Tedaviyi İzleyen Değişiklikler ve Değerlendirme Zorlukları

Prof. Dr. Duygu Düşmez Apa

Mersin Üniversitesi Tıp Fakültesi

Patoloji AD

Sunum planı

Giriş: Mikozis fungoides tanısındaki yöntem ve zorluklar

Sunum planı

- Giriş: Mikozis fungoides tanısındaki yöntem ve zorluklar
- **Tanıdan sonra neler oluyor?**

Sunum planı

- Giriş: Mikozis fungoides tanısındaki yöntem ve zorluklar
- Tanıdan sonra neler oluyor?
- **Mycosis Fungoides güncel tedavi seçenekleri nelerdir?**

Sunum planı

- Giriş: Mikozis fungoides tanısındaki yöntem ve zorluklar
- Tanıdan sonra neler oluyor?
- Mycosis Fungoides güncel tedavi seçenekleri nelerdir?
- **Tedavi nasıl etkili oluyor?**

Sunum planı

- Giriş: Mikozis fungoides tanısındaki yöntem ve zorluklar
- Tanıdan sonra neler oluyor?
- Mycosis Fungoides güncel tedavi seçenekleri nelerdir?
- Tedavi nasıl etkili oluyor?
- **Takip nasıl yapılıyor?**

Sunum planı

- Giriş: Mikozis fungoides tanısındaki yöntem ve zorluklar
- Tanıdan sonra neler oluyor?
- Mycosis Fungoides güncel tedavi seçenekleri nelerdir?
- Tedavi nasıl etkili oluyor?
- Takip nasıl yapılıyor?
- **Patolojinin yeri nedir?**

Sunum planı

- Giriş: Mikozis fungoides tanısındaki yöntem ve zorluklar
- Tanıdan sonra neler oluyor?
- Mycosis Fungoides güncel tedavi seçenekleri nelerdir?
- Tedavi nasıl etkili oluyor?
- Takip nasıl yapılıyor?
- Patolojinin yeri nedir?
- **Tanı ve takipte ileri yöntemler nelerdir?**

Sunum planı

- **Giriş: Mikozis fungoides tanısındaki yöntem ve zorluklar**
  - Tanıdan sonra neler oluyor?
  - Mycosis Fungoides güncel tedavi seçenekleri nelerdir?
  - Tedavi nasıl etkili oluyor?
  - Takip nasıl yapılıyor?
  - Patolojinin yeri nedir?
  - Tanı ve takipte ileri yöntemler nelerdir?

Erken MF Tanısı
(Klinik Kriterler)

- Topikal **steroid tedavisine dirençli** ya da tedavi kesildiğinde tekrarlayan **inatçı lezyon** vardır.

Erken MF Tanısı

(Klinik Kriterler)

- Lezyonlar **5 cm den büyük**, eritemli skuamlı atopik dermatit ve psöriazis benzeri **yama ve plak** lezyonlardır. Genellikle birden fazla sayıdadır.

Erken MF Tanısı
(Klinik Kriterler)

- **Poikiloderma** (Noktali pigmentasyon, telenjektazi, epidermal atrofi) MF taklitçisi lezyonlarda bulunmaz.

Erken MF Tanısı
(Klinik Kriterler)

- **Lenfadenopati**
  - Geç dönemde ortaya çıkar.
  - Deri dışı yayılımın ilk işaretidir.
  - Yaygın deri tutulumu bölgelerini drene eden lenf nodları öncelikle genişler.

Erken MF Tanısı
(Klinik Kriterler)

- **Visseral organ tutulumu**
  - akciğer, dalak, karaciğer gastrointestinal sistem

Erken MF Tanısı
(Klinik Kriterler)

- Öncül lezyonlar
  - **MF direk tümör evresi ile başlamaz**, öncül lezyonlar vardır. Tümör evresinde genellikle yama, plak, nodül ve ülser bir arada görülür.

MF Patolojik Tanı

- Mikozis fungoides histolojik olarak küçük -orta büyüklükte serebriform nükleuslu lenfositlerin üst dermis ve epidermise infiltrasyonu (**epidermotropizm**) ve intraepidermal yuvalanmalar (**Pautrier mikroapseleri**) ile karakterizedir.

AJH Educational Material

ANNUAL CLINICAL UPDATES IN HEMATOLOGICAL MALIGNANCIES:
A CONTINUING MEDICAL EDUCATION SERIES

Cutaneous T-cell lymphoma: 2011 update on diagnosis, risk-stratification, and management

Ryan A. Wilcox*

Table 3. Algorithm for the diagnosis of early MF[15]

Criteria	Major (2 points)	Minor (1 point)
Clinical		
Persistent and/or progressive patches and plaques plus	Any 2	Any 1
(1) Non–sun-exposed location		
(2) Size/shape variation		
(3) Poikiloderma		
Histopathologic		
Superficial lymphoid infiltrate plus	Both	Either
(1) Epidermotropism without spongiosis		
(2) Lymphoid atypia*		
Molecular/biologic: clonal TCR gene rearrangement	NA†	Present
Immunopathologic		
(1) CD2,3,5 less than 50% of T cells	NA†	Any 1
(2) CD7 less than 10% of T cells		
(3) Epidermal discordance from expression of CD2,3,5 or CD7 on dermal T cells		

— indicates not applicable.

*Lymphoid atypia is defined as cells with enlarged hyperchromatic nuclei and irregular or cerebriform nuclear contours.

†Not applicable since it cannot fulfill any major criteria.

blood 2007 110: 1713-1722
Prepublished online May 31, 2007;
doi:10.1182/blood-2007-03-055749

Revisions to the staging and classification of mycosis fungoides and Sézary syndrome: a proposal of the International Society for Cutaneous Lymphomas (ISCL) and the cutaneous lymphoma task force of the European Organization of Research and Treatment of Cancer (EORTC)

Elise Olsen, Eric Vonderheid, Nicola Pimpinelli, Rein Willemze, Youn Kim, Robert Knobler, Herschel Zackheim, Madeleine Duvic, Teresa Estrach, Stanford Lamberg, Gary Wood, Reinhard Dummer, Annamari Ranki, Gunter Burg, Peter Heald, Mark Pittelkow, Maria-Grazia Bernengo, Wolfram Sterry, Liliane Laroche, Franz Trautinger and Sean Whittaker

Öne Çıkan Histomorfolojik Parametreler

- Pautrier mikroapsesi,
- Etrafında halo içeren lenfositler,
- Ekzostoz,
- Uygunsuz epidermotropizm,
- Dermal lenfositlere oranla daha büyük epidermal lenfositler,
- Serebriform nükleer kontur içeren intraepidermal lenfositler,
- Bazalde sıralanma gösteren lenfositler
- "Orta -büyük lenfositler"in epidermotropizmi

Smoller BR, Bishop K, Glusac E, et al. Reassessment of histologic parameters in the diagnosis of mycosis fungoides. Am J Surg Pathol 1995;19:1423–1430.

AJH Educational Material

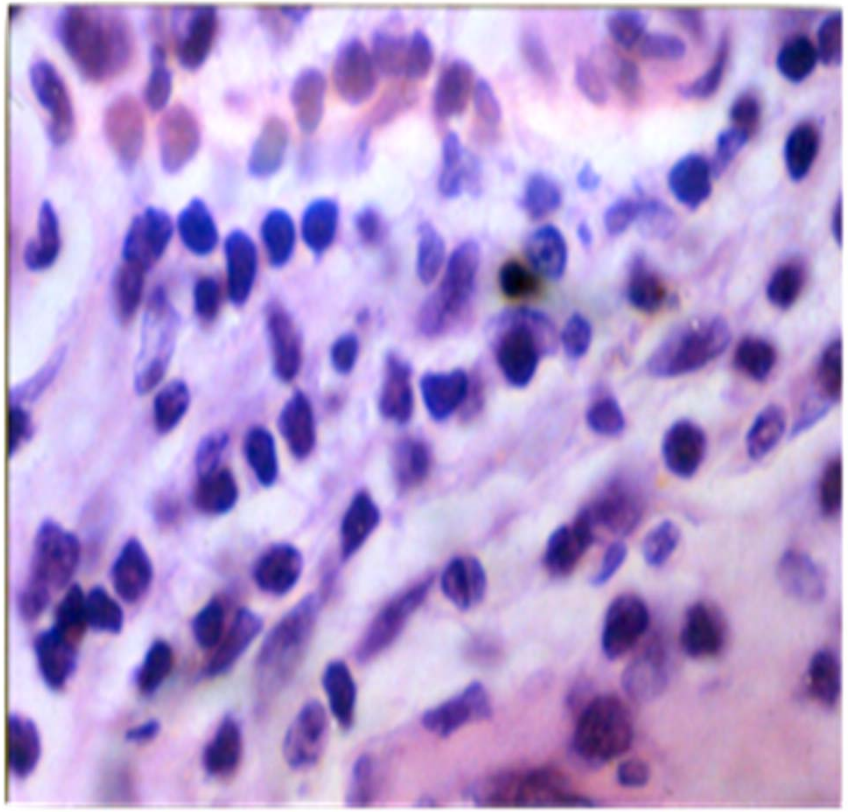
ANNUAL CLINICAL UPDATES IN HEMATOLOGICAL MALIGNANCIES:
A CONTINUING MEDICAL EDUCATION SERIES

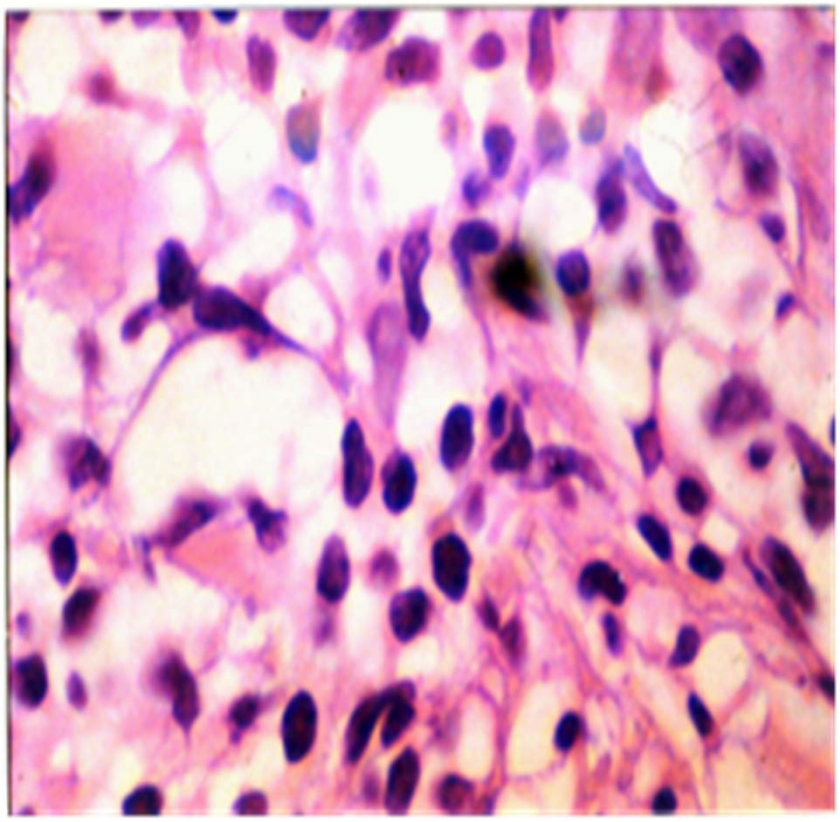
Cutaneous T-cell lymphoma: 2011 update on diagnosis, risk-stratification, and management

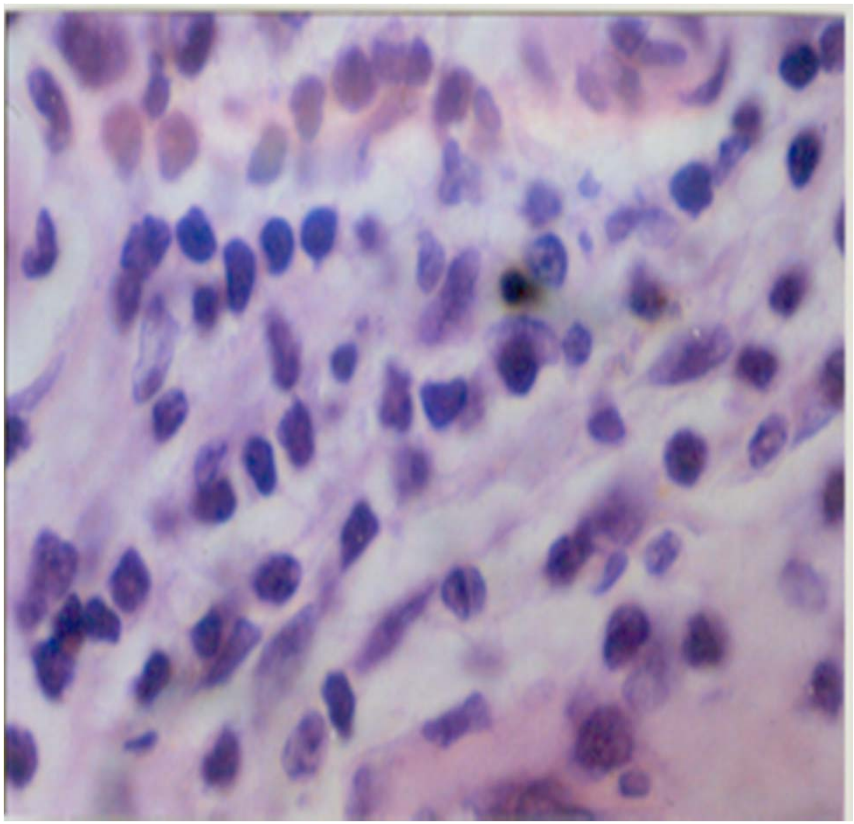
Ryan A. Wilcox*

Santucci M, Biggeri A, Feller AC, et al. Efficacy of histologic criteria for diagnosing early mycosis fungoides: An EORTC cutaneous lymphoma study group investigation. European Organization for Research and Treatment of Cancer. Am J Surg Pathol 2000;24:40–50.

