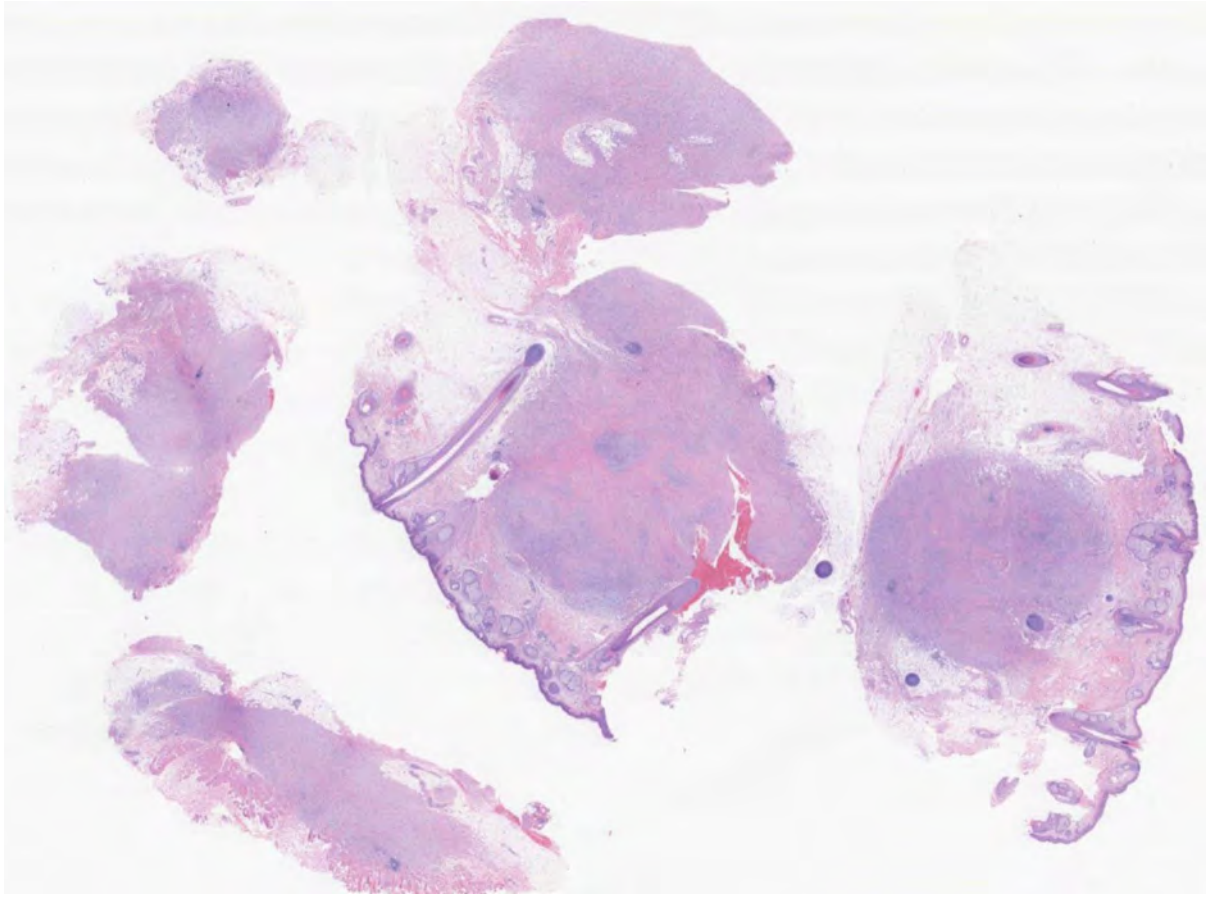
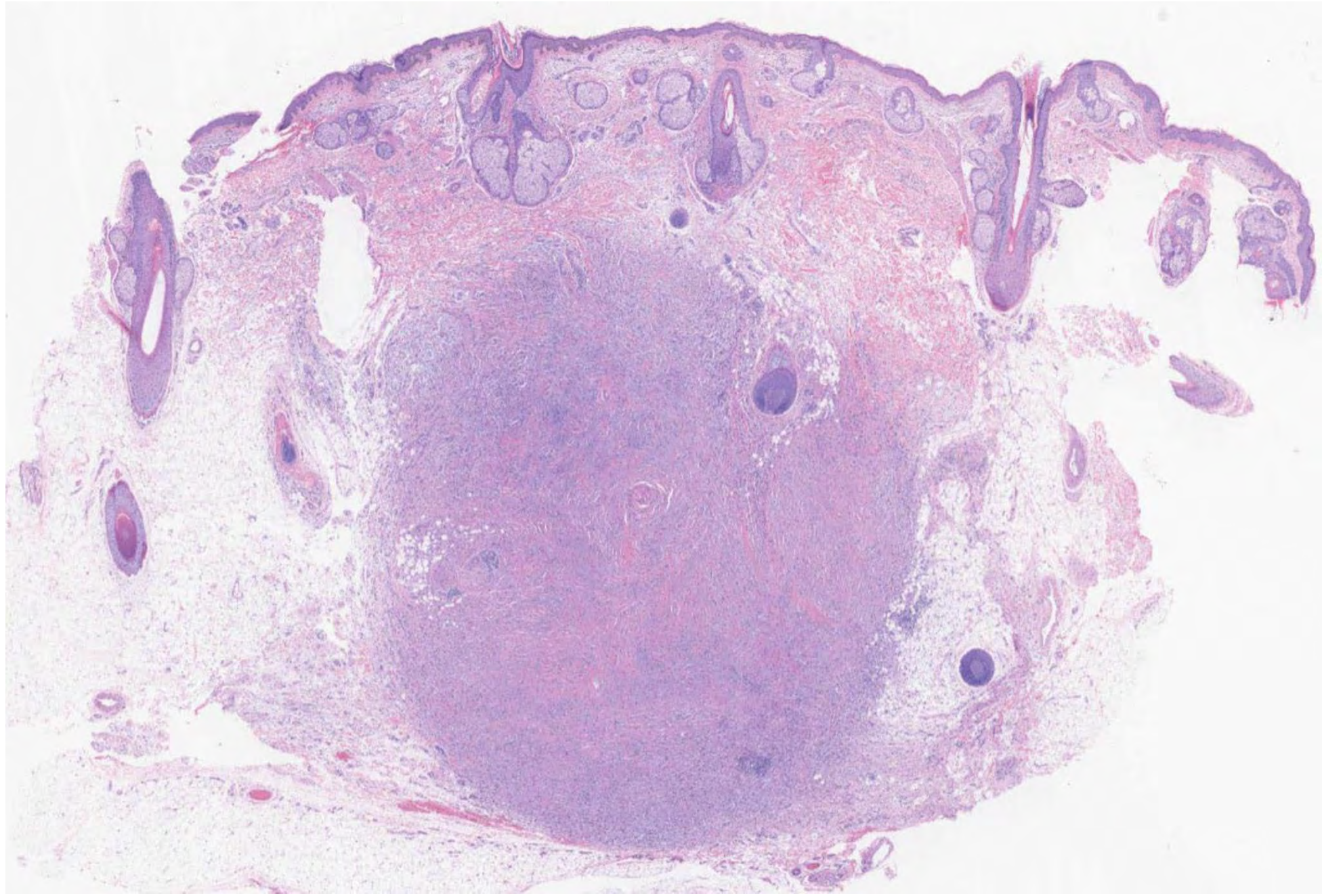
Graz, July 1, 2025

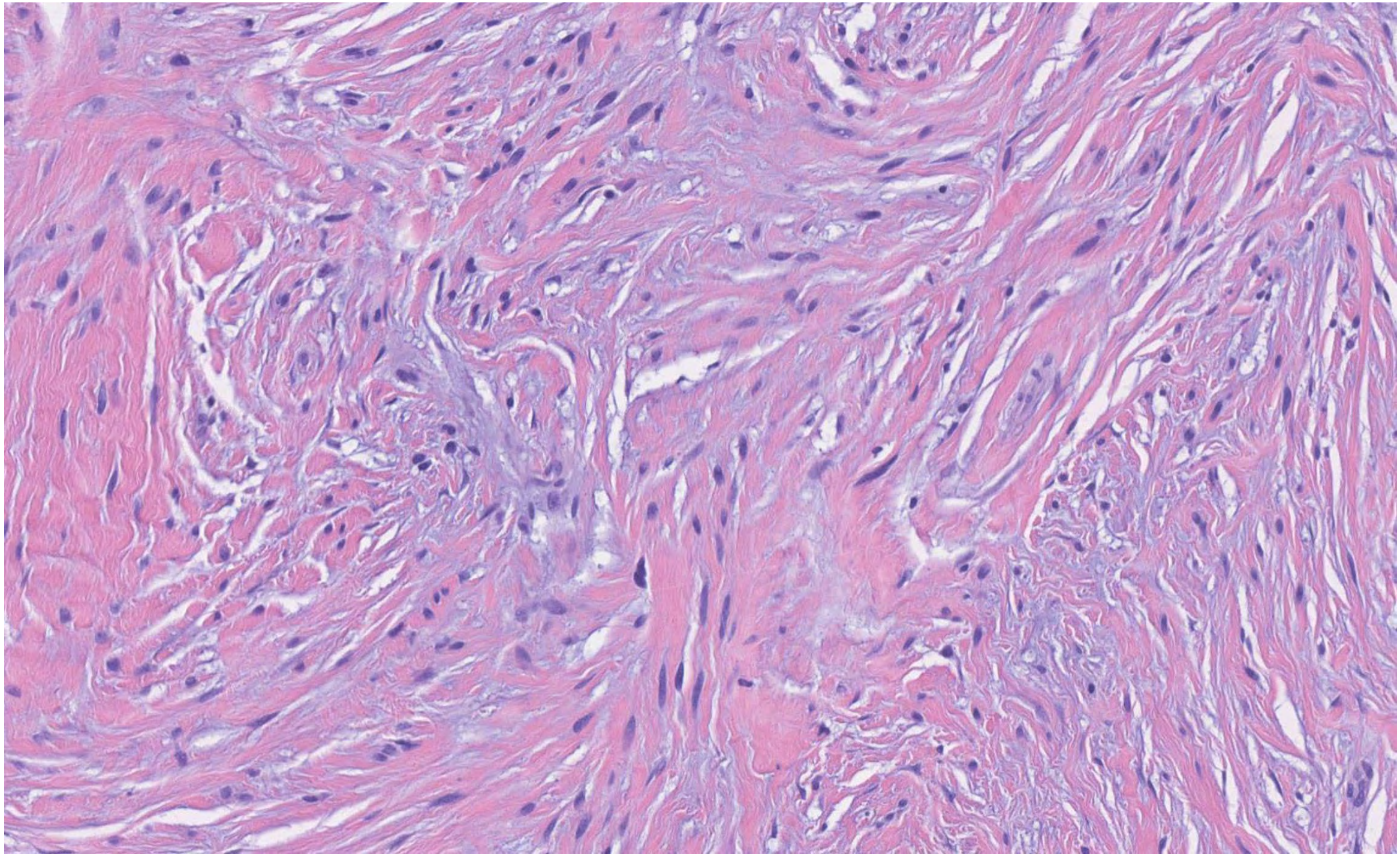
Desmoplastic Melanocytic Tumors

Memorial Sloan Kettering Cancer Center, NYC

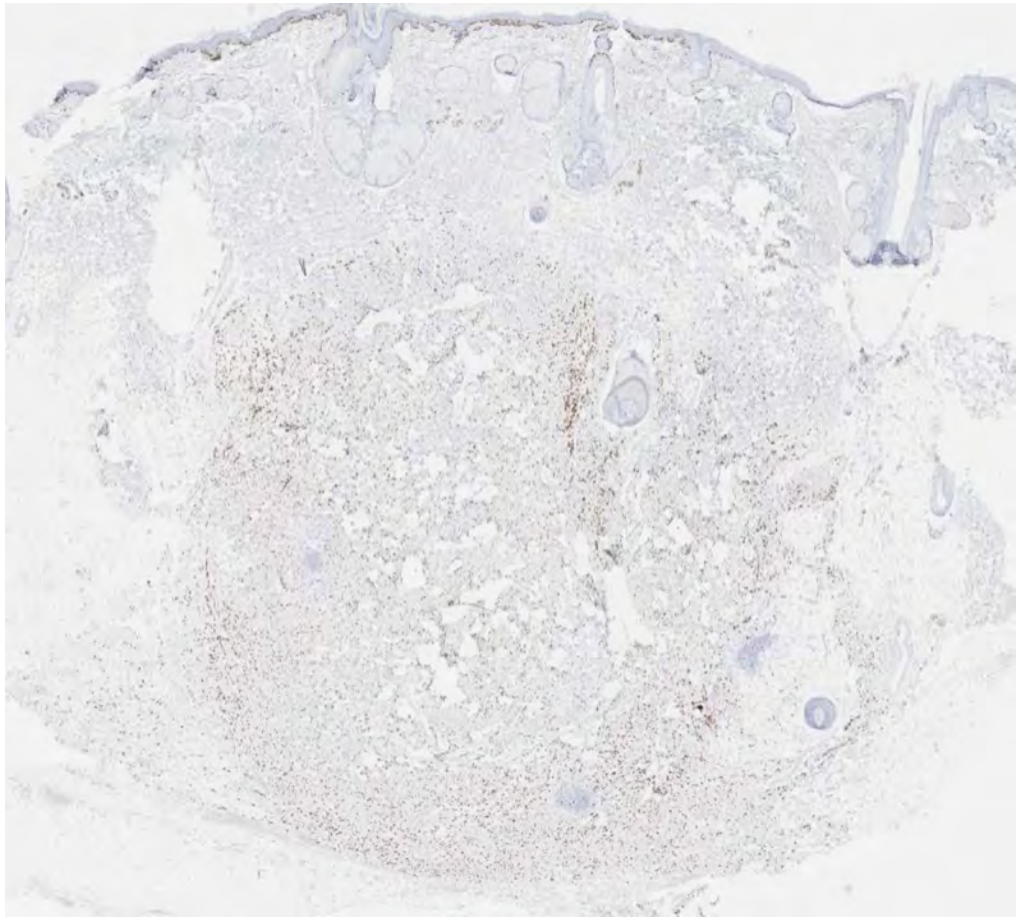
Case 1: 93M, nodule on cheek, r/o cyst

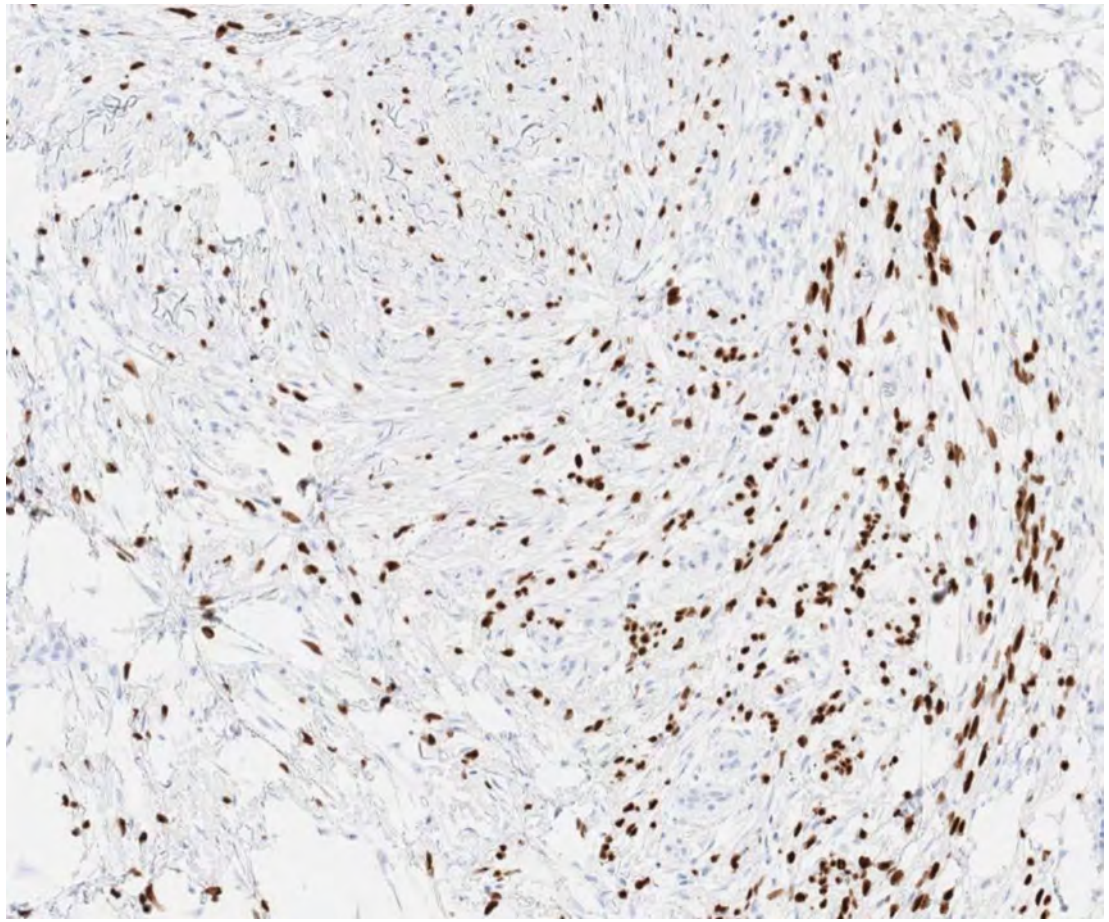






IHC – Sox10





93M, nodule on cheek, r/o cyst

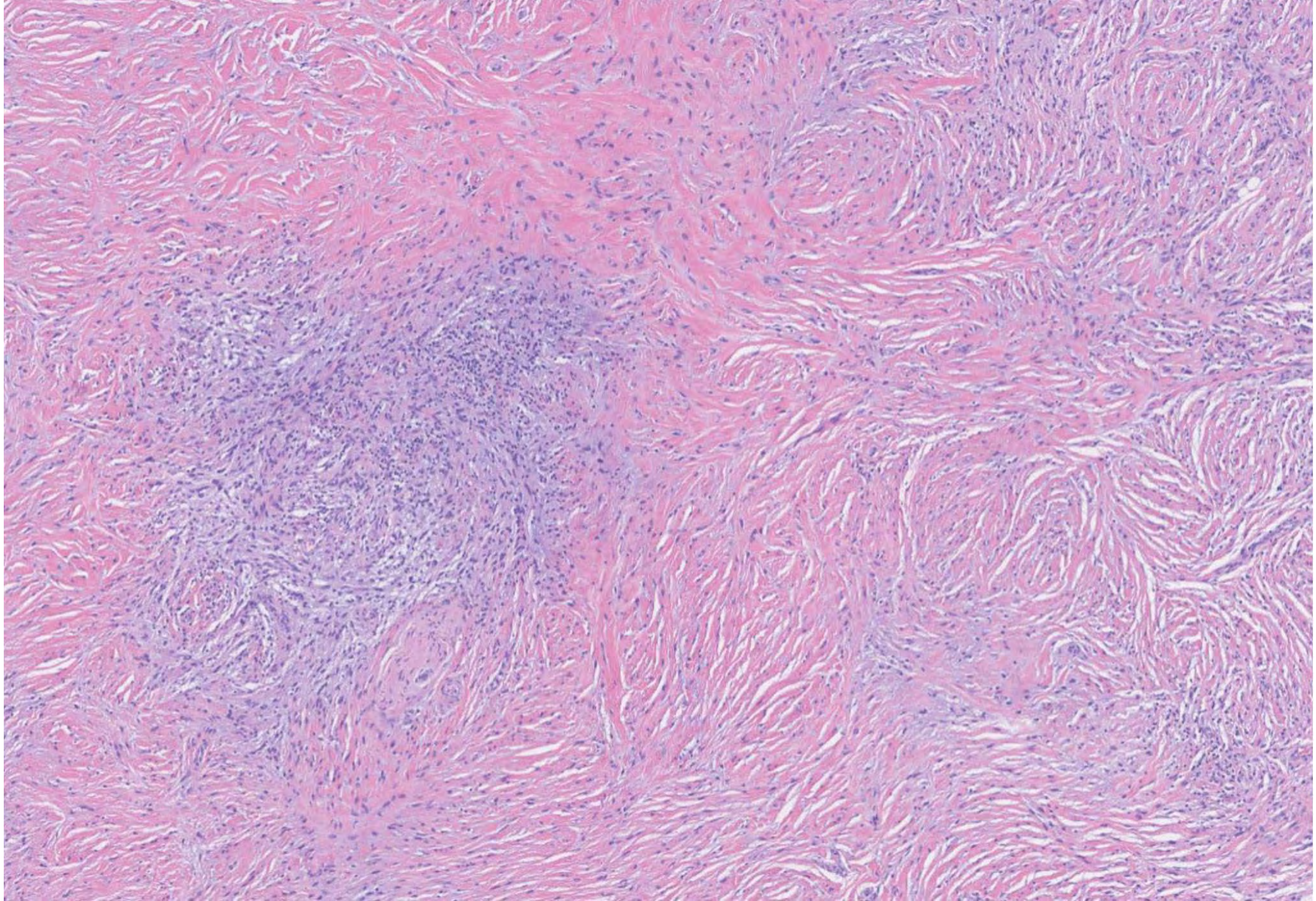
Specimens

A	Forehead, upper forehead excision, suture at 12 o'clock
B	Cheek, left cheek excision

Final Diagnosis

A. Skin, Upper Forehead, Excision:
Basal cell carcinoma; resection margins negative.

B. Left Cheek Excision:
Dermal spindle cell proliferation with neural features; see microscopic description.



Spectrum of Neurofibromatous Tumors

Hum Pathol. 2017 September ; 67: 1–10. doi:10.1016/j.humpath.2017.05.010.

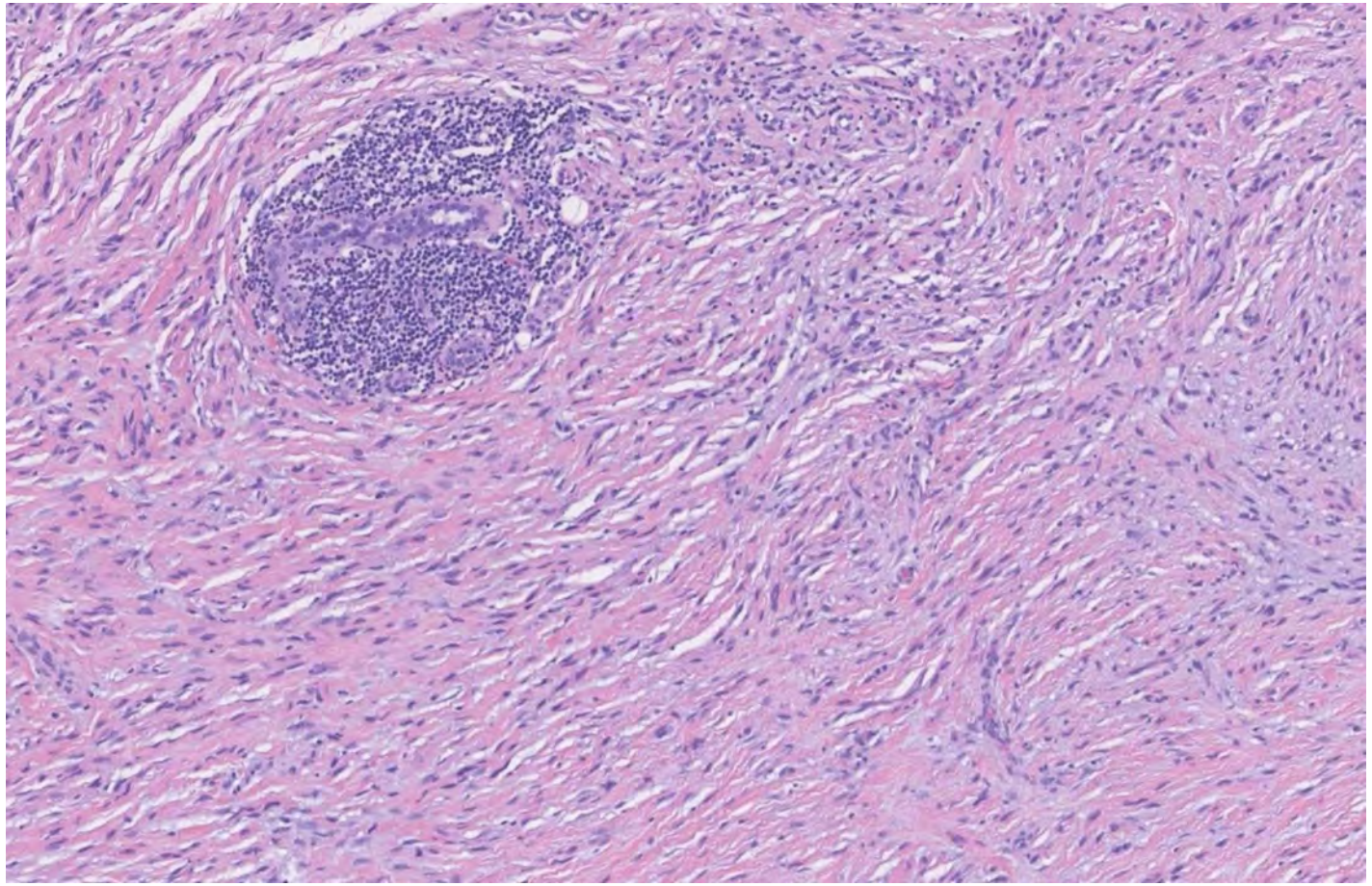
HISTOPATHOLOGIC EVALUATION OF ATYPICAL NEUROFIBROMATOUS TUMORS AND THEIR TRANSFORMATION INTO MALIGNANT PERIPHERAL NERVE SHEATH TUMOR IN NEUROFIBROMATOSIS 1 PATIENTS – A CONSENSUS OVERVIEW

Markku M. Miettinen, MD[1], **Cristina R. Antonescu, MD**[2], **Christopher D. M. Fletcher, MD**[3], **Aerang Kim, MD**[4], **Alexander J. Lazar, MD**[5], **Martha M. Quezado, MD**[1], **Karlyne M. Reilly, PhD**[6], **Anat Stemmer-Rachamimov, MD**[7], **Douglas R. Stewart, MD**[8], **David Viskochil, MD**[9], **Brigitte Widemann, MD**[10], and **Arie Perry, MD**[11]

Spectrum of Neurofibromatous Tumors

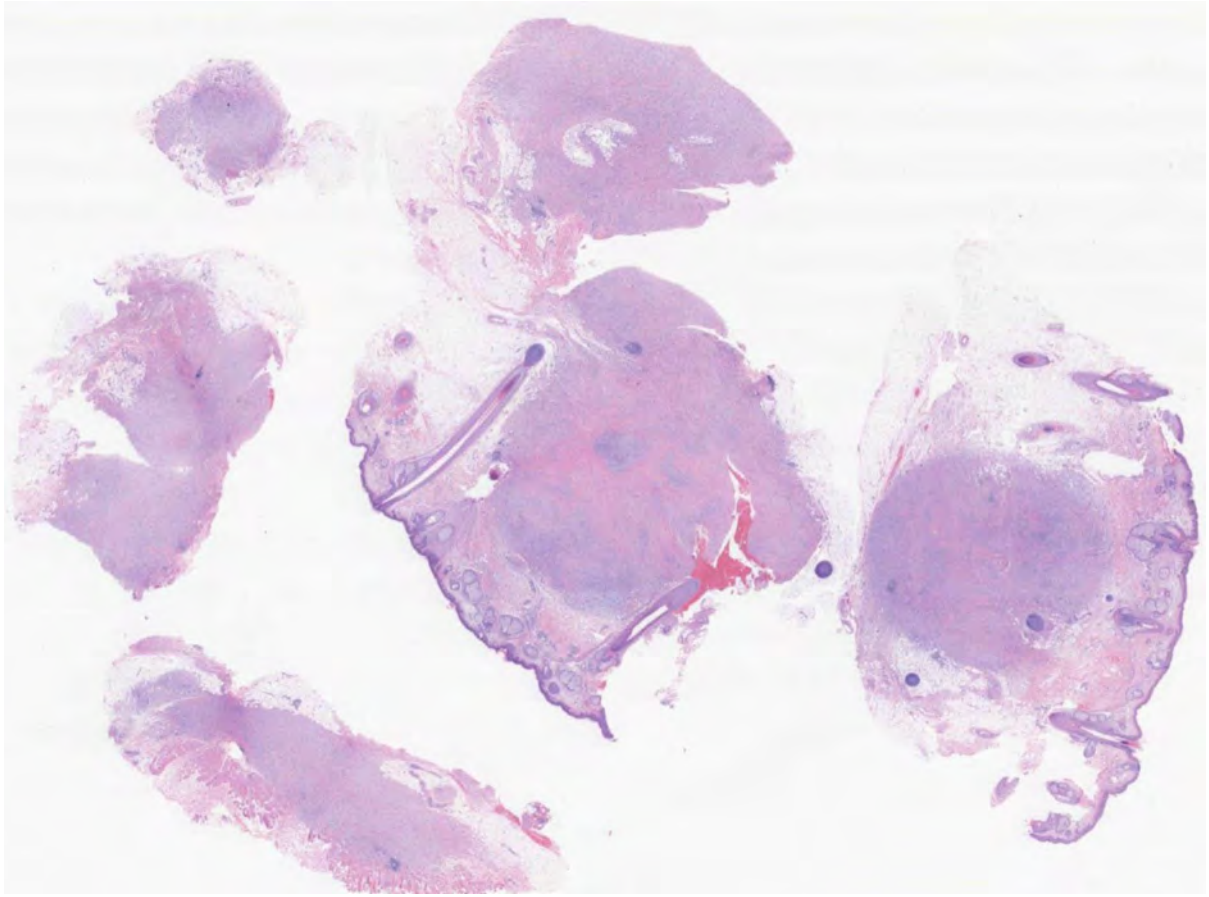
- Neurofibroma
- Neurofibroma with hypercellularity and atypia
- Atypical neurofibromatous tumor of uncertain malignant potential
- Low grade malignant peripheral nerve sheath tumor

