involve the trunk and limbs. Twelve years ago increasing numbers of cysts and comedones appeared on his face and scalp. Over the past 3 years he has lost most of his scalp hair. The widespread skin dryness gradually developed into a symmetrical follicular hyperkeratotic eruption affecting the trunk and limbs. In areas the follicular lesions coalesced into a more plaque-like appearance. At the same time ulcers on the trunk and limbs have developed periodically which heal with scarring over a period of several months. The clinical features are shown in Figures 1–3.

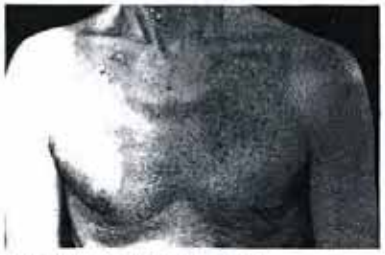
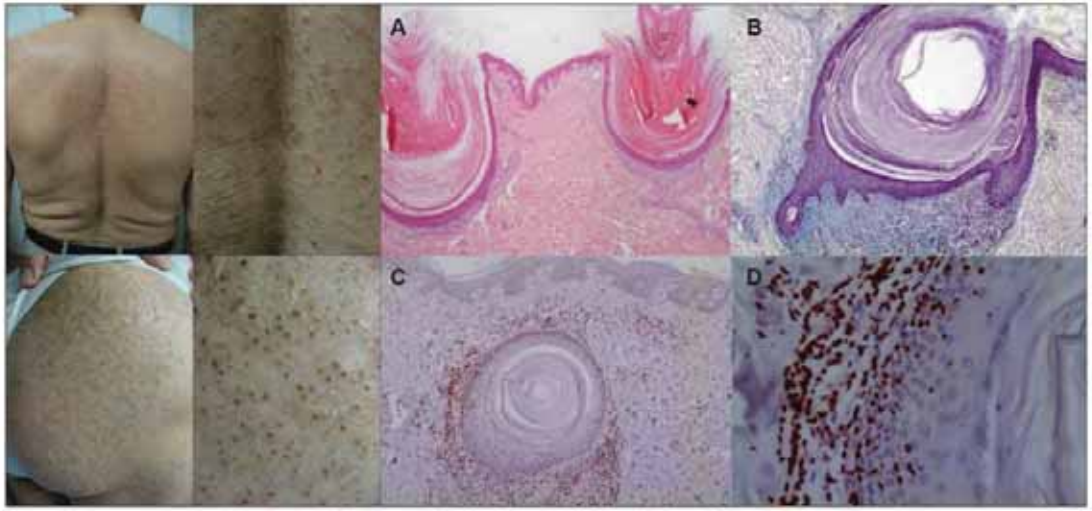


Figure 1. Follicular eruption on chest and arms.

Figure 2. Scalp showing comedones and hair loss.

Skin biopsies were taken in 1989 and 1990. These showed an upper dermal inflammatory infiltrate but there were no diagnostic features. Repeat biopsies taken in 1991 from the forearm, front of chest and back showed the features of mycosis fungoides (Figs 4 and 5). There is an upper dermal infiltrate showing marked epidermotropism, and destruction of the hair follicles, some of which show cystic dilatation. There are no changes of follicular mucinosis and stains for mucin

Correspondence: Dr S. Oliwiecki.



1. Piccinno R, Cocciolanzo M, Berti E, Baldini L. Radiotherapy of cutaneous B cell lymphomas: our experience in 21 cases. *Int J Radiat Oncol Biol Phys* 1993; 27: 385-9.
2. Dalle S, Thomas L, Balme B, Dumontet C, Thaddeemant C. *Primary cutaneous marginal zone lymphoma. Crit Rev Oncol Hematol*. 2009.
3. Fink-Puches R, Wolf IH, Zelouduk I, Kerl H, Cerroni L. Treatment of *primary cutaneous B-cell lymphoma with rituximab. J Am Acad Dermatol* 2005; 52: 847-53.
4. Kyrkonis MC, Siakantaris MP, Kalpadakis C, *et al*. Favorable outcome of primary cutaneous marginal zone lymphoma treated with *intralesional rituximab. Eur J Haematol* 2006; 77: 300-3.
5. Li C, Inagaki H, Kuo TT, Hu S, Okabe M, Eimoto T. Primary cutaneous marginal zone B-cell lymphoma: a molecular and clinicopathologic study of 24 asian cases. *Am J Surg Pathol* 2003; 27: 1061-9.
6. Monari P, Farruggia C, Calzavara Pinton PG. Borrelia burgdorferi-associated primary cutaneous marginal-zone B-cell lymphoma: a case report. *Dermatology* 2007; 215: 229-32.

doi:10.1684/ejd.2010.0987

Widespread comedones as the sole clinical manifestation of follicular mycosis fungoides

Mycosis fungoides (MF) is the commonest type of cutaneous T-cell lymphoma and can manifest with a variety of clinical presentations. Histologically, it is characterized by infiltration of the epidermis by medium-sized to large atypical T cells with cerebriform nuclei [1]. Hair follicle infiltration is a common histological feature of MF. It is usually clinically silent, however, folliculotropism-originated comedones, follicular keratosis, follicular papules and alopecia sometimes occur [2].

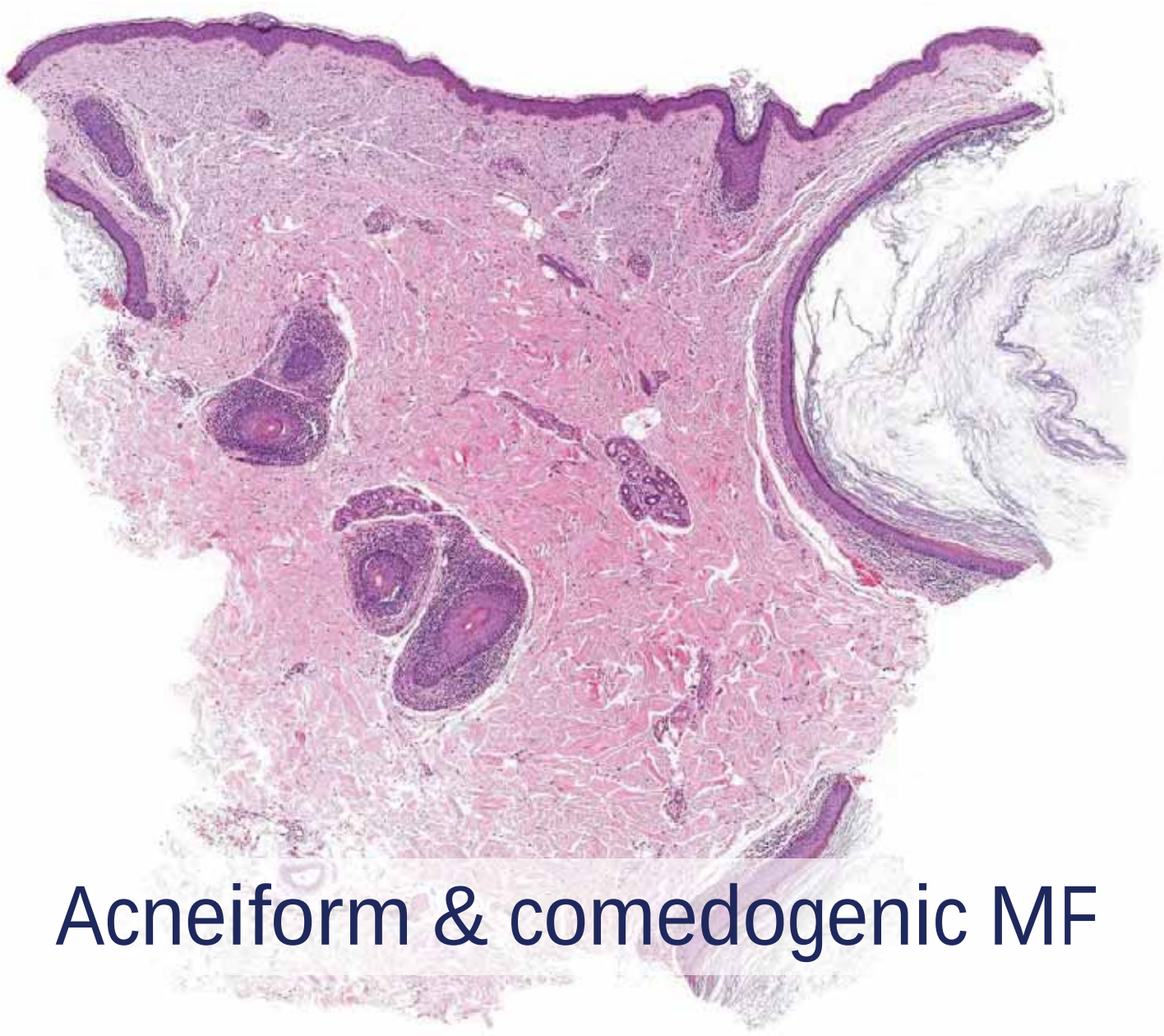
A 67-year-old man presented with disseminated comedones spread over the trunk, buttocks and thighs, mildly pruritic, with two years evolution (*figure 1*). There was clinically with various combinations of lesions. Rarely, as in our patient, a single type of lesions predominate and FMF cases in which comedones were the only presenting sign have been reported [3]. Clinical diagnosis may be difficult since the manifestations may look like acne or an acneiform eruption. It may require several biopsies to make a definitive diagnosis and sometimes the diagnosis may be only made by T-cell receptor gene rearrangement analysis [4]. Histopathologically, FMF is characterized by perifollicular and perivascular dermal infiltrates with variable infiltration of the follicular epithelium by medium-sized to large atypical T cells with cerebriform nuclei, sometimes accompanied by mucinosis. Infiltration of the interfollicular epidermis by atypical T cells is mostly absent (folliculotropism instead of epidermotropism). Generally, the neoplastic T lymphocytes are $CD3^+$, $CD4^+$ and $CD8^-$, as in classic MF [5]. The presence of a considerable number of $CD30^-$ blast cells has been associated with a worse prognosis [4]. Because of the perifollicular localization of the dermal infiltrates, FMF is generally less responsive to the standard therapies used with classic MF and it is believed to have a worse prognosis. Total skin electron beam irradiation is the preferred method of treatment, but complete remission occurs in only a few cases and unresponsiveness has been reported. A good alternative can be found in PUVA combined with interferon-α, or retinoids [4]. A case of FMF treated with narrow band UVB has recently been reported [6]. Chemotherapy should be restricted to those patients with extracutaneous involvement [4].

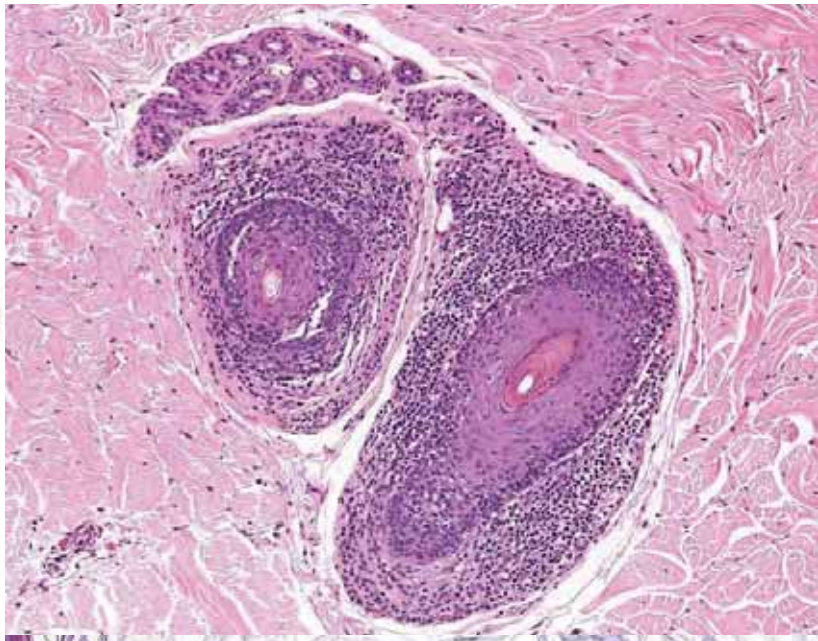
Comedones as the sole manifestation of FMF is rare. The diagnosis in these cases requires a high clinical index of suspicion to give an accurate diagnosis at presentation. The authors emphasize the importance of considering FMF in the differential diagnosis of widespread comedones, particularly as the only clinical manifestation of

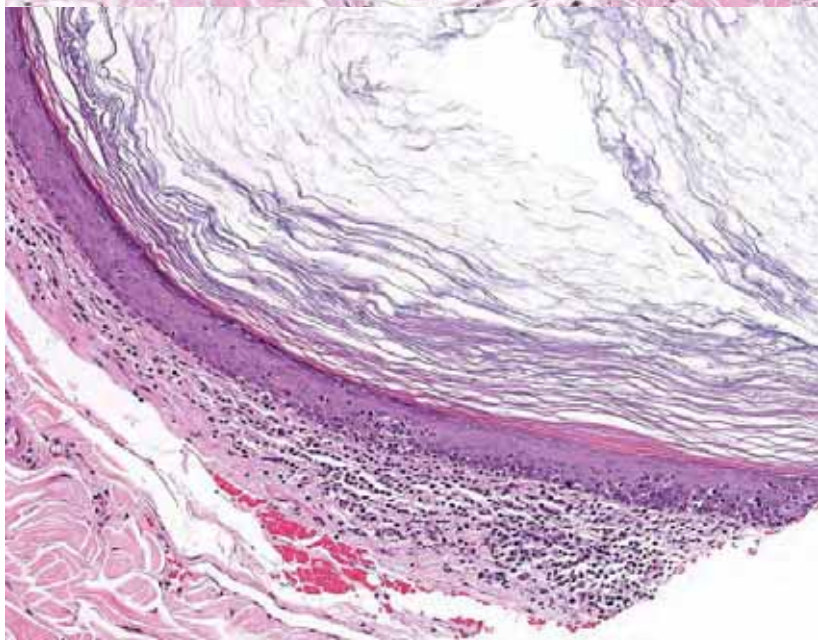
Torres T, et al. EJD, 2010

F, 60
Multiple closed comedones ("whiteheads") on the head & neck with some features of "milia en plaques"; partly inflamed comedo-like follicles on the trunk.

