The Royal College of Pathologists
Pathology: the science behind the cure

London, Dermatopathology Study Day 04.12.15

# Pigmented lesions of sun-damaged skin

**W.J. Mooi**

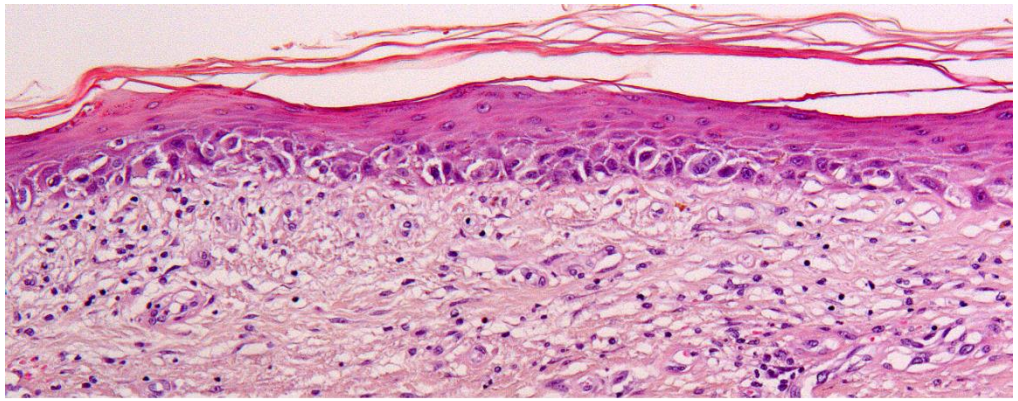
**Department of Pathology,**

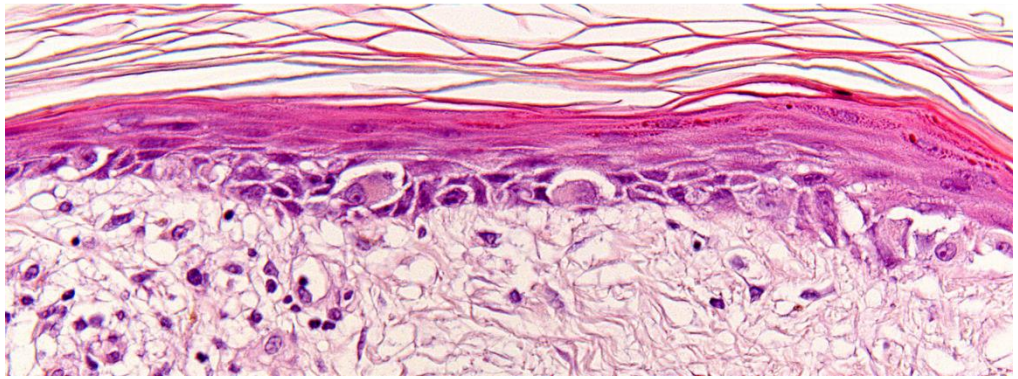
**VU university medical center, Amsterdam**

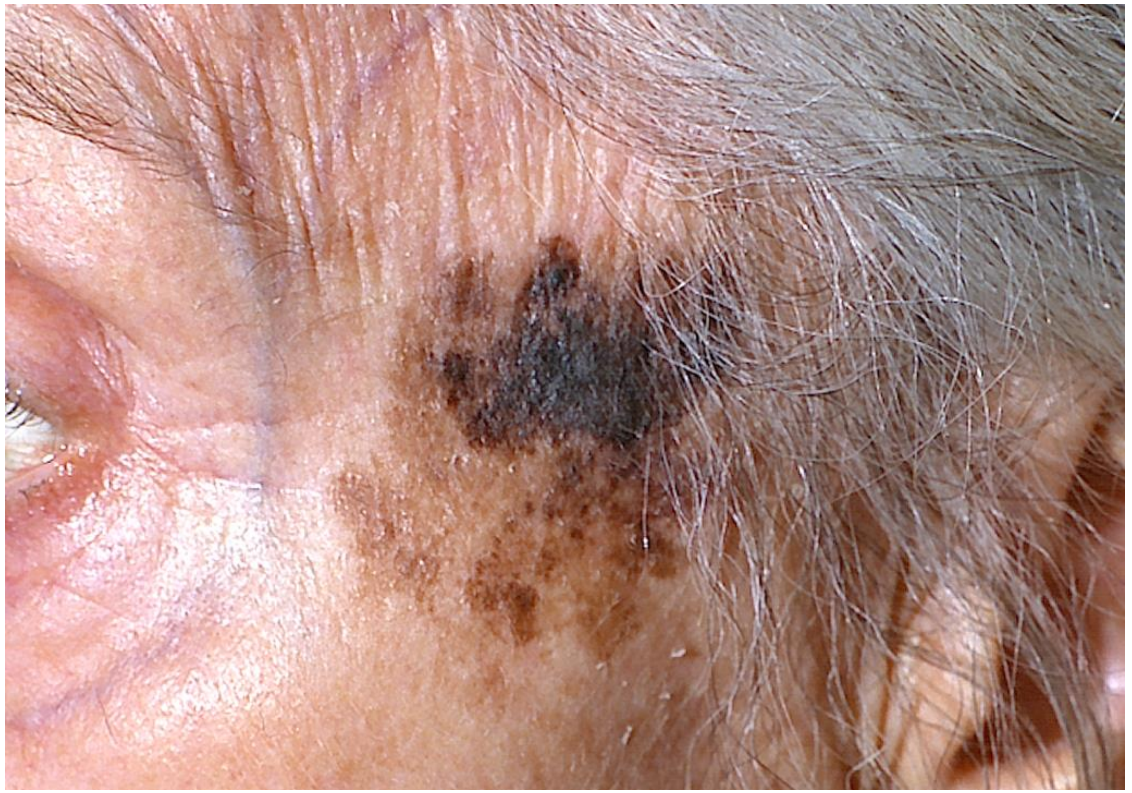
**wj.mooi@vumc.nl**


VITERZO

# Lentigo maligna



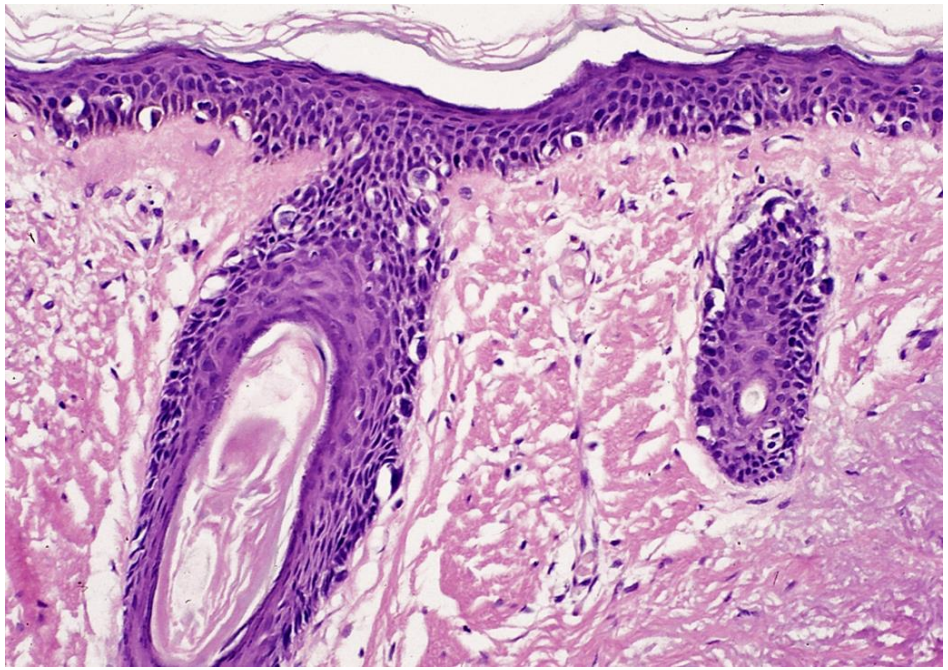


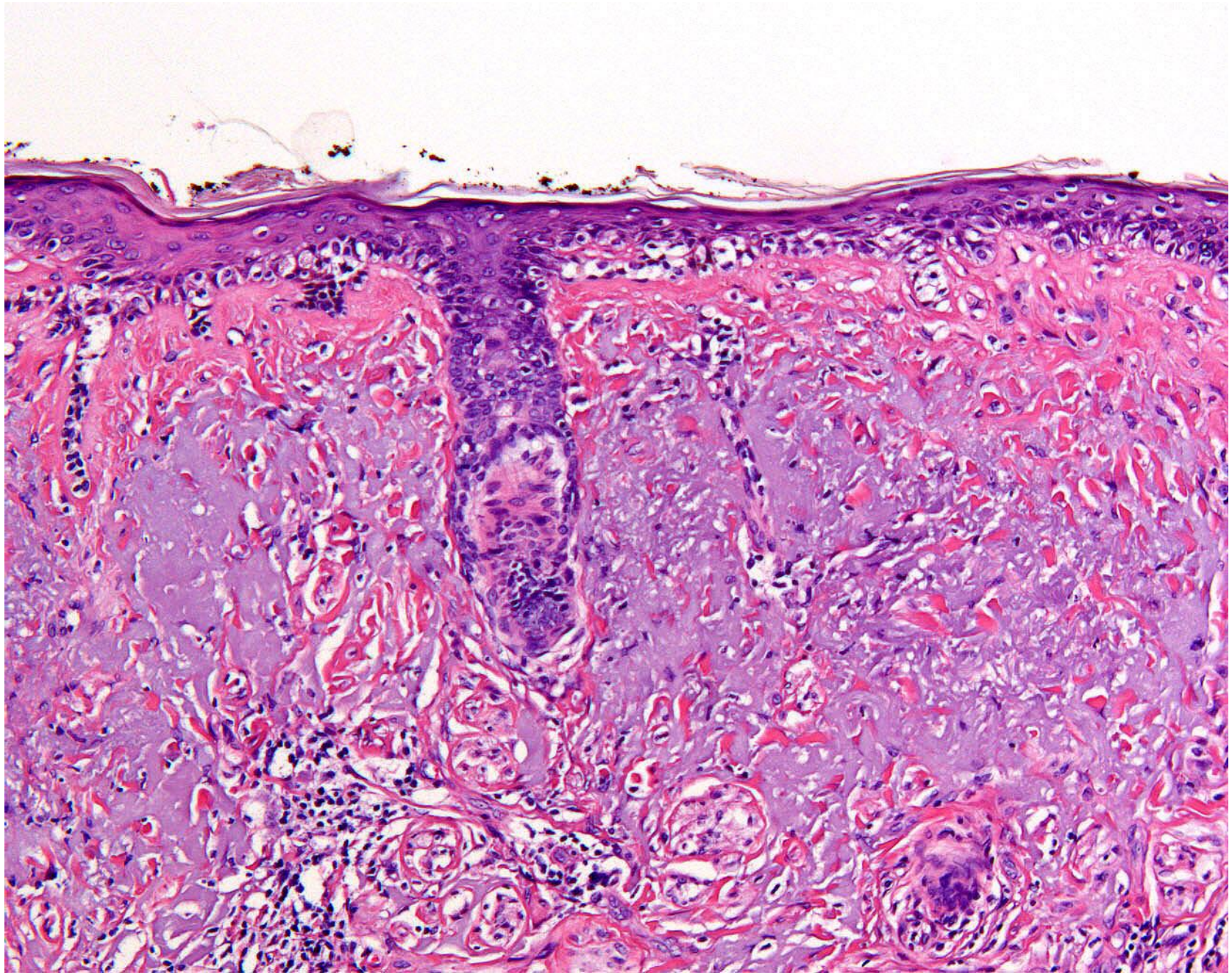


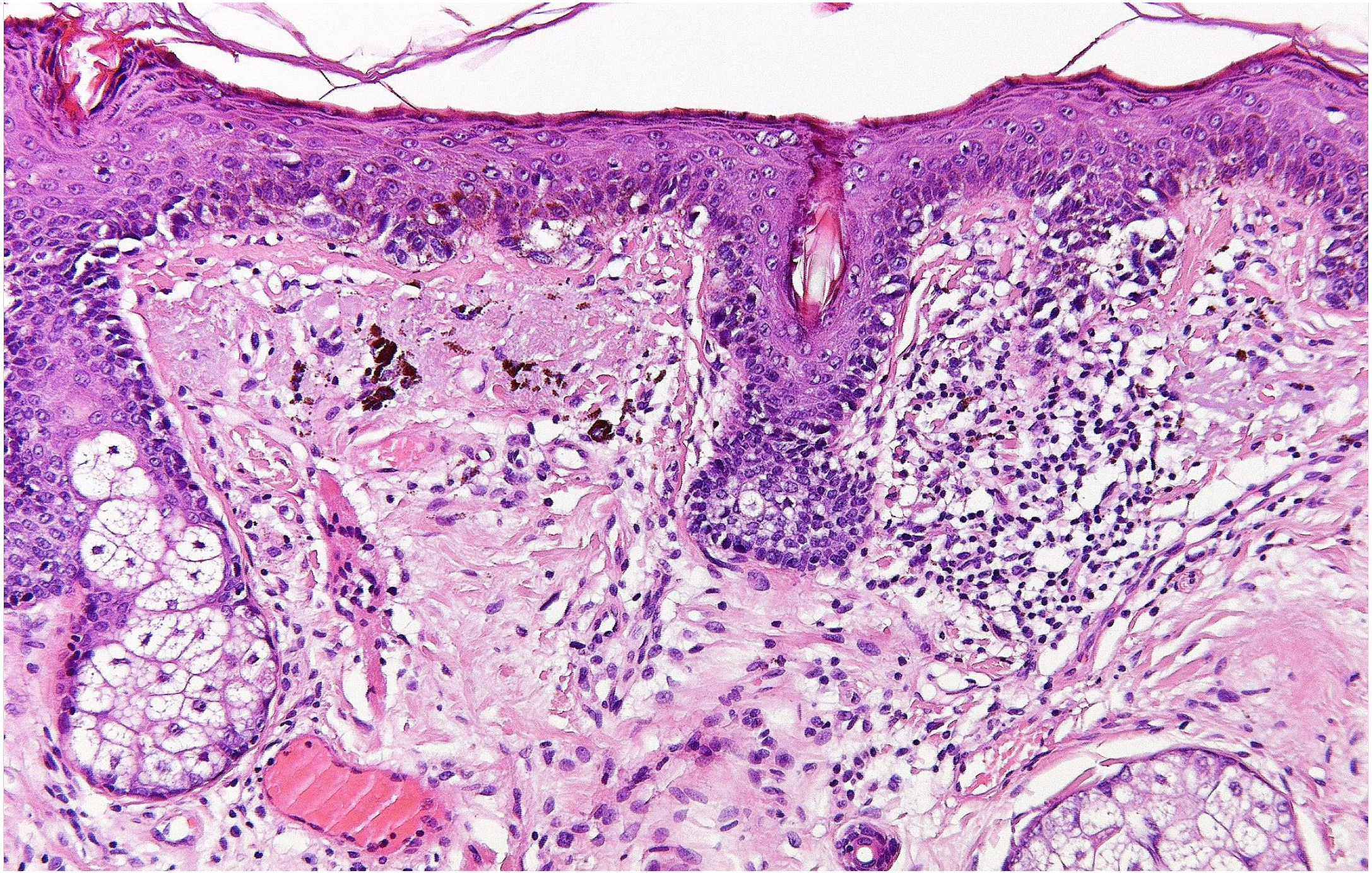
# Lentigo maligna

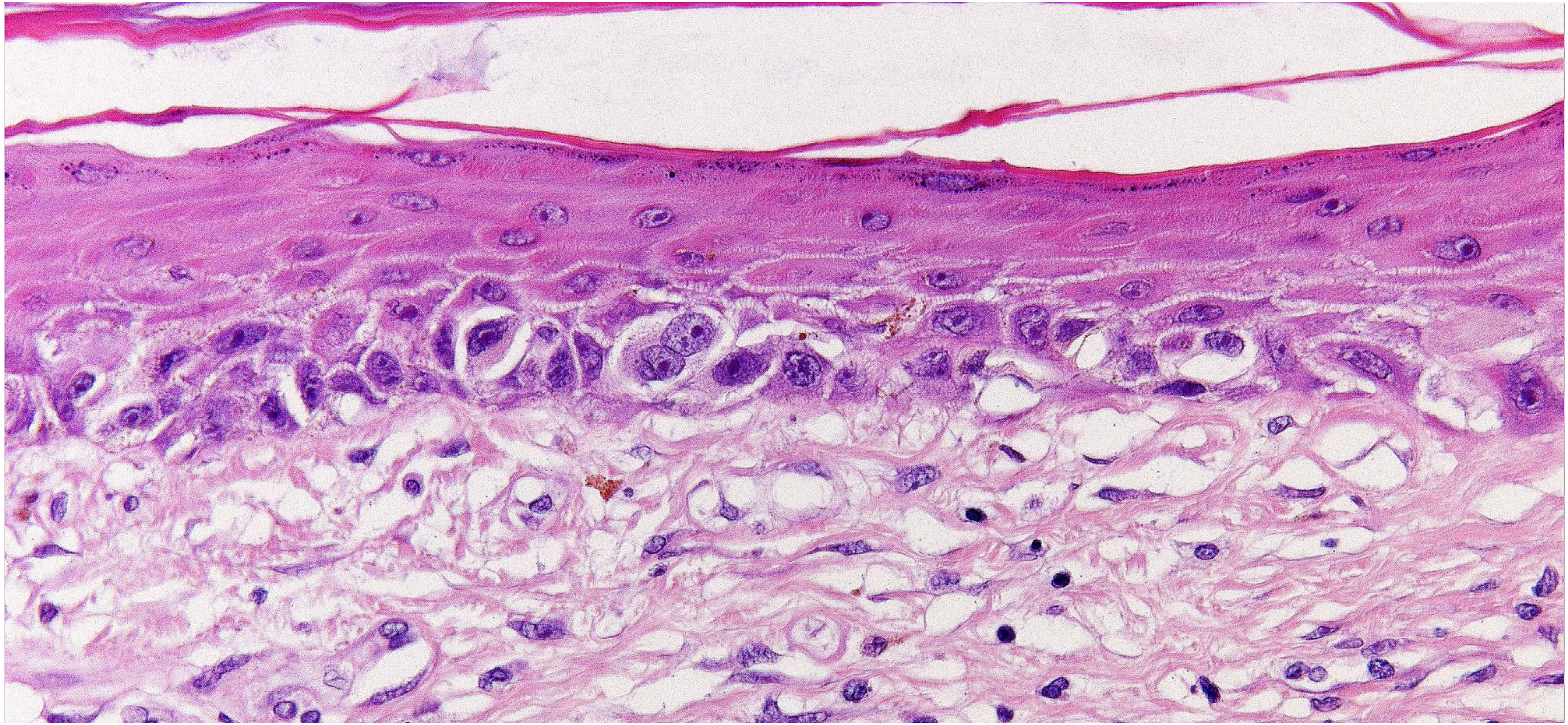
- Defining combination of features: a substantial proliferation of atypical melanocytes predominantly in lentiginous arrangement, limited to the epithelial compartment of sun-damaged skin, and manifesting as a flat, impalpable hyperpigmentation, usually with irregular contours and with variations of pigmentation.

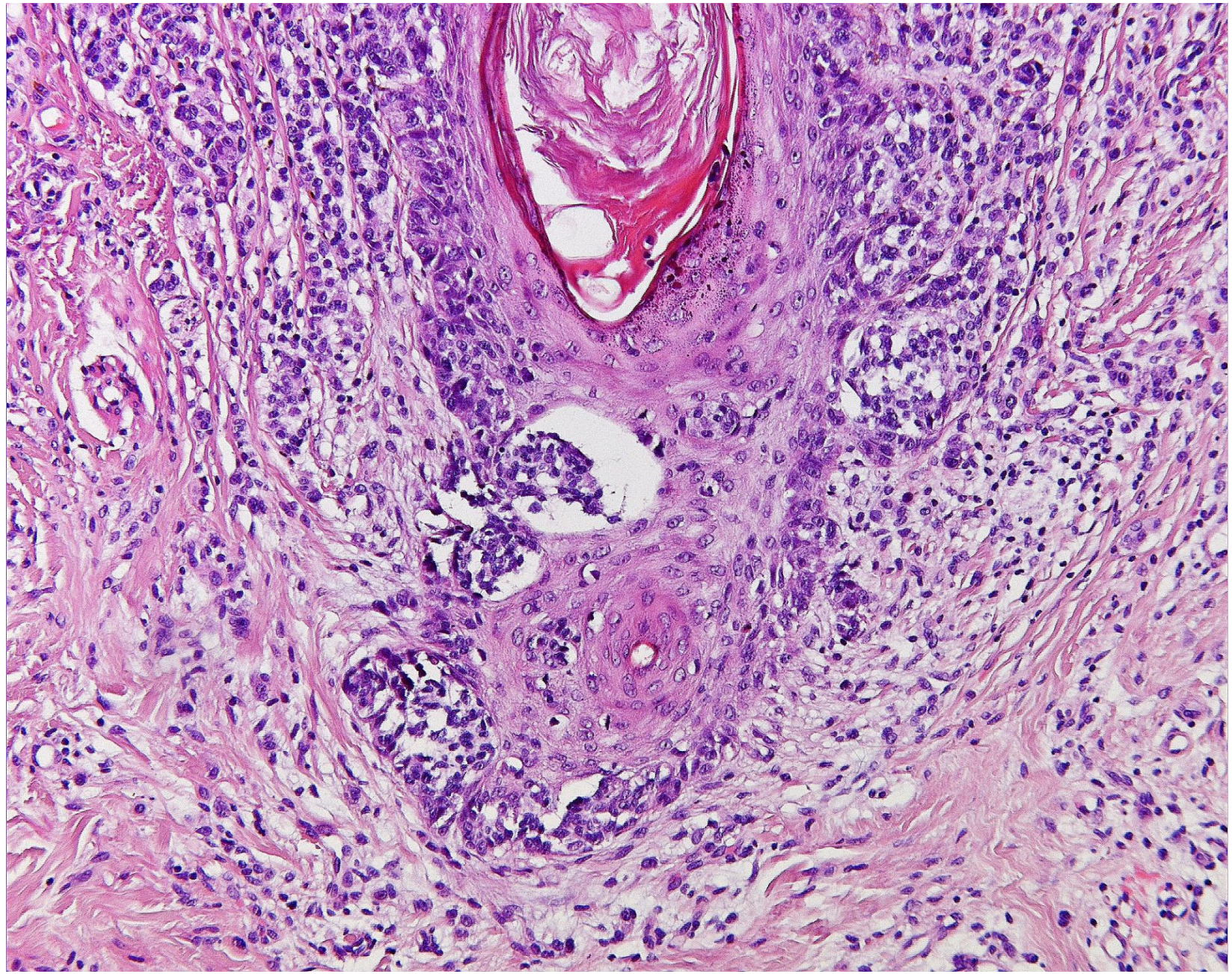
- Spread into hair follicles usually present
- Ascent of atypical melanocytes commonly present
- Nests are absent or present
- The epidermis is commonly flat and thin, but rete ridges may be present
- Cellularity, ascent, nesting, degree of atypia vary within the same lesion
- Lichenoid inflammatory response sometimes