Lymphocytic Aggregate

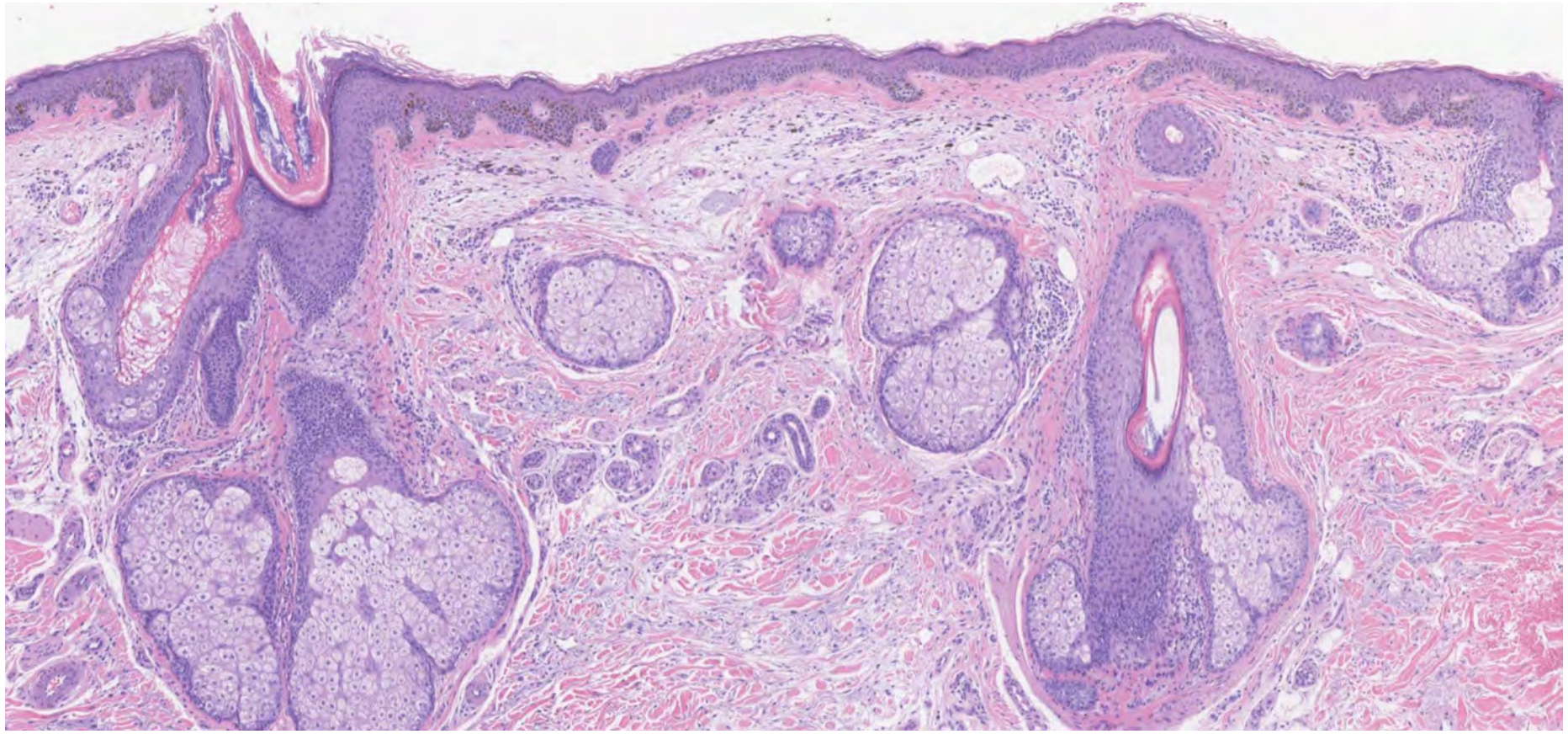


Multiple tissue sections

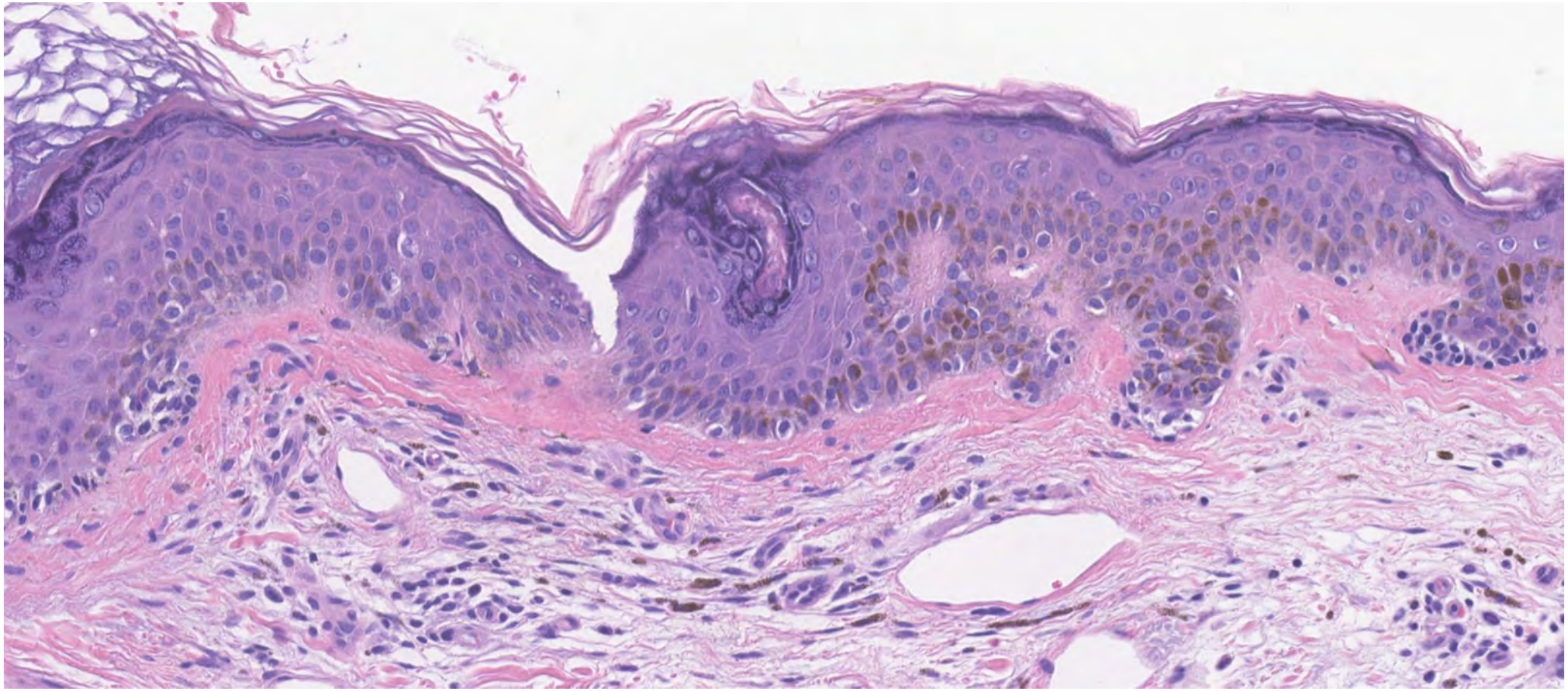
- 93 M
- Nodule on cheek

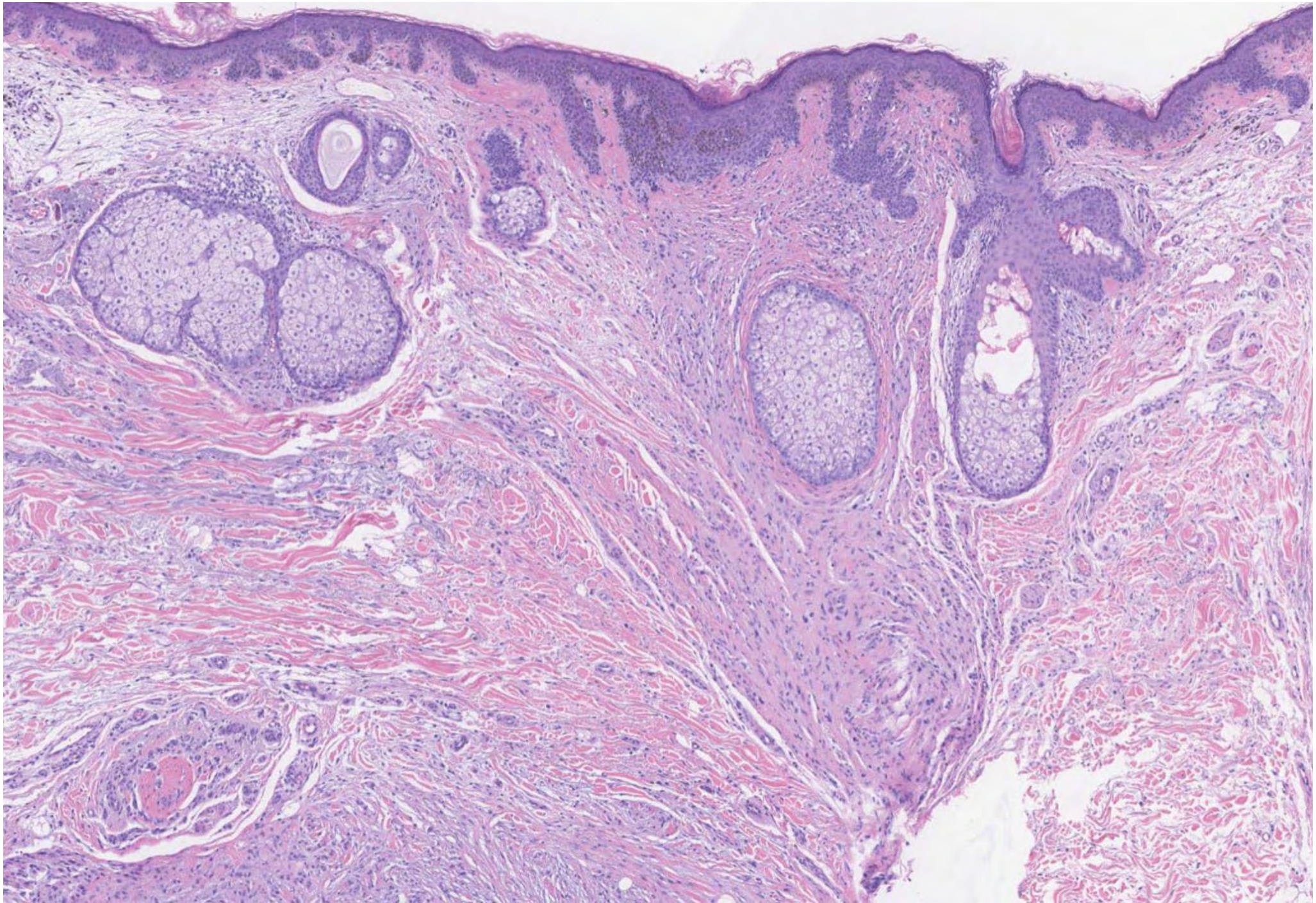


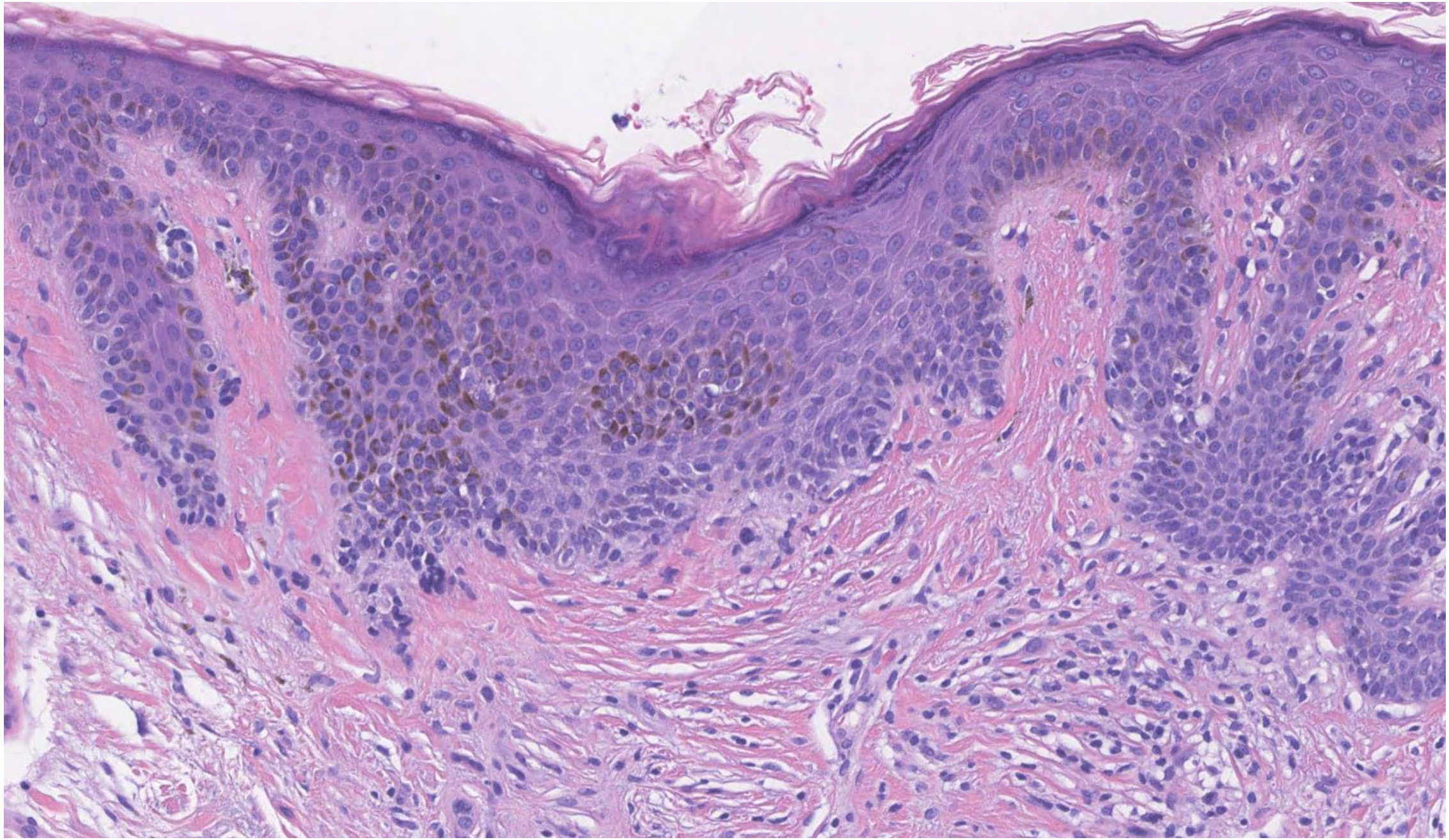
Skin overlying the nodule



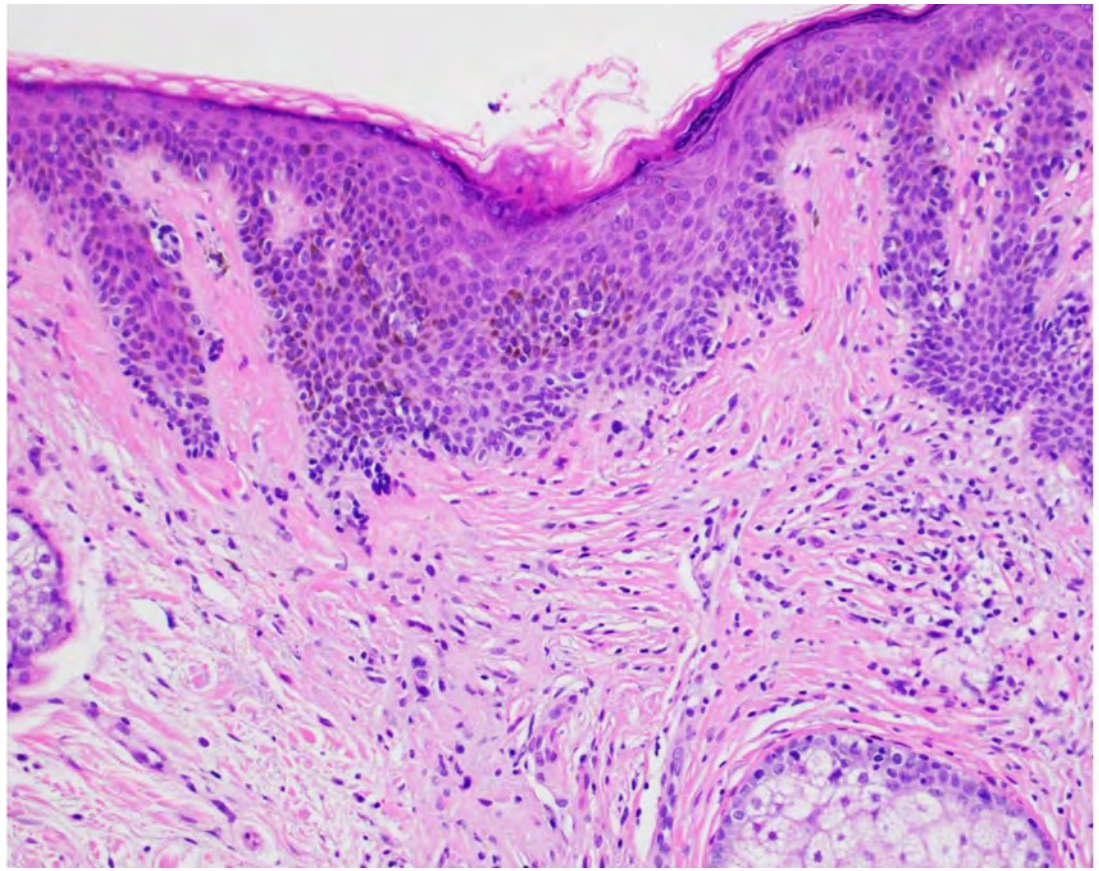
Junctional Melanocytic Proliferation



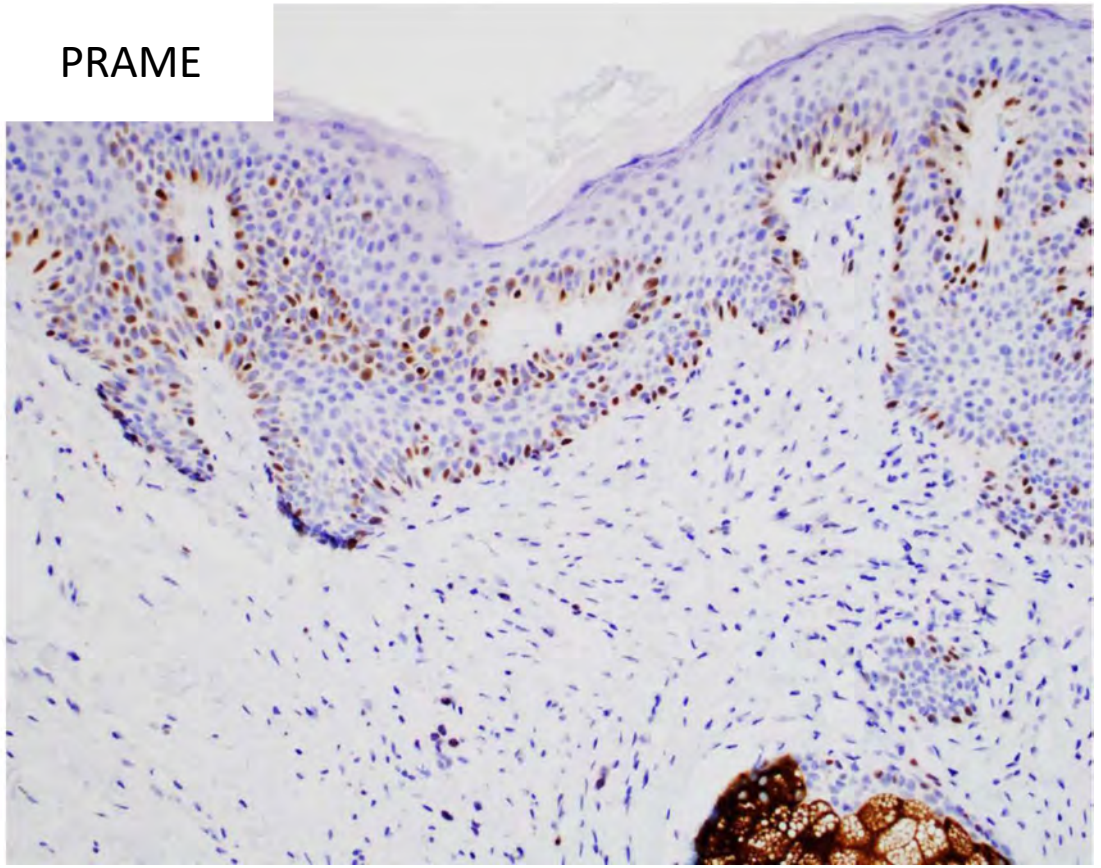




Associated melanoma in situ



PRAME



Case 1: Diagnosis

Desmoplastic Melanoma

The 2018 World Health Organization Classification of Cutaneous, Mucosal, and Uveal Melanoma

Detailed Analysis of 9 Distinct Subtypes Defined by Their Evolutionary Pathway

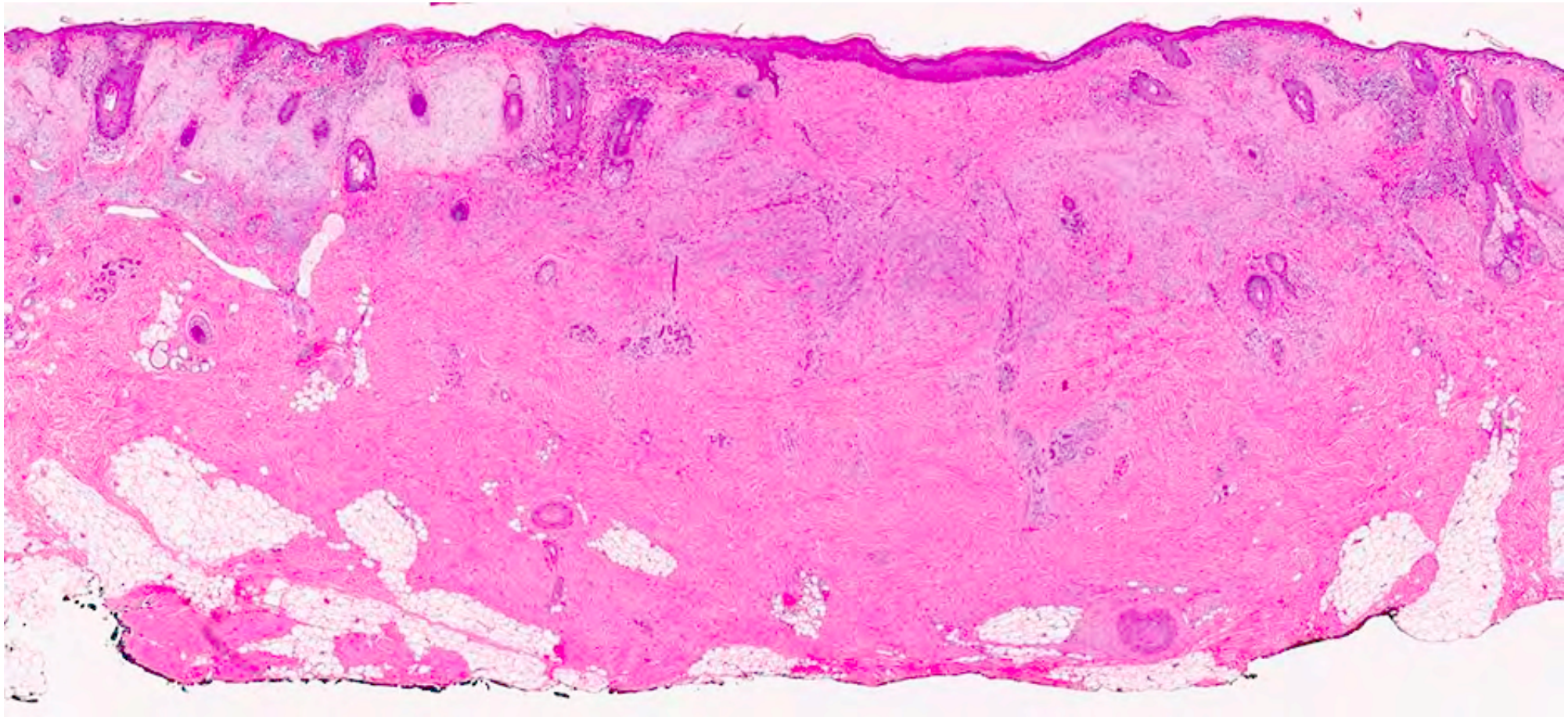
David E. Elder, MB ChB, FRCPA; Boris C. Bastian, MD, PhD; Ian A. Cree, MB ChB, PhD, FRCPath; Daniela Massi, MD, PhD; Richard A. Scolyer, MD, FRCPA, FRCPath

Table 1. Classification of Melanoma (Modified From 2018 WHO Classification)

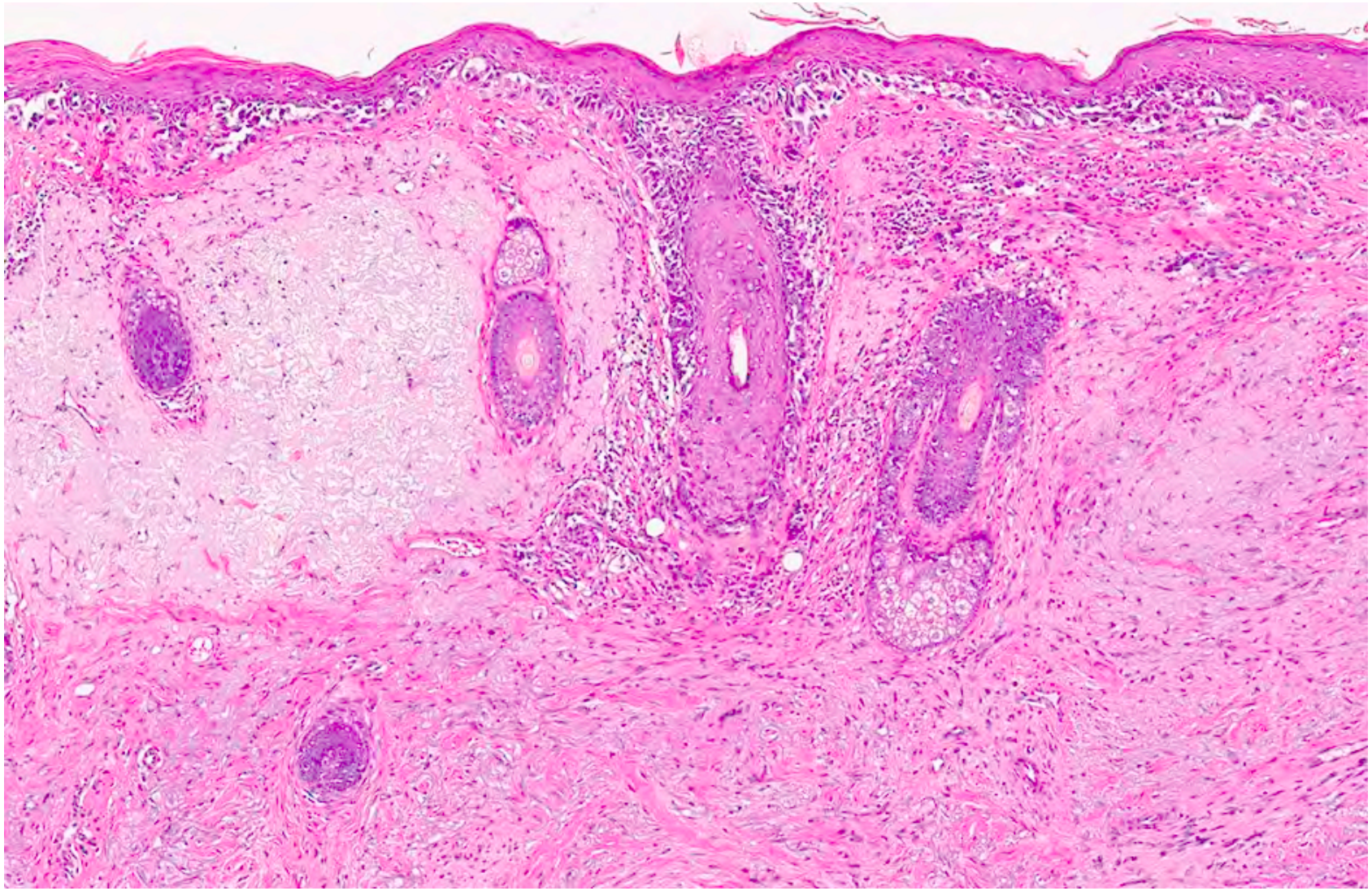
A. Melanomas typically associated with CSD
Pathway I. Superficial spreading melanoma/low-CSD melanoma
Pathway II. Lentigo maligna melanoma/high-CSD melanoma
Pathway III. Desmoplastic melanoma
B. Melanomas not consistently associated with cumulative solar damage (no CSD)
Pathway IV. Spitz melanomas
Pathway V. Acral melanoma
Pathway VI. Mucosal melanomas
Pathway VII. Melanomas arising in congenital nevi
Pathway VIII. Melanomas arising in blue nevi
Pathway IX. Uveal melanoma (not considered further in this review)
C. Nodular melanoma (may occur in any or most of the pathways)

Abbreviation: CSD, cumulative solar damage.

Desmoplastic Melanoma - Pathology



Desmoplastic Melanoma - Pathology



DM – Heterogenous Group of Tumors

- "Classic" Desmoplastic Melanoma
  - Chronically sun-damaged skin
  - Often associated with lentigo maligna
  - *De novo* primary dermal melanoma

- Desmoplastic melanoma not associated with chronic sun damage
  - May be associated with superficial spreading or acral melanoma
  - May be associated with a nevus
  - May be a *de novo* primary dermal melanoma

DM – Clinical Behavior

- Local persistence/recurrence more common

- Regional node metastasis less common

DM – Local Recurrence

- Anatomic site (wide clearance difficult in H&N region)
- Positive margins can be difficult to see
- Perineural invasion

Local Recurrence

Review Article

Local Recurrence Rates After Excision of Desmoplastic Melanoma: A Systematic Review and Meta-Analysis

Nina A. Ran, MD,* Surya Veerabagu, BA,† Christopher J. Miller, MD,* Rosalie Elenitsas, MD,* Emily Y. Chu, MD, PhD,* and Aimee E. Krausz, MD*

BACKGROUND Few prospective studies have evaluated local recurrence rates (LRR) after excision of desmoplastic melanoma (DM); however, several retrospective studies have reported high LRR.

OBJECTIVE To determine LRR after excision of DM and evaluate factors affecting LRR.

MATERIALS AND METHODS Systematic review of the PubMed, Embase, and Web of Science databases was performed to identify studies reporting local recurrence after excision of DM with conventional wide local excision (WLE), Mohs micrographic surgery (MMS), or staged excision (SE). Meta-analysis was performed to calculate summary LRR and pooled risk ratios (RR).

RESULTS Literature search identified 4 studies evaluating MMS or SE (total $n = 61$ DM). 53 studies assessed WLE ($n = 3,080$) and were analyzed quantitatively. The overall LRR after WLE of DM was 21% (95% CI, 0.16–0.28; $n = 2,308$). Local recurrence rate was higher with positive/unknown histologic excision margins (49%, 95% CI, 0.25–0.74; $n = 91$) versus negative histologic margins (11%, 95% CI, 0.07–0.17; $n = 1,075$; [$p < .01$]). Neurotropism was also associated with increased LRR (RR, 1.79; 95% CI, 1.34–2.38, $p < .01$; $n = 644$).

CONCLUSION DM has high LRR after WLE. Local recurrence risk was greatest with positive excision margins, indicating the importance of achieving negative microscopic margins. Greater study of MMS and SE for DM is required.

Dermatol Surg 2023; 49: 330 - 37

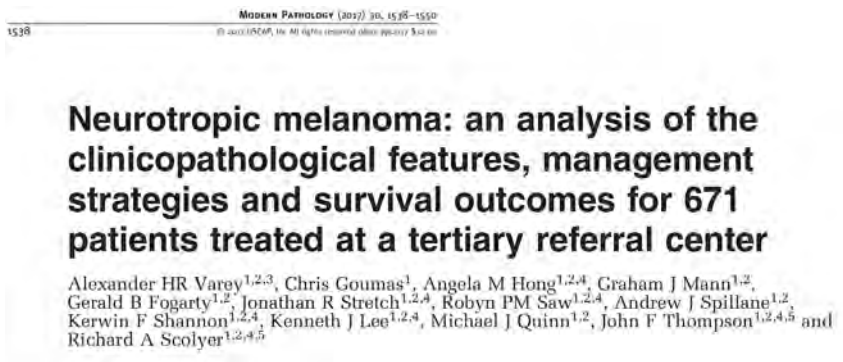
- LRR said to be 11%
- Studies from 1971 - 2021

DM – Local Recurrence Rates

- Egbert (UCSF) *Cancer 1988;62:2033-41* 48%
- Quinn (SMU) *Cancer 1998;83:1128-35* 11%
- Livestro (MGH) *J Clin Oncol 2005;23:6739-46* 7.9%
- Gyorki (MSKCC) *Ann Surg Oncol 2003;10:403-7* 4%
- Arora (UofM) *Cancer 2005;104:1462-7* 4%

How to Minimize Local Recurrence for DM

- Wide and deep excision
- Meticulous margin assessment
  - Comprehensive sampling and mapping
  - Use if IHC
- Post-operative XRT in selected cases



Modern Pathology (2017) 30, 1538–1550

1538

Neurotropic melanoma: an analysis of the clinicopathological features, management strategies and survival outcomes for 671 patients treated at a tertiary referral center

Alexander HR Varey[1,2,3], Chris Goumas[1], Angela M Hong[1,2,4], Graham J Mann[1,2], Gerald B Fogarty[1,2], Jonathan R Stretch[1,2,4], Robyn PM Saw[1,2,4], Andrew J Spillane[1,2], Kerwin F Shannon[1,2,4], Kenneth J Lee[1,2,4], Michael J Quinn[1,2], John F Thompson[1,2,4,5] and Richard A Scolyer[1,2,4,5]

Desmoplastic Melanoma – SLN Biopsy

Annals of Surgical Oncology, **10**(4):403–407
DOI: 10.1245/ASO.2003.04.003

Sentinel Lymph Node Biopsy for Patients With Cutaneous Desmoplastic Melanoma

David E. Gyorki, Klaus Busam, MD, Kathy Panageas, PhD, Mary Sue Brady, MD, and Daniel G. Coit, MD

27 patients with pure DM: Not a single SLN was positive

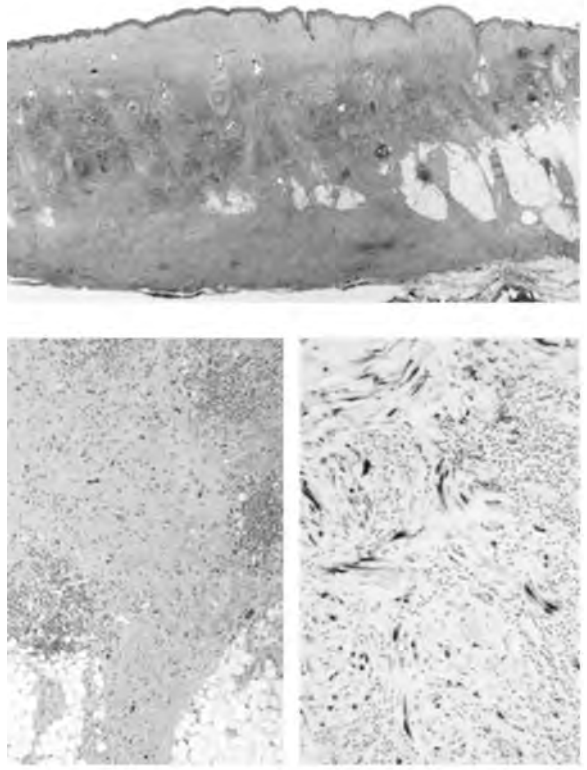


FIG. 1. Desmoplastic melanoma. (**A**) Scanning magnification shows a fibrosing tumor infiltrating the dermis and subcutis. (**B**) The tumor is composed of hyperchromatic spindle cells in a collagen-rich stroma and is focally associated with lymphoid aggregates. (**C**) The tumor cells are homogenously immunopositive for S-100 protein.

Different Data from University of Michigan

Desmoplastic and Neurotropic Melanoma

Analysis of 33 Patients with Lymphatic Mapping and Sentinel Lymph Node Biopsy

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Lori Lowe, M.D.[1,2]
Timothy S. Wang, M.D.[2]
Jennifer L. Schwartz, M.D.[2]
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Vernon K. Sondak, M.D.[3]
Timothy M. Johnson, M.D.[2–4]

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[2] Department of Dermatology, University of Michigan Medical Center, Ann Arbor, Michigan.

[3] Department of Surgery, University of Michigan Medical Center, Ann Arbor, Michigan.

[4] Department of Otorhinolaryngology, University of Michigan Medical Center, Ann Arbor, Michigan.

BACKGROUND. Desmoplastic and neurotropic melanoma (DNMM) occasionally metastasizes to regional lymph nodes and extranodal sites. The value of sentinel lymph node biopsy (SLNB) has not been demonstrated clearly for patients with DNMM. The authors report on the utility of SLNB in the management of patients with DNMM.

METHODS. The authors identified 33 patients with DNMM who were seen during a 5-year period in their institution who underwent lymphatic mapping and SLNB. Clinical and histopathologic data were reviewed.

RESULTS. Thirty-three patients with DNMM underwent SLNB (mean Breslow depth, 4.0 mm; median, 2.8 mm). There were 25 male patients and 8 female patients with a median age of 61 years (range, 31–86 years). Fifty-two percent of tumors presented in the head and neck region, and 24% were associated with lentigo maligna. Four of 33 patients (12%) without clinical evidence of metastatic disease who underwent SLNB had at least 1 positive sentinel lymph node. No additional positive lymph nodes were found in subsequent therapeutic regional lymphadenectomy in any of these four patients.

CONCLUSIONS. SLNB detected subclinical metastases of DNMM to regional lymph nodes. SLNB at the time of resection can provide useful information to guide early treatment and, coupled with lymphadenectomy in positive patients, may limit tumor spread and prevent recurrence at the draining lymph node basin. ***Cancer* 2004;100:598–604.**

4/33 patients with positive SLN

These tumors look different…

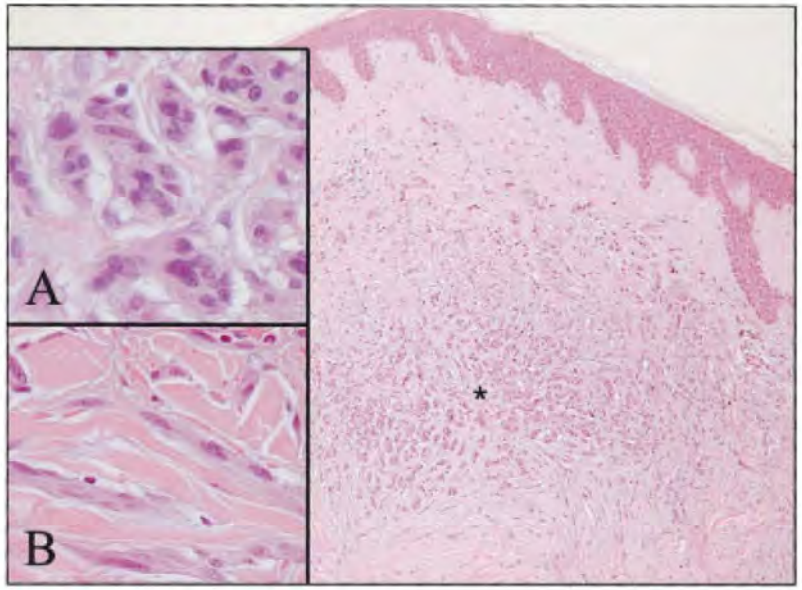


FIGURE 5. Desmoplastic and neurotropic melanoma from Patient 3 showed a small population of conventional epithelioid melanoma cells (asterisk and *inset A*) in the upper part of the tumor and atypical spindle cells invading the deep dermis accompanied by prominent desmoplasia (*inset B*).

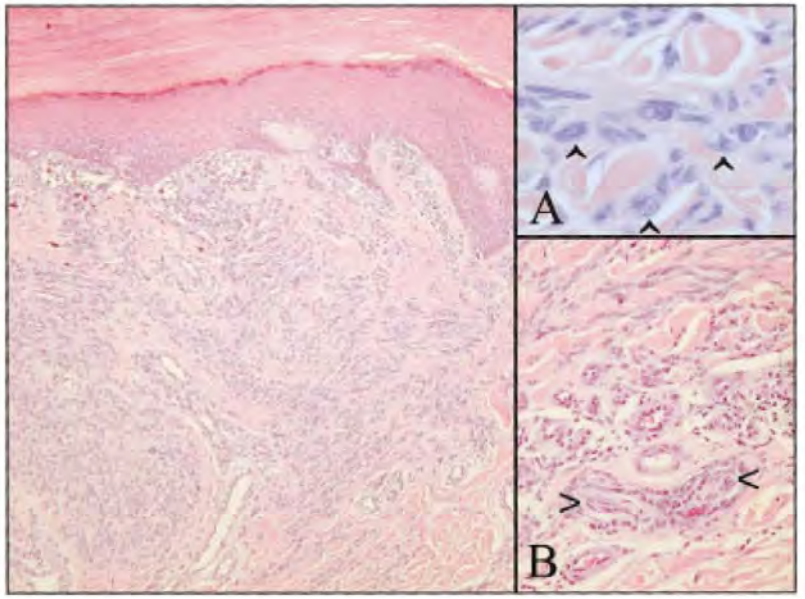
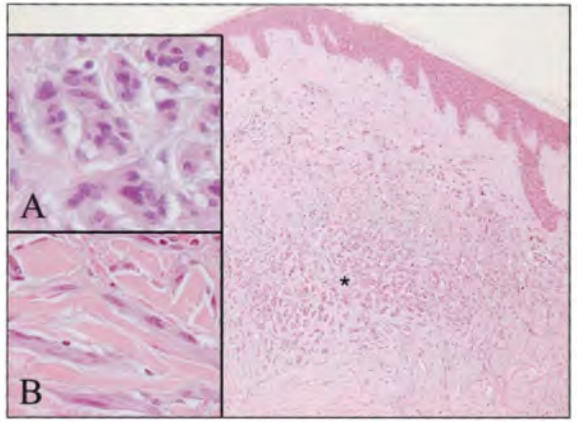


FIGURE 6. Desmoplastic and neurotropic melanoma arising in acral lentiginous melanoma from the foot of Patient 4 showed highly atypical spindle melanocytes infiltrating the dermis (arrowheads in inset A). Tumor cells displayed neurotropism surrounding and invading nerve twigs in deep dermis (arrowheads in inset B).

Metastases with Melan-A-positive epithelioid cells



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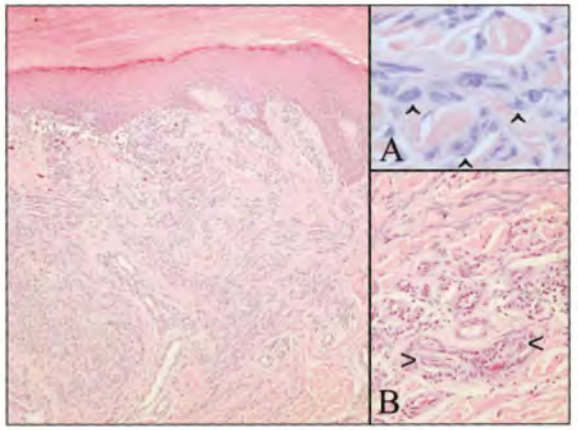

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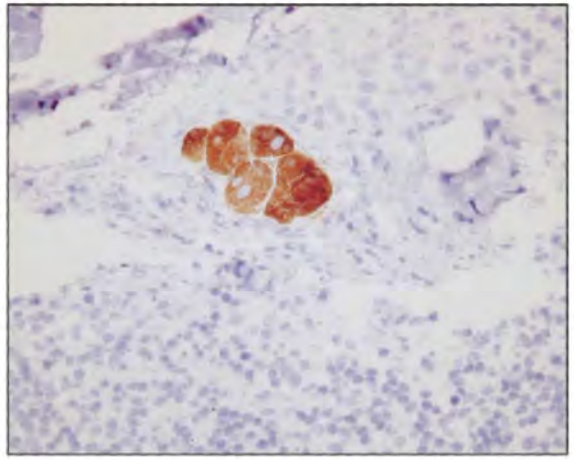


FIGURE 7. One of a few clusters of metastatic epithelioid melanoma in the lymph node parenchyma from Patient 3 was found to express melan-A.

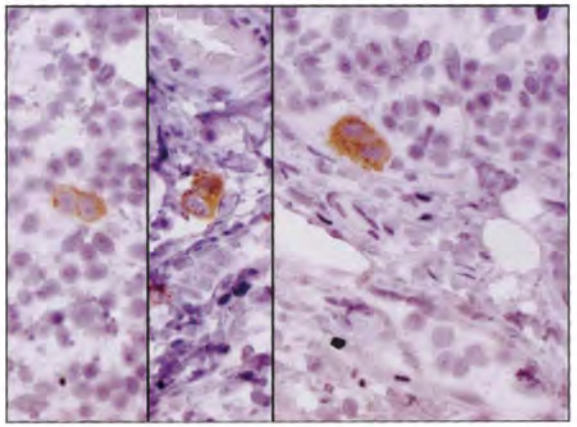
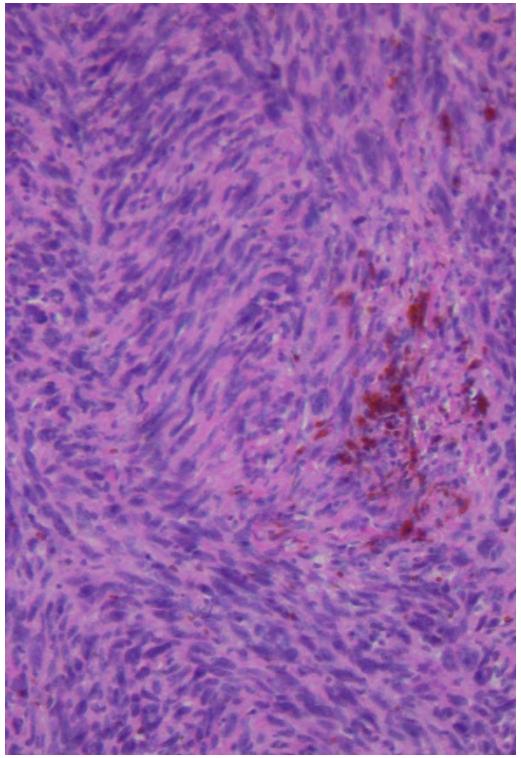
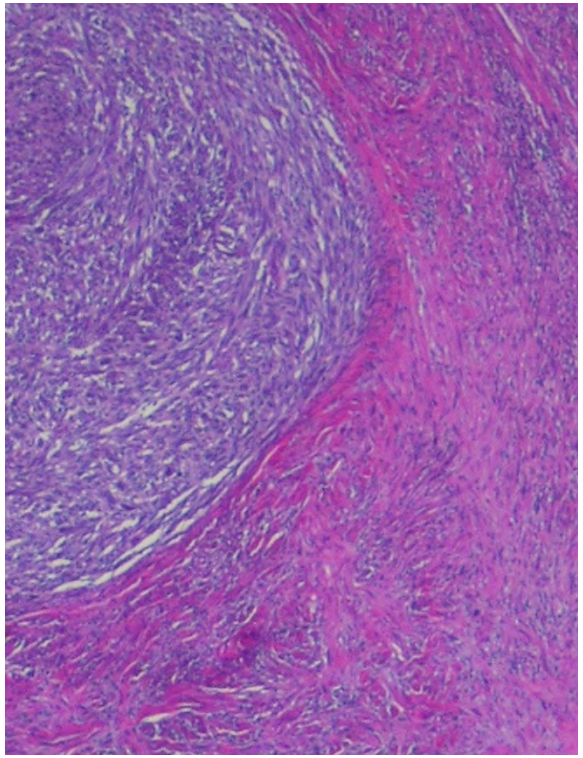


FIGURE 8. In the sentinel lymph node from Patient 4, a few clusters of melan-A positive, atypical epithelioid cells were identified in the parenchyma and peritrabecular areas, consistent with metastatic melanoma.