Consultation
Dr. H. Beltraminelli, Locarno

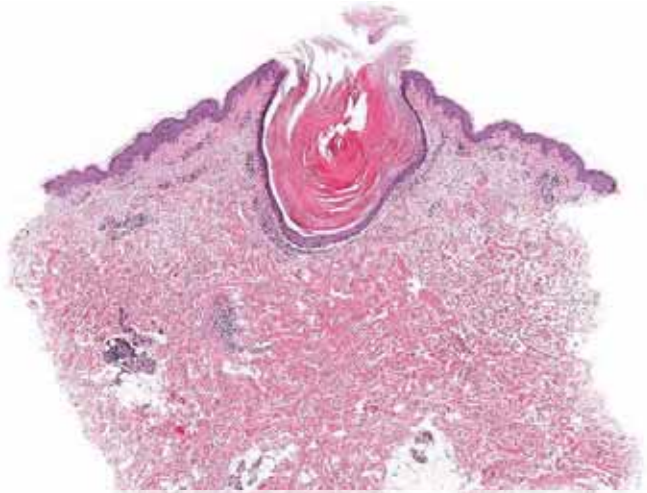


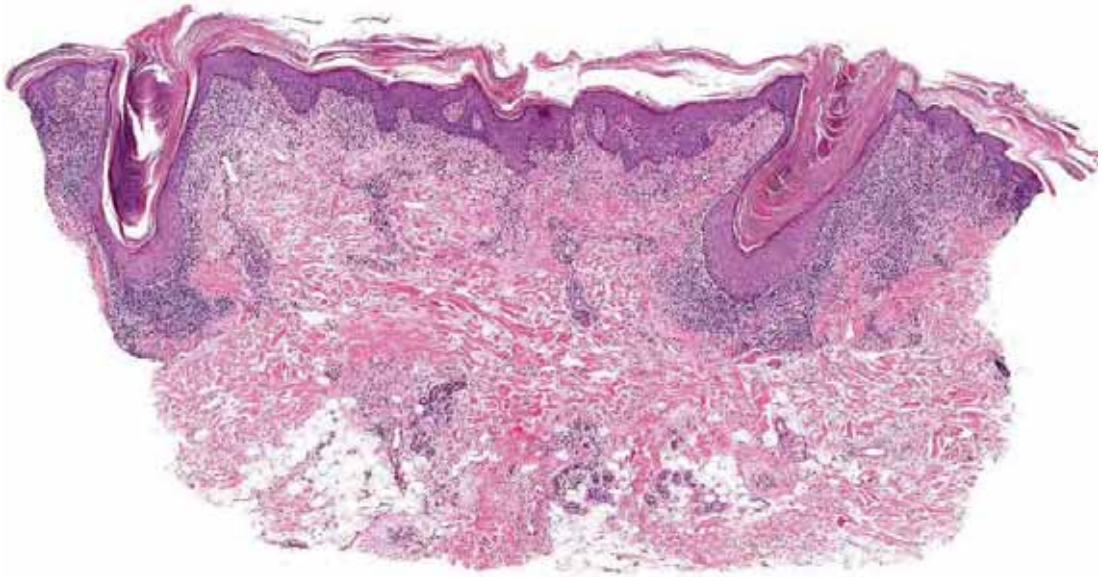


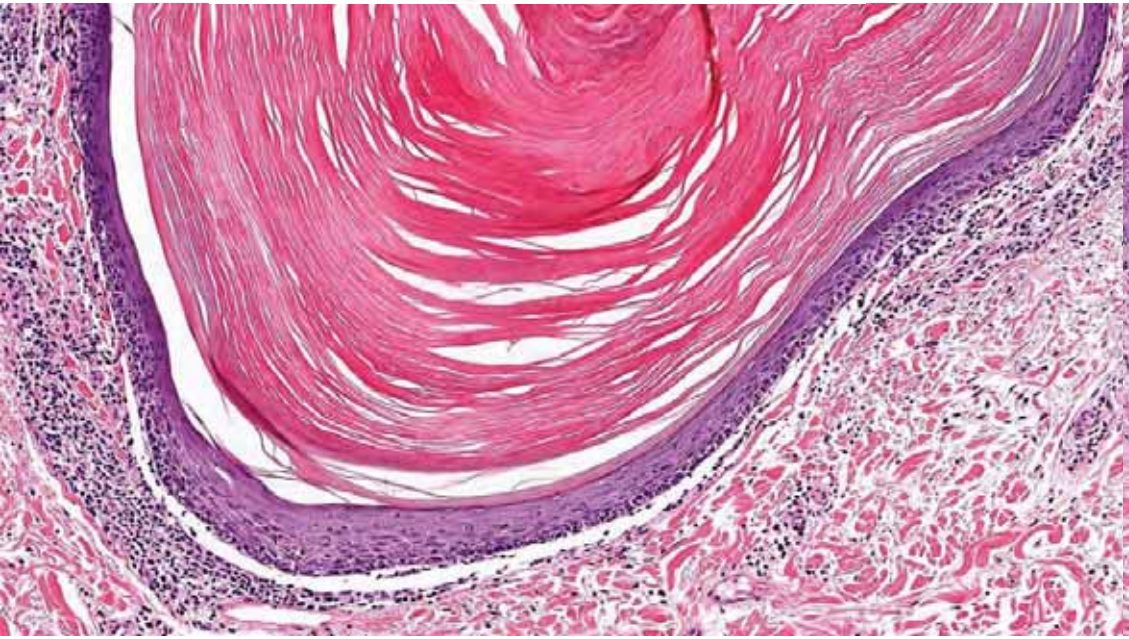


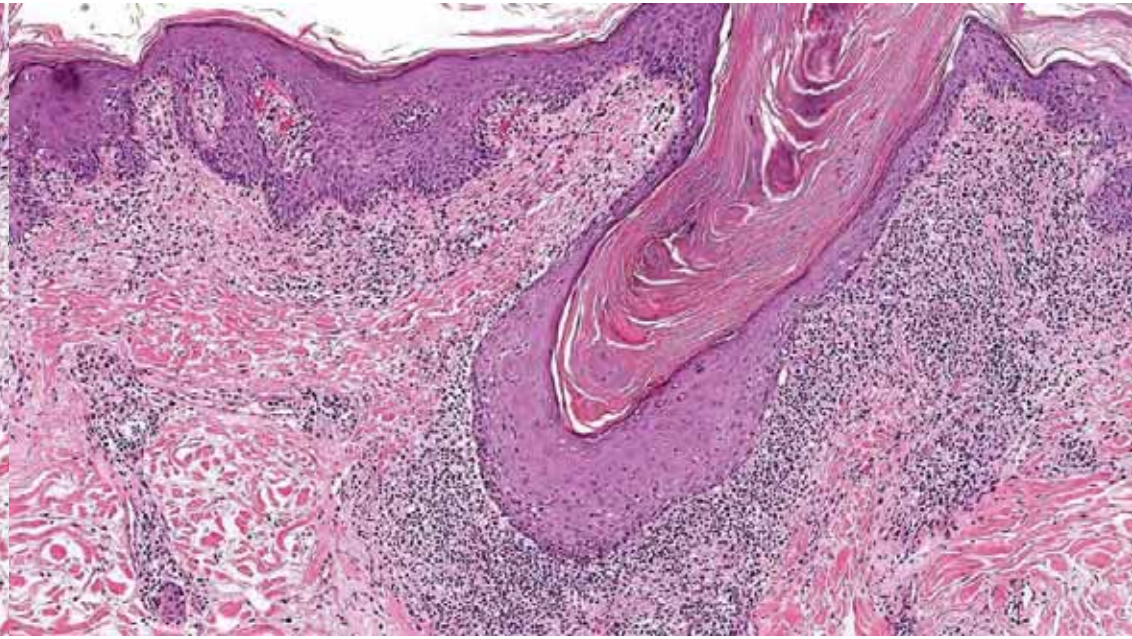
Acneiform & comedogenic MF

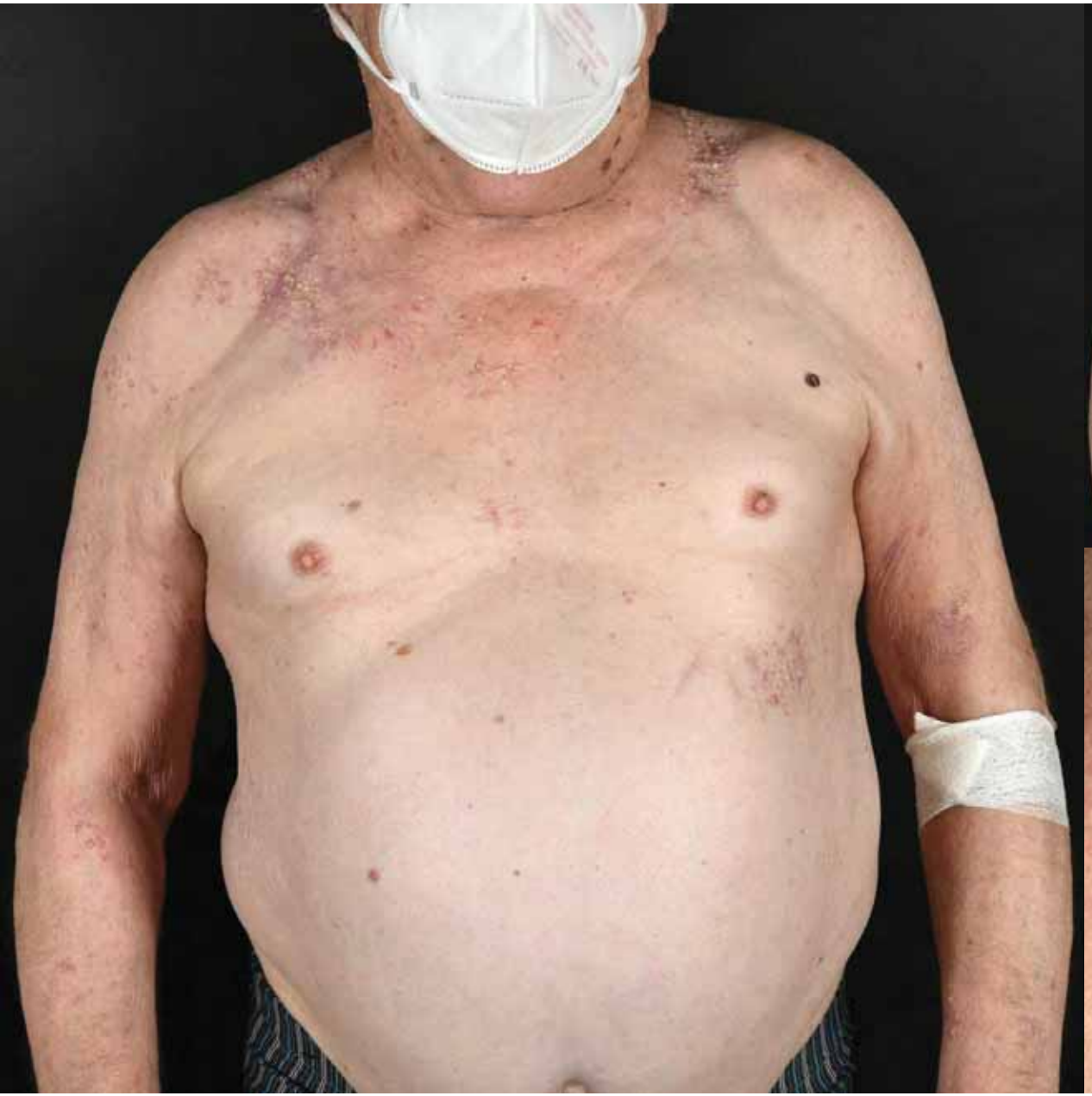
Comedogenic MF

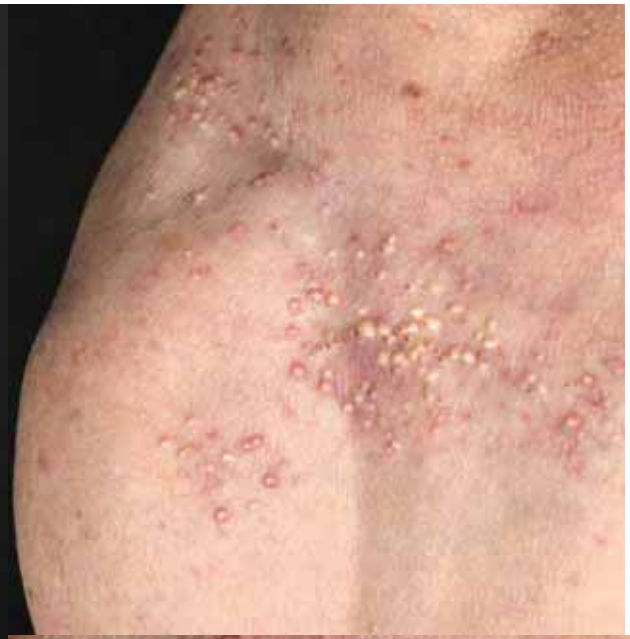


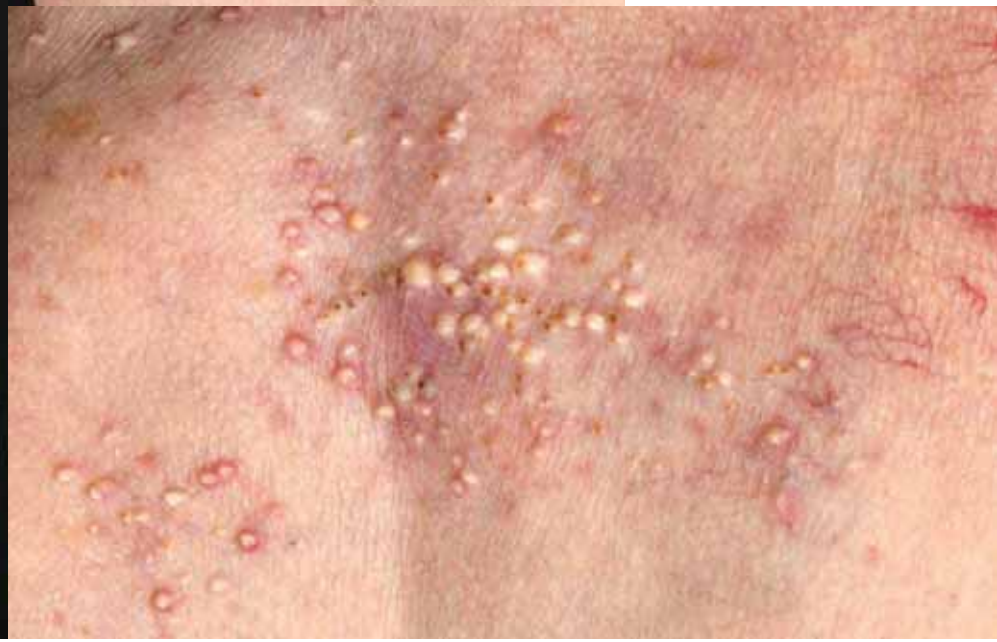








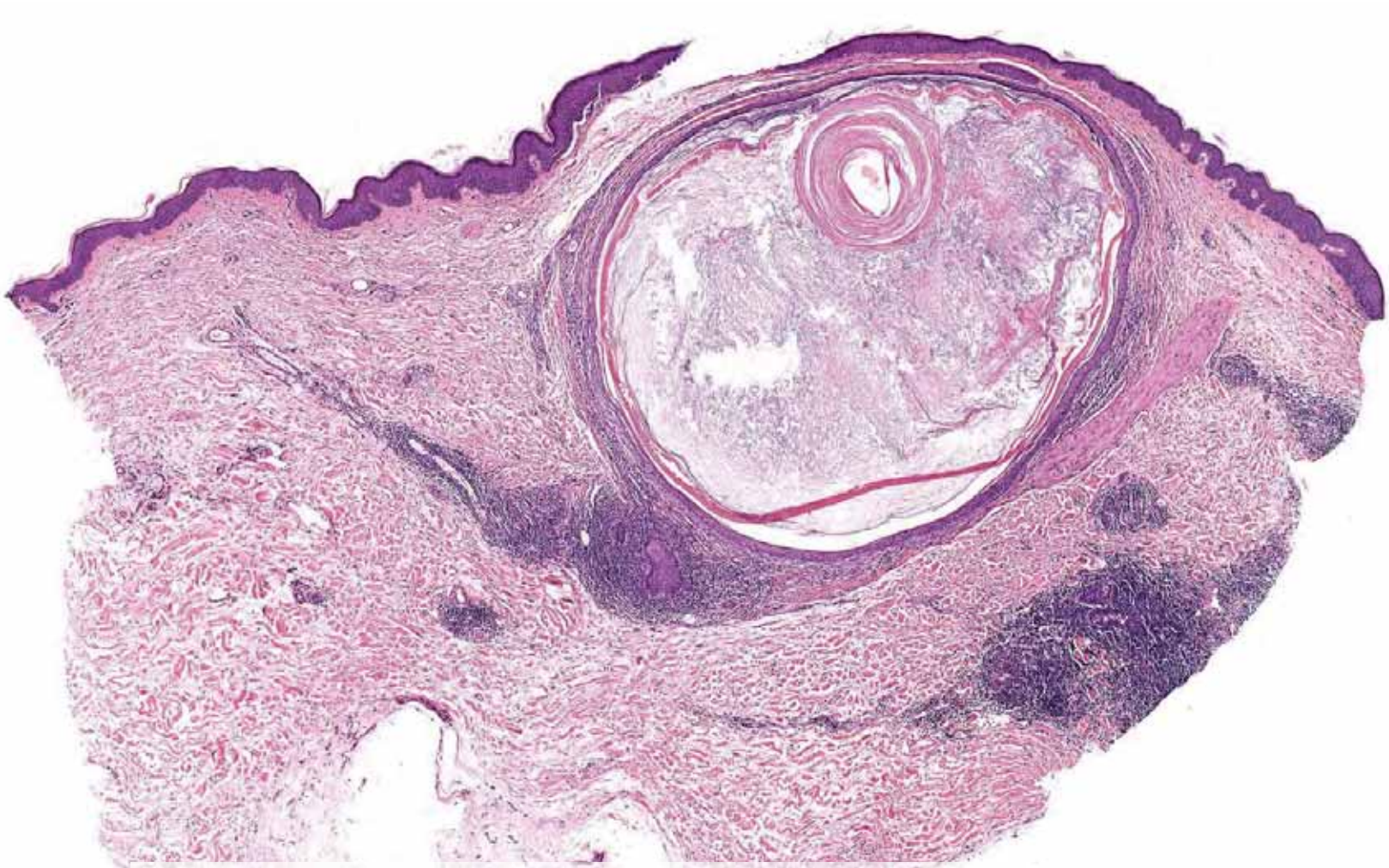


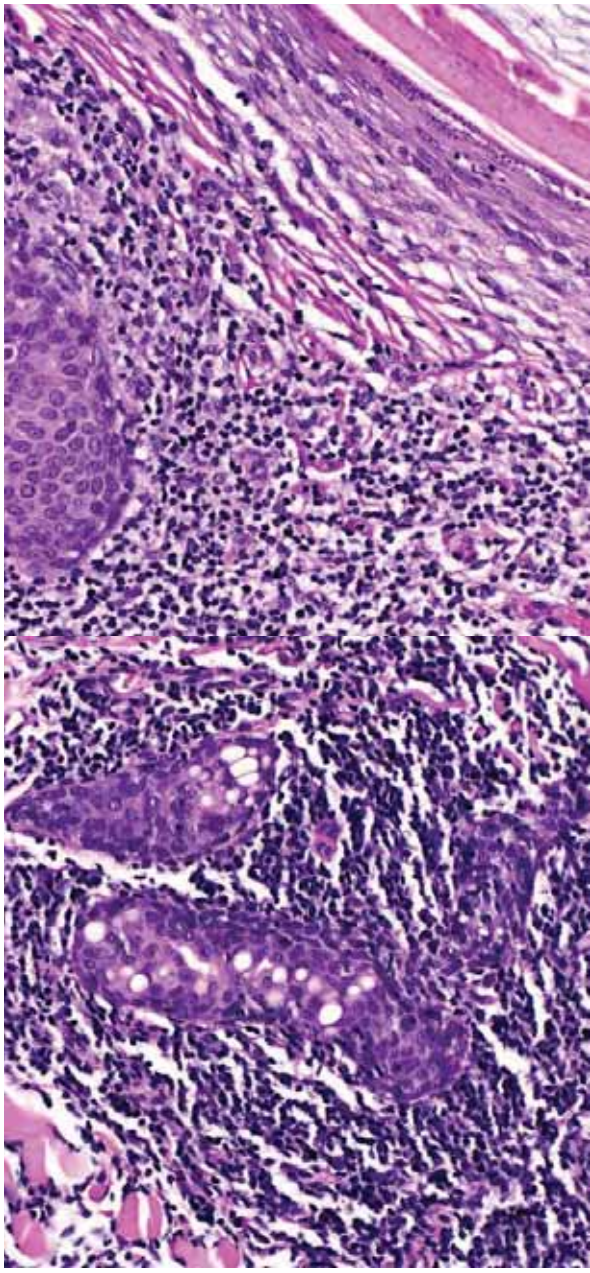


M, 71

Miliary cysts on the trunk and upper extremities of unknown duration.

A biopsy is taken.





Acneiform & comedogenic MF

(with syringotropism)

Acneiform & comedogenic pilotropic mycosis fungoides

- Lesions located to the hair follicles only may resemble an acneiform dermatitis clinically; Onset of small cysts and comedones can be observed rarely in long-standing pilotropic MF
- In my opinion, cases with acneiform follicular mucinosis located on the head & neck only should not be classified as pilotropic MF – but long-standing follow-up is mandatory!
- Cysts characterized histopathologically by a dense lymphoid infiltrate with epitheliotropic lymphocytes should rise suspicion of possible pilotropic MF *(but dense pilotropic / perifollicular infiltrates are not specific for MF !)*
- Clue (if present): syringotropism & syringometaplasia

Annales de dermatologie et de vénéréologie (2014) 141, 462–464

Formation médicale continue

DOCUMENT ICONOGRAPHIQUE

Mycosis fongoïde avec mucinose folliculaire révélé par un spinulosis des plis

Mycosis fungoides associated with follicular mucinosis manifested by lichen spinulosus in skinfolds

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Disponible sur internet le 2 juin 2014

Introduction

Le spinulosisme est l'hyperkératose de l'ostium folliculaire, symptôme observé dans différentes maladies telles que le lichen spinulosus [1], les démodécidoses [2], la dermatomyosite de Wong [3] et plus classiquement la kératose pilaire physiologique.

Observation

Une femme de 46 ans avait depuis une quinzaine d'années un prurit des plis des coudes sur lesquels, depuis un an, étaient apparues des lésions spinulosiques (Fig. 1). Des papules similaires étaient visibles dans les creux inguinaux (Fig. 2) et poplités, associées à une xérose cutanée diffuse modérée.

À partir de 2003, plusieurs examens histologiques étaient faits, montrant un infiltrat lymphocytaire dermique pilotrope et épidermotrope, dont le phénotype était CD3– CD8+, CD20–. Sur une même biopsie de l'aine était observée la coexistence de deux types de lésions pilaires avec infiltrat pilotrope : une kératose pilaire rétentionnelle avec dilatation ostiale (Fig. 3) et une mucinose folliculaire, confirmée par la coloration au bleu alcian (Fig. 4). L'étude des réarrangements de la chaîne gamma du récepteur T par PCR mettait en évidence une population clonale T majoritaire, identique en peau pathologique et en peau saine, mais différente de celle détectée dans le sang. Le diagnostic retenu était celui de mycosis fongoïde (MF) CD8 pilotrope avec mucinose folliculaire et kératose folliculaire rétentionnelle à type de spinulosis. Le bilan paraclinique comportant une radiographie pulmonaire, une échographie abdominale, une NFS, le dosage des LDH et des IgE était normal.

La patiente était traitée par chlorméthine (Caryolysine®) et dermocorticoïdes (bétaméthasone) permettant une rémission clinique complète en trois mois.

Une récidive, trois mois après l'arrêt de la chlorméthine, était traitée uniquement par dermocorticoïdes d'activité forte jusqu'à disparition complète des lésions.

Le bilan à quatre ans montrait une récidive discrète du spinulosis sans prurit depuis trois à quatre mois, dans les

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Journal of Cutaneous Pathology

Spiky follicular mycosis fungoides: a clinicopathologic study of 8 cases

Background: The early stages of follicular mycosis fungoides (FMF) have not been described previously in the literature.
Objective: Our goal was to better categorize the clinicopathologic features of early stages of FMF.
Methods: The clinical notes of patients with a diagnosis of FMF seen during the previous 5 years were reviewed to identify any cases that at presentation had only hyperkeratotic follicular lesions.
Results: Eight patients (five male, three female) with a mean age of 55.4 years were enrolled. Noteworthy, FMF was not a clinical consideration in any of these patients initially. Patients presented with disseminated, slightly erythematous, hyperkeratotic, spiky follicular papules which, histopathologically, showed hyperkeratotic columns protruding from follicular plugging in concert with selective infiltration of the infundibular epithelium by atypical, mostly CD4+, lymphocytes. T-cell clonality was demonstrated in four of eight cases. The mean duration of the lesions before diagnosis was 17.1 months. The course was indolent in most of the cases (median follow up: 18 months), whilst progression to overt FMF was noted in two patients.
Limitations: The number of cases is small and follow up relatively short.
Conclusions: Spiky FMF is a deceptive clinicopathologic presentation of FMF that has been poorly described and that can mimic numerous follicular disorders.

Keywords: Follicular mycosis fungoides, Hyperkeratotic spicules, Keratosis pilaris, Spiky

Tomasini C, Kempf W, Novelli M, Fava P, Annessi G, Rongioletti F, Fierro MT, Quaglino P. Spiky follicular mycosis fungoides: a clinicopathologic study of eight cases. J Cutan Pathol 2015; 42: 164–172. © 2014 John Wiley & Sons A/S. Published by John Wiley & Sons Ltd

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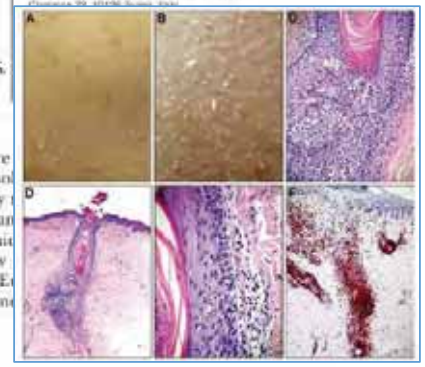

Mycosis fungoides (MF) is a low-grade cutaneous T-cell lymphoma characterized by epidermotropic T lymphocytes with clonal skin expansion that usually presents with scaling erythematous patches which, over time, may progress to plaques and tumors.[1] As there are numerous distinct variants of MF, diagnosis may be a challenge, especially in their early stage; as there MF histopathol However, early of these varian aggressive clinic In the new Organization-E Research an


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Calvin Klein
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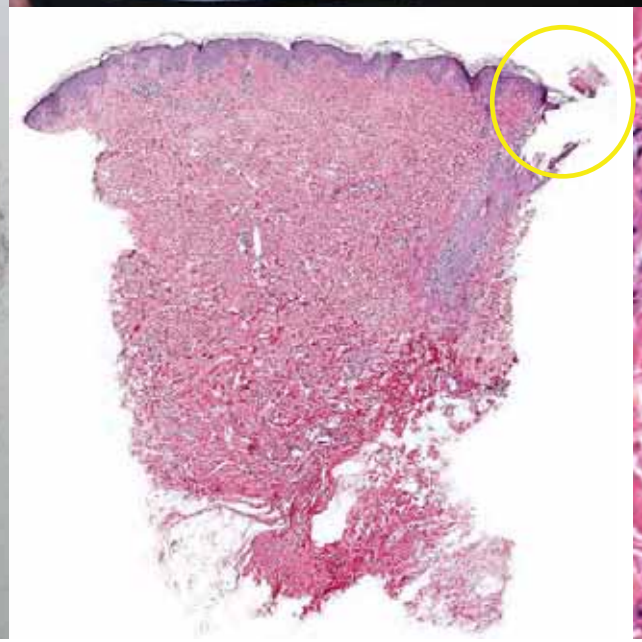
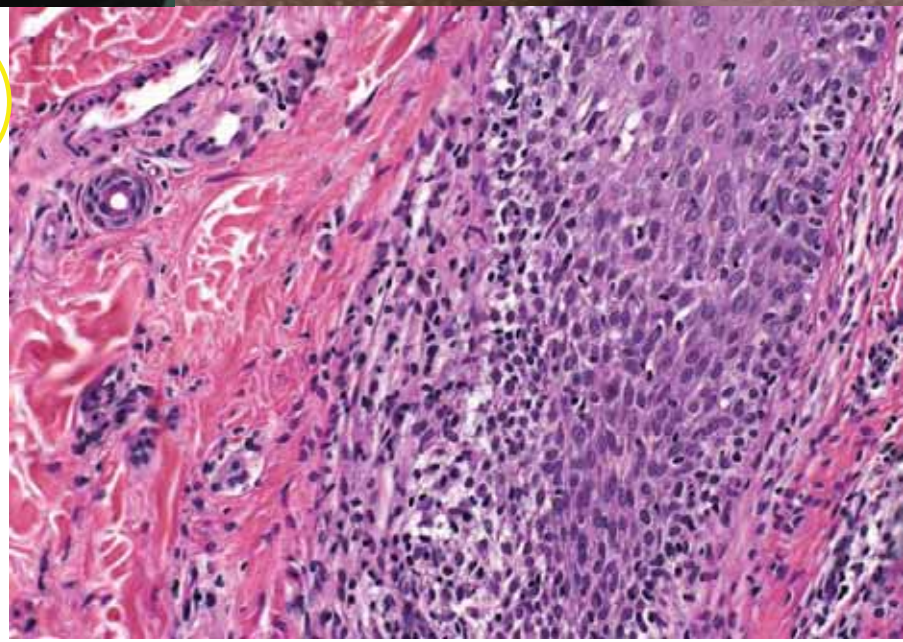
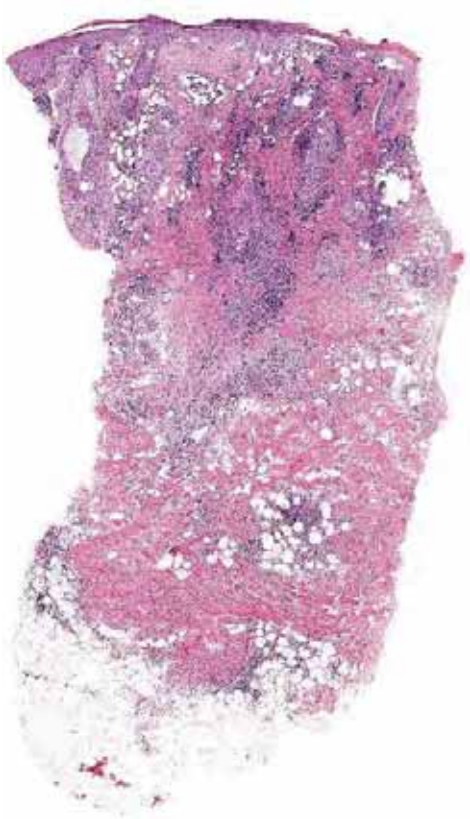
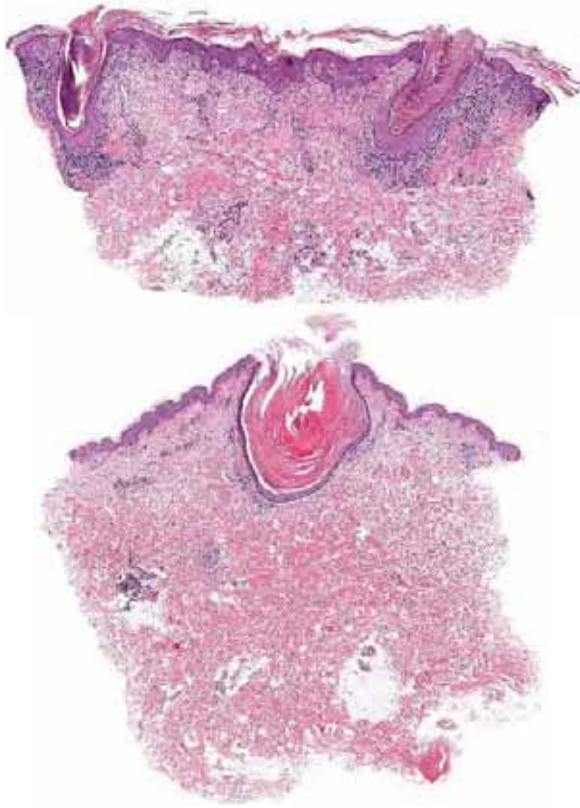




Is acneiform / comedogenic / hyperkeratotic / cystic follicular mucinosis always MF ?

In my opinion, most cases of acneiform follicular mucinosis (and variants) restricted to the head & neck are not associated with clear-cut MF; on the other hand, most patients with generalized acneiform lesions, comedones and cysts have MF. Histopathological features of head & neck vs. generalized cases are indistinguishable.





Epidermal mucinosis in mycosis fungoides

Brian J. Nickoloff, M.D., Ph.D., *Stanford, CA*

In many cases of mycosis fungoides there is widening of the epidermal intercellular spaces (i.e., spongiosis) and papillary dermal fibrosis with minimal papillary dermal edema. Twenty biopsies of mycosis fungoides, stained with a modified colloidal iron procedure, were analyzed to substantiate the notion that the spongiosis resulted from the formation of an osmotic gradient because of intercellular acidic mucopolysaccharide deposition. In nineteen of twenty cases of patch-plaque mycosis fungoides, there was positive intercellular deposition of acidic mucopolysaccharides. In addition to the contribution of acidic mucopolysaccharides to the process of spongiosis, the biologic significance of epidermal mucin deposition is discussed. Mycosis fungoides should be added to the growing list of diseases in which there is epidermal mucinosis. (J Am Acad Dermatol 15:83-86, 1986.)

Spongiosis has been variably defined by dermatopathologists, but basically it can be identified when the intercellular space between keratinocytes is widened (as noted in a review by Stenn et al[1]). There are various causes of spongiosis and varying degrees of spongiosis, which in the extreme form produces microvesicle formation. From a pathophysiologic standpoint, the precise mechanism of spongiosis is unclear.[1,2] One previous hypothesis implicated the pathogenetic formation of an osmotic gradient toward the epidermis.[1] In this hypothesis, epidermal cells were suggested to produce extracellular ions or proteins that, by the establishment of a Gibbs-Donnan equilibrium, would draw fluid across the basement membrane zone by osmotic forces.[1] My colleagues and I[3] have previously speculated that follicular spongiosis results from the intercellular deposition of water-binding acidic mucopolysaccharides that were recognized by positive colloidal iron staining. We suggested that follicular spongiosis and follicular mucinosis differ by virtue of the degree of follicular mucin deposition but that intercellular mucin could be identified in both cases in which there was increased widening of the spaces between follicular epithelium.

In many cases of the patch-plaque stage of mycosis fungoides, widening of the intercellular space where the atypical lymphocytes are infiltrating has been observed, and this report documents the presence of colloidal iron–positive material in these zones. Thus mycosis fungoides should be added to the list of diseases (basal cell carcinoma, verruca vulgaris, keratoacanthoma, squamous cell carcinoma, and spongiotic dermatitis) in which there is epidermal mucinosis.[4] In contrast to this study's cases of mycosis fungoides, in which the epidermal mucinosis is accompanied by a papillary dermis with coarse or thickened collagen, the allergic contact dermatitis and other types of spongiotic dermatitis, in which there may be general epidermal mucinosis, are accompanied by papillary dermal edema. This differential diagnostic point is emphasized because of the possible diagnostic dilemma that arises in distinguishing mycosis fungoides from other dermatitides that have variable degrees of widened intercellular spaces and lymphocytic infiltrates.[5]

MATERIALS AND METHODS

The last fourteen consecutive patients (1984 to 1985) with the patch or plaque stage of mycosis fungoides whose biopsies were processed in the Stanford Der-

From the Department of Dermatology, Stanford University Medical Center.

Reprint requests to: Dr. Brian J. Nickoloff, Director of Dermatopathology, R-166, Stanford University Medical Center, Stanford, CA 94305.