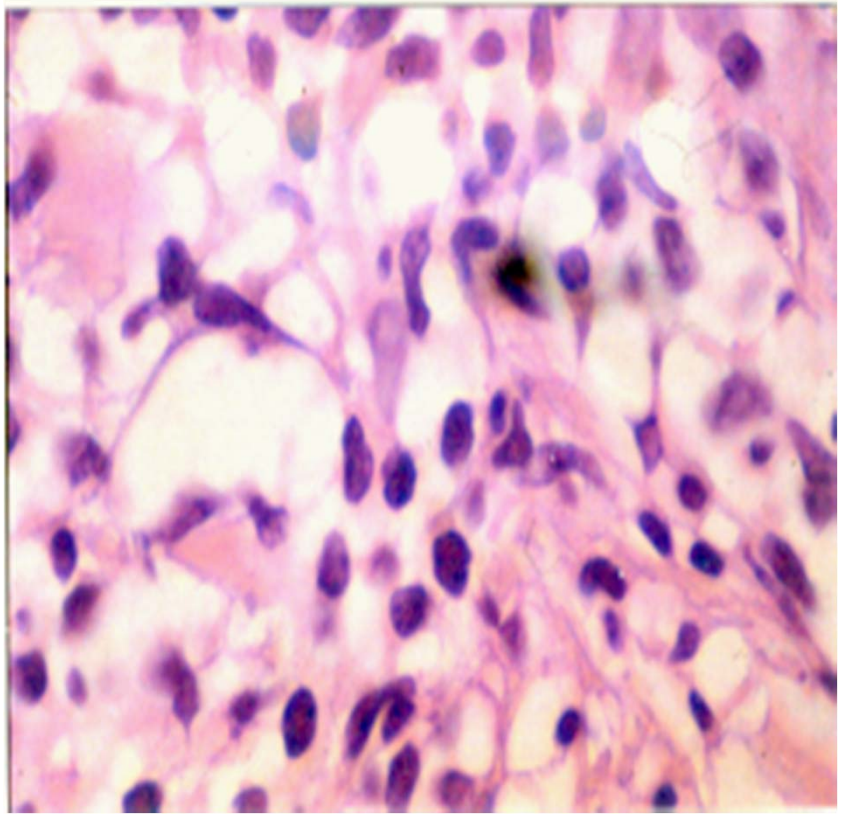
?



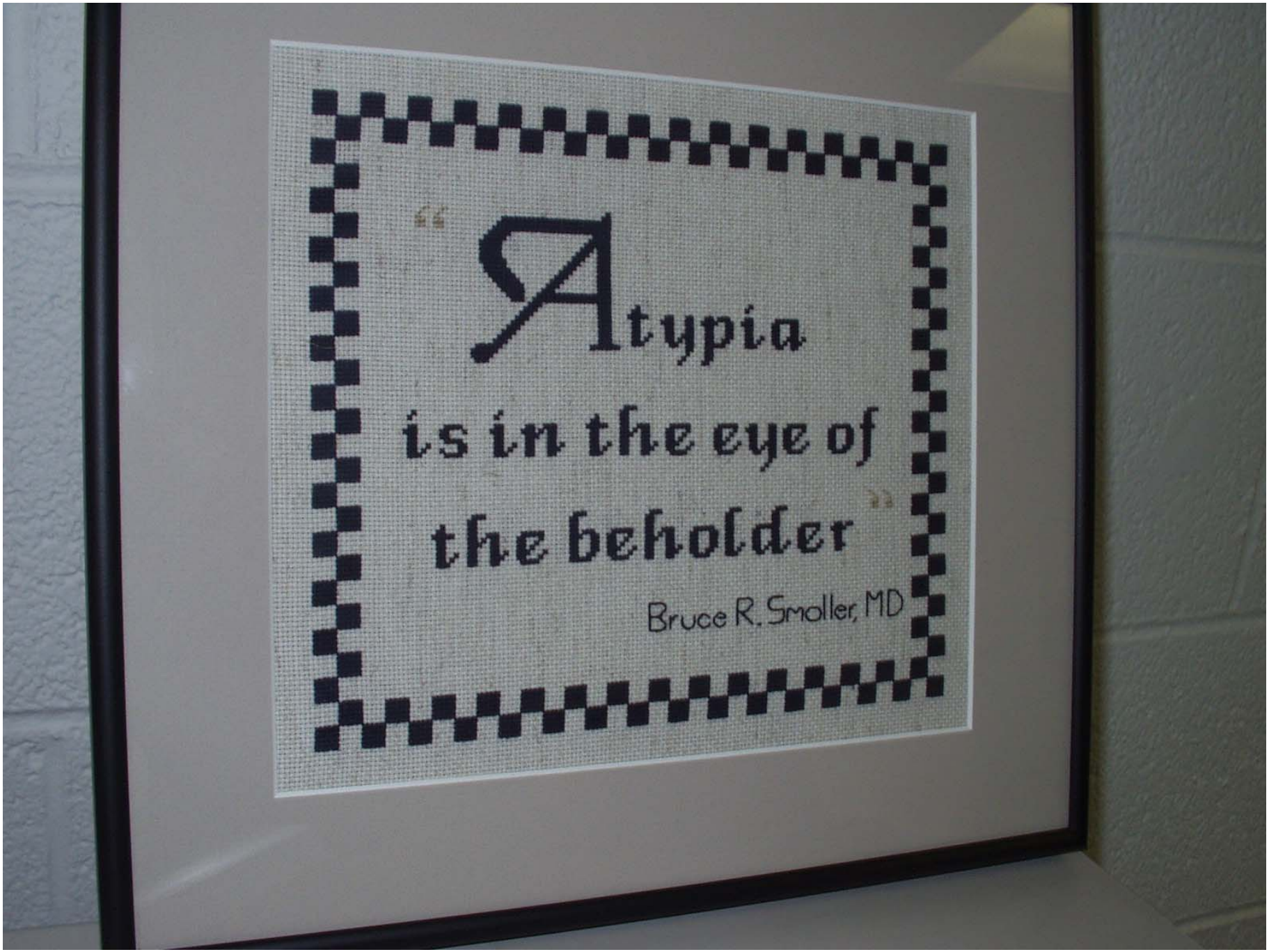




Mycosis fungoides



Spongiotic dermatitis


"Atypia
is in the eye of
the beholder"
Bruce R. Smoller, MD

- Bu bulgular spesifik veya sensitif değildir.
- Pautrier mikroapsesi MF olgularında dahi %37,5 bulunurken, non MF olgularında %2.1‘inde de bulunabilmektedir.
- Bu sebeplerle biopsi raporları genellikle “MF ile uyumlu” olarak çıkmakta bu da klinisyende şüphe ve hoşnutsuzluk yaratmaktadır.

MF Tanısında İleri Teknikler

- MF olgularının hemen tamamında **klonal CD4+ hücre proliferasyonu** vardır. PCR ile TCR gen rearrangement bakılarak bu proliferasyon **% 52-90 olguda** saptanabilir.

MF Tanısında İleri Teknikler

- Bu lezyonlardaki **tüm hücreler tümöral değildir, birçoğu reaktif** niteliktedir.
  - CD 4 ve CD 8’ den oluşan heterojen T-hücre infiltrasyonu vardır.
  - Erken (yama) dönemi lezyonlarda lazer mikrodiseksiyon ile epidermisde monoklonal T hücre varlığı tespit edilmektedir.
  - Dermisdeki hücrelerin birçoğu ise poliklonal T hücrelerinden oluşmaktadır.

MF Tanısında İleri Teknikler

- Bazı inflamatuar hastalıklarda da monoklonal üretim oluşabilir (örn PLEVA)

MF Tanısında İleri Teknikler

- MF için tanısal histopatolojik kriterler içermeyen ancak PCR'da klonal T hücre topluluğu bulunan lezyonlar **"klonal dermatit-abortif /latent lenfoma** " kavramının oluşmasına yol açmıştır.
- Bu lezyonlar uzun süreli takiplerde sadece histomorfolojik kriterler ile tanınan büyük plak parapsöriazis olgularına göre 4 kez daha fazla MF' e dönüşmüşlerdir.

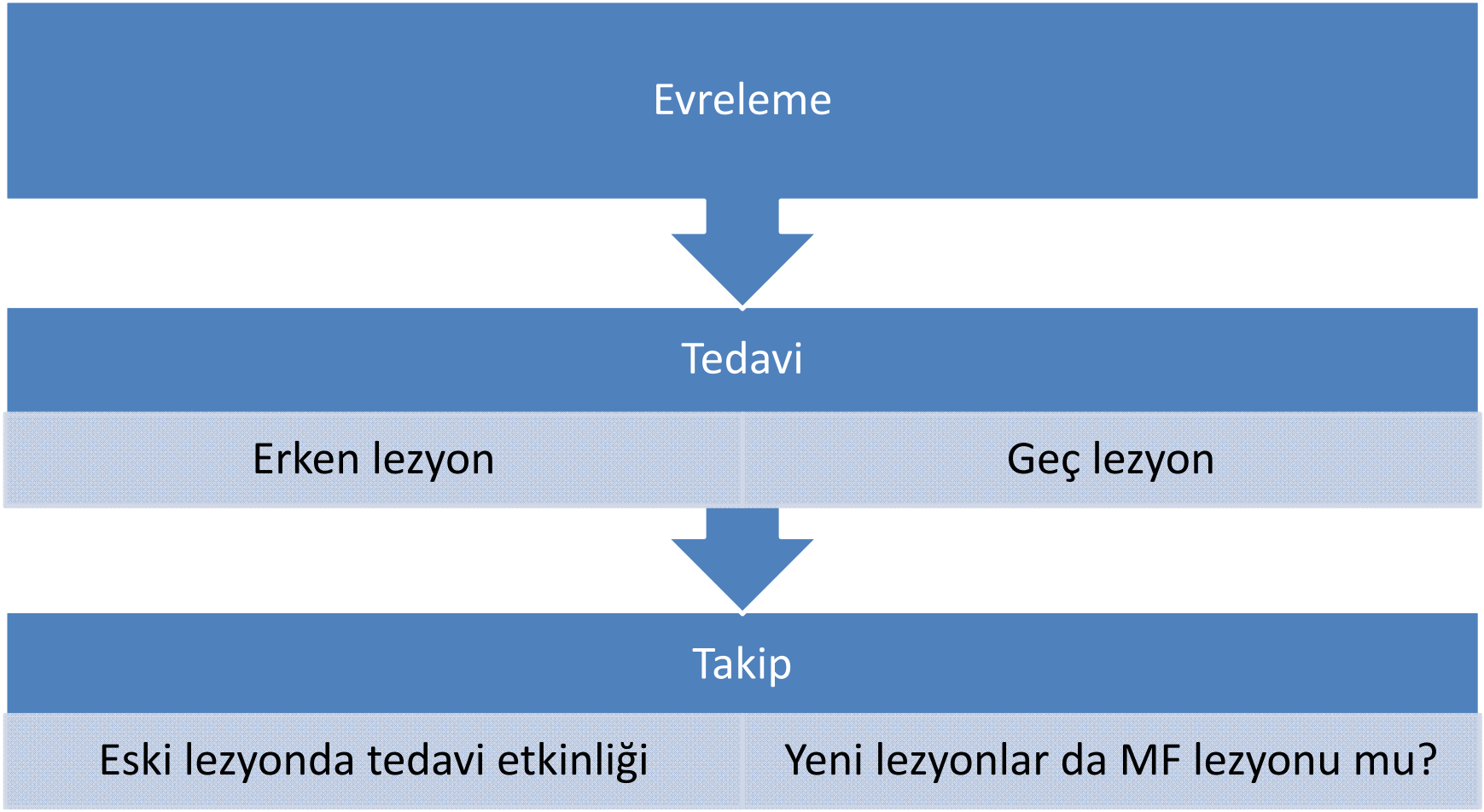
Fung MA, Murphy MJ, Hoss DM, Grant-Kels JM. Practical evaluation and management of cutaneous lymphoma. J Am Acad Dermatol 2002; 46:325-57.

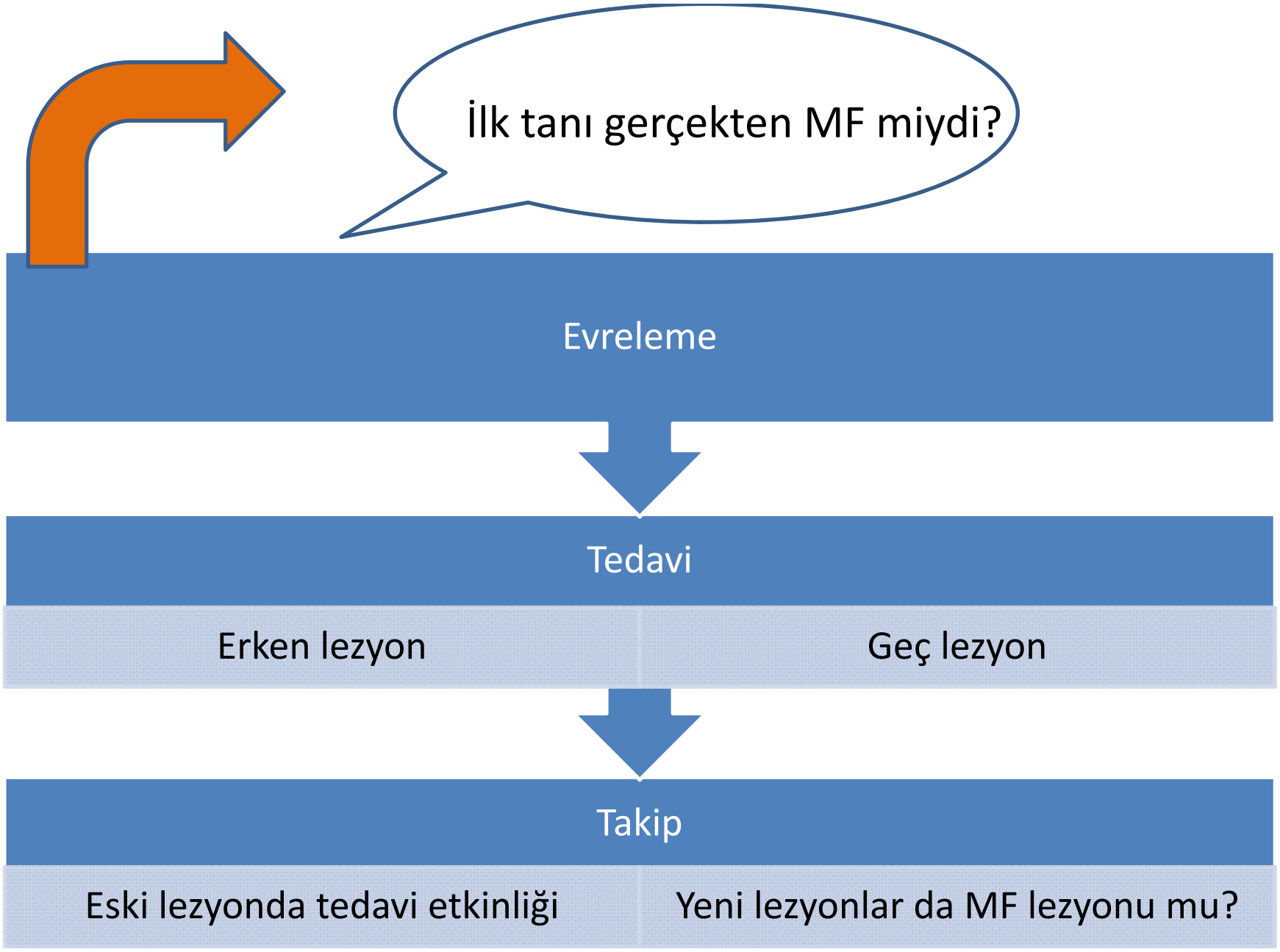
- MF histopatolojik tanısı için tam gelişmiş plaktan yeni çıkan lezyonlara dek çok sayıda biopsi almak gereklidir.
- Biopsiden 2-4 hafta önce tüm topikal ve sistemik tedaviler kesilmelidir, aksi takdirde tanı koydurucu kriterlerde silinmeye neden olunabilir.


merit MERSIN
Çukurowa

Tanıdan Sonra Neler Oluyor?