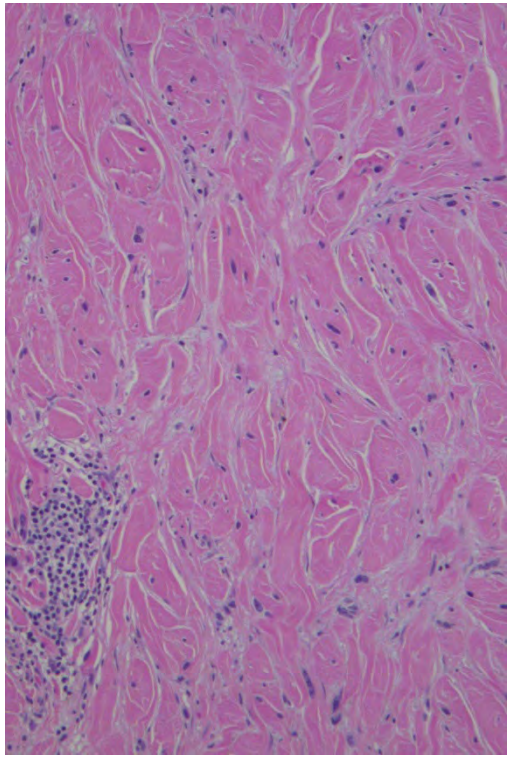
Pure vs mixed vs non-desmoplastic Melanoma



Solid spindle cell

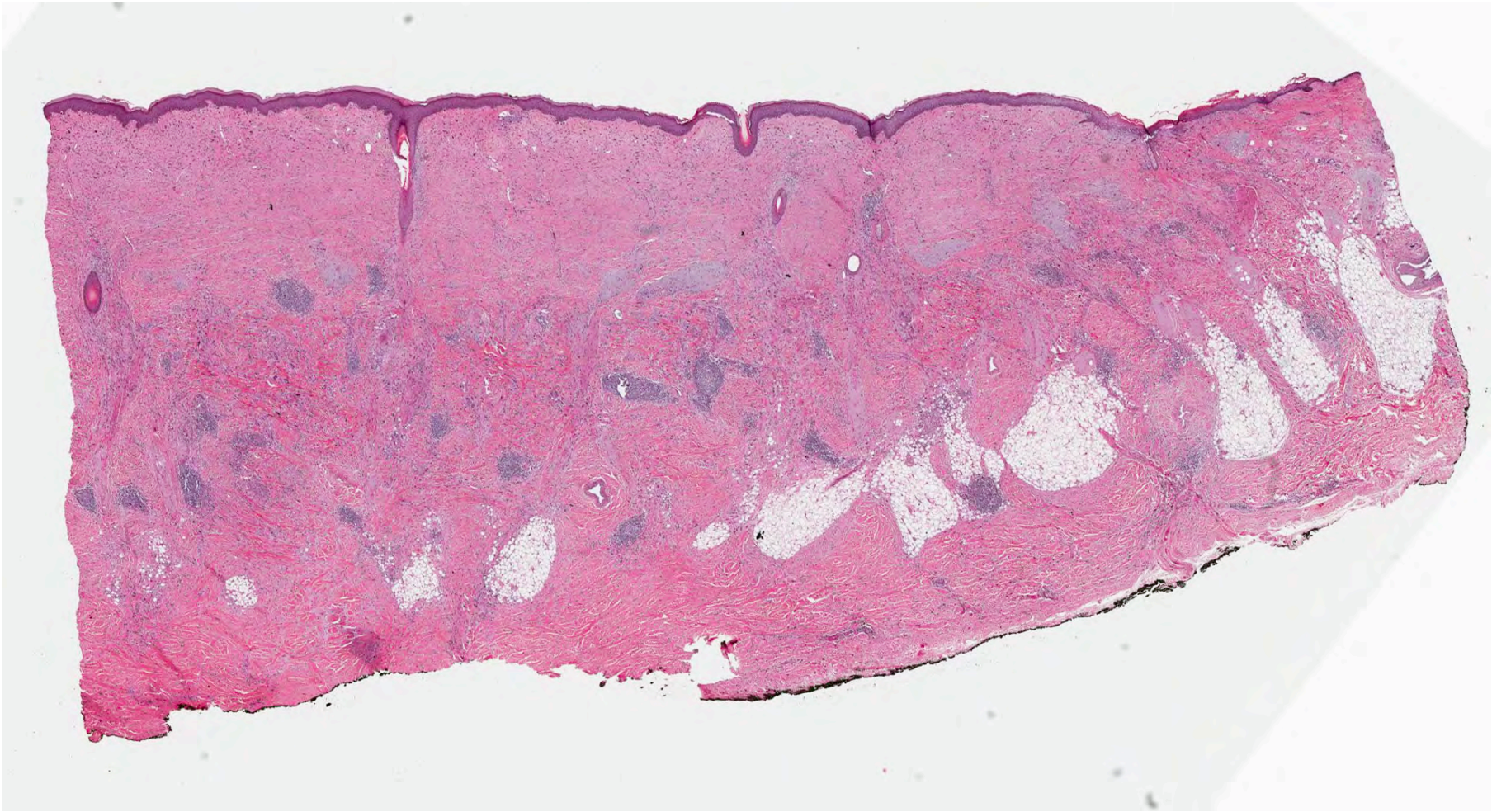


Combined (mixed) DM

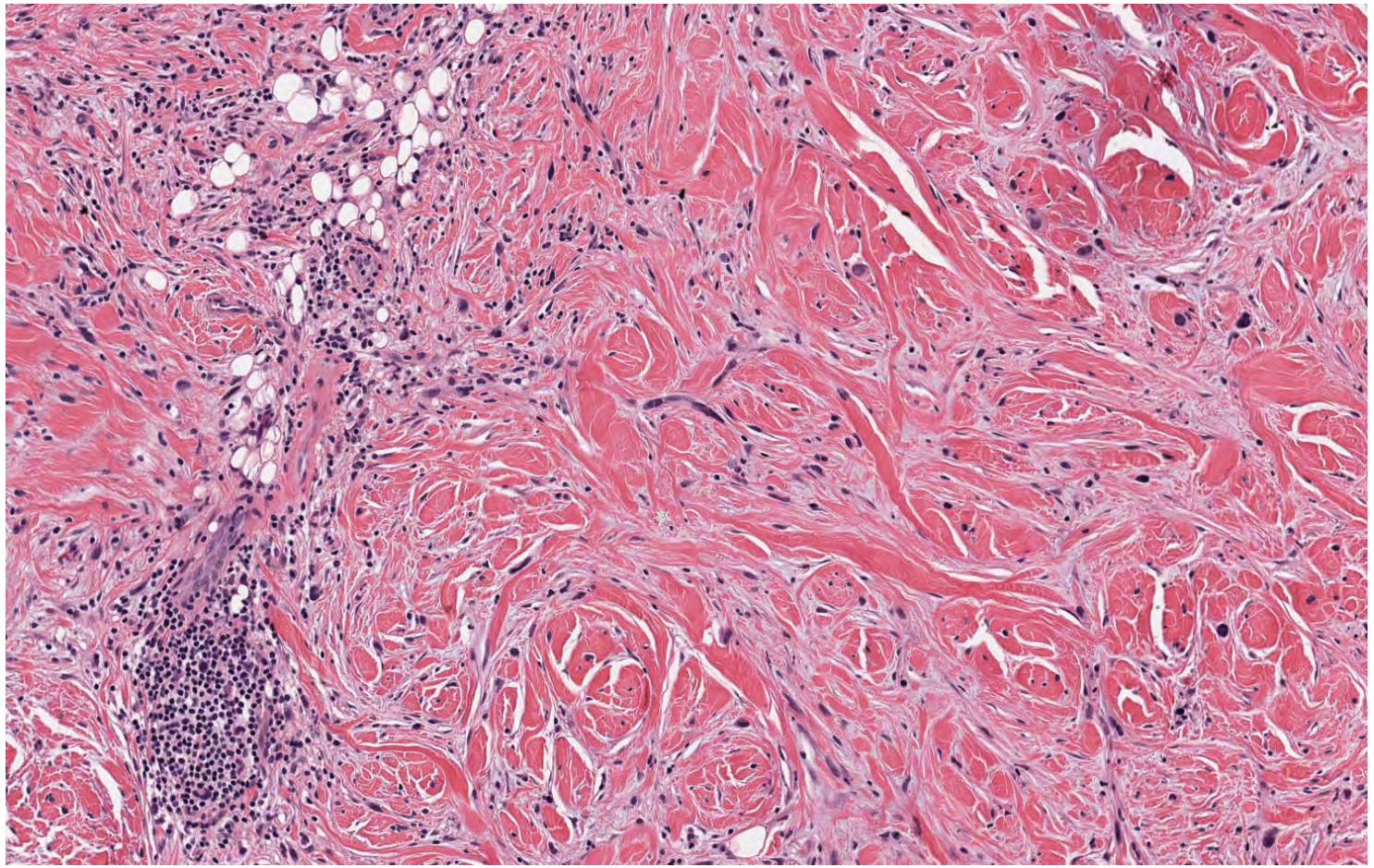


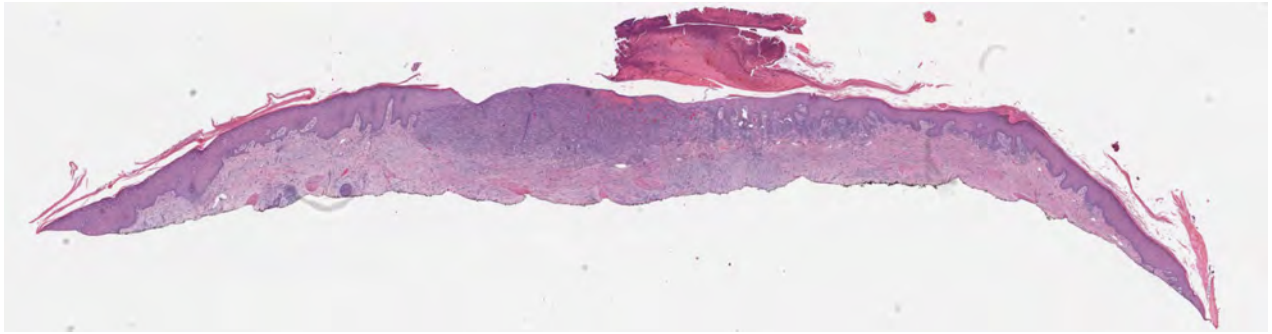
Pure DM

Pure Desmoplastic Melanoma

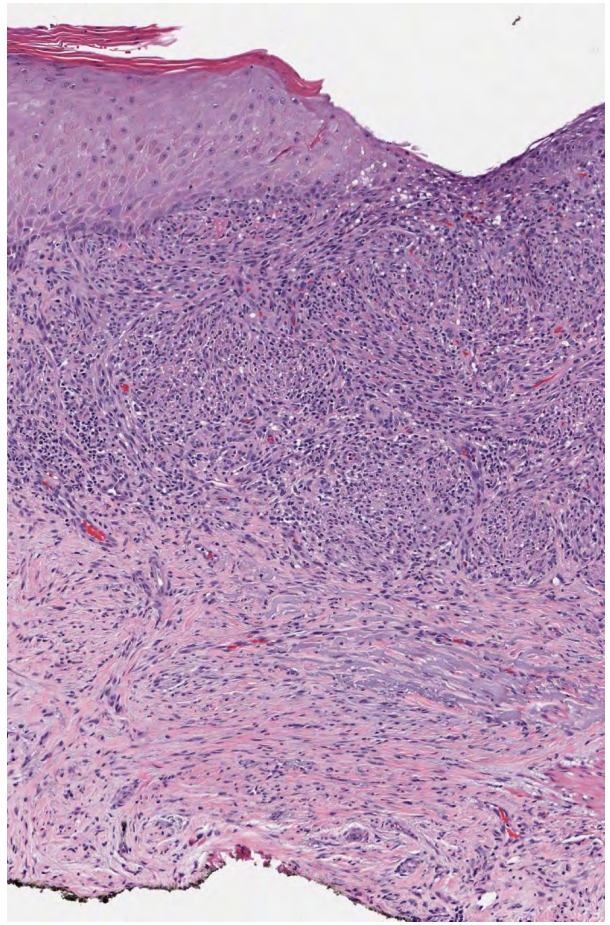


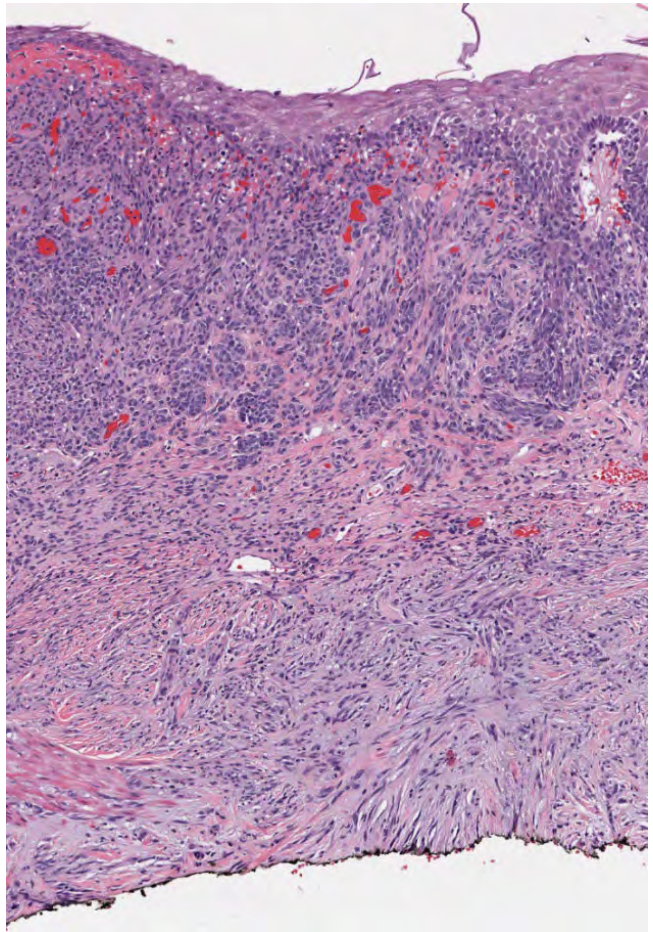
Pure Desmoplastic Melanoma





Mixed Desmoplastic Melanoma





Non-desmoplastic

Desmoplastic

Mixed Desmoplastic Melanoma

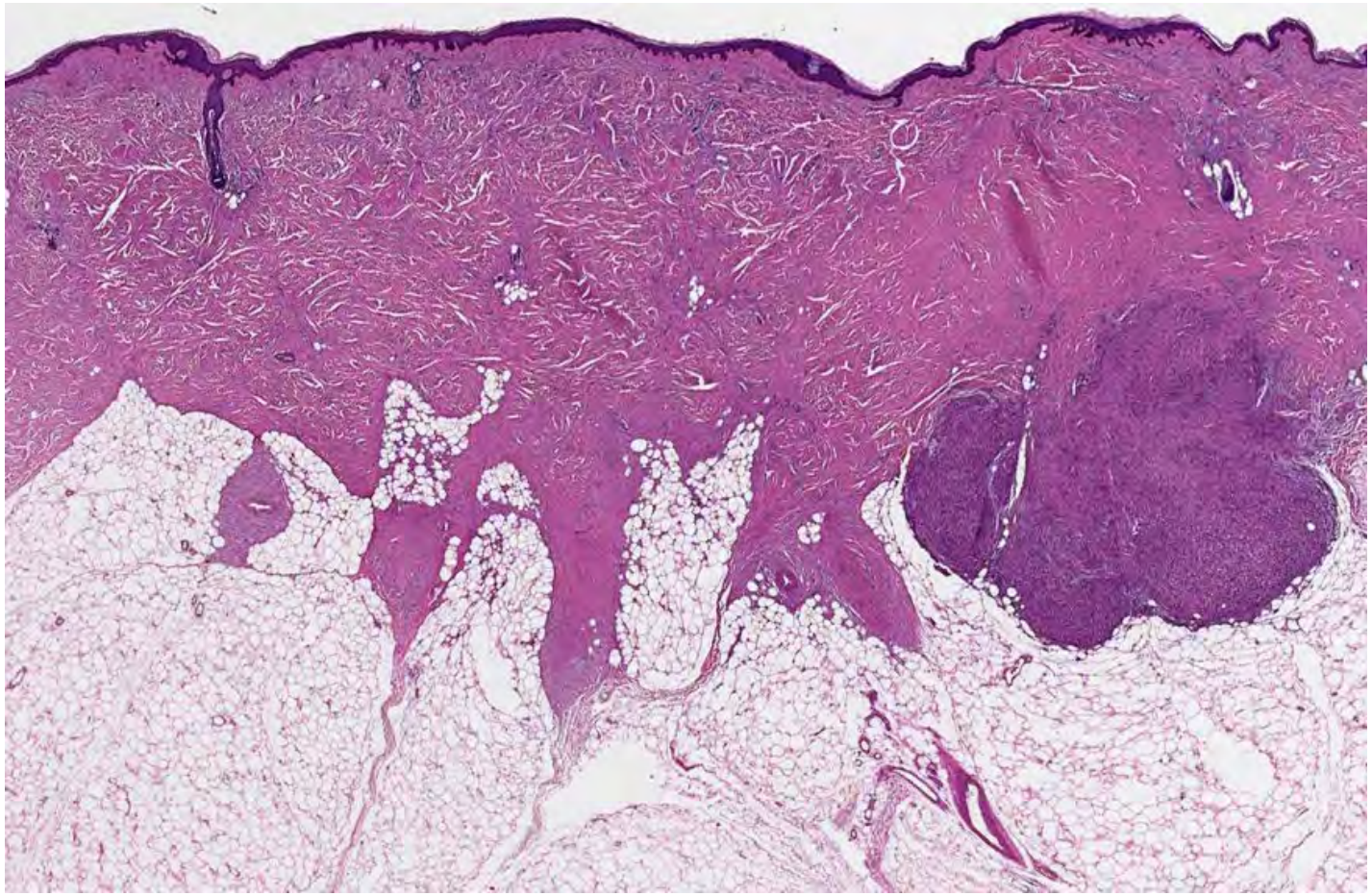


Table 2 SLNB outcomes for included studies.

	Study	Median breslow thickness (mm)	Primary outcome		Secondary outcome		Positive SLNB association with DFS, MSS and OS
			SLNB patients (n)	SLNB positive (%)	MDM SLNB positive (n)/total cases (n)	PDM SLNB positive (n)/total cases (n)	
1	Jaroszewski 2001	6.5[a]	12	0 (0%)	–	–	–
2	Gyorki 2003	2.2	24	0 (0%)	–	–	–
3	Su 2004	2.8	33	4 (12.1%)	–	–	–
4	Livestro 2005	2.6	25	2 (8%)	–	–	Reduced MSS
5	Pawlik 2006	2.9	65	4 (6.2%)	3/19 (15.8%)	1/46 (2.2%)	Reduced DFS for MDM vs PDM
6	Posther 2006	4.4[a]	12	0 (0%)	–	–	–
7	Thelmo 2006	3.9[a]	16	0 (0%)	–	–	–
8	Cummins 2007	2.3	15	1 (6.7%)	–	–	–
9	Maurichi 2009	1.9 MDM 2.1 PDM	100	9 (9%)	7/51 (13.7%)	2/49 (4.1%)	–
10	Murali 2010	2	252	17 (6.7%)	11/129 (8.5%)	6/123 (4.9%)	Reduced DFS Reduced DFS for MDM vs PDM
11	Wasif 2011	3.0[a]	505	14 (2.8%)	–	–	–
12	Mohebati 2012	6.1[a]	21	0 (0%)	0/7 (0%)	0/14 (0%)	–
13	Eppsteiner 2012	3.5	165	8	–	–	Reduced MSS
14	Broer 2013	3.9[a]	22	4 (18.2%)	2/8 (25%)	2/14 (14.3%)	–
15	Egger 2013	2.6	47	8 (17.0%)	–	–	Reduced DFS With ulcerated primary, reduced OS
16	Han 2013	3.7	205	28 (13.7%)	15/61 (24.6%)	6/67 (9.0%)	Reduced MSS
		Total	**1519**	**99 (6.5%)**	**38/275 (13.8%)**	**17/313 (5.4%)**	

[a] Mean.

Journal of Plastic, Reconstructive & Aesthetic Surgery (2017) 70, 274–280

JPRAS
An International Journal of Surgical Reconstruction
www.JPRASurg.com

Review

Is sentinel lymph node biopsy warranted for desmoplastic melanoma? A systematic review

Jonathan A. Dunne*[,a,b], Justin C.R. Wormald [c], Jessica Steele [d], Elizabeth Woods [d], Joy Odili [d], Barry W.E.M. Powell [d]

Department of Plastic and Reconstructive Surgery, St George's Hospital, Blackshaw Rd, Tooting, London, SW17 0QT, United Kingdom

Received 6 August 2016; accepted 8 November 2016

"…we would not recommend SLN biopsy in pure desmoplastic melanoma"

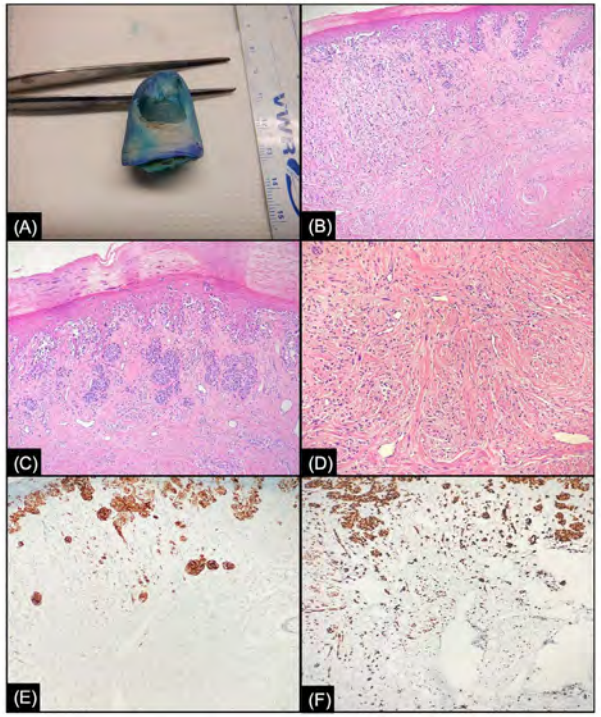
Received: 14 April 2023 | Revised: 18 September 2023 | Accepted: 24 September 2023
DOI: 10.1111/cup.14542

CASE STUDY

JCP WILEY

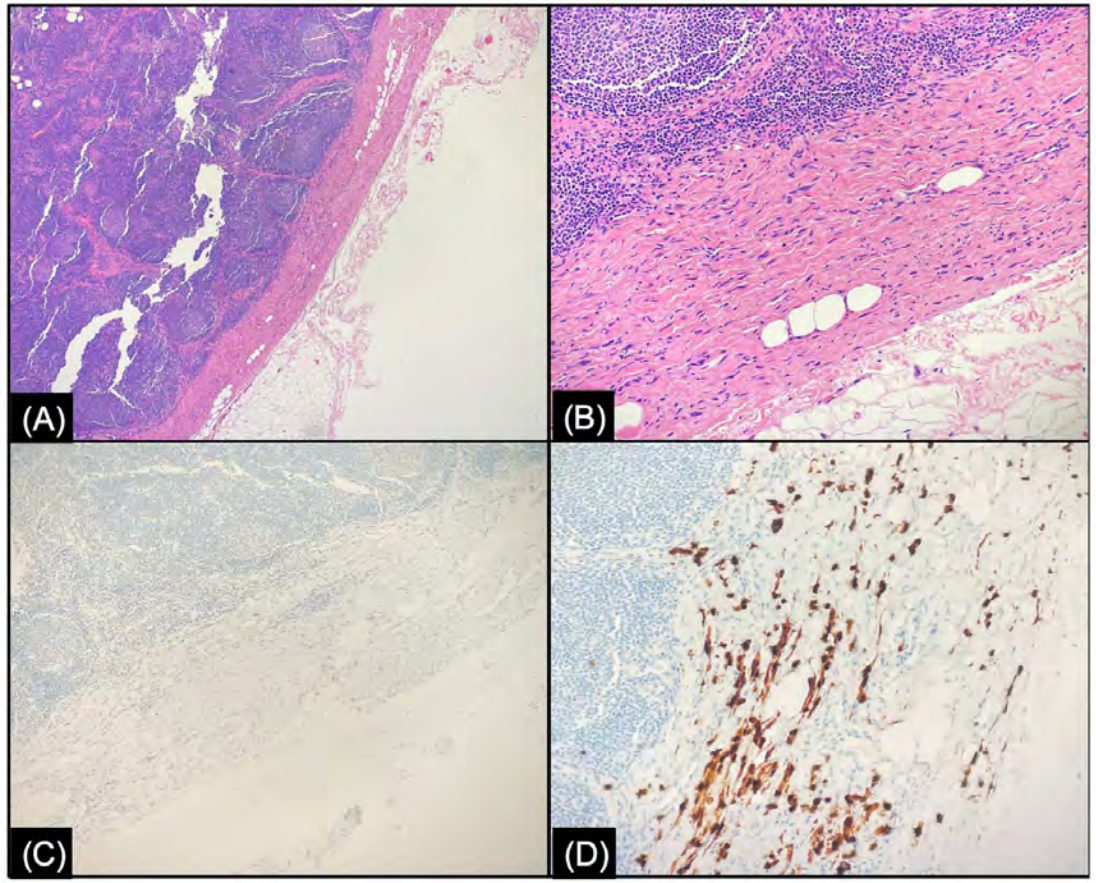
The utility of SOX10 in mixed type desmoplastic melanoma with lymph node metastasis of the spindle cell component: A cautionary tale of inattentional blindness

Ahmed Shah MD, MSc[1] | Katelynn Campbell MD[2] | Allison Osmond MD, MSC, FRCPC[2]



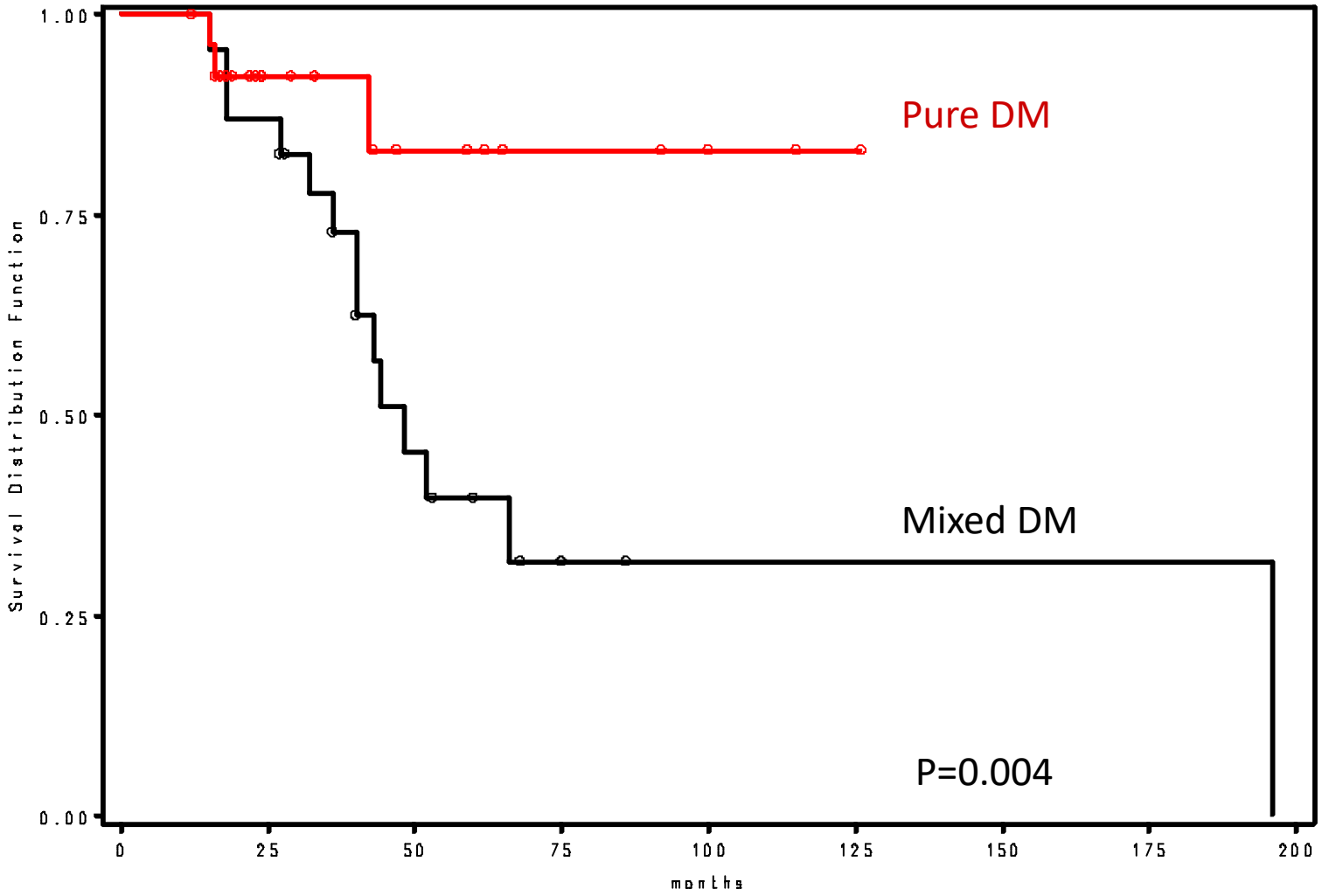
CAUTION!

DM: Use S100P or Sox10 for SLN analysis



Survival Advantage for Desmoplastic Melanoma

Among ≥ 4 mm Thick Melanomas



Am J Surg Pathol 2004;28:1518-25

Survival Advantage for Pure Desmoplastic Melanoma

DOI: 10.1111/jdv.15753 JEADV

ORIGINAL ARTICLE

Differences between pure desmoplastic melanoma and superficial spreading melanoma in terms of survival, distribution and other clinicopathologic features

M.D. Howard,[1,2,*] E. Wee,[3] R. Wolfe,[2] C.A. McLean,[1,4] J.W. Kelly,[1] Y. Pan[1]

[1]Victorian Melanoma Service, Alfred Hospital, Melbourne, Vic., Australia
[2]School of Public Health and Preventive Medicine, Monash University, Melbourne, Vic., Australia
[3]Department of Dermatology, St Vincent's Hospital Melbourne, Melbourne, Vic., Australia
[4]Department of Pathology, Alfred Hospital, Melbourne, Vic., Australia
*Correspondence: M. Howard. E-mail: matthew.david.howard@gmail.com

Abstract

Background Pure desmoplastic melanoma (pDM) is an uncommon subtype of malignant melanoma with comparative high rates of local recurrence and low rates of sentinel lymph node positivity. The melanoma-specific survival (MSS) of pDM compared to other melanoma subtypes is unclear, with conflicting reports and lack of multivariable analyses.

Objectives We aimed to describe clinicopathological characteristics of a cohort of patients with pDM and to compare the MSS of pDM with superficial spreading melanoma (SSM).

Methods A prospective cohort study was performed of all primary invasive cutaneous pDM with known tumour location and thickness reviewed at a tertiary referral centre over 21 years.

Results A total of 119 primary cutaneous invasive pDMs from 3570 total invasive cutaneous melanomas were included. Compared to 2272 SSMs, and due largely to their greater average thickness, patients with pDM had worse MSS (unadjusted hazard ratio, HR, 2.56, 95% confidence interval, CI, 1.56–4.22). After adjustment for clinicopathologic factors (including thickness, ulceration, mitotic rate, age and sex), there was evidence that patients with pDM had an improved MSS (adjusted HR, 0.49; 95% CI, 0.28–0.87). Median thickness of head and neck pDM was greater than non-head and neck pDM ($P < 0.001$). There was reduced univariable MSS in head and neck pDM compared to the rest of the body.

Conclusions Decreased univariable MSS of patients with pDM compared to SSM was explained by the increased frequency of adverse clinicopathologic features at diagnosis, in particular the greater Breslow thickness of pDM. After adjustment, patients with pDM had half the chance of melanoma-specific death compared to SSM. Head and neck pDM were thicker at diagnosis compared to the rest of the body, which may account for its poorer survival compared to the rest of the body.

Received: 27 March 2019; Accepted: 6 June 2019

- 119 pDM vs 2272 CM
- Pure DM had better MSS
- ”Patients with pDM had half the chance of melanoma-specific death”

How reproducible is the classification of DM?

Pathology (March 2023) 55(2), pp. 223–226

MELANOCYTIC TUMOUR PATHOLOGY

Interobserver agreement in the histopathological classification of desmoplastic melanomas

CECILIA LEZCANO[1], MARIANNE BERWICK[2], LI LUO[2], RAYMOND BARNHILL[3], LYN M. DUNCAN[4], PEDRAM GERAMI[5], LORI LOWE[6], JANE L. MESSINA[7], RICHARD A. SCOLYER[8,9,10,11], BENJAMIN WOOD[12], IWEI YEH[13], ARTUR ZEMBOWICZ[14], KLAUS J. BUSAM[1]

- 30 cases of WSI reviewed by 11 dermatopathologists
- Interobserver agreement on subtype of DM (pure vs mixed): Kappa = 0.64, $p<0.0001$ (substantial agreement)

Pathology (March 2023) **55(2)**, pp. 214–222

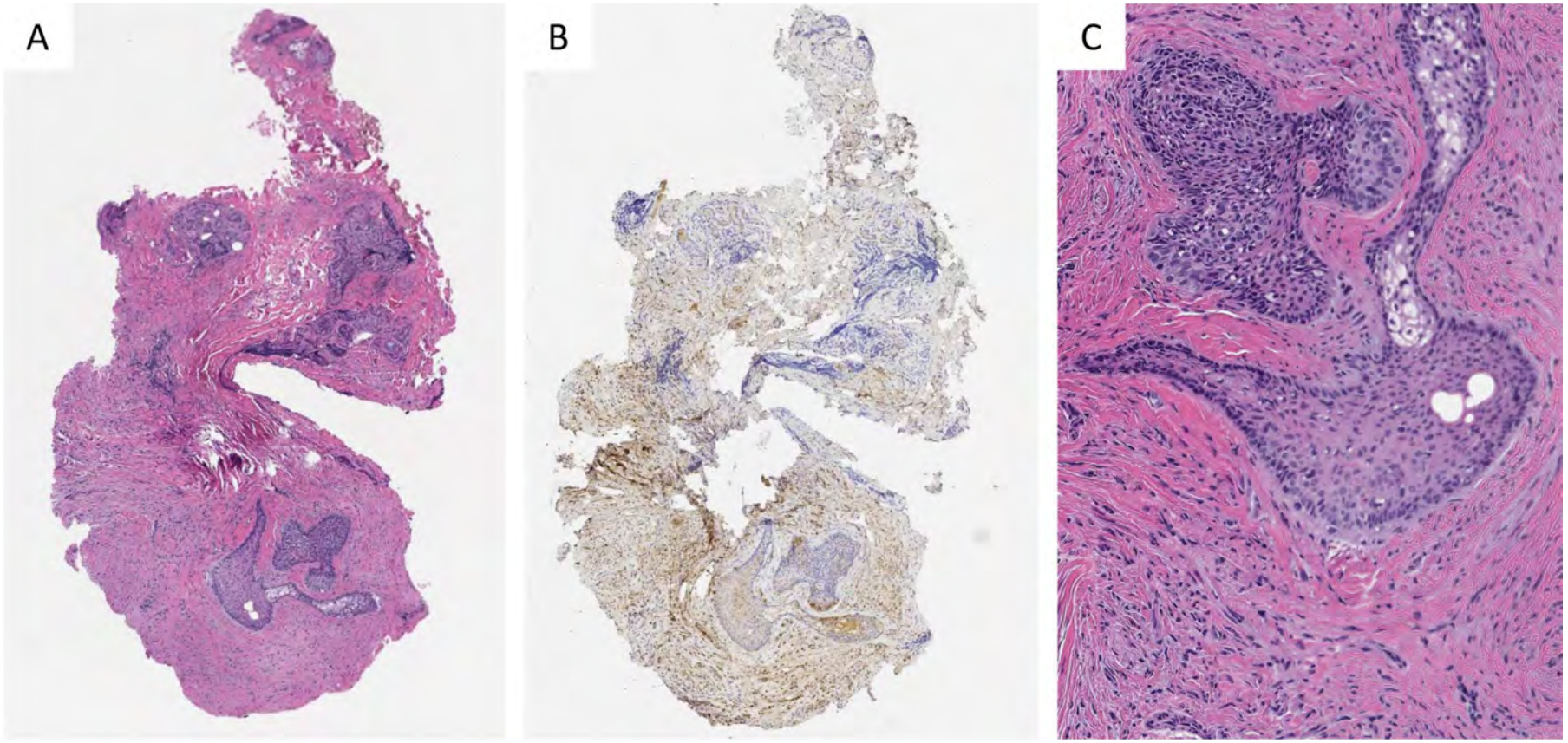
MELANOCYTIC TUMOUR PATHOLOGY

Representativeness of initial skin biopsies showing pure desmoplastic melanoma: implications for management

R. V. Rawson[1,2,3,4], I. A. Vergara[1,2,5], J. R. Stretch[1,2,6], R. P. M. Saw[1,2,6], J. F. Thompson[1,2,6], S. N. Lo[1], R. A. Scolyer[1,2,3,4,5], K. J. Busam[7]

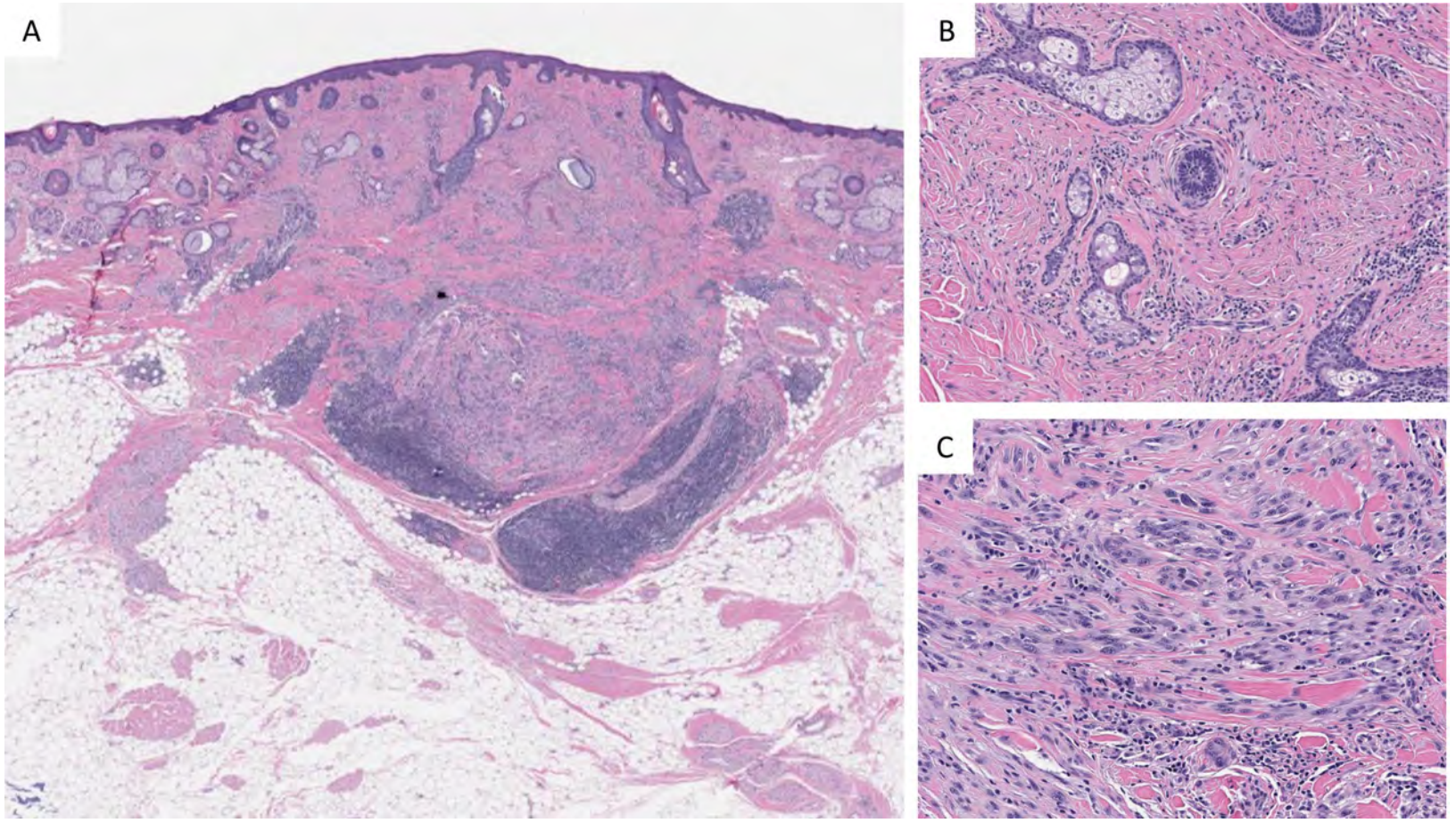
- 91/101: Biopsy and excision concordant for pure DM
- 10/101: Changed to mixed DM upon review of excision

Desmoplastic Melanoma – “Pure” on BX



70F, cheek – r/o cyst, foreign body, scar

Mixed Desmoplastic Melanoma



CANCER DISCOVERY

News in Brief

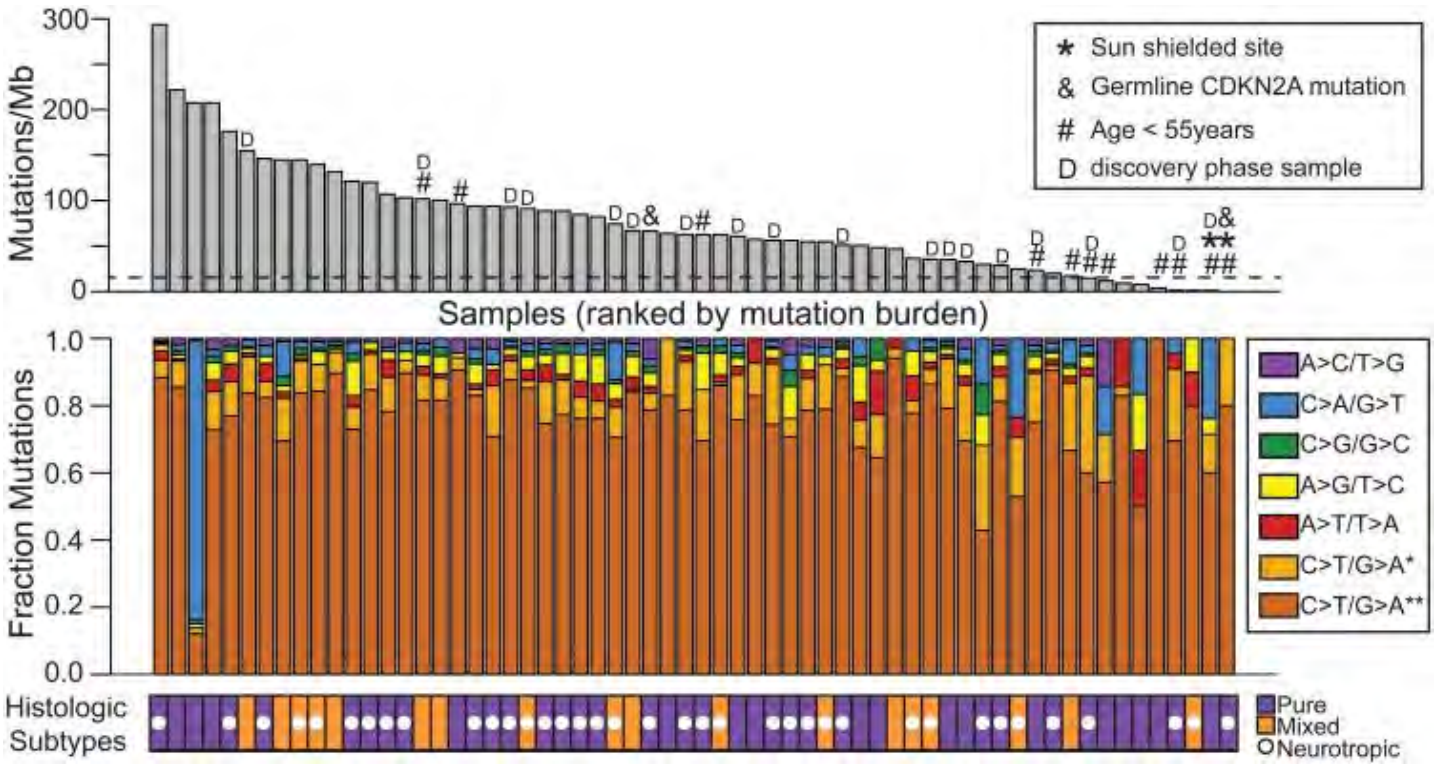
Desmoplastic Melanoma Carries High Mutation Burden

DOI: 10.1158/2159-8290.CD-NB2015-134 Published November 2015

Published in final edited form as:
Nat Genet. 2015 October ; 47(10): 1194–1199. doi:10.1038/ng.3382.