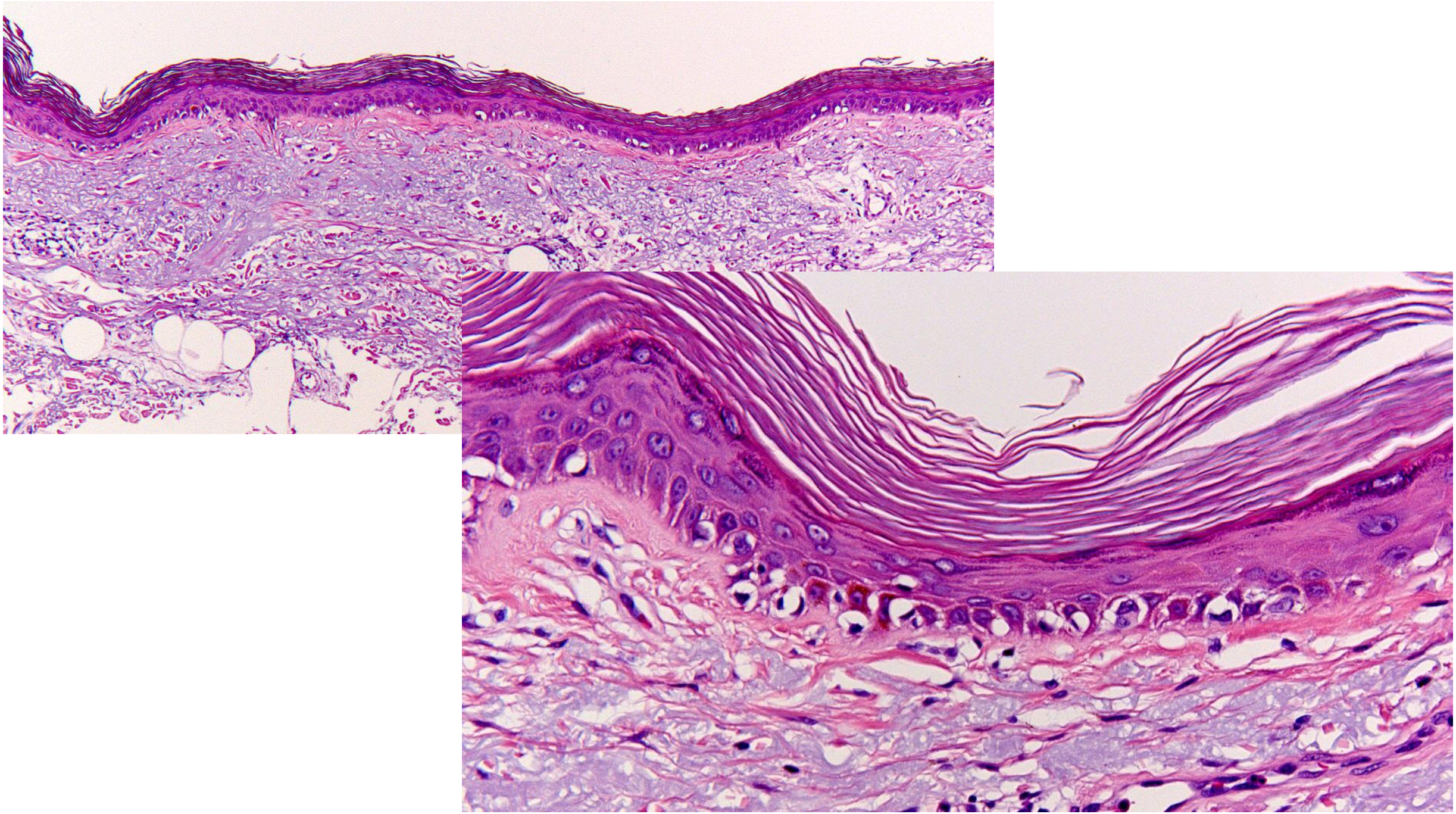


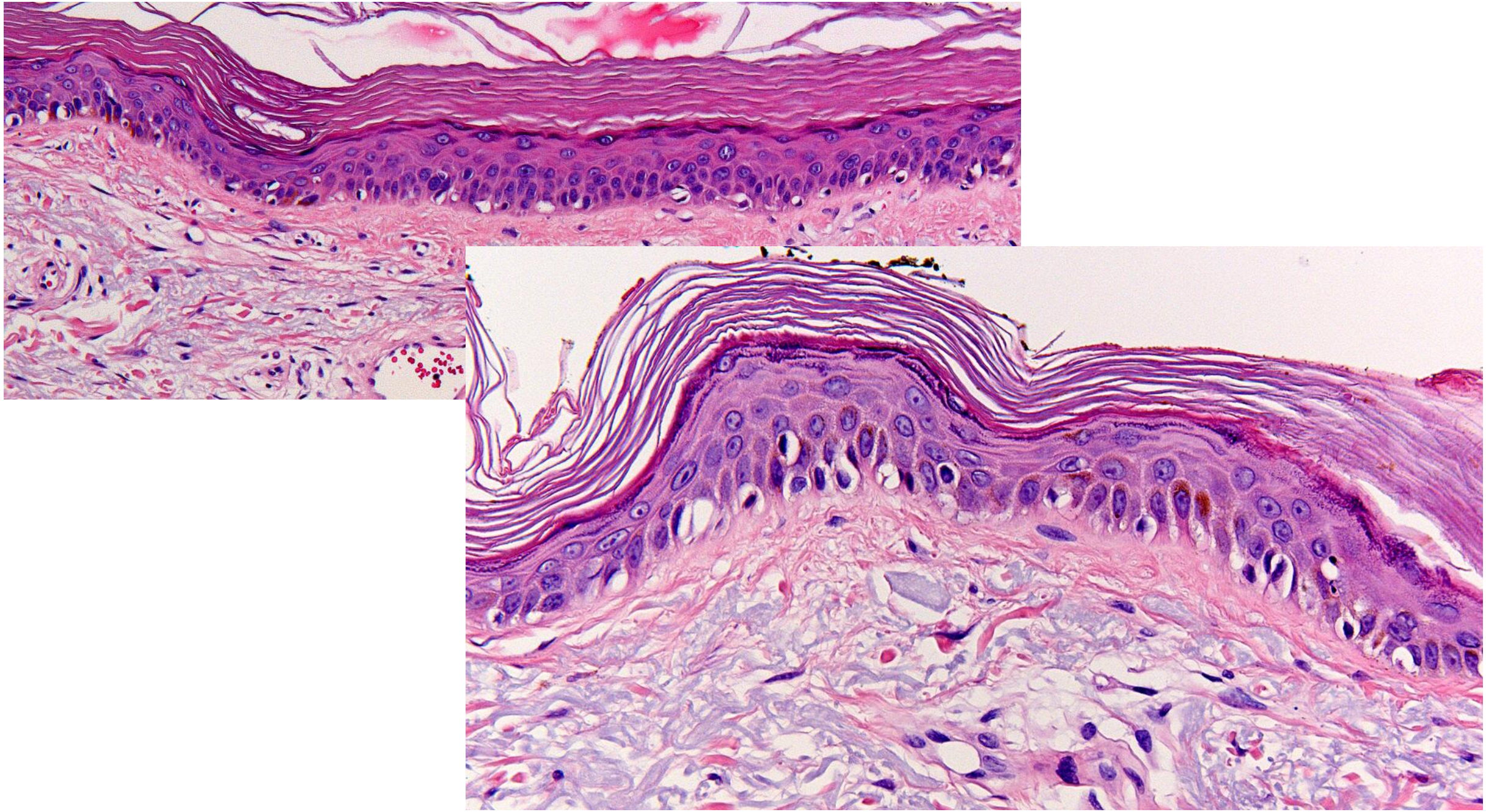




# Lentigo maligna: some diagnostic problems

- Distinction between paucicellular LM and reactive melanocytic hyperplasia in sun-damaged skin
- ‘Grading’ of severity; assessment of risk of invasion: compromised by variations within the same lesion
- Interpretation of small numbers of dermal melanocytes in conjunction with LM
  - Small dermal melanocytic naevi
  - Scattered isolated dermal ? pre-existent melanocytes
- Lichenoid inflammatory response obscuring LM





# Paucicellular lentigo maligna versus reactive melanocyte hyperplasia in sun-damaged skin

| LENTIGO MALIGNA | REACTIVE MELANOCYTIC HYPERPLASIA |
|---|---|
| Lentiginous spread with or without nests | Lentiginous spread only; no nests |
| Melanocytes often directly side-to-side (rather than separated by basal keratinocytes) | Melanocytes usually not directly side-to-side |
| Spread well into hair follicles | Spread into hair follicles is not marked |
| Ascent common | Ascent uncommon |
| Marked cytological atypia in at least some of the cells common | Marked cytological atypia is uncommon |

The assessment of resection margins in LM may yield less than equivocal results, because of overlap of features of LM and reactive melanocyte proliferation and atypia

# Paucicellular lentigo maligna versus reactive melanocyte hyperplasia in sun-damaged skin

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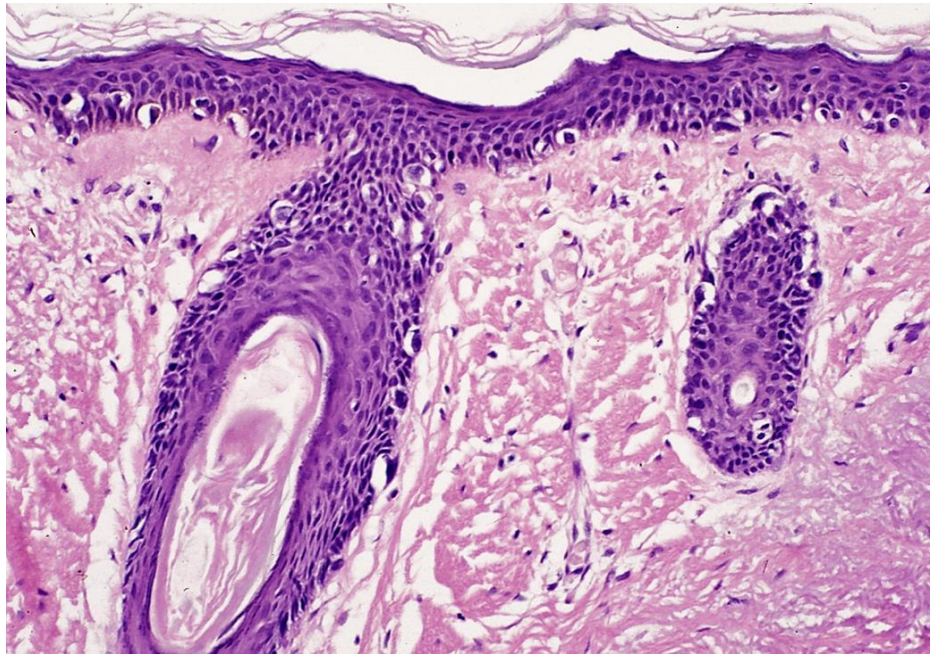
| Ascent common | Ascent uncommon |
| Marked cytological atypia in at least some of the cells common | Marked cytological atypia is uncommon |
| Clinically: single hyperpigmented lesion | Clinically: no obvious single pigmented lesion |

The assessment of resection margins in LM may yield less than equivocal results, because of overlap of features of LM and reactive melanocyte proliferation and atypia

# Lentigo maligna

- Defining features: a substantial proliferation of atypical melanocytes predominantly in lentiginous arrangement, within the epithelial compartment of sun-damaged skin, ***manifesting as a flat impalpable hyperpigmentation, usually with irregular contours and variations of pigmentation.***

- Spread into hair follicles usually present
- Ascent of atypical melanocytes commonly present
- Nests are absent or present
- Rete ridges may be present and may be elongated (e.g., overgrowth of LM on solar lentigo)
- Cellularity, ascent, nesting, degree of atypia are variable within the same lesion
- Lichenoid inflammatory response may closely mimick lichenoid keratosis



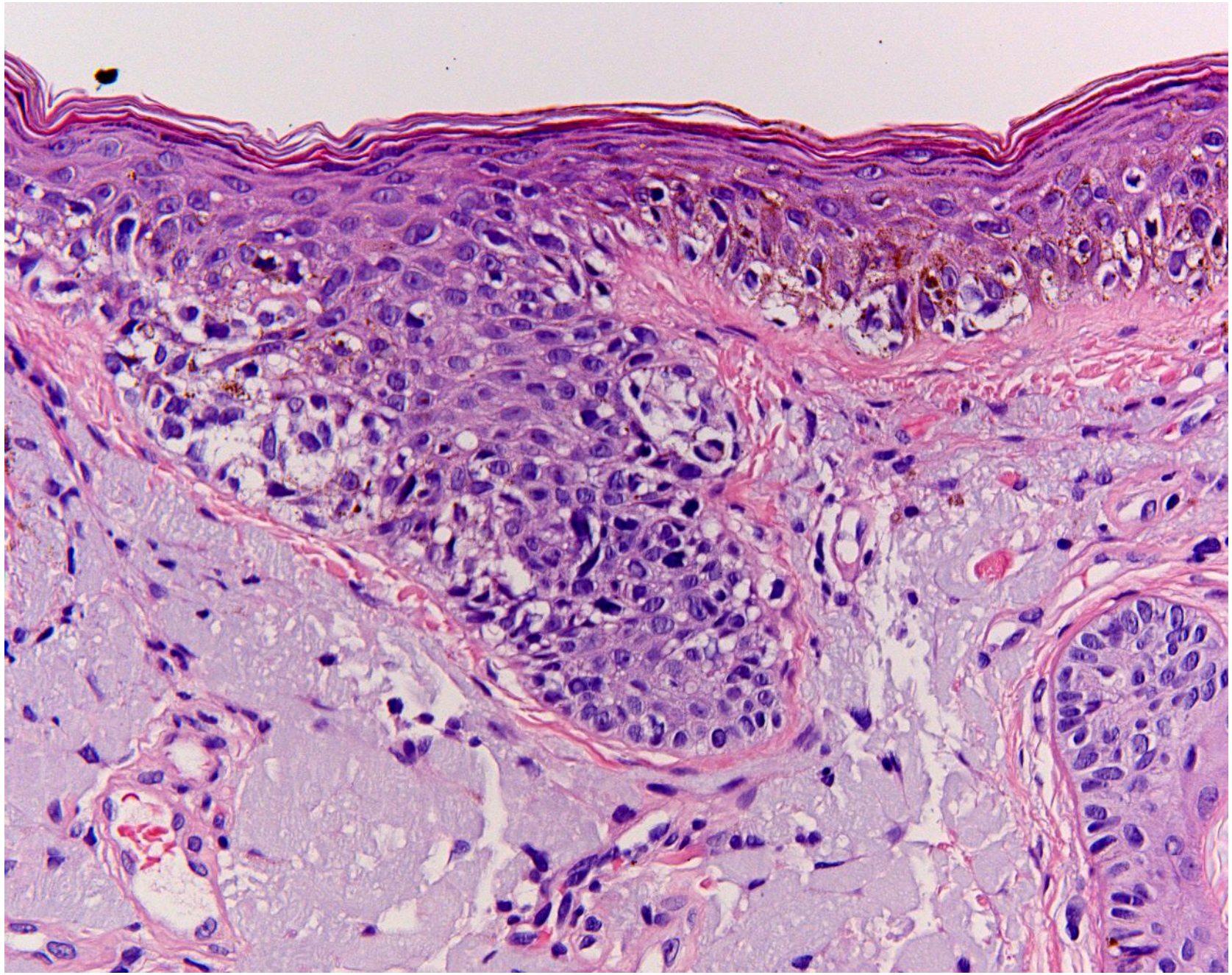

Hokusai: The Great Wave off Kanagawa

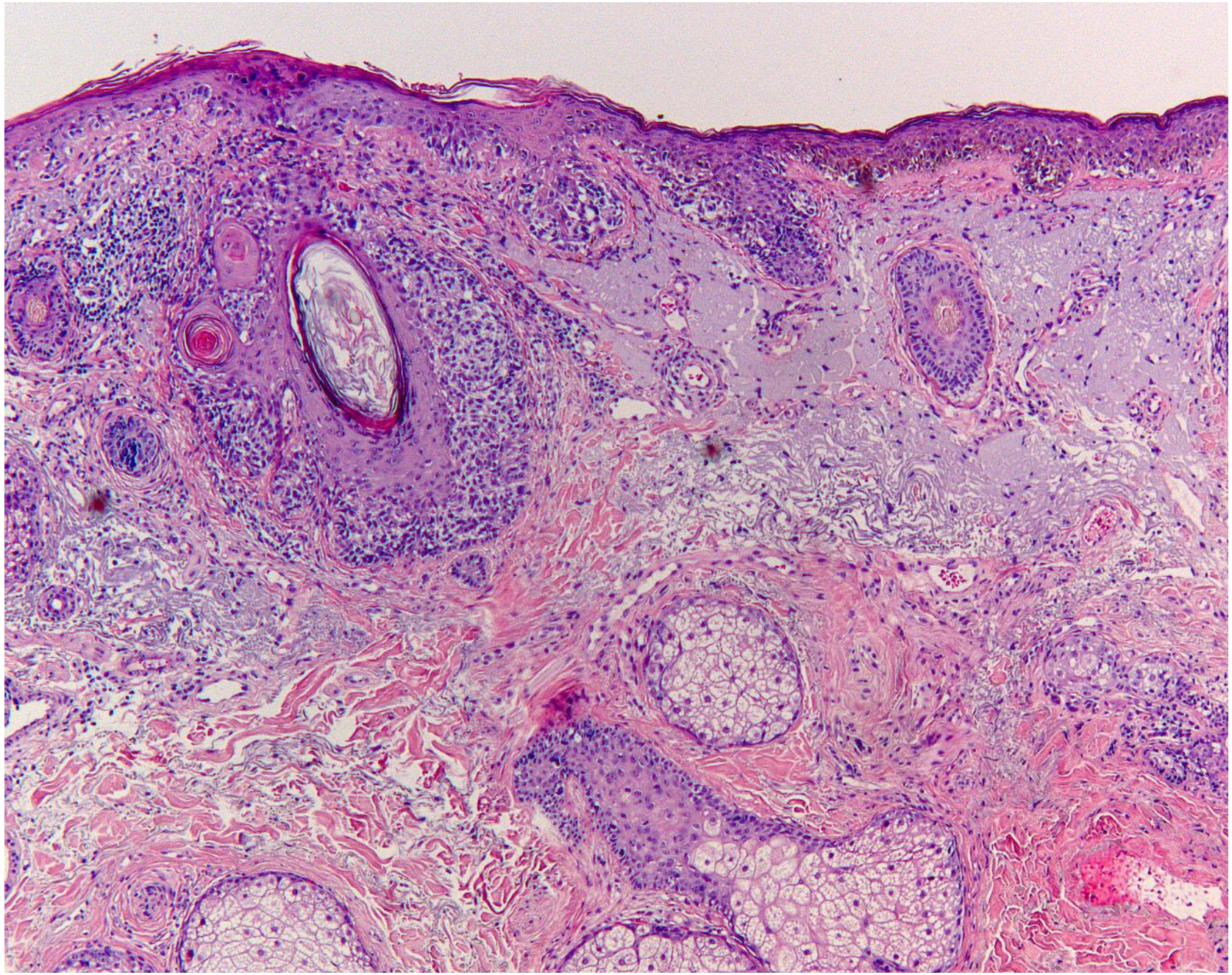
Review of 50 cases of lentigo maligna: two subsets of lesions.

1. Lentigo maligna: atypical melanocytic hyperplasia *only*;
2. Malignant melanoma in situ, lentigo maligna type: melanocytic hyperplasia and, *in addition*:
    1. individual cells and nests of cells at varying layers of the epidermis,
    2. confluence of the melanocytes replacing the basilar region,
    3. uniformity of the cytological atypia,
    4. nesting of uniformly atypical melanocytes.

It is proposed that the lesions that have been termed lentigo maligna represent a spectrum of atypia and that the application of some of the traditional features for the diagnosis melanoma may permit the segregation of more and less aggressive lesions.

Flotte TJ, Mihm MC. Lentigo maligna and malignant melanoma in situ, lentigo maligna type. *Hum Pathol*. 1999; **30**: 533-6.





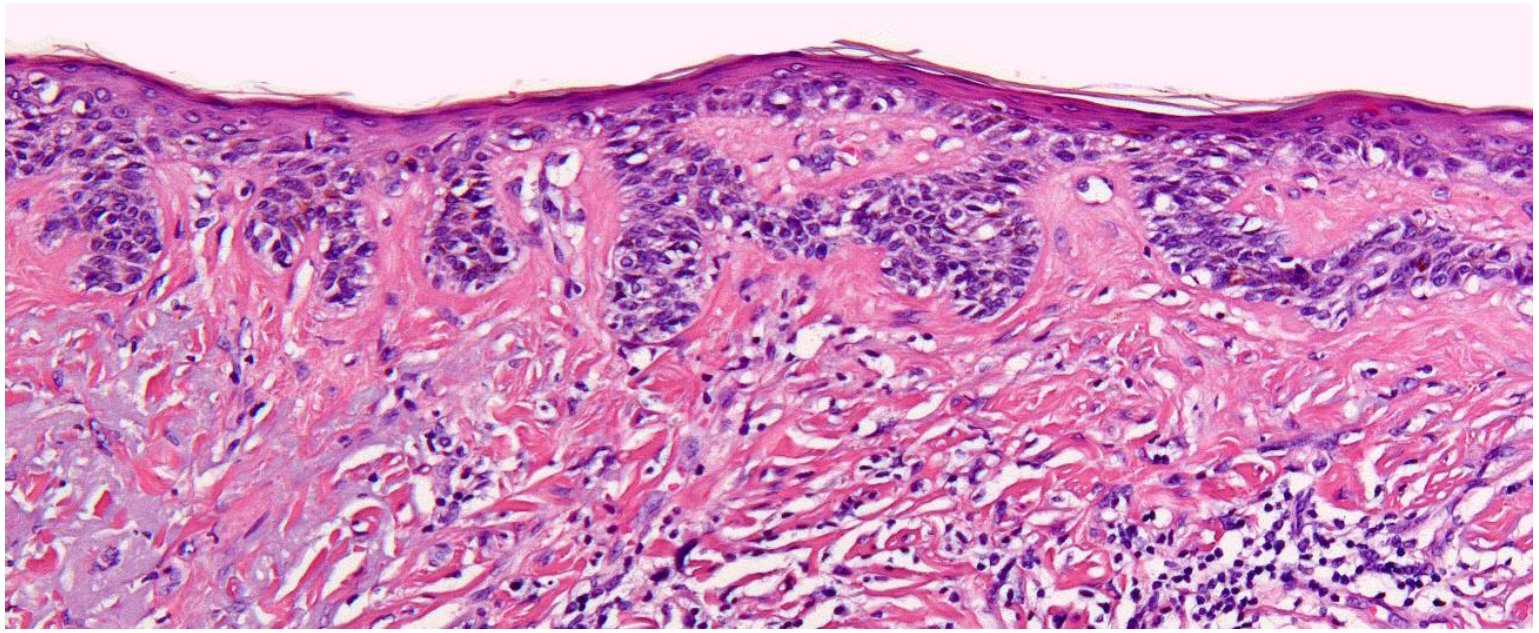
The intraepidermal component of 42 consecutive cases of invasive malignant melanoma, lentigo maligna type was evaluated. All of the cases evaluated showed features diagnostic of malignant melanoma in situ, lentigo maligna type, in the epidermis overlying the invasive dermal component.