Tanıdan Sonra Neler Oluyor?




İlk tanı gerçekten MF miydi?
Evreleme
Tedavi
Erken lezyon
Geç lezyon
Takip
Eski lezyonda tedavi etkinliği
Yeni lezyonlar da MF lezyonu mu?

Evreleme

TNMB EVRELEMESİ 1979
Mycosis Fungoides Cooperative Group

- T1 Toplam vucut alanının <%10 tutan yama, plak, papül
- T2 Toplam vucut alanının >%10 tutan eritem, yama, plak, papül
- T3 Tümör
- T4 Yaygın eritrodermi

Table. — Staging of Cutaneous T-Cell Lymphoma: TNMB Classification

Classification	Description		
T: Skin			
T0	Lesions clinically and/or histopathologically suggestive of CTCL		
T1	Limited plaques, papules, or eczematous patches covering <10% of skin surface		
T2	Generalized plaques, papules, or erythematous patches covering ≥10% of skin surface		
T3	Cutaneous tumors		
T4	Generalized erythroderma		
N: Lymph Nodes			
N0	No palpable lymphadenopathy, lymph node pathology negative for CTCL		
N1	Palpable lymphadenopathy; lymph node pathology negative for CTCL		
N2	No palpable lymphadenopathy, lymph node pathology positive for CTCL		
N3	Palpable lymphadenopathy, lymph node pathology positive for CTCL		
M: Viscera			
M0	No visceral organ involvement		
M1	Visceral organ involvement, pathology present		
B: Blood			
B0	Atypical circulating cells not present (<5%)		
B1	Atypical circulating cells present (≥5%)		
Stage	**T**	**N**	**M**
IA	1	0	0
IB	2	0	0
IIA	1–2	1	0
IIB	3	0–1	0
III	4	0–1	0
IVA	1–4	2–3	0
IVB	1–4	0–3	1

Adapted from Bunn PA Jr, Lamberg SI. Report of the Committee on Staging and Classification of Cutaneous T-cell Lymphomas. *Cancer Treat Rep.* 1979;63:725-728.

Evreleme

Table 1. Tumor-node-metastasis-blood (TNMB) staging as proposed by the ISCL/EORTC (10)

Skin	
T1	Limited patches, papules, and/or plaques covering < 10% of skin surface
T2	Patches, papules, and/or plaques covering ≥ 10% of skin surface
T3	One or more tumors (≥1 cm in diameter)
T4	Confluence of erythema covering ≥80% body surface area
Node*	
N0	No clinically abnormal peripheral lymph nodes, biopsy not required
N1a	Clinically abnormal peripheral lymph nodes, histopathology: dermatopathic lymphadenopathy, clone negative
N1b	Clinically abnormal peripheral lymph nodes, histopathology: dermatopathic lymphadenopathy, clone positive
N2a	Clinically abnormal peripheral lymph nodes, histopathology: early involvement of MF, clone negative
N2b	Clinically abnormal peripheral lymph nodes, histopathology: early involvement of MF, clone positive
N3	Clinically abnormal peripheral lymph nodes, histopathology: partial or complete effacement of lymph node architecture
Nx	Clinically abnormal peripheral lymph nodes, no histologic confirmation
Visceral	
M0	No visceral organ involvement
M1	Visceral involvement
Blood	
B0a	Absence of significant blood involvement, clone negative
B0b	Absence of significant blood involvement, clone positive
B1a	Low tumor burden: > 5% of peripheral blood lymphocytes are atypical cells but does not meet the criteria of B2, clone negative
B1b	Low blood tumor burden: > 5% of peripheral blood lymphocytes are atypical cells but does not meet the criteria of B2, clone positive
B2	High blood tumor burden: ≤ 1000/μl Sezary cells with positive clone

*For details on histopathological classification of lymph nodes in MF, see (73, 74).

ISCL, International Society for Cutaneous Lymphomas; EORTC, European Organization for the Research and Treatment of Cancer; MF, mycosis fungoides.

- 2007 yılında ISCL ve EORTC TNM sınıflaması revize edilerek önemli bir prognostik faktör olan dolaşımda atipik hücre varliği (B) de sınıflamada kullanılmaya başlandı.

Evreleme

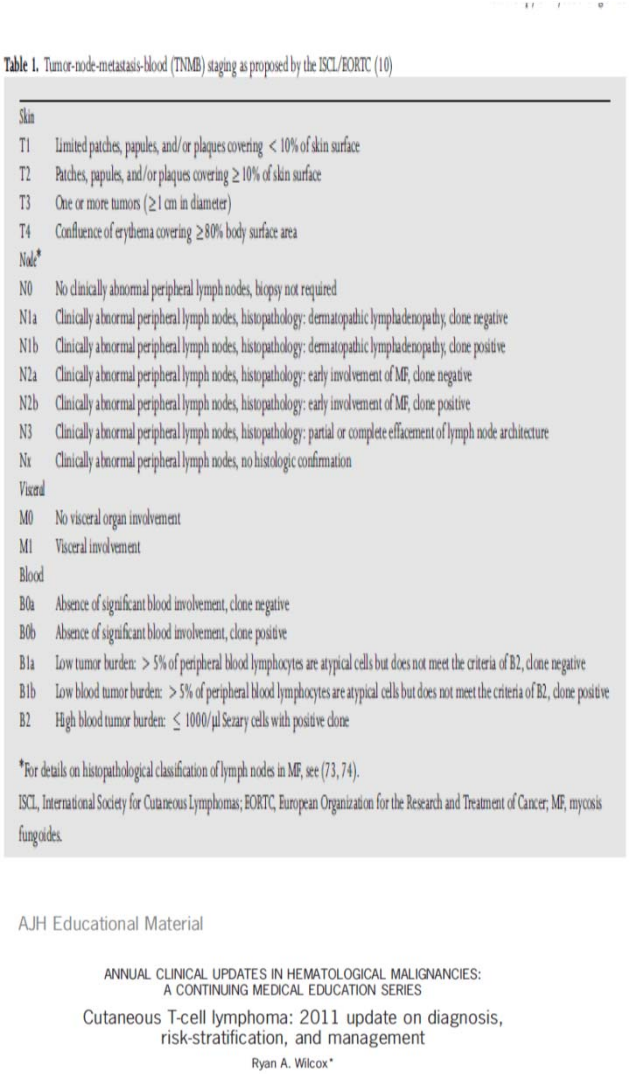


Table 1. Tumor-node-metastasis-blood (TNMB) staging as proposed by the ISCL/EORTC (10)

Skin	
T1	Limited patches, papules, and/or plaques covering < 10% of skin surface
T2	Patches, papules, and/or plaques covering ≥ 10% of skin surface
T3	One or more tumors (≥ 1 cm in diameter)
T4	Confluence of erythema covering ≥ 80% body surface area
Node*	
N0	No clinically abnormal peripheral lymph nodes, biopsy not required
N1a	Clinically abnormal peripheral lymph nodes, histopathology: dermatopathic lymphadenopathy, clone negative
N1b	Clinically abnormal peripheral lymph nodes, histopathology: dermatopathic lymphadenopathy, clone positive
N2a	Clinically abnormal peripheral lymph nodes, histopathology: early involvement of MF, clone negative
N2b	Clinically abnormal peripheral lymph nodes, histopathology: early involvement of MF, clone positive
N3	Clinically abnormal peripheral lymph nodes, histopathology: partial or complete effacement of lymph node architecture
Nx	Clinically abnormal peripheral lymph nodes, no histologic confirmation
Visceral	
M0	No visceral organ involvement
M1	Visceral involvement
Blood	
B0a	Absence of significant blood involvement, clone negative
B0b	Absence of significant blood involvement, clone positive
B1a	Low tumor burden: > 5% of peripheral blood lymphocytes are atypical cells but does not meet the criteria of B2, clone negative
B1b	Low blood tumor burden: > 5% of peripheral blood lymphocytes are atypical cells but does not meet the criteria of B2, clone positive
B2	High blood tumor burden: ≤ 1000/μl Sezary cells with positive clone

*For details on histopathological classification of lymph nodes in MF, see (73, 74).

ISCL, International Society for Cutaneous Lymphomas; EORTC, European Organization for the Research and Treatment of Cancer; MF, mycosis fungoides.

AJH Educational Material

ANNUAL CLINICAL UPDATES IN HEMATOLOGICAL MALIGNANCIES:
A CONTINUING MEDICAL EDUCATION SERIES

Cutaneous T-cell lymphoma: 2011 update on diagnosis, risk-stratification, and management

Ryan A. Wilcox*

Erken evre MF hastaları

- **Evre I** Yama ve plak lezyonlar
  - evre IA Toplam vucut alanının %”10’undan azı
  - evre IB %10’dan fazlası
- **Evre IIA** Yama ve plak dönemi klinik olarak anormal lenf nodu olan T1, T2 olgular

İleri evre MF hastaları

- Tümör (T3) ve eritrodermi (T4),
- parsiyel ya da komplet lenf nodu tutulumu (N3),
- visseral metastaz (M1),
- yaygın lösemik tutulum (B2)
- PCR ile kanda ve lenf nodunda klonalite

EVRELEMEDE LENF NODLARI

Node*	
N0	No clinically abnormal peripheral lymph nodes, biopsy not required
N1a	Clinically abnormal peripheral lymph nodes, histopathology: dermatopathic lymphadenopathy, clone negative
N1b	Clinically abnormal peripheral lymph nodes, histopathology: dermatopathic lymphadenopathy, clone positive
N2a	Clinically abnormal peripheral lymph nodes, histopathology: early involvement of MF, clone negative
N2b	Clinically abnormal peripheral lymph nodes, histopathology: early involvement of MF, clone positive
N3	Clinically abnormal peripheral lymph nodes, histopathology: partial or complete effacement of lymph node architecture
Nx	Clinically abnormal peripheral lymph nodes, no histologic confirmation
Visceral	

- N evrelemesinde MF/SS hastalarında histopatolojik olarak “pozitif” veya “negatif “ olarak değerlendirilen lenf nodlarıyla ilgili herhangi bir tanımlama vermez
- Geçerli sınıflamada normal lenf nodlarından biopsi önermemektedir, ancak **1.5 cm’den büyük sert fikse lenf nodları** için biopsi önerilmektedir.
  - Biopsi için tutulan deri bölgesini drene eden en büyük lenf nodu veya radyolojik olarak PET görüntüleme sisteminde en çok madde tutan lenf nodu seçilmelidir.

Lenf Nodu Tutulumu

Table 5. Histopathologic staging of lymph nodes in mycosis fungoides and Sézary syndrome

Updated ISCL/EORTC classification	Dutch system[58]	NCI-VA classification[13,57,59]
N_1	Grade 1: dermatopathic lymphadenopathy (DL)	LN_0: no atypical lymphocytes LN_1: occasional and isolated atypical lymphocytes (not arranged in clusters) LN_2: many atypical lymphocytes or in 3-6 cell clusters
N_2	Grade 2: DL; early involvement by MF (presence of cerebriform nuclei > 7.5 μm)	LN_3: aggregates of atypical lymphocytes; nodal architecture preserved
N_3	Grade 3: partial effacement of LN architecture; many atypical cerebriform mononuclear cells (CMCs) Grade 4: complete effacement	LN_4: partial/complete effacement of nodal architecture by atypical lymphocytes or frankly neoplastic cells

Dutch sistem

- Atipik lenfositlerin büyüklüğü
- Lenf nodu yapısal bozulmanın derecesi

NCI/VA

(*National Cancer Institute-Veterans Administration*)

- Tutulan lenf nodundaki atipik lenfosit oranı

blood 2007 110: 1713-1722
Prepublished online May 31, 2007;
doi:10.1182/blood-2007-03-055749

Revisions to the staging and classification of mycosis fungoides and Sézary syndrome: a proposal of the International Society for Cutaneous Lymphomas (ISCL) and the cutaneous lymphoma task force of the European Organization of Research and Treatment of Cancer (EORTC)

Elise Olsen, Eric Vonderheid, Nicola Pimpinelli, Rein Willemze, Youn Kim, Robert Knobler, Herschel Zackheim, Madeleine Duvic, Teresa Estrach, Stanford Lamberg, Gary Wood, Reinhard Dummer, Annamari Ranki, Gunter Burg, Peter Heald, Mark Pittelkow, Maria-Grazia Bernengo, Wolfram Sterry, Liliane Laroche, Franz Trautinger and Sean Whittaker

Prognoz

- MF düşük dereceli bir lenfomadır.
  - Yama evresinden plak, tümör ve deri dışı yayılım evresine geçiş on yıllar içerisinde olur.
- Hastalık daha çok yaşlılarda ortaya çıkar.
  - birçok hastada plak ve tümör evresine geçiş izlenmez.
  - Genç hasta grubunda progresyon riski fazladır.
- Hastalıktan ölüm yaklaşık %15-20 civarında tahmin edilmektedir.
  - Bir grup hasta ise hızlı ve agresif bir seyir göstererek deri dışı yayılım gösterir ve sepsis ve ağır enfeksiyon gibi komplikasyonlar nedeni ile kaybedilir
- **En önemli prognostik parametreler** evre ve deri lezyonlarının tipidir.
  - 10 yıllık yaşam beklentisi
    - %10'dan az alan kapsayan sınırlı yama/plak MF olgularında %97-98,
    - %10'dan fazla alan kapsayan yaygın yama/plak MF olgularında % 83,
    - Tümör evresinde %42,
    - histolojik olarak lenf nodu tutulumu gösterilmiş olgularda %20 oranındadır.

TEDAVİ

Erken Evre MF Tedavisi

- Erken evre yama plak MF lezyonlarında prognoz iyi olduğundan toksik yan etkilerden kaçınmak için "**bekle ve gör**" stratejisi uygulanır.
- Dermatolog ve onkolog gözetiminde deriye yönelik tedaviler (kortikosteroidler, alkilleyici ajanlar ve bexarotene) uygulanır. Klinik ve patolojik komplet remisyon oranı %63 kadardır.
- Erken evre MF tedavisinde ultraviole ışınları (UVA ve UVB) ve total vücut elektron beam tedavisi kullanılır.

Fototerapi

UVA ve UVB- her ikisi de MF tedavisinde etkilidir.
Ultraviole ışınları deride mutajenik ve immünolojik etkilere sahiptir.
Lenfosit apoptozu fototerapinin en önemli etkisidir.
T lenfositler UV ışınlarına oldukça duyarlıdırlar

UVA

- Psöralen PUVA ile kullanıldığında (fotokemoterapi) fotoaktivasyon sonucu DNA bağları oluşturur ve tümör hücresinde apoptoza yol açar. Komplet remisyon %90 oranındadır.
- Vitiligo ve psöriazis tedavisinde de kullanılır.
- UVB'den farklı olarak derin dermise penetre olur, dermal fibroblasts, dendritik hücreler, lenfositler, mast hücreleri ve granülositleri etkiler.