Exome sequencing of desmoplastic melanoma identifies recurrent NFKBIE promoter mutations and diverse activating mutations in the MAPK pathway

A. Hunter Shain[1,2,3], **Maria Garrido**[1,2,3], **Thomas Botton**[1,2,3], **Eric Talevich**[1,2,3], **Iwei Yeh**[1,2,3], **J. Zachary Sanborn**[4], **Jongsuk Chung**[5], **Nicholas J. Wang**[6,7], **Hojabr Kakavand**[8,9], **Graham J. Mann**[8,9], **John F. Thompson**[8,9,10], **Thomas Wiesner**[11], **Ritu Roy**[2], **Adam B. Olshen**[2,12], **Alexander Gagnon**[1,2,3], **Joe W. Gray**[6,7], **Nam Huh**[5], **Joe S. Hur**[13], **Klaus J. Busam**[14], **Richard A. Scolyer**[8,9,10], **Raymond J. Cho**[3,16], **Rajmohan Murali**[14,15,16], and **Boris C. Bastian**[1,2,3,16]

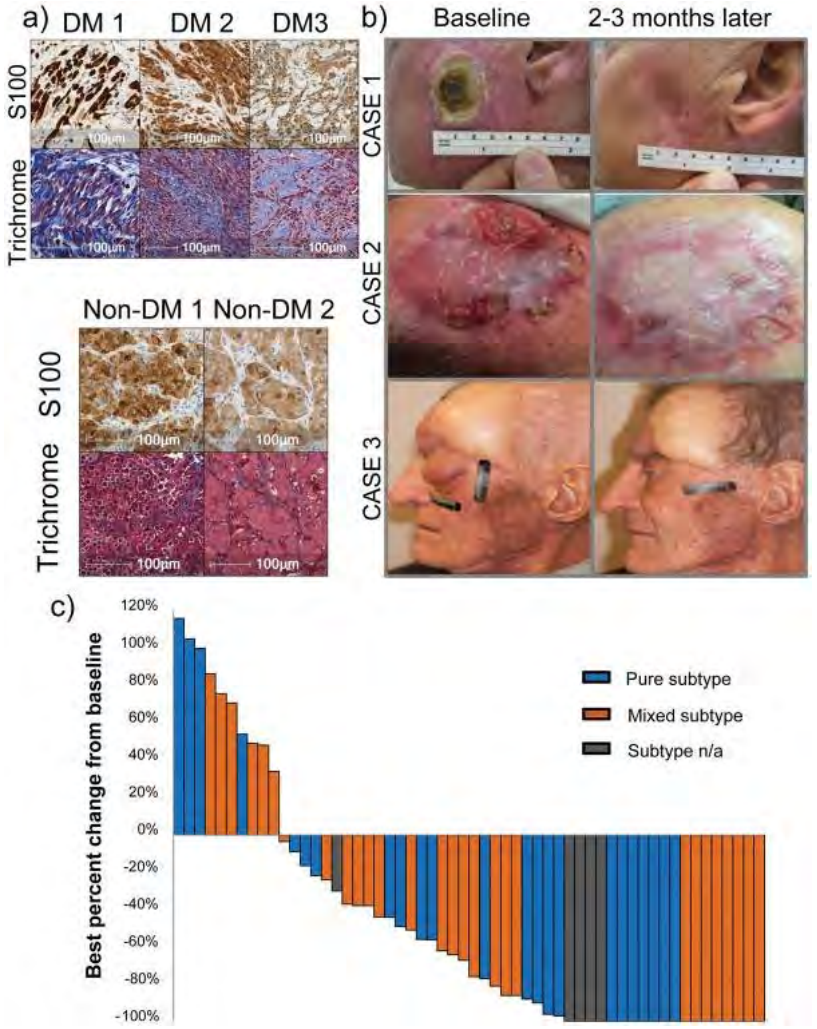


LETTER

doi:10.1038/nature25187

High response rate to PD-1 blockade in desmoplastic melanomas

Zeynep Eroglu[1,2*], Jesse M. Zaretsky[1*], Siwen Hu-Lieskovan[1*], Dae Won Kim[2,3], Alain Algazi[4], Douglas B. Johnson[5], Elizabeth Liniker[6], Ben Kong[7], Rodrigo Munhoz[8,9], Suthee Rapisuwon[10], Pier Federico Gherardini[11], Bartosz Chmielowski[1], Xiaoyan Wang[1], I. Peter Shintaku[1], Cody Wei[1], Jeffrey A. Sosman[5†], Richard W. Joseph[12], Michael A. Postow[8,9], Matteo S. Carlino[6,7,13], Wen-Jen Hwu[3], Richard A. Scolyer[6,13,14], Jane Messina[2], Alistair J. Cochran[1], Georgina V. Long[6,13,15] & Antoni Ribas[1]



- 60 patients with advanced DM treated with anti PD-1/PD-L1
- Tumor response to treatment in 42/60 patients
- 14/17 tumors had NF1 mutations
- IHC: More PD-L1-positive cells and CD8+ T- cells in DM

Nature 2018; 553: 347 - 350

Desmoplastic Melanoma – Diagnostic Pitfall

Pitfalls in the Diagnosis of Malignant Melanoma

Findings of a Risk Management Panel Study

David B. Troxel, MD

Unrecognized Desmoplastic Melanoma (3 Claims)

More than half of these were shave biopsies (often misdiagnosed microscopically as dermatofibroma). Most desmo-

Am J Surg Pathol 2003; 27:1278-83.

Medicolegal Issues with Regard to Melanoma and Pigmented Lesions in Dermatopathology

Amanda Marsch, MD[a], Whitney A. High, MD, JD, MEng[a,b,*]

Suggestion 6: Beware of Desmoplastic Melanoma

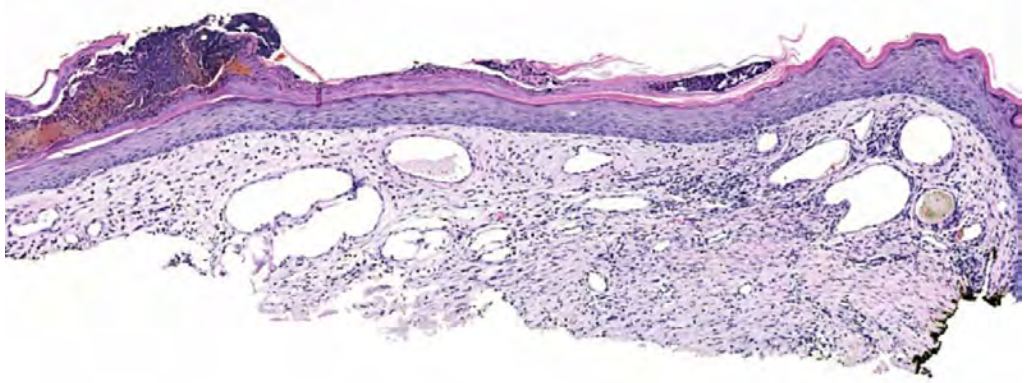
Desmoplastic melanoma (DM) is a rare spindle cell malignancy that usually develops on the sun-damaged skin of elderly patients. However, these elderly patients are also predisposed to other spindle cell neoplasms, such as spindle cell squamous carcinoma and atypical fibroxanthoma. Characteristic histopathologic features of DM include spindle-shaped melanocytes, prominent

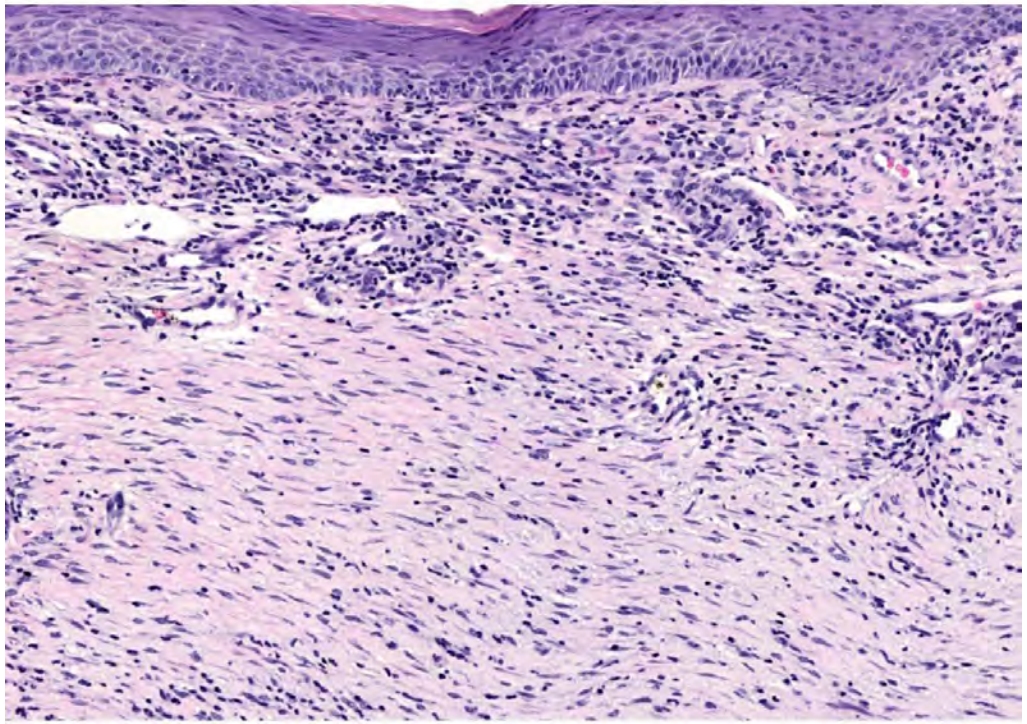
Dermatol Clin. 2012;30:593-615

DM Pathology – Differential Diagnosis

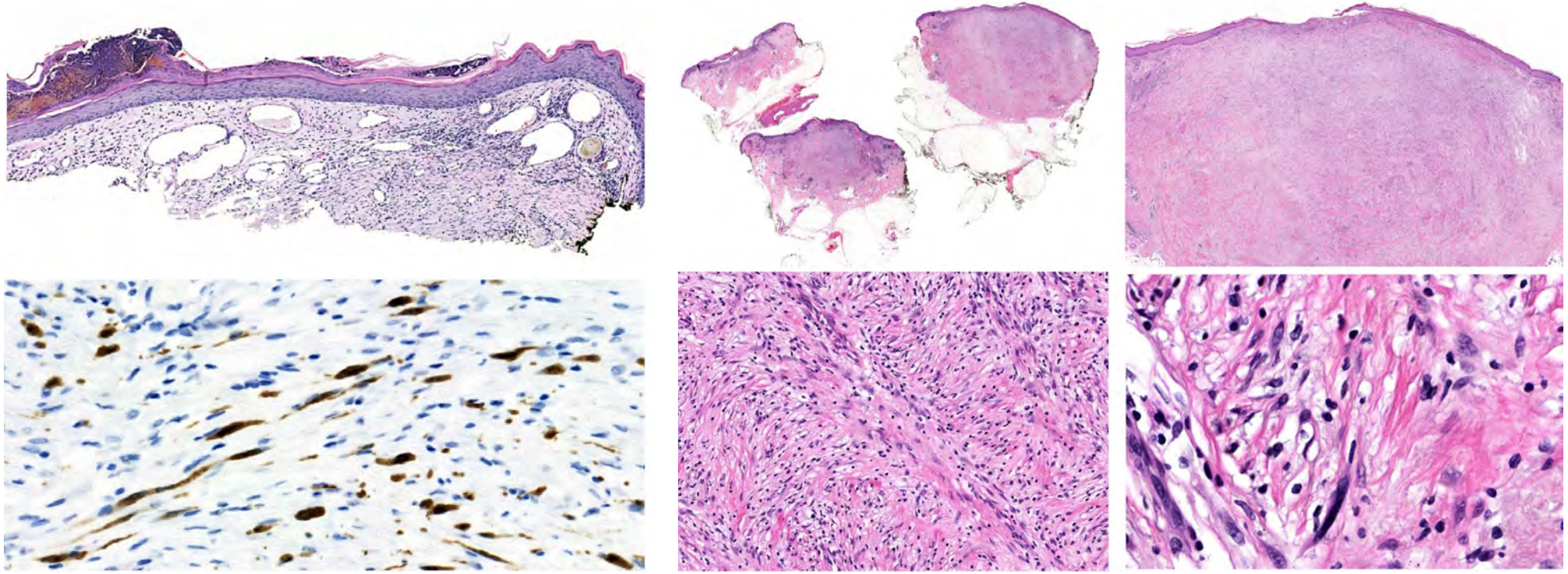
- DM vs benign fibrosing lesion
  - DM vs scar
  - DM vs dermatofibroma or nerve sheath tumor
  - DM vs desmoplastic melanocytic nevus (acquired or congenital)
- DM vs non-melanocytic malignant tumor
  - Spindle cell sarcoma with desmoplasia
  - Desmoplastic carcinoma (usually desmoplastic SCC)

DM – Confusion with a scar





Desmoplastic Melanoma



S100P/Sox10-positive cells in scars

SOX10 expression in cutaneous scars: a potential diagnostic pitfall in the evaluation of melanoma re-excision specimens

Sir,

The distinction of scar tissue from desmoplastic melanoma is sometimes problematic, particularly in melanoma re-excision specimens. Misdiagnosis may result in under-treatment or over-treatment and have adverse consequences for the patient. Interpretation can be complicated by the labelling of occasional mildly atypical cells for S100 protein which have been interpreted as immature fibroblasts/myofibroblasts, dendritic cells or nerve sheath-derived cells.[1,2] SOX10 has some myoepithelial cells and has been touted as a more sensitive and specific marker for melanocytic tumours than S100.[5,6]

Ramos-Herberth *et al.* studied the utility of SOX10 for identifying melanomas in excision and biopsy specimens (n = 26, including 9 desmoplastic melanomas), and distinguishing them from scar tissue (n = 18).[3] Using a three tiered grading system (0, negative; 1, weak; 2, strong), they reported that fibroblasts in scars expressed SOX10 weakly in contrast to desmoplastic melanomas, which stained strongly (average staining intensity 0.6 versus 2).

Similarly, Plaza *et al.* studied SOX10 immunoexpression in 40 desmoplastic melanomas and compared this to control cases of scars (n = 24), dermatofibromas (n = 16) and fibromatoses (n = 23).[4] They reported that all cases of scar were negative for SOX10, whereas all desmoplastic melanomas

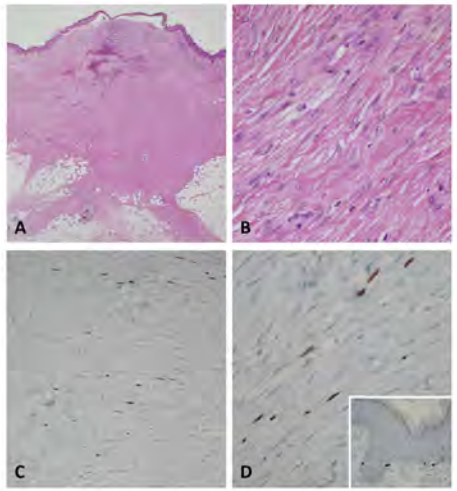


Fig. 1 (A) Low power view of scar (H&E). (B) High power view of scar (H&E). (C) High power view of scar showing distribution of sparse SOX10 positive cells (SOX10). (D) High power view of SOX10 positive cells. The SOX10 positive cells probably represent schwannian cells (SOX10). Inset: Basal melanocytes serve as an internal control (SOX10).

Jackett LA, McCarthy SW, Scolyer RA. Pathology. 2016;48:626-8.

The American Journal of Dermatopathology *24(4): 309–312, 2002*

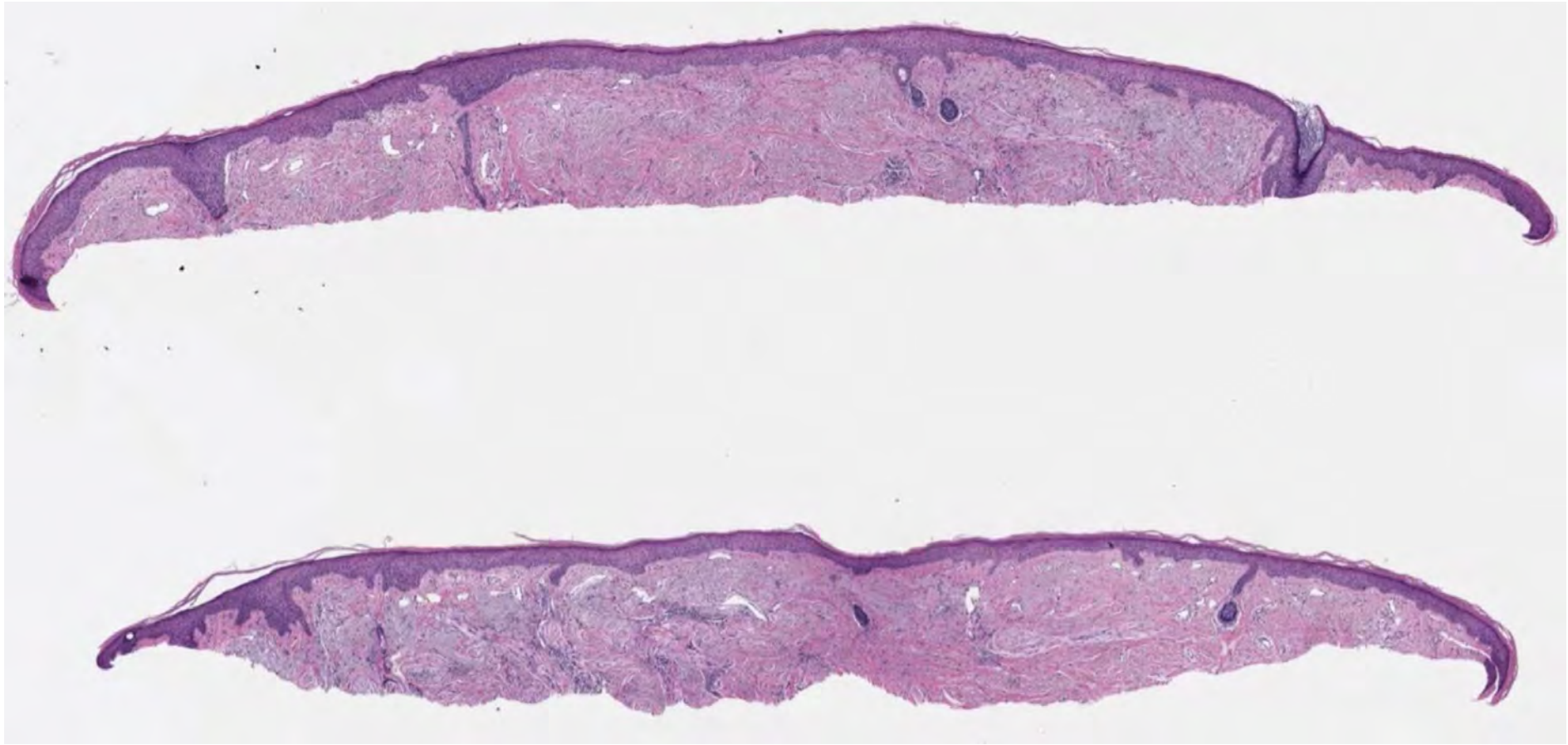
S100-Positive Spindle Cells in Scars

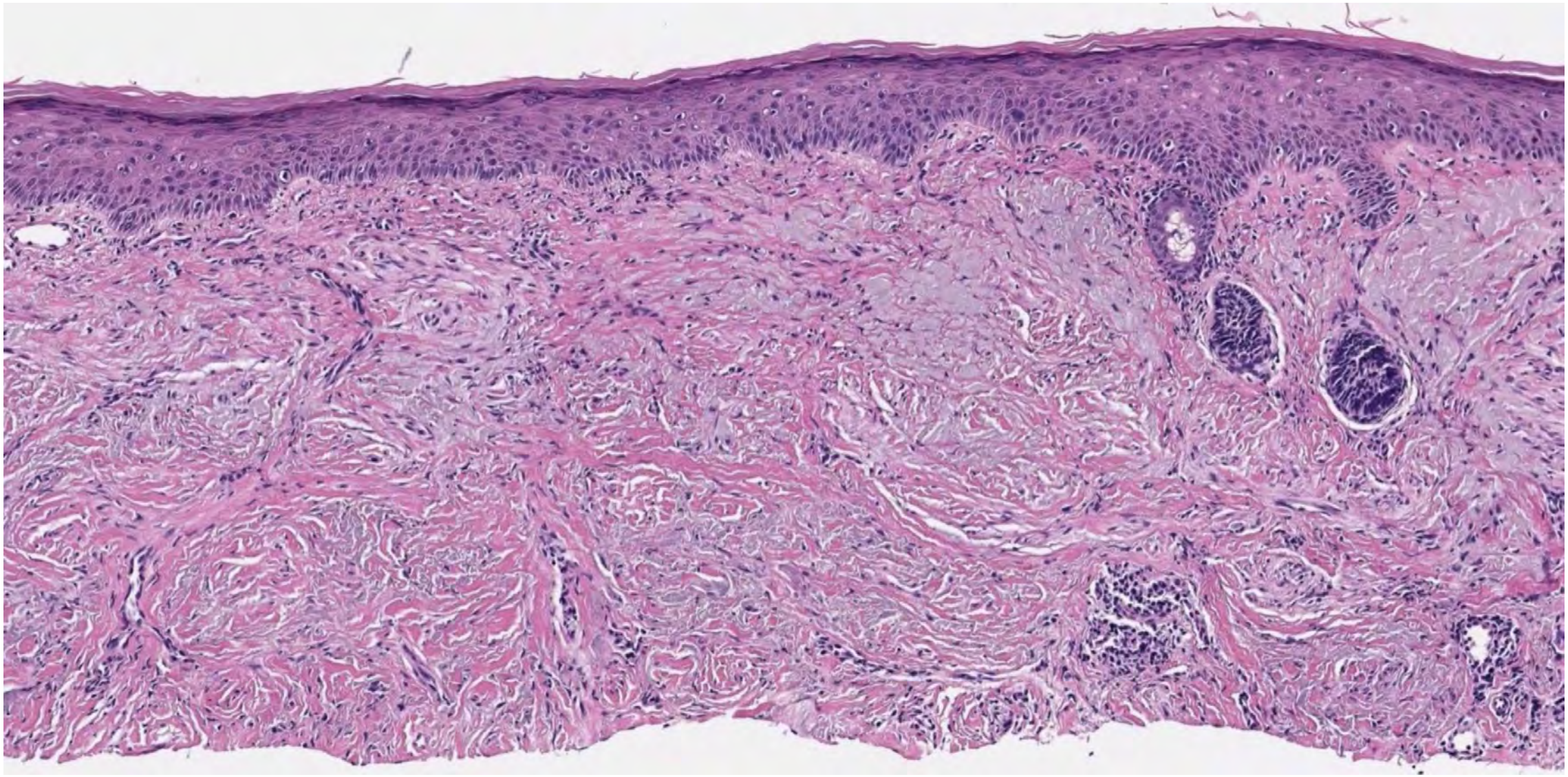
A Diagnostic Pitfall in the Re-Excision of Desmoplastic Melanoma

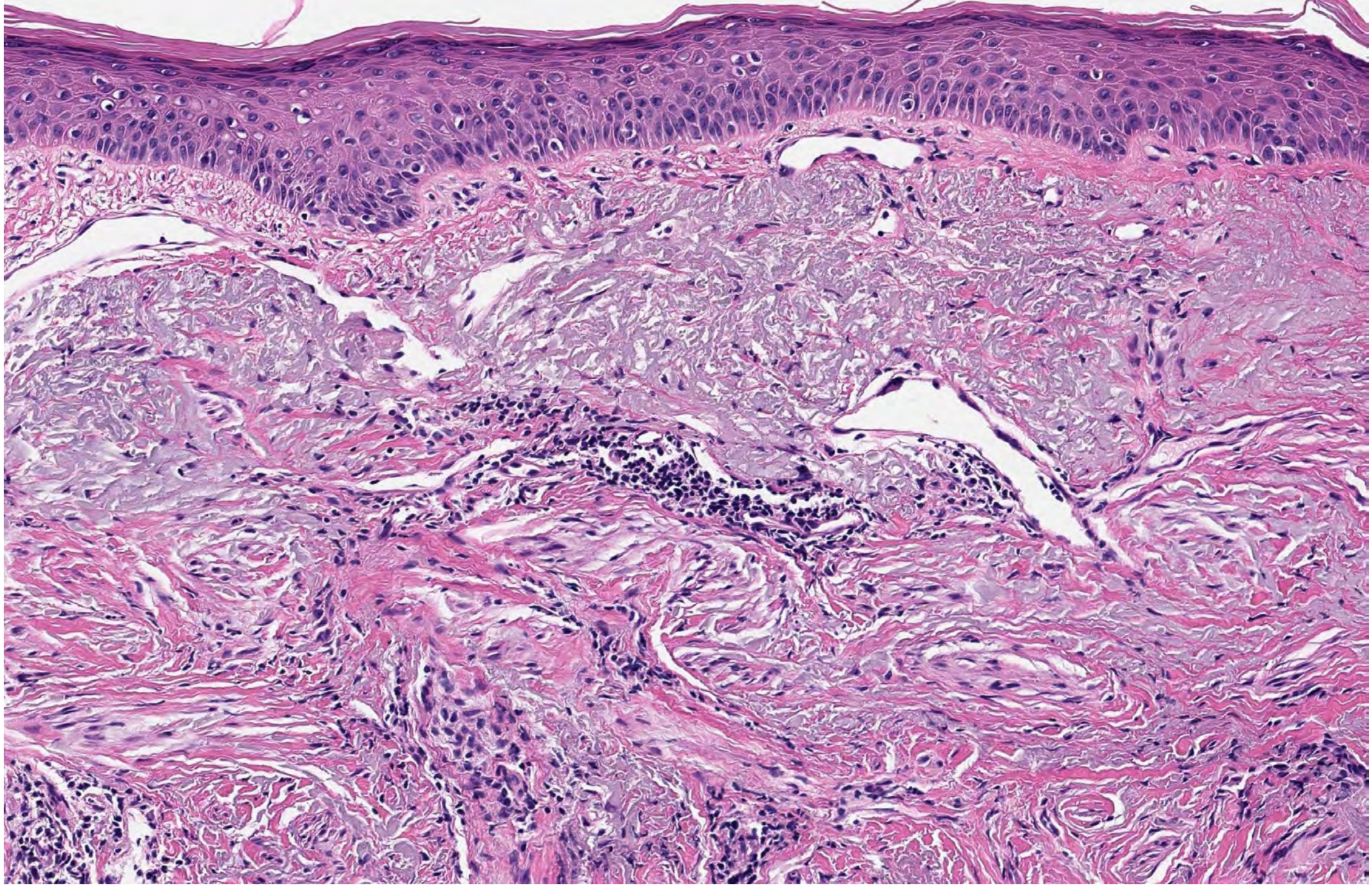
Joe A. Chorny, M.D., and Ronald J. Barr, M.D.

Case 2: 75M with nasal induration and erythema

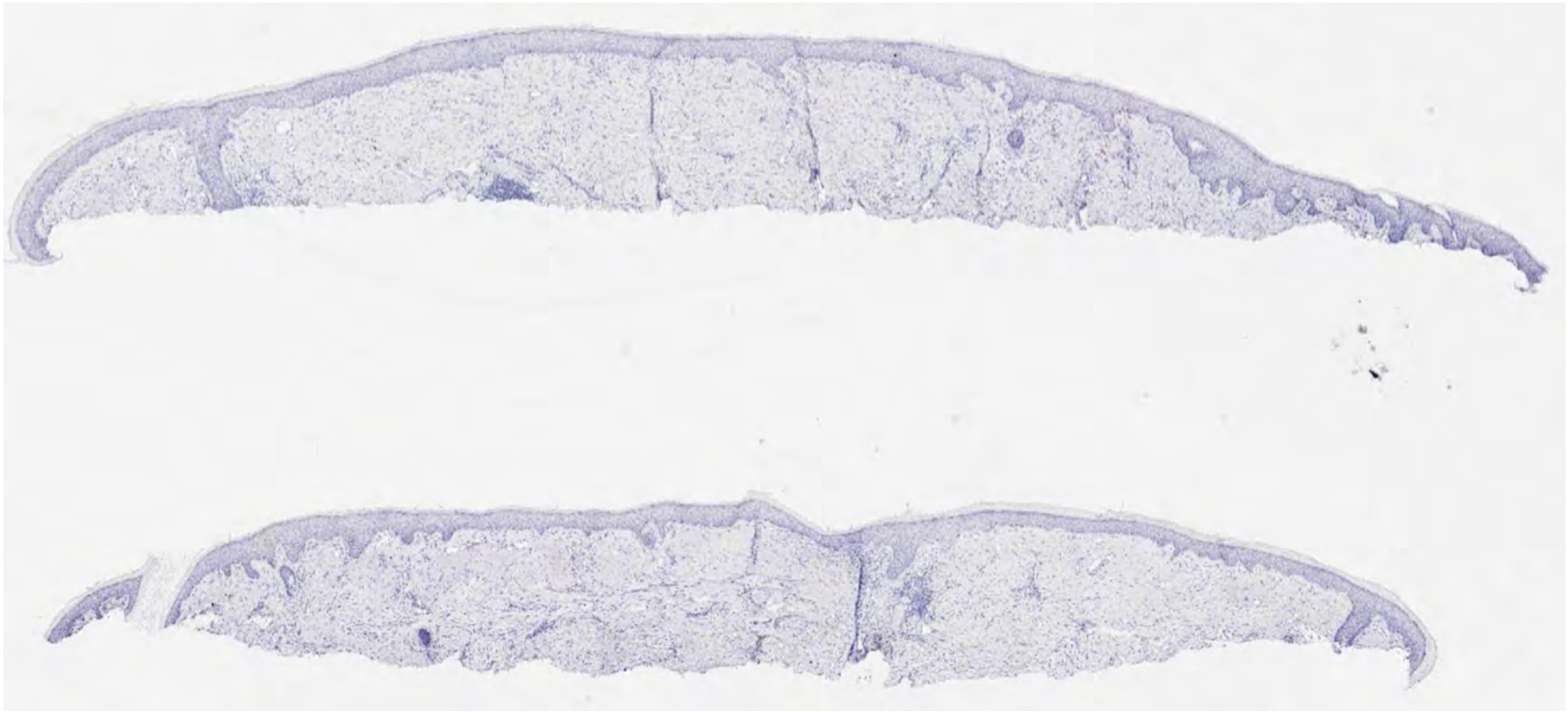
1st Biopsy: Shave



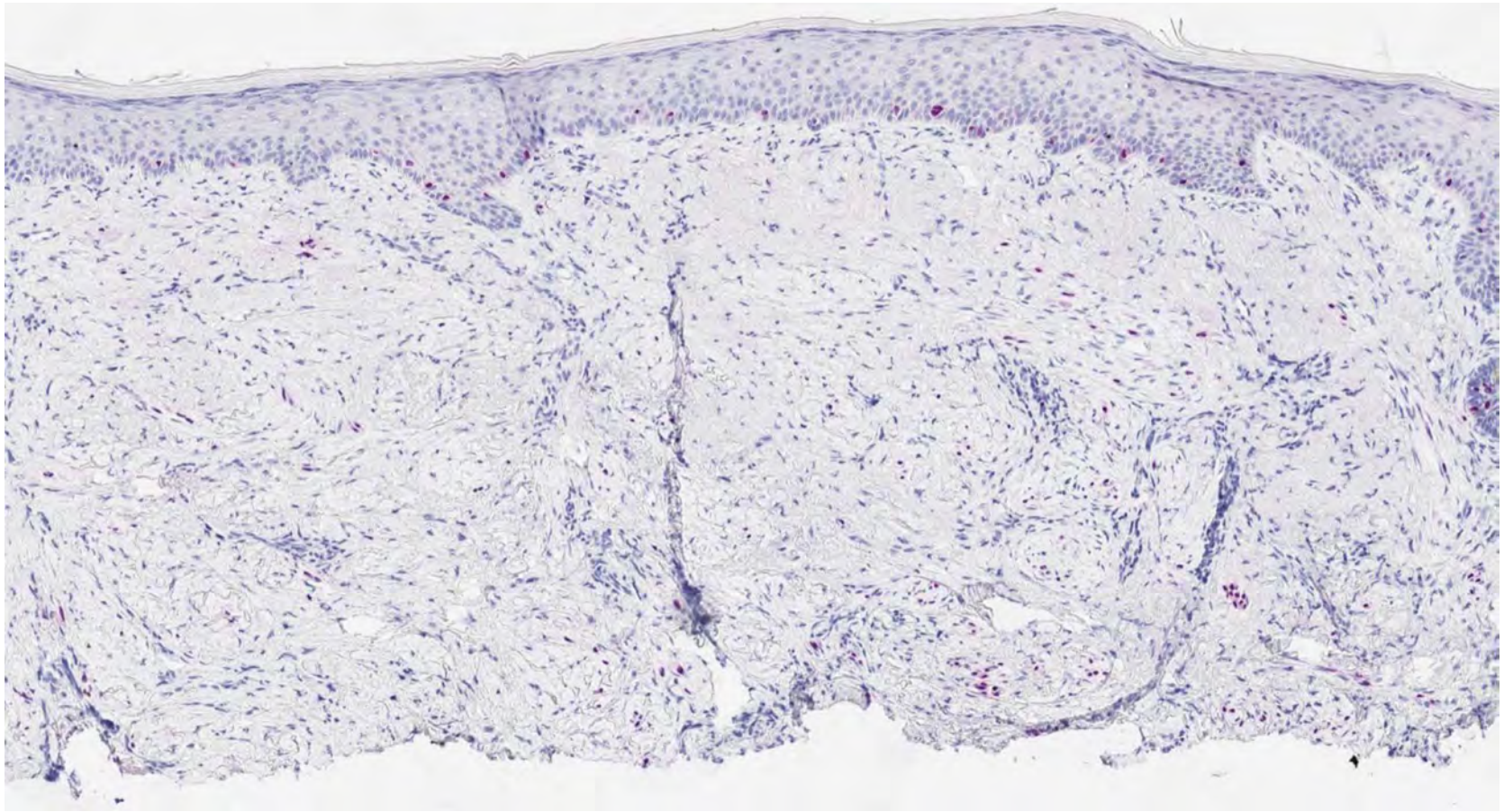




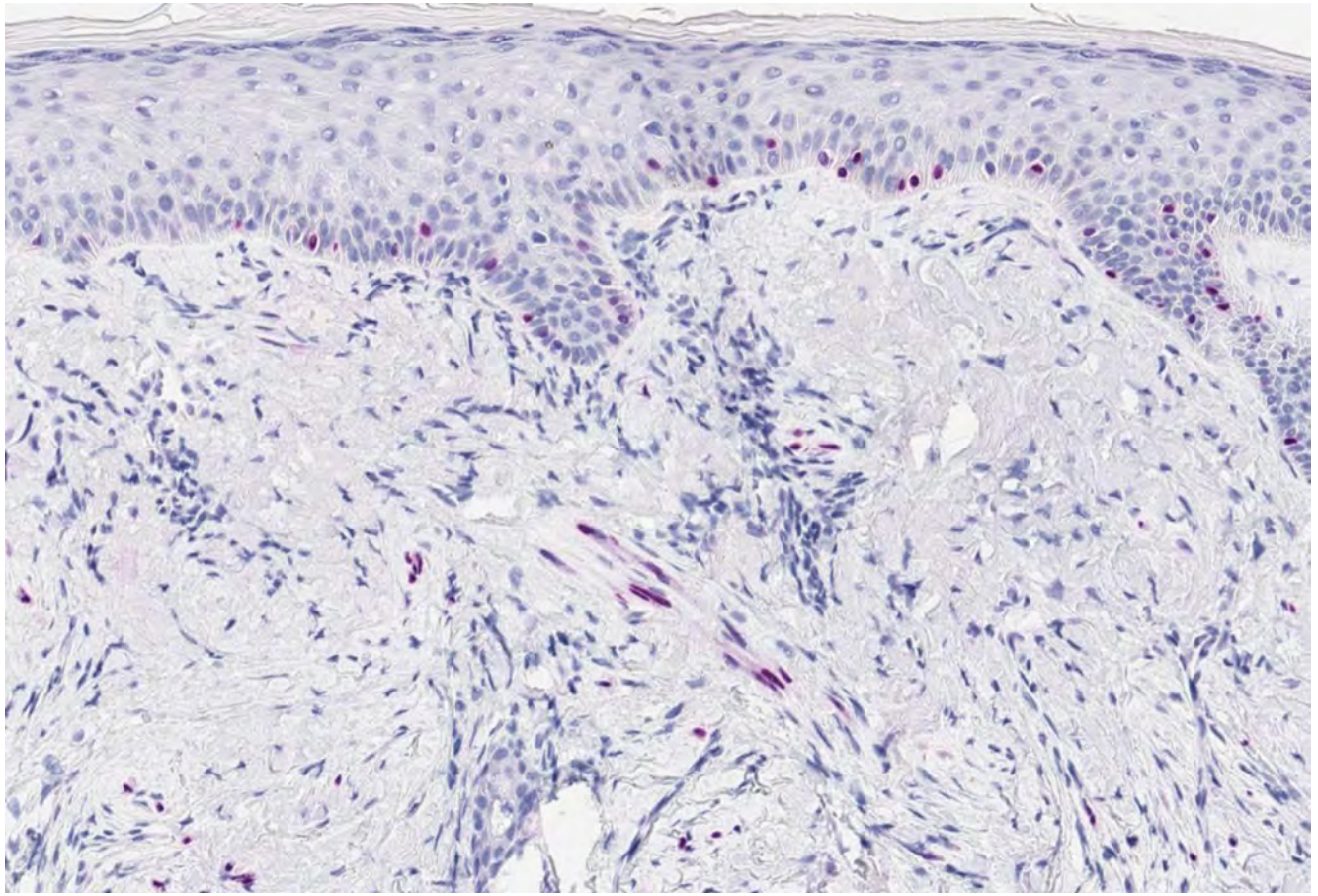
IHC - Sox10



IHC - Sox10



IHC - Sox10



Pathology Report

AMENDMENT SECTION

09/17/2019: *** ADDENDUM REPORT *** -
This case has been reviewed by intradepartmental dermatopathologists and, while this could represent the top of a scar, a deeper biopsy is advised to rule out a spindle cell neoplasm.

DERMATOPATHOLOGY REPORT

RESULTS

DIAGNOSIS:

NOSE-

SURFACE OF SCAR
Note: This case has been reviewed by [redacted] who concurs.

CLINICAL INFORMATION

?SCAR VS SCLEROTIC BCC VS SPINDLE CELL TUMOR

What is your diagnosis ?