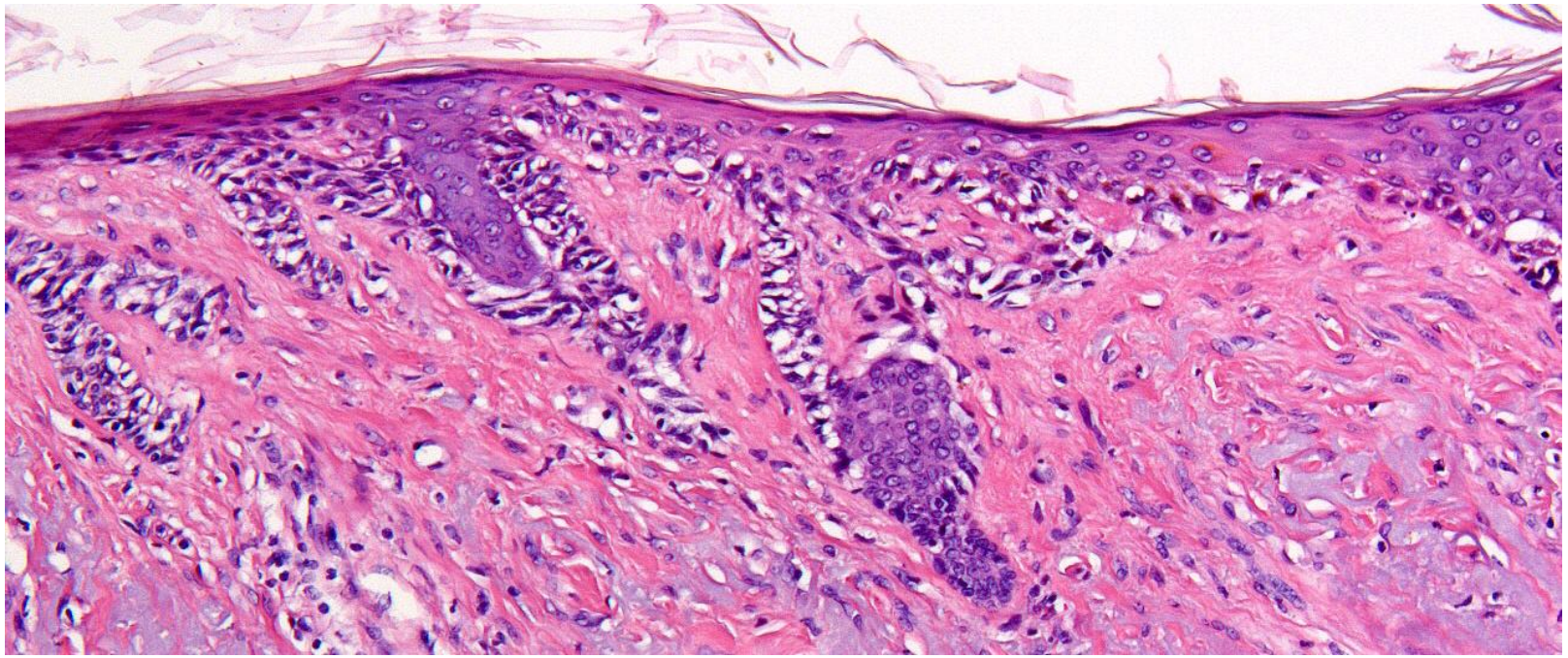
We conclude that **invasive lentigo maligna melanoma arises in association with those lesions that we have termed *malignant melanoma in situ, lentigo maligna type***, which may represent a step in the progression between atypical melanocytic hyperplasia (lentigo maligna) and invasive melanoma. This finding supports the distinction of these entities and may have therapeutic implications.

Tannous ZS, Lerner LH, Duncan LM, Mihm MC, Flotte TJ.
Progression to invasive melanoma from malignant melanoma in situ, lentigo maligna type. *Hum Pathol*. 2000; **31**: 705-8

# Lentigo maligna: pitfalls resulting from the presence of other lesions

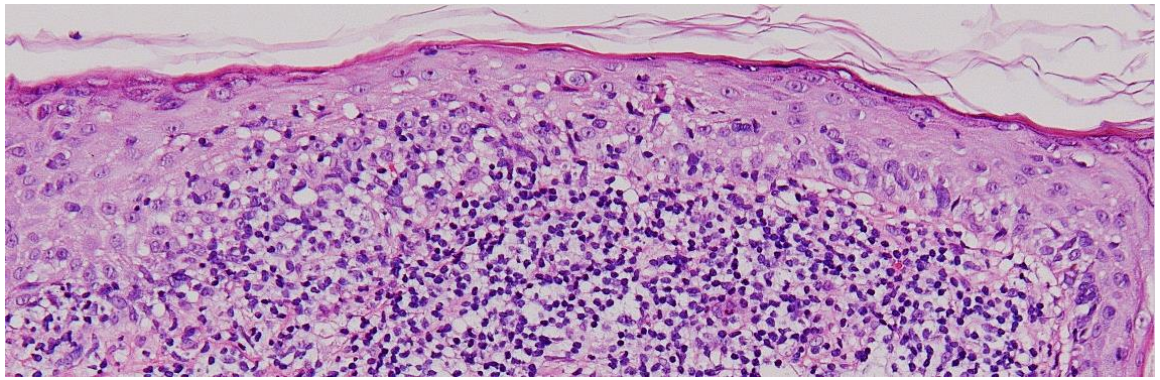
- Solar lentigo
  - Danger: absence of epidermal atrophy may be misconstrued as evidence against LM
- Actinic keratosis
  - Danger: failure to identify LM; misinterpretation of melanocytic proliferation as a reactive process
- Intradermal naevus
  - Danger: misinterpretation as evidence of invasive growth



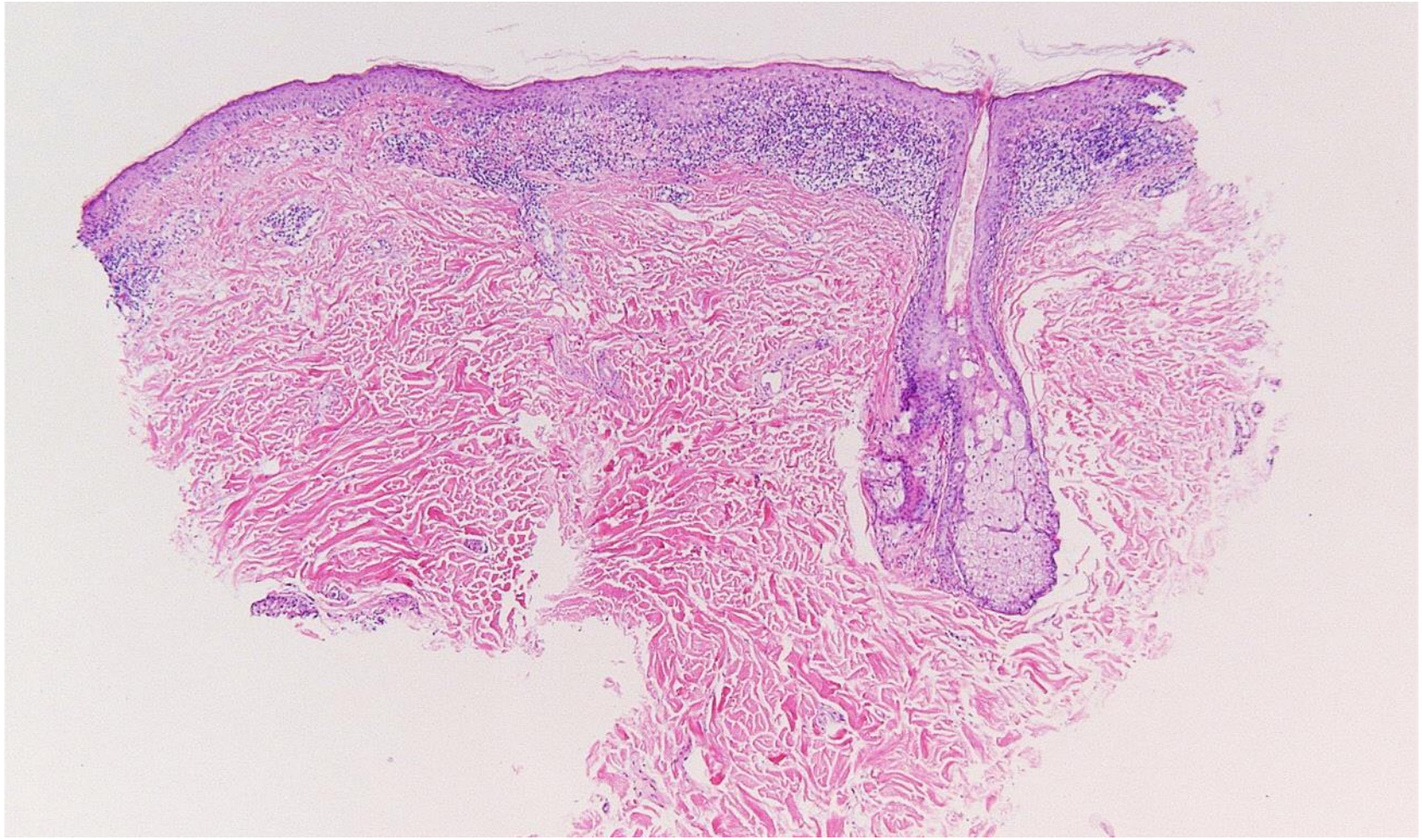


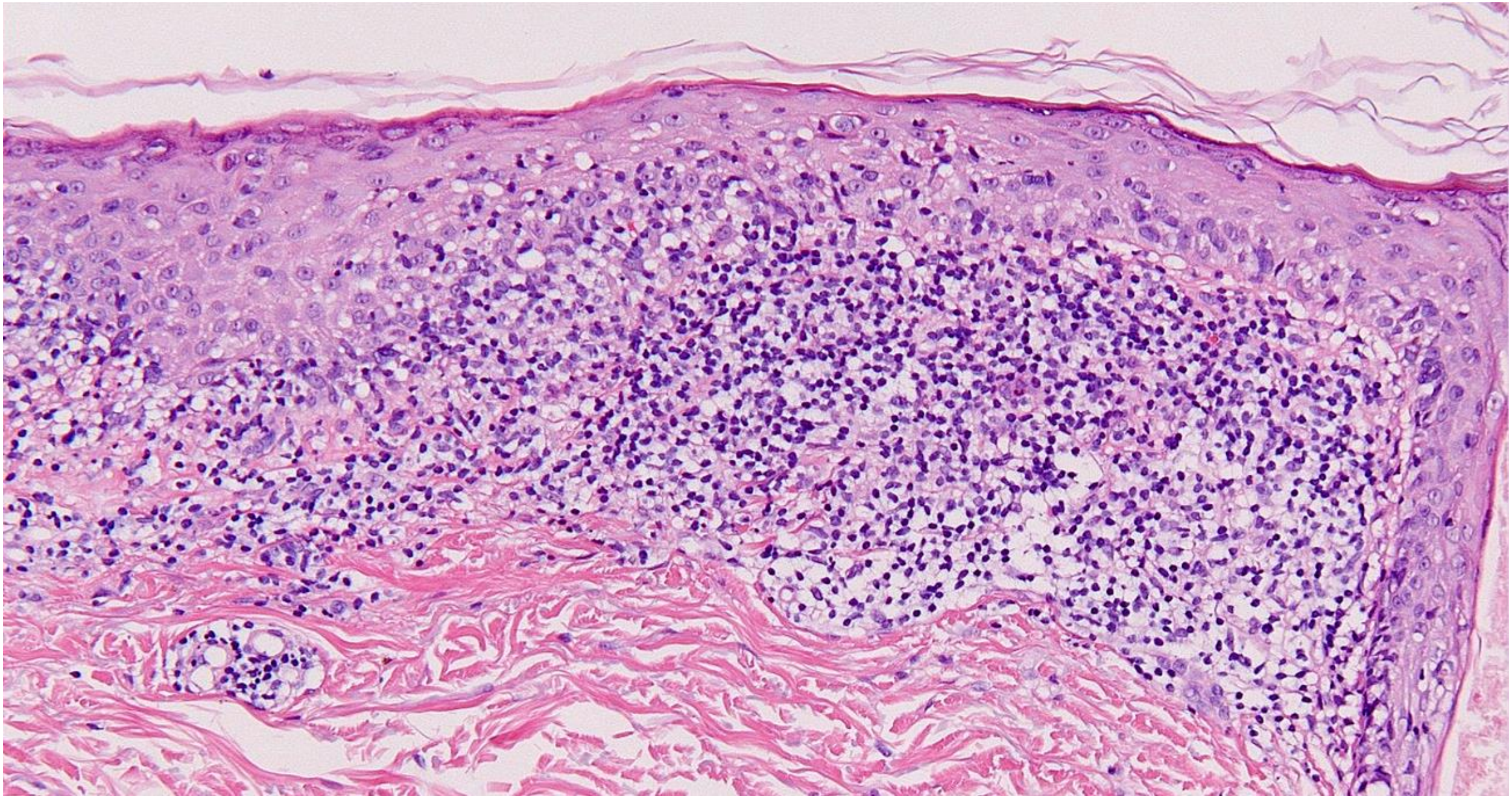
# Lentigo maligna: lichenoid inflammatory response

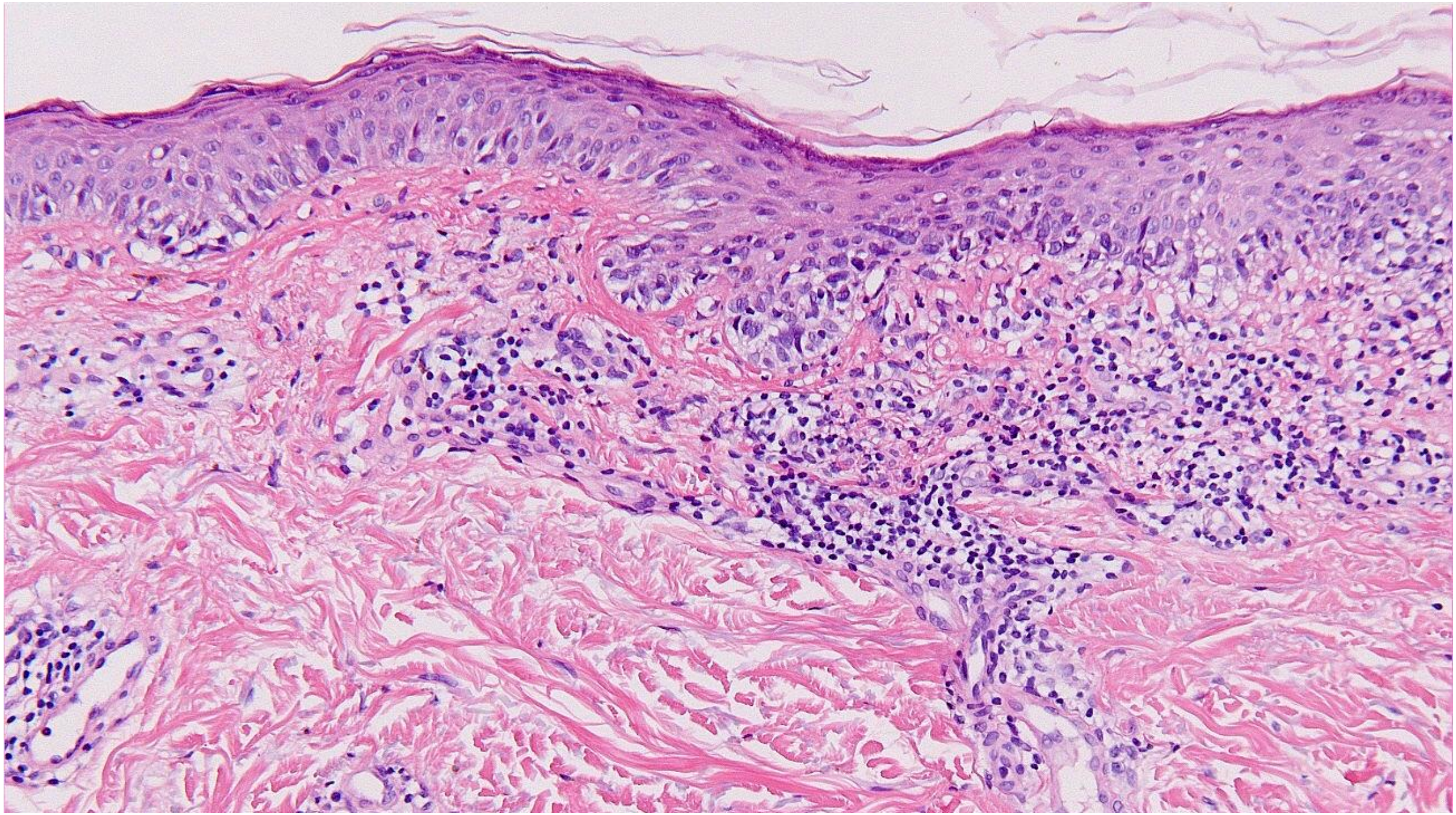
- The atypical melanocytic proliferation may not be noticed, and the lesion may be misinterpreted as lichenoid keratosis, atrophic lichen planus, lupus erythematosus &c.
- Conversely, focal junctional Melan-A positivity in lichenoid inflammation may be misinterpreted as evidence of LM

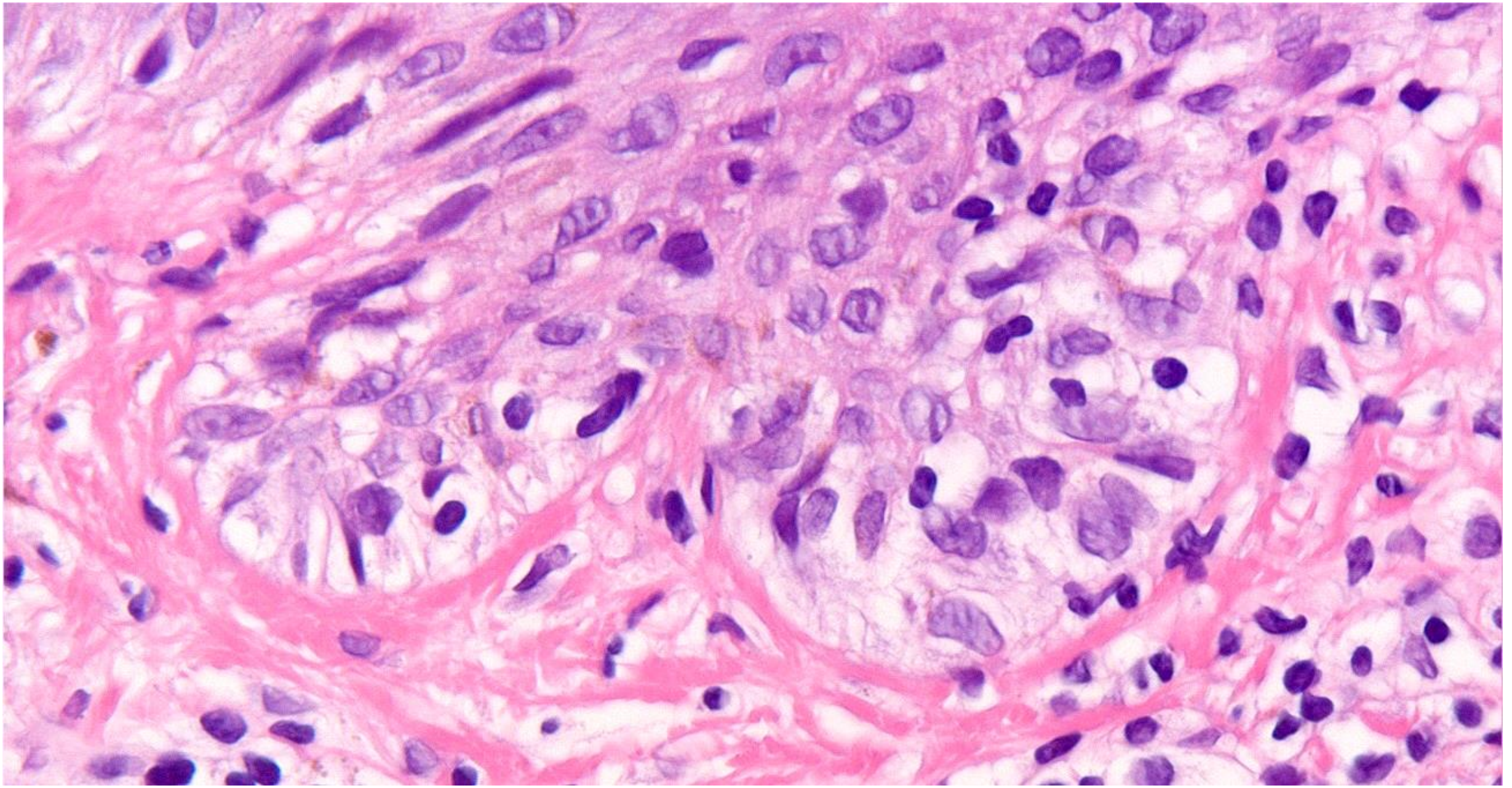


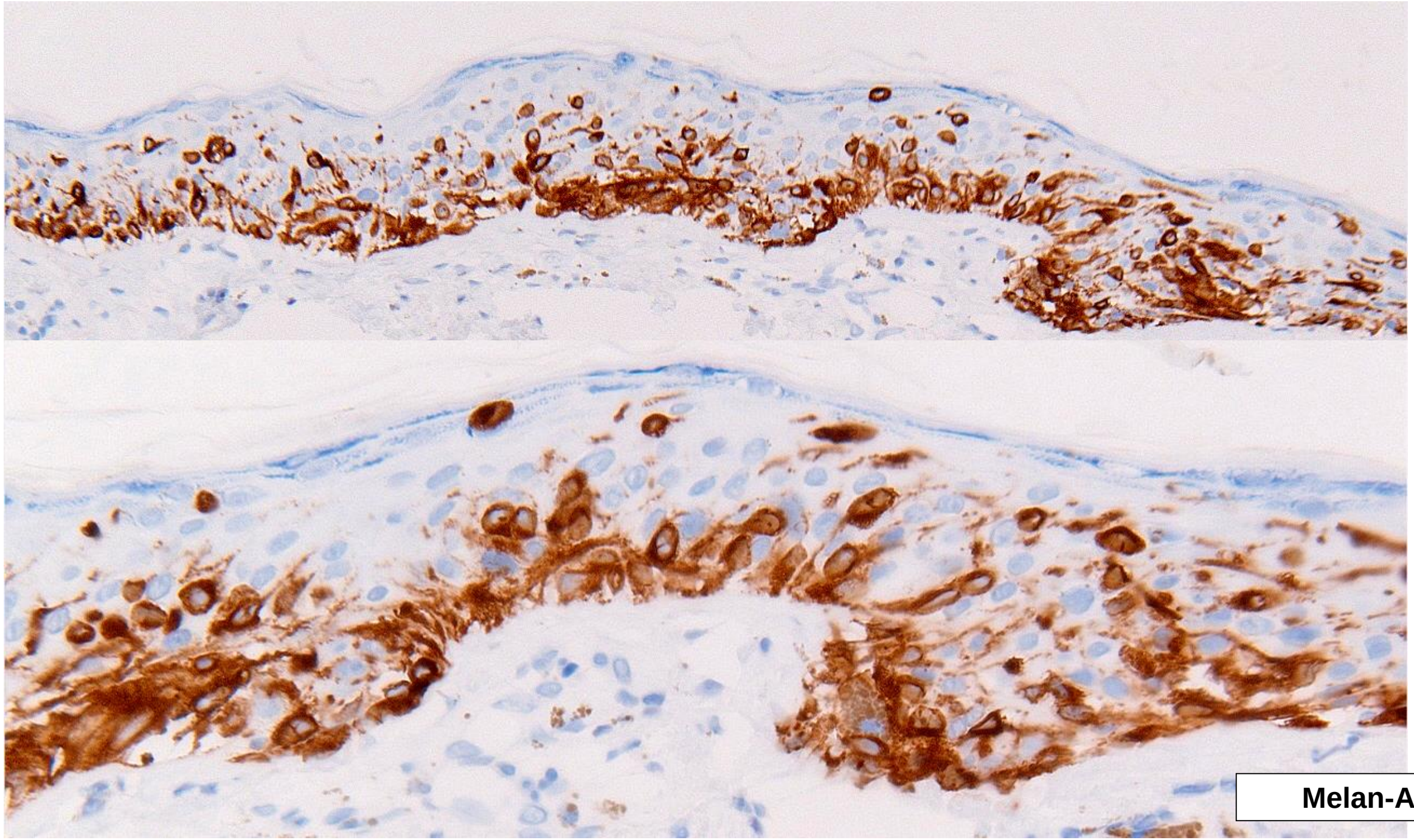
Female, 40 yrs. Punch biopsy, skin of back.
Superficial BCC?