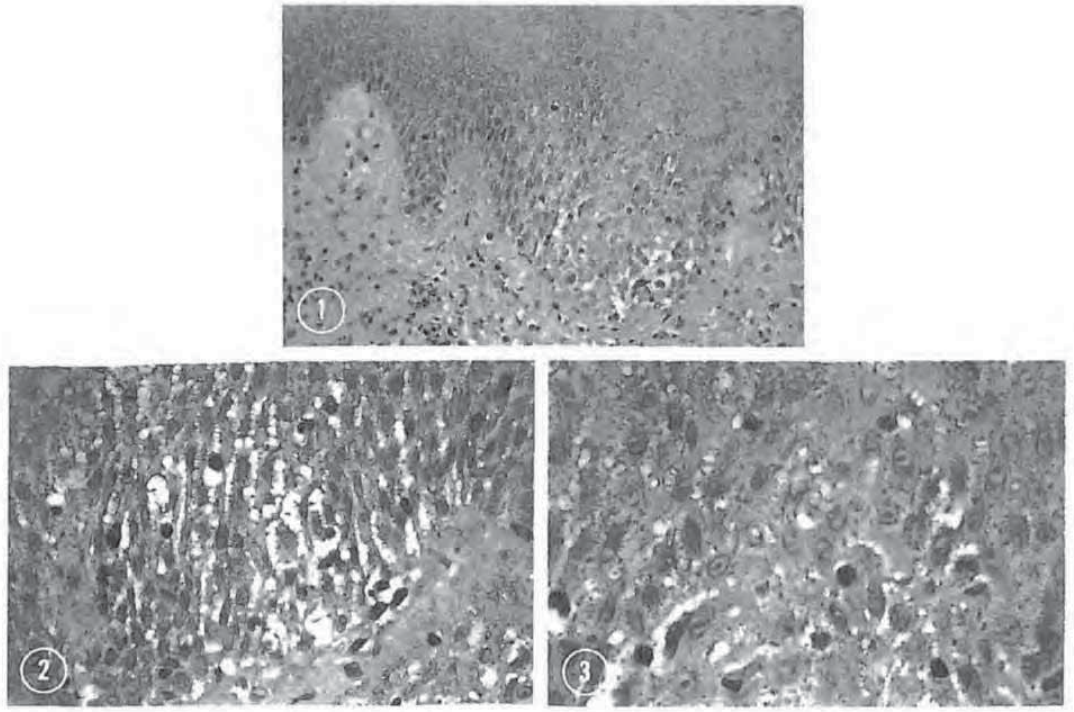
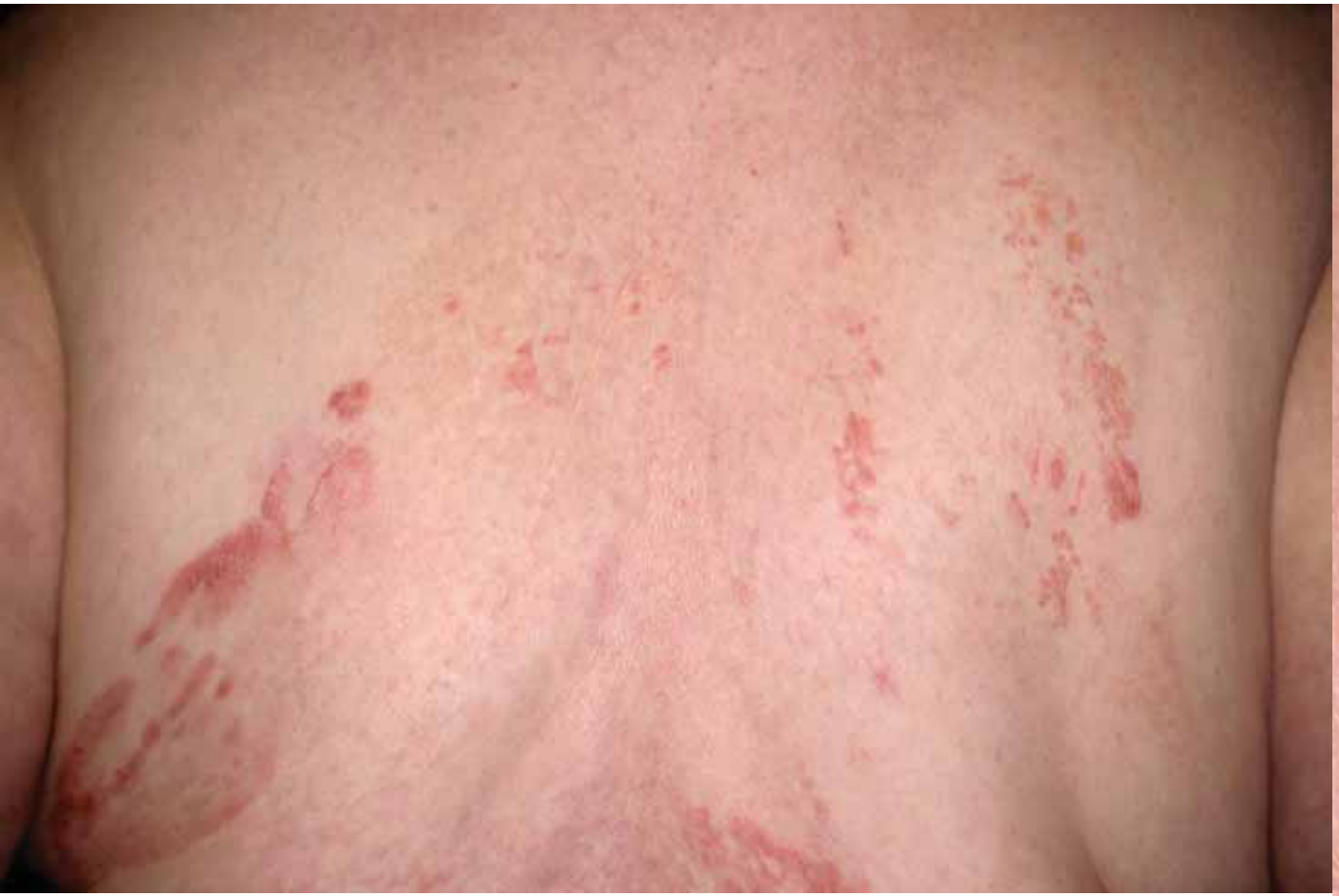
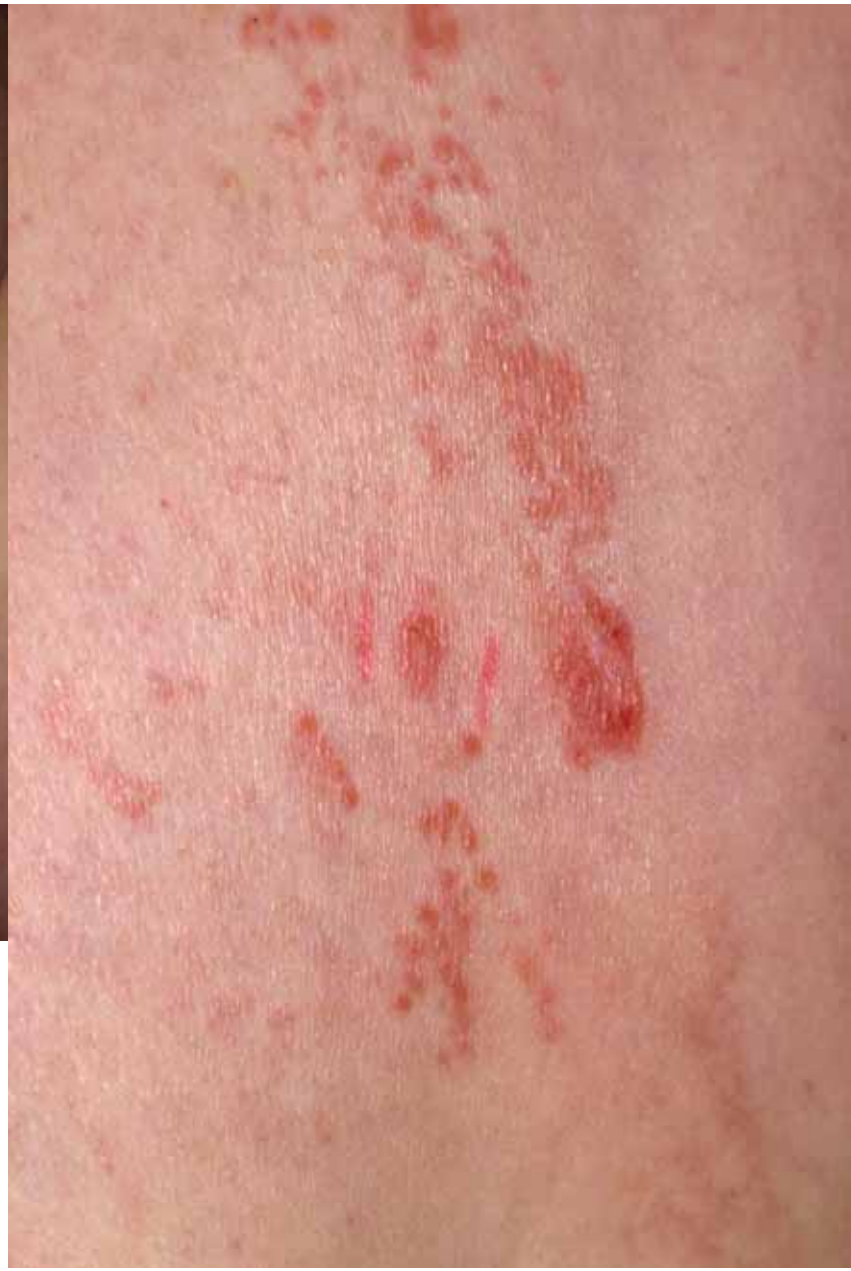


Fig. 1. Patch stage of mycosis fungoides. Spongiosis and intercellular colloidal iron–positive material are most prominent in the mid and lower epidermis. The lower epidermis is infiltrated by enlarged hyperchromatic lymphocytes. The papillary dermis is fibrotic, with scattered atypical lymphocytes. (×250.)

Figs. 2 and 3. Higher magnification confirms the widened intercellular spaces containing colloidal iron–positive material. The infiltrating lymphocytes are markedly hyperchromatic, with irregular nuclear contours. (Fig. 2: ×500; Fig. 3: ×700.)





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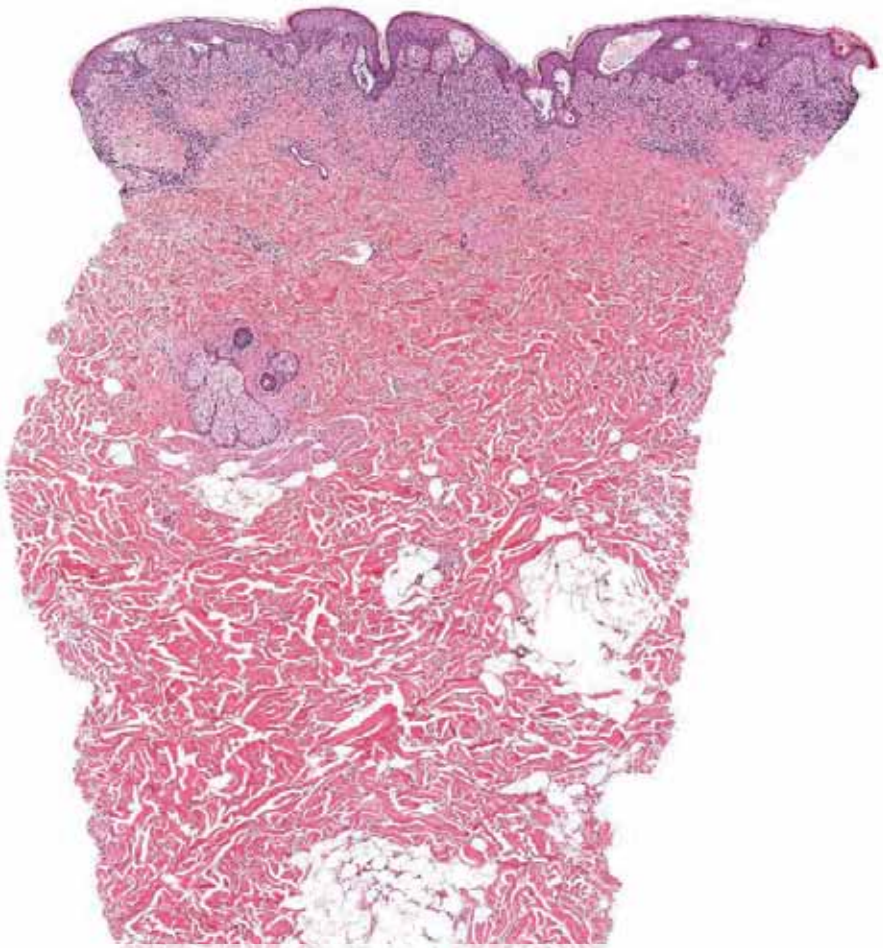
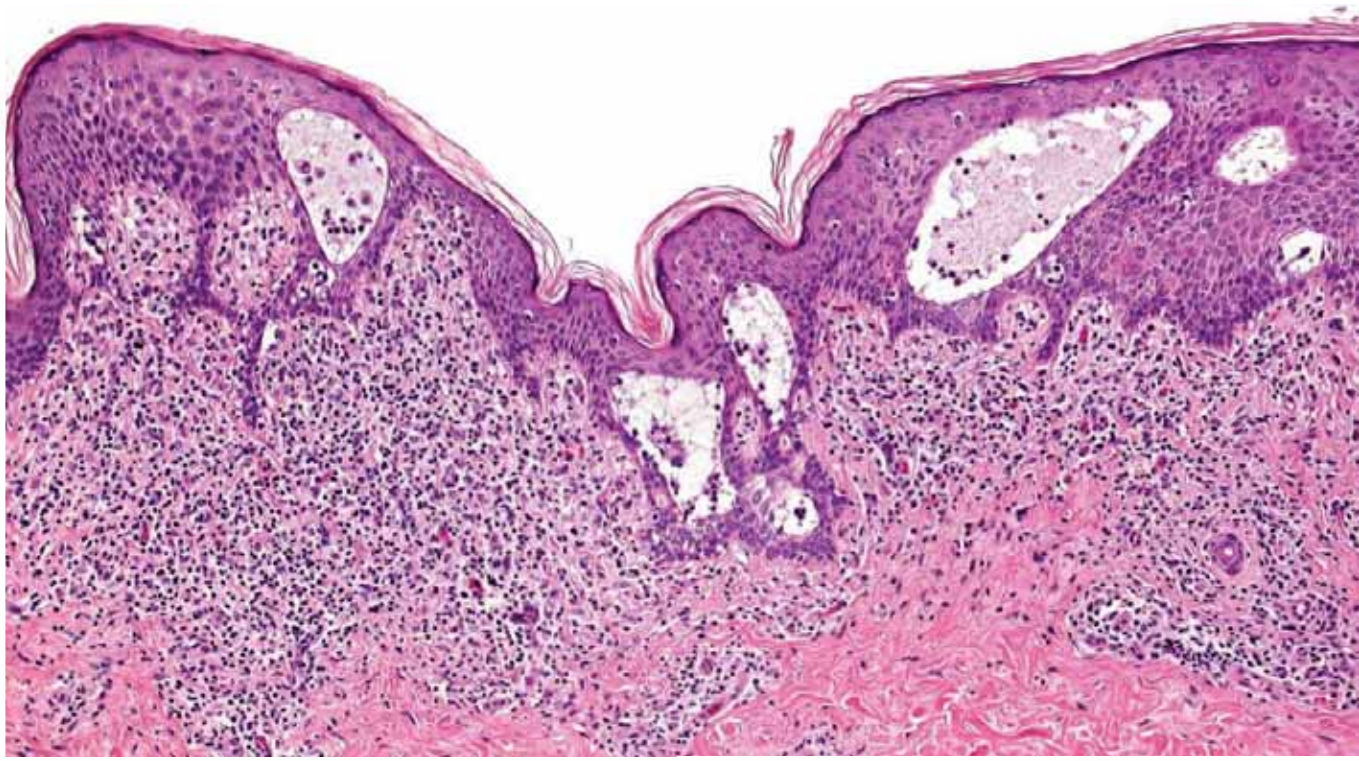
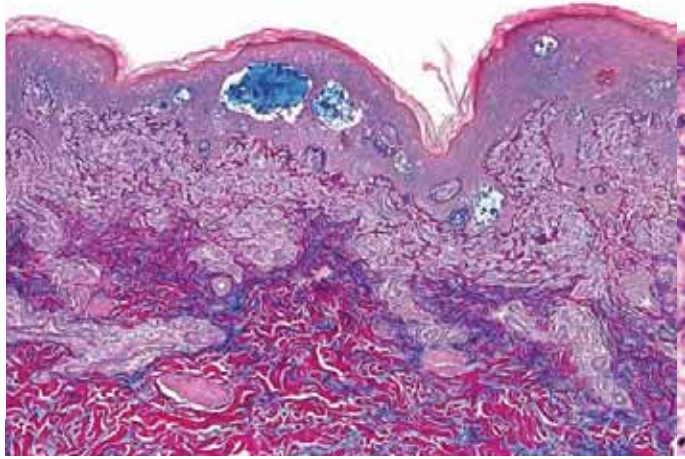
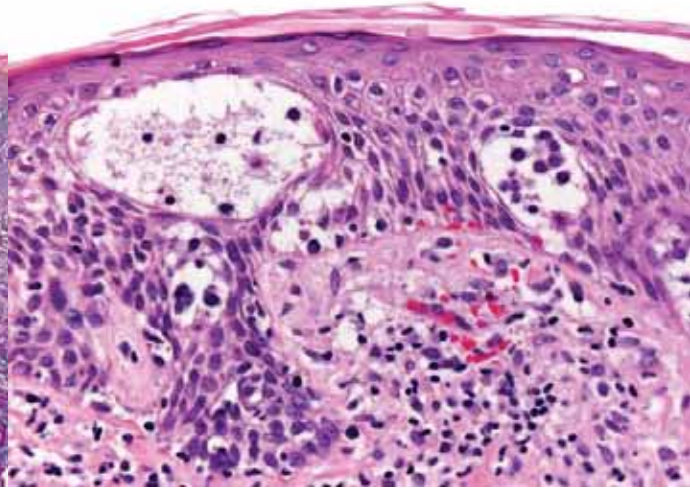
According to the patient lesions on the trunk and upper extremities for approximately 5 years.

A biopsy is taken.