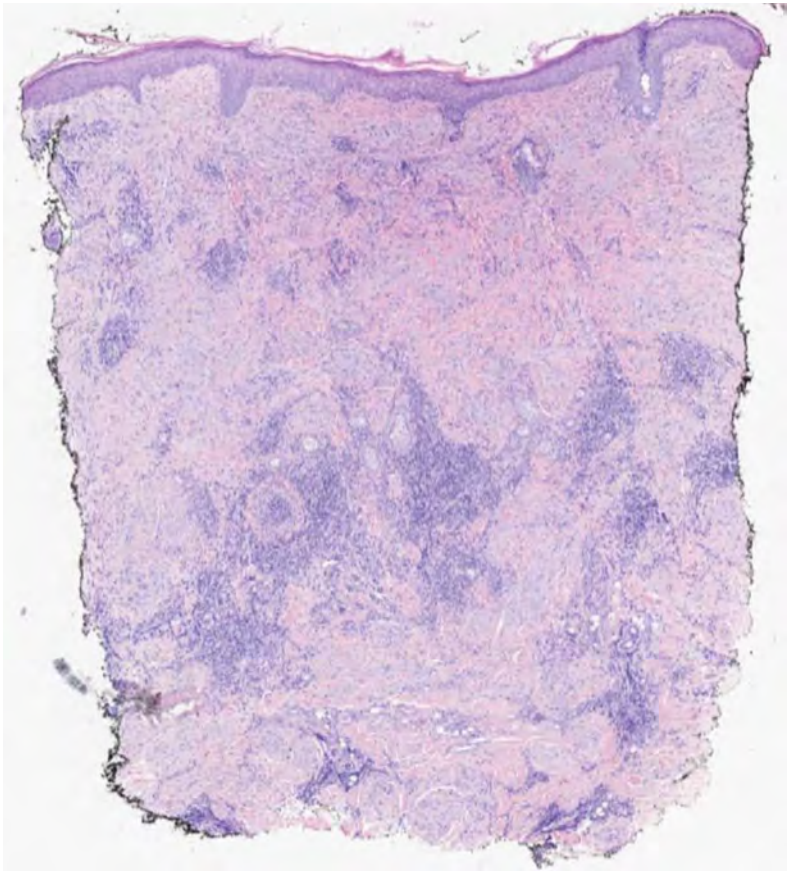
A. Scar

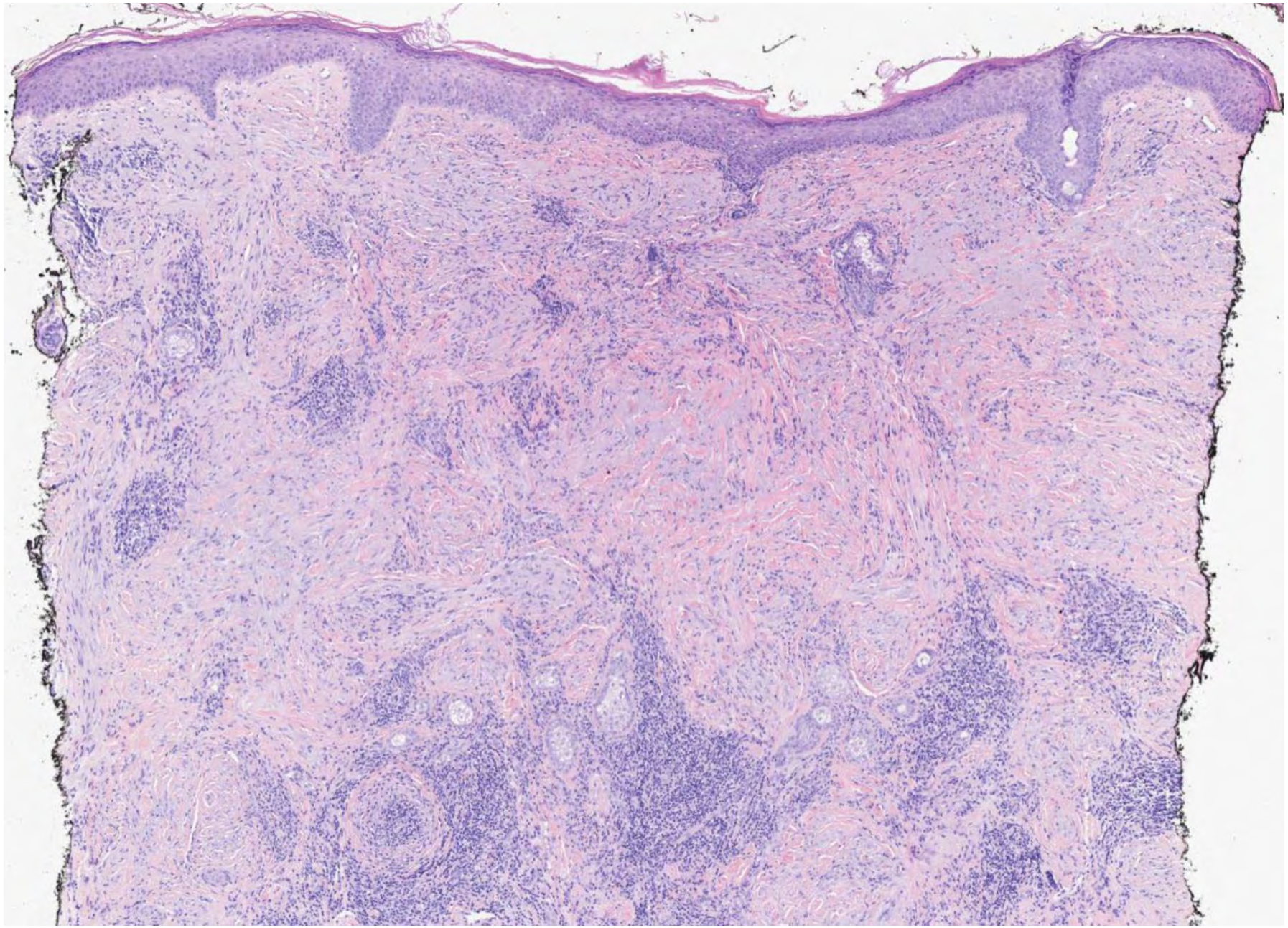
B. Desmoplastic melanoma

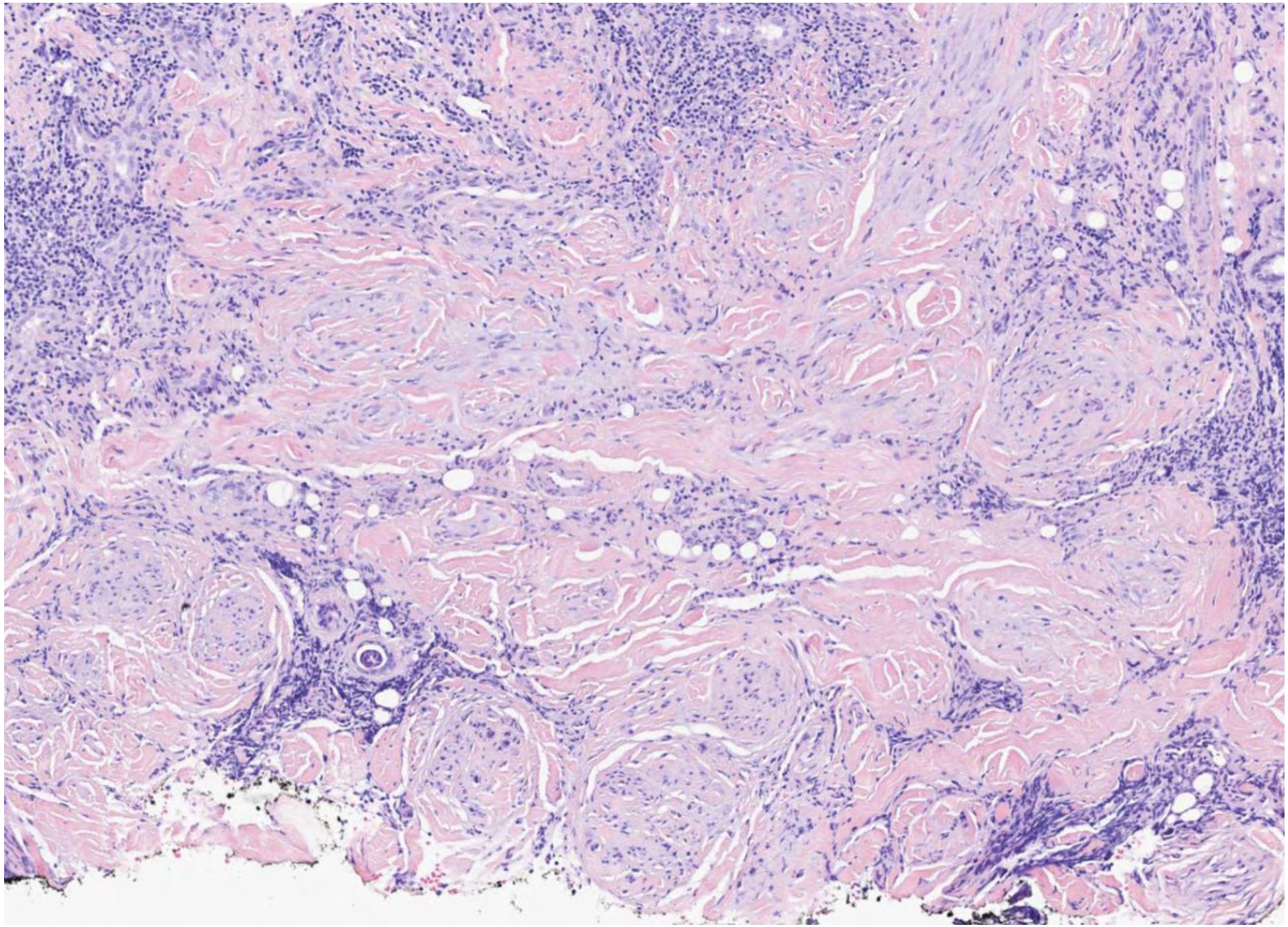
C. Other

D. I am not sure (yet)

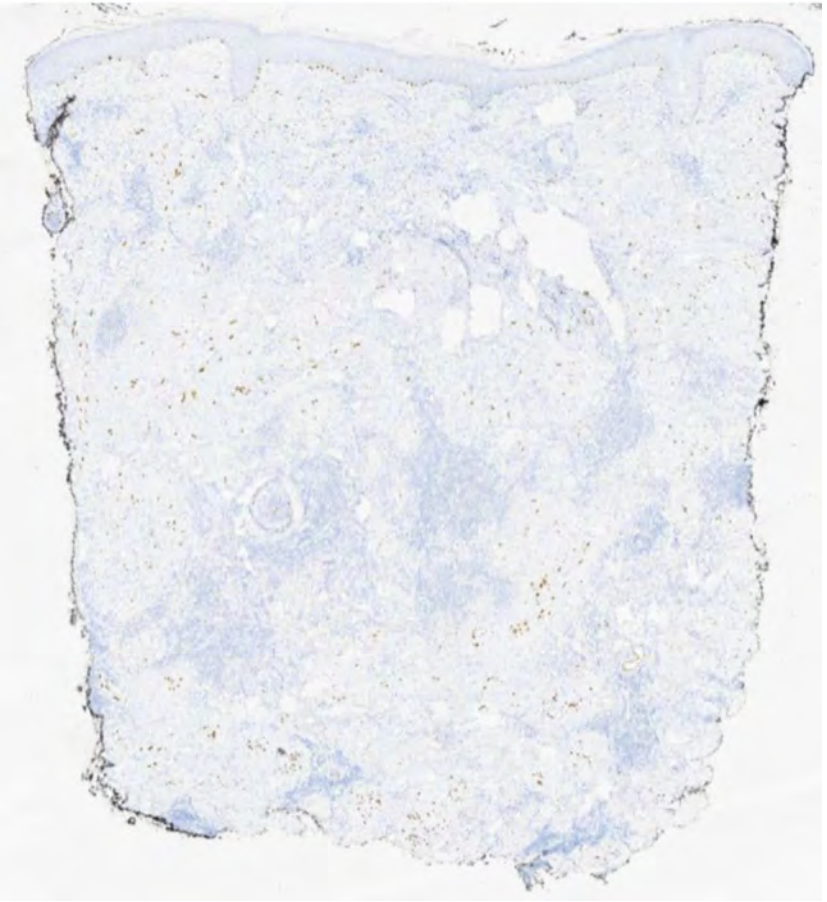
2nd Biopsy: Punch

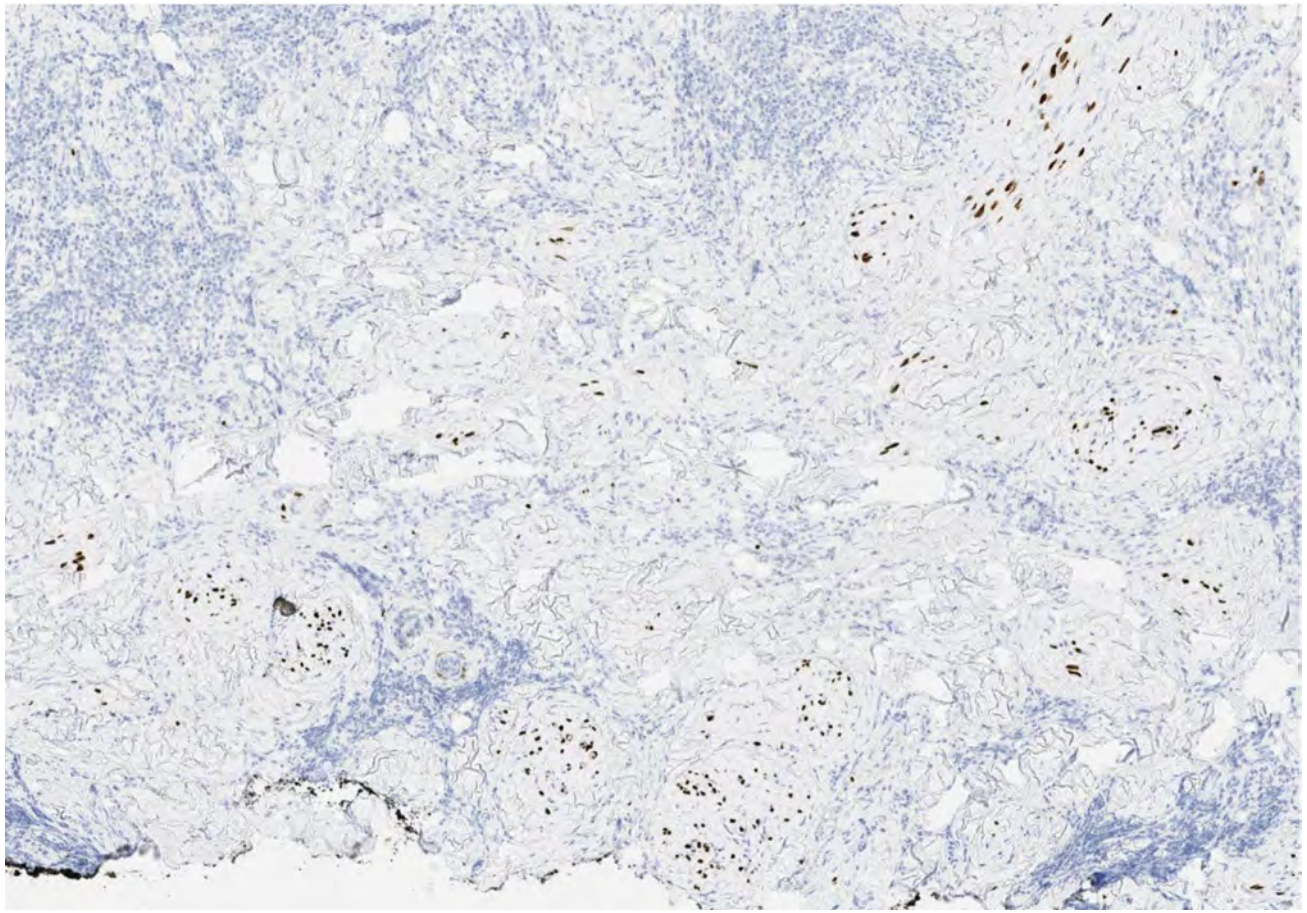




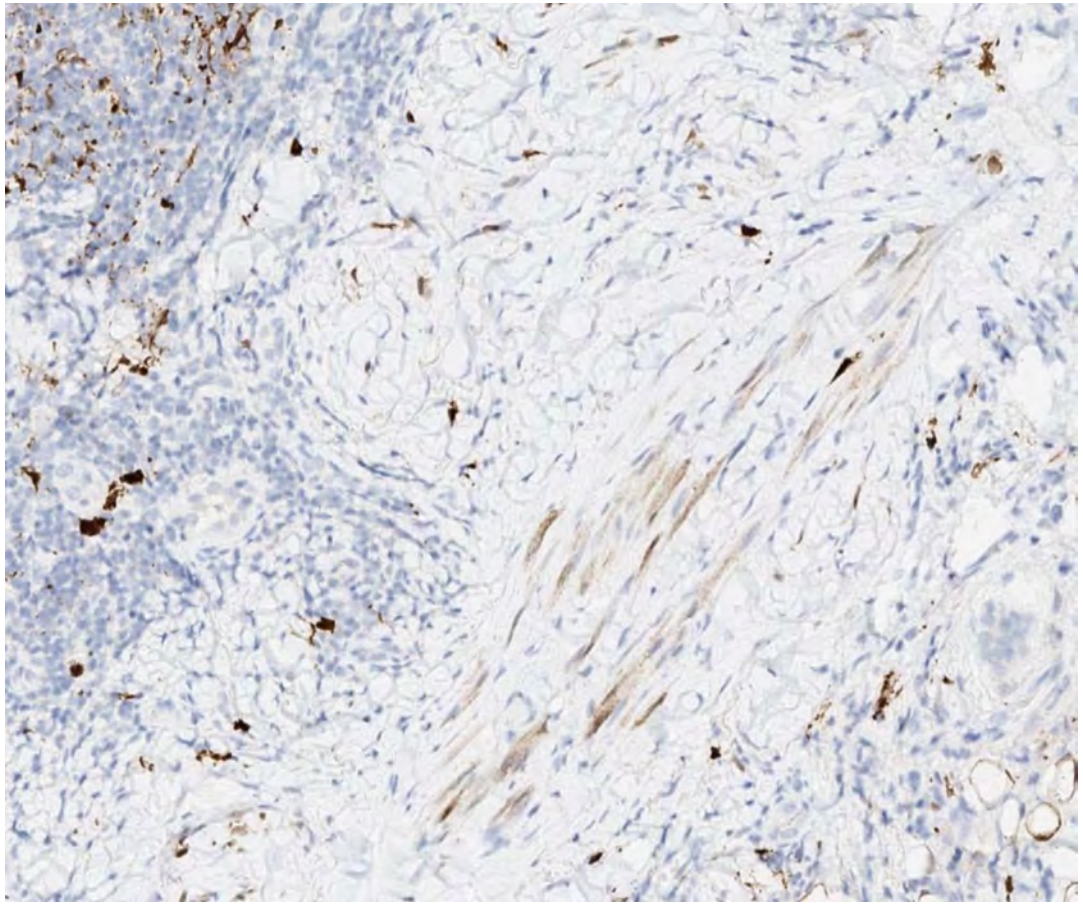


IHC - Sox10





IHC - S100

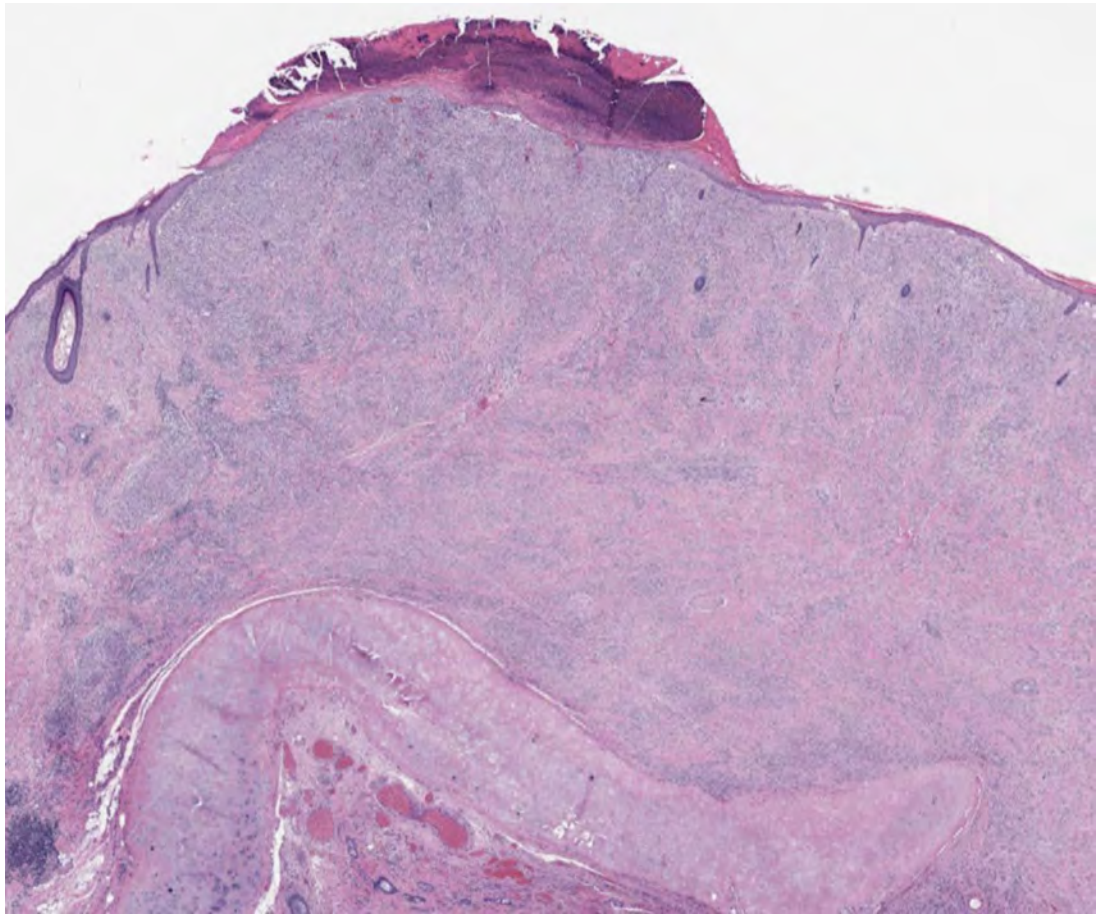


Case 2 - Diagnosis

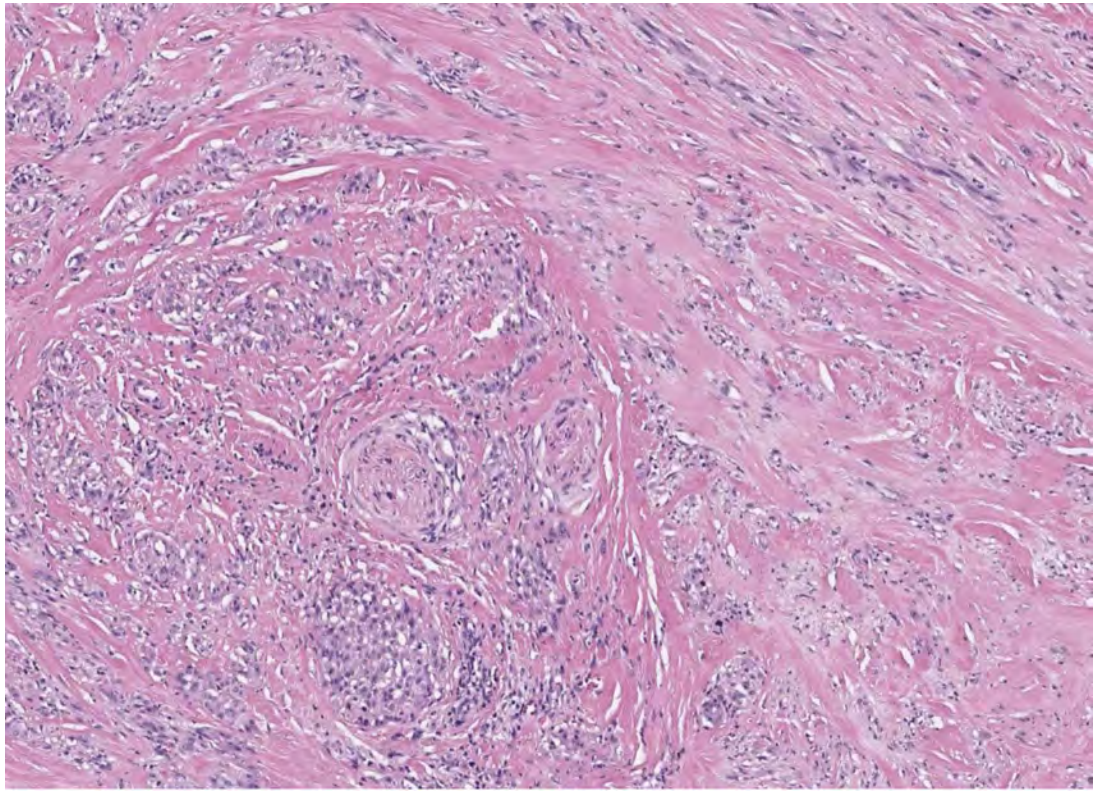
DESMOPLASTIC MELANOMA

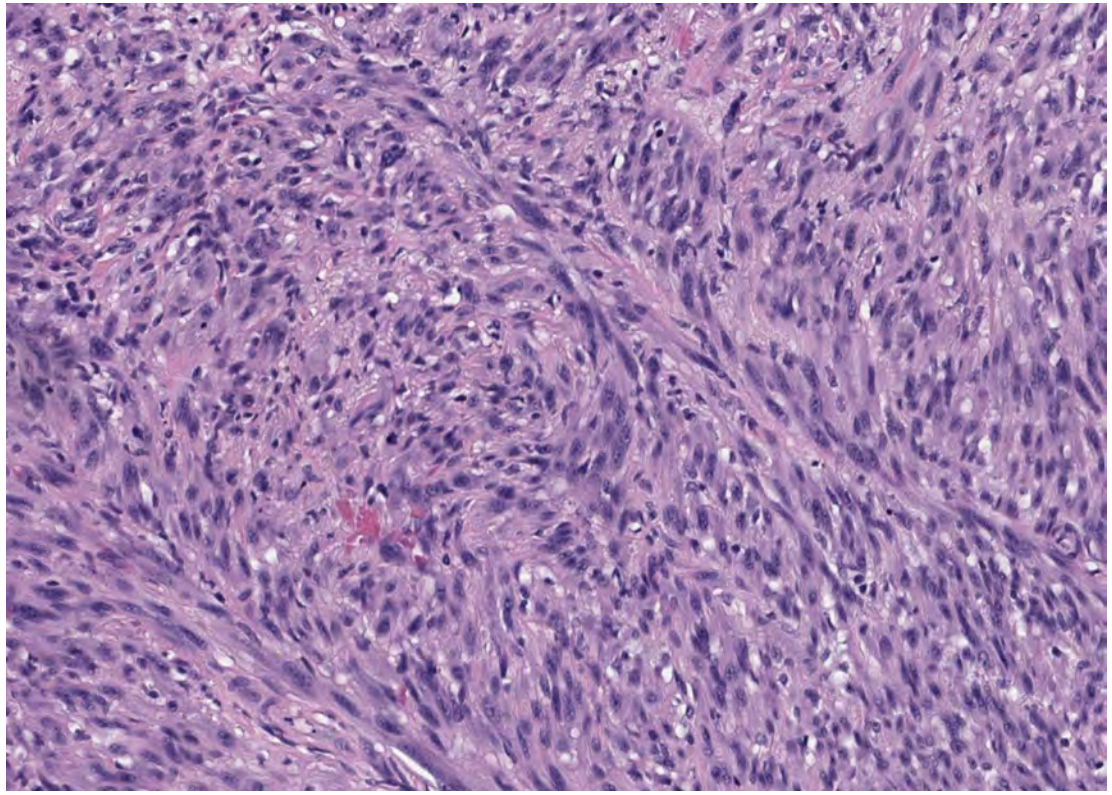
Rhinectomy

Histopathology of Excision

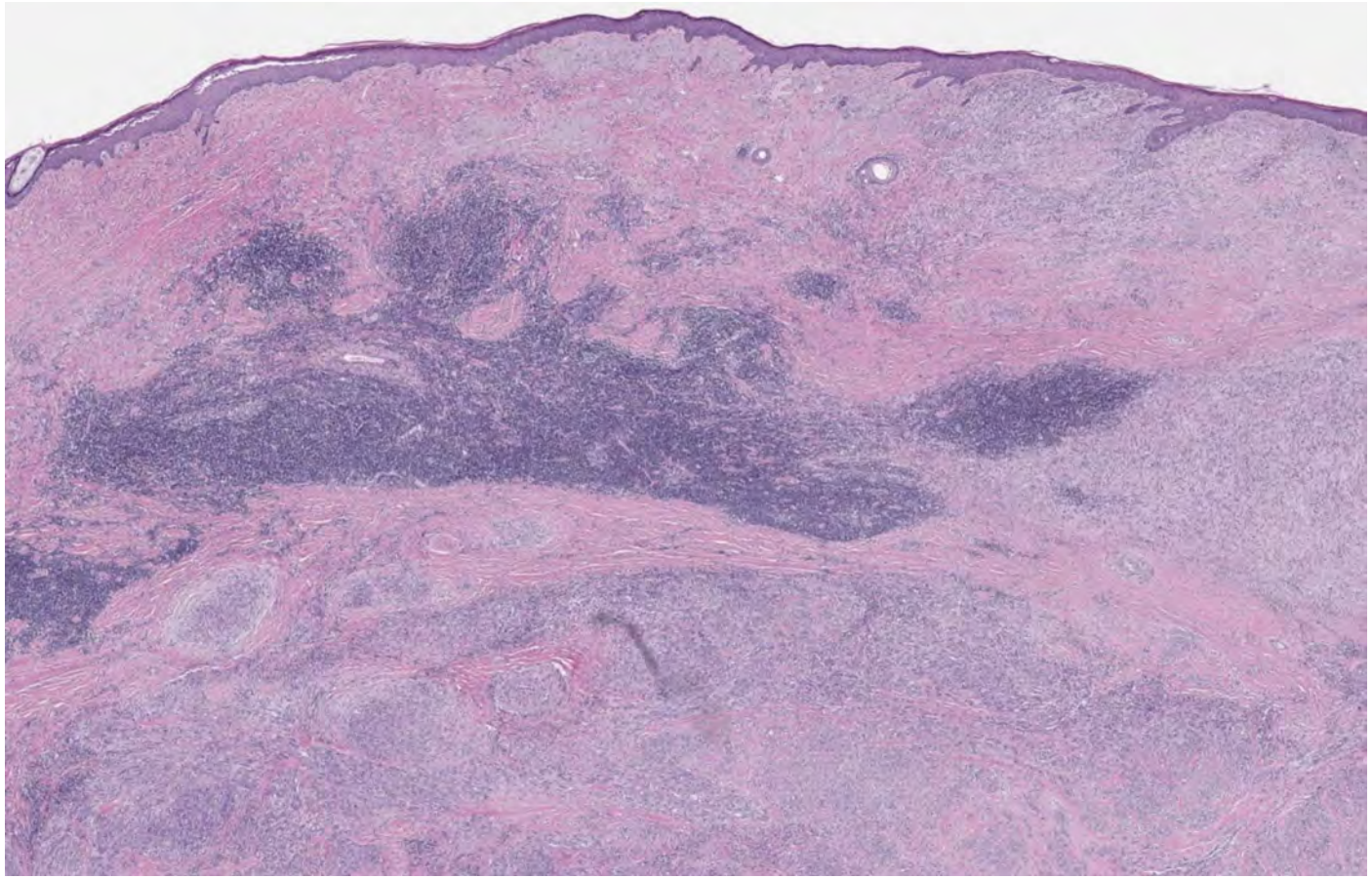


Case 2: Mixed Desmoplastic Melanoma





Desmoplastic Melanoma with CLL



Lessons from case

- The diagnosis of DM can be challenging and is often delayed
- Diagnostic problems are related to amelanotic clinical presentation, subtlety of histopathologic findings and partial sampling
- More than 1 biopsy and IHC may be needed for diagnosis

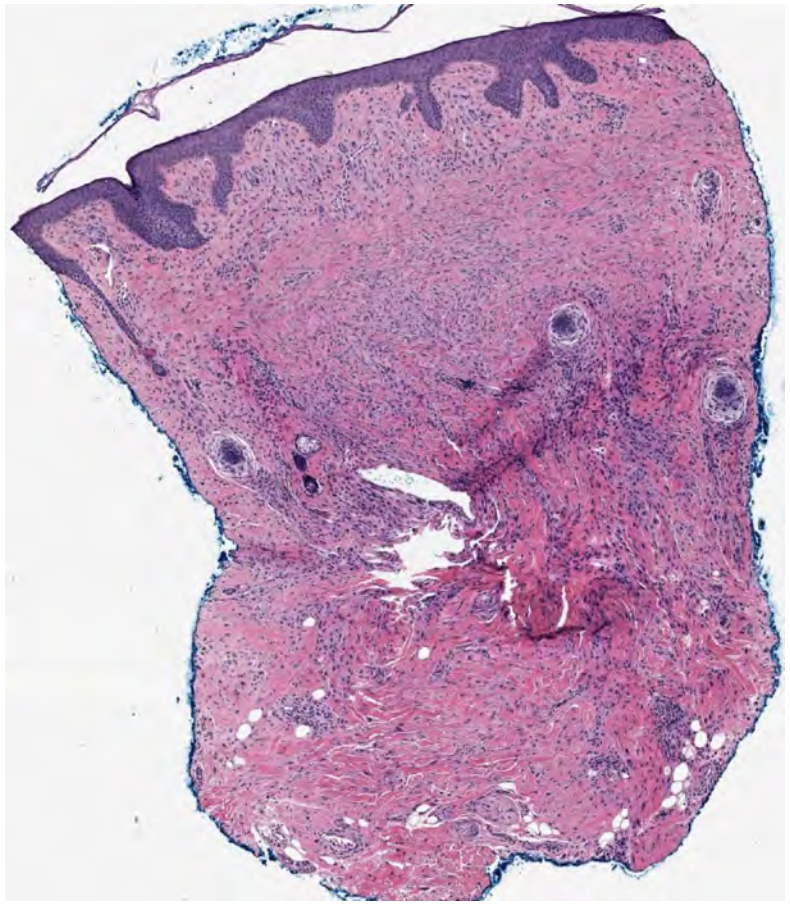
Desmoplastic Nevus vs Melanoma

- Desmoplastic Spitz Nevus
- Sclerosing Blue Nevus
- Other Melanocytic Nevi with Desmoplasia

Desmoplastic Spitz Nevus

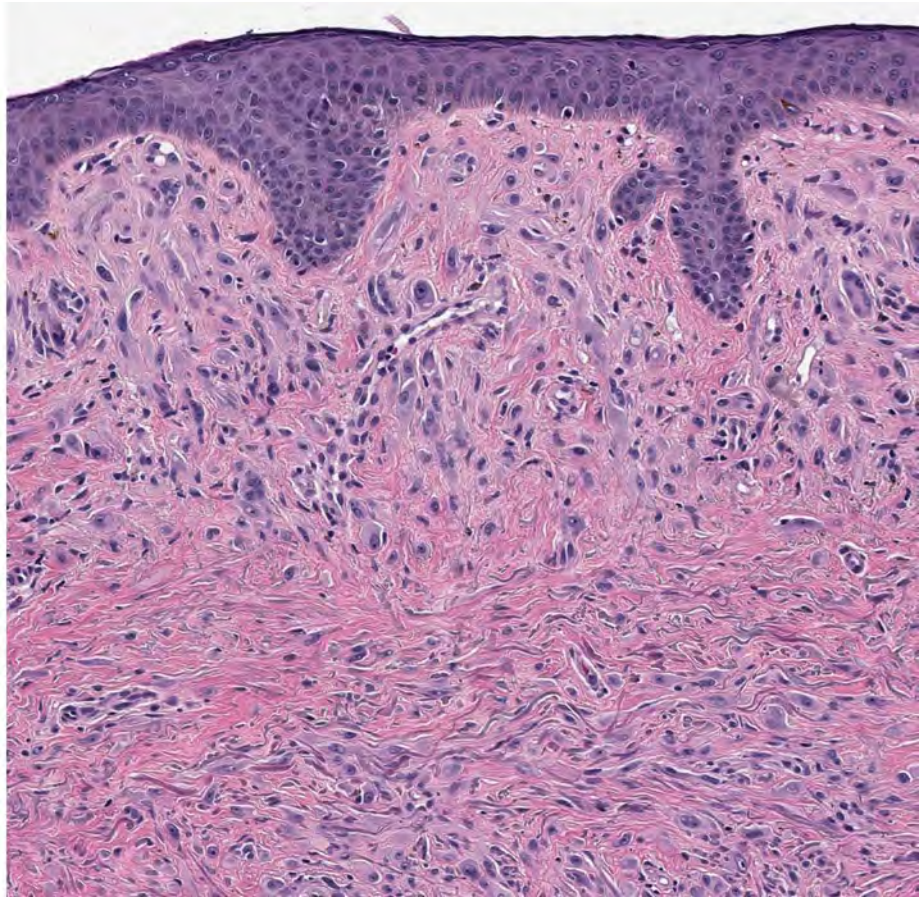
- Spitzoid cytology
- Immunoreactivity for Melan-A and p16
- Molecular findings, if needed

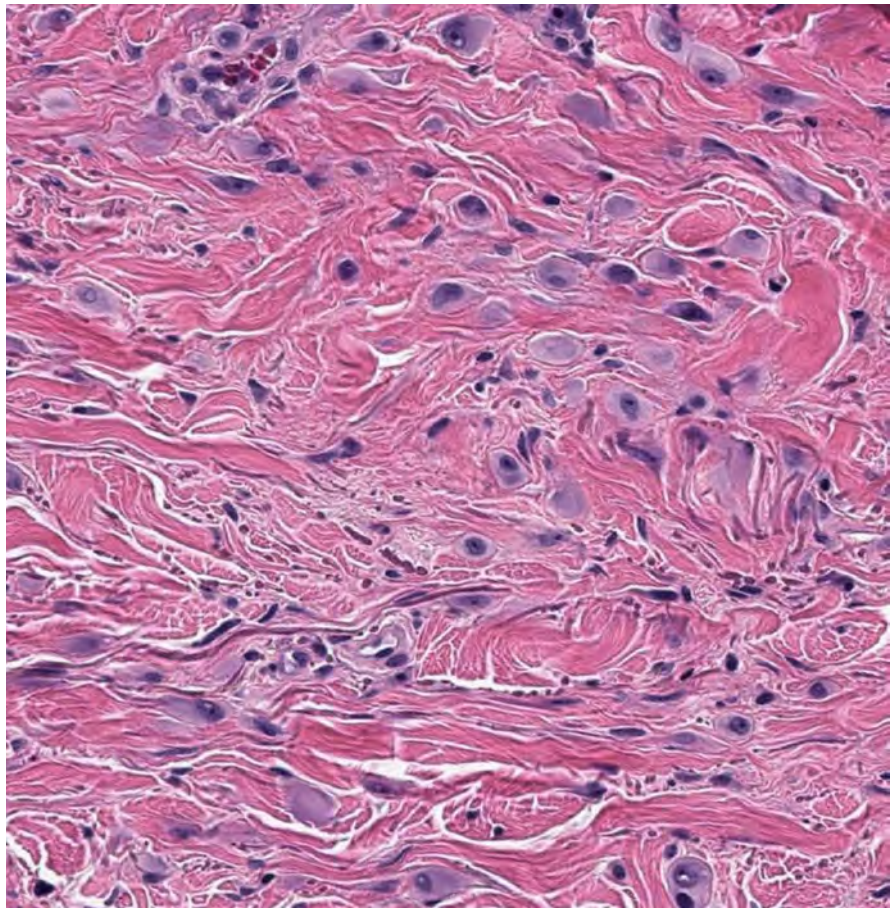
Case 3: What is Your Diagnosis?