UVB

- Dar veya geniş bant **UVB** ise psörolan'e ihtiyaç duymaz. Klinik ve patolojik cevap oranları yüksektir. Günümüzde daha çok dar bant kullanılmaktadır.
- UVB UVA'ya oranla daha çok enerji içerir, ancak derinin derin katmanlarına erişemez. Bu nedenle UVB daha çok Langerhans hücreleri ve epidermal keratinositleri etkiler.

ELSEVIER
Seminars in Cutaneous Medicine and Surgery
Phototherapy in the Age of Biologics
Daniel Walker, BS, and Heidi Jacobe, MD, MSCS

İleri Evre MF tedavisi

- İleri evre MF tedavisi çoklu disipliner yaklaşım gerektirir. Hastanın yaşına performansına hastalığın yaygınlığına, ve önceki tedavilere göre kişiye özel tedavi planı uygulanmalıdır.
  - Topikal tedaviler,
  - Biyolojik ajanlar (bexarotene, interferon alfa)
  - sistemik kemoterapötikler

MF Klinik Takibinde Kriterler Patolojinin Yeri

Therapy

Eur J Dermatol 2008; 18 (6): 660-2

Ting XIAO
Li-Xin XIA
Zhen-Hai YANG
Chun-Di HE
Xing-Hua GAO
Hong-Duo CHEN

Department of Dermatology,
No. 1 Hospital of China Medical University,
155 North Nanjing Street, Shenyang
110001, China

Reprints: H.-D. Chen
<chenhd@cae.cn>

Article accepted on 22/7/2008

Narrow-band ultraviolet B phototherapy for early stage mycosis fungoides

Recently there have been some reports concerned the treatment of early stage mycosis fungoides (MF) with narrow-band ultraviolet B (NB-UVB) phototherapy. In most of the previous reports, NB-UVB phototherapy was given three times a week on non-consecutive days. Our aim was to evaluate the effect of a twice weekly regimen of NB-UVB phototherapy in the treatment of early-stage MF. Eight patients with early stage MF received NB-UVB phototherapy twice weekly. Six patients (75%) had a complete response in a mean of 23.4 treatments, two (25%) had a partial response. Upon discontinuation of treatment, four patients with complete response relapsed in a mean time to relapse of 5 months. The twice weekly regimen of NB-UVB phototherapy is effective and well-tolerated in the treatment of early stage MF.

Key words: mycosis fungoides, narrow-band ultraviolet B, phototherapy

MF Klinik Takibinde Kriterler Patolojinin Yeri

Therapy

Eur J Dermatol 2008; 18 (6): 660-2

Ting XIAO
Li-Xin XIA
Zhen-Hai YANG
Chun-Di HE
Xing-Hua GAO
Hong-Duo CHEN

Department of Dermatology,
No. 1 Hospital of China Medical University,
155 North Nanjing Street, Shenyang
110001, China

Reprints: H.-D. Chen
<chenhd@cae.cn>

Article accepted on 22/7/2008

Narrow-band ultraviolet B phototherapy for early stage mycosis fungoides

Recently there have been some reports concerned the treatment of early stage mycosis fungoides (MF) with narrow-band ultraviolet B (NB-UVB) phototherapy. In most of the previous reports, NB-UVB phototherapy was given three times a week on non-consecutive days. Our aim was to evaluate the effect of a twice weekly regimen of NB-UVB phototherapy in the treatment of early-stage MF. Eight patients with early stage MF received NB-UVB phototherapy twice weekly. Six patients (75%) had a complete response in a mean of 23.4 treatments, two (25%) had a partial response. Upon discontinuation of treatment, four patients with complete response relapsed in a mean time to relapse of 5 months. The twice weekly regimen of NB-UVB phototherapy is effective and well-tolerated in the treatment of early stage MF.

Key words: mycosis fungoides, narrow-band ultraviolet B, phototherapy

Methods

Before treatment, all patients received a work-up of a complete medical history, a complete physical and skin examination, some laboratory examinations (including complete blood cell count, liver and kidney function tests, serum lactate dehydrogenase levels, CD4/CD8 flow cytometry, blood smear for Sezary cells), chest X-ray and skin biopsy. Lymph node biopsy was performed in 3 patients

Determination of clinical response

The clinical response to NB-UVB phototherapy was based on determining the percentage of total body surface area affected by the disease. It was determined as follows: complete response (CR), at least 95% clearing of lesions; patial response (PR), at least 50% but less than 95% clearing; no response (NR), less than 50% clearing [1]. Relapse was defined as clinically significant disease requiring further treatment. The follow-up period ranged from 7 to 60 months (mean ± SD, 26.9 ± 19.7 months).

JEADV ISSN 1468-3083

ORIGINAL ARTICLE

Narrowband UVB phototherapy for early-stage mycosis fungoides: evaluation of clinical and histopathological changes

G Gökdemir,*† B Barutcuoğlu,† D Sakız,‡ A Köşlü†

†Dermatology Clinic and ‡Pathology Clinic, Sisli Etfal Research and Training Hospital, Istanbul, Turkey

Determination of clinical and histopathological response and statistical analysis

Clinical response was defined as follows: complete response (CR), more than 90% reduction in skin lesions; partial response (PR), 50–90% reduction in the lesions; and no response (NR), less than 50% reduction in the skin lesions. Before and after therapy, a skin biopsy specimen was taken from each patient for histological examination. The specimens were processed routinely and stained with haematoxylin–eosin (H&E) for light microscopic examination. Histopathological response was determined as follows: CR, the absence of epidermotropism and Pautrier microabscesses and marked reduction in a dense infiltrate of atypical lymphocytes with irregular nuclei and mitosis in the epidermis and dermis; PR, marked reduction in epidermotropism and sparsely scattered atypical lymphocytes in the epidermis and dermis; NR, no changes in histological findings.

Efficacy of narrowband UVB phototherapy in early stage of mycosis fungoides

clearing of skin lesions. Biopsies before and at the end of the treatment were examined to evaluate histological improvement. Maintenance therapy was accomplished by

67.8 J/cm^2) (Table 1). Histological examination of the control biopsies revealed loss of the characteristic features of MF. There was no correlation between the previous

Kural Y, Onsun N, Aygin S, Demirkesen C, Buyukbabani N. Efficacy of narrowband UVB phototherapy in early stage of mycosis fungoides. J Eur Acad Dermatol Venereol 2006;20: 104-5

Takipte PCR

British Journal of Dermatology 2003; 148: 265–271.

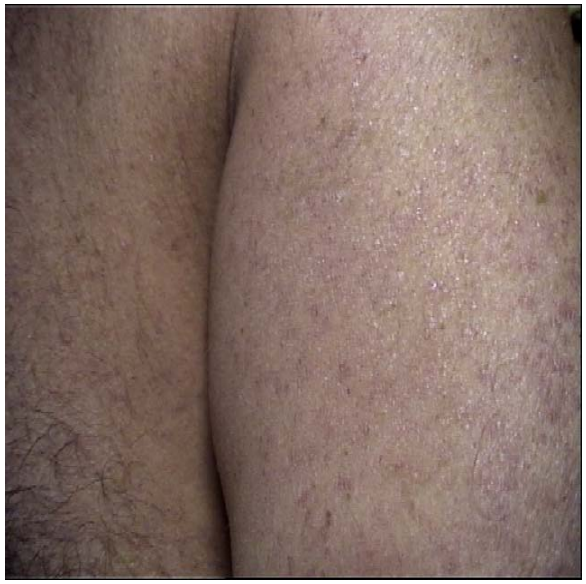
Dermatopathology

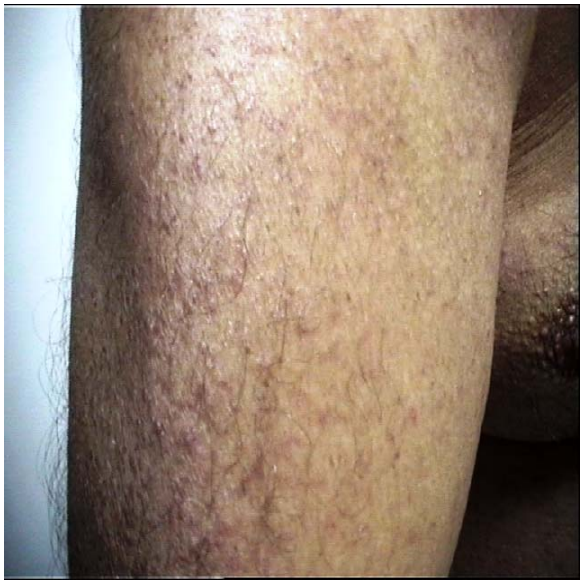
Minimal residual disease in mycosis fungoides follow-up can be assessed by polymerase chain reaction

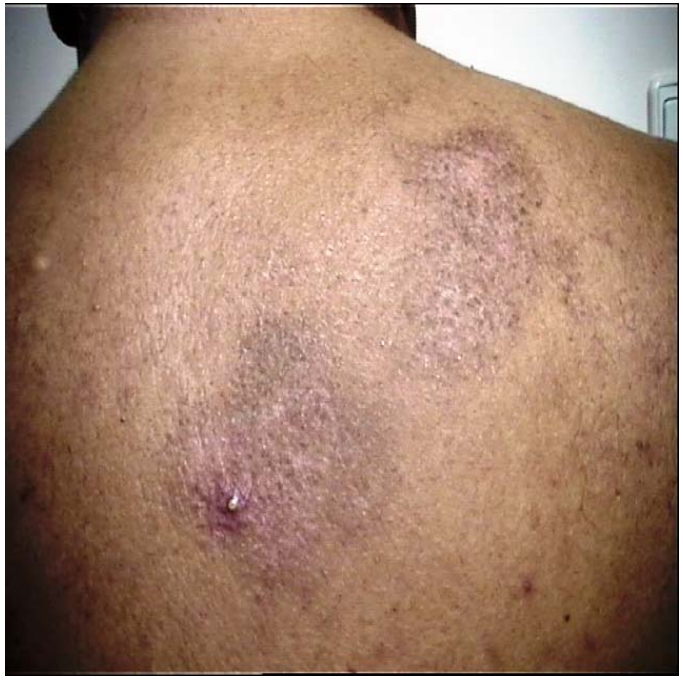
E. POSZEPCZYNSKA-GUIGNE, M. BAGOT, J. WECHSLER,* J. REVUZ, J-P. FARCET† AND M-H. DELFAU-LARUE†

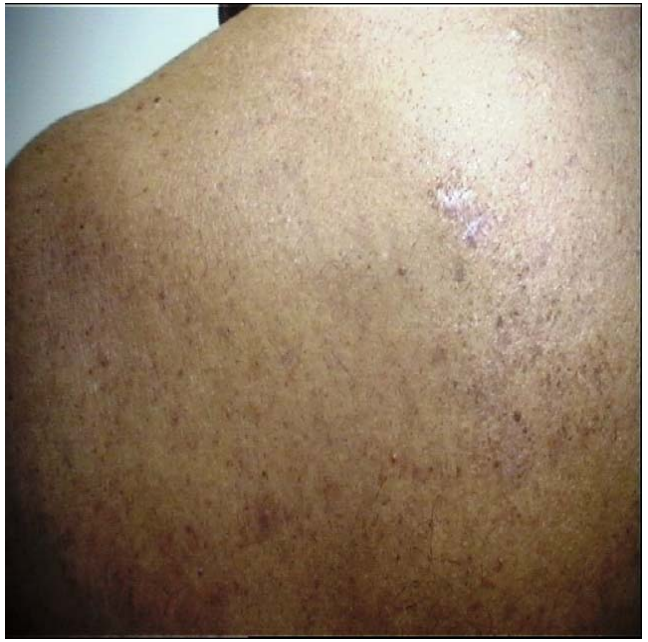
*Departments of Dermatology, *Pathology and †Immunology, Henri Mondor Hospital, University Paris XII, APHP, 51 avenue du Maréchal-de-Lattre-de-Tassigny, 94010 Créteil cedex, France*

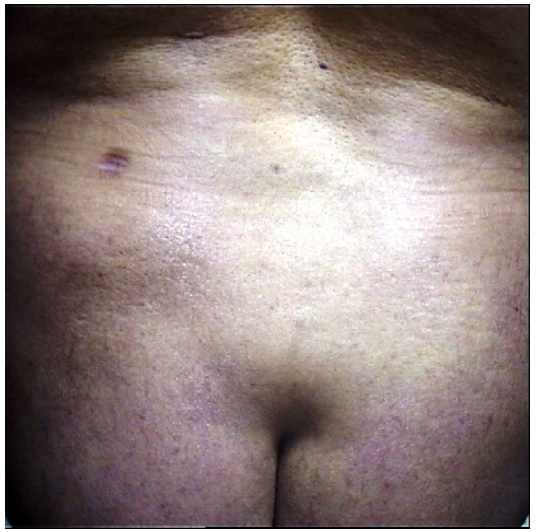
- Tedavi öncesi ve sonrası kan ve PCR sonuçları karşılaştırılan bir çalışmada “atipik lenfositler” ve “epidermotropizm” olmayan biopsiler histolojik olarak remisyonda kabul edilmiş.
- Klinik olarak devam eden (persiste) olguların:
  - Histopatoloji %29,
  - PCR %77 sinde MF tespit edilebilmiş.
- Histolojik remisyondaki olgularda % 31 oranında ise “minimal rezidüel hastalık” tanımlanmış.