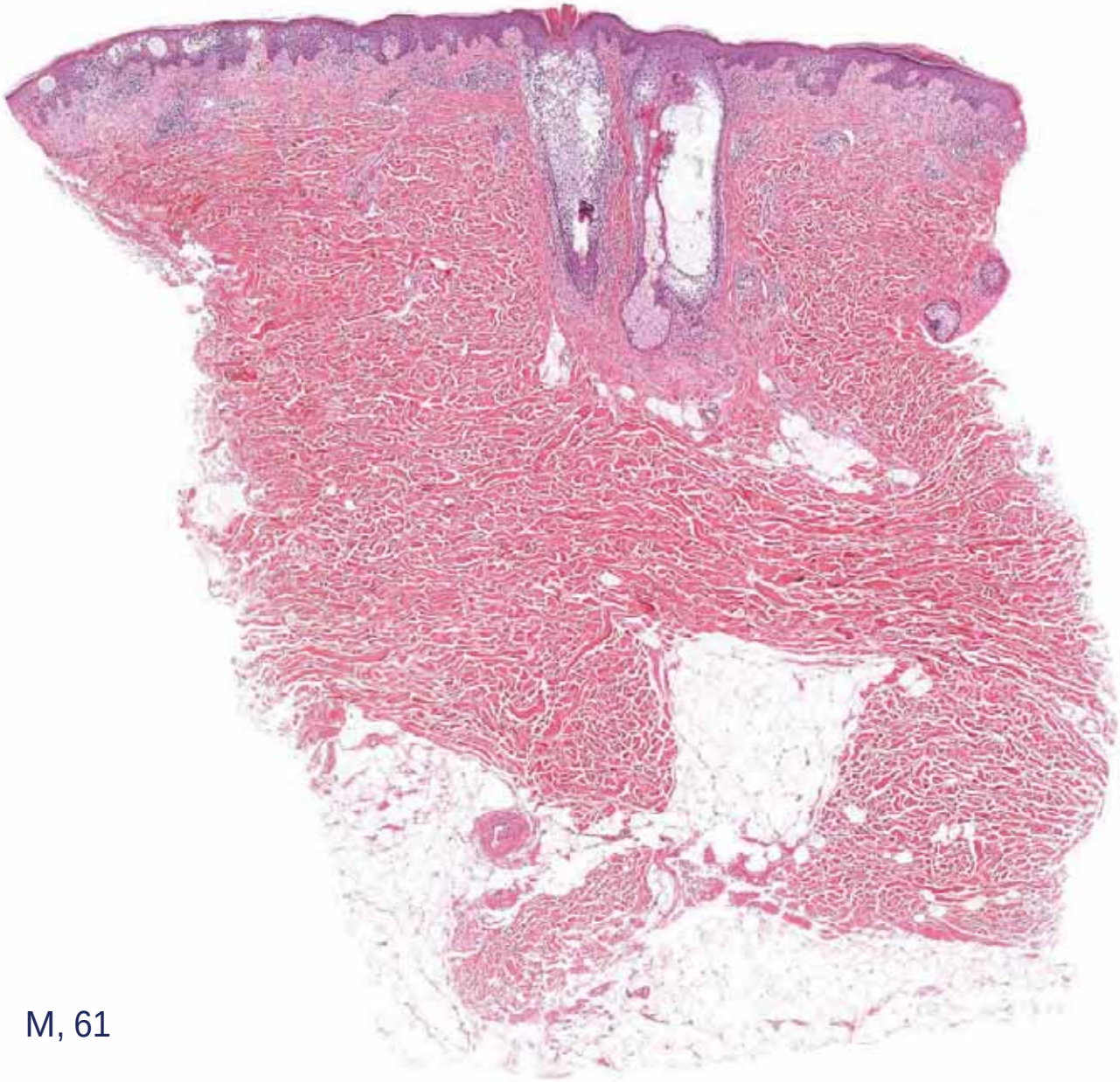






Mycosis fungoides

with epidermal mucinosis



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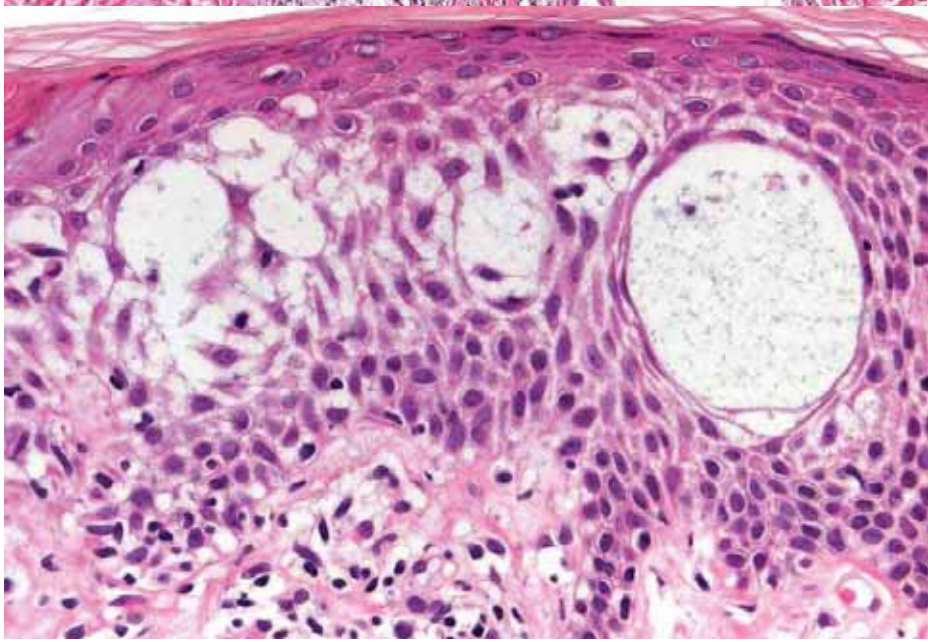
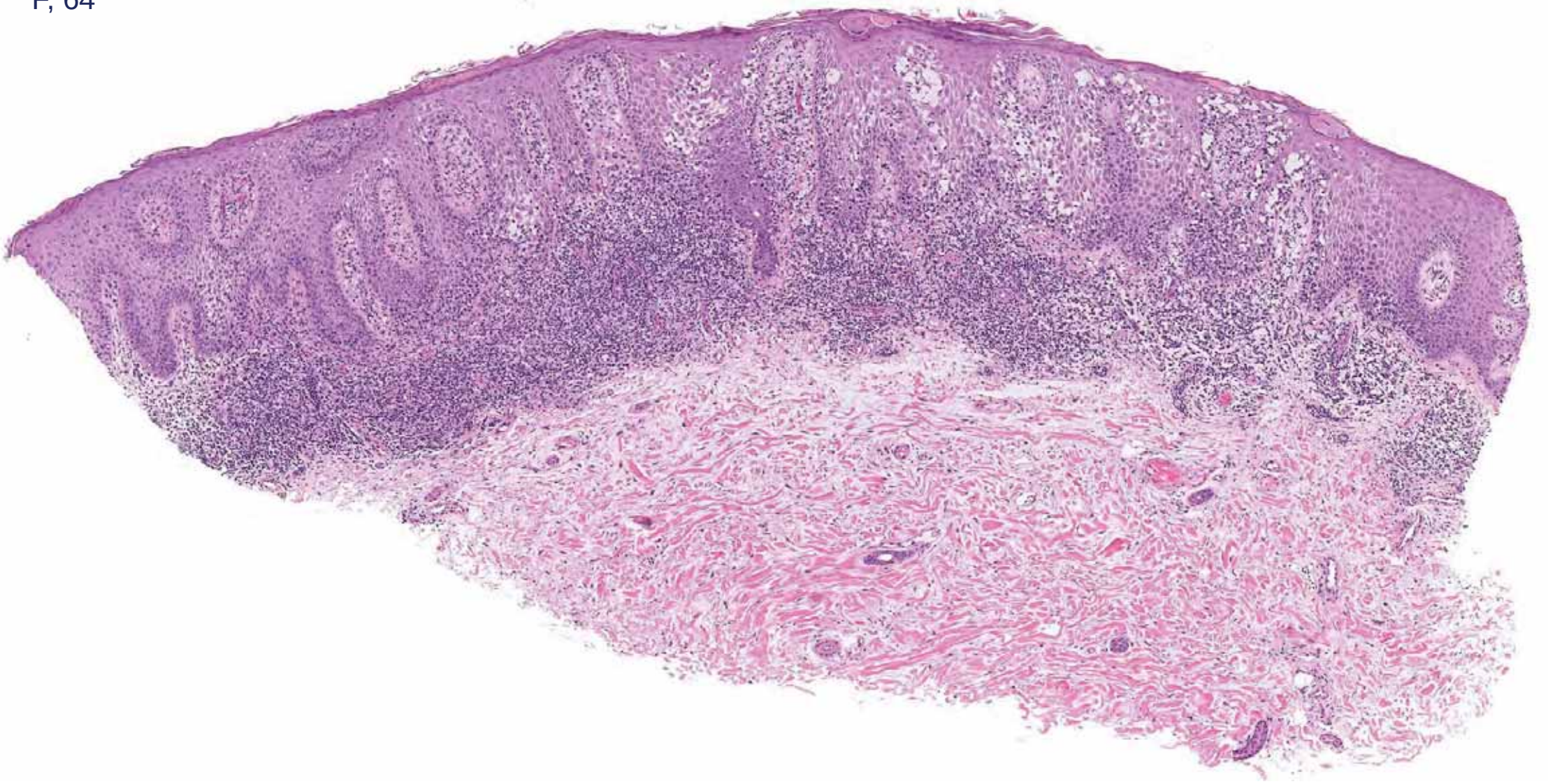
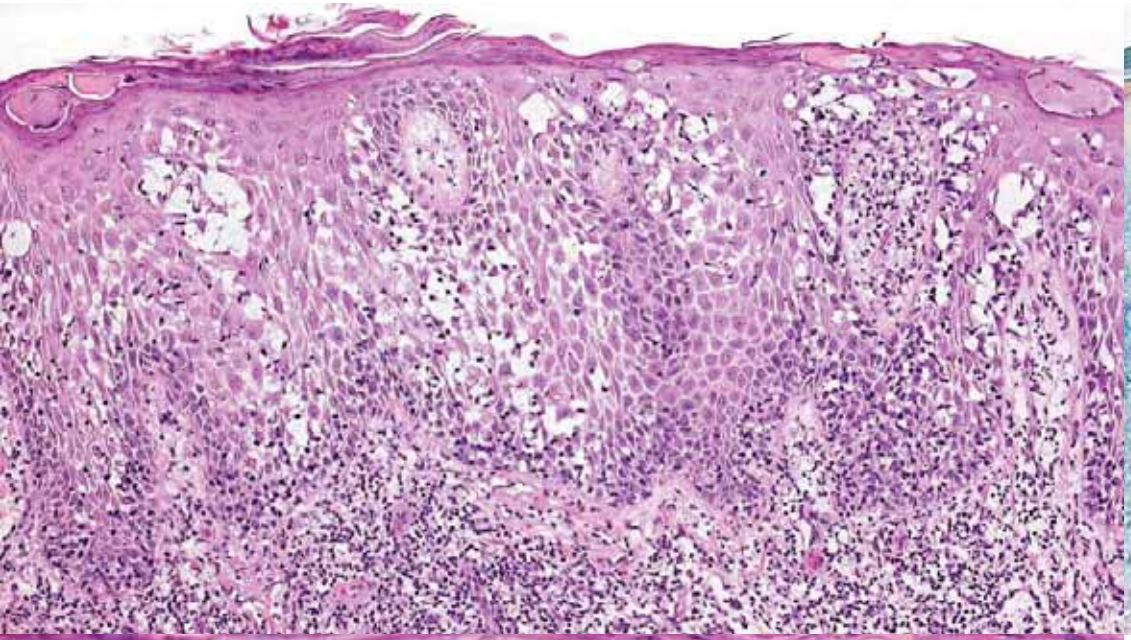
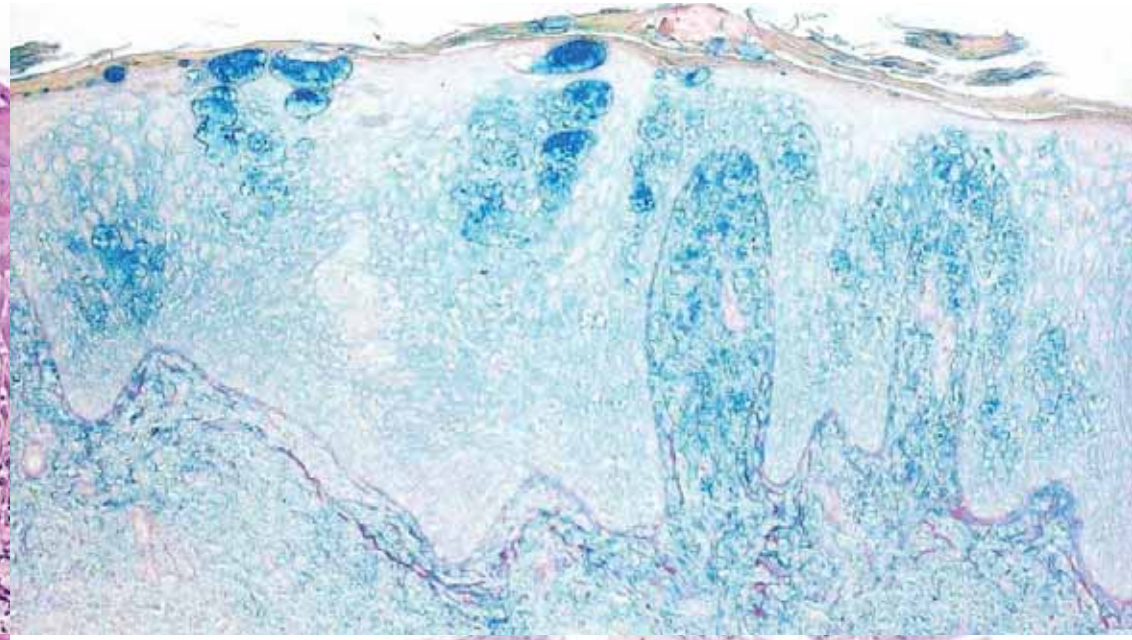
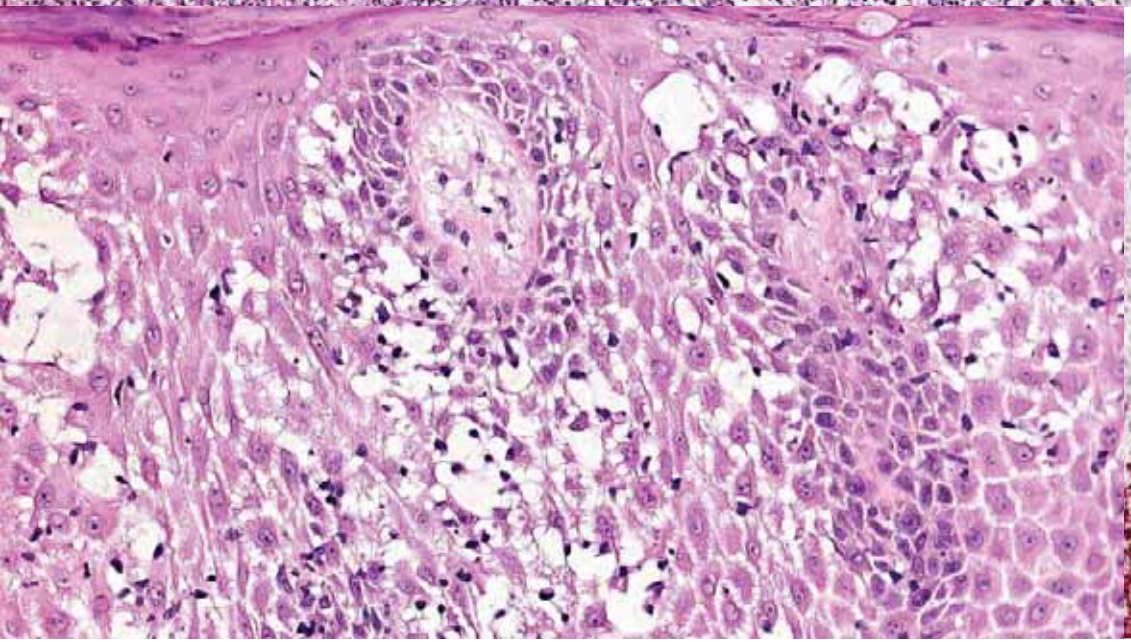


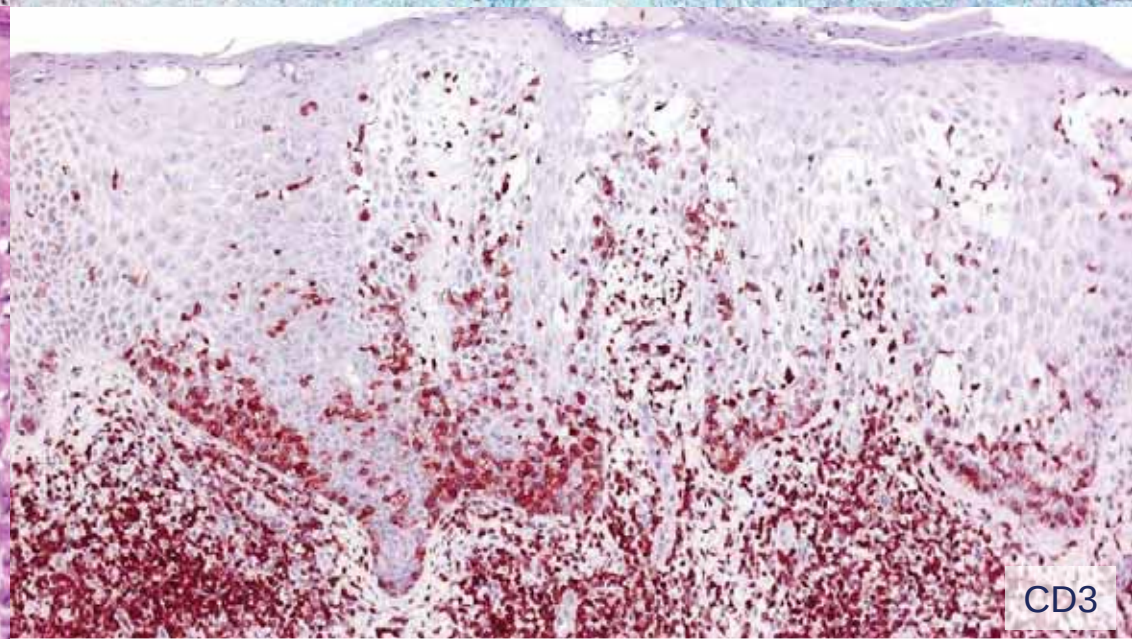
F, 64







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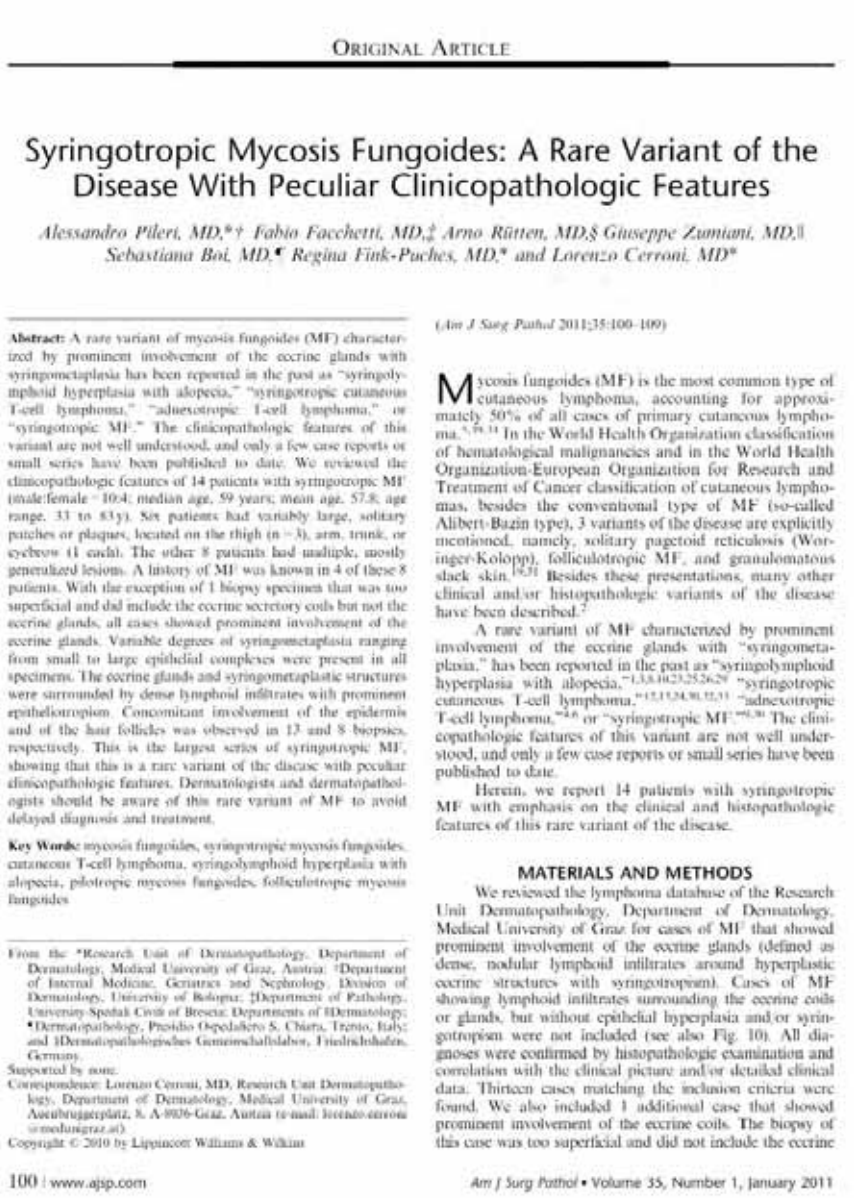

ORIGINAL ARTICLE

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

Alessandro Pileri, MD,† Fabio Facchetti, MD,‡ Arno Rütten, MD,§ Giuseppe Zumiani, MD,‖ Sebastiana Boi, MD,¶ Regina Fink-Puches, MD,* and Lorenzo Cerroni, MD**

Abstract: A rare variant of mycosis fungoides (MF) characterized by prominent involvement of the eccrine glands with syringometaplasia has been reported in the past as "syringolymphoid hyperplasia with alopecia," "syringotropic cutaneous T-cell lymphoma," "adnexotropic T-cell lymphoma," or "syringotropic MF." The clinicopathologic features of this variant are not well understood, and only a few case reports or small series have been published to date. We reviewed the clinicopathologic features of 14 patients with syringotropic MF (male:female = 10:4; median age, 59 years; mean age, 57.8; age range, 33 to 83 y). Six patients had variably large, solitary patches or plaques, located on the thigh (n = 3), arm, trunk, or eyebrow (1 each). The other 8 patients had multiple, mostly generalized lesions. A history of MF was known in 4 of these 8 patients. With the exception of 1 biopsy specimen that was too superficial and did include the eccrine secretory coils but not the eccrine glands, all cases showed prominent involvement of the eccrine glands. Variable degrees of syringometaplasia ranging from small to large epithelial complexes were present in all specimens. The eccrine glands and syringometaplastic structures were surrounded by dense lymphoid infiltrates with prominent epitheliotropism. Concomitant involvement of the epidermis and of the hair follicles was observed in 13 and 8 biopsies, respectively. This is the largest series of syringotropic MF, showing that this is a rare variant of the disease with peculiar clinicopathologic features. Dermatologists and dermatopathologists should be aware of this rare variant of MF to avoid delayed diagnosis and treatment.

Key Words: mycosis fungoides, syringotropic mycosis fungoides, cutaneous T-cell lymphoma, syringolymphoid hyperplasia with alopecia, pilotropic mycosis fungoides, folliculotropic mycosis fungoides

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Supported by none.

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Mycosis fungoides (MF) is the most common type of cutaneous lymphoma, accounting for approximately 50% of all cases of primary cutaneous lymphoma.[1–3,13,14] In the World Health Organization classification of hematological malignancies and in the World Health Organization-European Organization for Research and Treatment of Cancer classification of cutaneous lymphomas, besides the conventional type of MF (so-called Alibert-Bazin type), 3 variants of the disease are explicitly mentioned, namely, solitary pagetoid reticulosis (Woringer-Kolopp), folliculotropic MF, and granulomatous slack skin.[1,9,11] Besides these presentations, many other clinical and/or histopathologic variants of the disease have been described.[2]

A rare variant of MF characterized by prominent involvement of the eccrine glands with "syringometaplasia," has been reported in the past as "syringolymphoid hyperplasia with alopecia,"[1,3,8,10,23,25,26,29] "syringotropic cutaneous T-cell lymphoma,"[4,5,15,15,24,30,32,33] "adnexotropic T-cell lymphoma,"[4,6] or "syringotropic MF."[9,11,30] The clinicopathologic features of this variant are not well understood, and only a few case reports or small series have been published to date.

Herein, we report 14 patients with syringotropic MF with emphasis on the clinical and histopathologic features of this rare variant of the disease.

MATERIALS AND METHODS

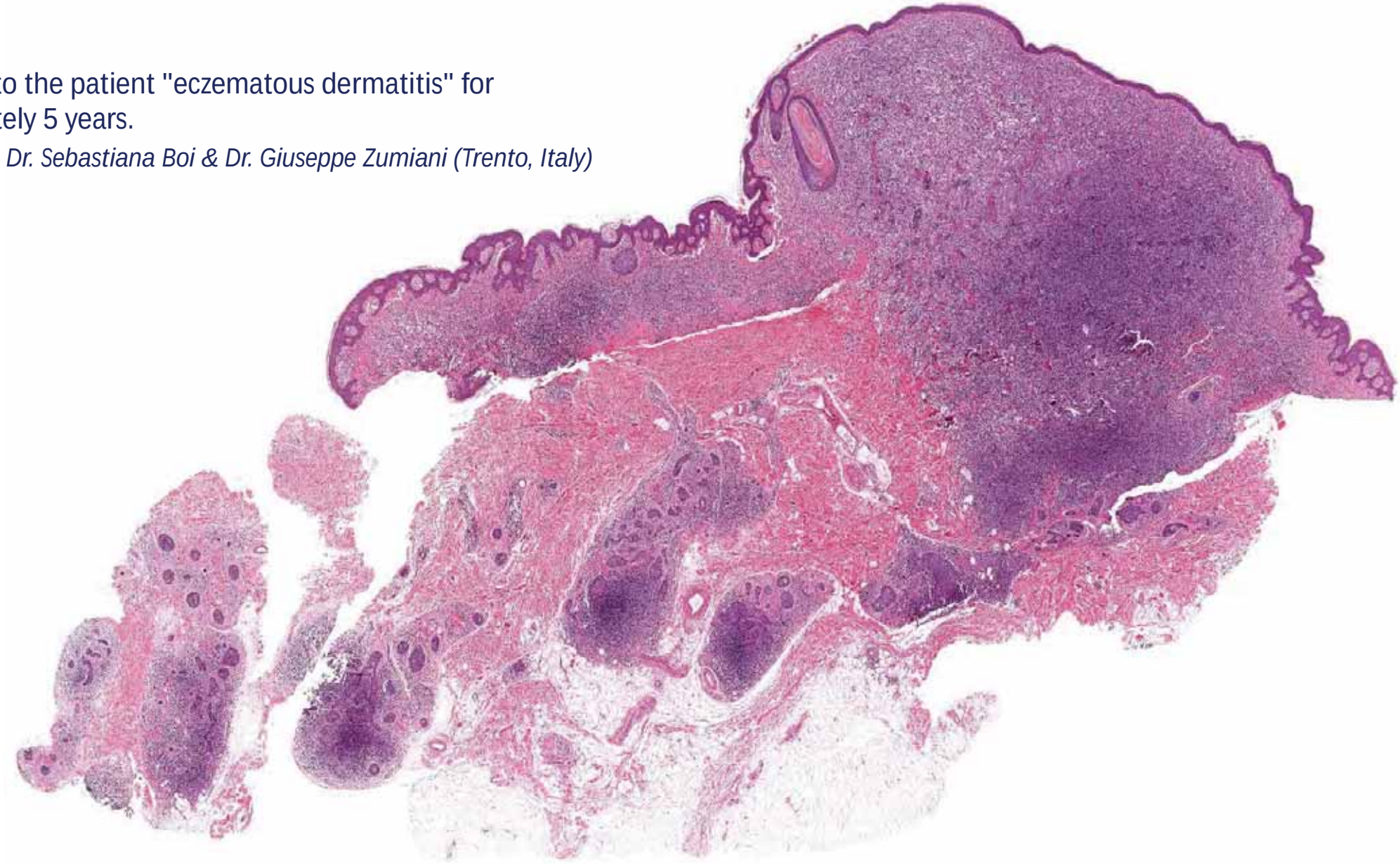
We reviewed the lymphoma database of the Research Unit Dermatopathology, Department of Dermatology, Medical University of Graz for cases of MF that showed prominent involvement of the eccrine glands (defined as dense, nodular lymphoid infiltrates around hyperplastic eccrine structures with syringotropism). Cases of MF showing lymphoid infiltrates surrounding the eccrine coils or glands, but without epithelial hyperplasia and/or syringotropism were not included (see also Fig. 10). All diagnoses were confirmed by histopathologic examination and correlation with the clinical picture and/or detailed clinical data. Thirteen cases matching the inclusion criteria were found. We also included 1 additional case that showed prominent involvement of the eccrine coils. The biopsy of this case was too superficial and did not include the eccrine

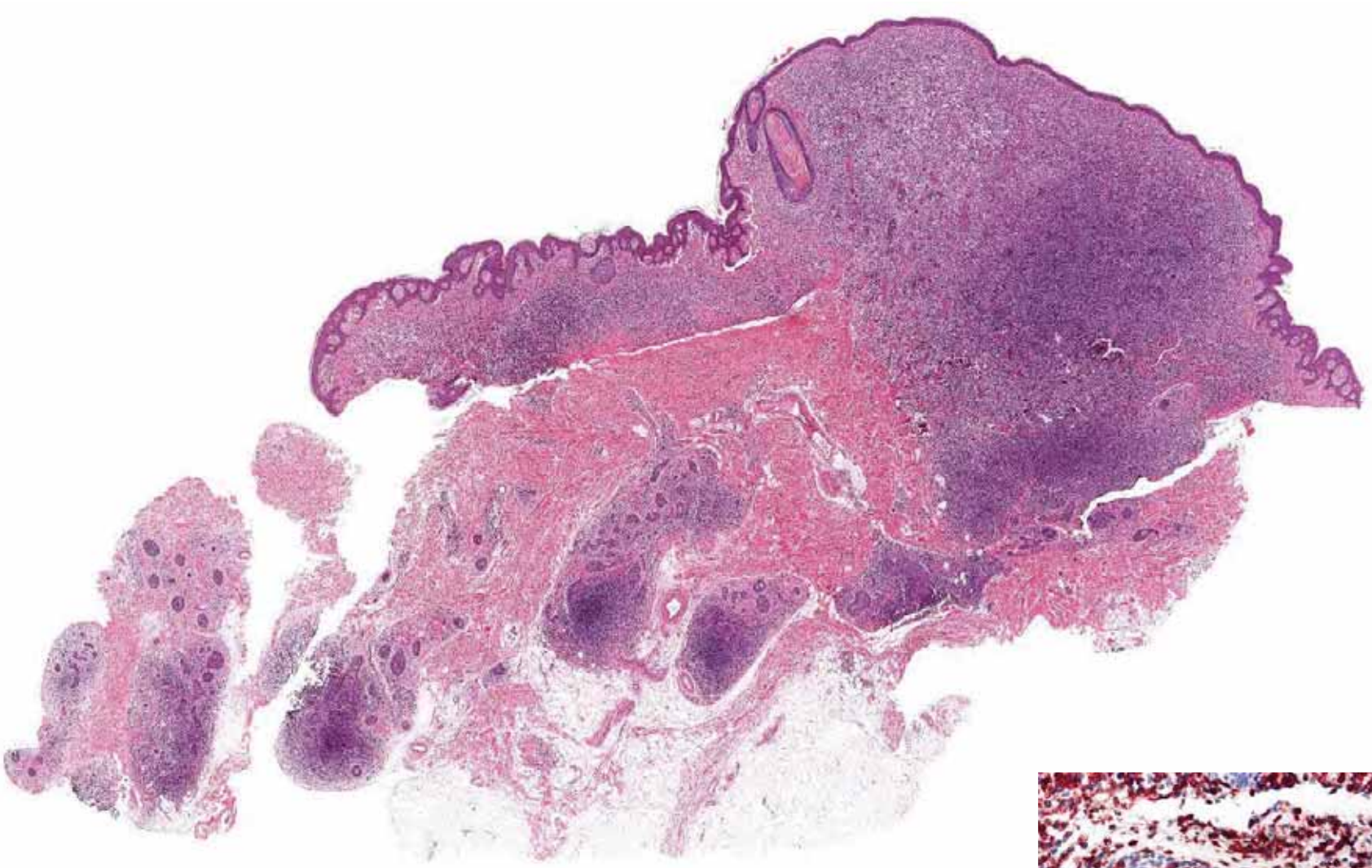
- Clinicopathologic variant of mycosis fungoides; sometimes solitary lesions
- Clinical manifestations oft different from "conventional" MF
- Prominent involvement of the eccrine glands; syringometaplasia
- Oft concomitant involvement of the hair follicles *(syringotropic-pilotropic MF; "syringolymphoid hyperplasia with alopecia")*

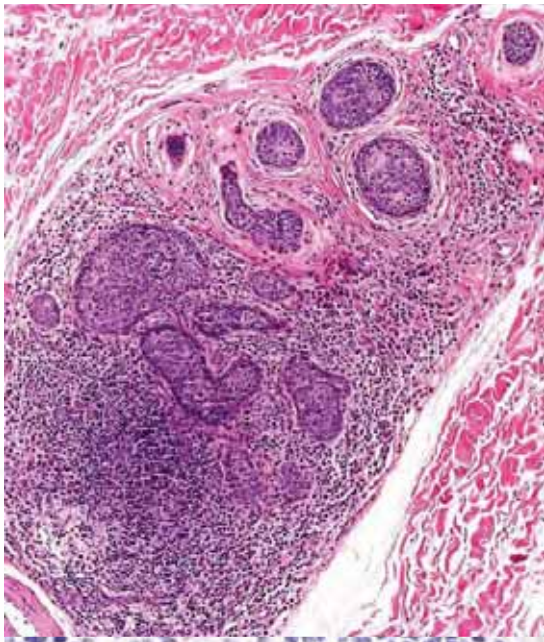
F, 33

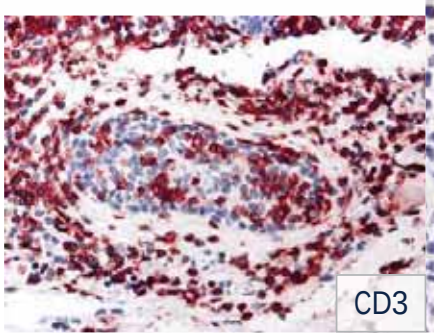
According to the patient "eczematous dermatitis" for approximately 5 years.