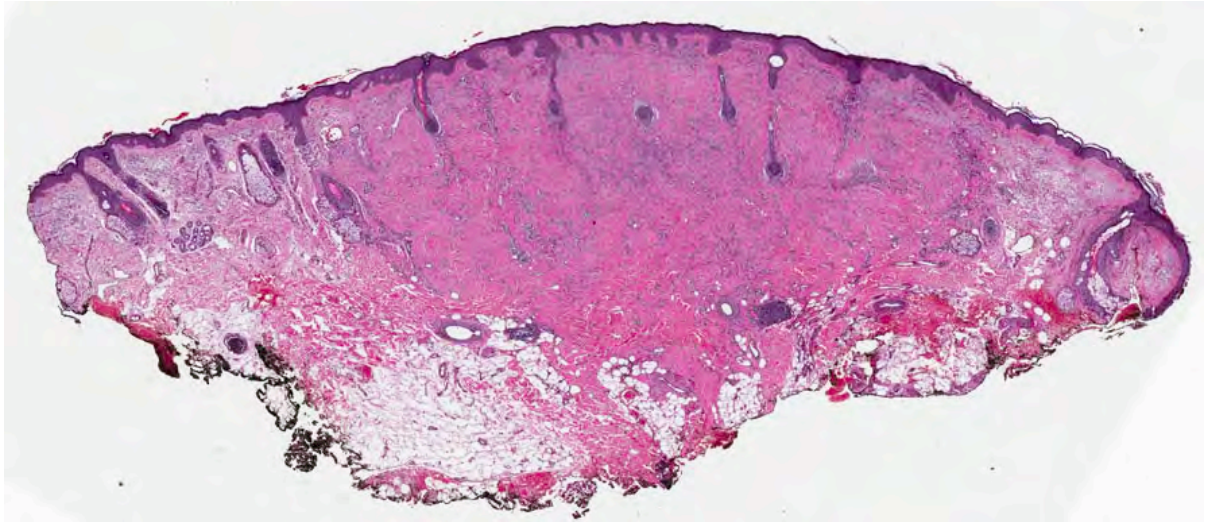
- 64 M
- Nodule on ear

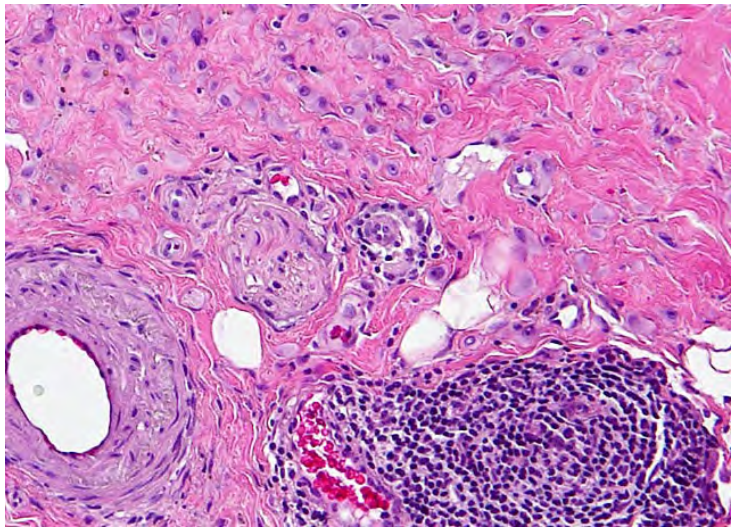
What is Your Diagnosis?

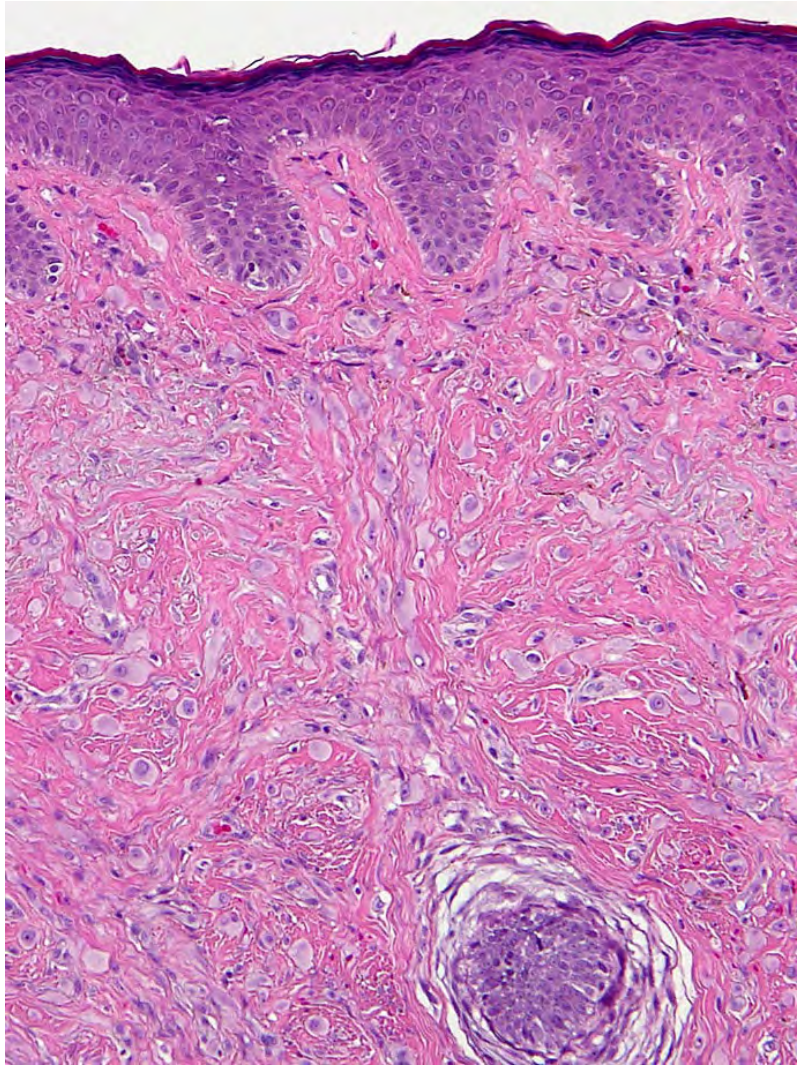




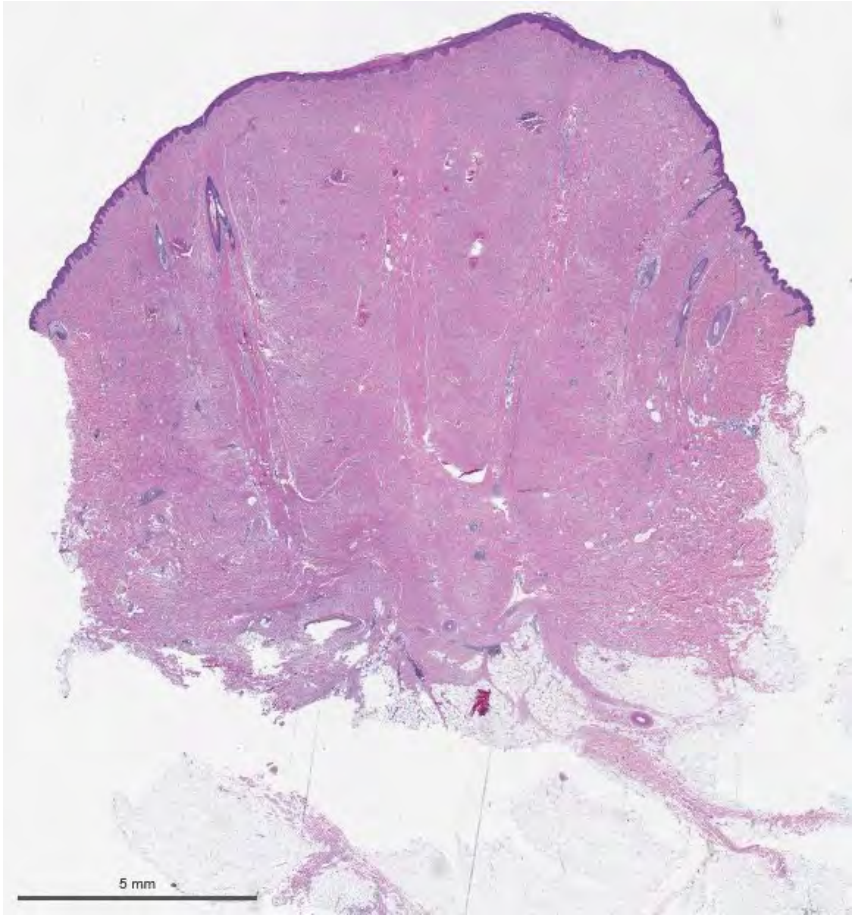
Diagnosis: Desmoplastic Spitz Nevus

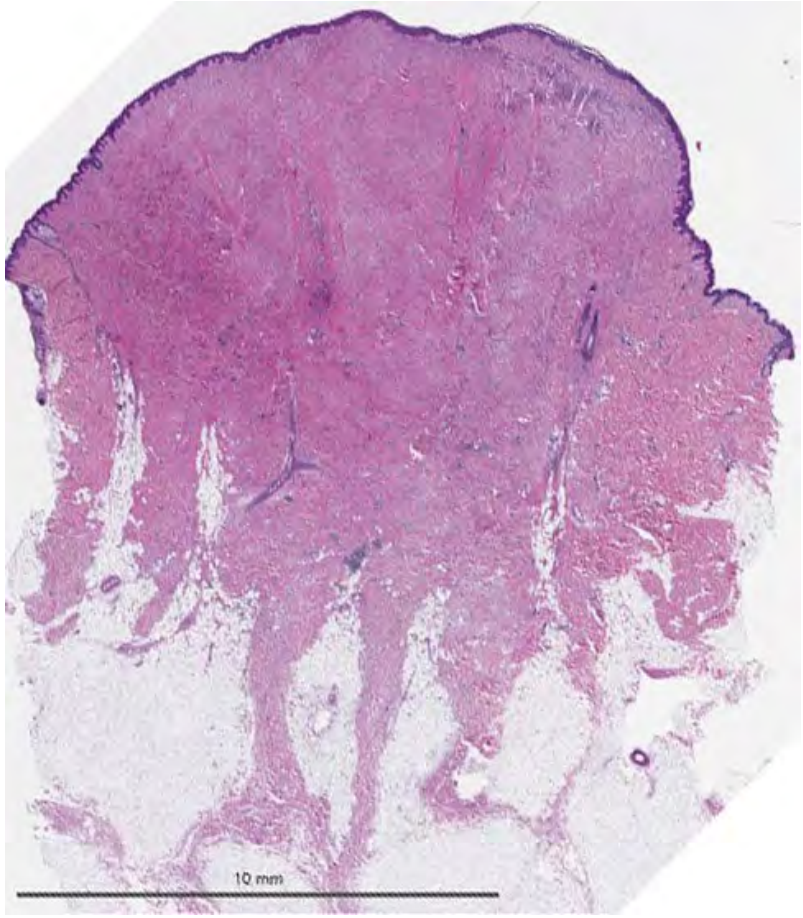


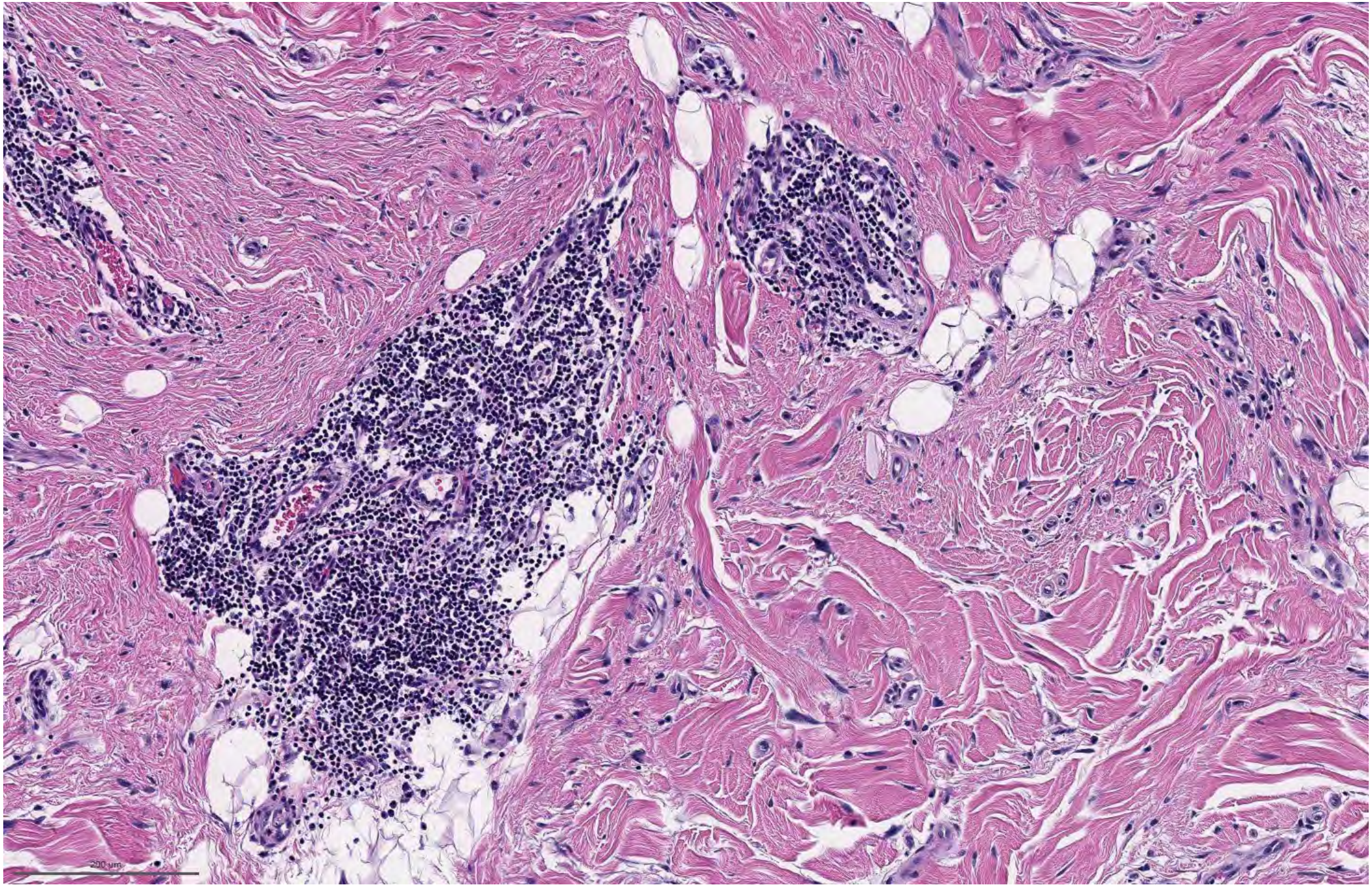




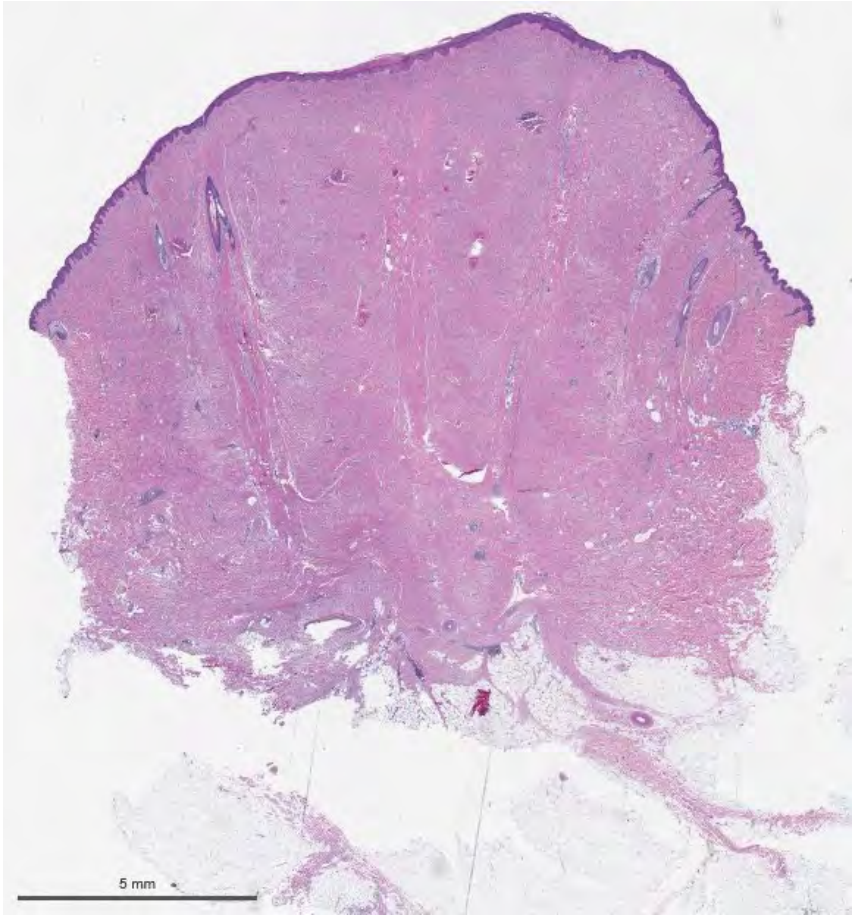
Case 4: What is Your Diagnosis?

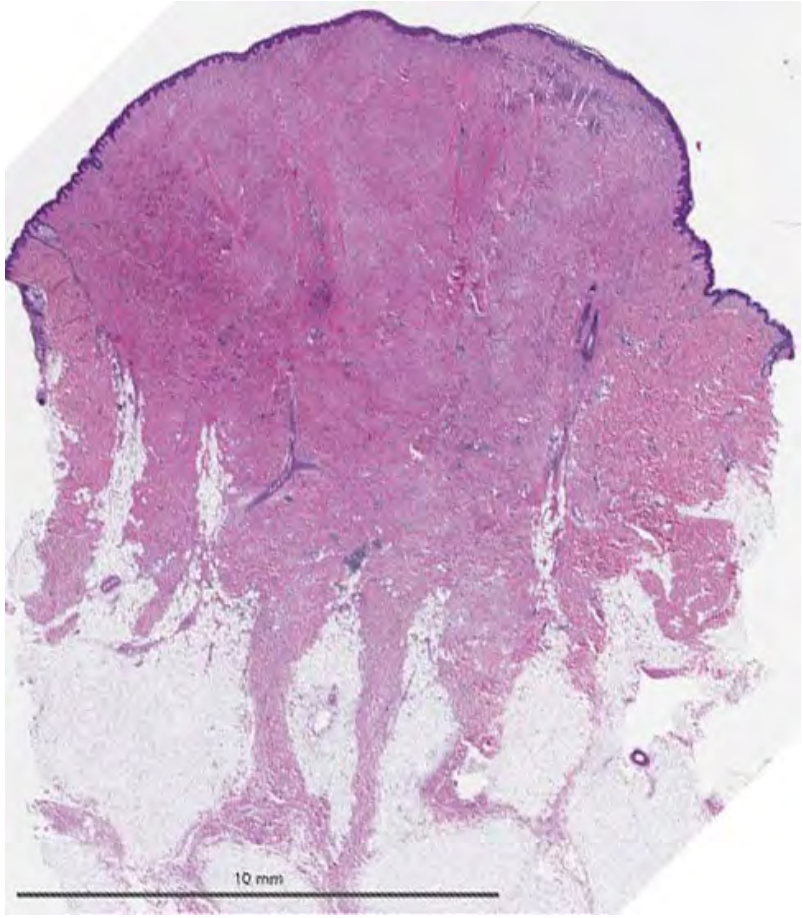




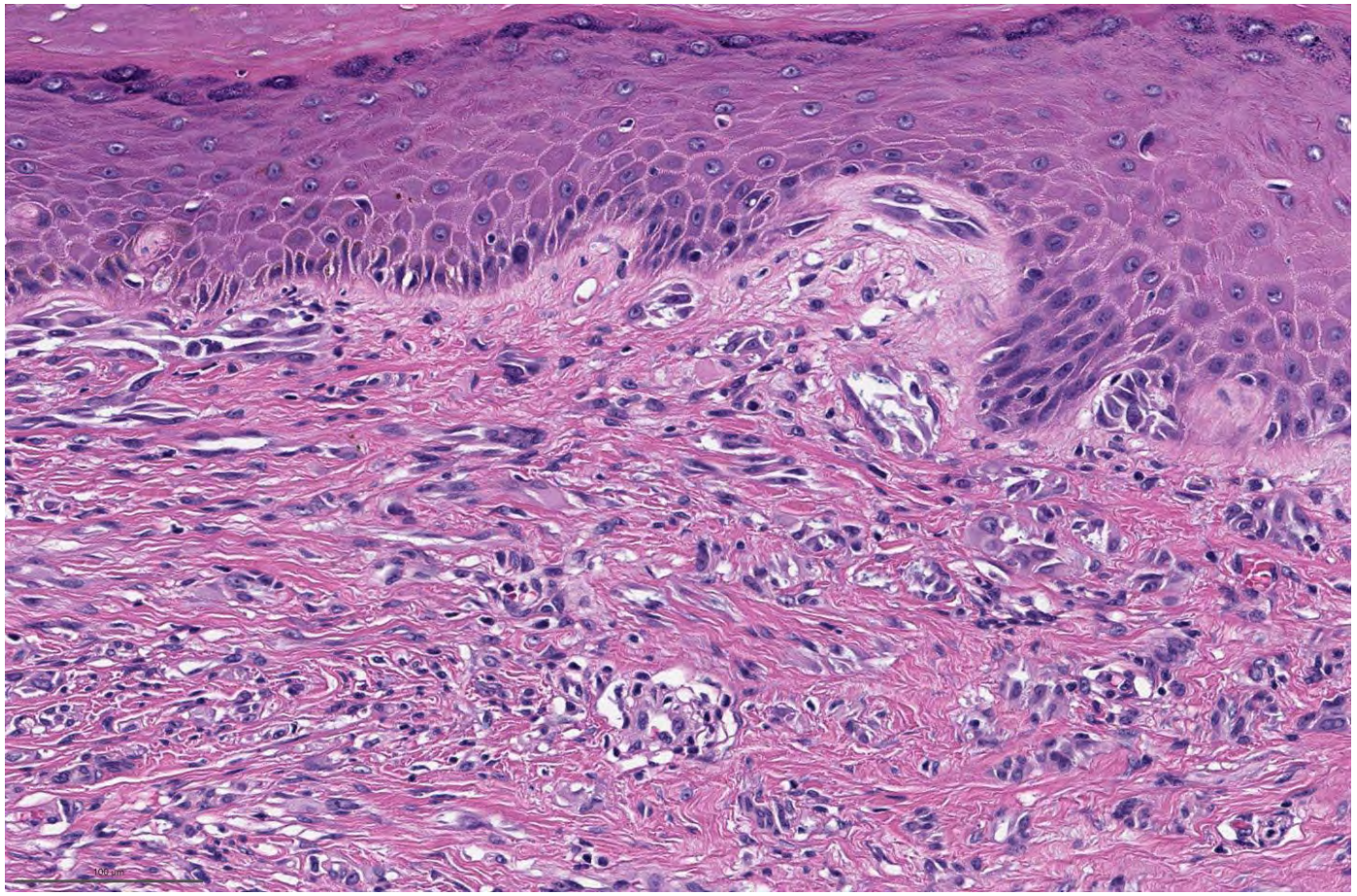

200 µm

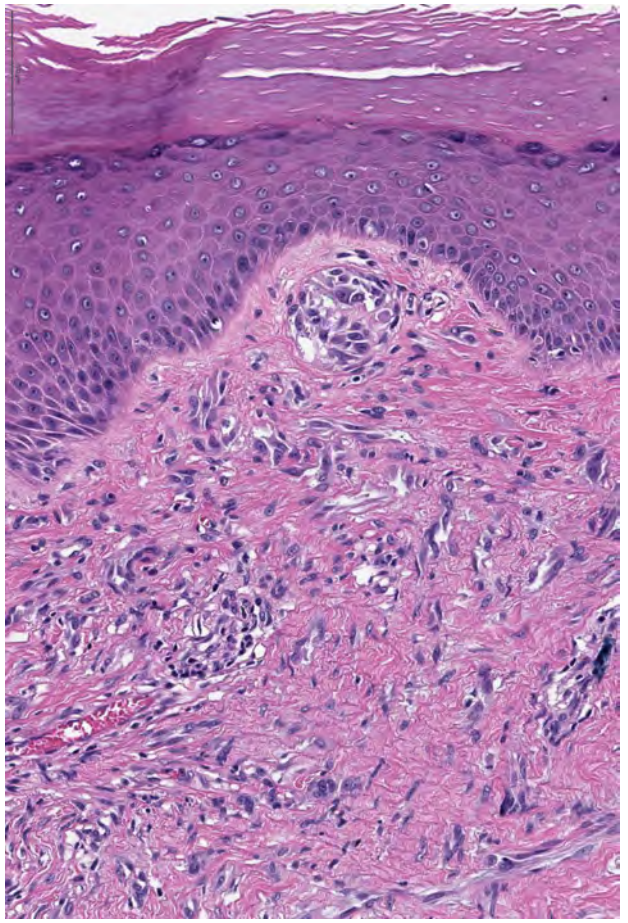
Case 4: 17M, skin of back



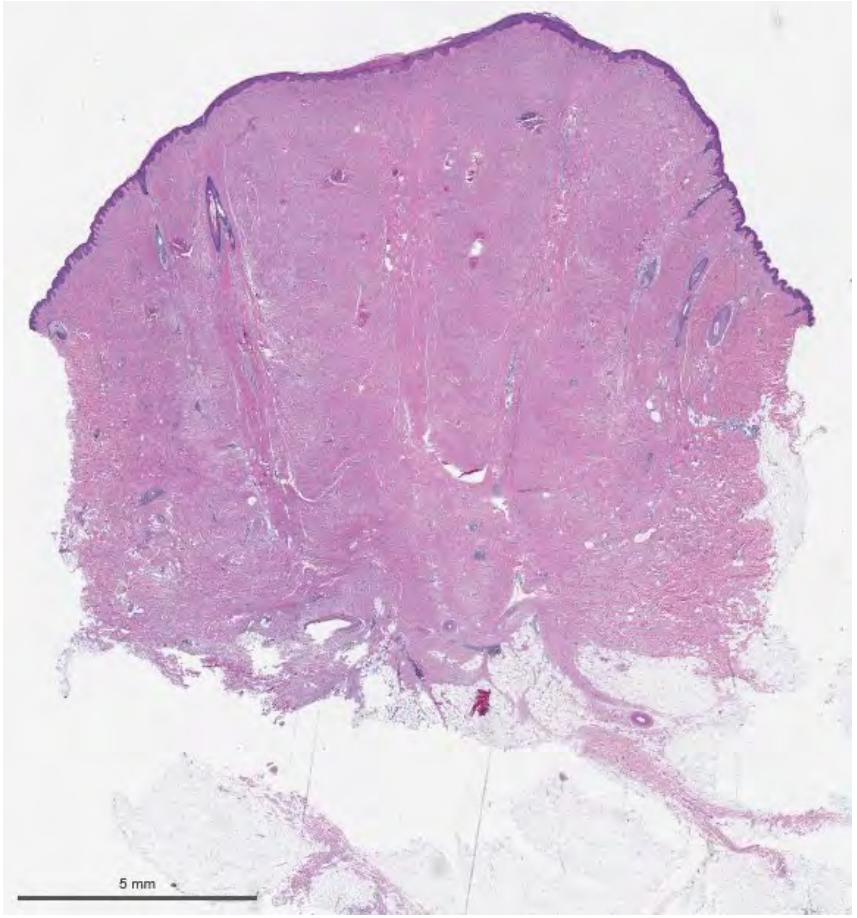


Desmoplastic Melanocytic Tumor; 17 M, back





Diagnosis: Desmoplastic Spitz Nevus



17 M, back

PWWP2A-
ROS1 FUSION

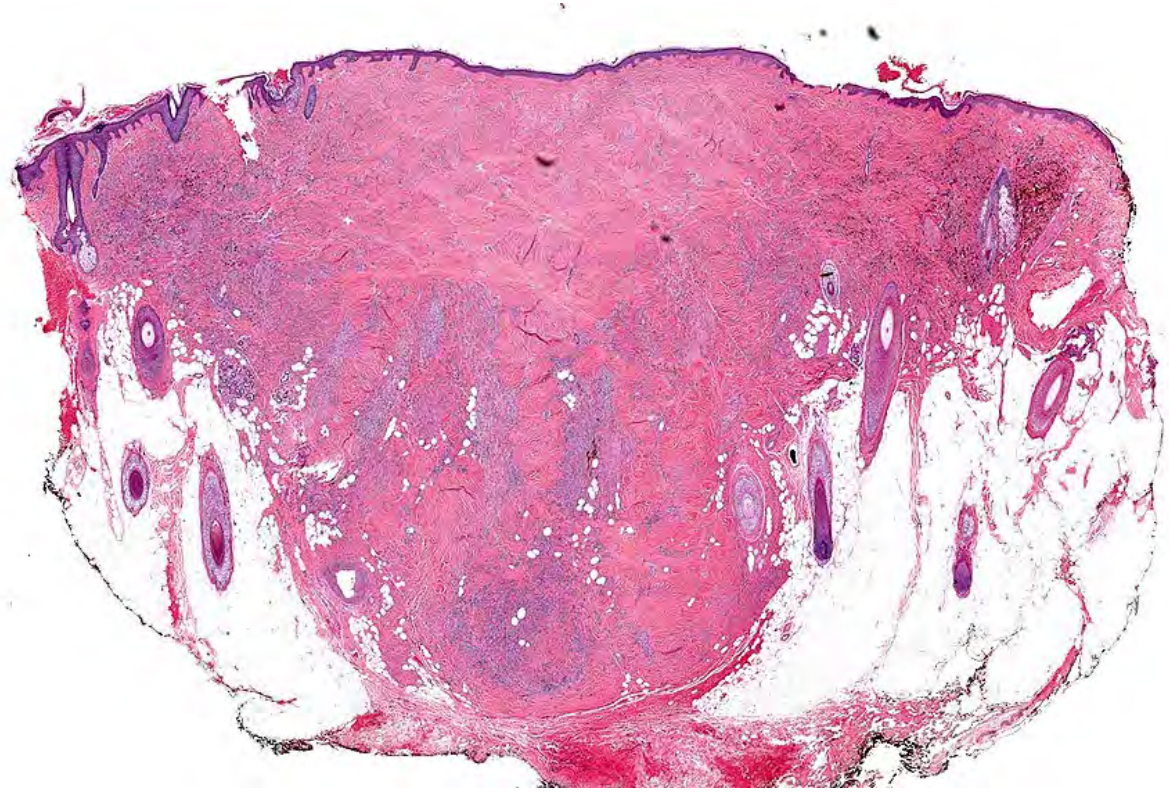
Desmoplastic Spitz Nevus vs Melanoma - Clues

- Clinical presentation
- Histopathology (spitzoid cytology)
- IHC: Melan-A, p16
- Molecular (HRAS aberrations, gene fusions)

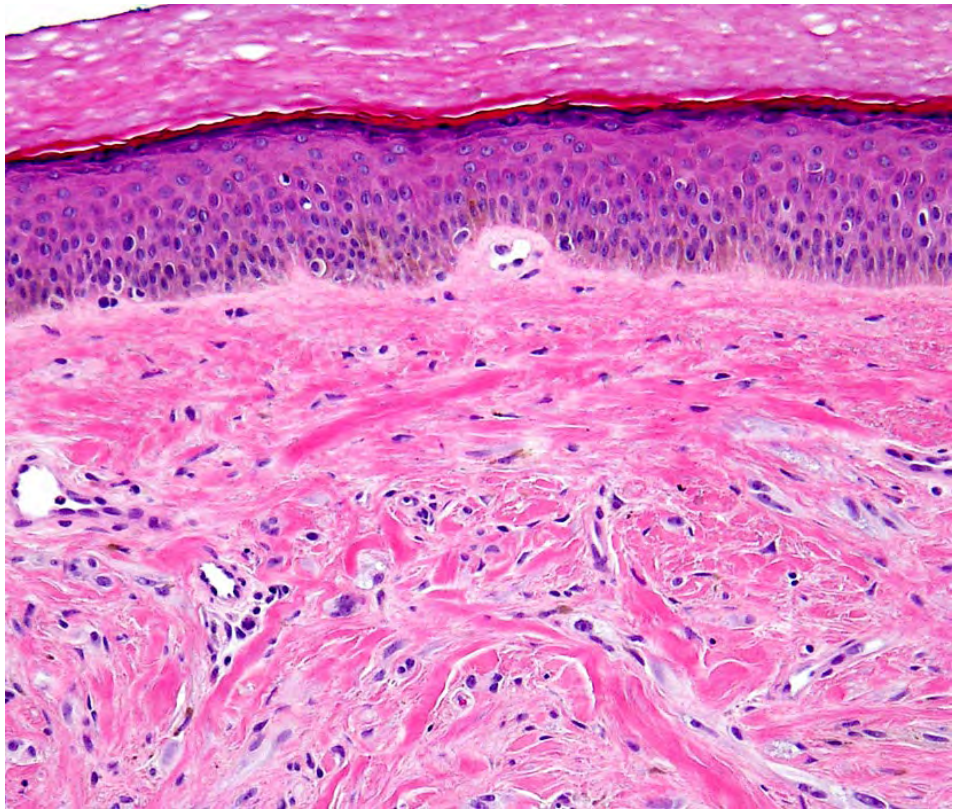
Sclerosing BN vs DM

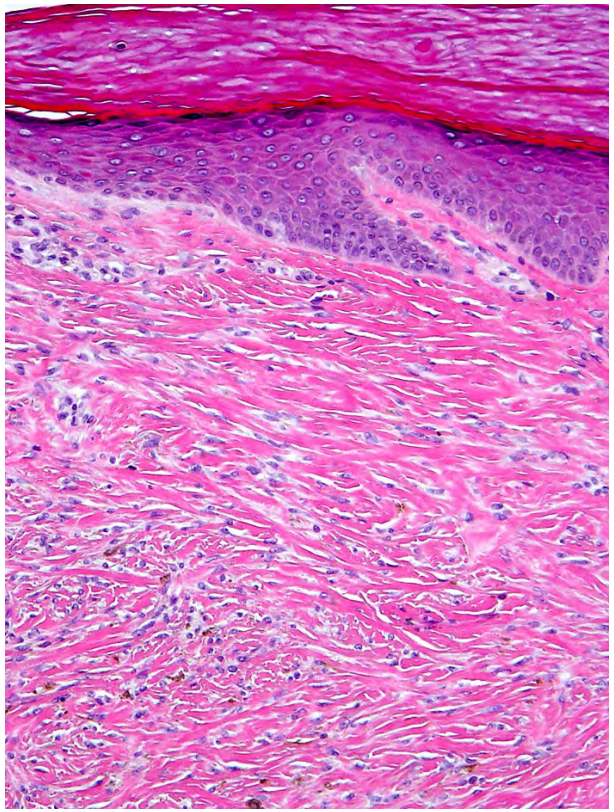
- Slender pigmented fusiform and dendritic melanocytes, often accompanied by melanophages
- Immunoreactivity for Melan-A, HMB-45
- Mutation profile, if needed