Melan-A

# Ducking Stray "Magic Bullets": A Melan-A Alert

John C. Maize, Jr., M.D., Jack S. Resneck, Jr., M.D.,
Philip E. Shapiro, M.D., Timothy H. McCalmont, M.D., and
Philip E. LeBoit, M.D.

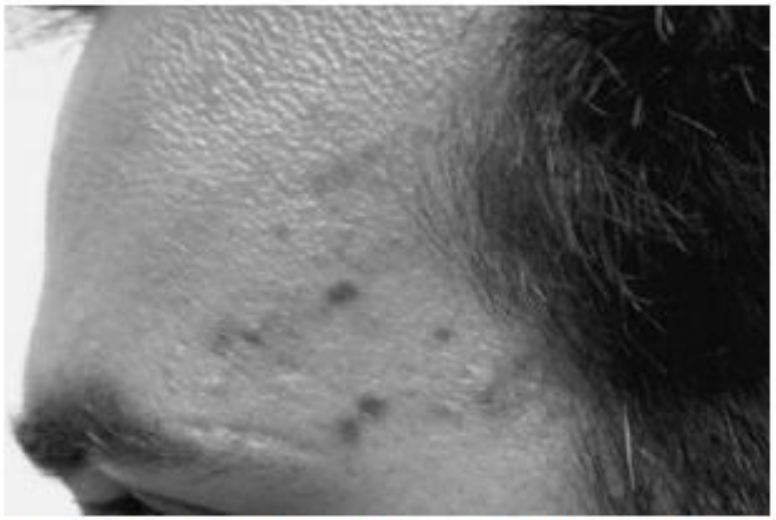


**FIG. 1.** There are ill-defined gray macules on the left temple of this Indian man in his mid-thirties.

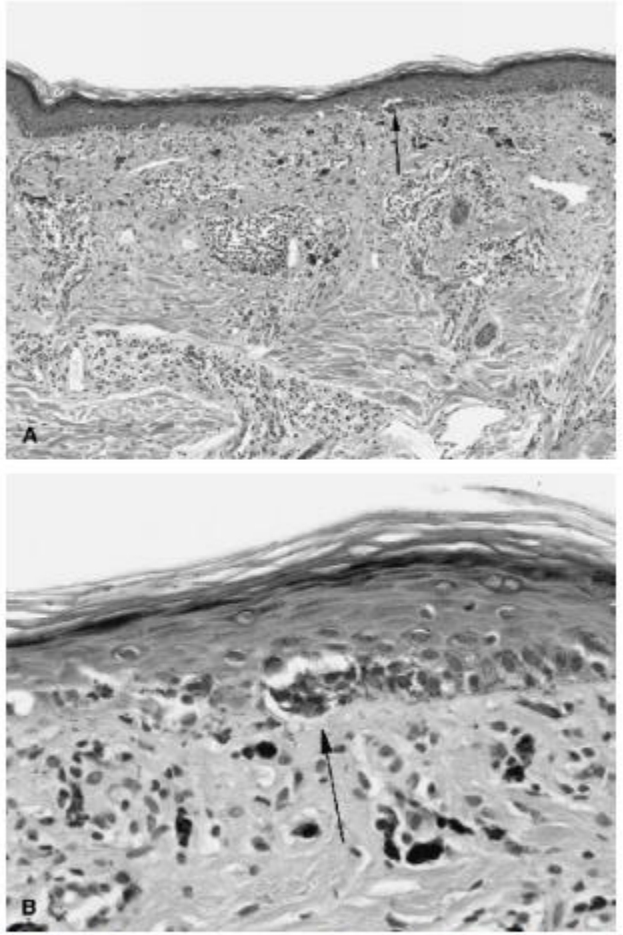



**FIG. 2.** A biopsy from a macule shown in Figure 1 reveals an effaced epidermis, scattered lymphocytes and melanophages in the upper dermis, and apparent nests along the junction (arrow; **A**). Note the nest-like aggregate (arrow) at the dermoepidermal junction with many melanophages in the subjacent dermis (**B**).

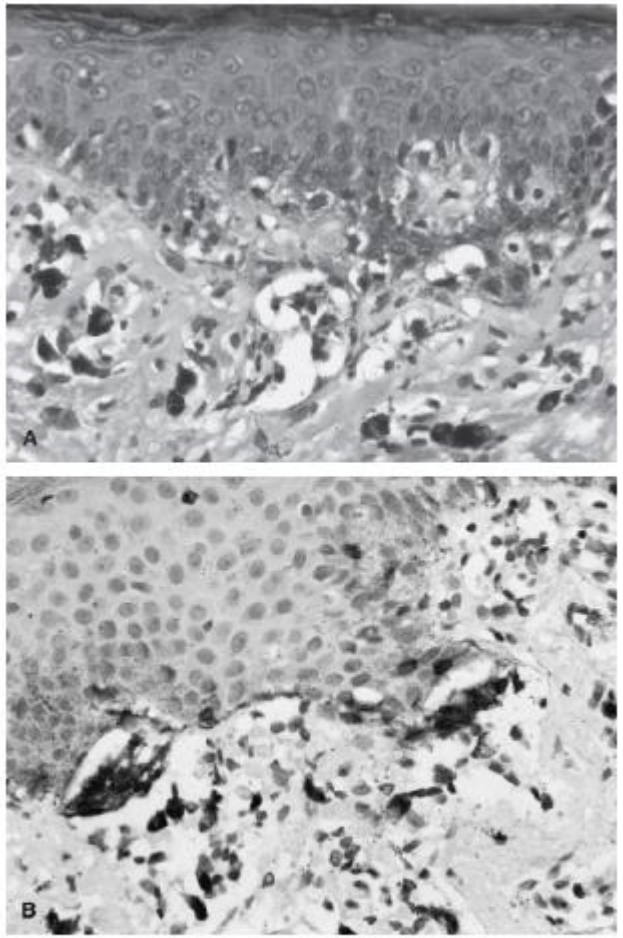



**FIG. 3.** A second biopsy from the patient in Figure 1 again reveals nests strongly resembling nests of melanocytes, this one apparently bridging adjacent rete ridges. There are many nearby melanophages (**A**). These nest-like structures label with a Melan-A immunoperoxidase stain using a red chromagen (**B**, and **on the cover**).

*Am J Dermatopathol* 2003; **25**: 162-5

*J Cutan Pathol* 2015: 42: 394–399
*doi: 10.1111/cup.12479*
*John Wiley & Sons. Printed in Singapore*



Journal of
Cutaneous Pathology

# Melanocytic tumors with intraepidermal melanophages: a report of five cases with review of 231 archived cutaneous melanocytic tumors

Dermal melanophages are frequently encountered in both benign melanocytic nevi and malignant melanoma. In contrast, intraepidermal melanophages (IEM) are under-recognized in melanocytic lesions and their biologic significance is not understood. Herein, we report the clinical and histopathologic features of five melanocytic lesions featuring IEM encountered prospectively in our dermatopathology practice at the University of Chicago. Two hundred and thirty-one (231) archived skin primary melanocytic proliferations were also investigated retrospectively in a de-identified, archival teaching set collection. Nineteen of 231 of the archived cases were positive for IEM. Among the total 24 IEM-positive cases (5 prospective and 19 archived cases), 13 were categorized as Spitz nevi ($p < 0.0001$) and 3 as atypical Spitz tumors ($p = 0.0152$). Fourteen of 24 cases with IEM also exhibited intracorneal melanocytes ($p < 0.0001$). IEM are evidently not rare, especially in spitzoid melanocytic neoplasms. IEM in our series were significantly correlated with intracorneal melanocytosis, possibly indicating an association between IEM and suprabasal melanocytosis and/or transepidermal elimination of melanocytes.

**Masakazu Fujimoto[1,2], Juliana L. Basko-Plluska[1], Thomas Krausz[3], Maria Angelica Selim[4] and Christopher R. Shea[1]**

[1]Department of Medicine, Section of Dermatology, The University of Chicago Medicine, Chicago, IL, USA,
[2]Department of Diagnostic Pathology, Kyoto University Hospital, Kyoto, Japan,
[3]Department of Pathology, The University of Chicago Medicine, Chicago, IL, USA, and
[4]Department of Pathology, Duke University Medical Center, Durham, NC, USA

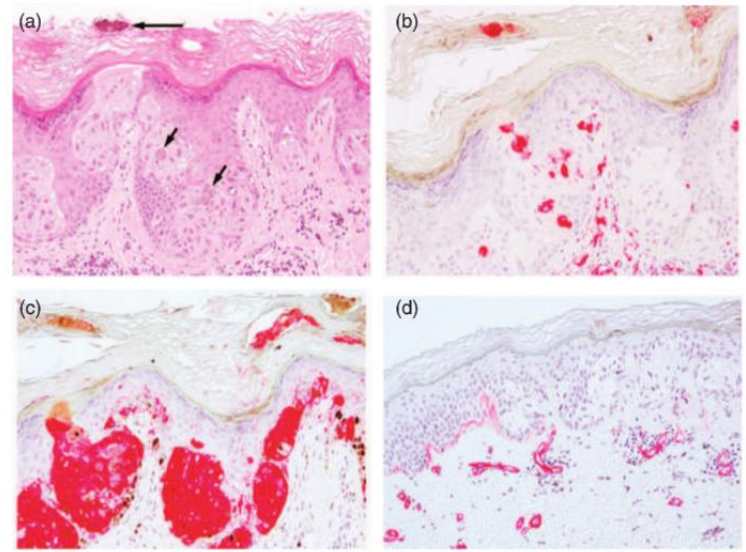



*Fig. 1.* Melanophages, index case 5: the diagnosis was atypical junctional melanocytic proliferation. A) Atypical melanocytes are arranged in irregular nests at the basal layer of the epidermis. Melanophages (short arrows) are seen within melanocytic nests. Intracorneal melanocytes (long arrow) are also seen. B) CD68 immunostaining confirms the presence of intraepidermal melanophages and also highlights the macrophages in the intracorneal melanocytic nests. C) Melan A staining highlights intracorneal melanocytes. D) Collagen IV expression is absent on right-hand portion, which was interpreted as focal effacement of basement membrane.

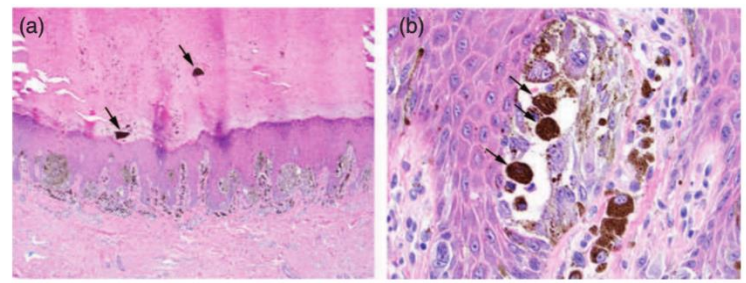
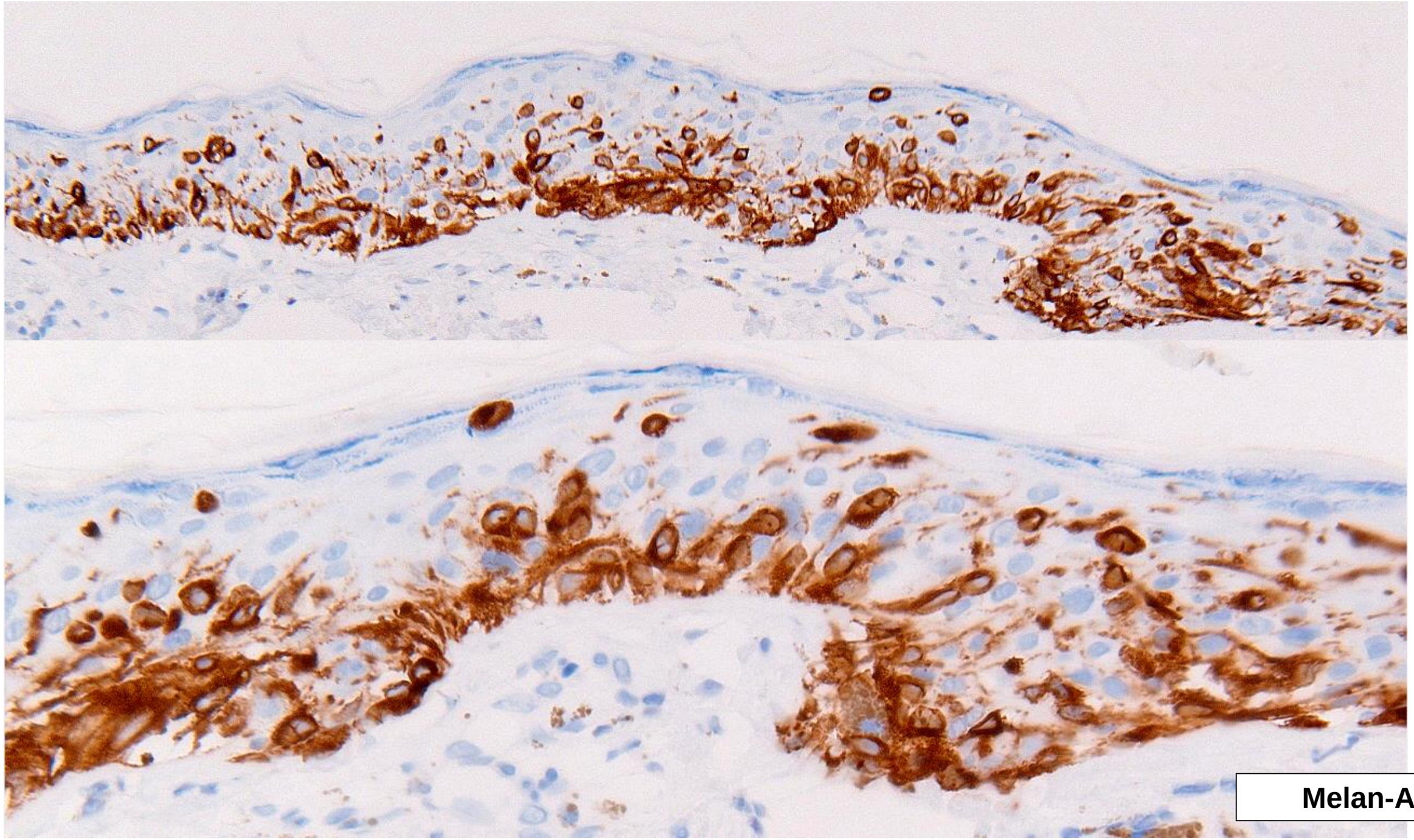
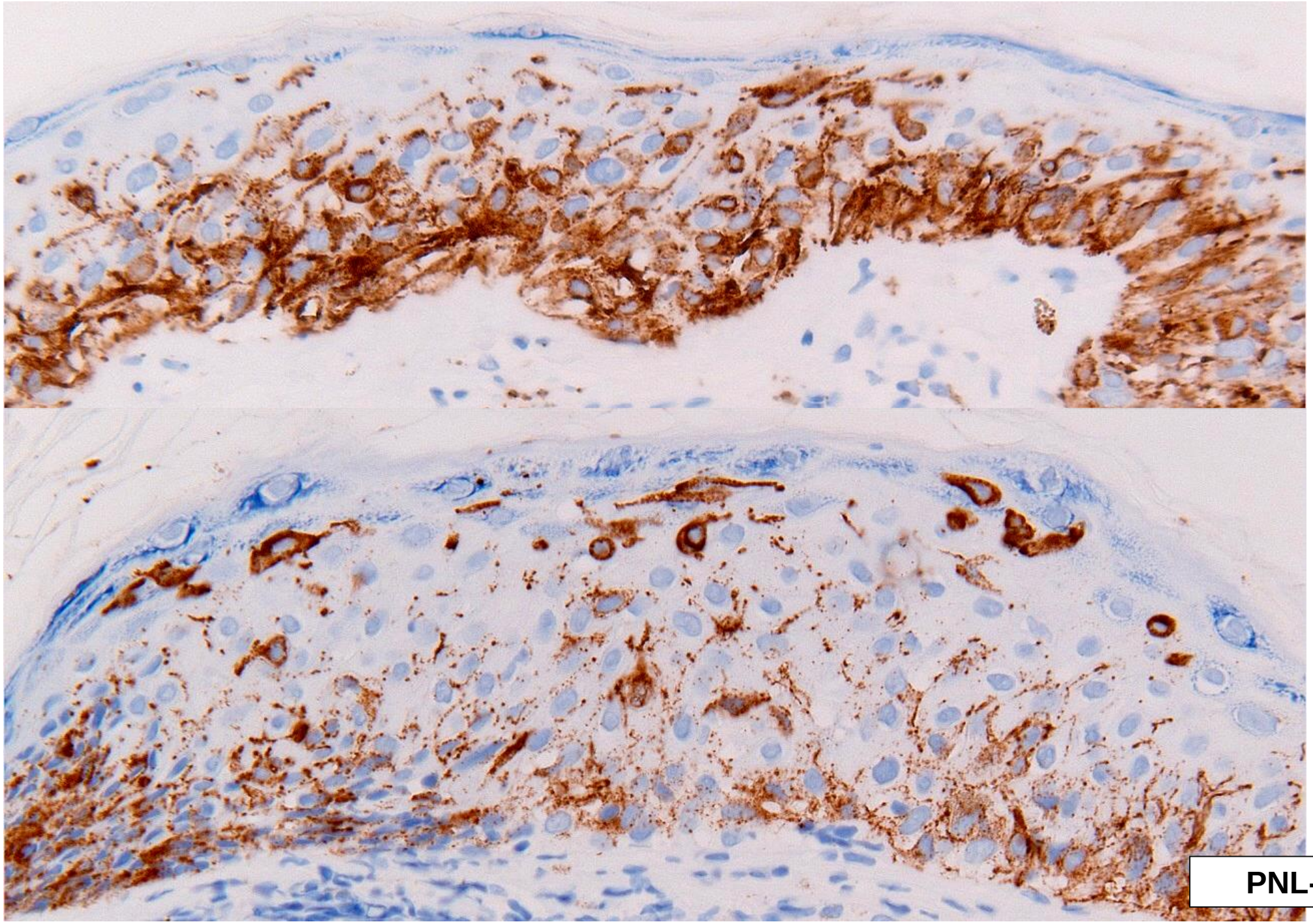



*Fig. 2.* Intraepidermal melanophages , a representative case from the archived cases: the diagnosis is Spitz nevus with both intraepidermal melanophages and intracorneal melanocytes. A) There is a well-circumscribed proliferation of melanocytes arranged in nests at the basal layer of the epidermis. Clusters of degenerated melanocytes (arrows) are present in the stratum corneum. B) Melanophages (arrows) are seen in an epidermal nest of epithelioid melanocytes. Intradermal melanophages are also seen.