Consultation Dr. Sebastiana Boi & Dr. Giuseppe Zumiani (Trento, Italy)





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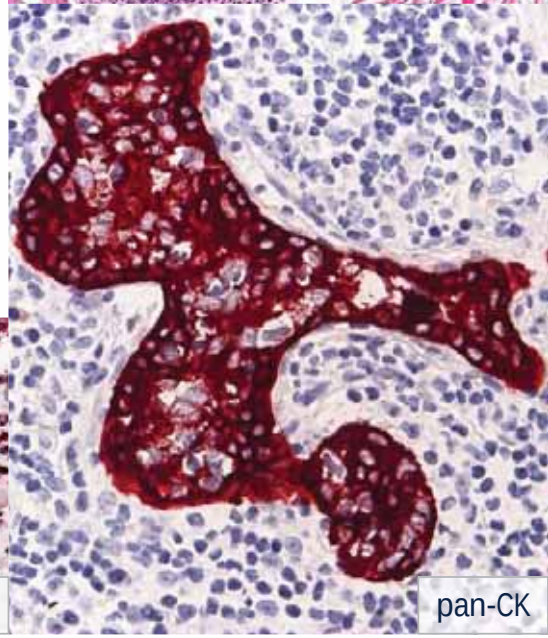
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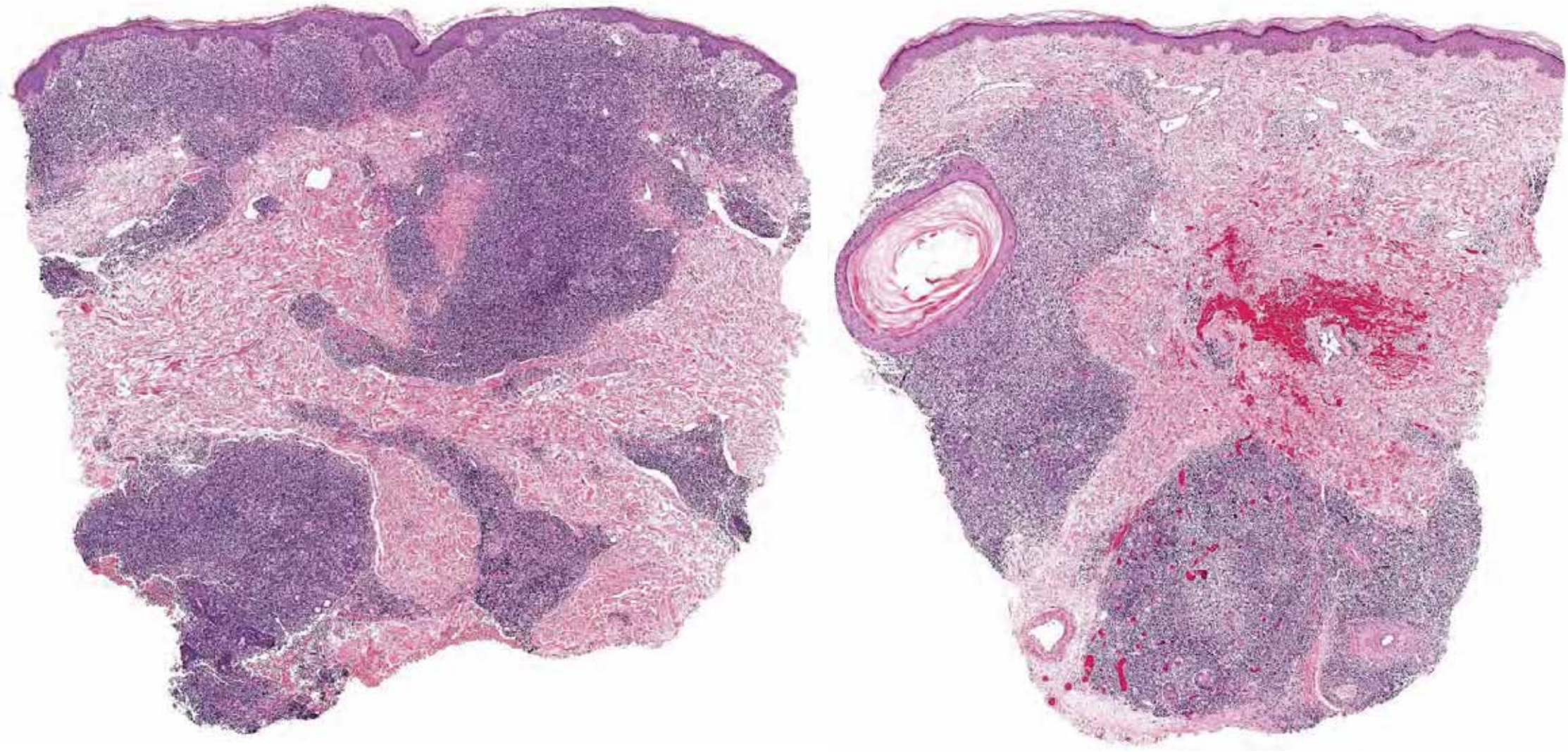
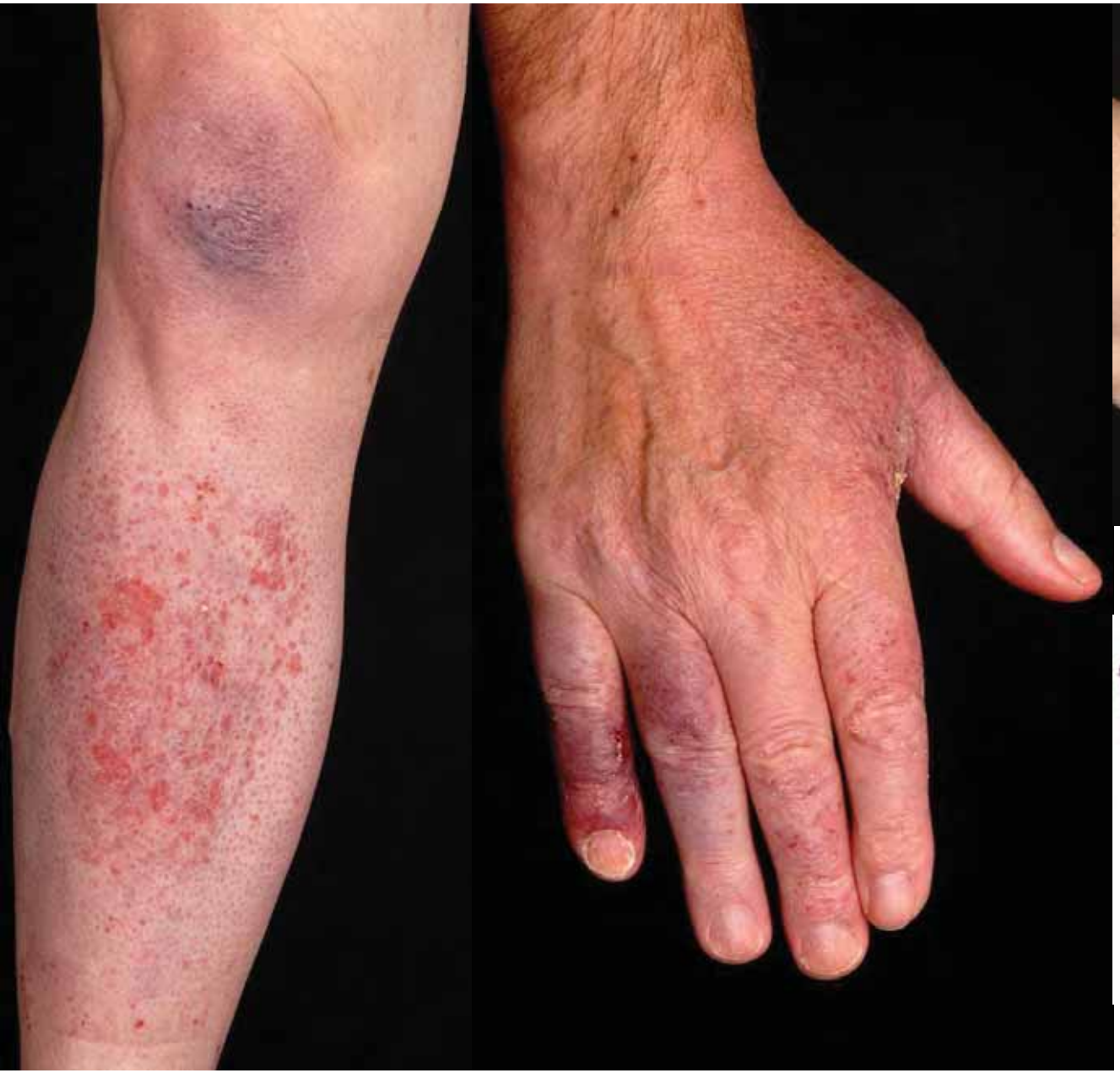
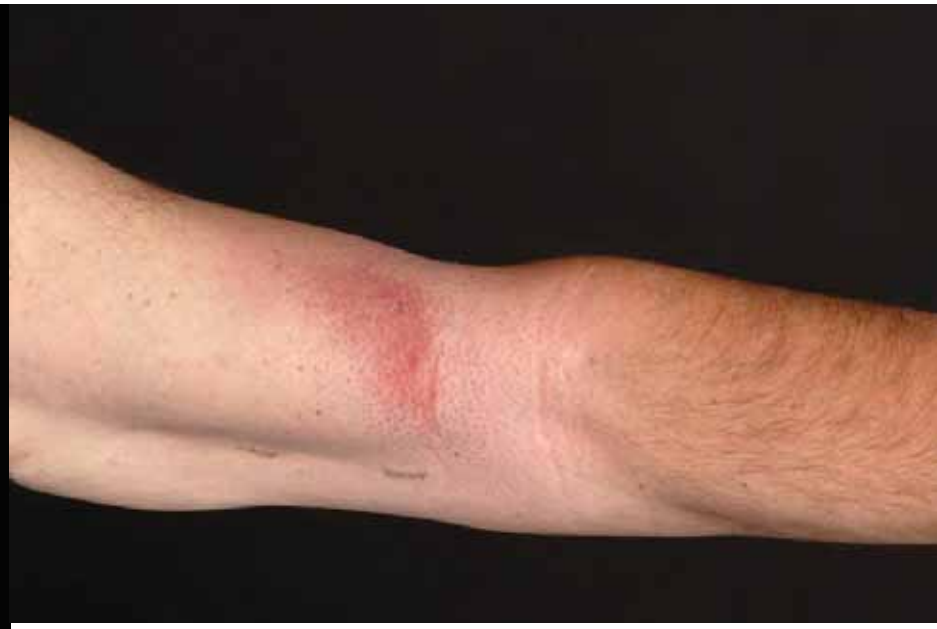
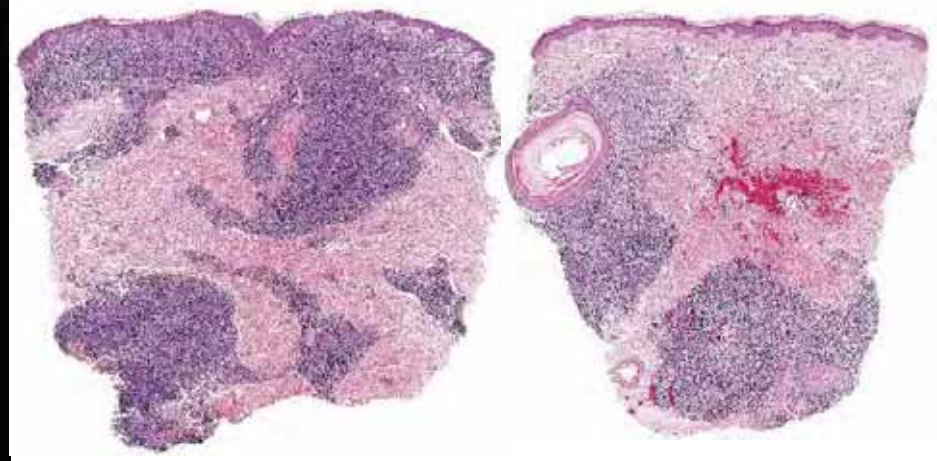


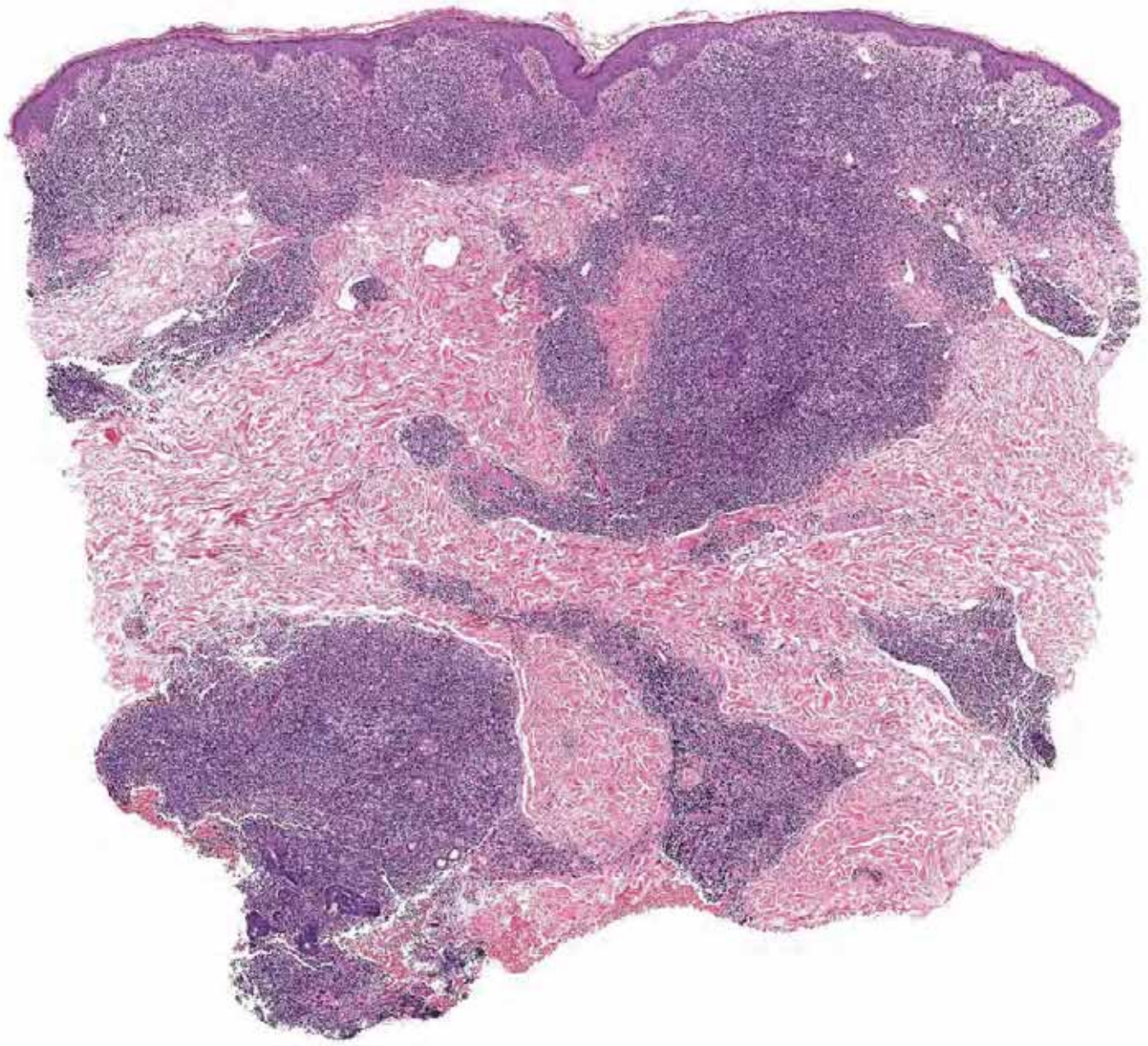
M, 64

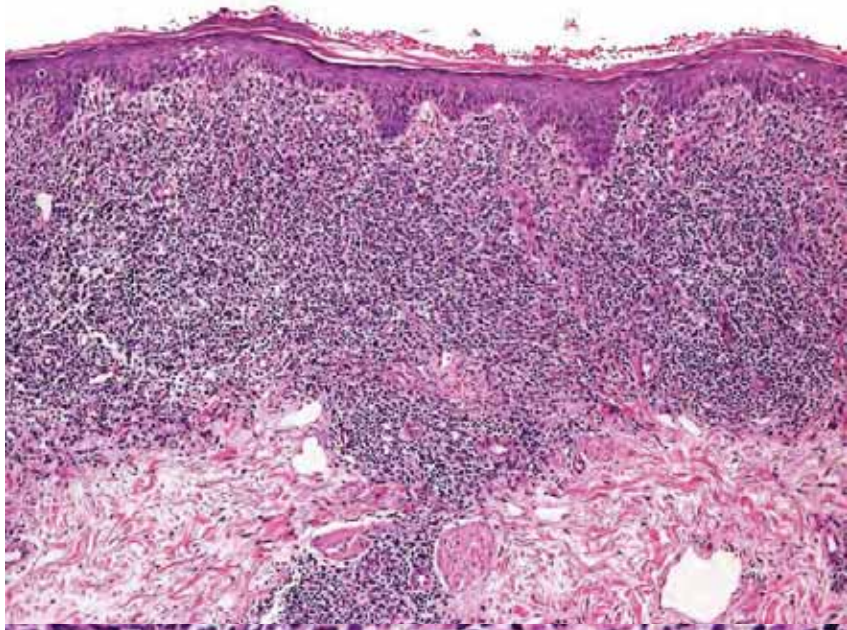
According to the patient skin lesions on the upper and lower extremities present for years.