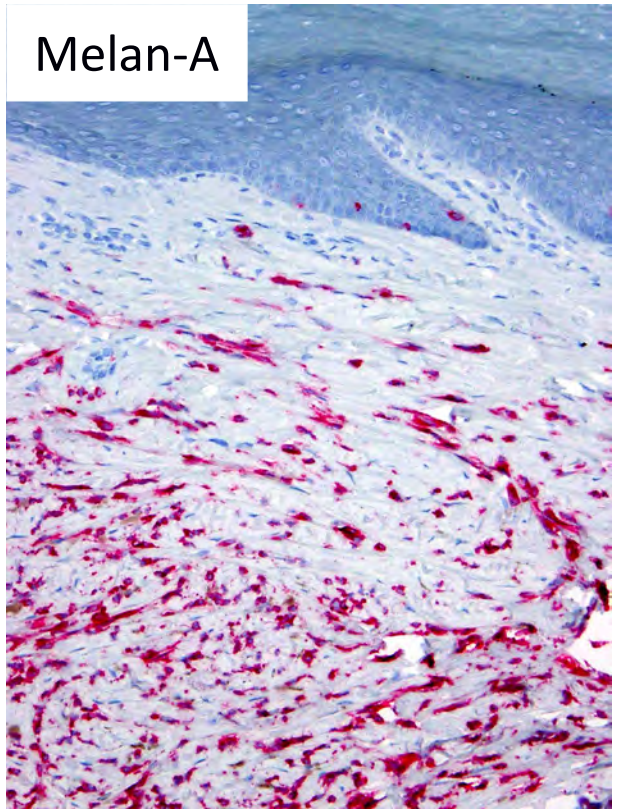
Sclerosing Blue Nevus



Sclerosing Blue Nevus

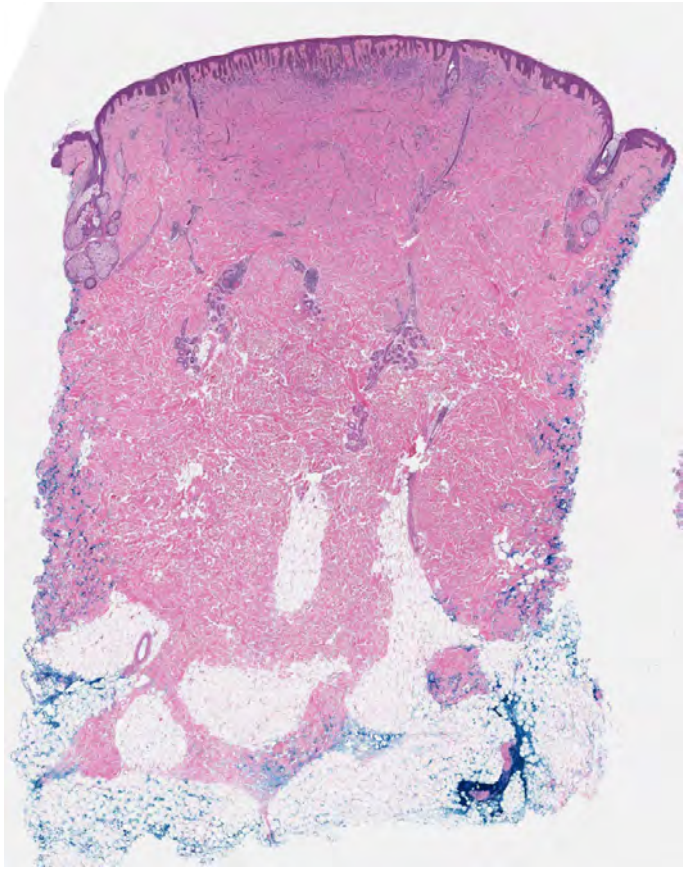


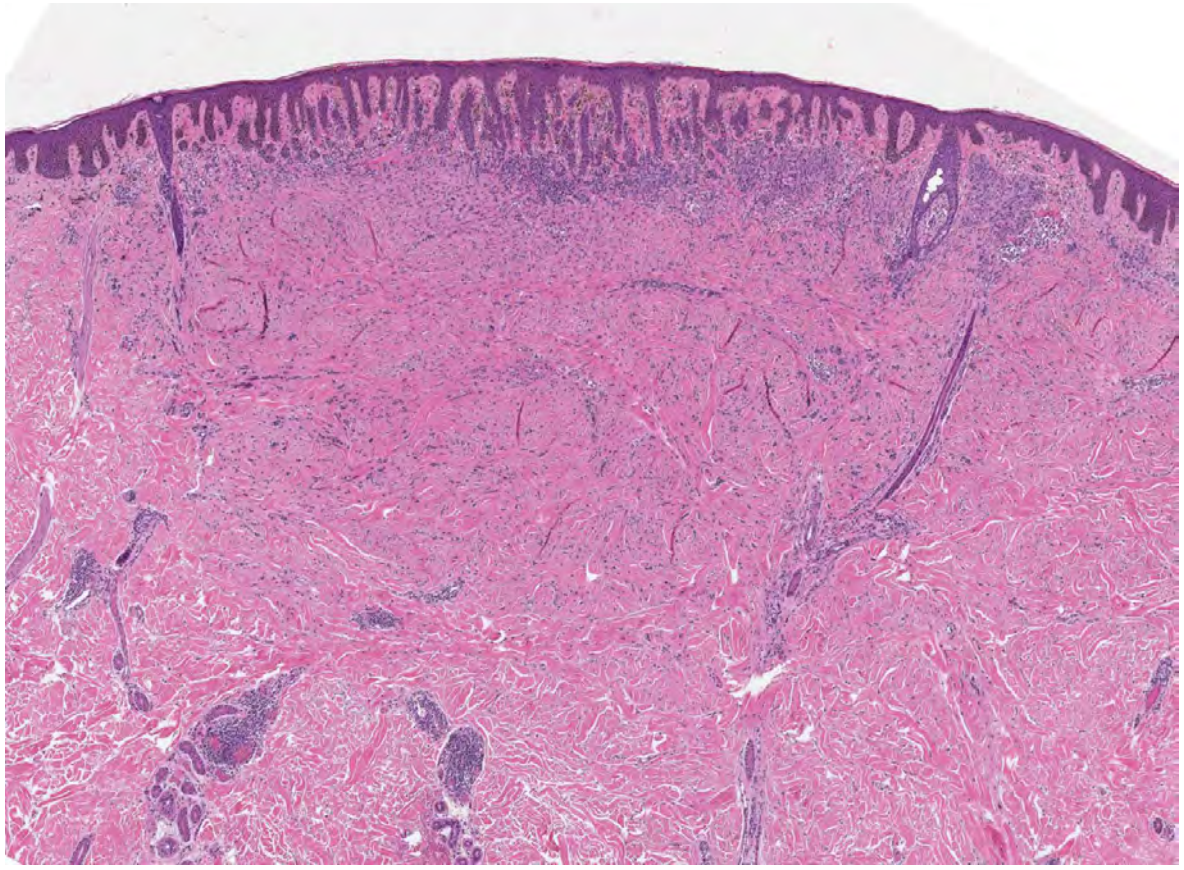




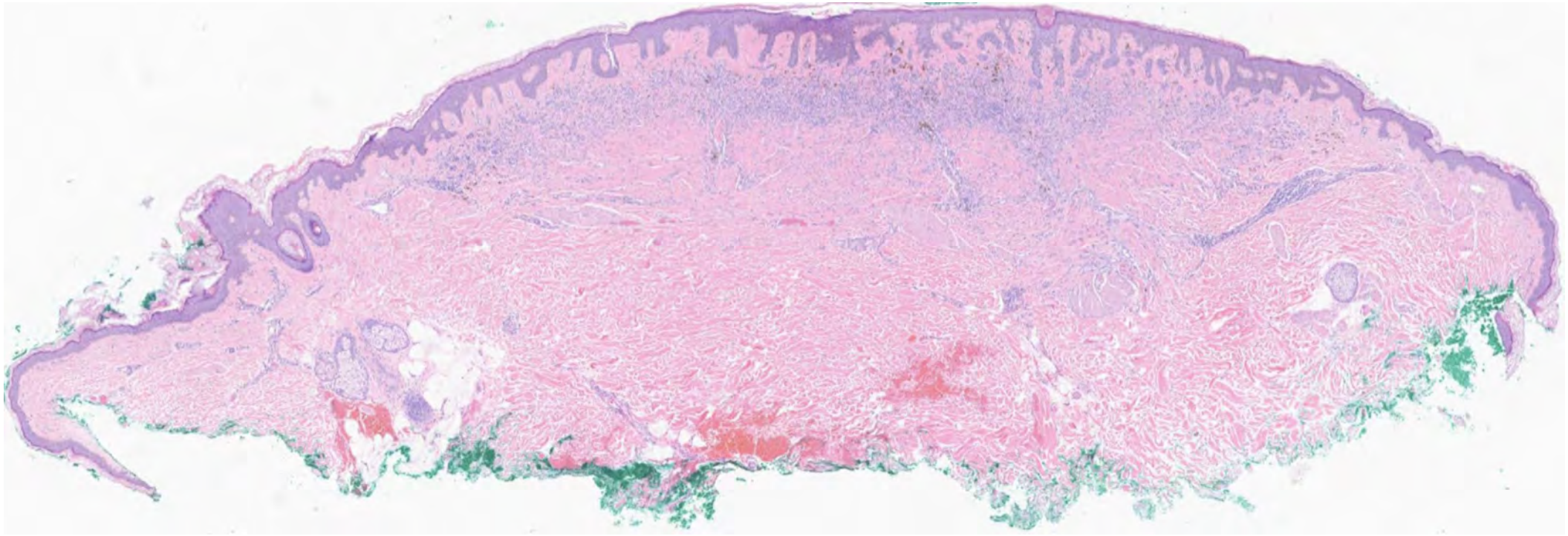
Bland Cytology

Compound Nevus with Desmoplasia

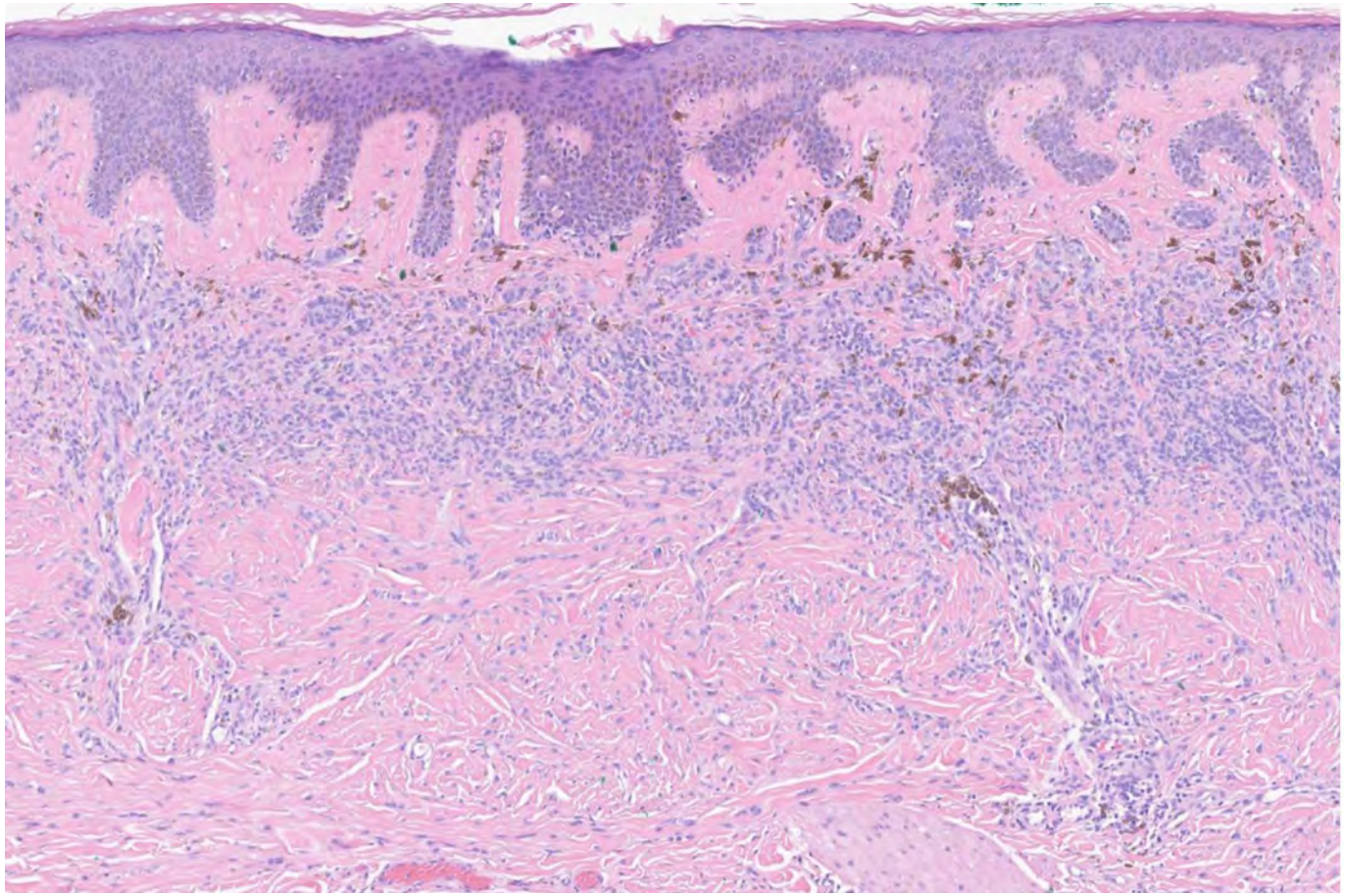




Melanocytic Nevus with *MAP2K1* Mutation



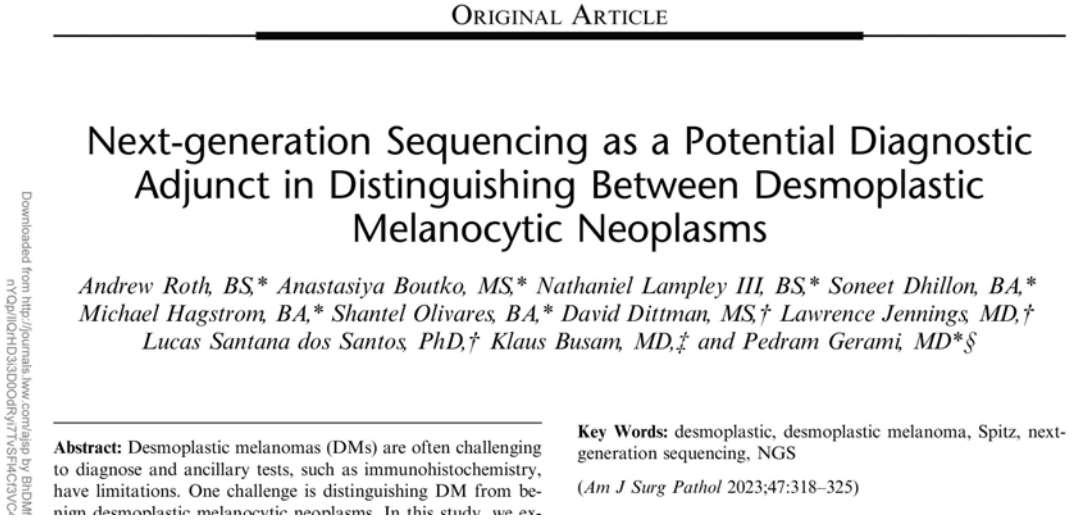
Melanocytic Nevus with *MAP2K1* Mutation



Desmoplastic Melanocytic Nevi

- Small diameter and limited depth, usually
- Symmetric silhouette
- Superficial compound nevus with evidence of maturation
- Cytologically different from desmoplastic melanoma
- IHC: Usually positive for p16, Melan-A

NGS for the Diagnosis of Desmoplastic Melanocytic Tumors



ORIGINAL ARTICLE

Next-generation Sequencing as a Potential Diagnostic Adjunct in Distinguishing Between Desmoplastic Melanocytic Neoplasms

Andrew Roth, BS, Anastasiya Boutko, MS,* Nathaniel Lampley III, BS,* Soneet Dhillon, BA,* Michael Hagstrom, BA,* Shantel Olivares, BA,* David Dittman, MS,† Lawrence Jennings, MD,† Lucas Santana dos Santos, PhD,† Klaus Busam, MD,‡ and Pedram Gerami, MD*§*

Abstract: Desmoplastic melanomas (DMs) are often challenging to diagnose and ancillary tests, such as immunohistochemistry, have limitations. One challenge is distinguishing DM from be-

Key Words: desmoplastic, desmoplastic melanoma, Spitz, next-generation sequencing, NGS

(*Am J Surg Pathol* 2023;47:318–325)

- Diagnostic Value
  - Desmoplastic Spitz or blue nevi (characteristic mutations or gene fusions)
- Limitations
  - Low TMB does not exclude DM

NGS for the Diagnosis of Desmoplastic Melanocytic Tumors

Desmoplastic Melanoma

76F

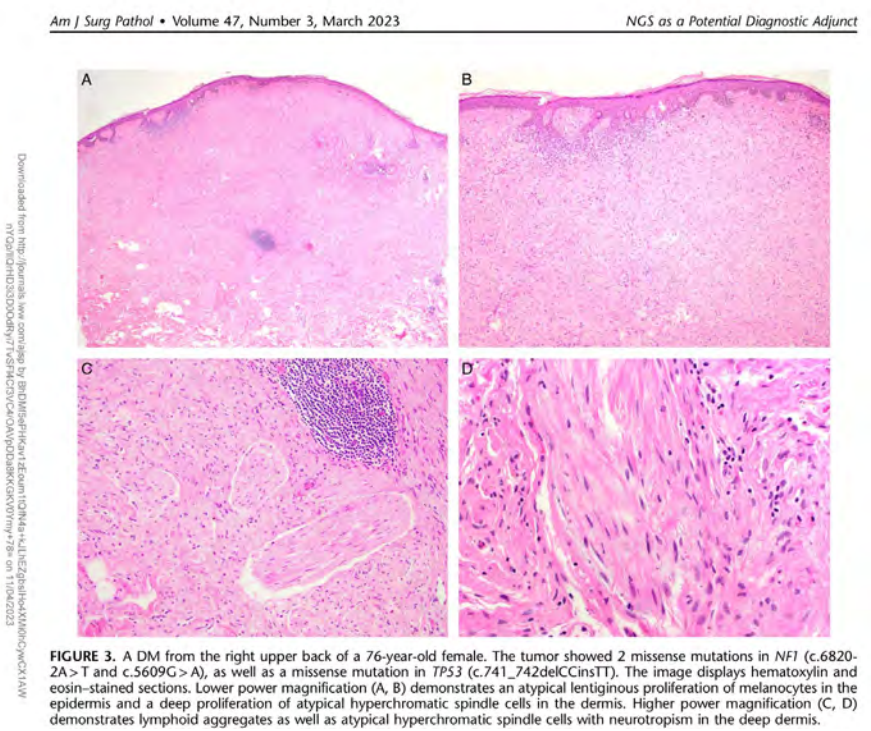


FIGURE 3. A DM from the right upper back of a 76-year-old female. The tumor showed 2 missense mutations in *NF1* (c.6820-2A>T and c.5609G>A), as well as a missense mutation in *TP53* (c.741_742delCCinsTT). The image displays hematoxylin and eosin–stained sections. Lower power magnification (A, B) demonstrates an atypical lentiginous proliferation of melanocytes in the epidermis and a deep proliferation of atypical hyperchromatic spindle cells in the dermis. Higher power magnification (C, D) demonstrates lymphoid aggregates as well as atypical hyperchromatic spindle cells with neurotropism in the deep dermis.

(NF1 and TP53 mutations)

Desmoplastic Nevus

5F

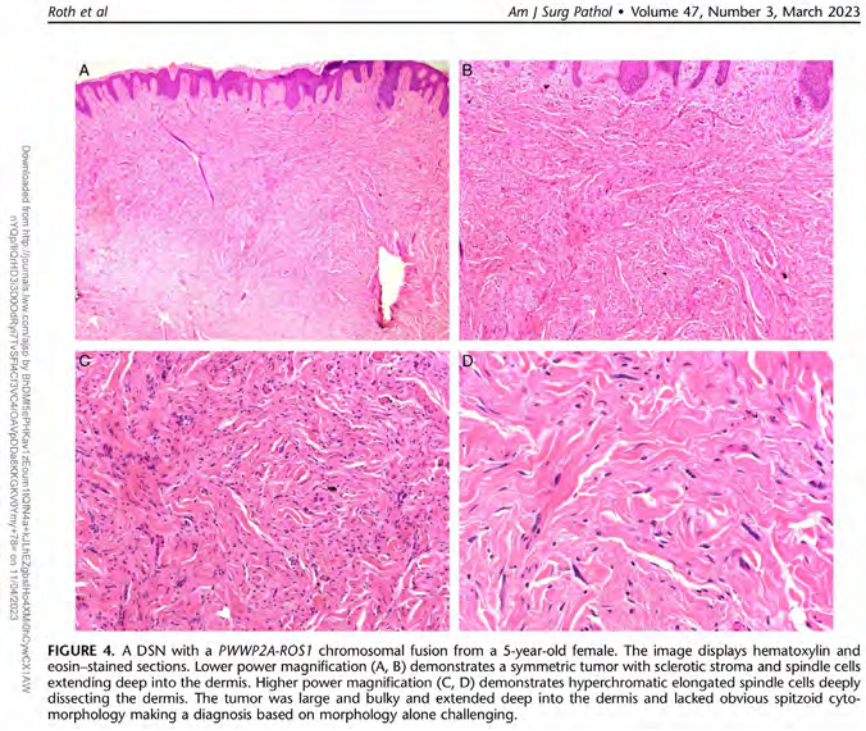


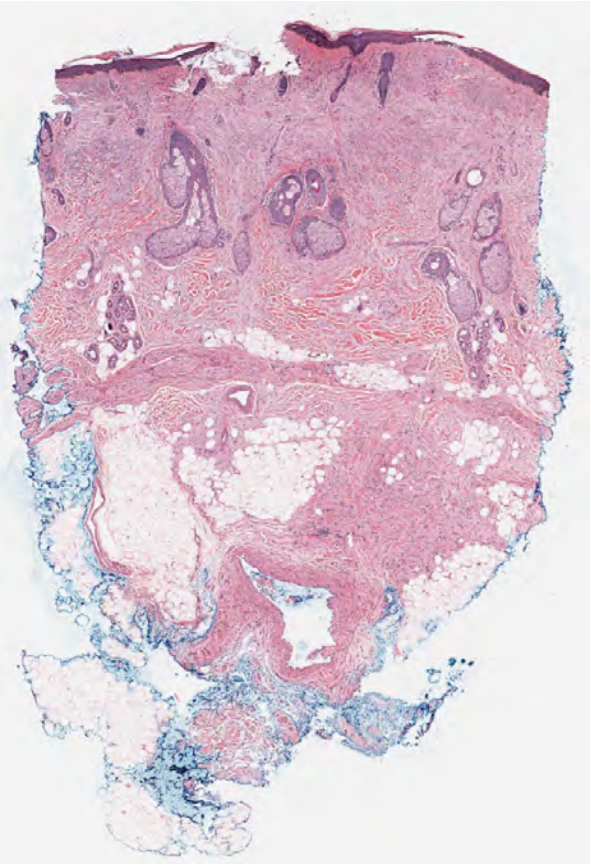
FIGURE 4. A DSN with a *PWWP2A-ROS1* chromosomal fusion from a 5-year-old female. The image displays hematoxylin and eosin–stained sections. Lower power magnification (A, B) demonstrates a symmetric tumor with sclerotic stroma and spindle cells extending deep into the dermis. Higher power magnification (C, D) demonstrates hyperchromatic elongated spindle cells deeply dissecting the dermis. The tumor was large and bulky and extended deep into the dermis and lacked obvious spitzoid cytomorphology making a diagnosis based on morphology alone challenging.

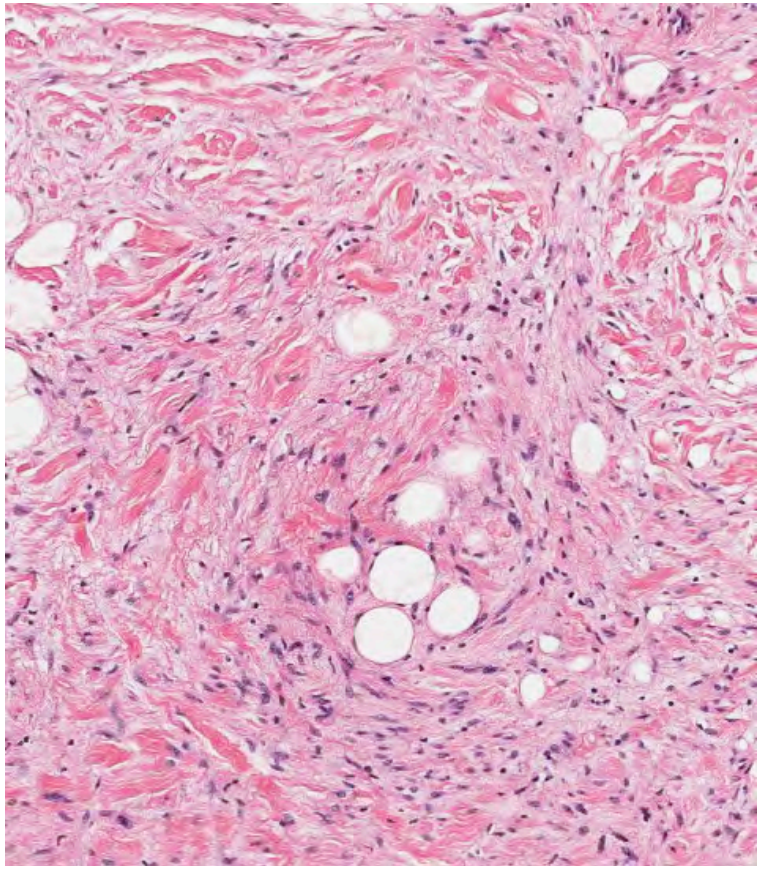
(PWWP2A-ROS1 fusion)

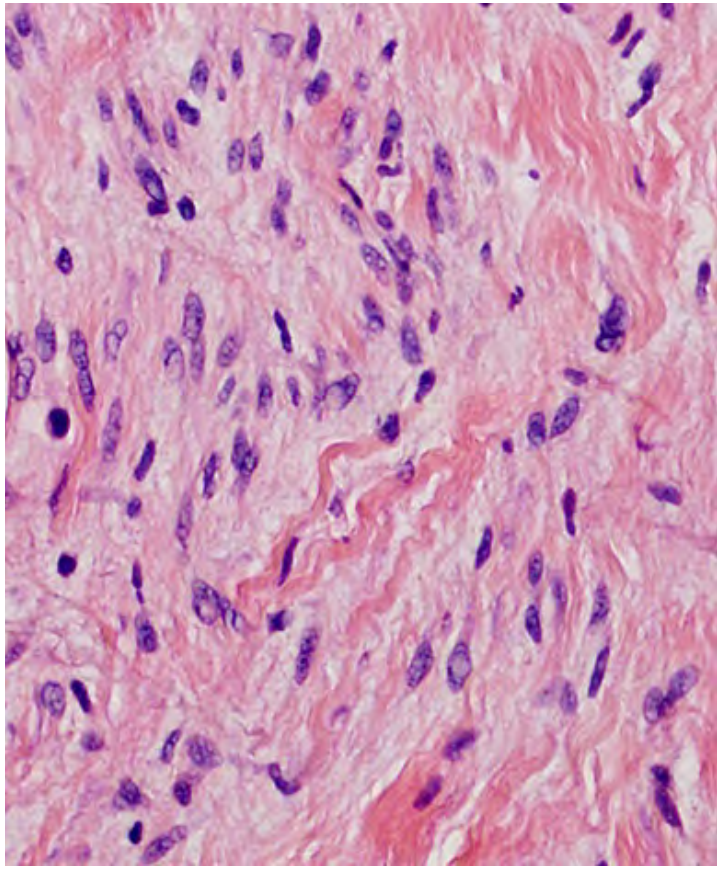
Desmoplastic Neurotropic Melanoma vs Nerve Sheath Tumors

- Neurofibroma
- Schwannoma
- Gene fusion-associated nerve sheath tumors
- MPNST

Neurofibroma vs Desmoplastic Melanoma

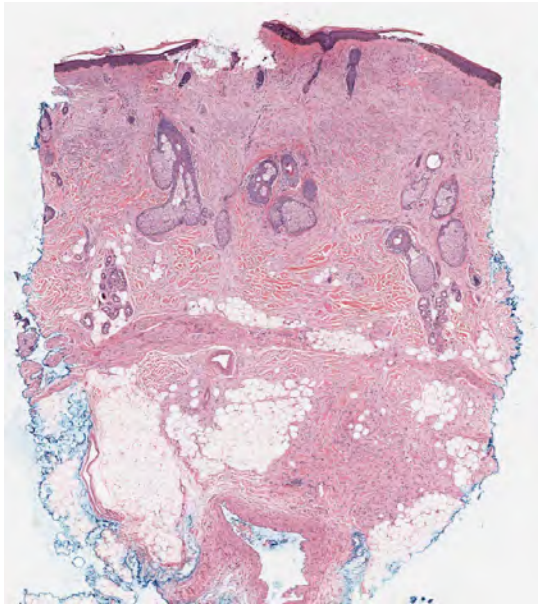


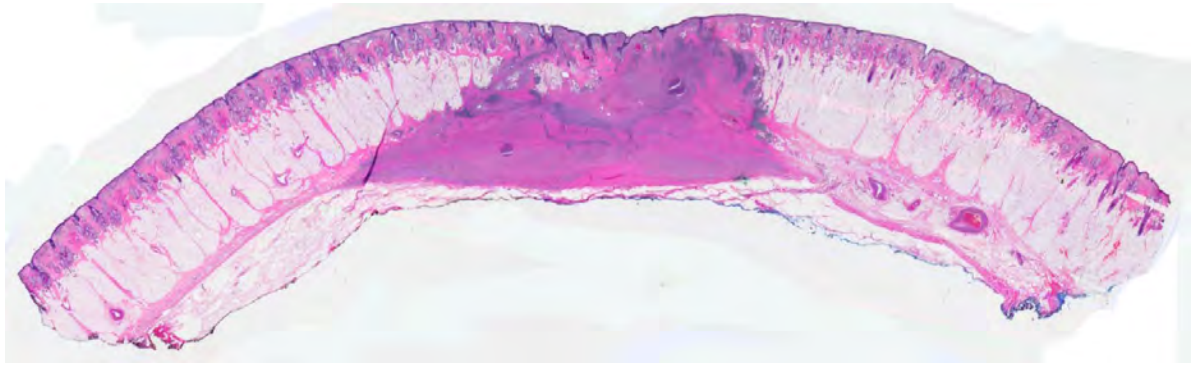




69M, forehead; r/o “neurofibroma”

DM Misdiagnosed as Neurofibroma





J Cutan Pathol 2013: 40: 985–987
doi: 10.1111/cup.12206
John Wiley & Sons. Printed in Singapore.

Journal of
Cutaneous Pathology

Letter to the Editor

Fingerprint CD34 immunopositivity to distinguish neurofibroma from an early/paucicellular desmoplastic melanoma can be misleading

Keywords: early/paucicellular desmoplastic melanoma, fingerprint CD34 immunopositivity, neurofibroma

To the Editor,

In the August 2011 issue of the *JCP*, Yeh and McCalmont present a study which concludes that *CD34 fingerprint immunoreactivity* is useful in distinguishing neurofibroma from early desmoplastic melanoma, especially if the fingerprint involves more than 60% of a tumor's cross-sectional area.[1]

We recently encountered a biopsy of a paucicellular spindle cell tumor (Fig. 1A) on the temple of a 64-year-old man with a similar histopathologic

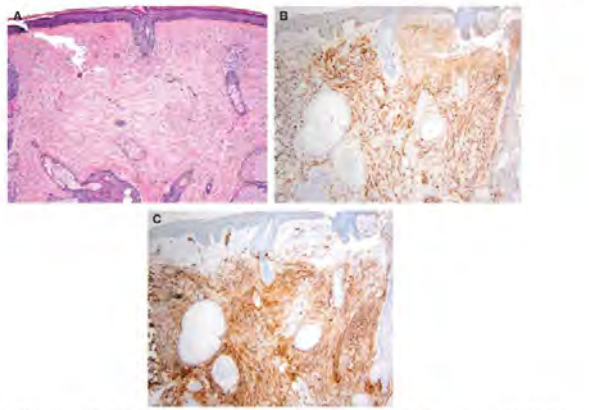
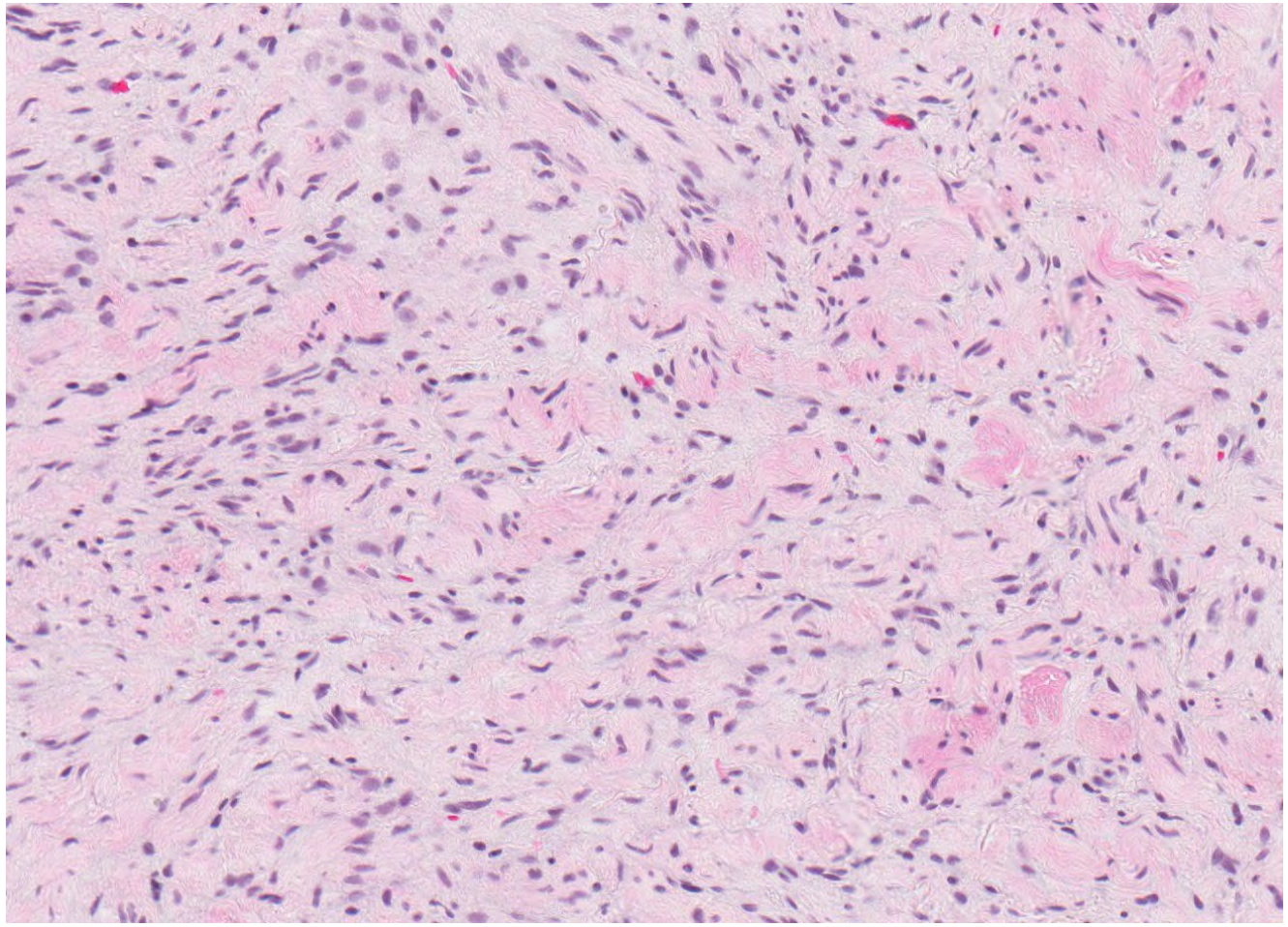


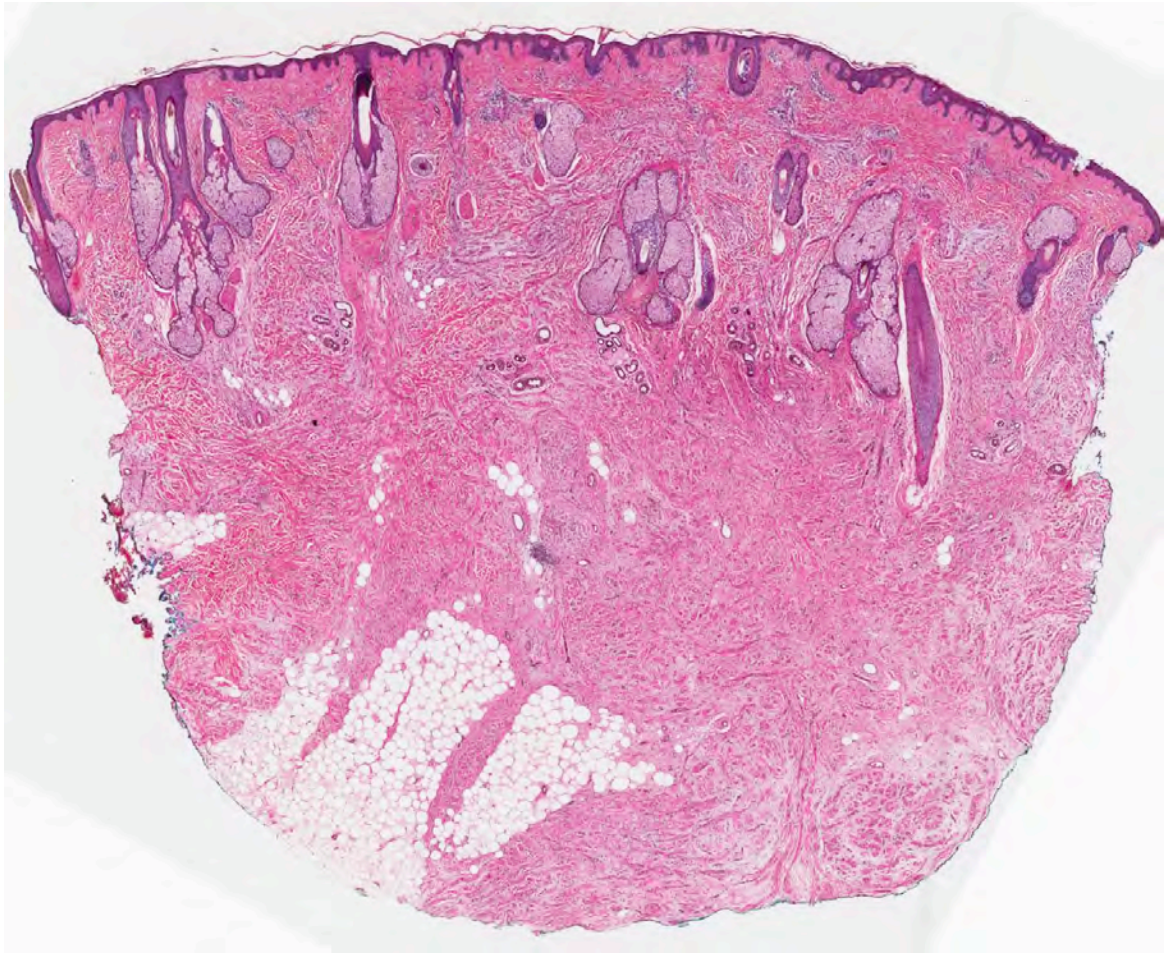
Fig. 1. A) Original biopsy specimen. Paucicellular spindle cell proliferation. Hematoxylin–eosin, original magnification ×10. B) Original biopsy specimen. S100 immunostain, original magnification ×10. C) Original biopsy specimen. CD34 immunostain, original magnification ×10.

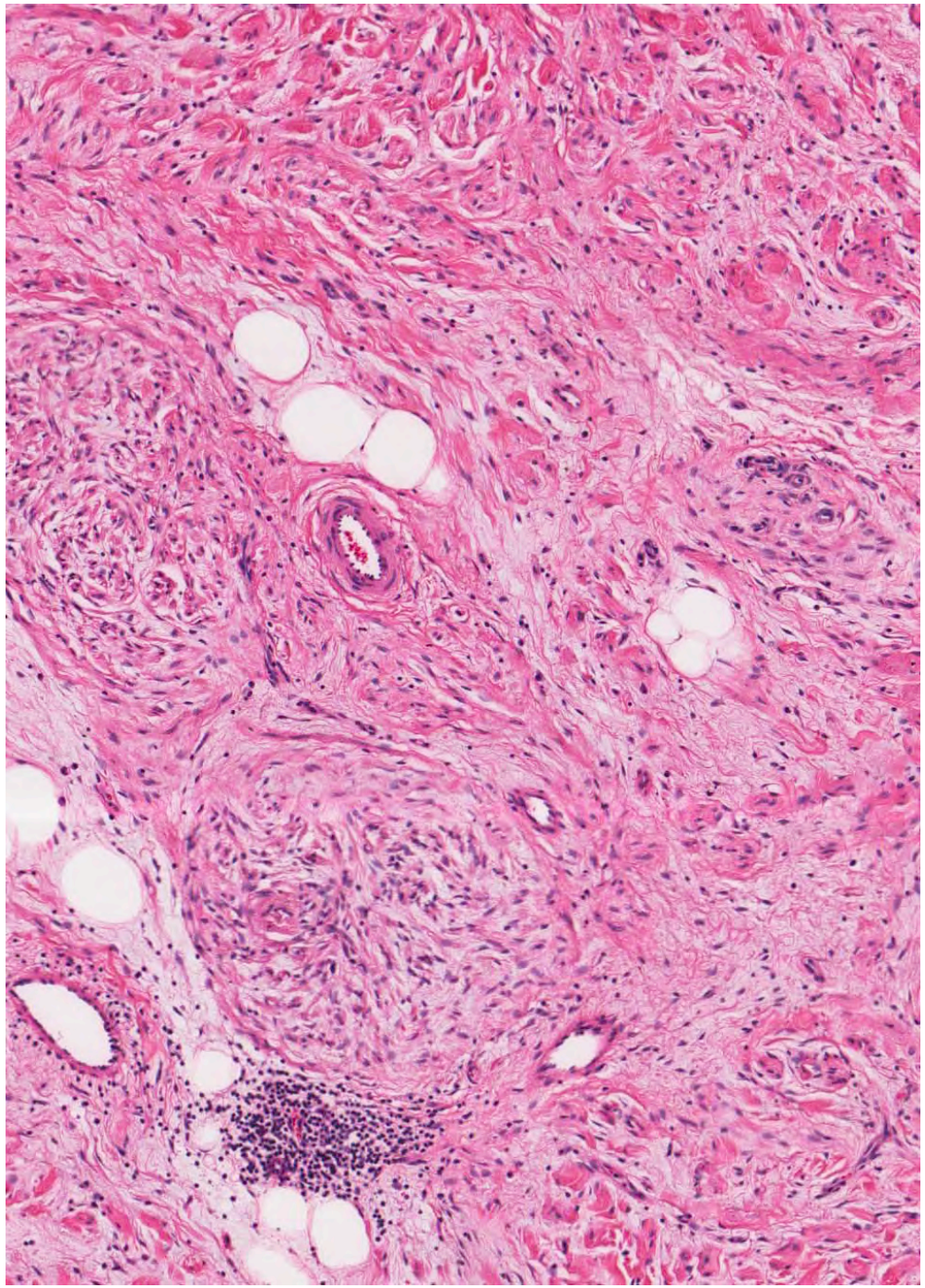
Desmoplastic Melanoma Misdiagnosed as Neurofibroma



23M, nodule on cheek, r/o “ruptured cyst”