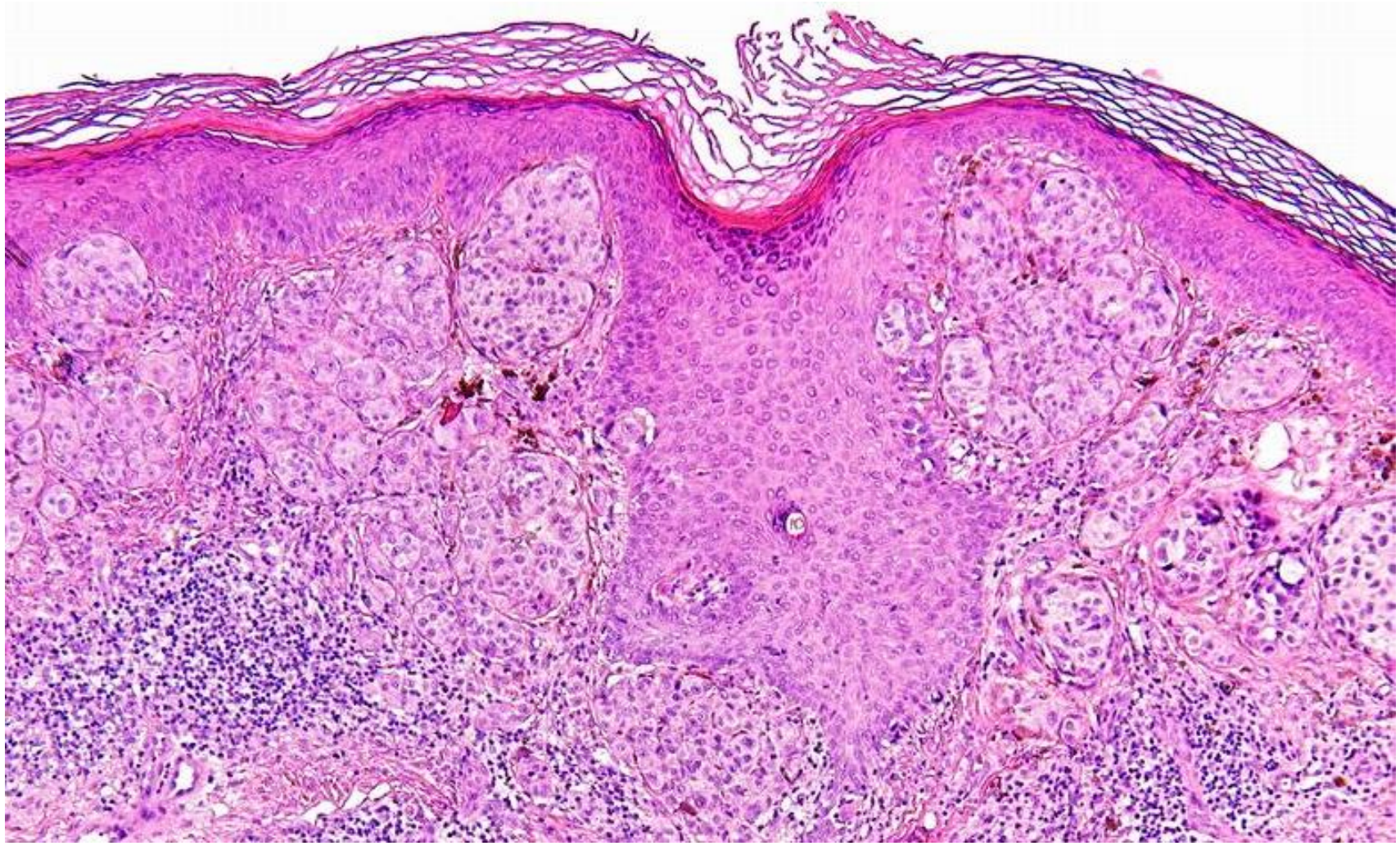


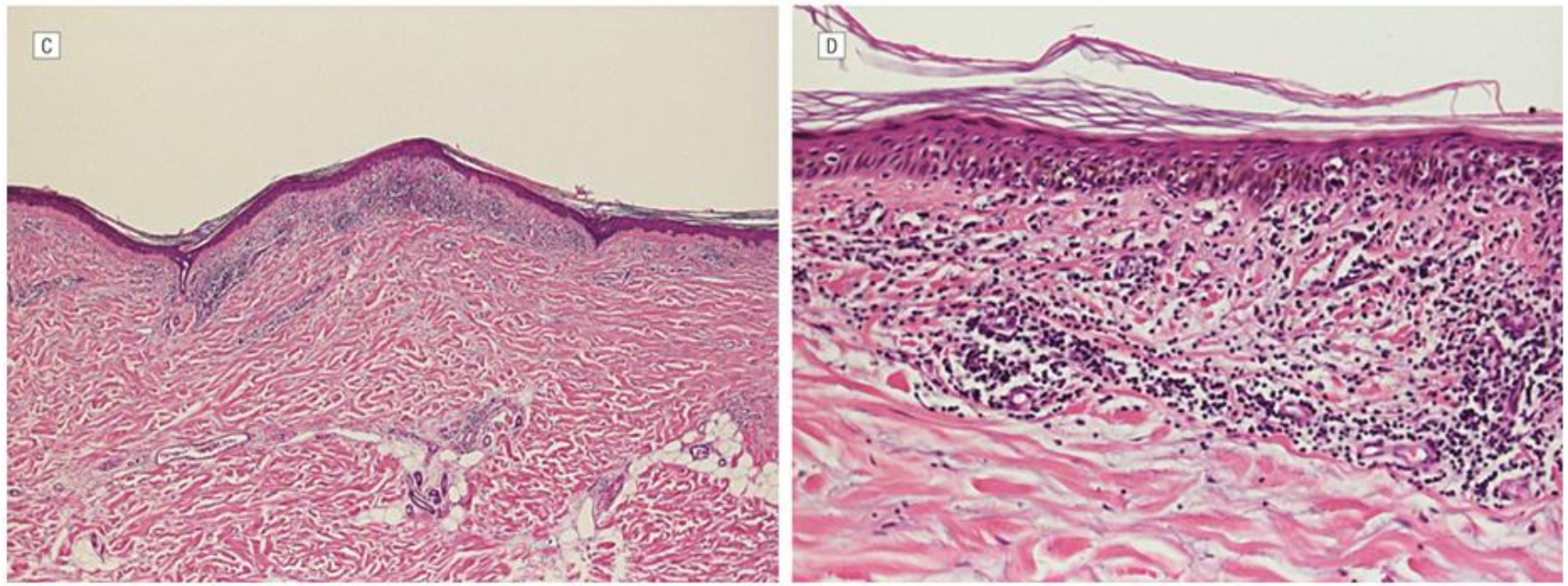
Melan-A



PNL-2

# Locally recurrent 2 years later




C
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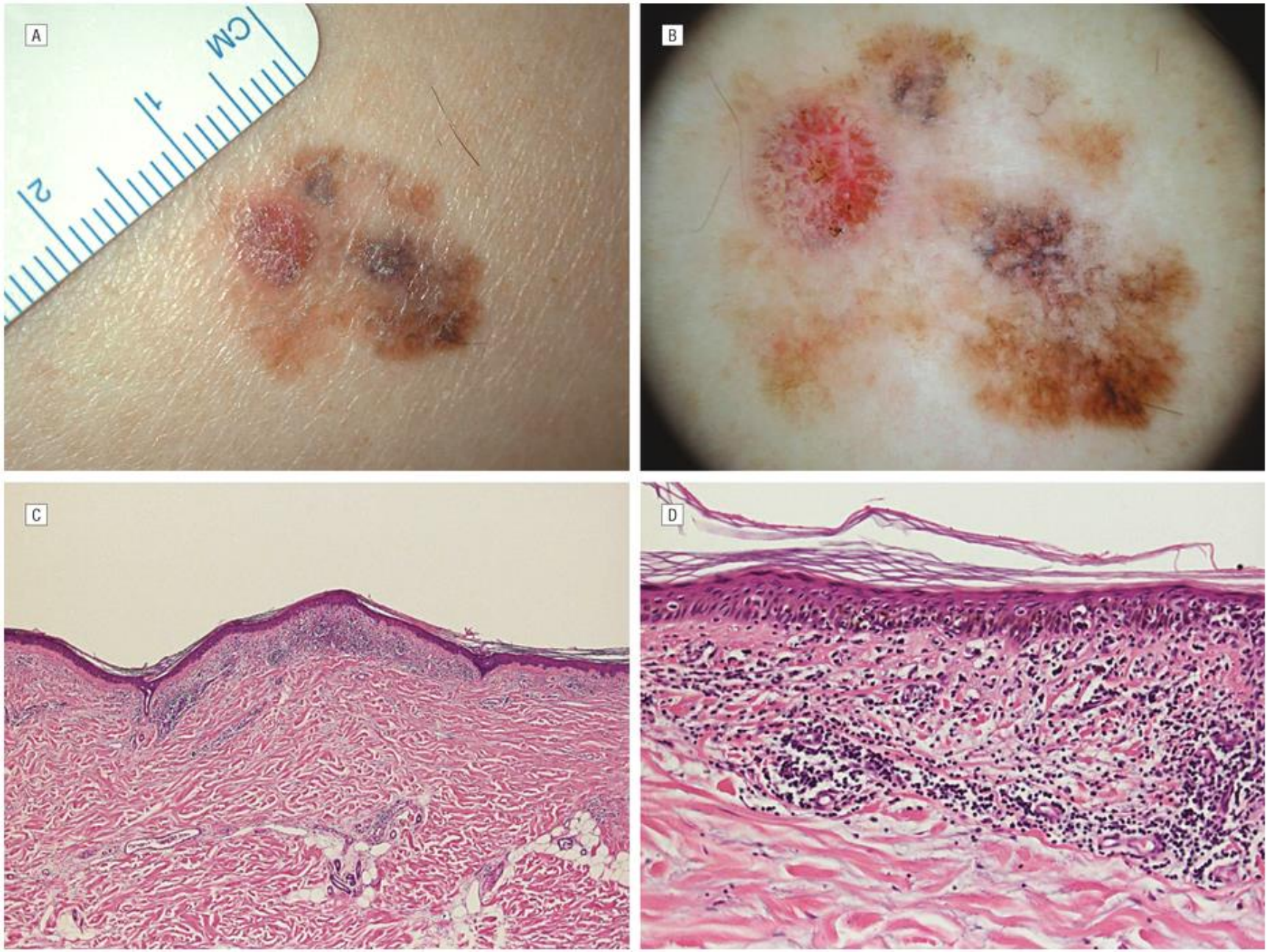
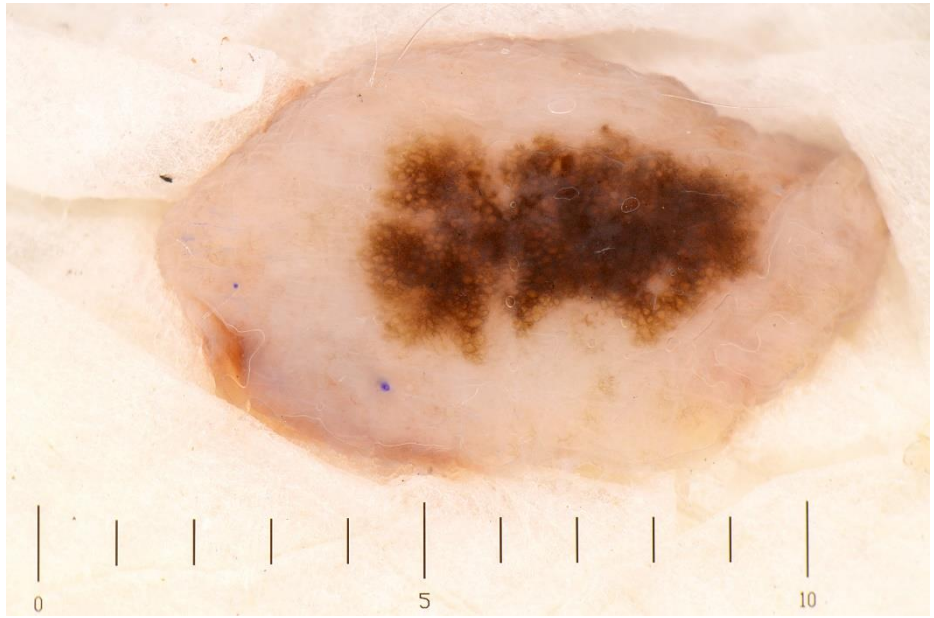
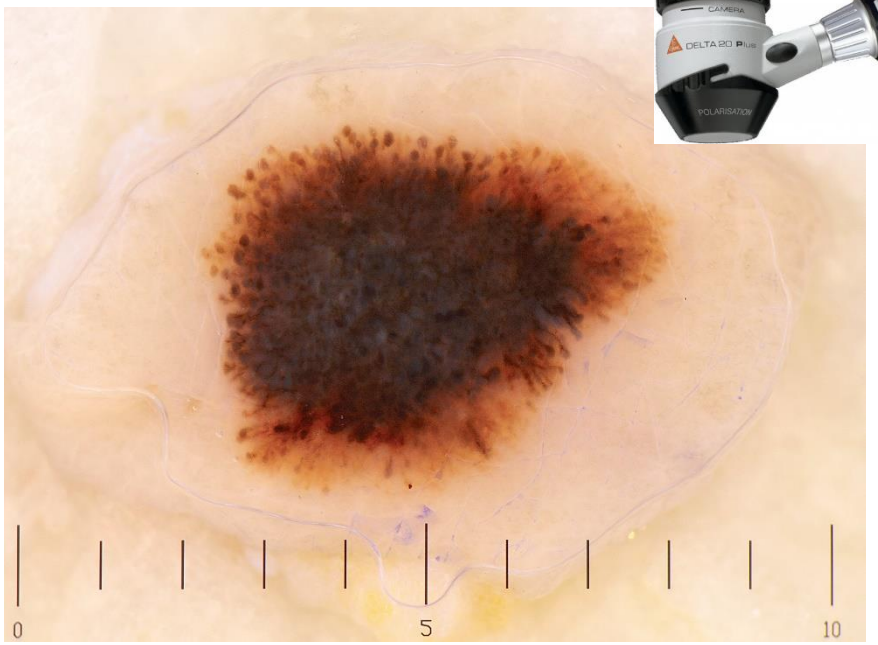
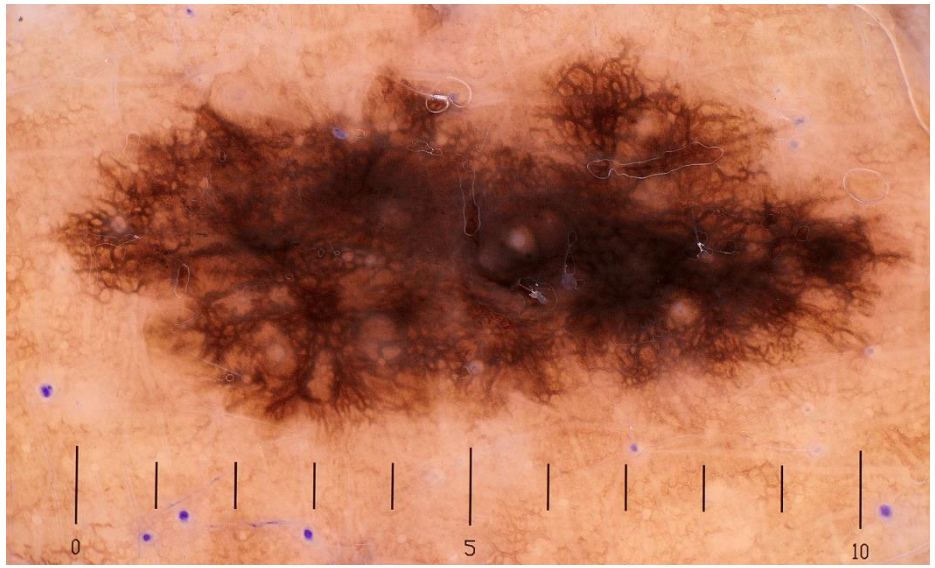


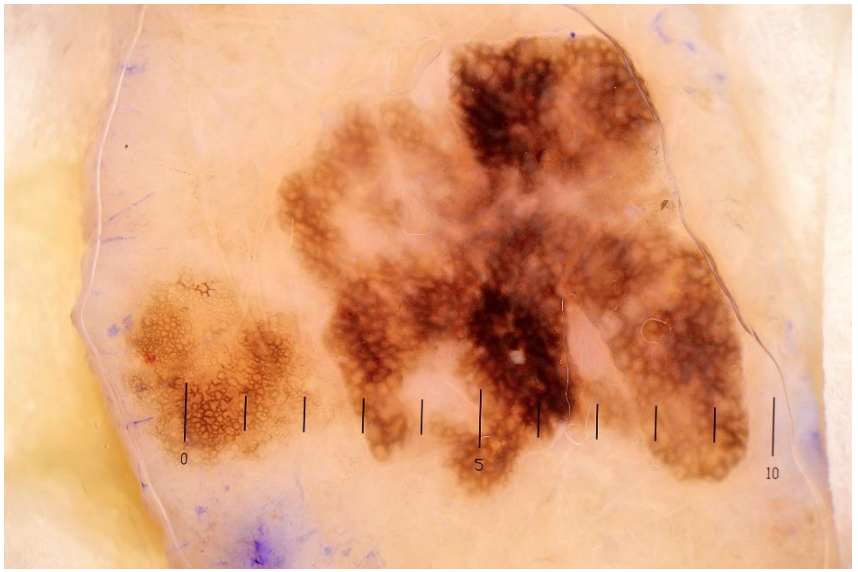

Soyer HP et al., *Arch Dermatol*. 2005; **141**: 209-211

# Specimendermatoscopy

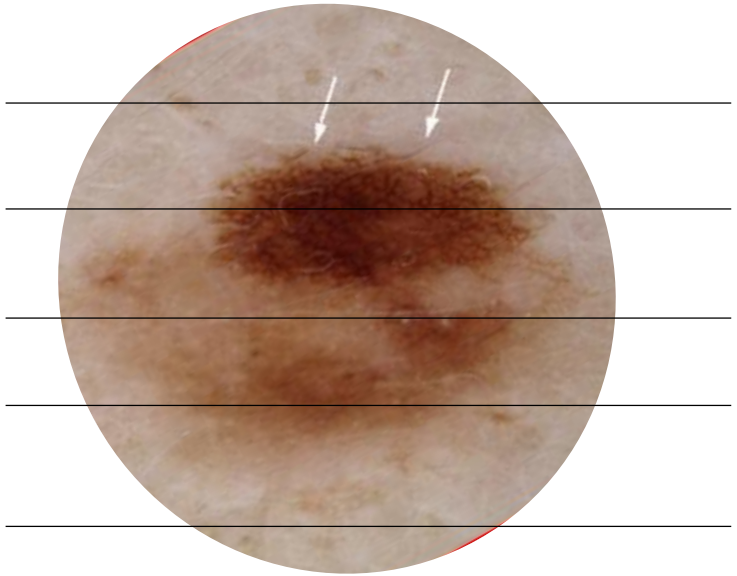


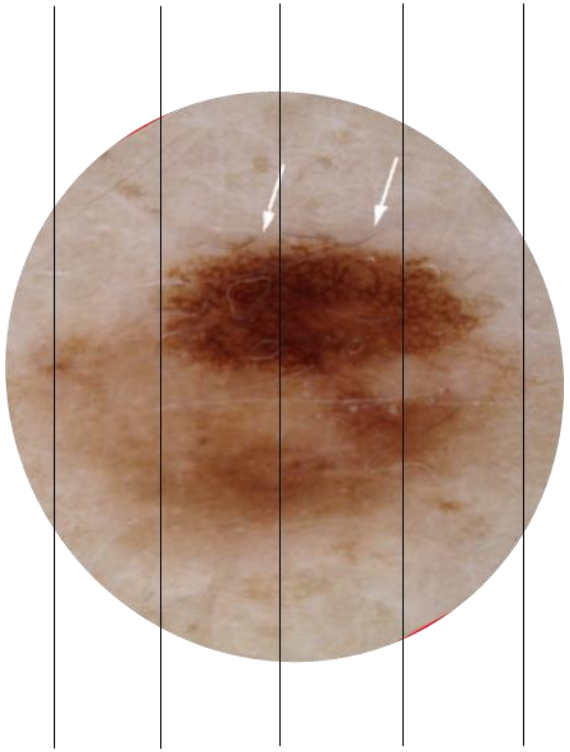



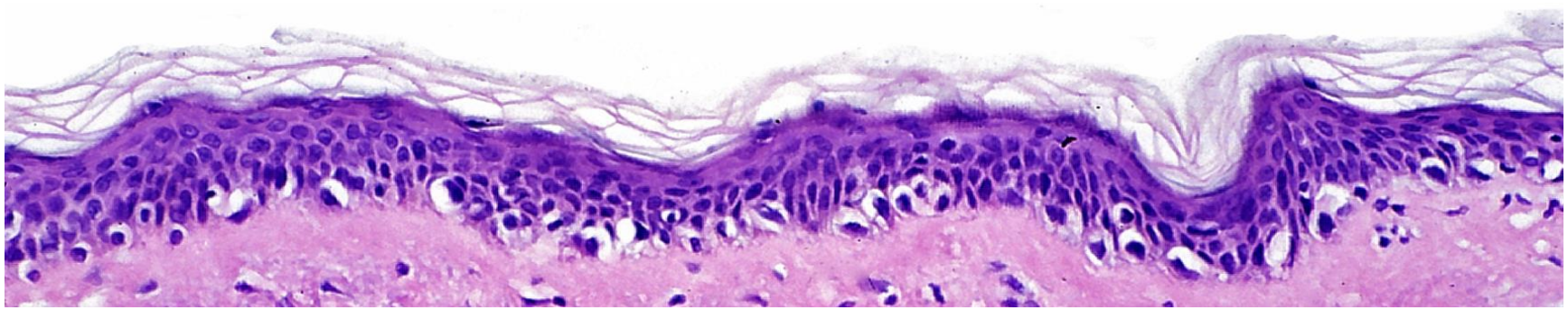

# Specimen dermoscopy: also an aid in the sectioning of specimen





# Lentigo maligna prognosis and management

- Life-time chance of progression to invasive melanoma is estimated to be a few percent;
  - may be higher in younger cohorts: increased sun exposure at young ages; increased life span
  - prevalence of small LM is not known
    - An unknown percentage does not come to clinical attention (especially small lesions and elderly patients)
- Trials of lentigo maligna therapies generally take local recurrence of LM as (intermediate) end point. A better end point would be: chance of invasive melanoma (or, better still: death of melanoma)
- 'Lentigo premaligna' would perhaps be a better term



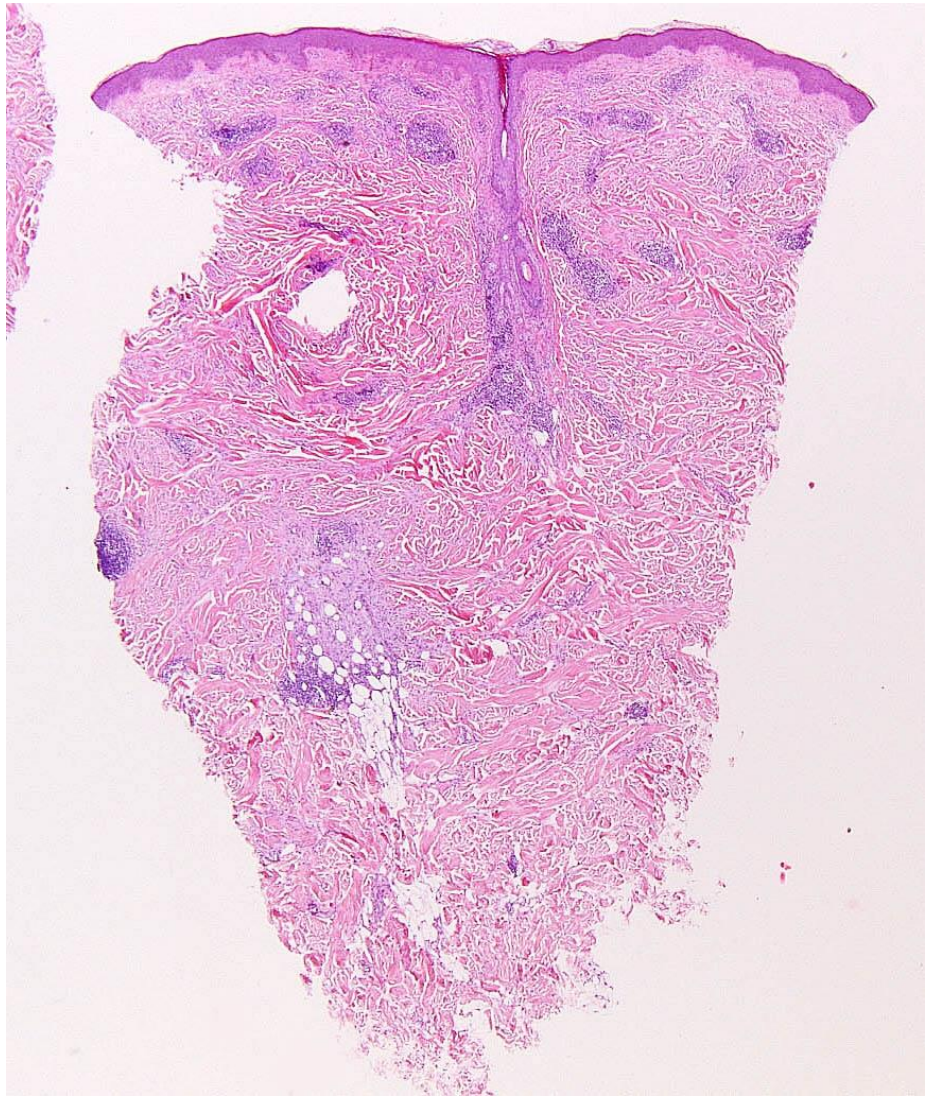
# Desmoplastic melanoma

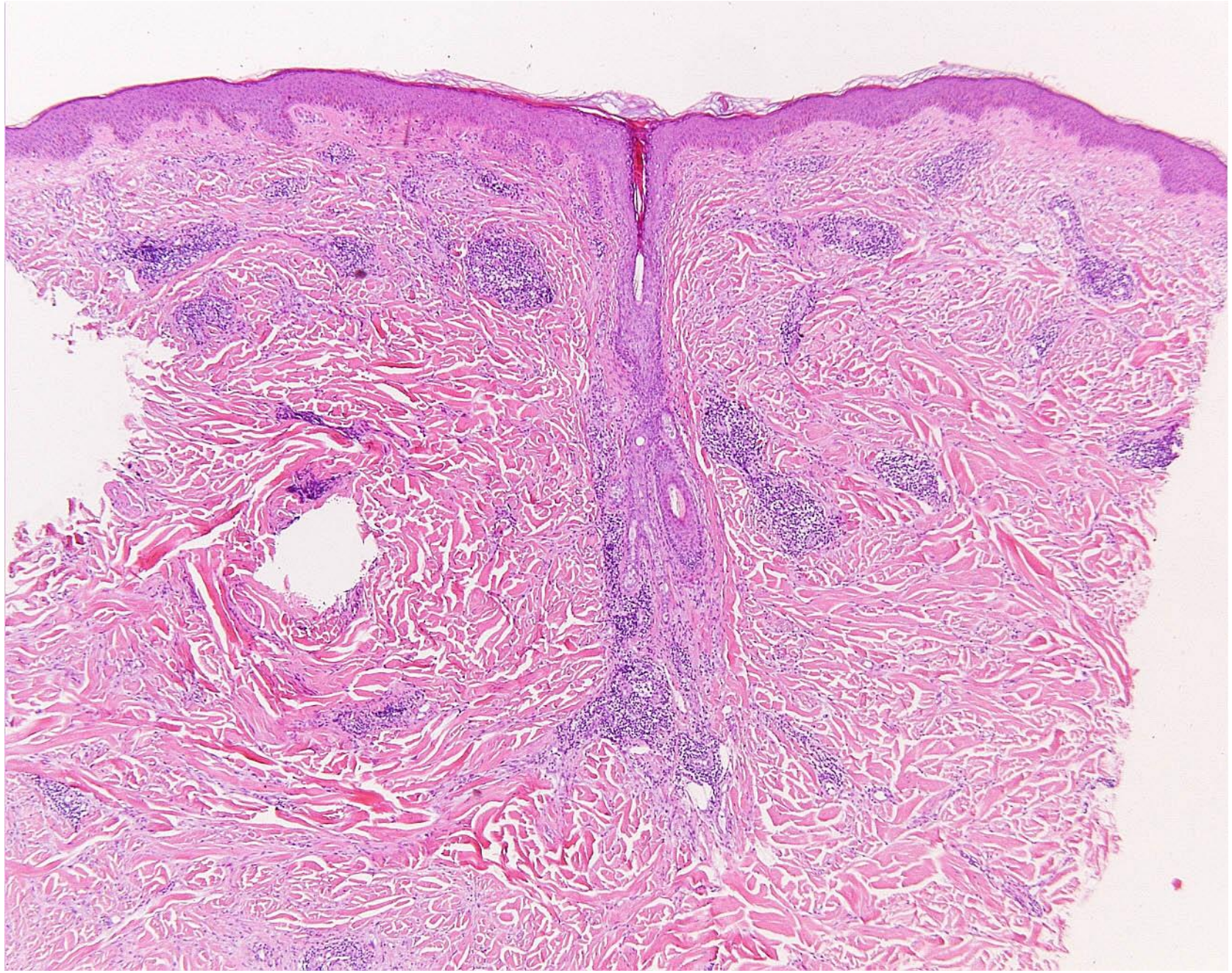
- Intradermal atypical spindle-cell proliferation associated with newly formed fibrillar collagen
- S-100 and Sox-10 positive. Melan-A, HMB-45, PNL2, MITF-M negative
- Associated intraepithelial or compound melanocytic proliferation (benign or malignant) may or may not be present
- Histological evidence of chronic solar damage of the skin
- Poorly defined borders. Resection margins of initial biopsy practically always positive
- Intraneural and perineural spread more common than in melanomas of other types
- Lymphogenous spread exceedingly uncommon in pure desmoplastic melanoma, but hematogenous spread to distant organs may well occur