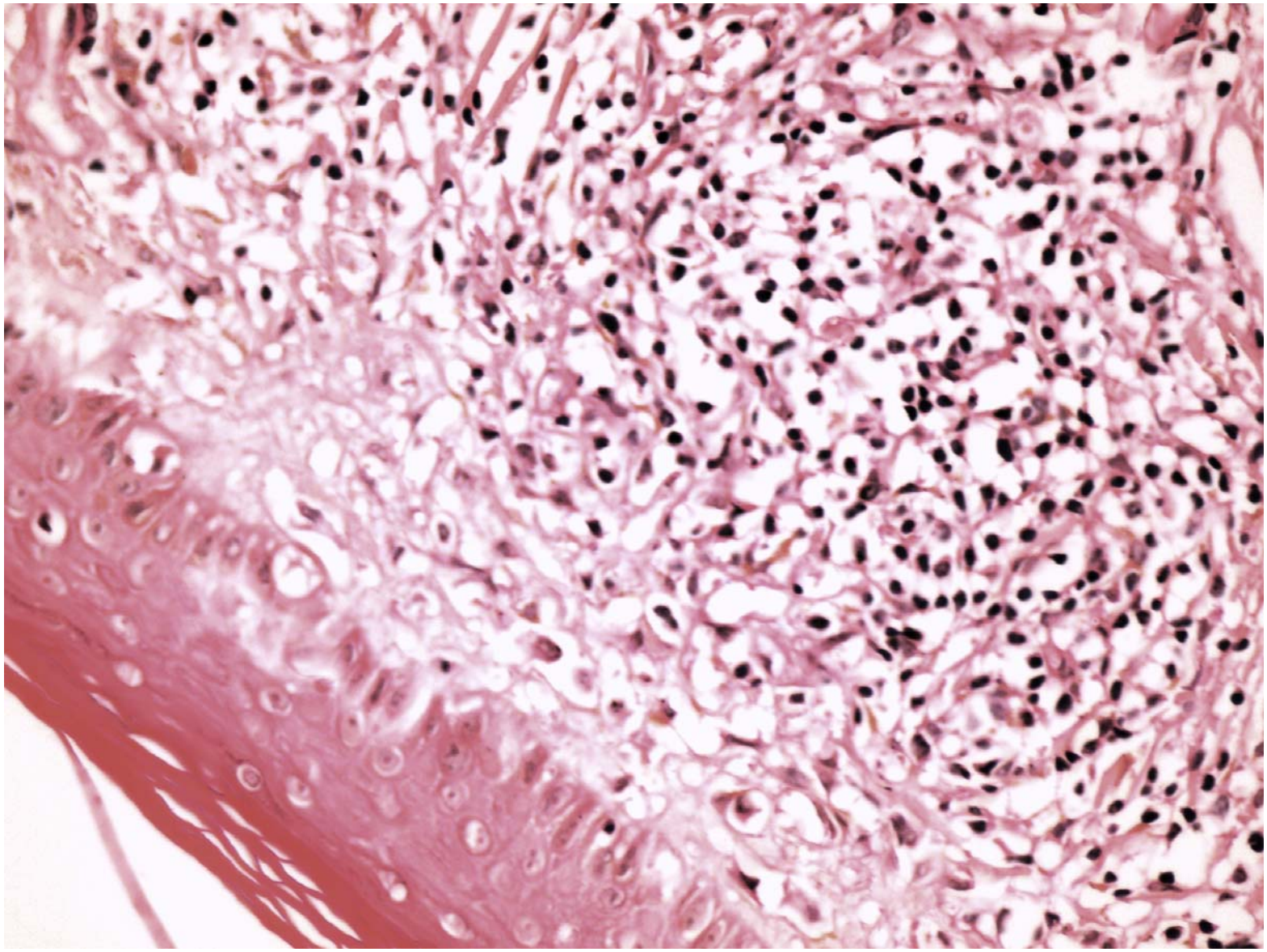




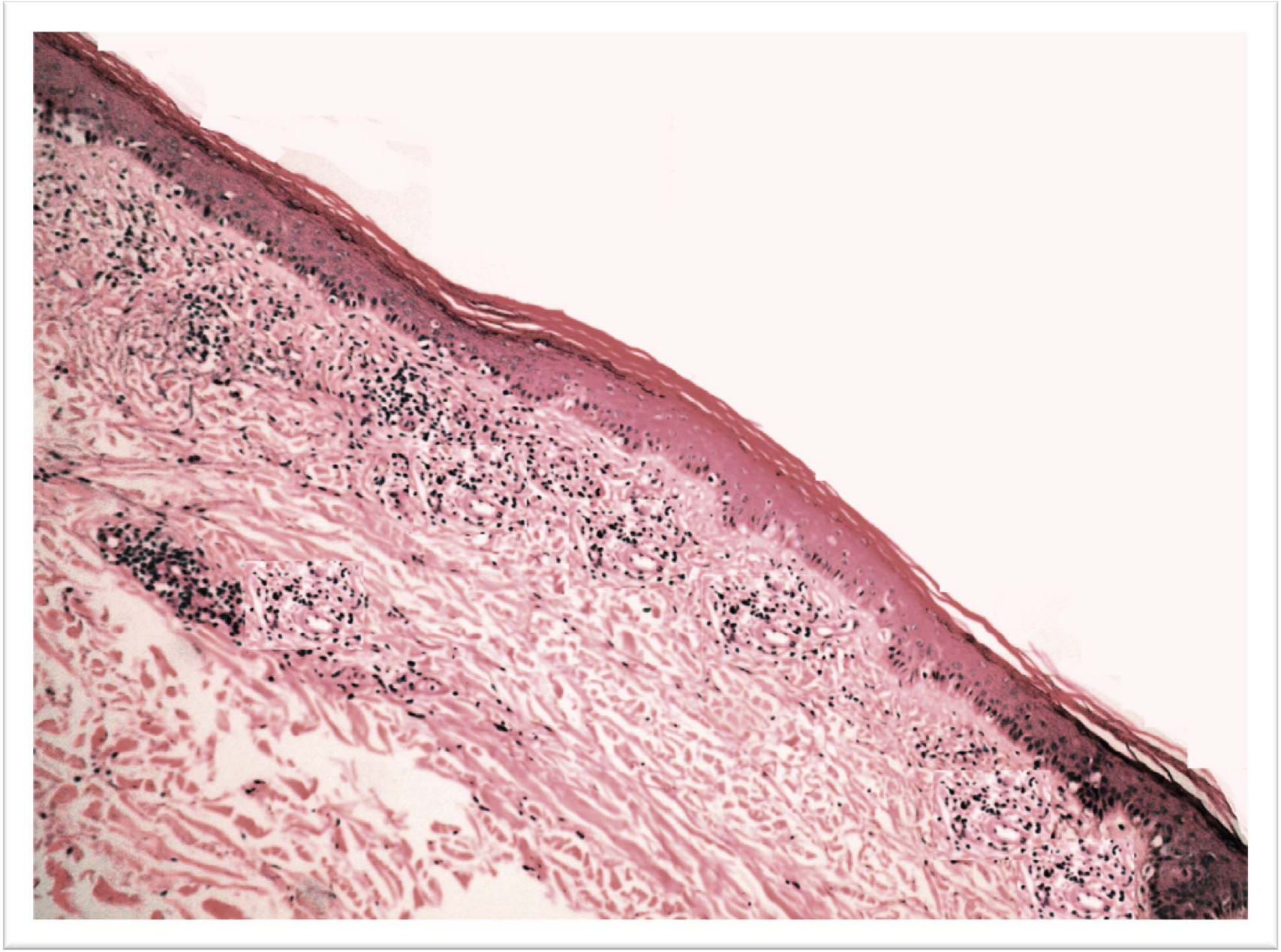




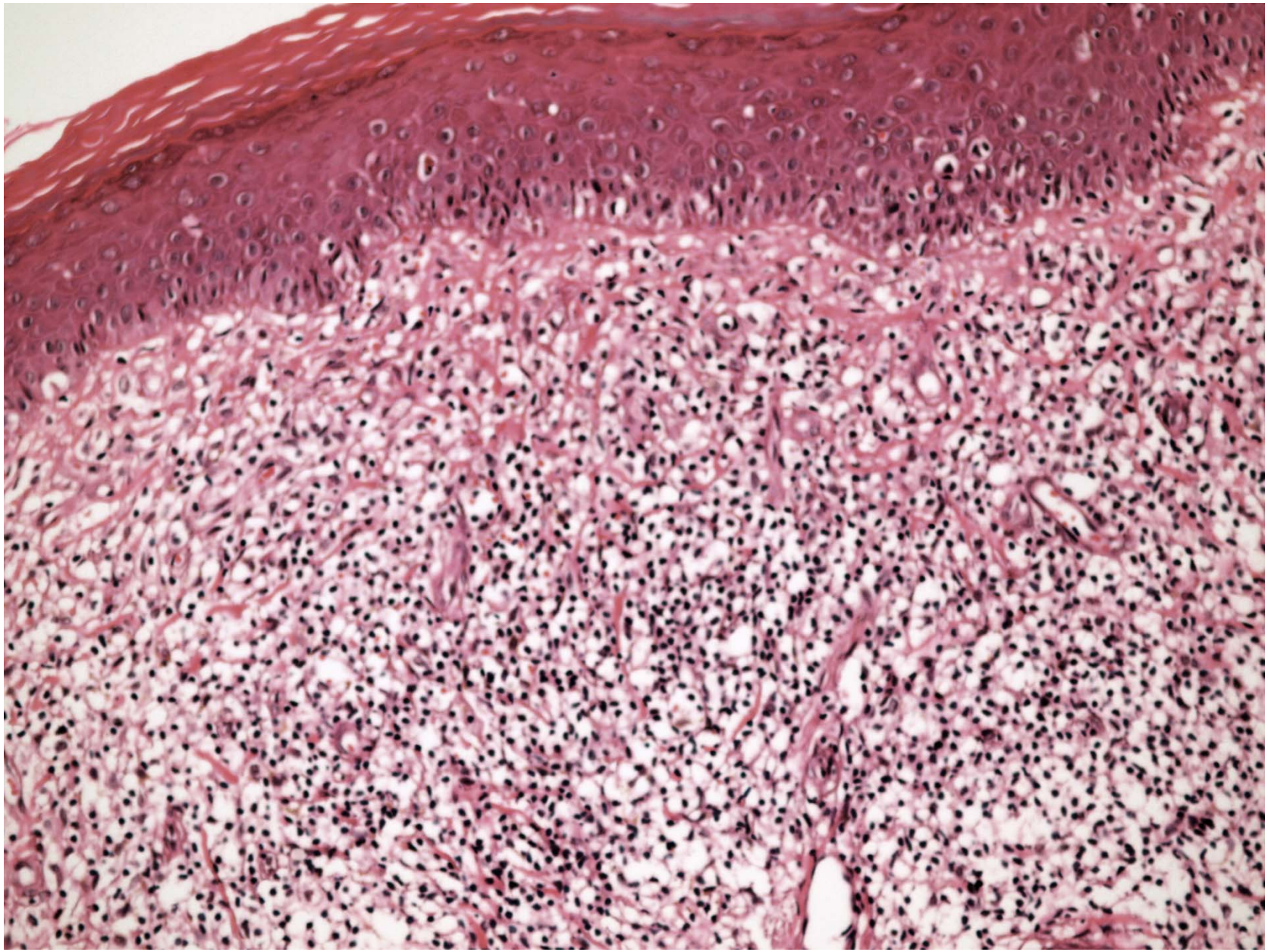




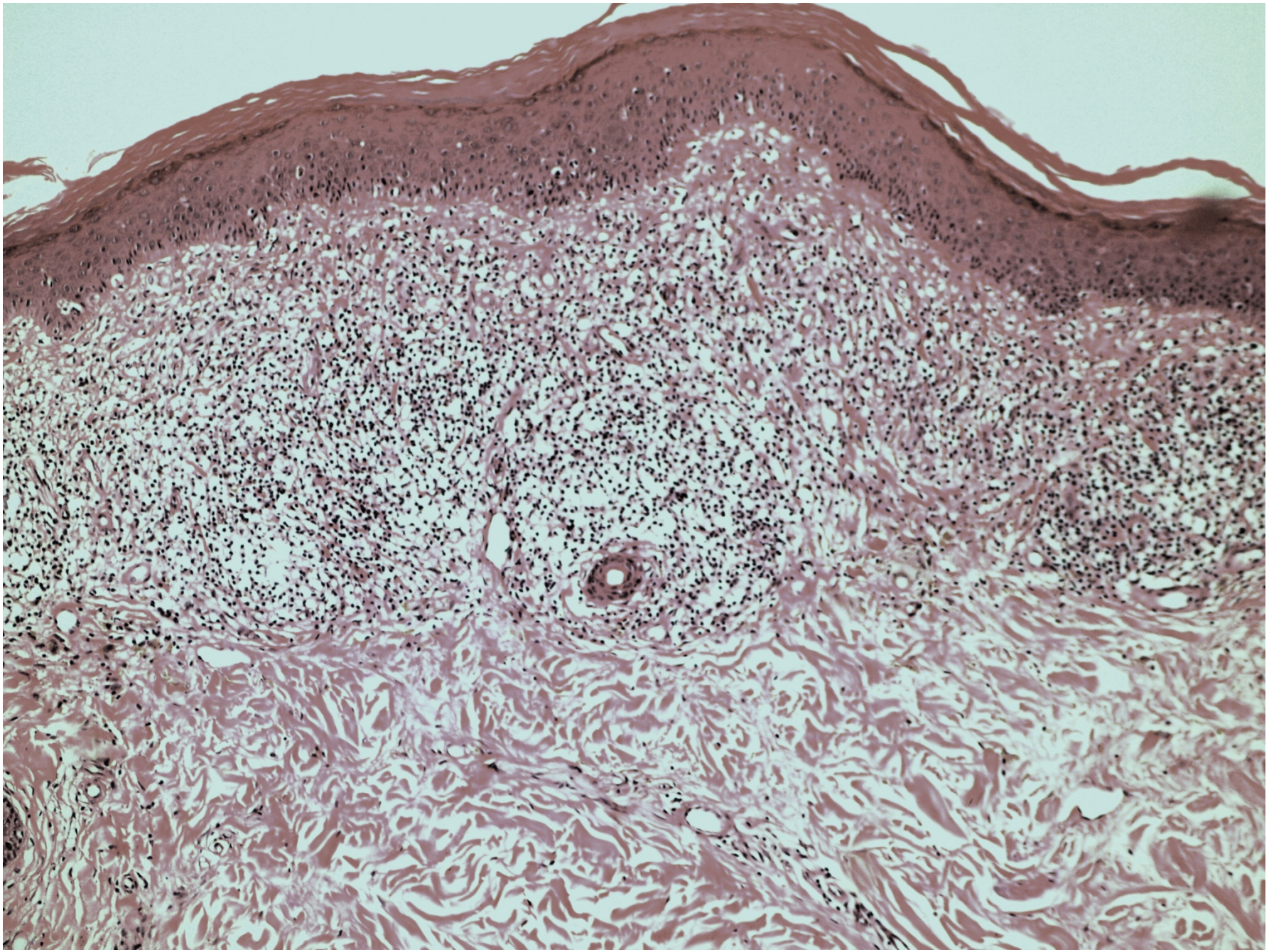
tö



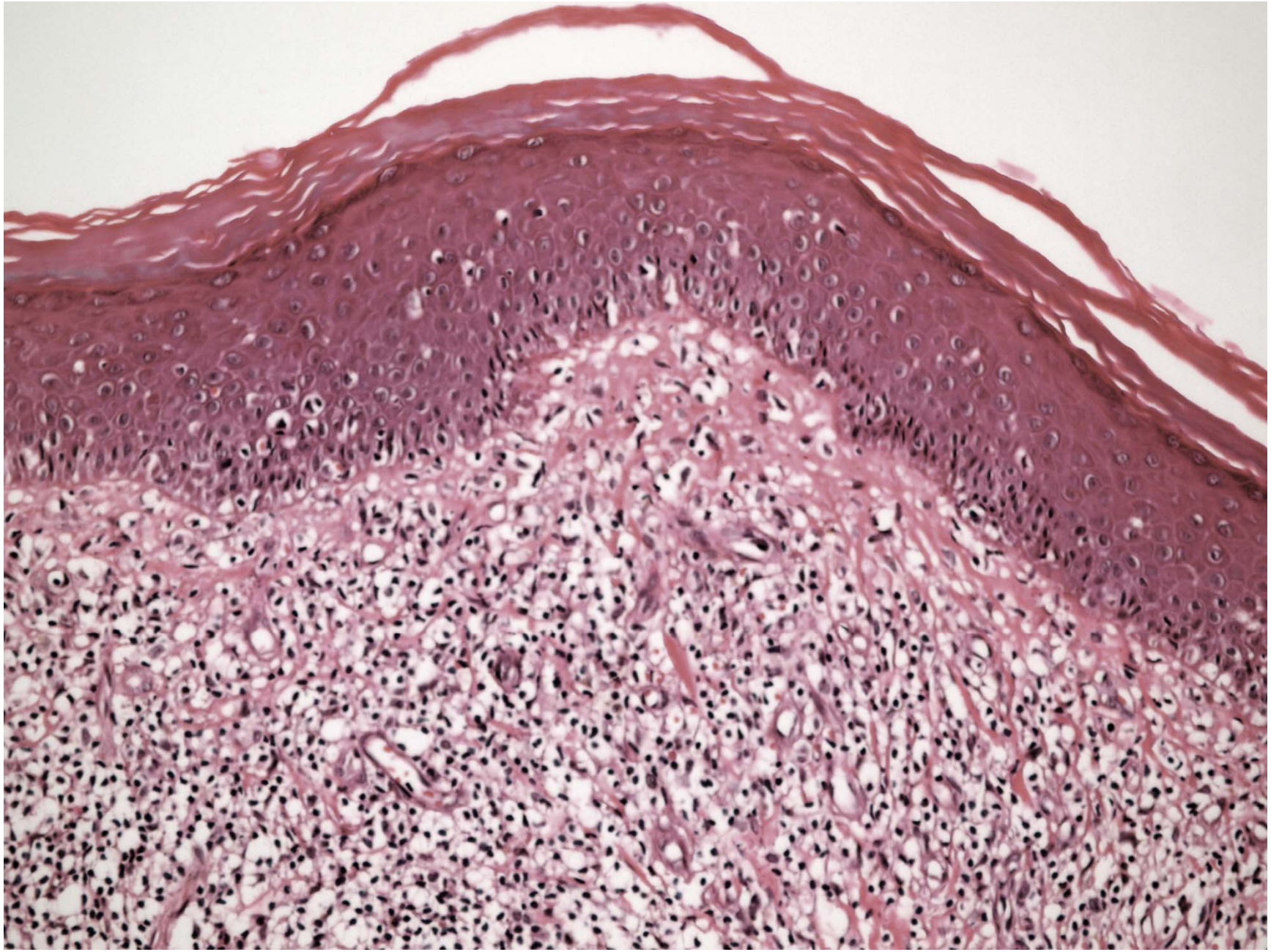
ts



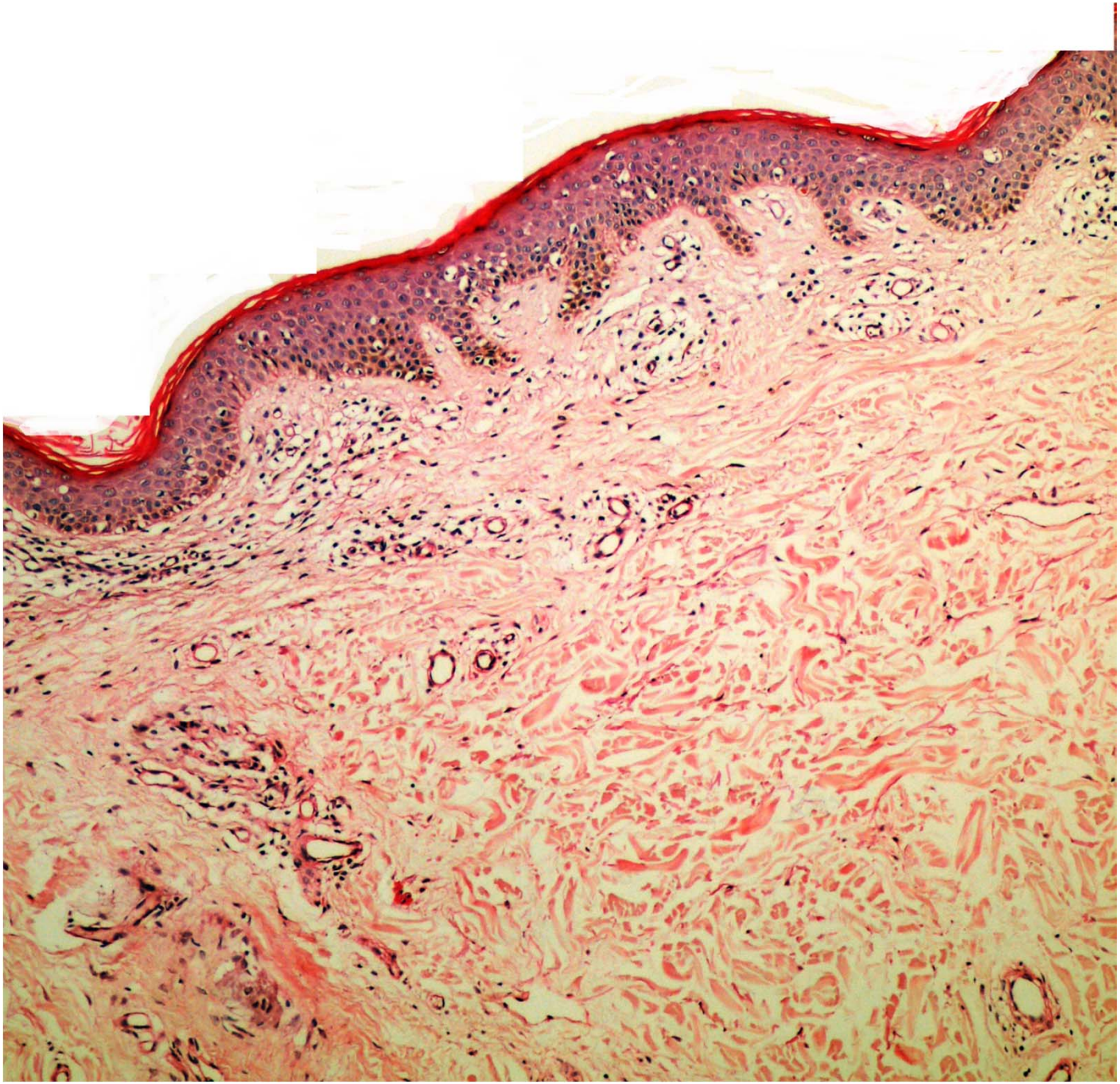
ts



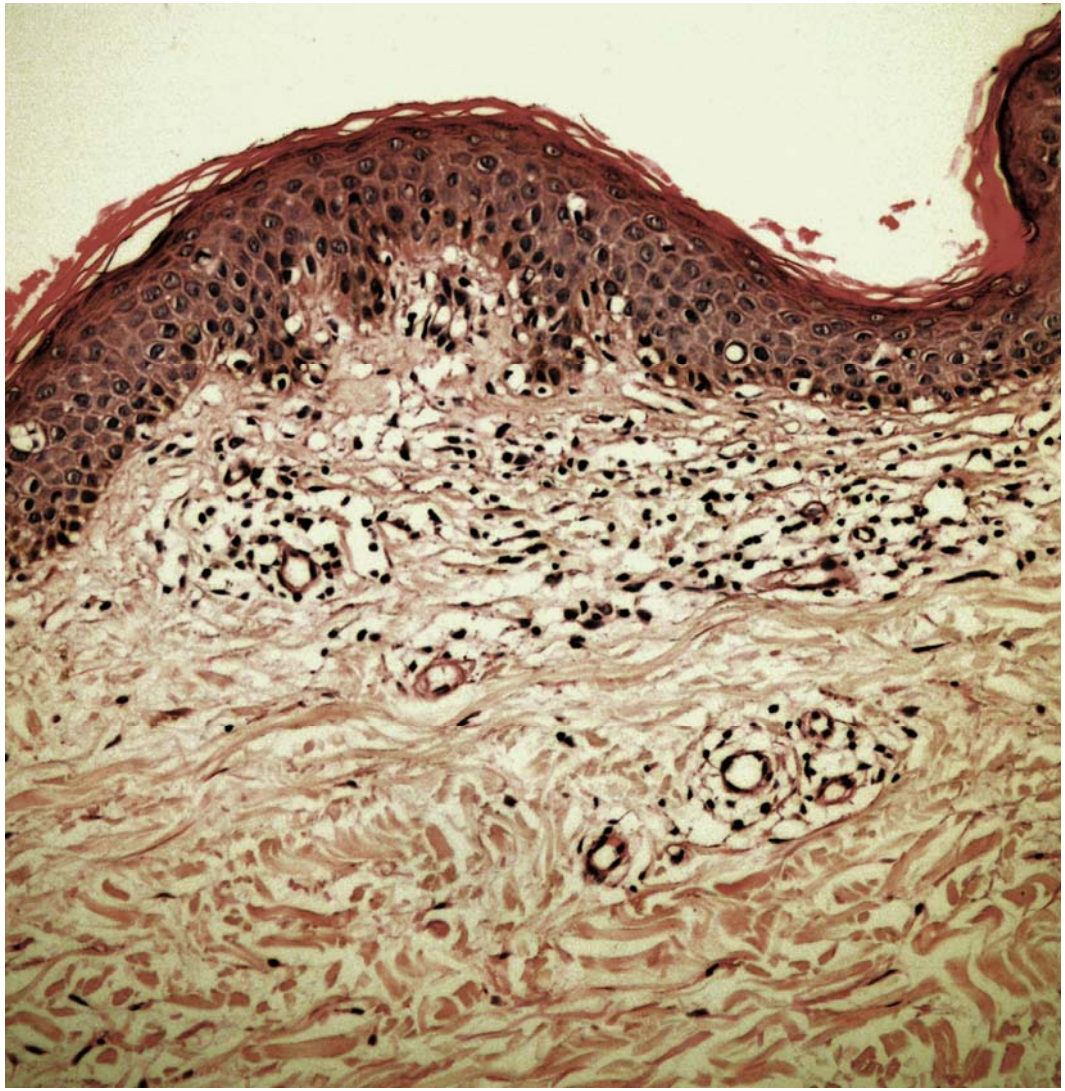
ts



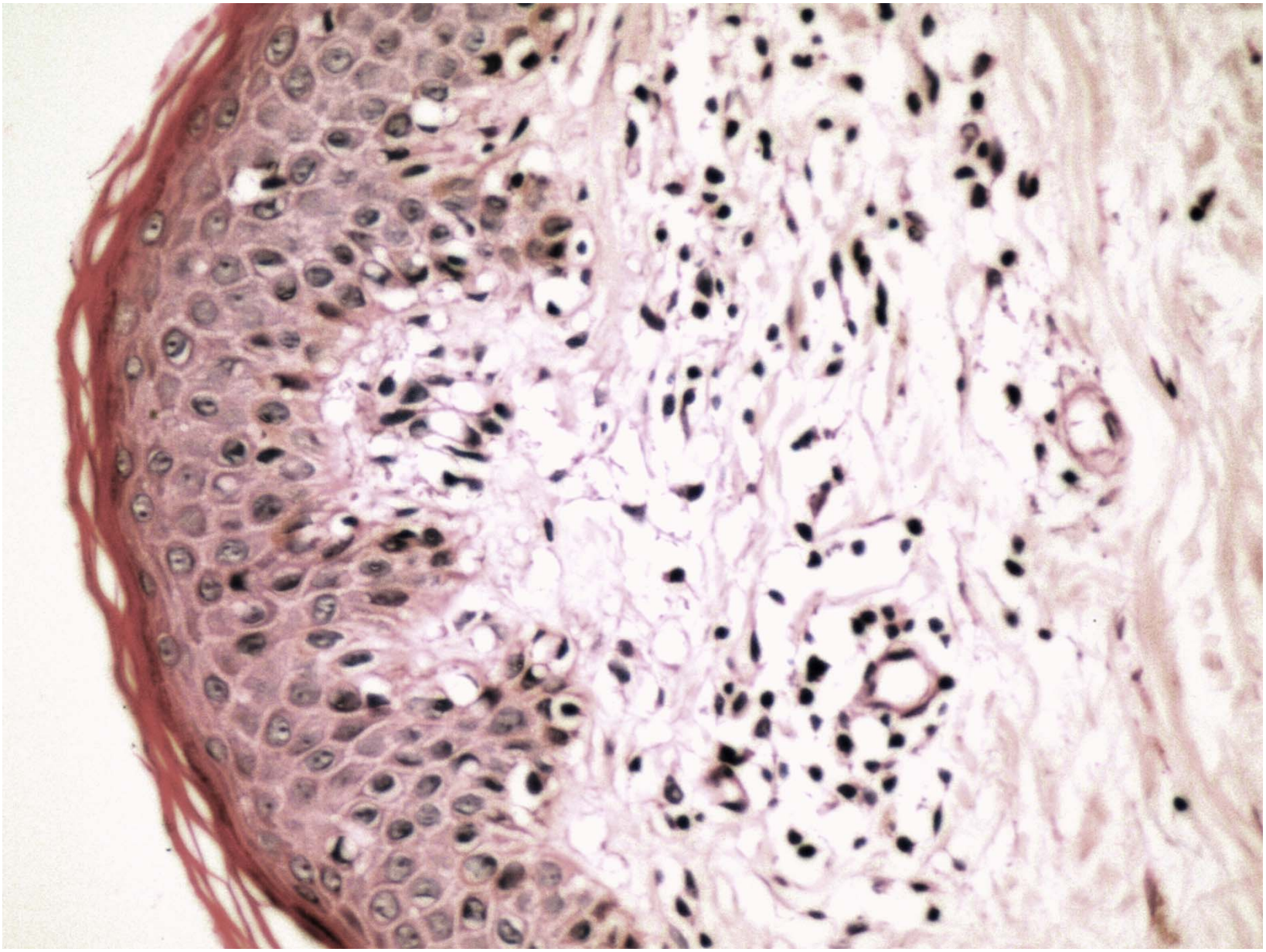
ts



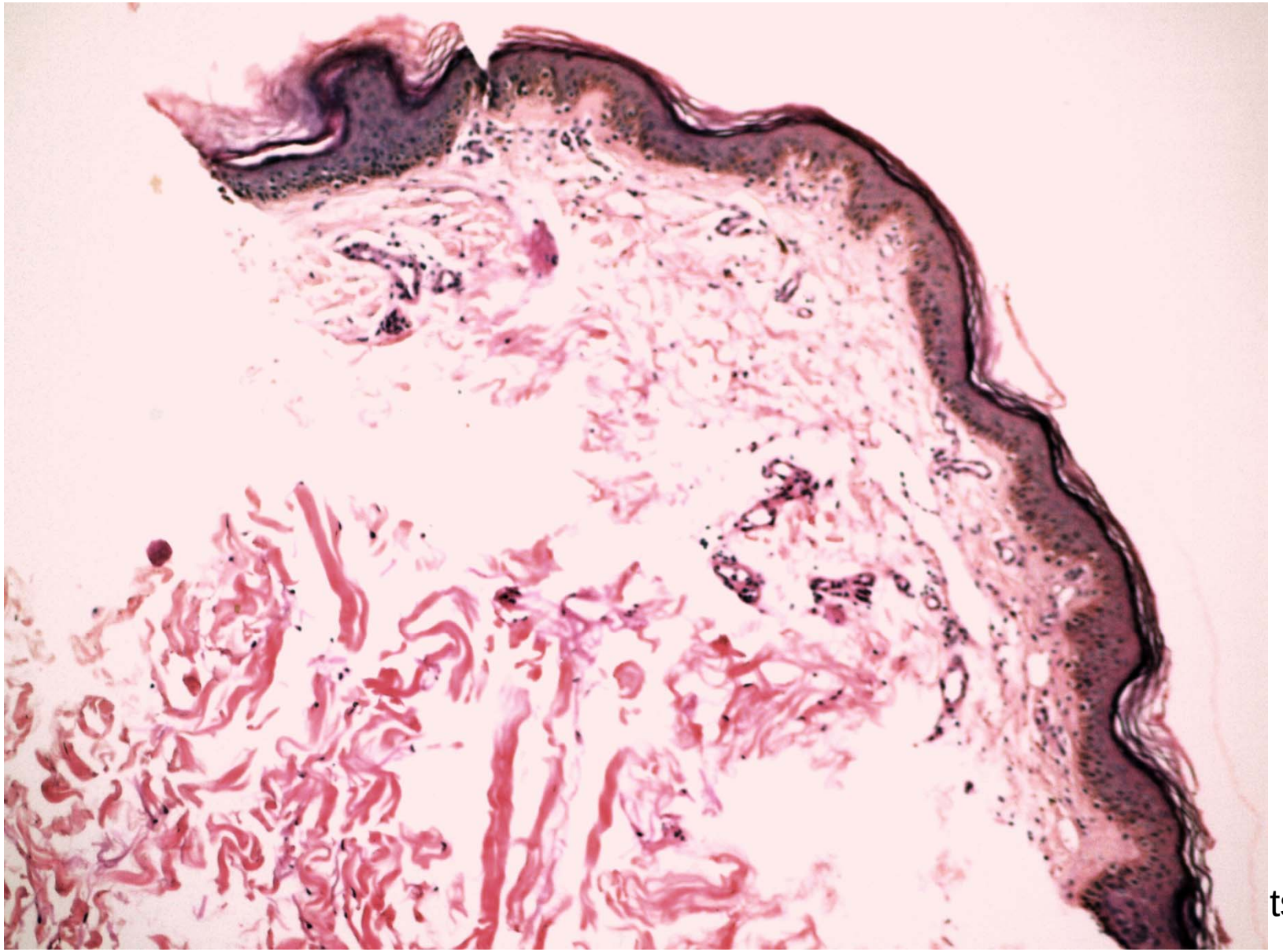
tö



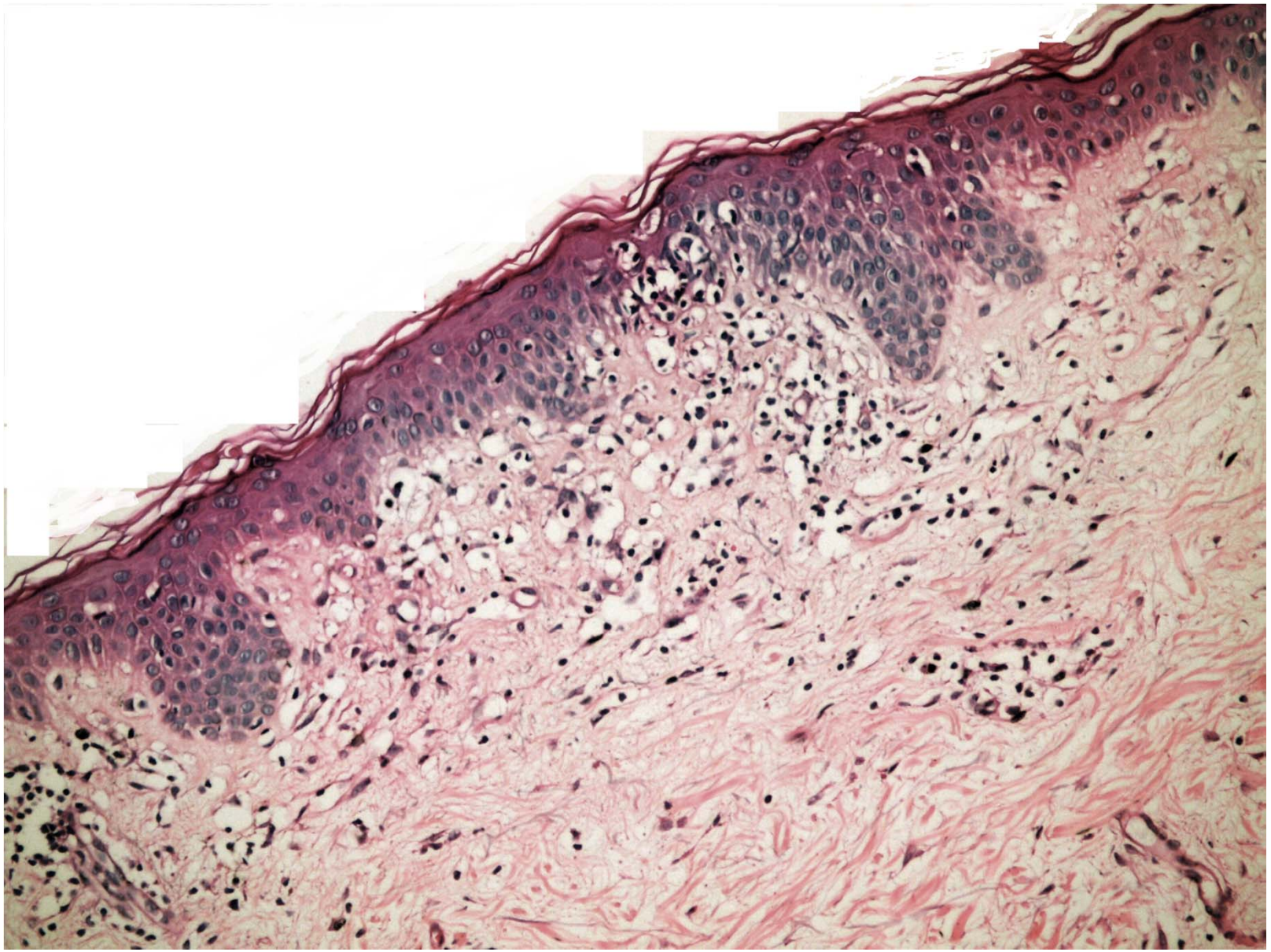
tö



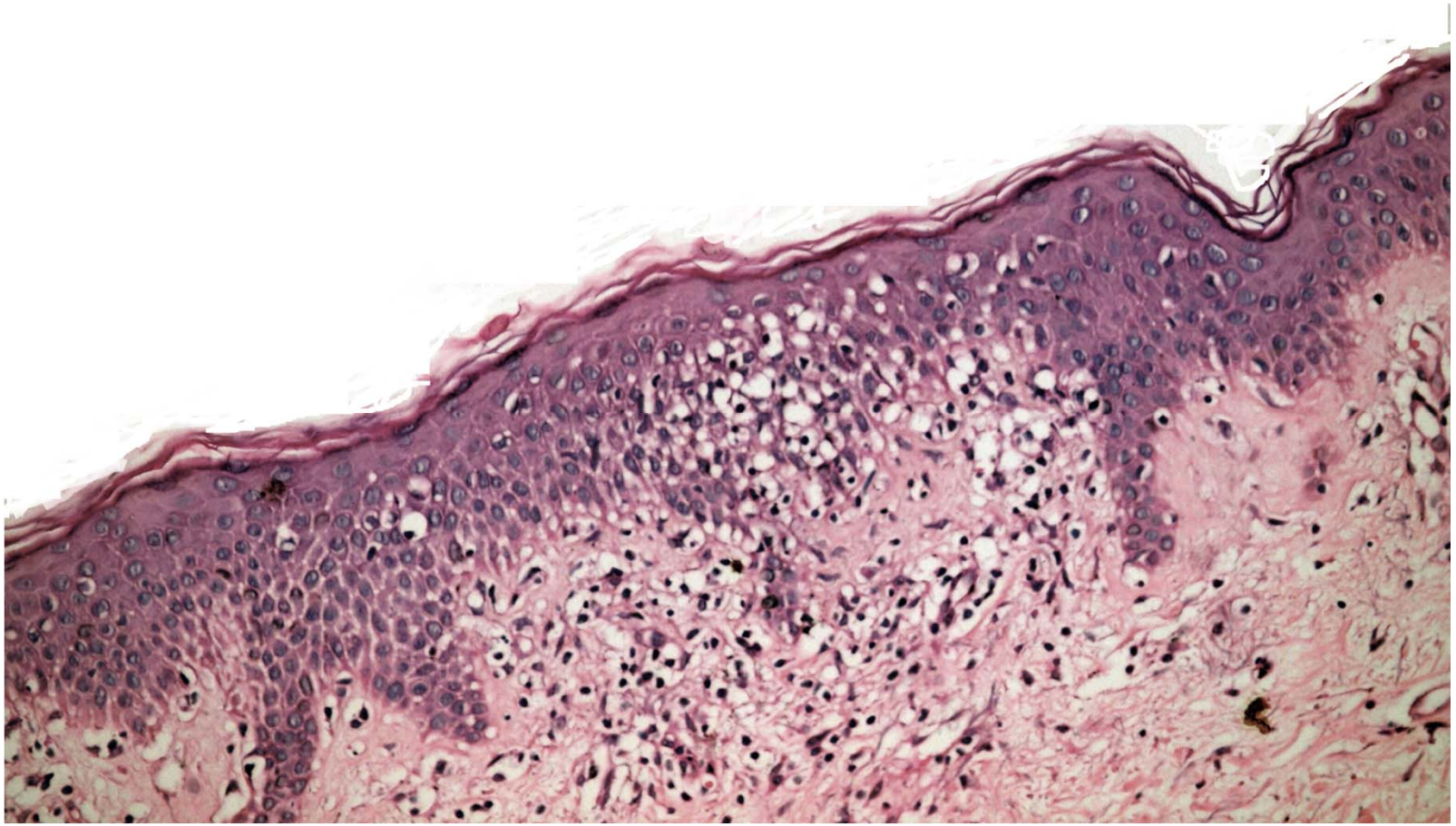
tö



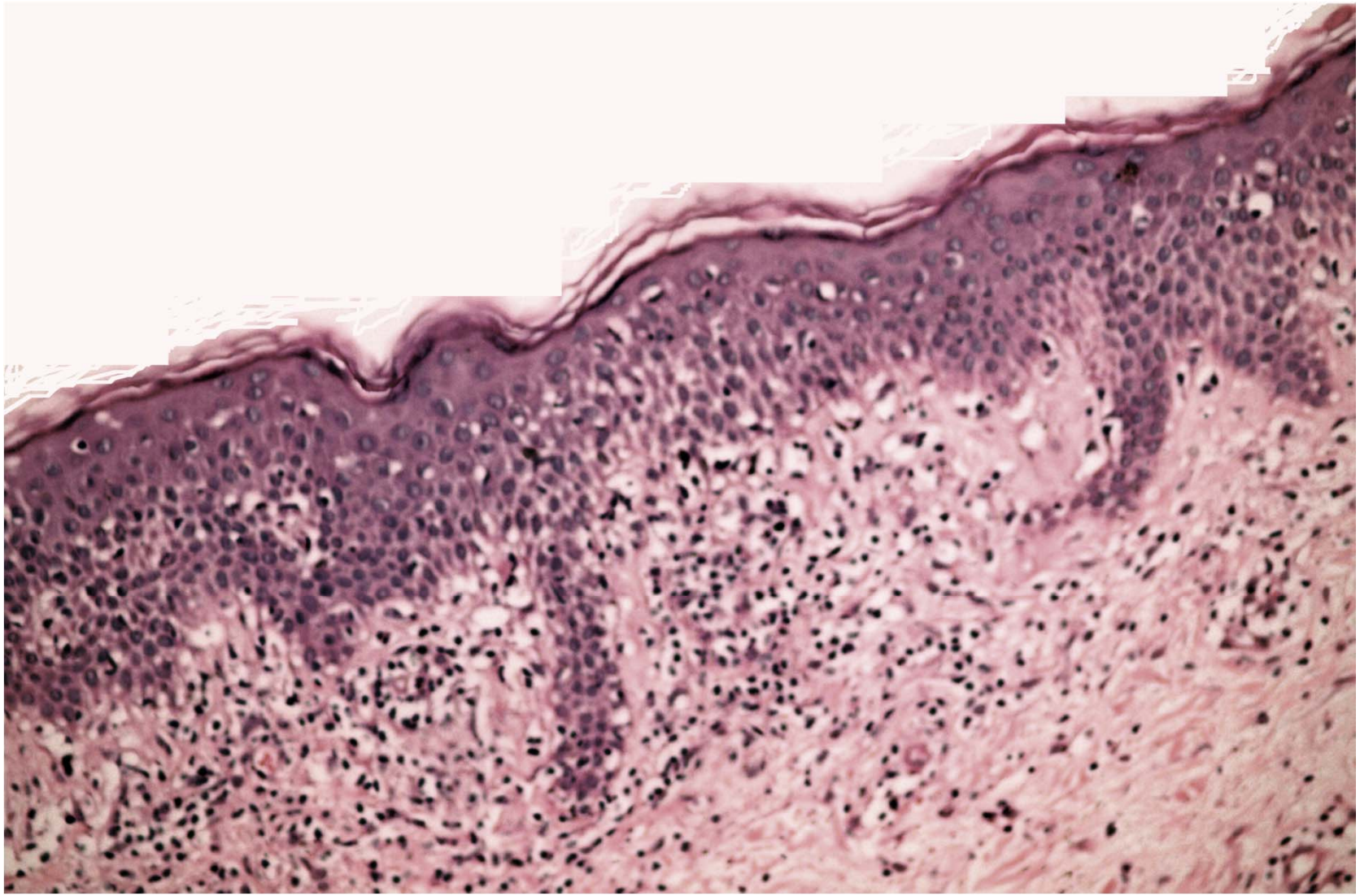
ts



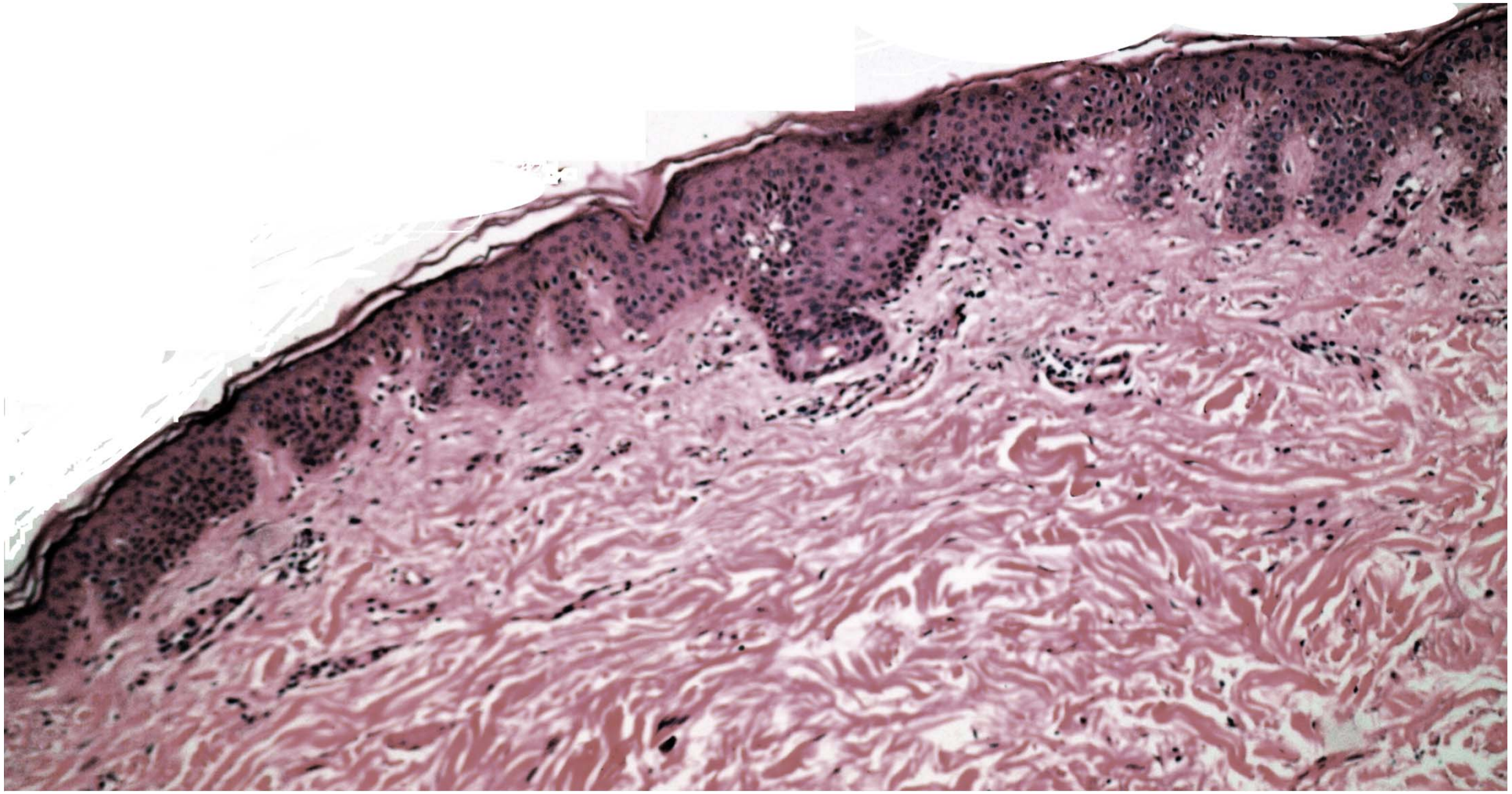
tö



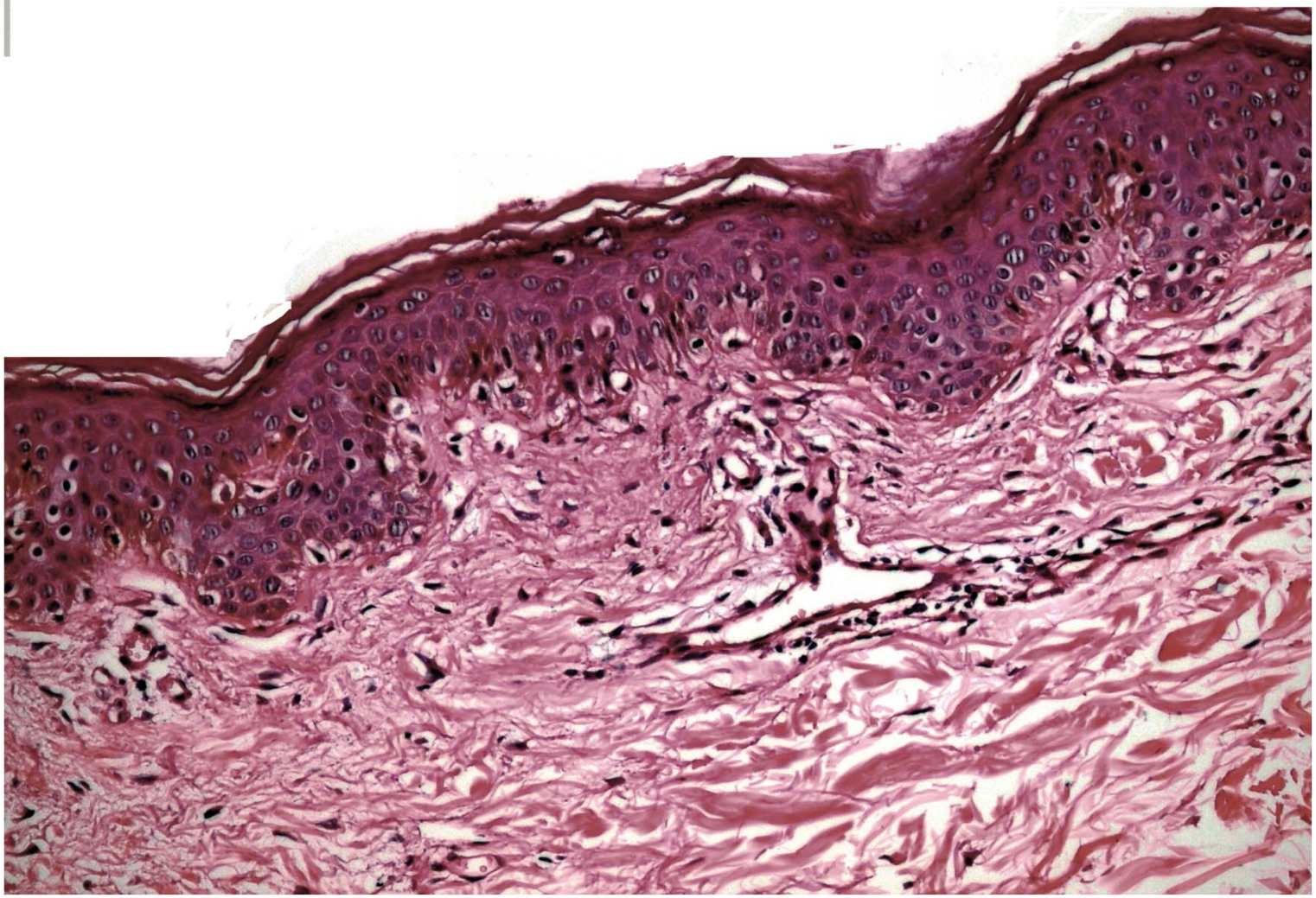
tö



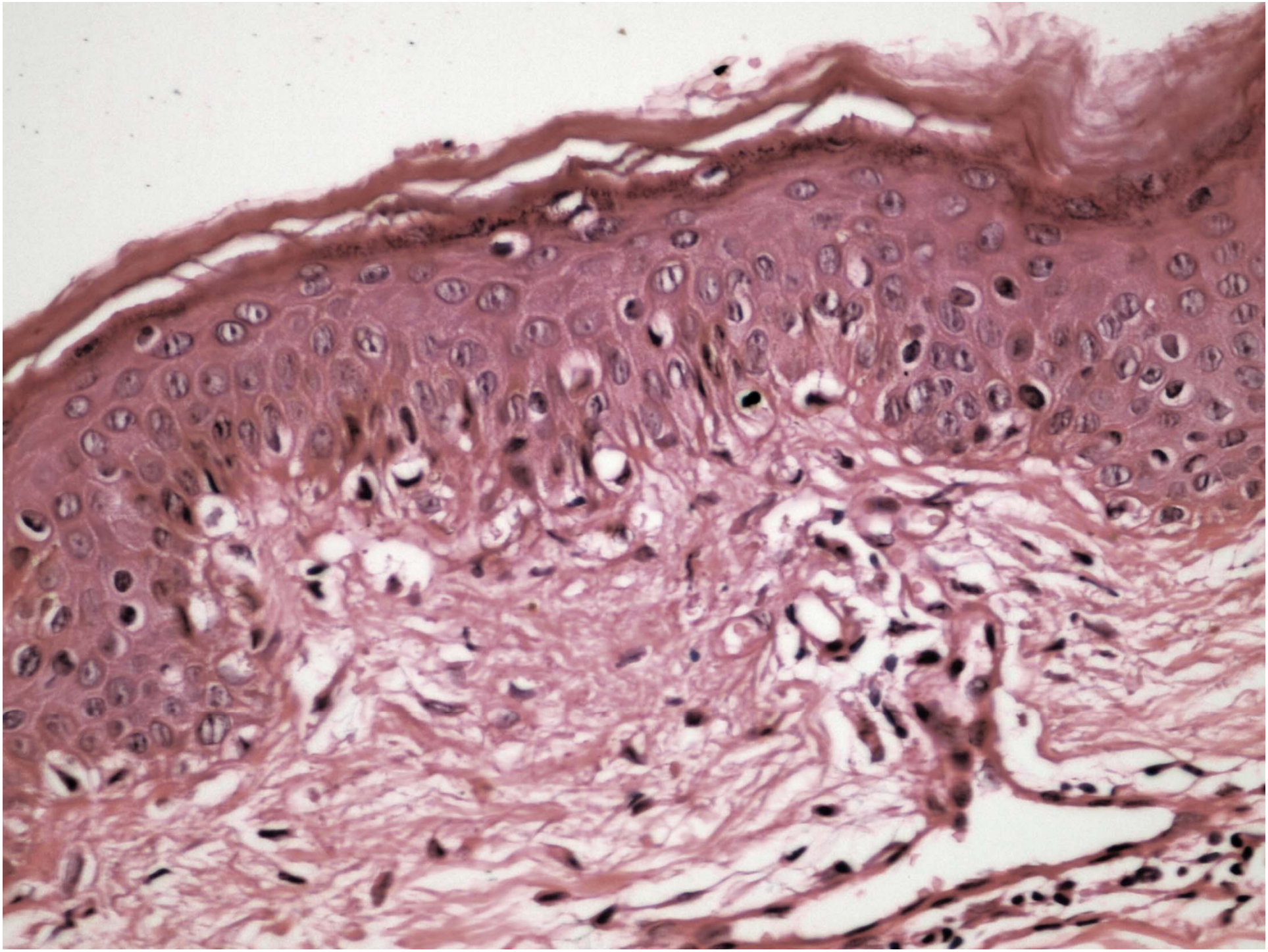
tö



ts



ts



Histopathological Changes Seen in Mycosis Fungoides Patients After Phototherapy

Duygu Dusmez Apa, MD, Ebru Serinsoz Pfeiffer, MD, PhD, Kiymet Baz, MD, Emine Arzu Kanik, PhD, and Pinar İnandioğlu, MD

TABLE 1. Histomorphologic Parameters

Histomorphological Feature	Biopsy				Response			
	Before (n = 23)	After (n = 23)	Specificity %	Sensitivity %	Yes (n = 13)	No (n = 10)	Specificity %	Sensitivity %