23M, cheek, 2nd biopsy

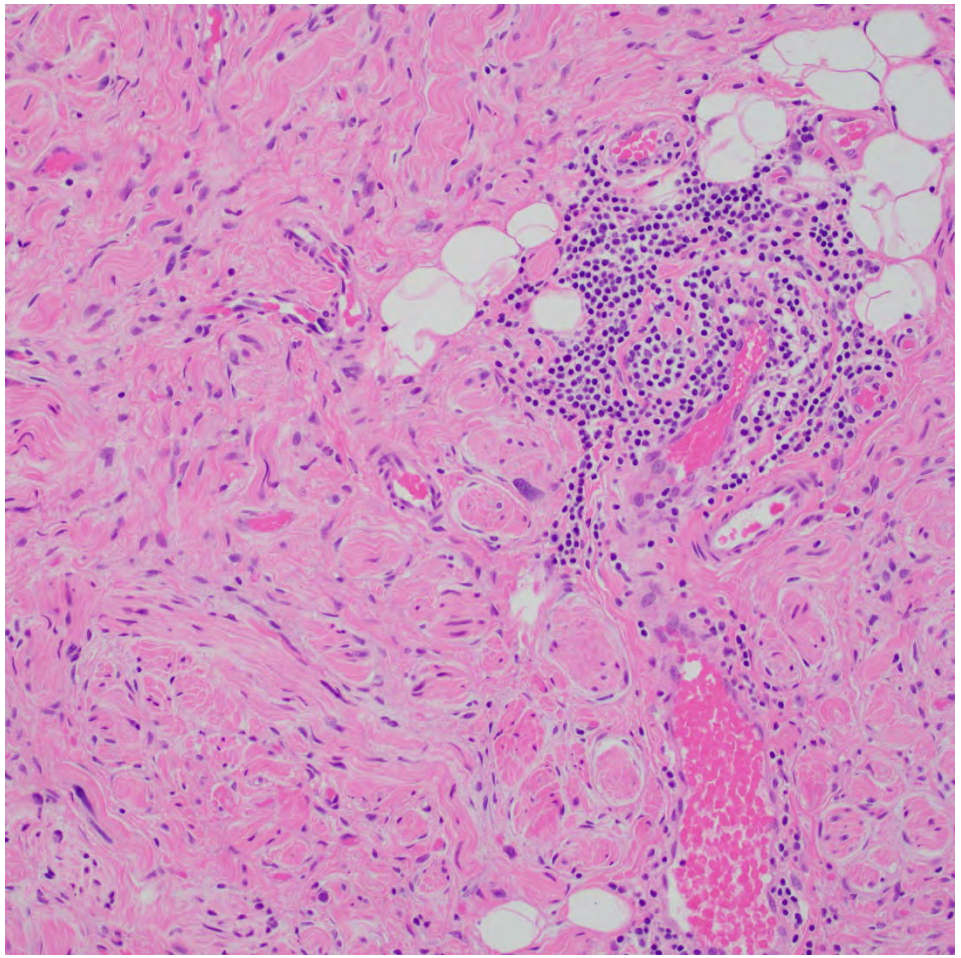




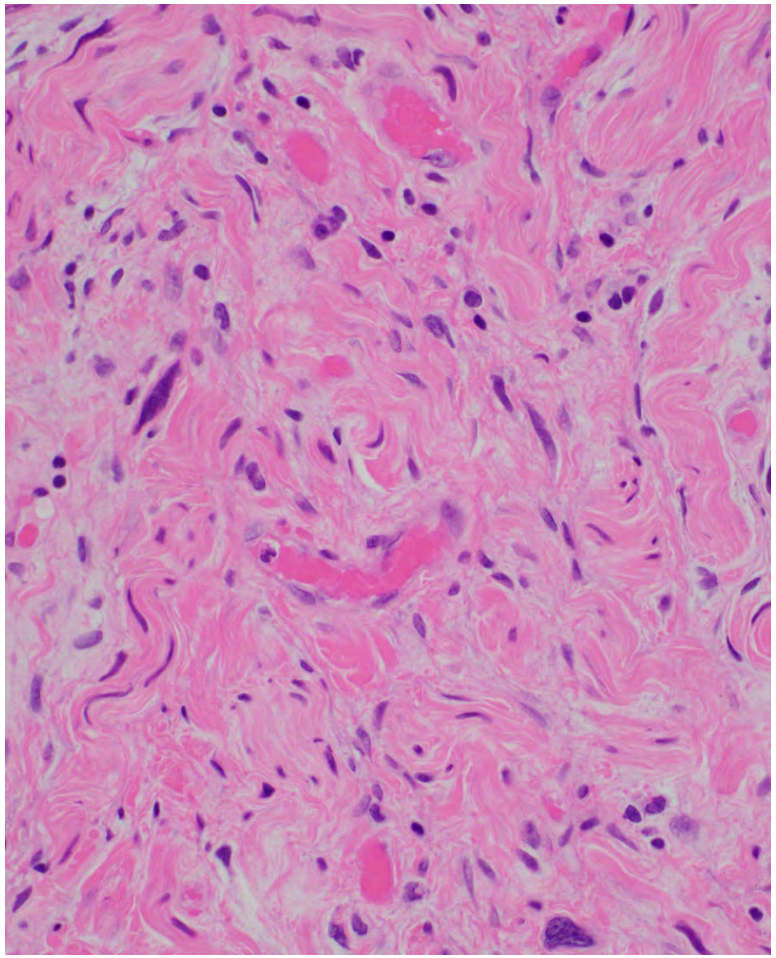
Clue # 1

Lymphoid aggregate

Clue # 2

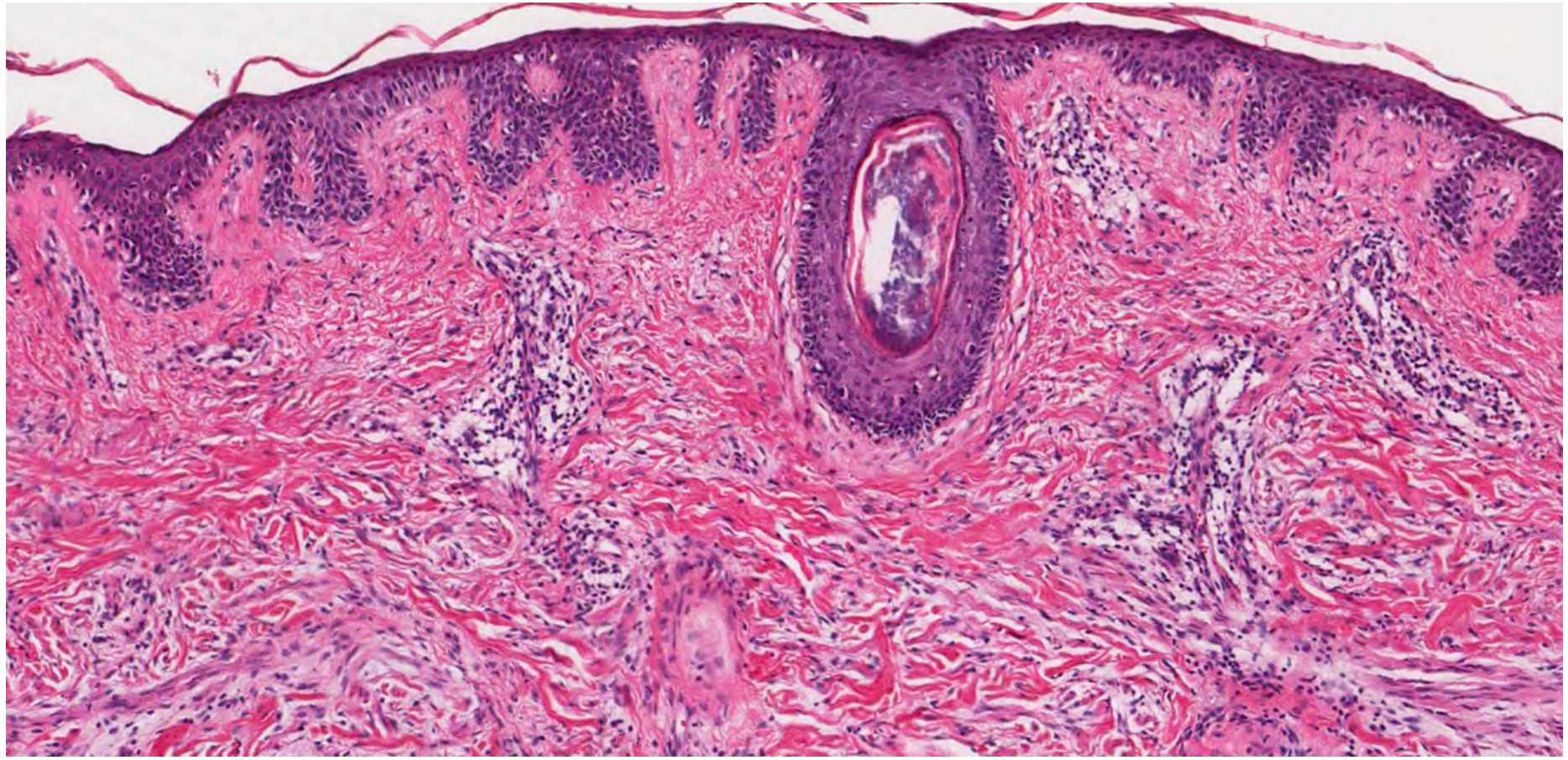


Hyperchromatic spindle cells



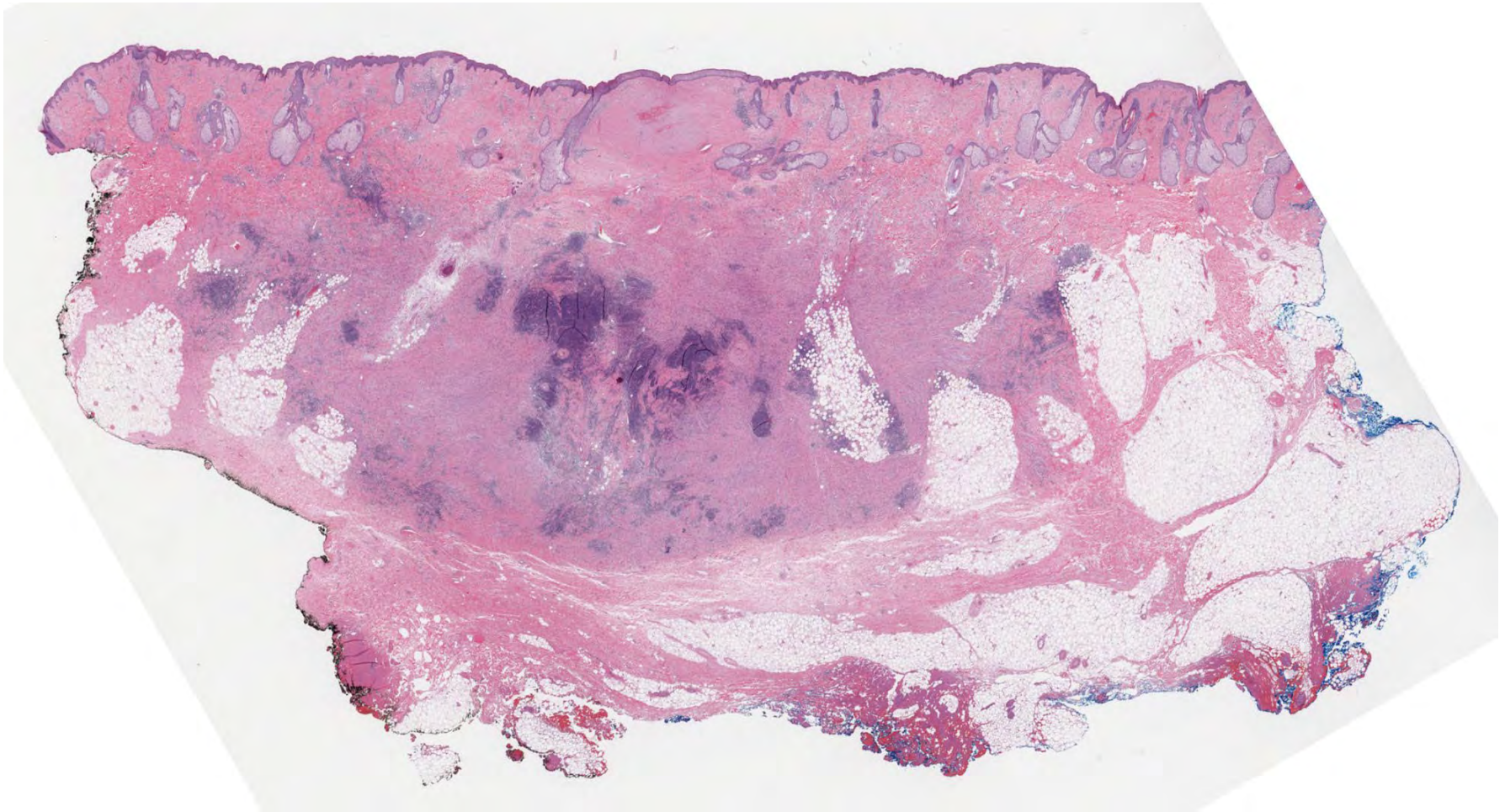
Nuclear Atypia

Clue # 3



Proliferation of solitary units of melanocytes at DE-junction

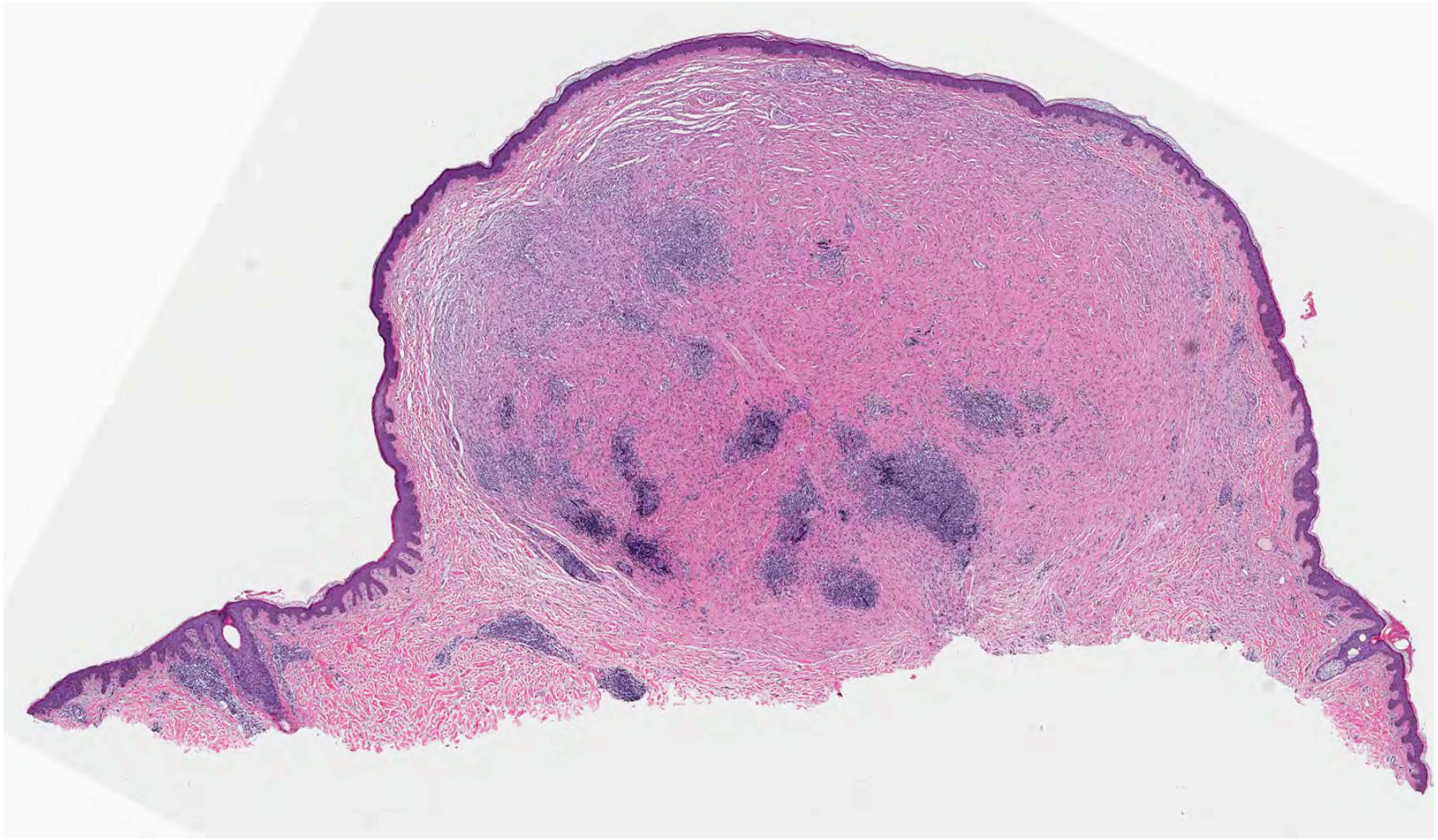
Desmoplastic Melanoma



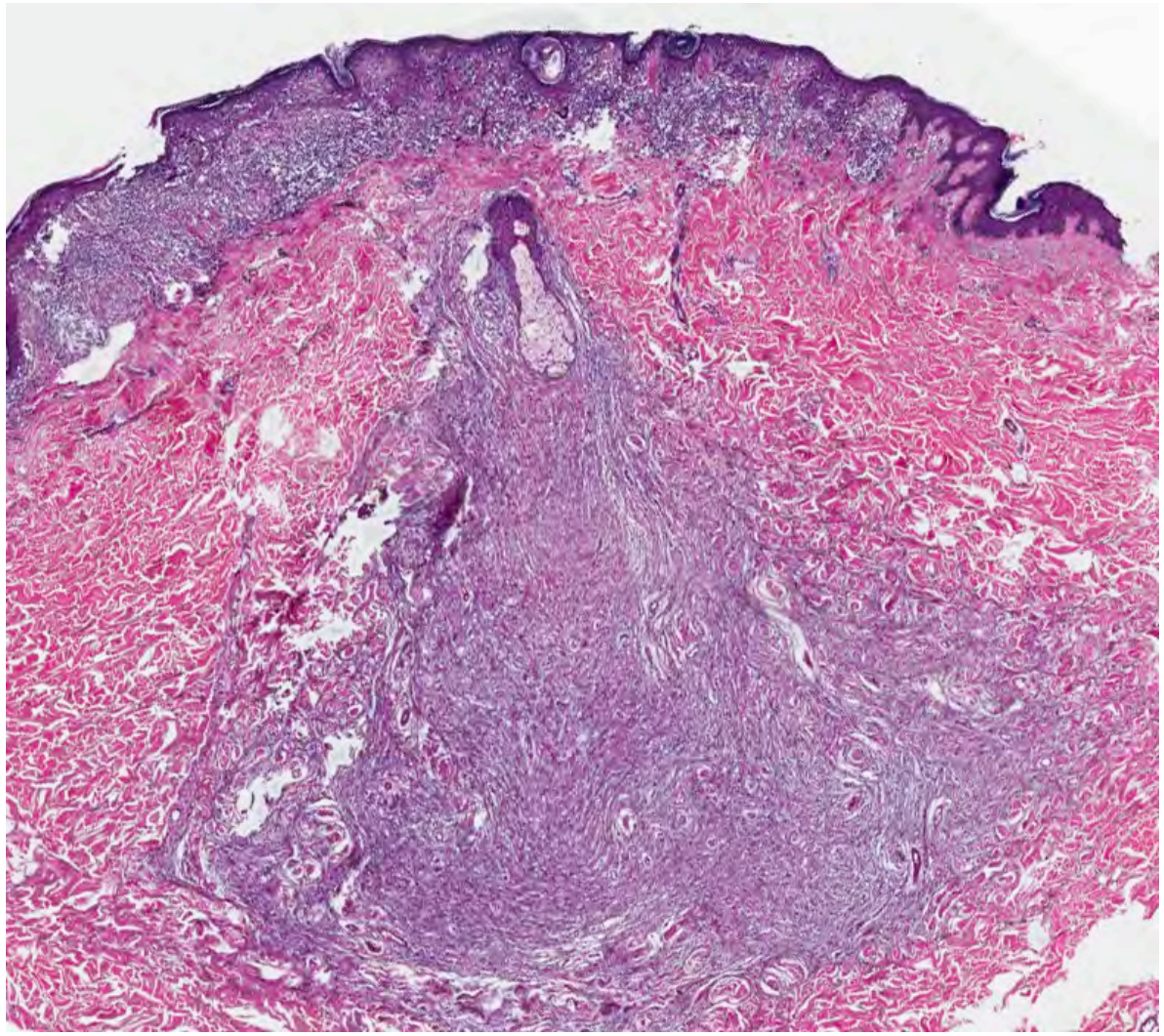
Microscopic clues: DM vs NF

- **Associated melanoma in situ**
- Spindle cells in papillary dermis (no grenz zone)
- Lymphocytic aggregates
- Atypia

Neurofibroma with lymphocytic aggregates



Collision of Melanoma and Neurofibroma

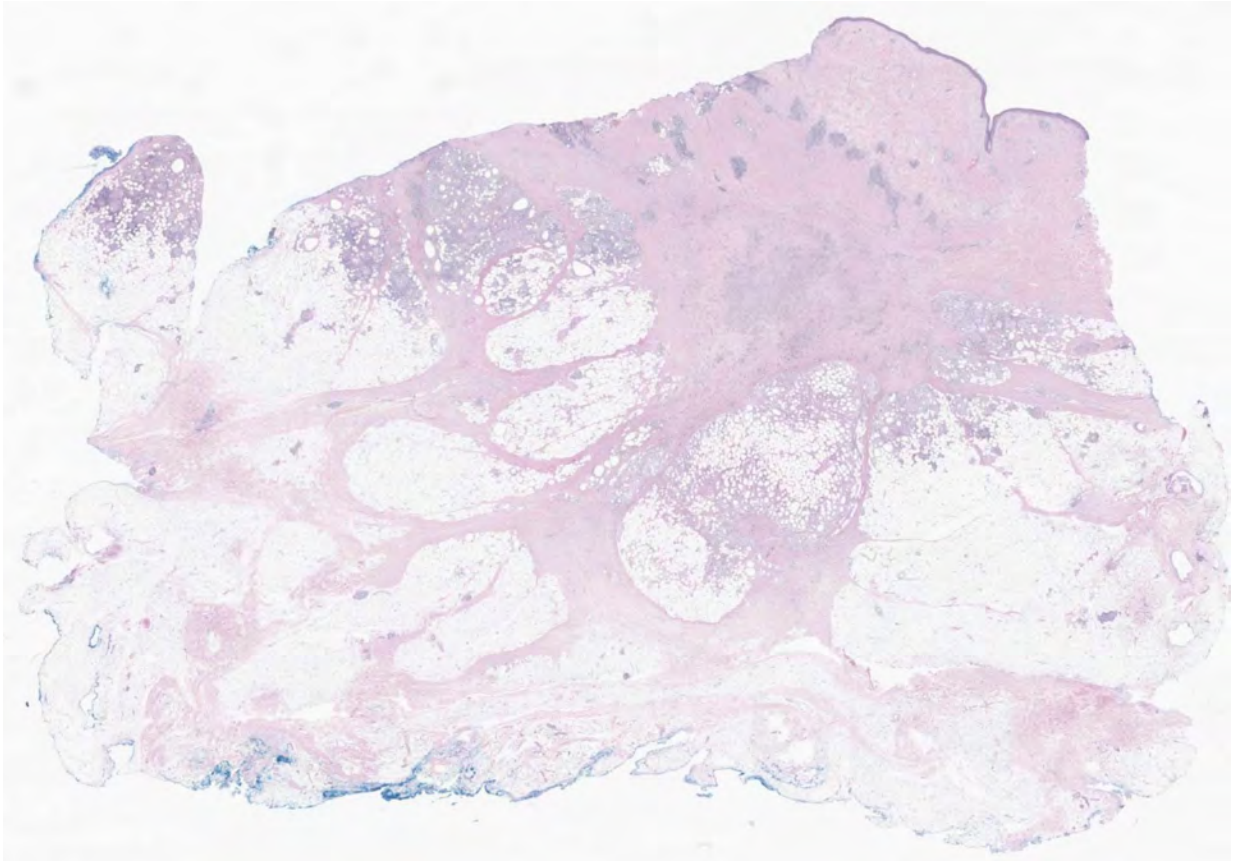


Lessons from Case

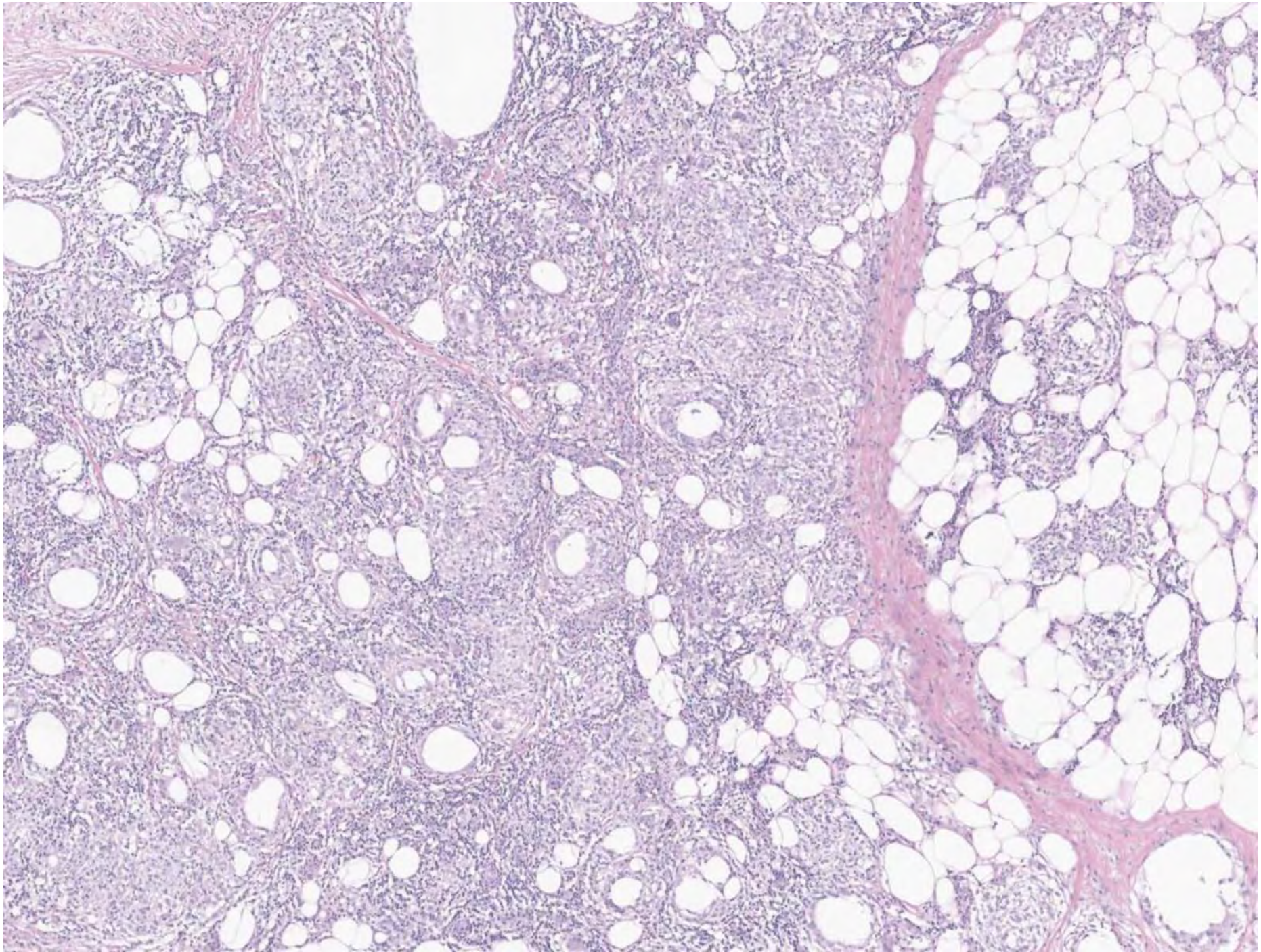
- Desmoplastic melanoma may be misdiagnosed as neurofibroma
  - Clues: MIS, nuclear atypia, lymphoid aggregates, grenz zone
- Neurofibroma may be misdiagnosed as desmoplastic melanoma
  - Clues: clinical setting of neurofibromatosis, collision scenario

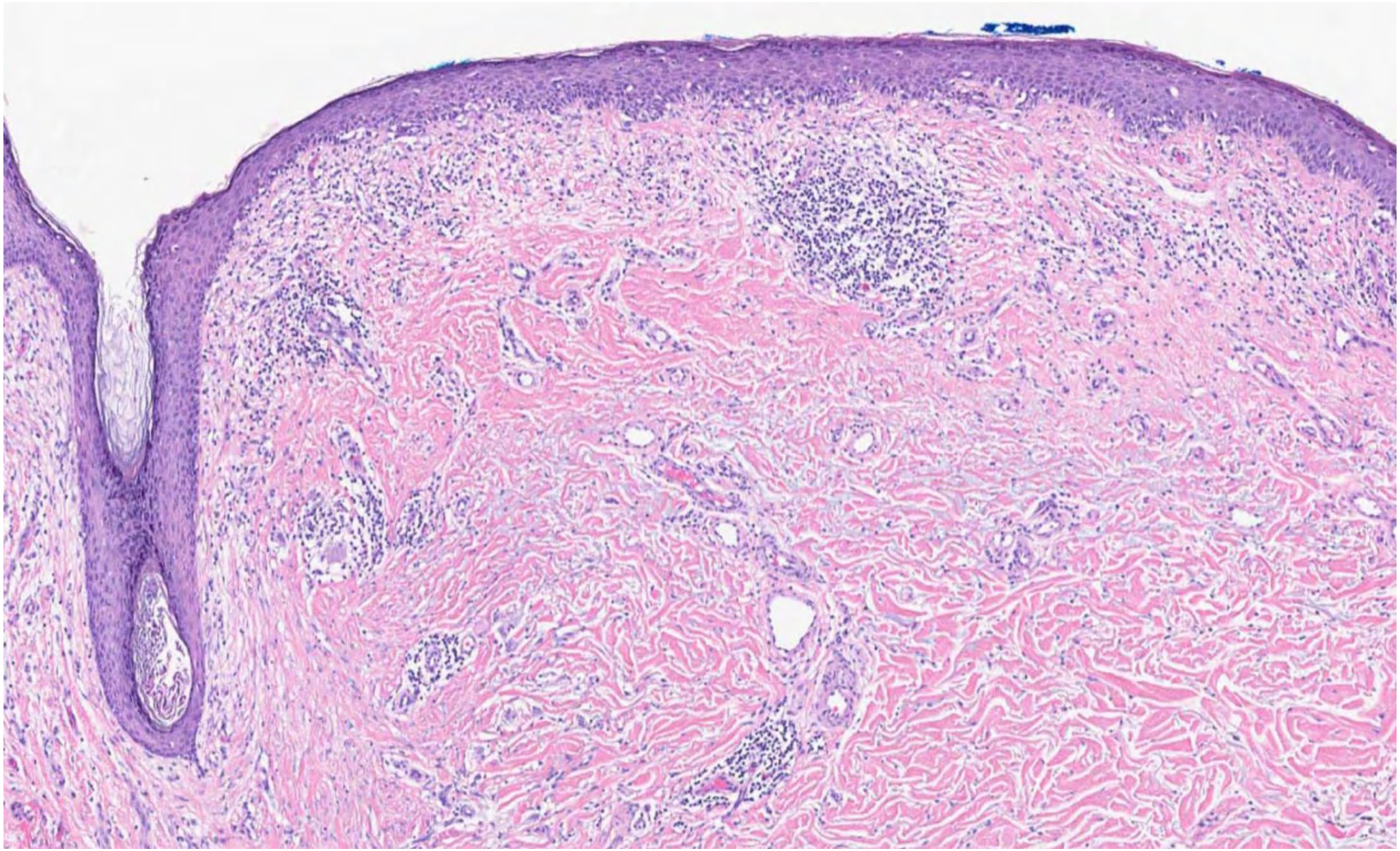
Be ready for the unexpected…

- 79M
- h/o lymphoma

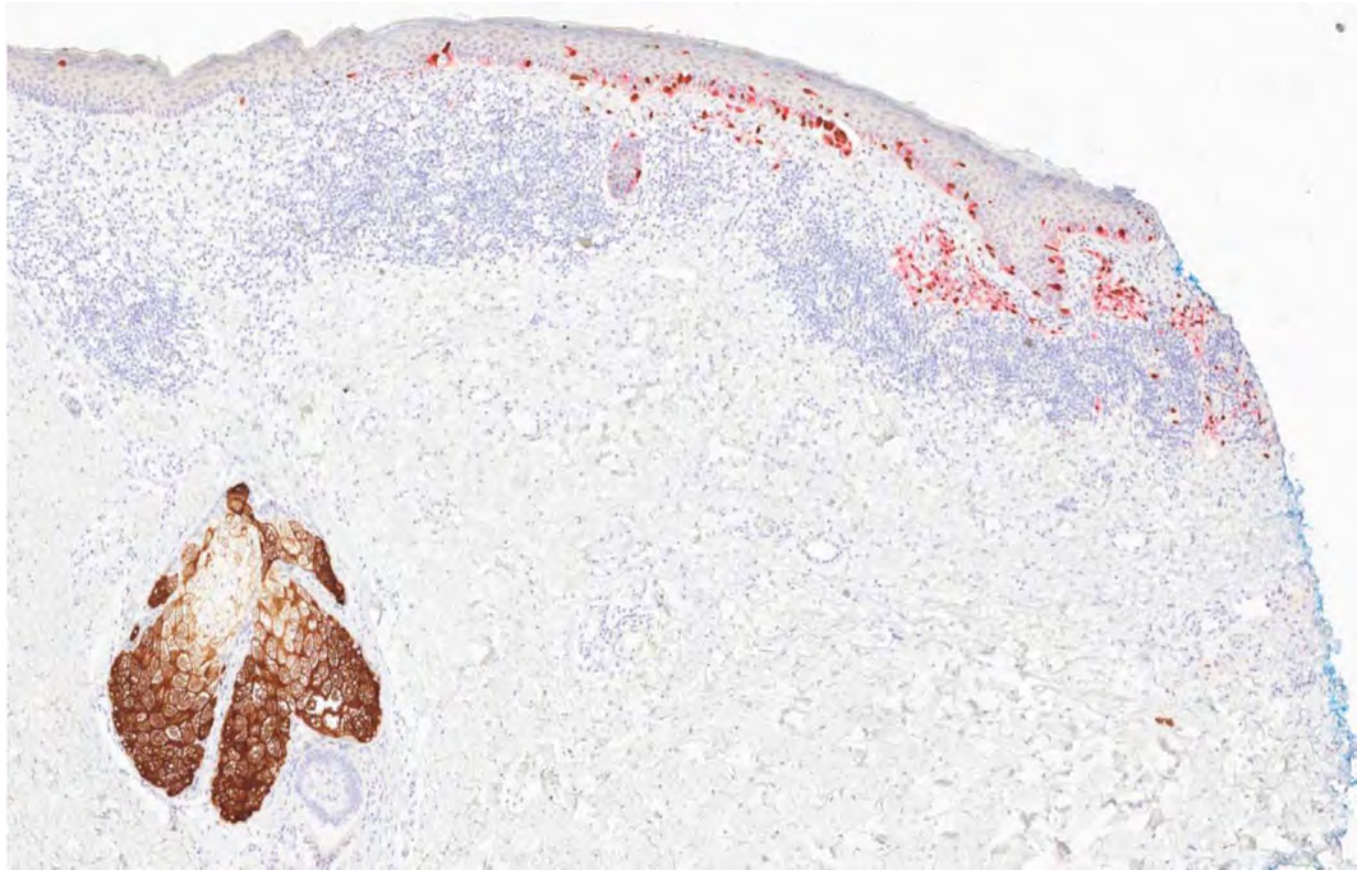


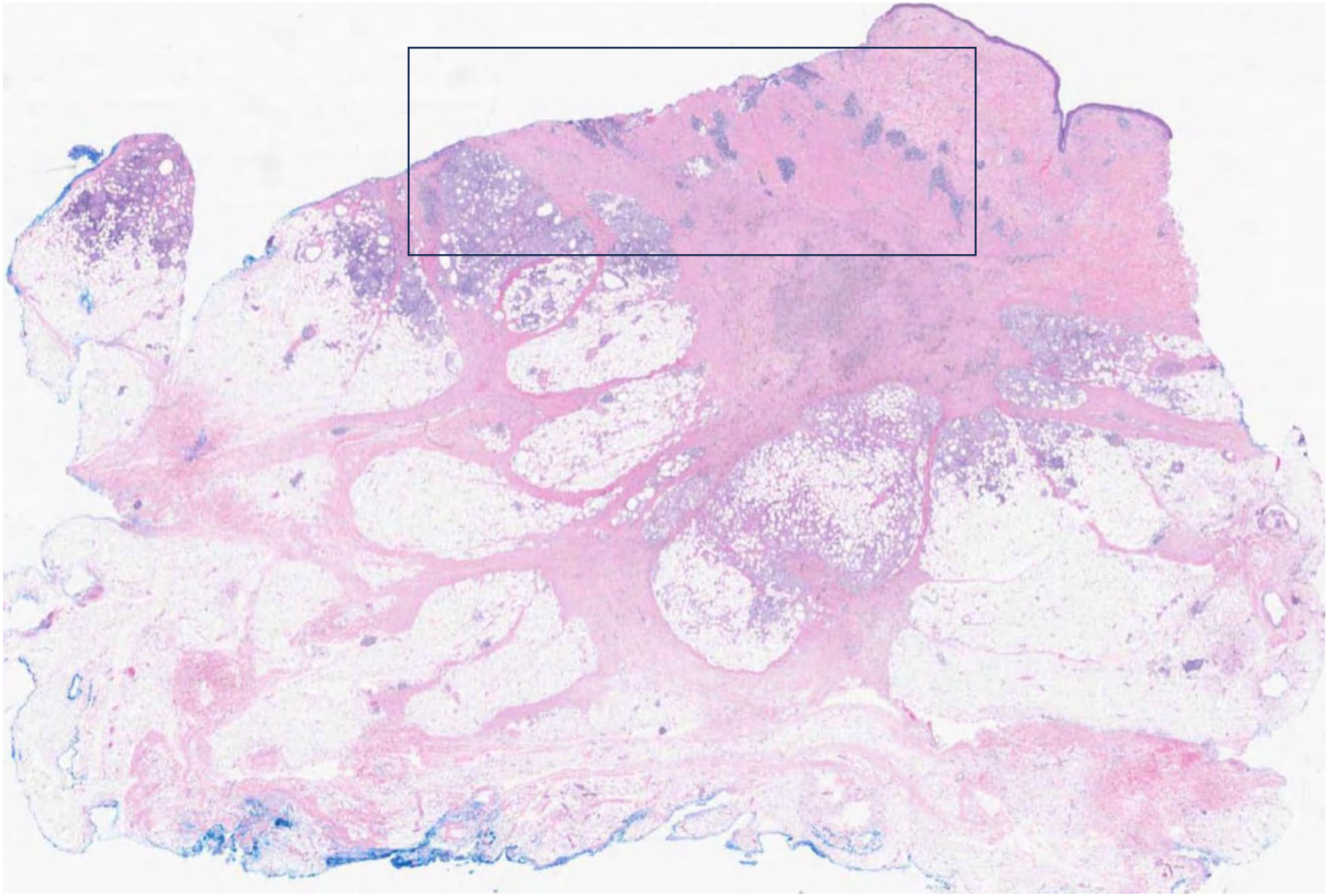
https://mskcc.pathpresenter.net/public/display?token=2afc3f30





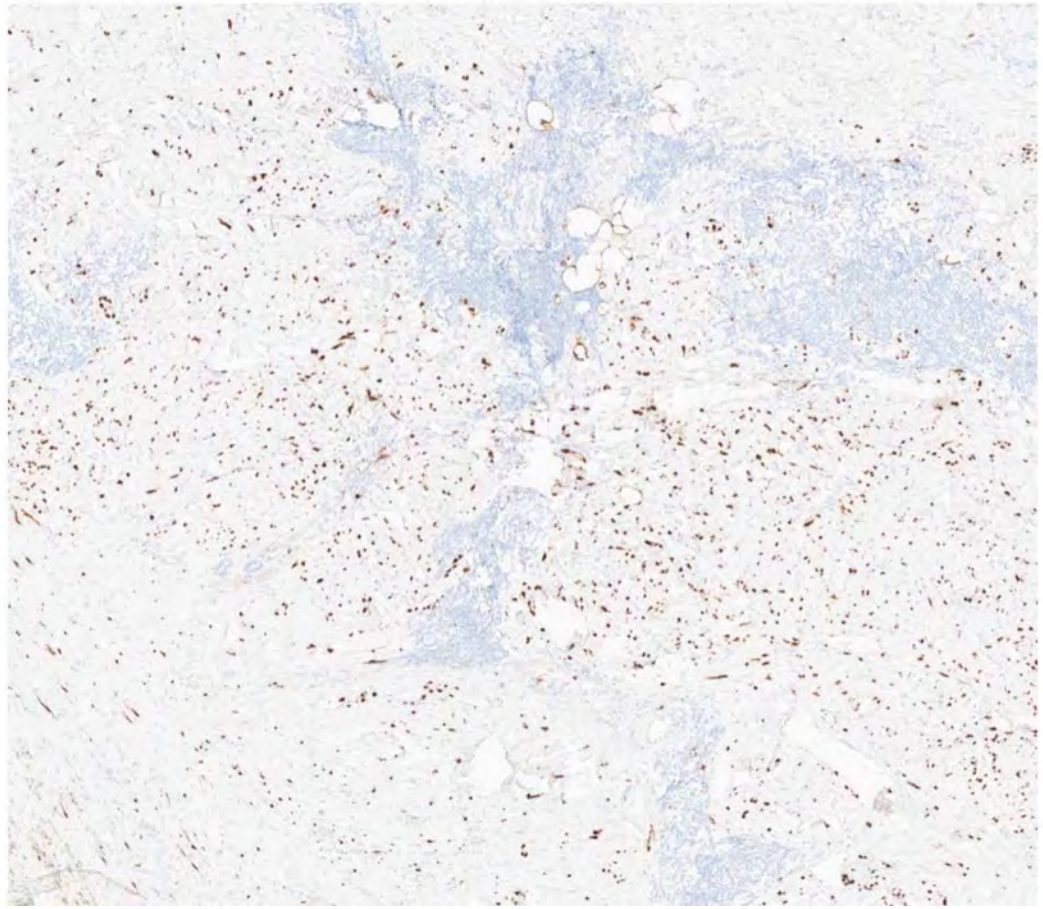
IHC for PRAME





Desmoplastic Melanoma

IHC for Sox 10



Summary – Key Points

- DM is a distinct variant of melanoma

- Beware of diagnostic pitfalls
  - Sampling
  - Mimicry (scar, fibromas, desmoplastic nevi, nerve sheath tumors, other)
  - IHC

Acknowledgements

- Colleagues at MSKCC
- Patients at MSKCC
- Colleagues at other institutions
- My family

busamk@mskcc.org

Thank You!