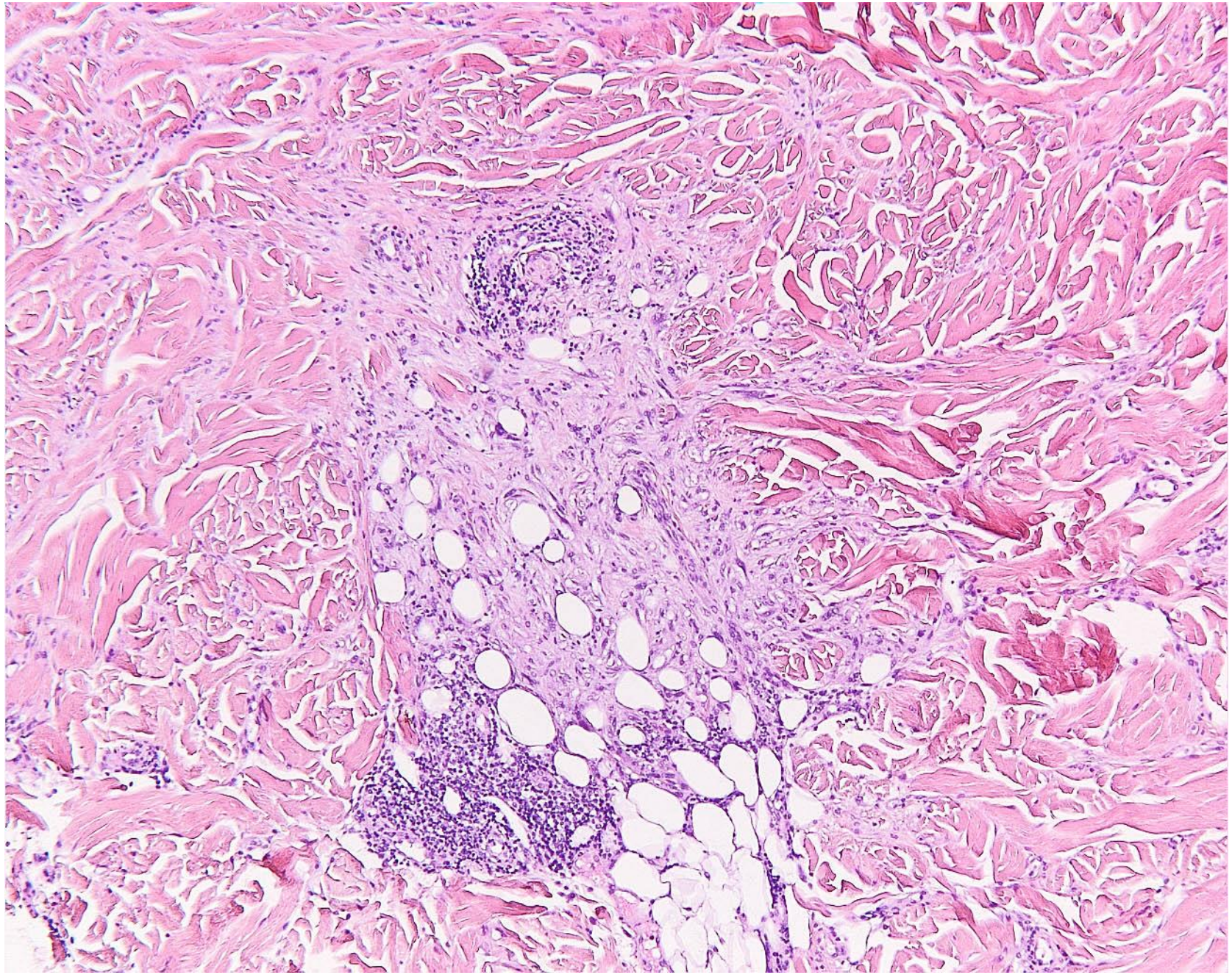
# Desmoplastic melanoma: caveats and pitfalls

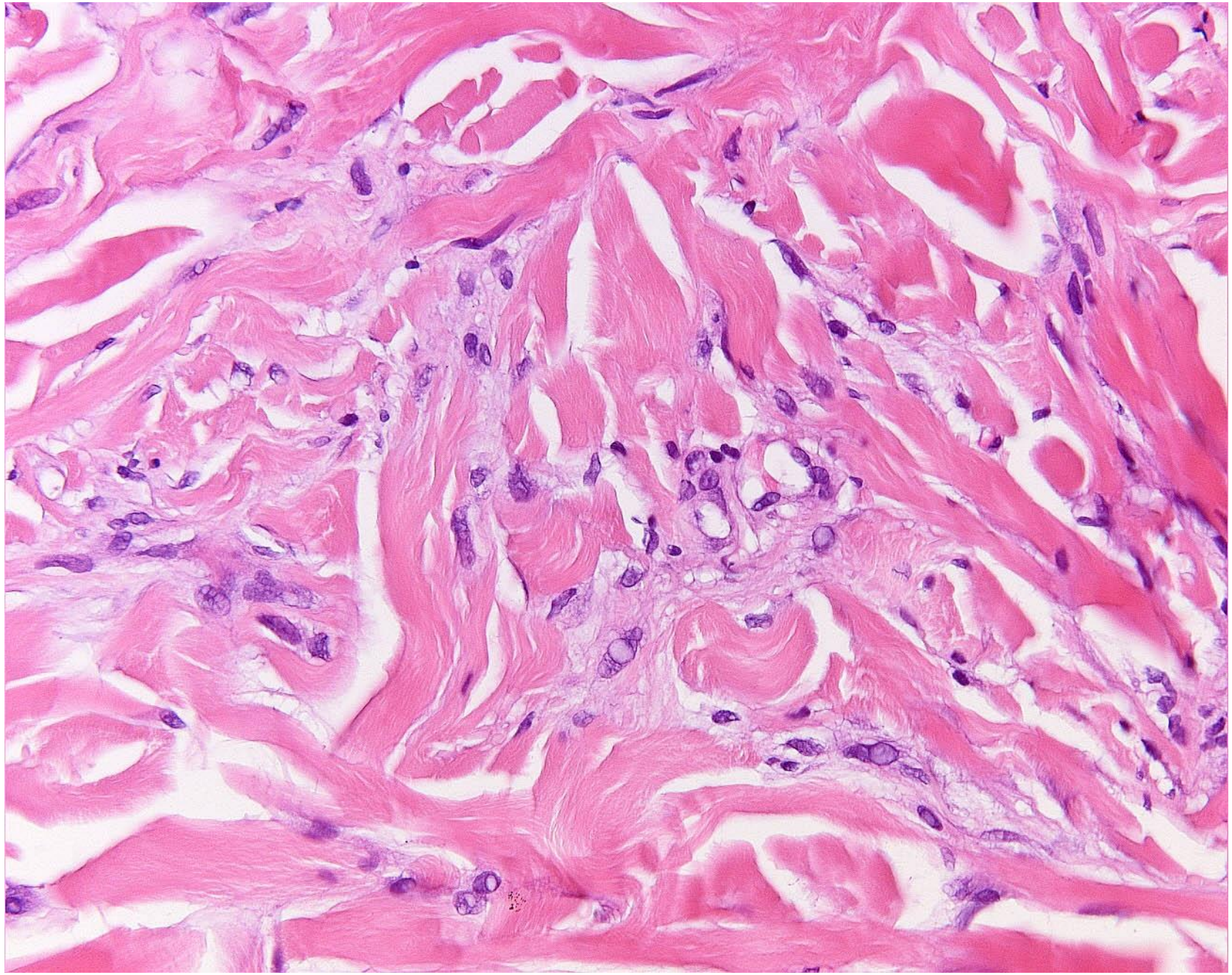
- Often not suspected clinically
- Easily overlooked or misinterpreted histologically
  - Paucicellular
  - Amelanotic
  - Some resemblance to scar tissue
  - Intraepidermal component absent or subtle
  - Associated superficial non-desmoplastic melanoma that gets all the attention
  - Multiple pathologies in skin biopsy
- Danger of overdiagnosis in case of a small lesion with no or minimal atypia, presenting in the wrong context (younger patient; no actinic damage); DD: desmoplastic spindle-cell naevus

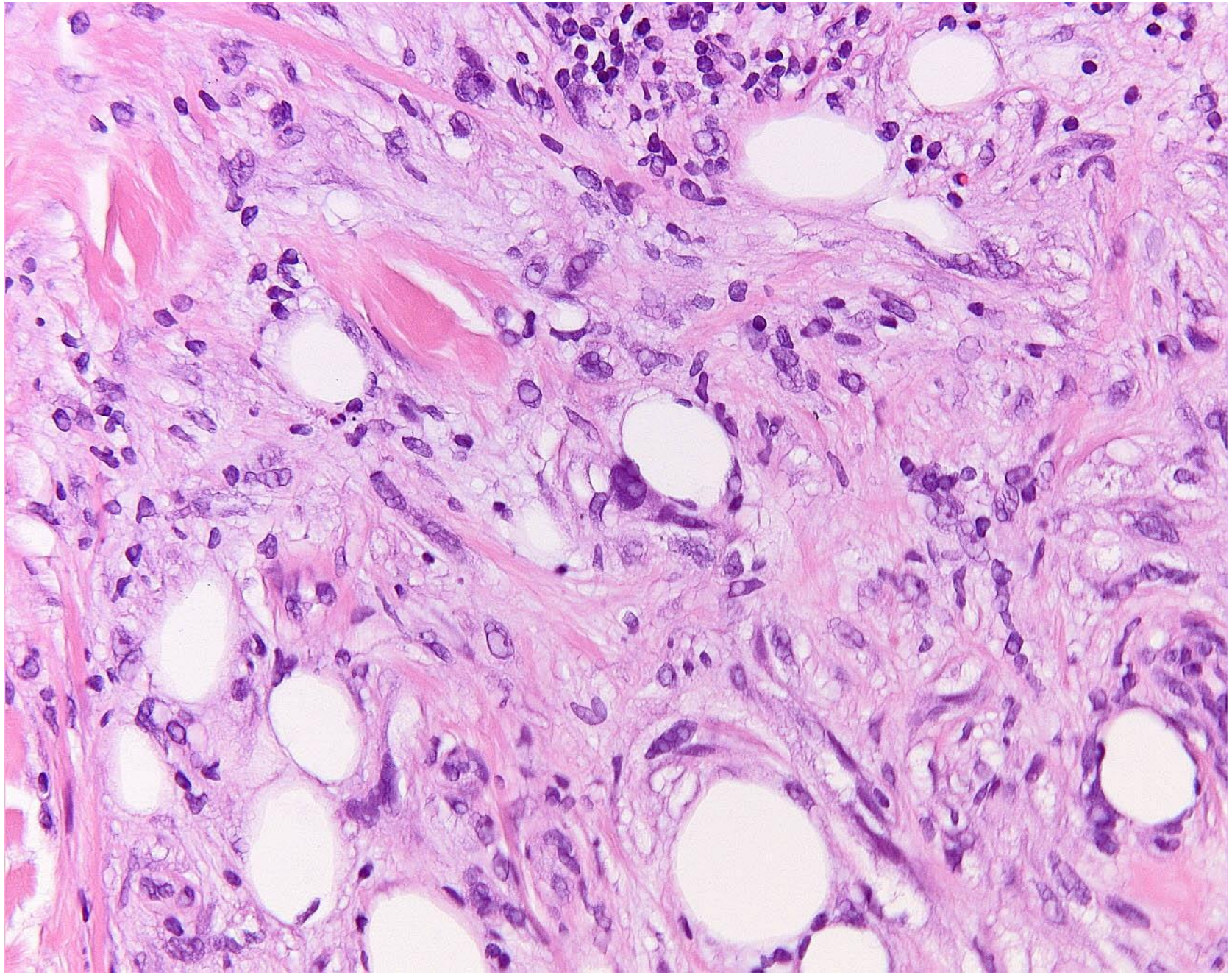
Female, 59 years. Punch biopsy, nodule, skin of back. Inflammatory disorder? Amelanotic melanoma?

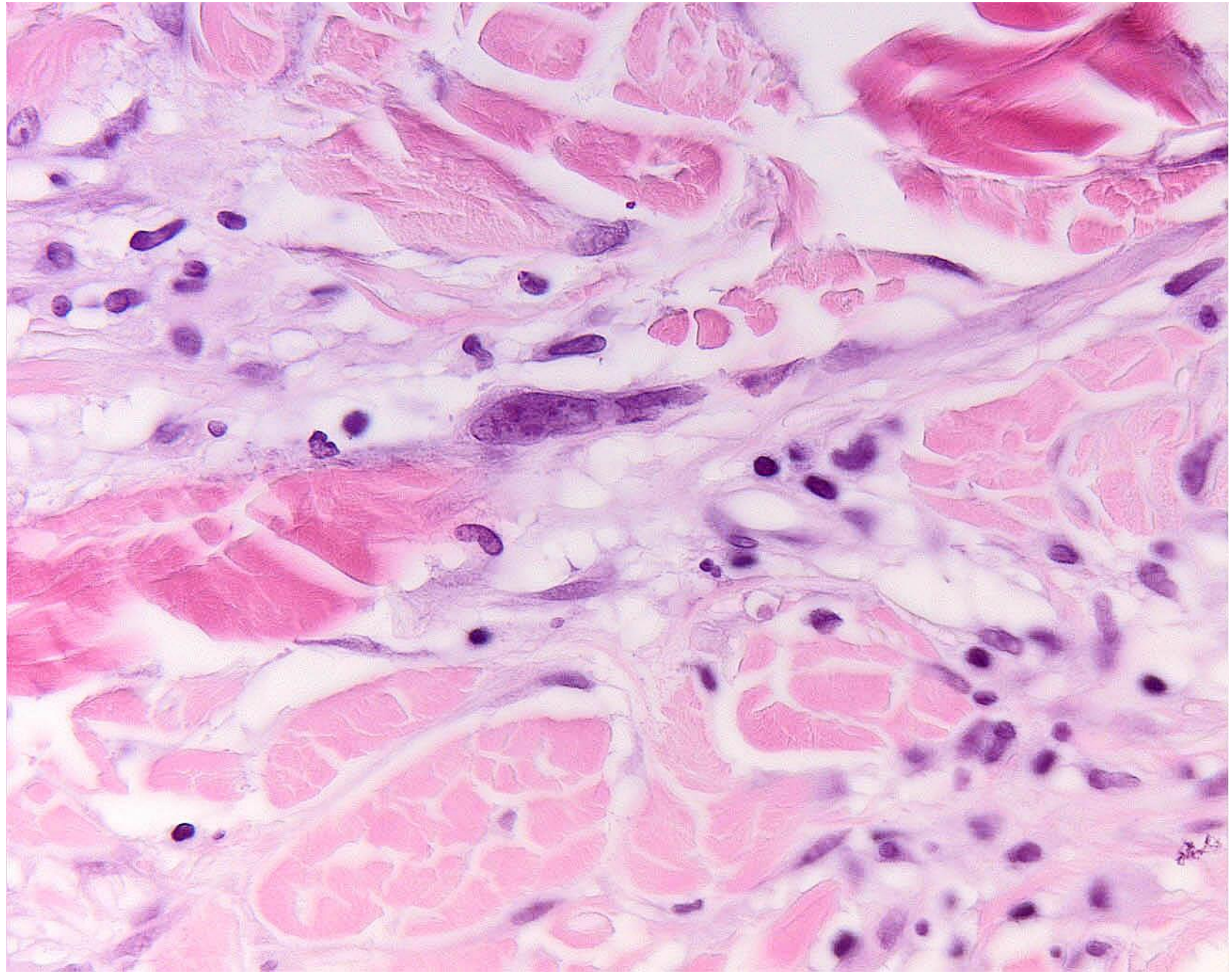


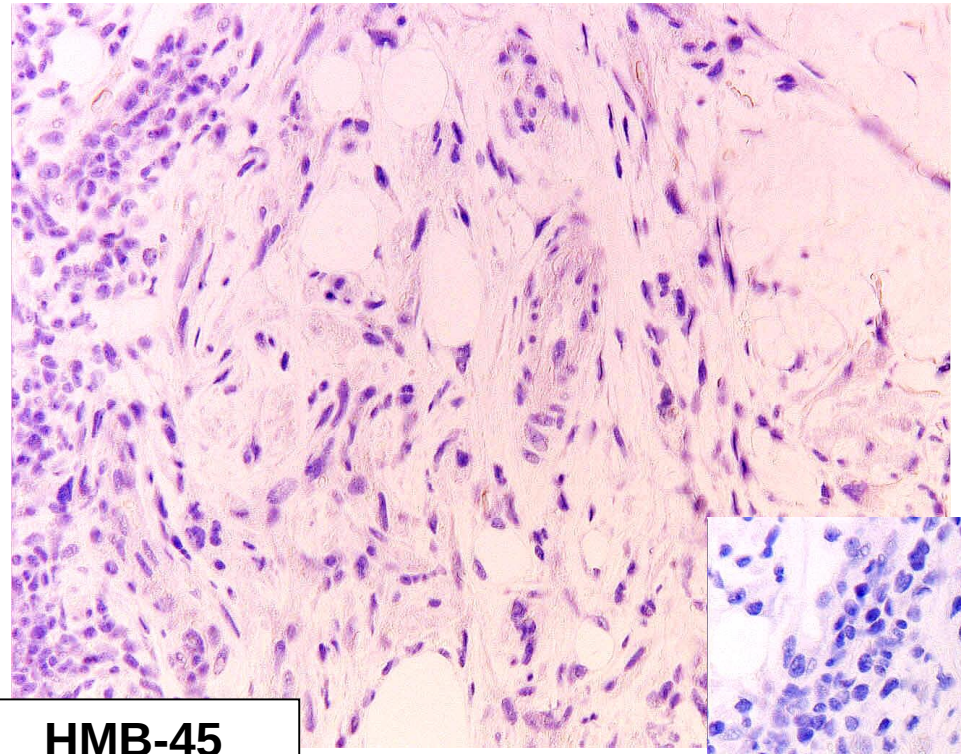












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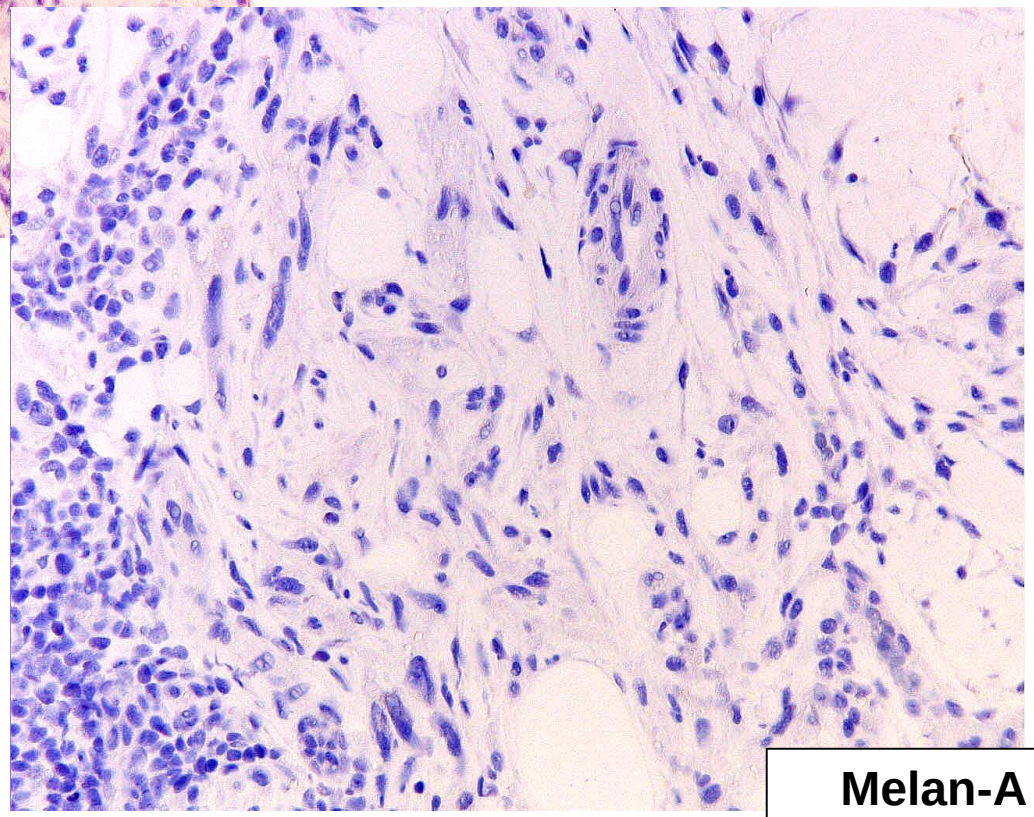
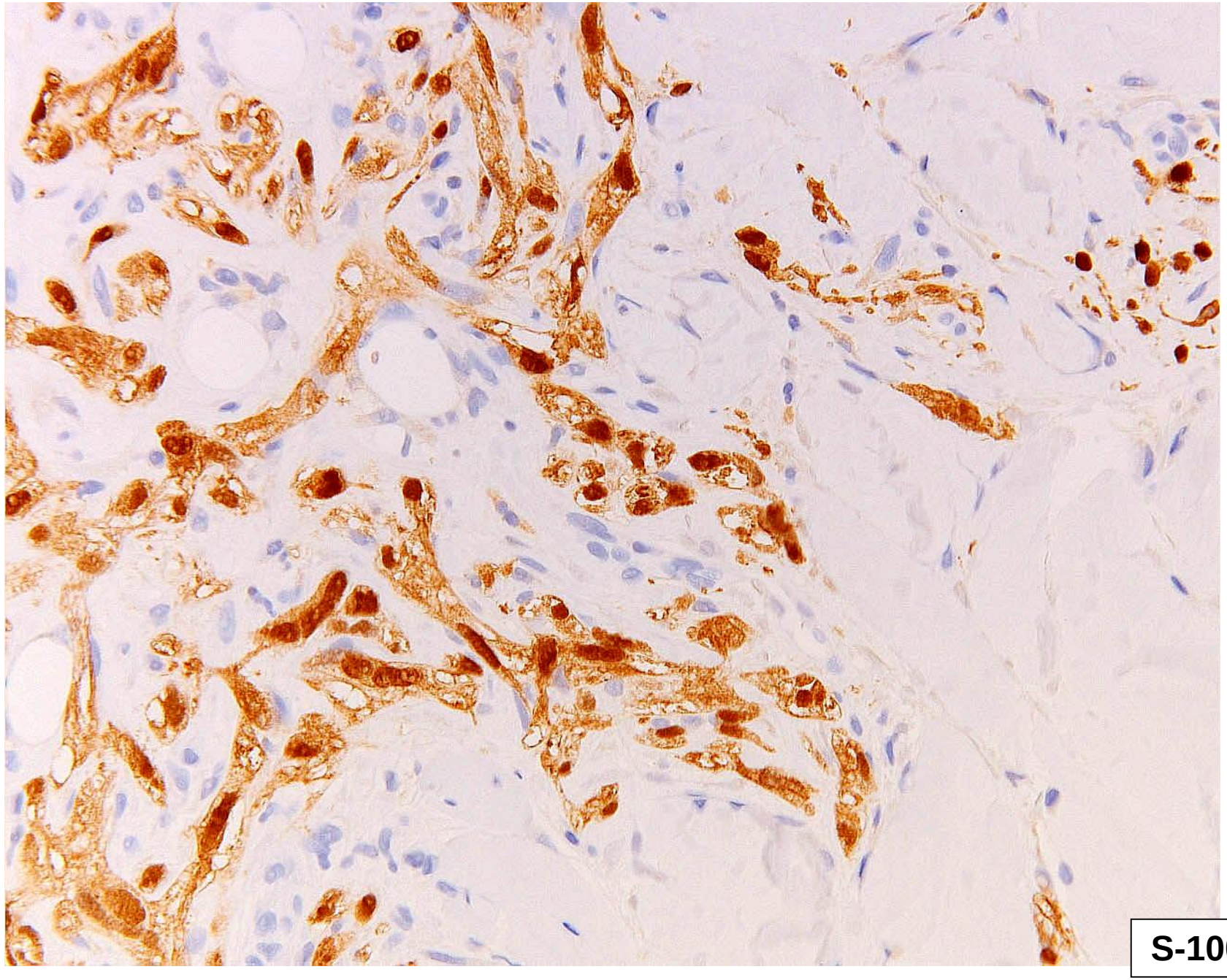