Epidermotropism								
Single cells	23	23	0.0	100.0	13	10	0.0	100.0
Halo	23	21	0.0	91.3	11	10	15.4	100.0
Linearly arranged cells	7	2	69.6	8.7	0	2	100.0	20.0
Pagetoid spread	19	12	17.4	52.2	6	6	53.8	60.0
Pautrier microabscesses	13	6	43.8	26.0	2	4	84.6	40.0
Stratum corneum								
Normal	12	12	47.8	52.2	5	7	61.5	70.0
Parakeratosis	5	2	78.3	8.7	1	1	92.3	10.0
Hiperkeratosis	6	9	73.9	39.1	7	2	46.2	20.0
Absence of spongiotic microvesicles	12	9	47.8	39.1	3	6	76.9	60.0
Epidermis								
Normal	6	3	73.9	13.0	2	1	84.6	10.0
Atrophic	16	17	30.4	73.9	10	7	23.1	70.0
Hiperplastic	1	2	95.7	8.7	1	2	92.3	20.0
Inflammatory infiltrate								
Superficial perivascular	10	6	56,5	26.1	4	2	69.2	20.0
Lichenoid	12	7	47.8	30.4	3	4	76.9	40.0
No inflammation	1	10	95.7	43.5	6	4	53.8	40.0
Dilated vessels	6	6	73.9	26.1	4	2	69.2	20.0
Dermal fibrosis								
No	15	10	34.8	43.5	5	5	61.5	50.0
1	8	1	65.2	4.3	0	1	100	10.0
2	0	10	100.0	43.5	6	4	53.8	40.0
3	0	2	100.0	8.7	2	0	84.6	0.0
Other dermal cells								
Extravasated erythrocytes	5	6	78.3	26.1	3	3	76.9	30.0
Plasma cells	1	0	95.7	0.0	0	0	100.0	0.0