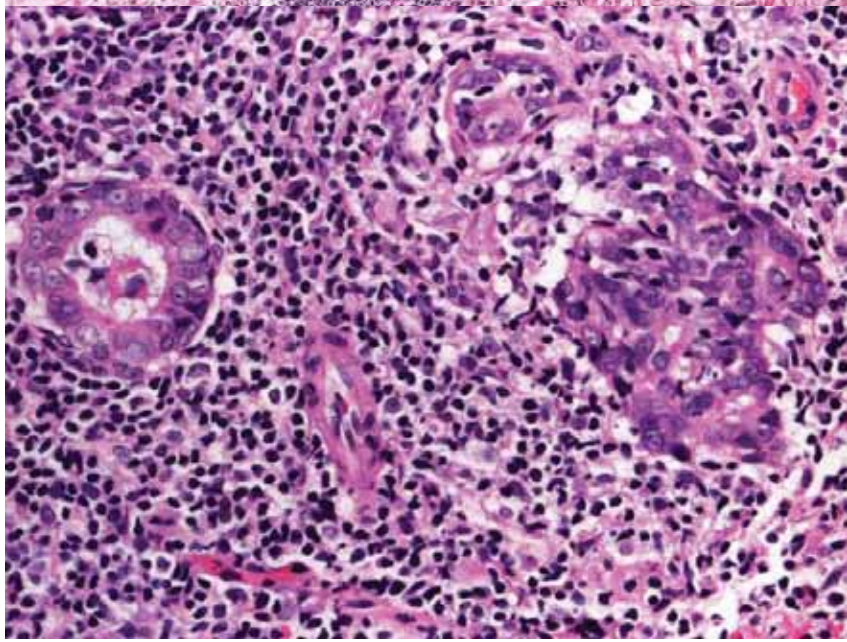


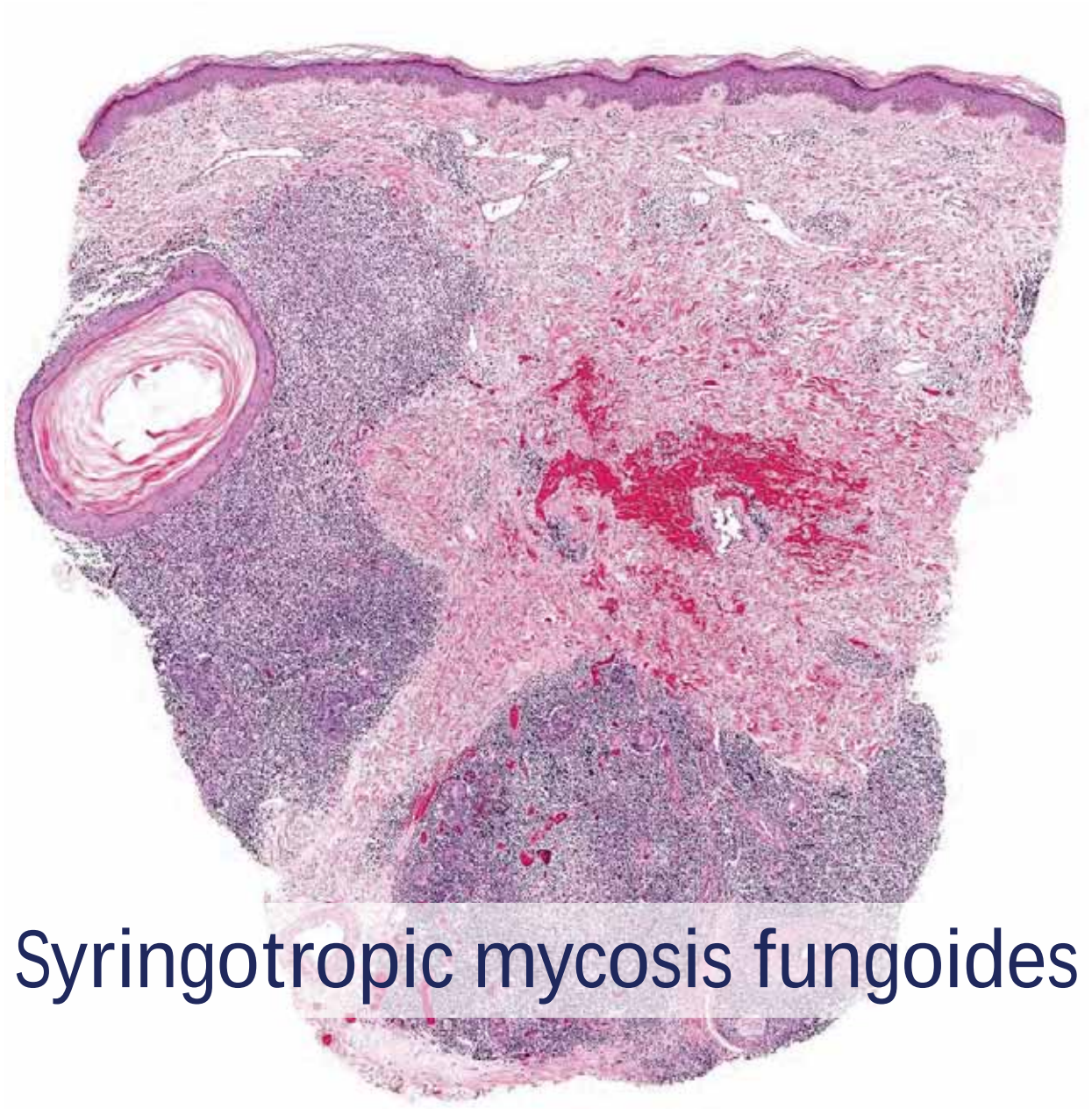




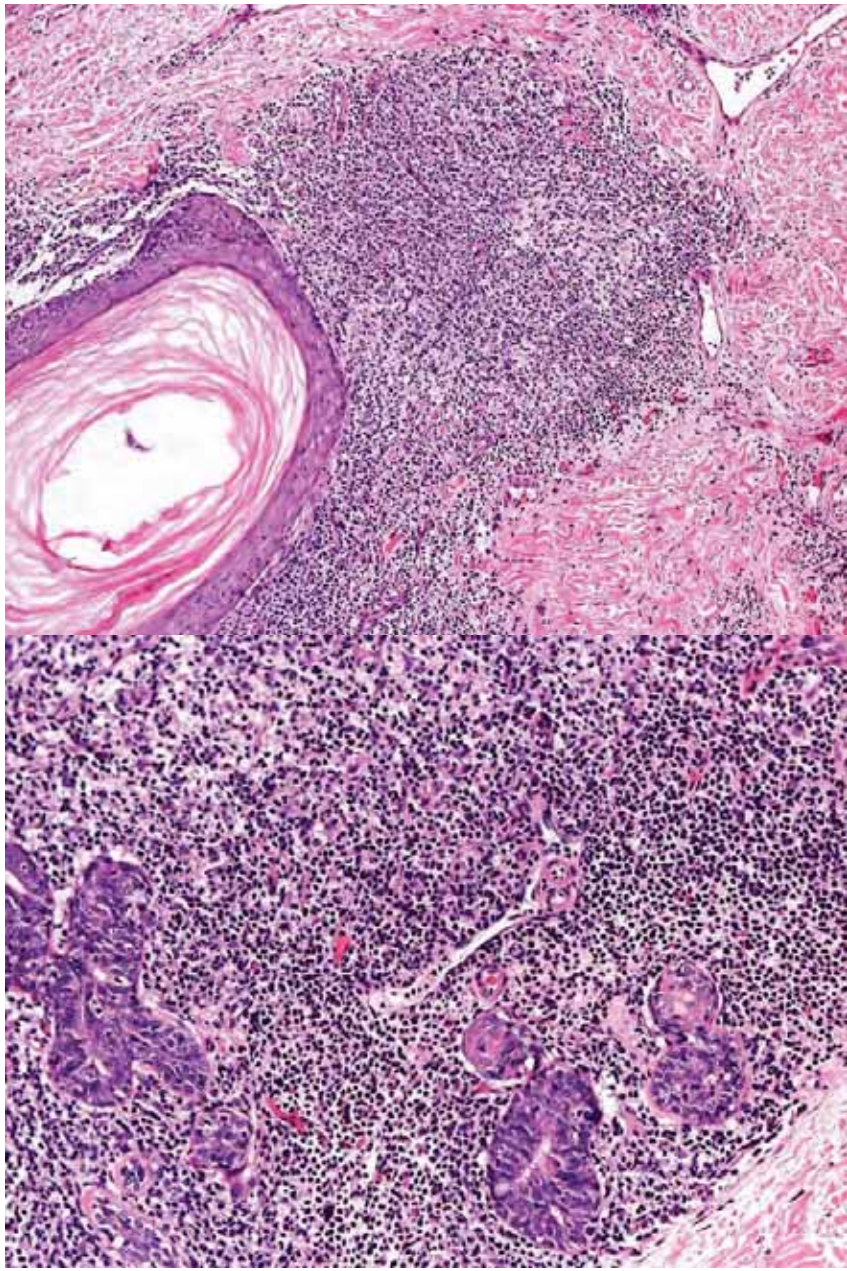


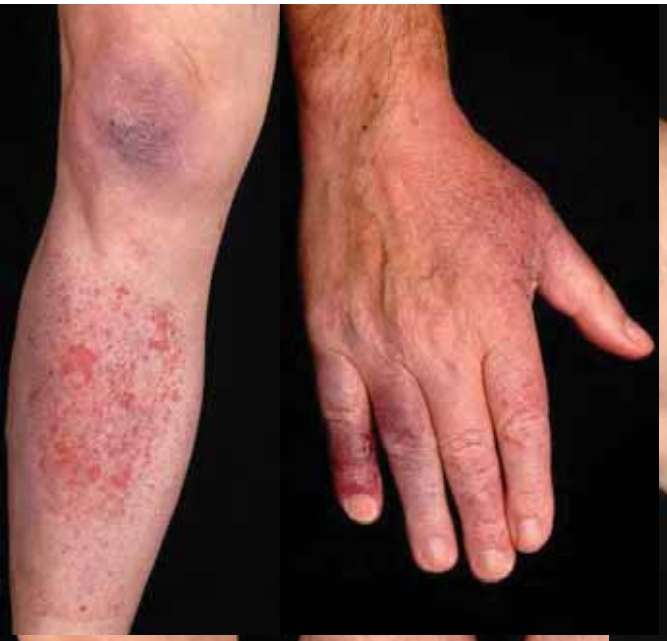


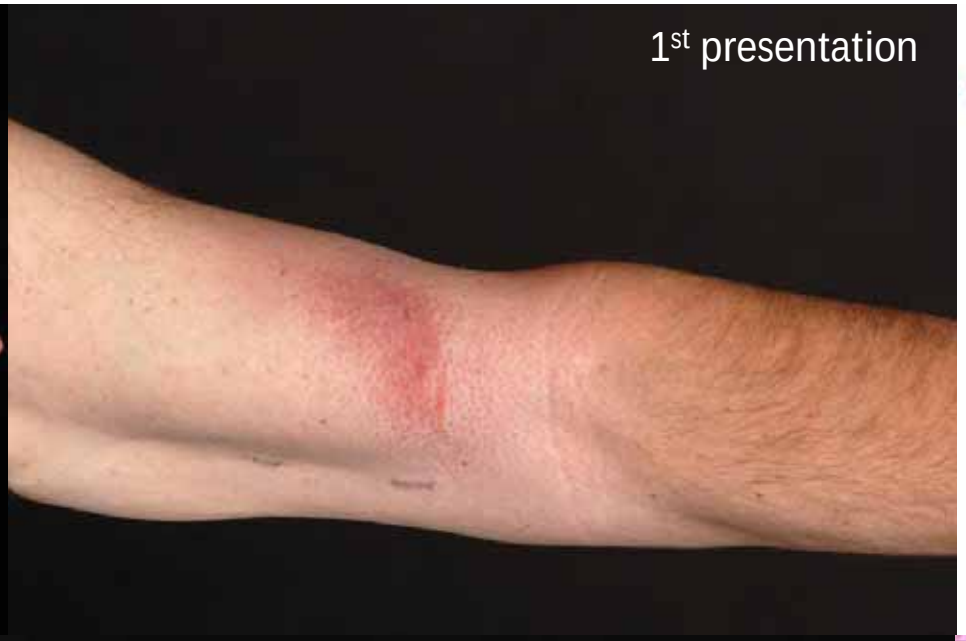




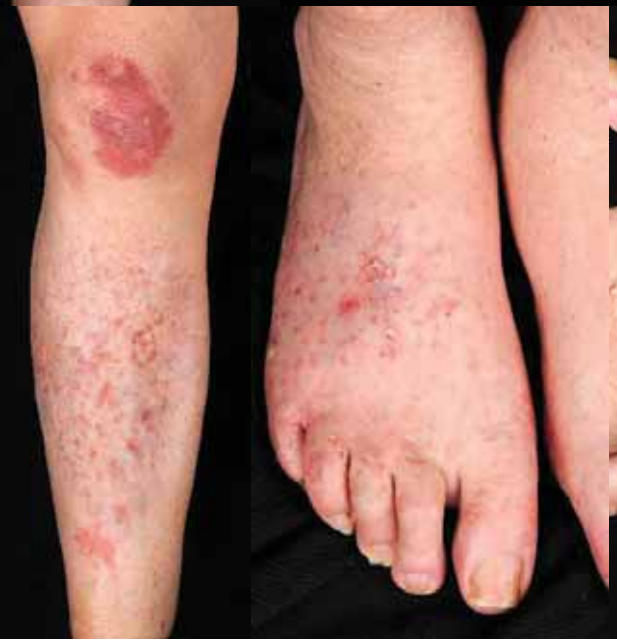
Syringotropic mycosis fungoides

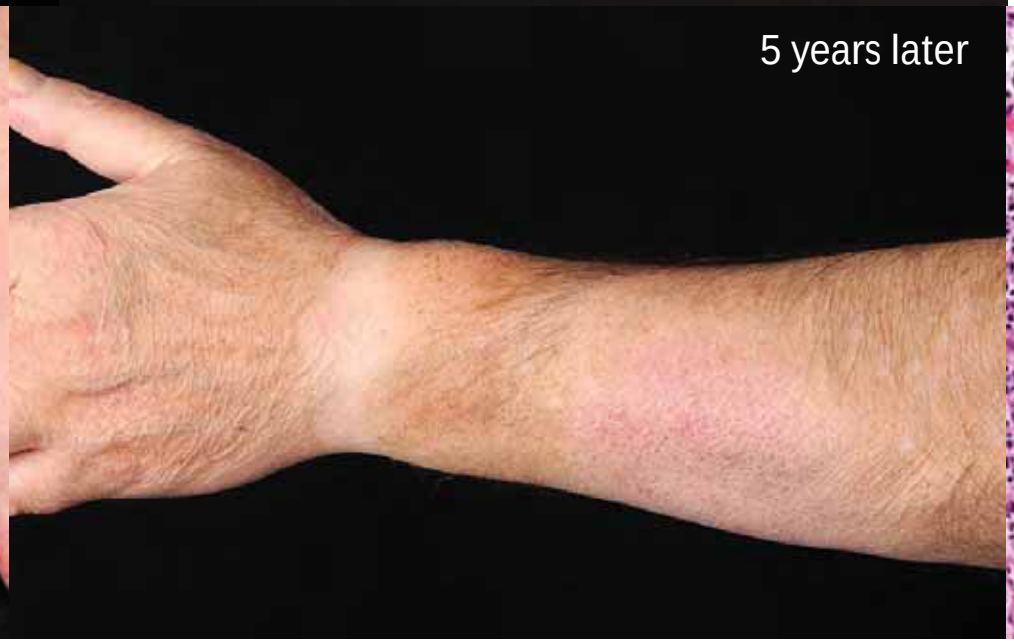


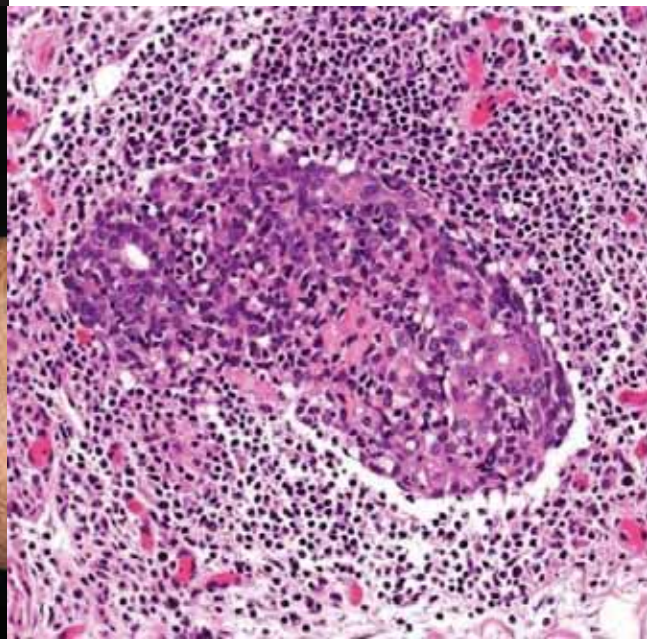


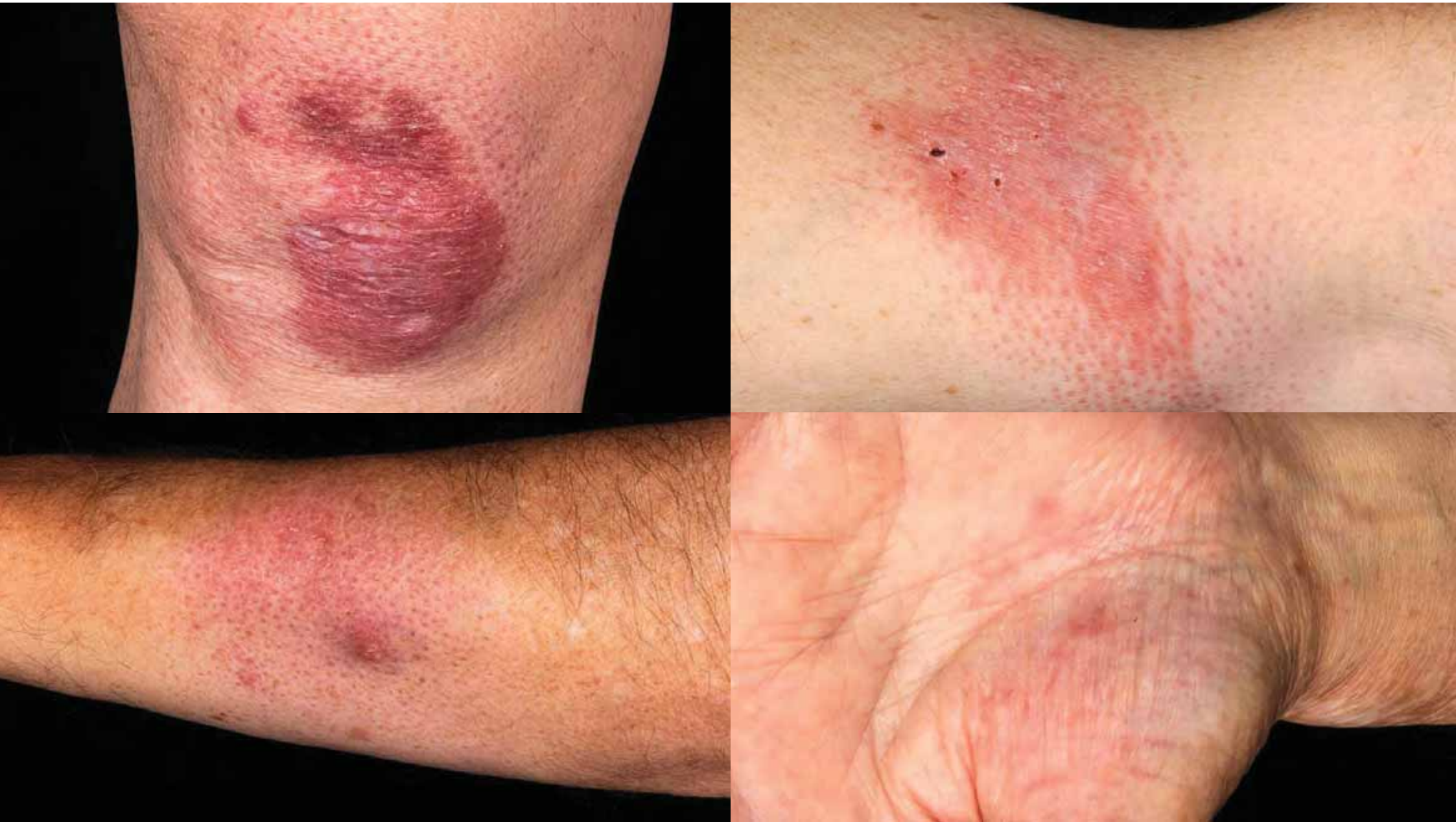

1st presentation

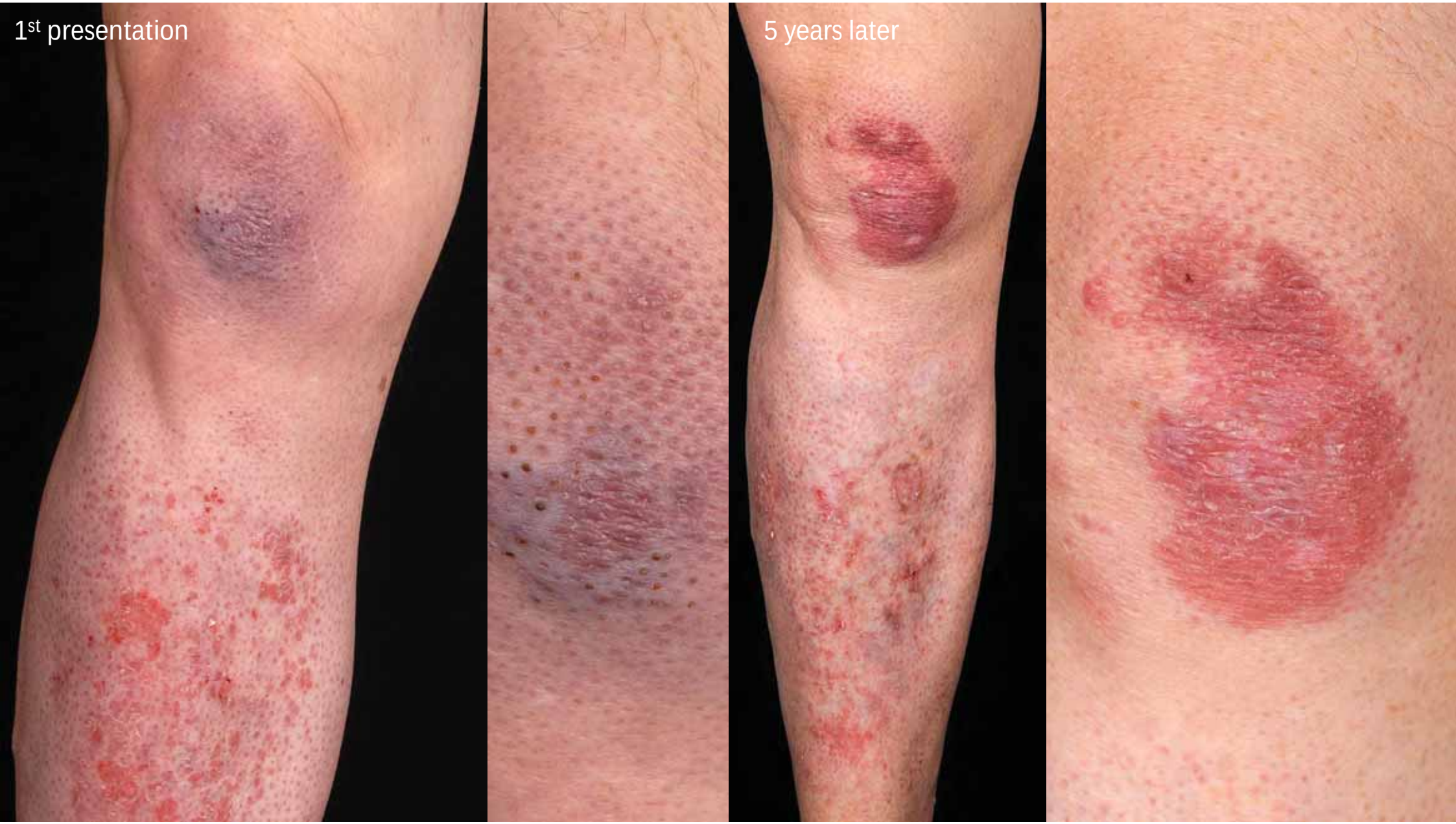

New biopsy




5 years later

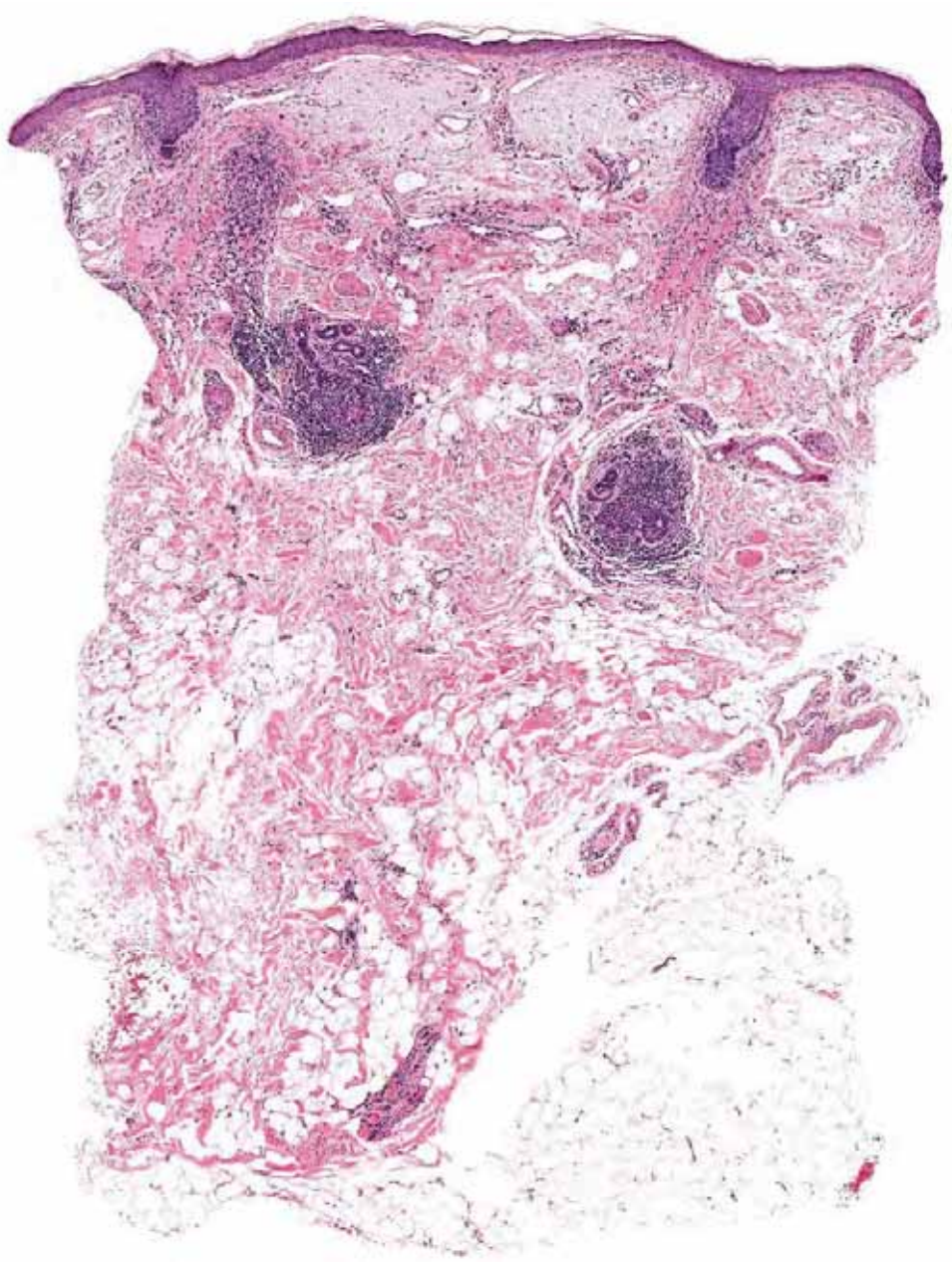


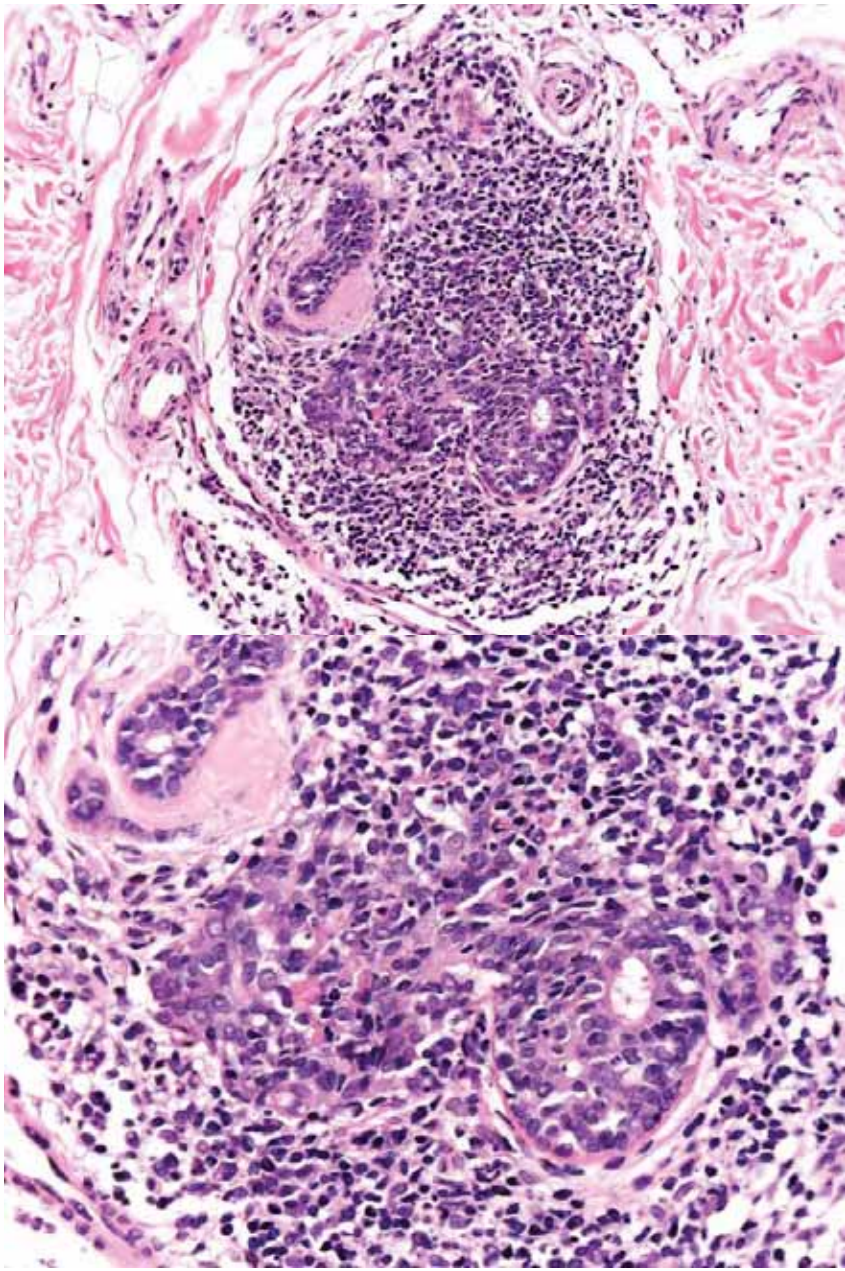


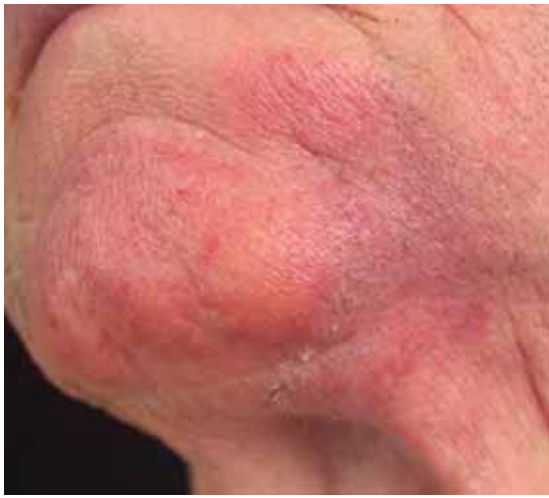

1st presentation
5 years later

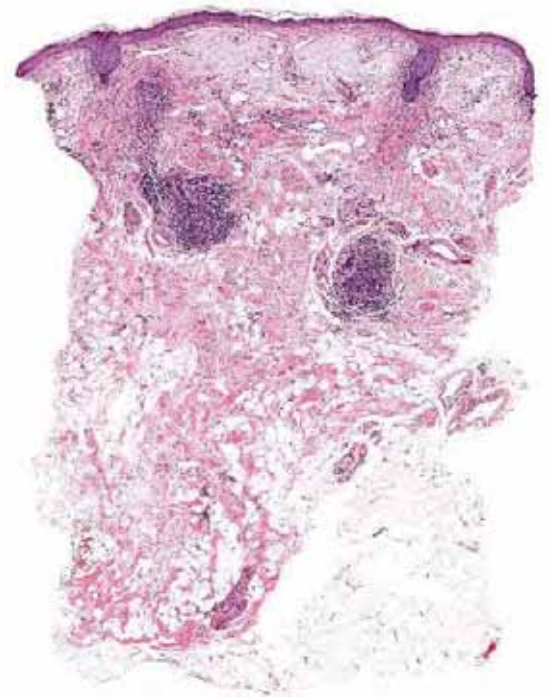
M, 83

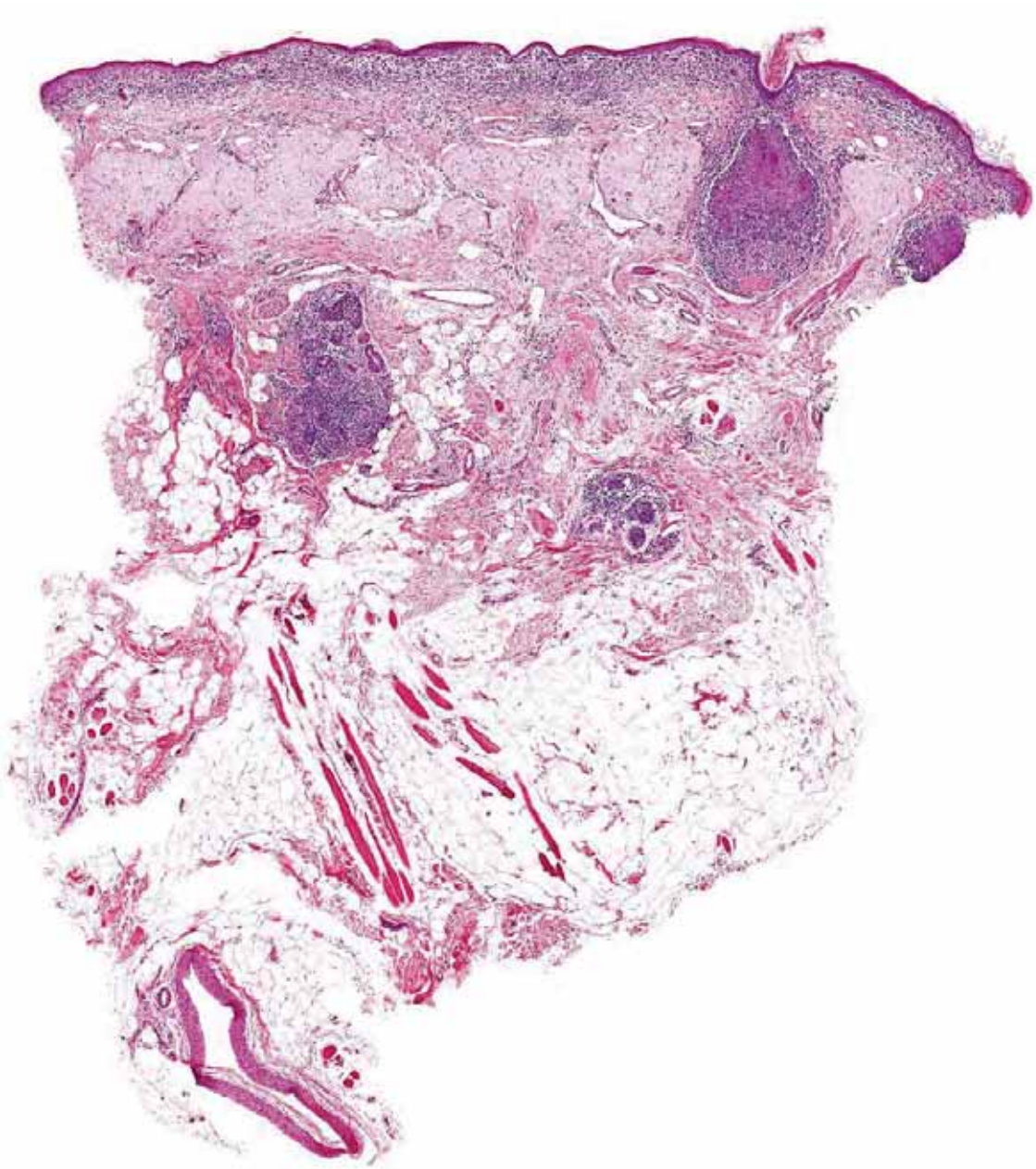
According to the patient "swelling" of the face for a few days. No improvement after 1 week of oral antibiotics.