Melan-A



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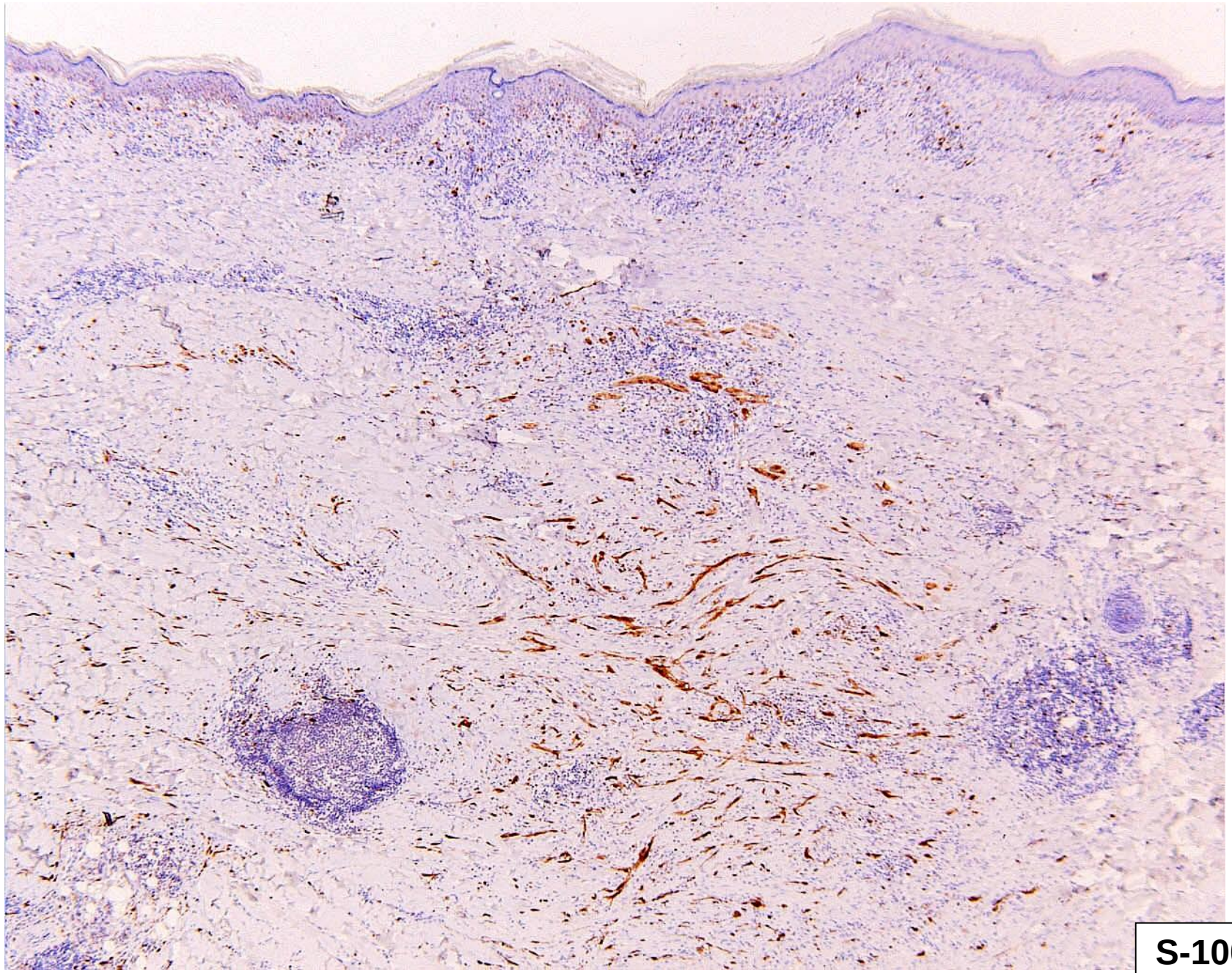

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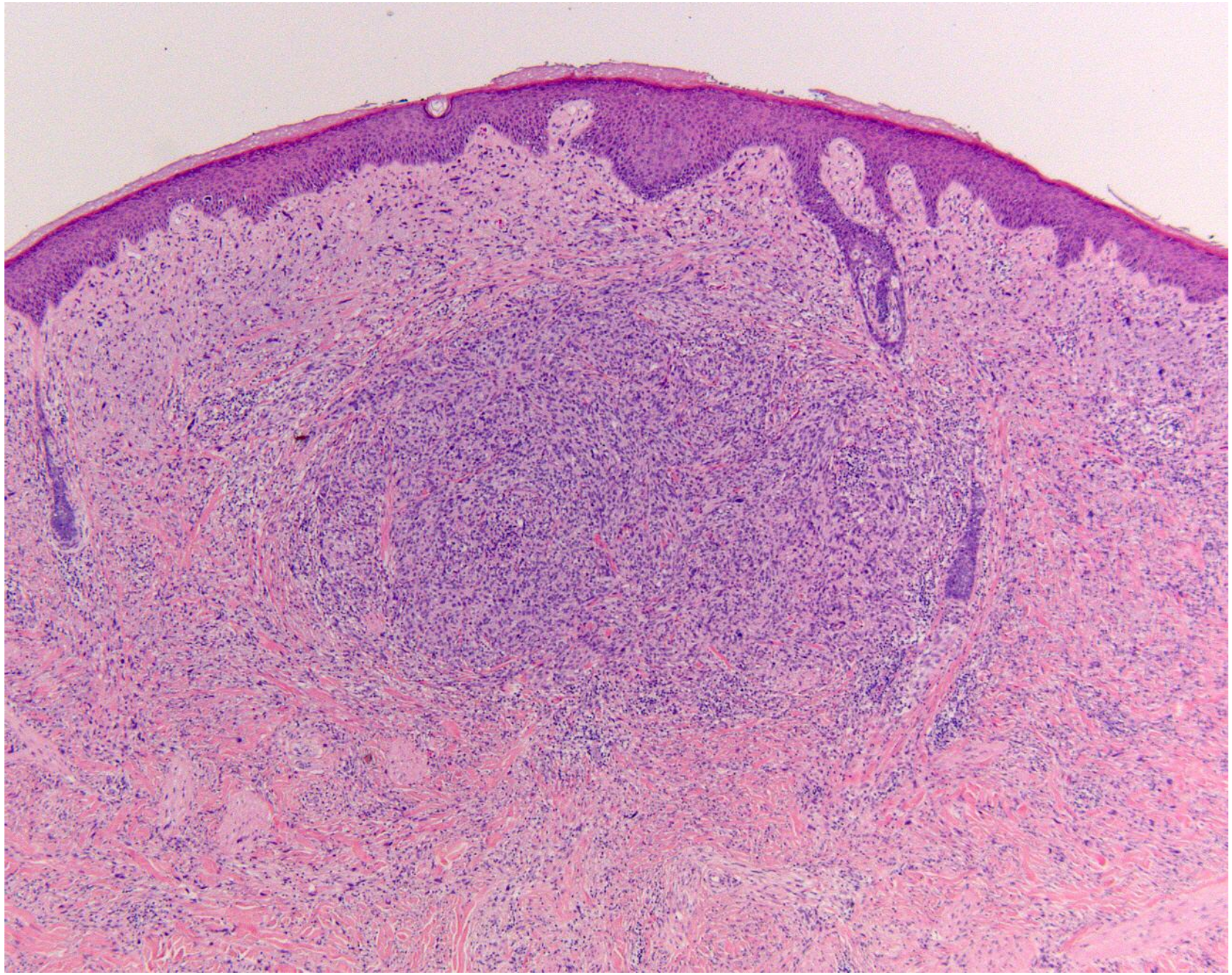
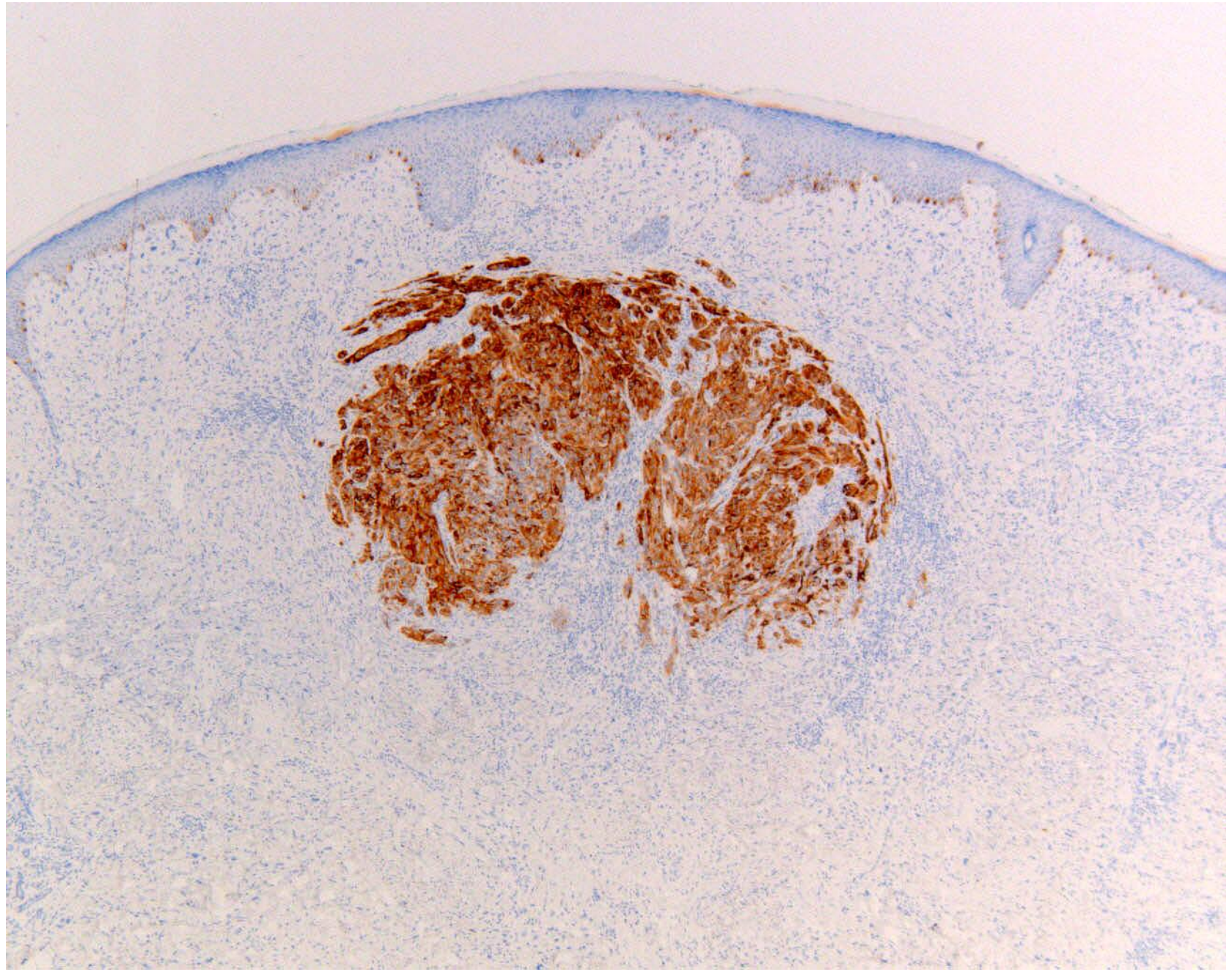
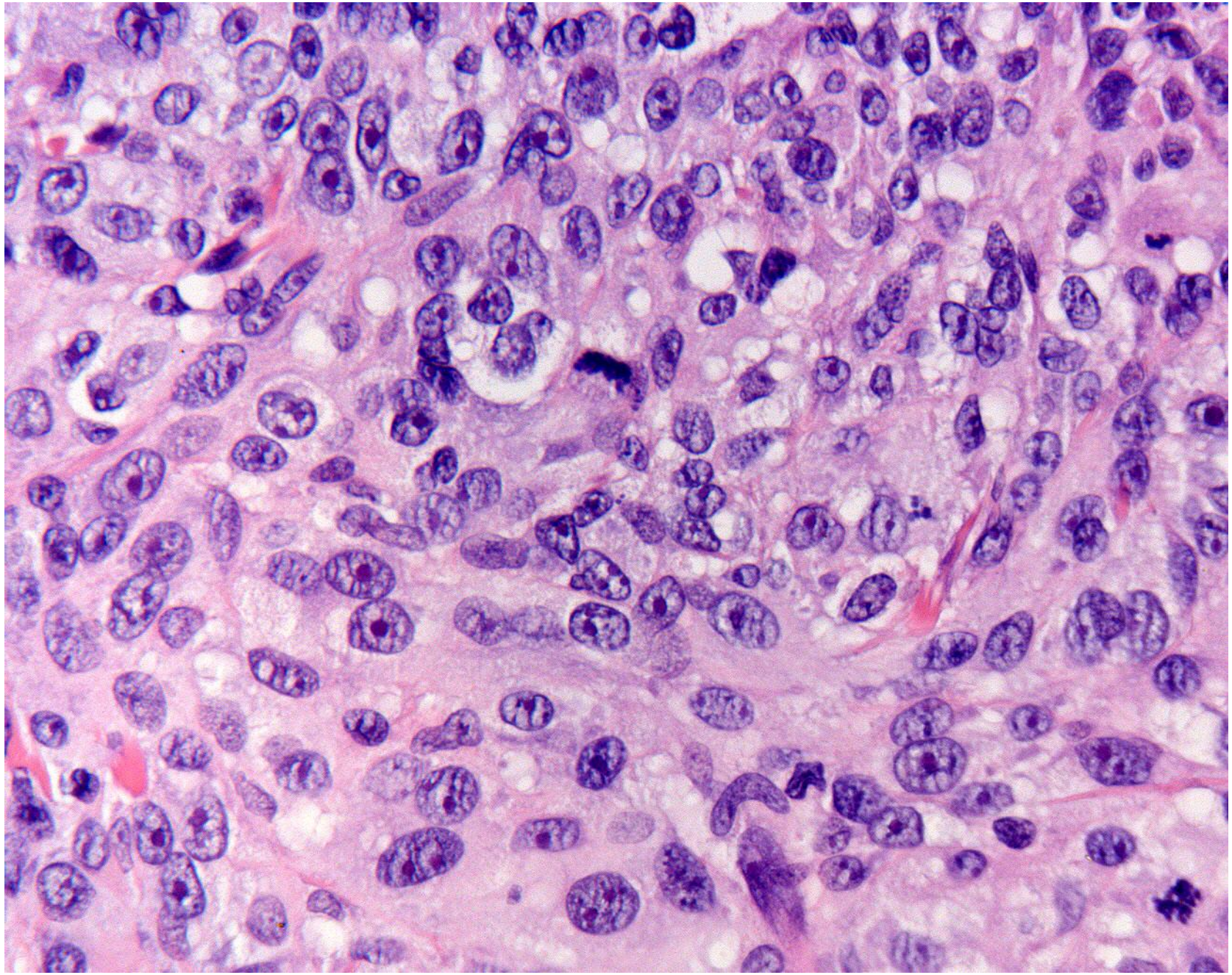
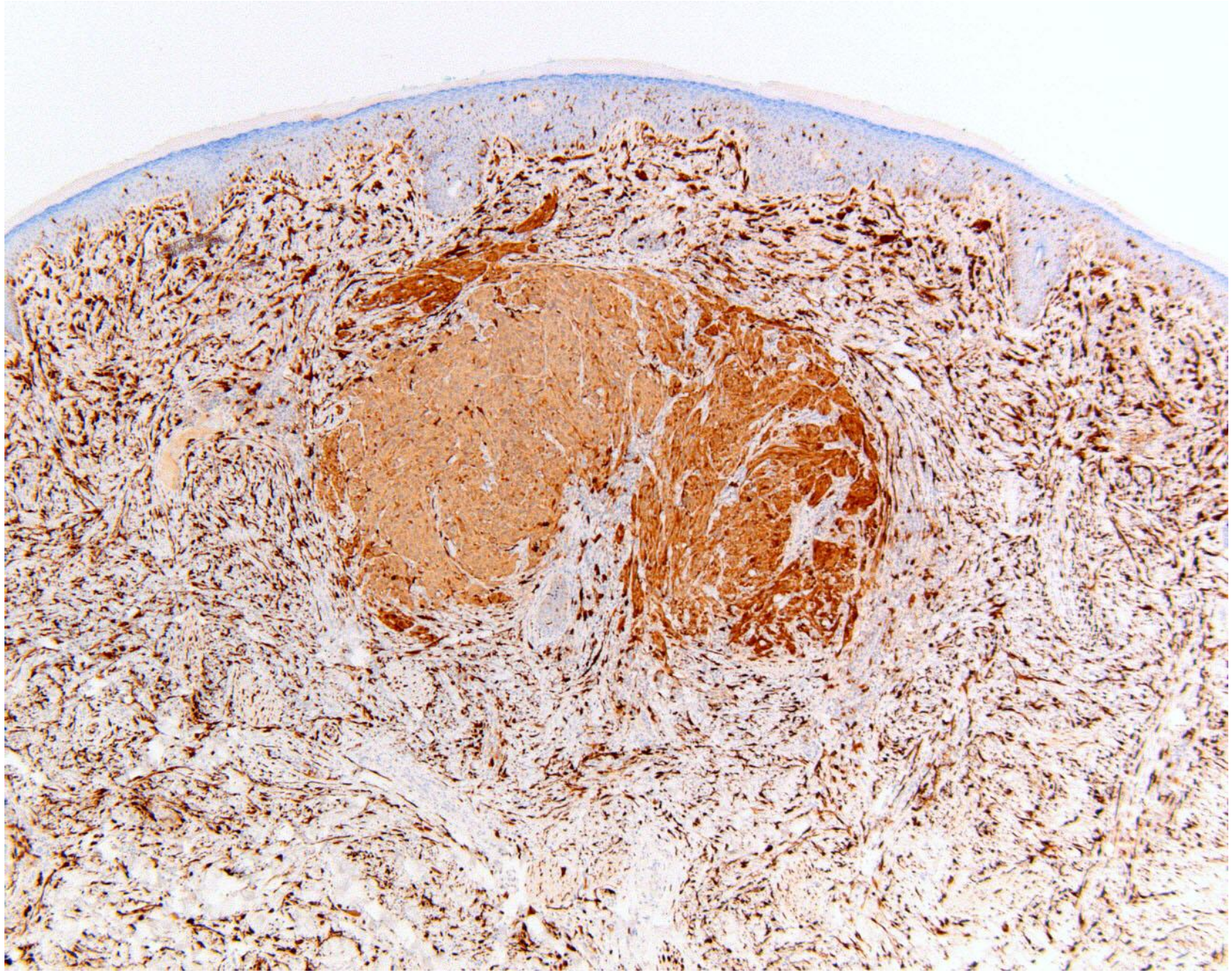
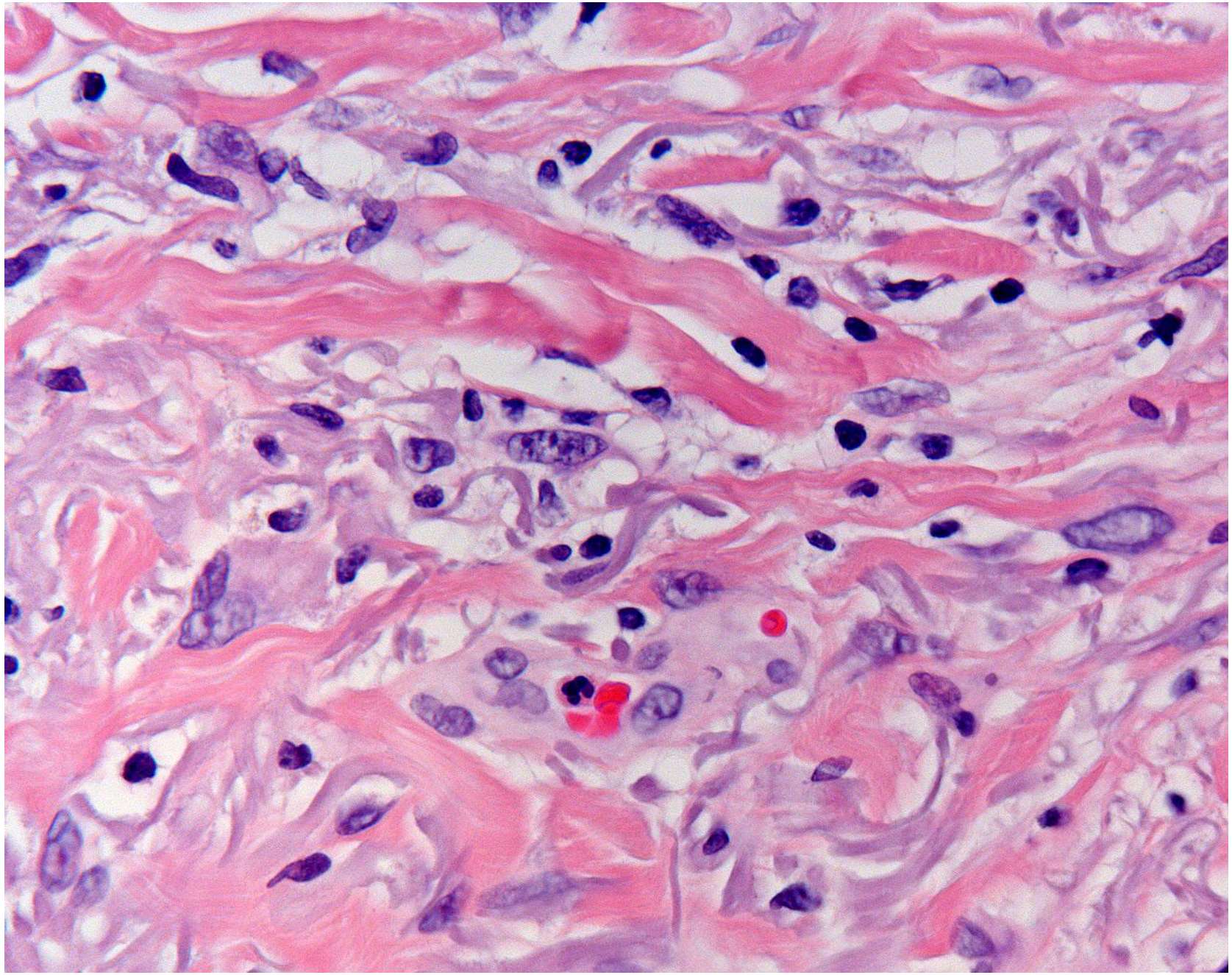
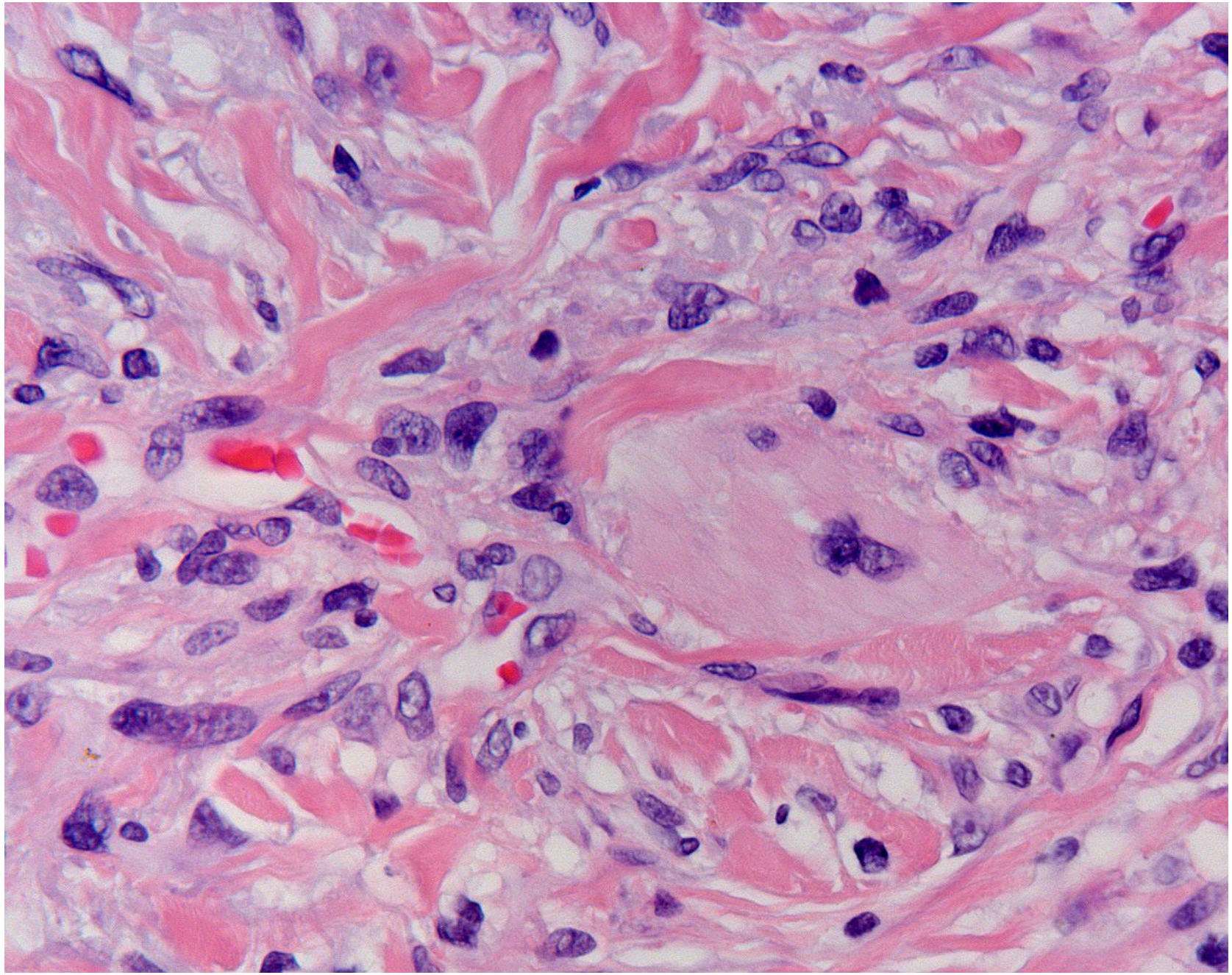