Eosinophils	4	3	82.6	13.0	2	1	84.6	10.0
Melanophages	14	10	39.1	43.0	3	7	76.9	70.0

CLINICOPATHOLOGIC CORRELATION

Histopathological Changes Seen in Mycosis Fungoides Patients After Phototherapy

Duygu Dusmez Apa, MD, Ebru Serinsoz Pfeiffer, MD, PhD, Kiymet Baz, MD, Emine Arzu Kanik, PhD, and Pinar İnandioğlu, MD

TABLE 2. SS ($P < 0.05$) and CIs of the Association Between Histomorphological Parameters Before and After Therapy

Parameter	Feature	CI %	SS
Single cells	Sensitive	85.18 to 100	$P < 0.0001$
Parakeratosis	Specific	56.30 to 92.54	$P = 0.0066$
Epidermal hyperplasia	Specific	78.05 to 99.89	$P < 0.0001$
No inflamation	Specific	78.05 to 99.89	$P < 0.0001$
Two and 3 dermal fibrosis	Specific	85.18 to 100.0	$P < 0.0001$
Erythrocytes	Specific	56.30 to 92.54	$P = 0.0066$
Plasma cells	Specific	78.05 to 99.89	$P < 0.0001$
Eosinophils	Specific	61.22 to 95.05	$P = 0.018$

CI, confidence intervals; SS, Statistical Significance.

TABLE 3. SS ($P < 0.05$) and CIs of the Association Between Histomorphological Parameters in Responder and Nonresponder Groups

Parameter	Feature	CI %	SS
Linearly arranged cells	Specific	75.29 to 100.0	$P < 0.0001$
Pautrier microabscesses	Specific	54.55 to 98.08	$P = 0.0004$
Parakeratosis	Specific	63.97 to 99.81	$P < 0.0001$
Epidermal hyperplasia*	Specific	63.97 to 99.81	$P < 0.0001$
Dermal fibrosis 1	Specific	75.29 to 100.0	$P < 0.0001$
Dermal fibrosis 3	Specific	54.55 to 98.08	$P = 0.0004$
Plasma cells	Specific	75.29 to 100.0	$P < 0.0001$
Eosinophils	Specific	54.55 to 98.08	$P = 0.0004$

Rather than reporting single epidermal atypical cells, importance should be given to more "active" parameters in posttreatment skin biopsies. These active parameters may be "Pautrier microabscess" and "linearly arranged cells." Pretreatment biopsies should always be reevaluated and mentioned in the final report.

A pathology report of a MF patient who has undergone successful phototherapy should describe changes resulting from phototherapy—such as fibrosis or "lack of dermal inflammation" and the absence of active epidermal cellular changes such as "Pautrier microabscess" or "linearly arranged cells."

TEŞEKKÜRLER