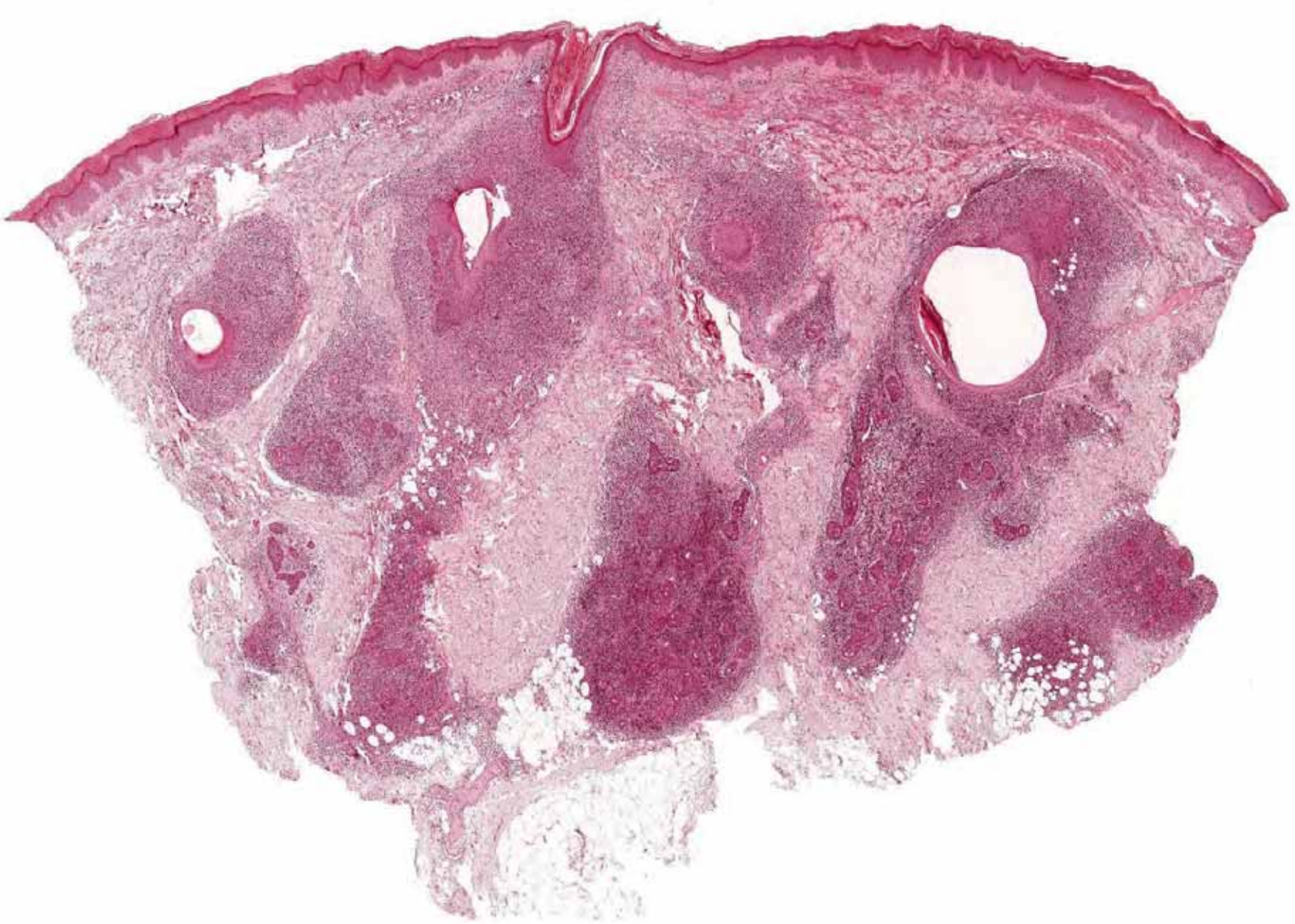


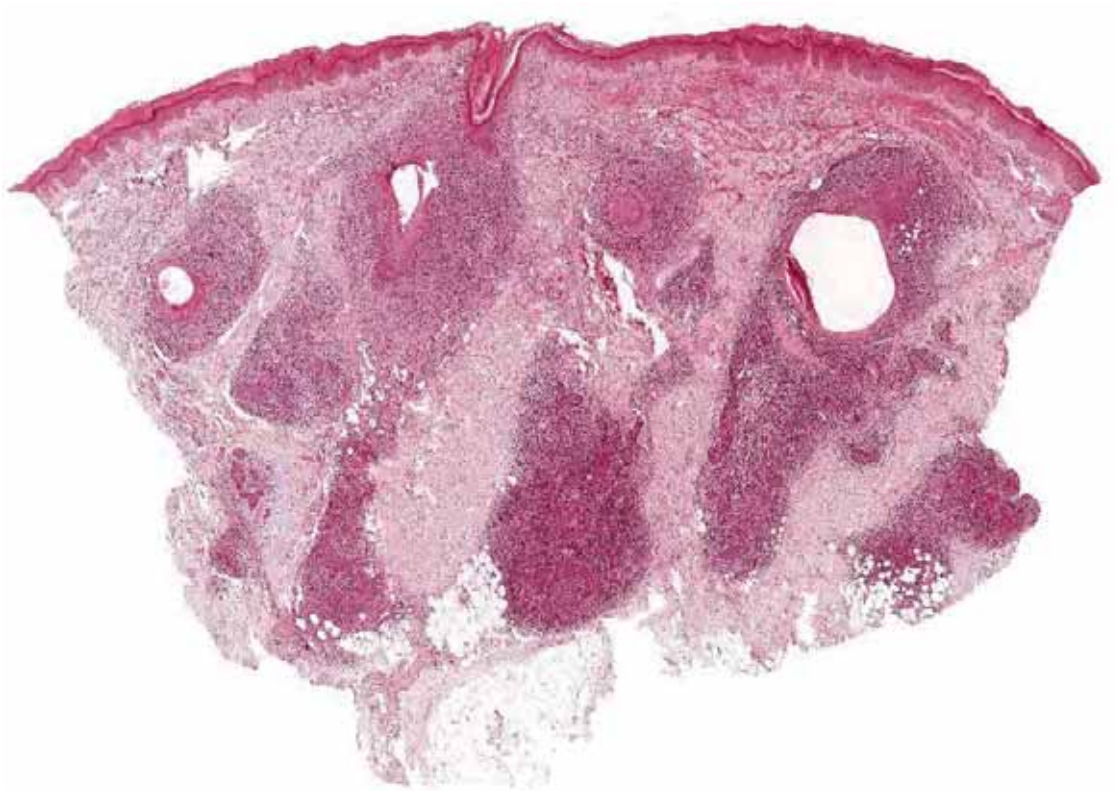
2 years later (85)

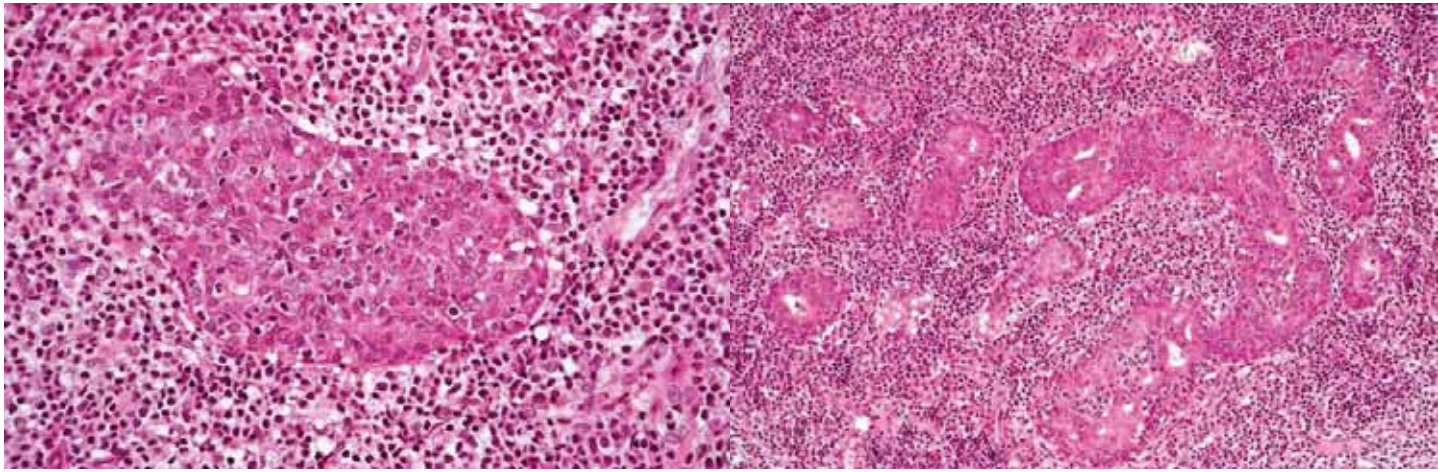
M, 58

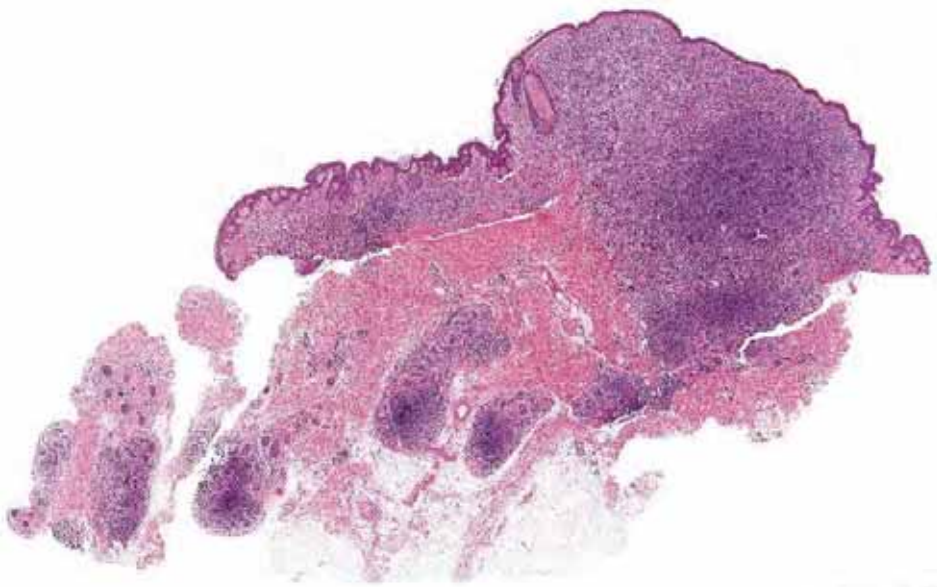
According to the patient "eczematous dermatitis" for approximately 5 years.

Consultation Dr. Fabio Facchetti (Brescia, Italy)

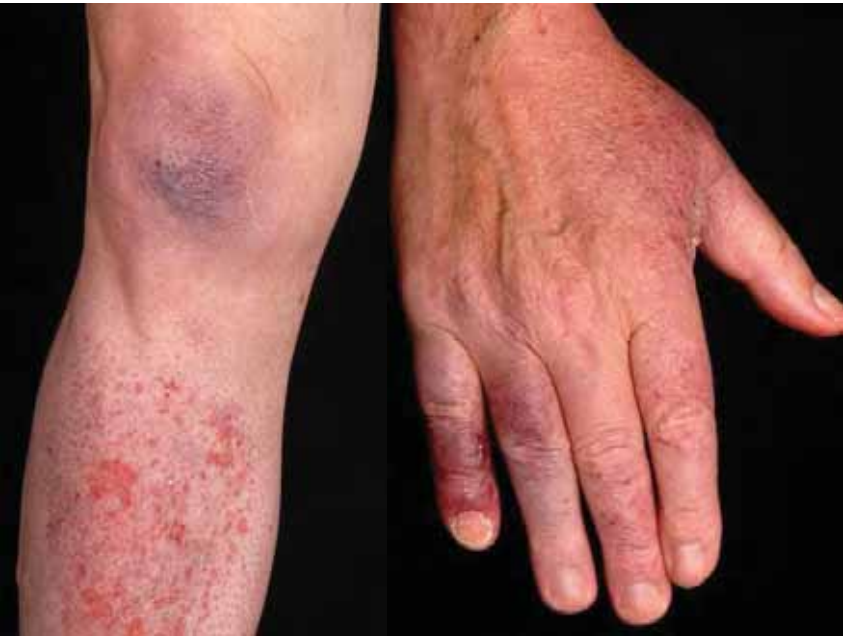


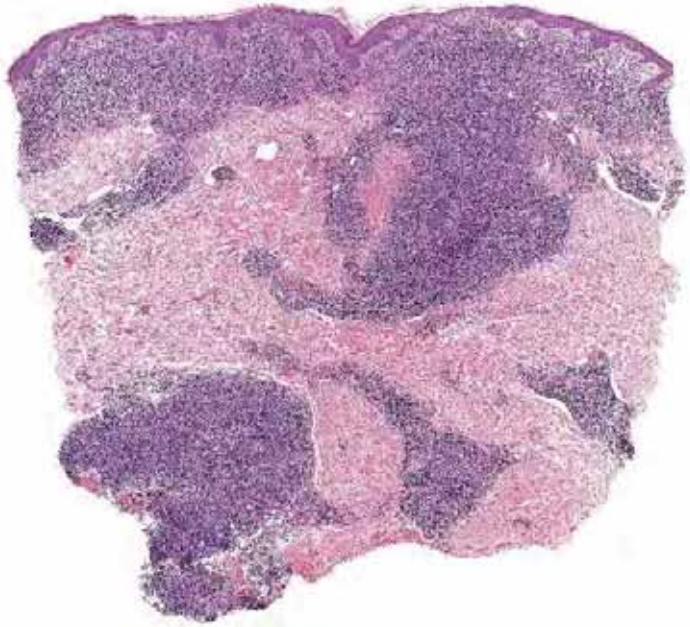


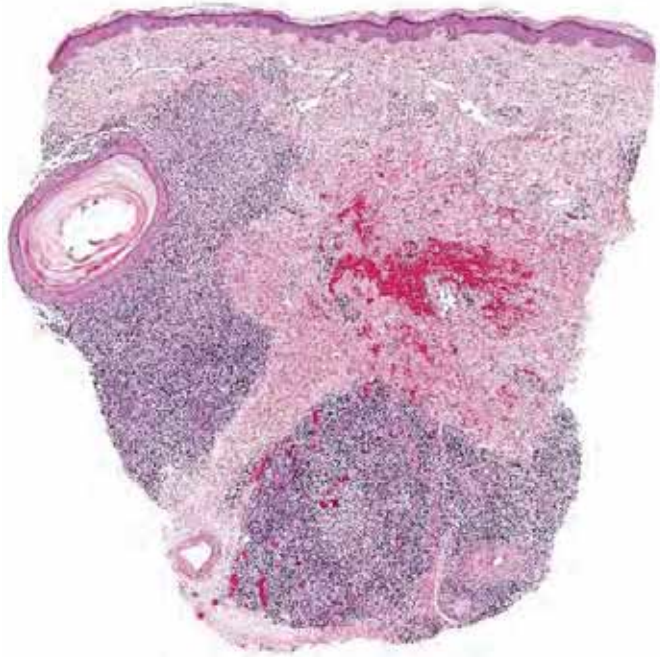




Syringotropic MF is a variant of MF with peculiar clinical features, and with histopathological features completely different from the band-like, epidermotropic infiltrate seen in "conventional" MF







CASE REPORT

Generalized lichen spinulosus and secondary follicular mucinosis

Justine C. Gallo, MB ChB,[a] Johann de Wet, MB ChB, MMed,[b] Willem Izak Visser, MB ChB, MFamMed, MMed,[a] Henry F. Jordaan, MB ChB, MMed, M Acad (SA),[c] and Johann W. Schneider, MB ChB, MMed (Anat Path)[b]

Key words: lichen spinulosus; lymphoma-associated follicular mucinosis; secondary follicular mucinosis.

INTRODUCTION

Lichen spinulosus (LS) is a follicular keratotic disorder and a variant of keratosis pilaris. LS usually shows a localized distribution, but a rare, generalized variant exists in the setting of chronic diseases such as HIV and Crohn's disease.[1,2]

Follicular mucinosis (FM) can occur in a primary idiopathic form, or as a secondary phenomenon due to inflammatory skin conditions such as eczema or lymphoma-associated follicular mucinosis (LAFM).[3] In this case report, we describe a healthy young adult who presented with generalized LS and associated incidental, secondary FM.

Abbreviations used:

CD: cluster of differentiation
FM: follicular mucinosis
LAFM: lymphoma-associated follicular mucinosis
LS: lichen spinulosus

CASE REPORT

A 21-year-old female was referred with xerosis, generalized spiny skin lesions, and a provisional diagnosis of eczema that did not improve on a medium-strength topical corticosteroid. She did not report other medical ailments, medication, atopy, or allergies, and a personal or family history of similar skin lesions was absent.

Clinical examination revealed multiple minute digitate hyperkeratosis which were folliculocentric. The distribution symmetrically involved the face, neck, trunk, and upper limbs (Fig. 1, *A* and *B*). Perilesional erythema, palmoplantar keratoderma, or signs of a nutritional deficiency were absent.

Histopathological assessment of hematoxylin and eosin stained sections from a 3-mm punch biopsy obtained from her back showed keratin plugs within hair follicle infundibula, sparse perifollicular lymphocytes, and cystic spaces in the outer root sheath of hair follicles and sebaceous glands (Fig 2). An Alcian blue–periodic acid–Schiff stain confirmed mucin within the spaces (Fig. 3). Immunohistochemistry revealed cluster of differentiation (CD)3- and predominantly CD4-positive small T lymphocytes. CD8 positive T lymphocytes comprised a minority of the cells, while CD20 positive small B lymphocytes and CD30 positive cells were inconspicuous. T-cell receptor gene rearrangement testing failed for technical reasons and was not repeated.

The preferred diagnosis of LS and secondary FM was made using a diagnostic algorithm (Fig 4) from the article titled "Multiple minute digitate hyperkeratosis (MMDH): A proposed algorithm for the digitate keratoses".[4] Vitamin A levels were normal.

She was started on isotretinoin 0.5 mg/kg and topical emollients. After 3 weeks of isotretinoin

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Funding sources: None.

IRB approval status: Stellenbosch University Human Research Ethics Committee (HREC) approval. HREC reference no: C22/03/006.

Patient consent: Written consent was obtained from the participant and consent forms are on file. Consent was obtained for the publication of medical information and patient photographs in print and online by the authors. The patient was aware that the information may be made publicly available.

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https://doi.org/10.1016/j.jdcr.2023.01.017

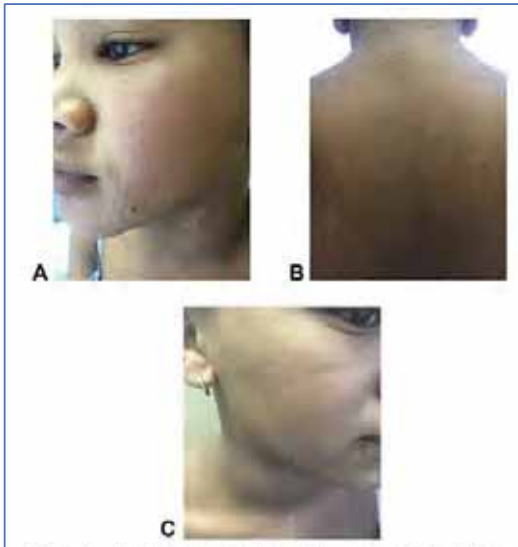


Fig 1. A, Multiple minute digitate hyperkeratosis, folliculocentric, of the left cheek and nose. Note: Dennie-Morgan lines and postinflammatory hypopigmentation on the neck. **B,** Multiple minute digitate hyperkeratosis, folliculocentric, symmetrically distributed, on the back. **C,** Drastically reduced lesions on the right cheek following treatment with a systemic retinoid.

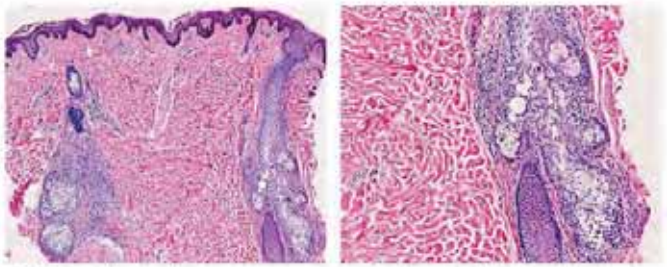


Fig 2. Two folliculo-sebaceous structures are depicted, surrounded by lymphocytes. Lymphocytes are also present within the follicular epithelium. Note tiny spaces within the epithelium. (Hematoxylin and eosin stain ×40 and ×100)

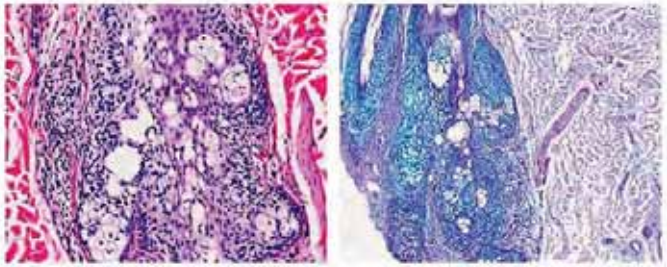
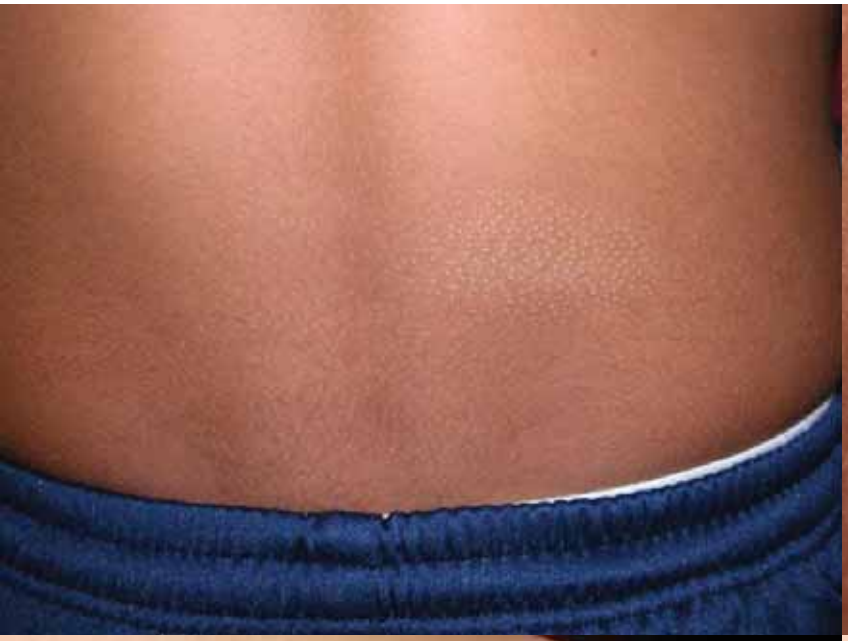
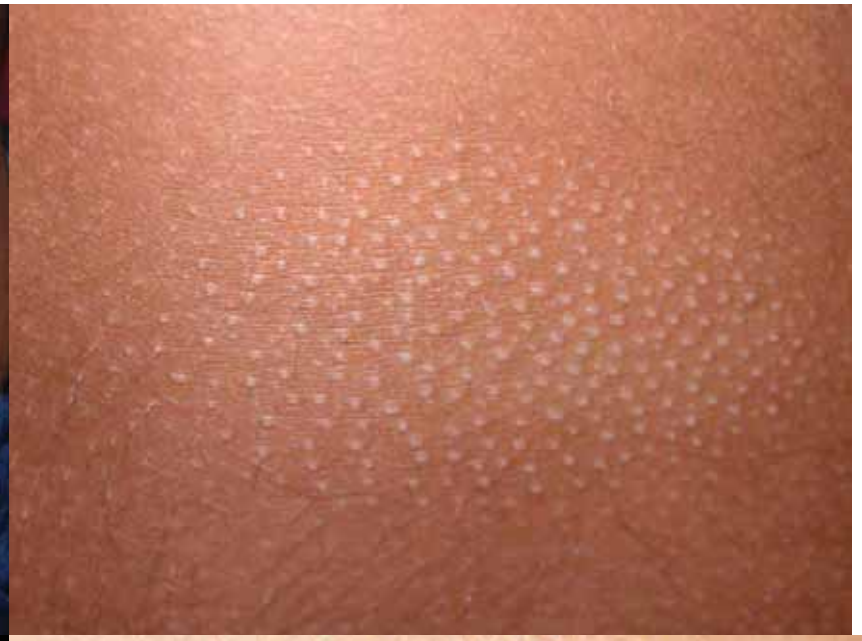


Fig 3. Mucin demonstrated within the spaces and within the follicular keratinocytes. (*Alcian Blue*, ×100). The apparently empty spaces contain wisps of mucin, implying the loss of mucin during processing of the specimen.