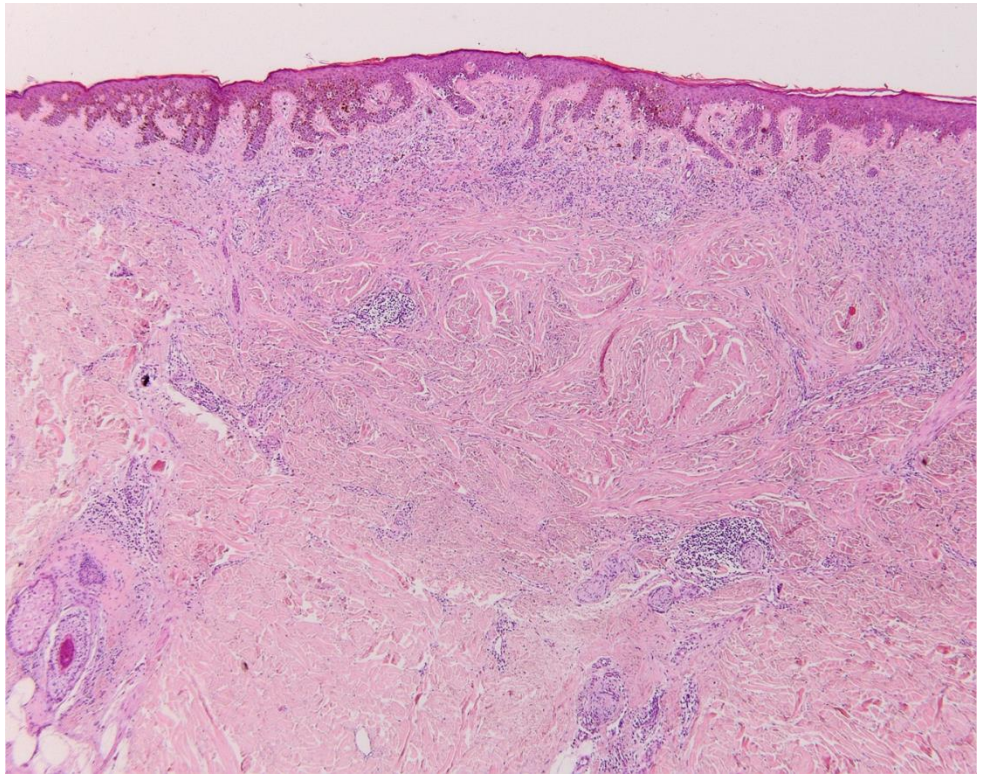




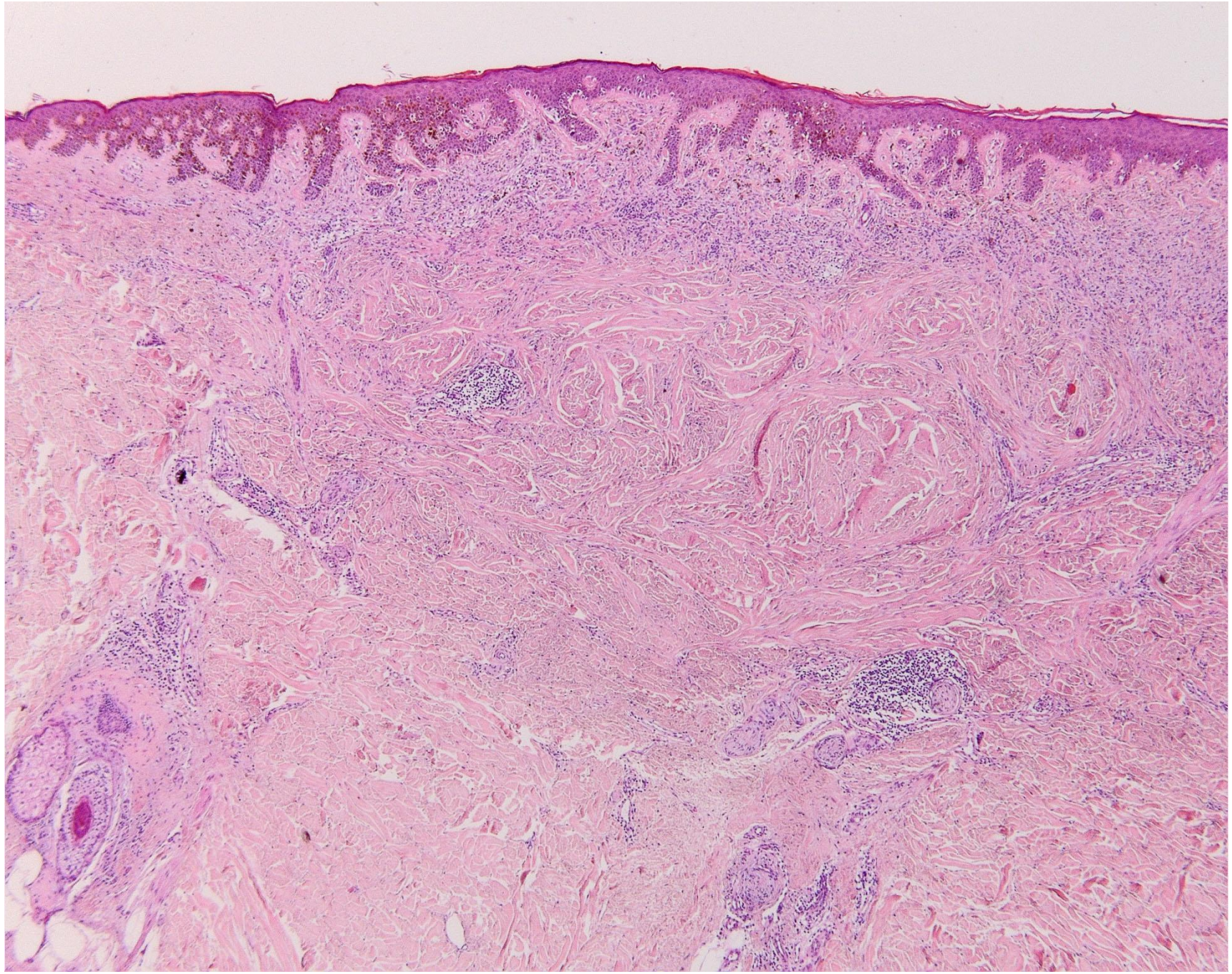


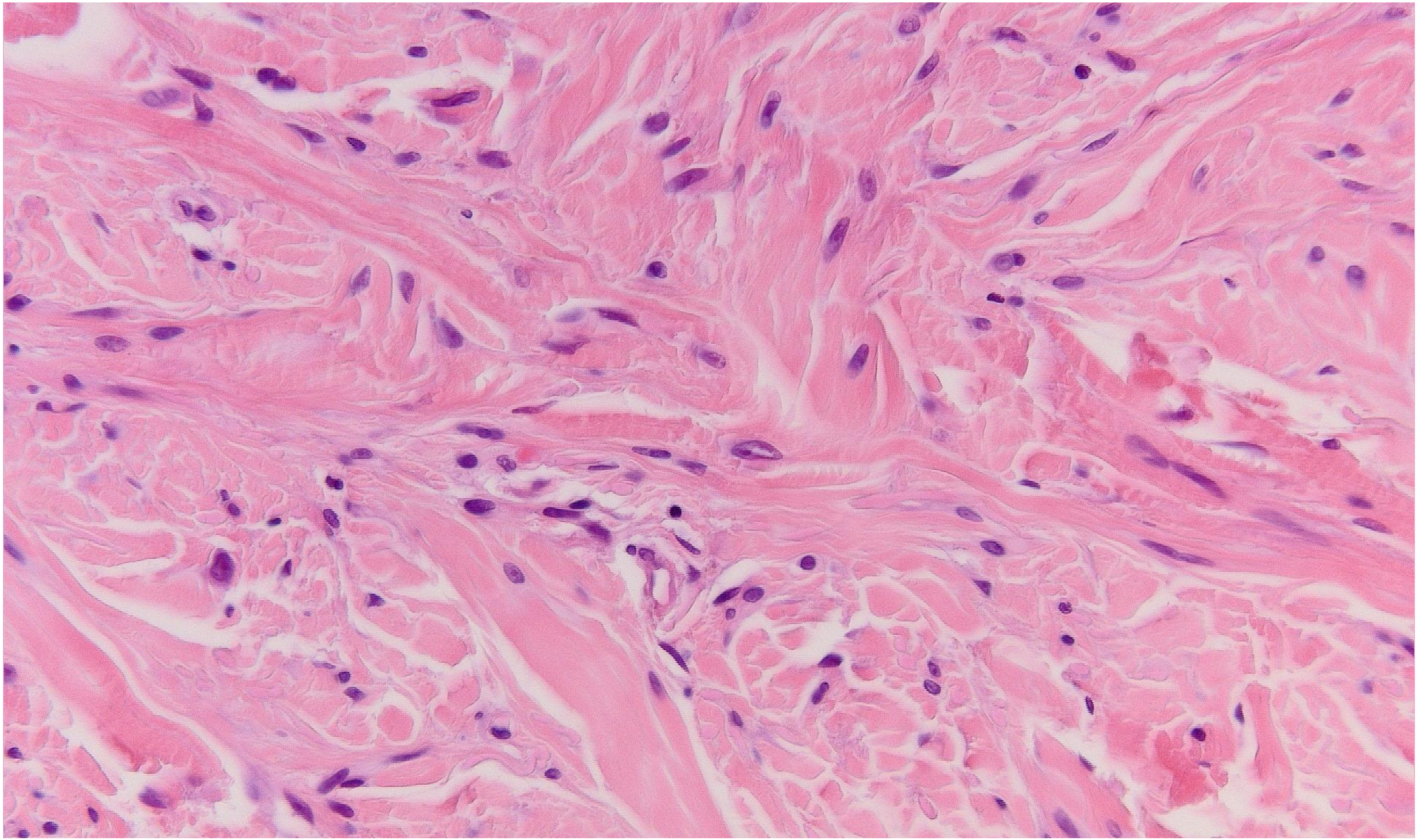


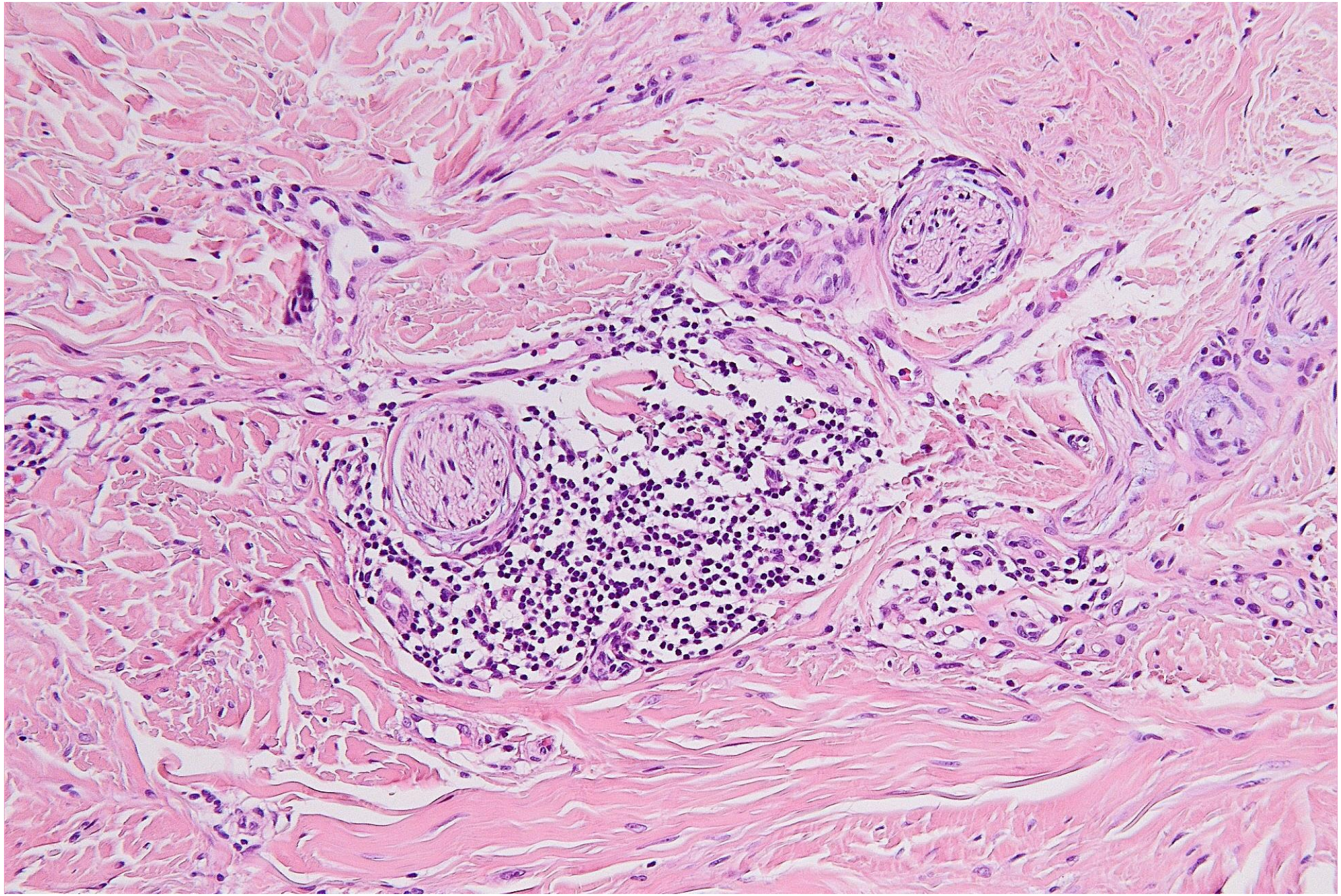
# Desmoplastic naevus: a benign simulator of desmoplastic melanoma



Kiuru M, Patel RM, Busam KJ. Desmoplastic melanocytic nevi with lymphocytic aggregates. *J Cutan Pathol*. 2012; **39**: 940-4.







J Cutan Pathol 2012: 39: 940–944
doi: 10.1111/j.1600-0560.2012.01962.x
John Wiley & Sons. Printed in Singapore



Journal of
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# Desmoplastic melanocytic nevi with lymphocytic aggregates

Desmoplastic melanocytic nevi can be difficult to distinguish from desmoplastic melanoma. The presence of lymphocytic aggregates in association with a sclerosing melanocytic proliferation is commonly regarded as a feature in support of a diagnosis of desmoplastic melanoma. However, the finding is not specific for melanoma. Herein

**Maija Kiuru[1], Rajiv M. Patel[2] and Klaus J. Busam[3]**

[1]Department of Dermatology, Weill Medical College of Cornell University, New York, NY, USA

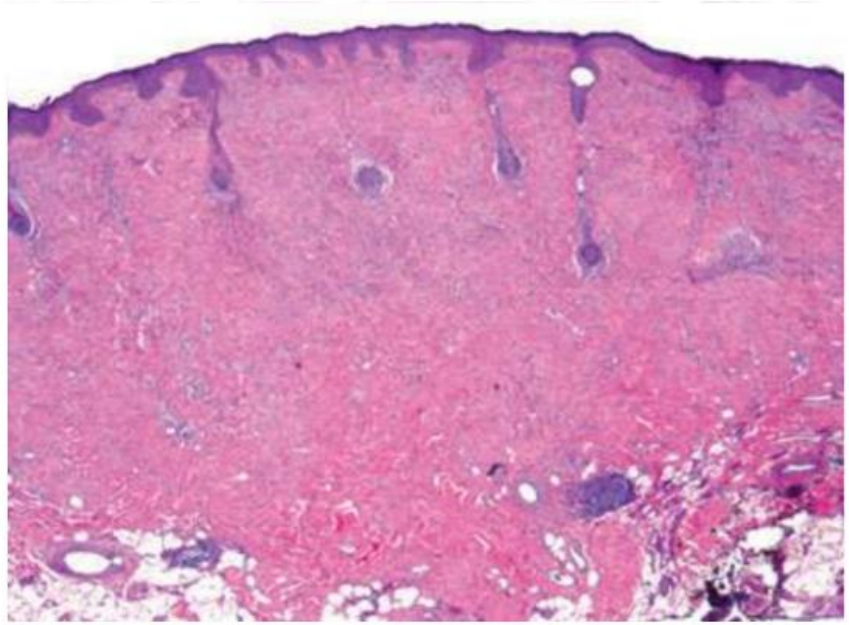

*Fig. 1.* Wedge-shaped symmetric silhouette of an intradermal paucicellular sclerosing nevus with lymphocytic aggregates in the reticular dermis.

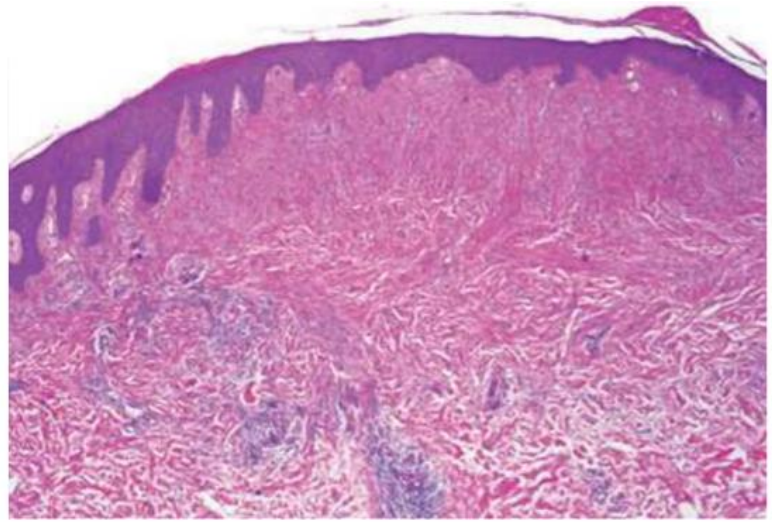

*Fig. 2.* Compound melanocytic nevus with sclerosis. Nests of melanocytes are present at the dermoepidermal junction and in the superficial dermis. Solitary units of melanocytes predominate within sclerotic dermis. Lymphocytic aggregates are present at the base.

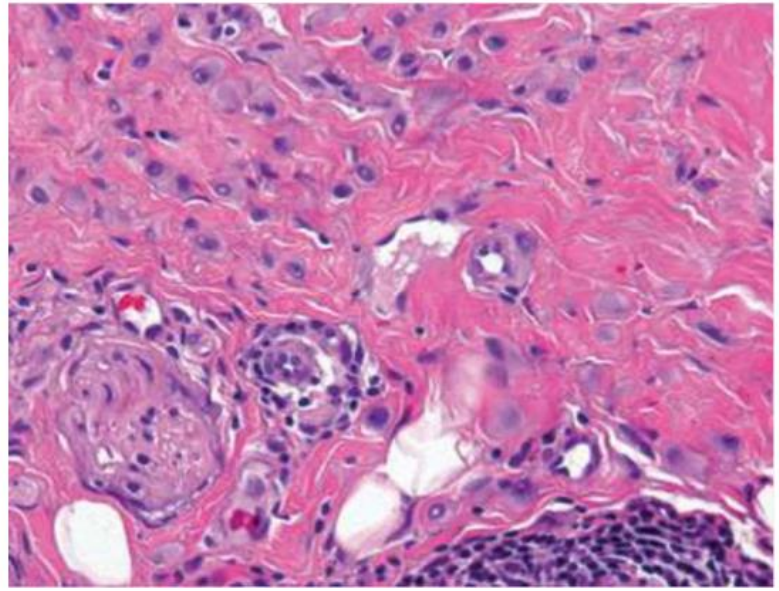

*Fig. 3.* Sclerosing Spitz nevus with epithelioid melanocytes adjacent to a lymphocytic aggregate.

# The end