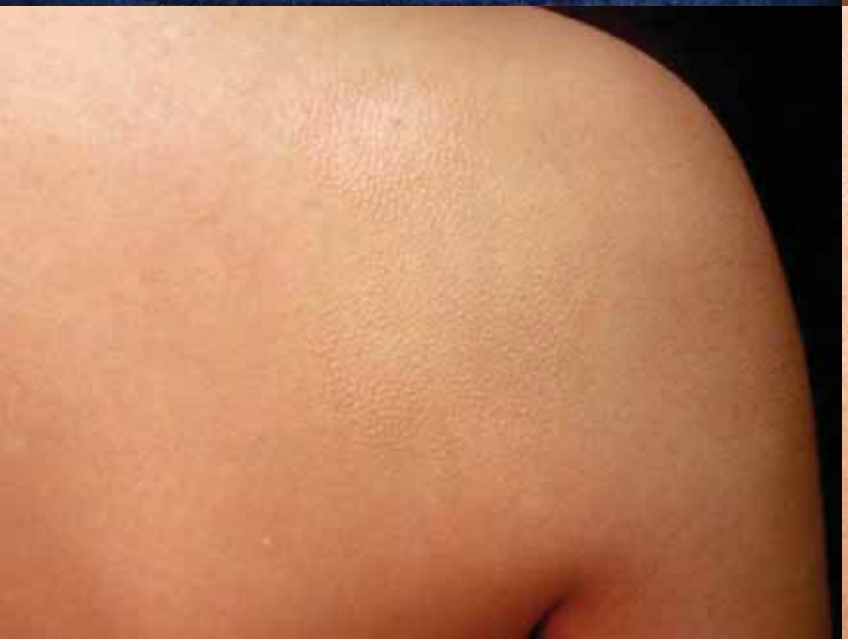


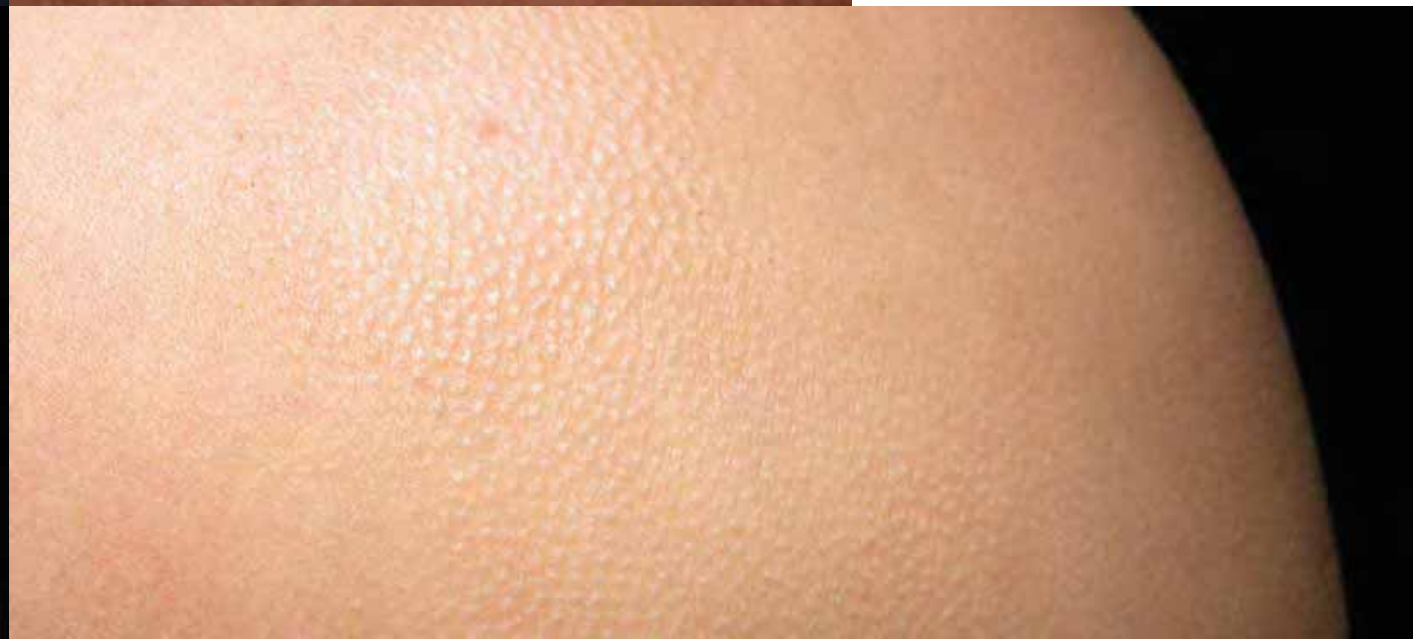
M, 10

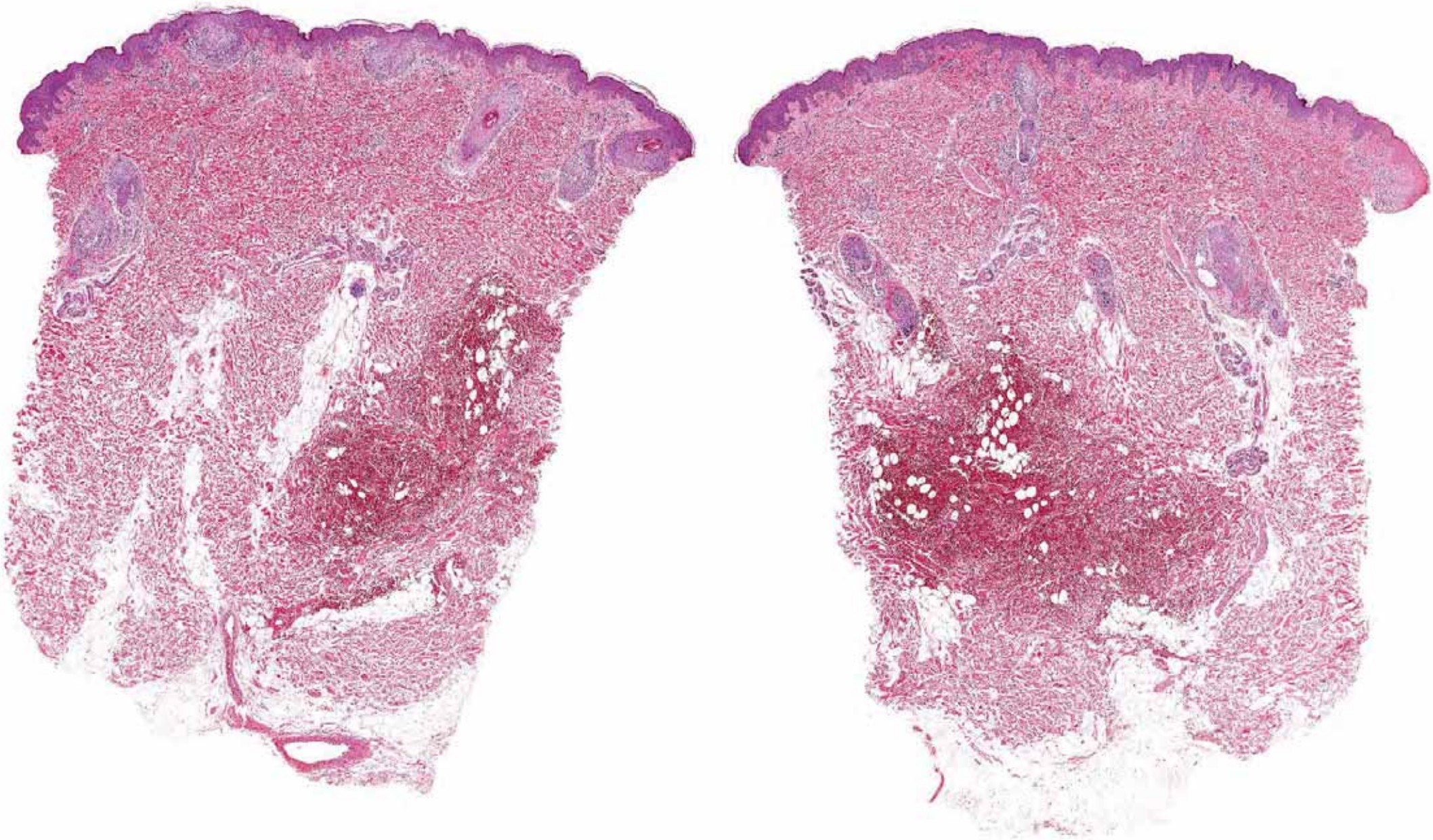
Two plaques of "lichen spinulosus" on the right lumbal region and right shoulder.

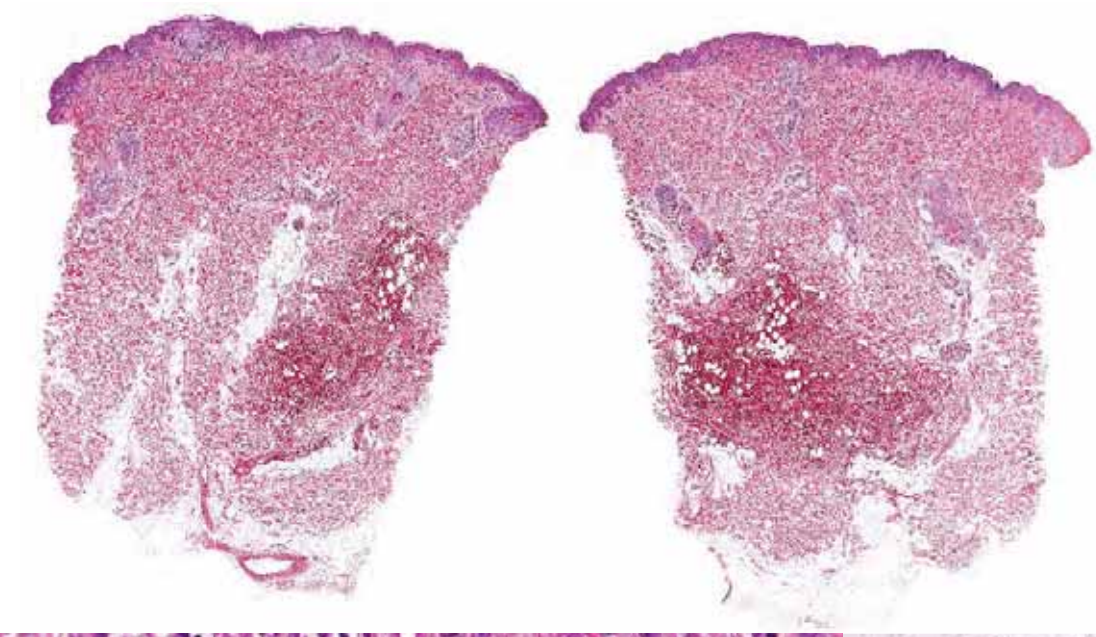
Two biopsies are taken.

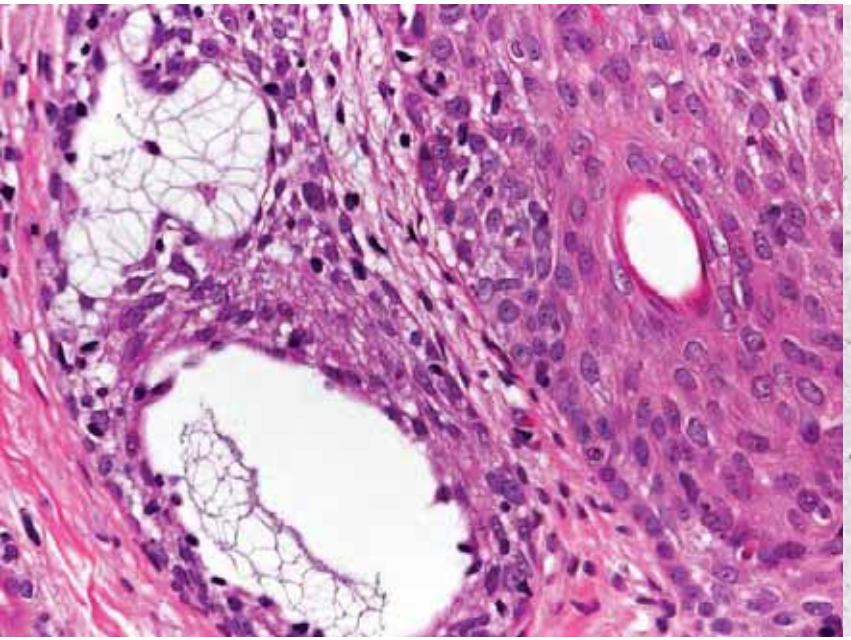
(Courtesy of L. Requena, Madrid)

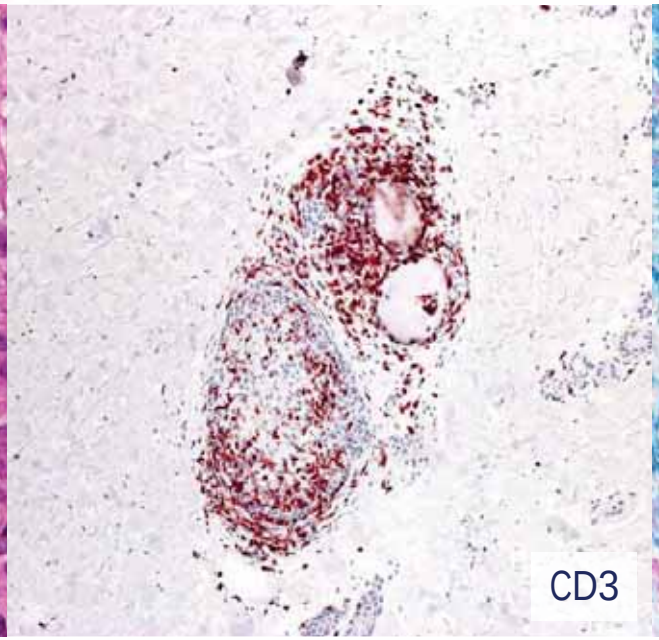








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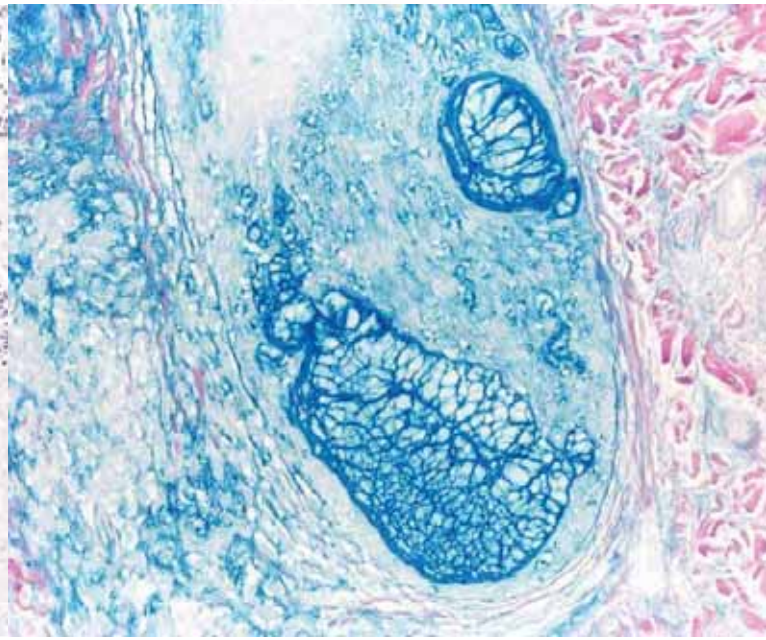
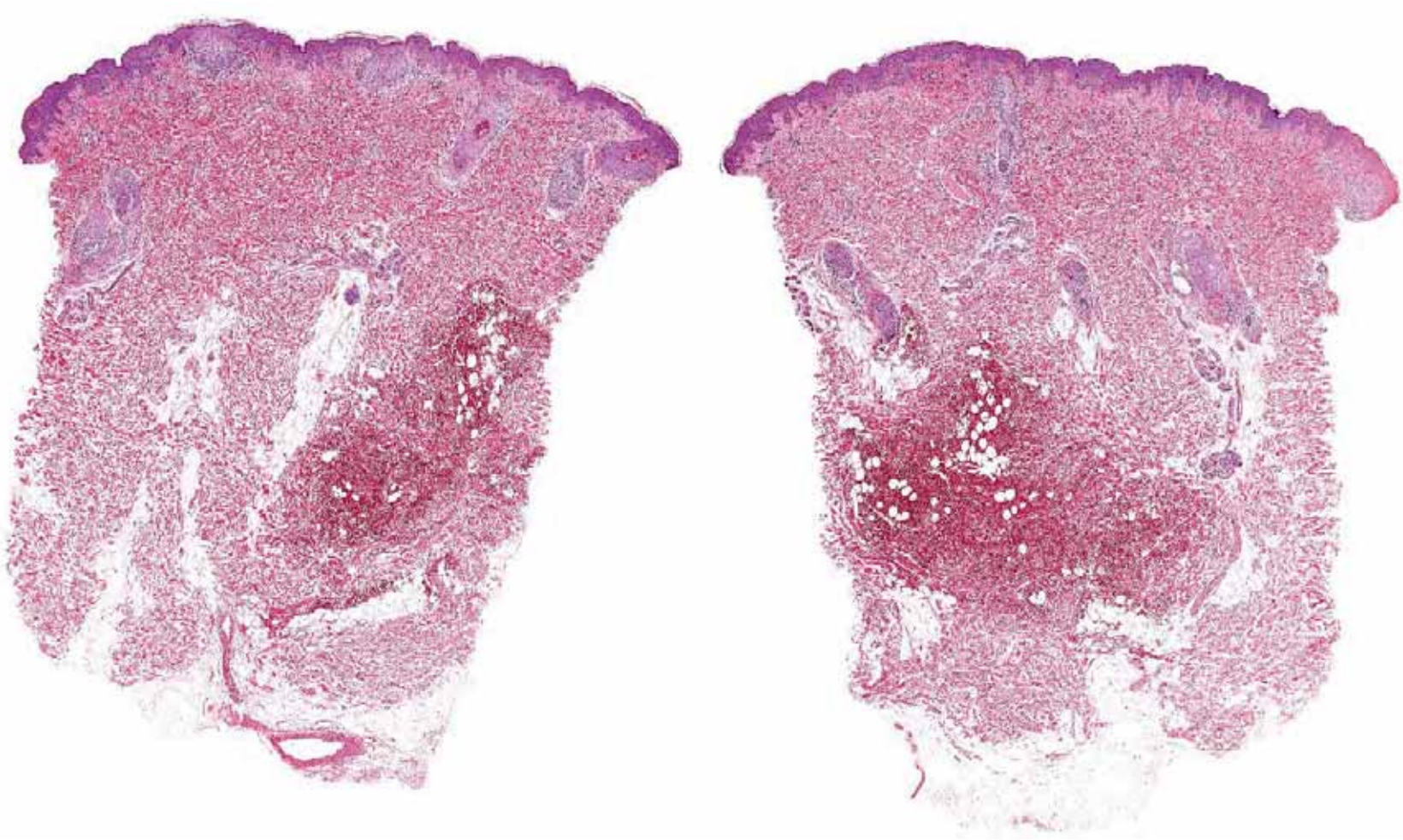
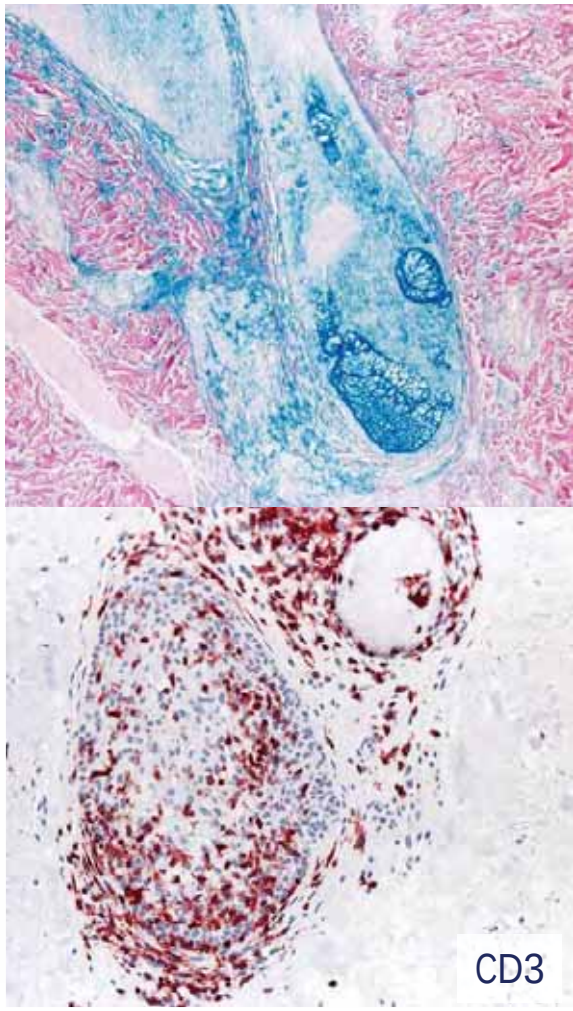
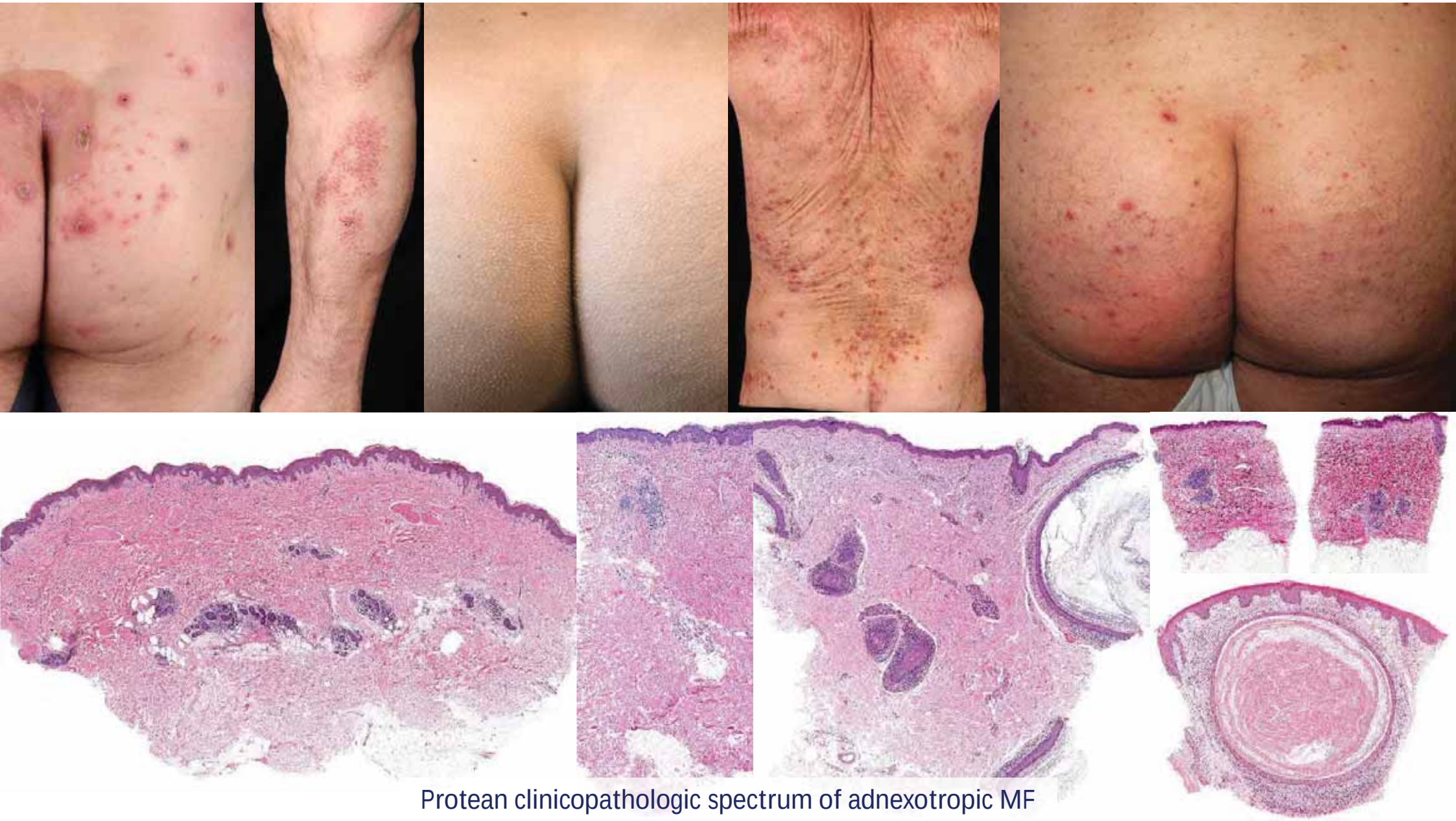






Criteria arguing against lichen spinulosus

Prominent follicular mucinosis in two distinct biopsies; Absence of follicular hyperkeratosis and dilated follicular opening; Presence of many pilotropic lymphocytes



Protean clinicopathologic spectrum of adnexotropic MF

Adnexotropic mycosis fungoides

- A variant observed in all ages including children; pilotropic & syringotropic patterns may be present in the same lesion
- Clinical as well as histopathological features oft different from "conventional" MF, and a source of diagnostic pitfall
- Solitary lesions on the face considered "benign"; however, classification of "benign alopecia mucinosa" yet unclear (and debated)
- Morphological, phenotypic and molecular features don't allow to separate MF-associated cases from "benign" ones
- Destruction of adnexal structures may result in granulomatous infiltrates, fibrosis, edema; sometimes the adnexotropic pattern may be inferred only from the architecture of the infiltrate *(adnexal structures wiped off by neoplastic cells)*
- In "benign" cases (children and adolescents; lesions restricted to the head & neck): conservative approach; avoid aggressive treatment