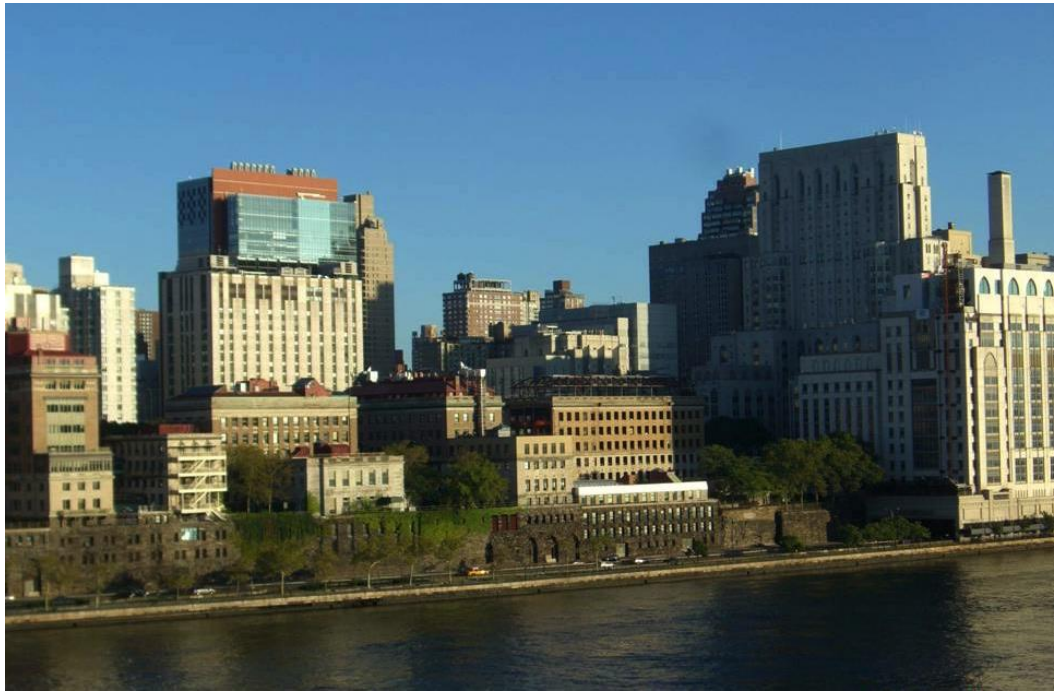
Trento, May 09, 2024

Diagnostically Challenging Melanocytic Tumors



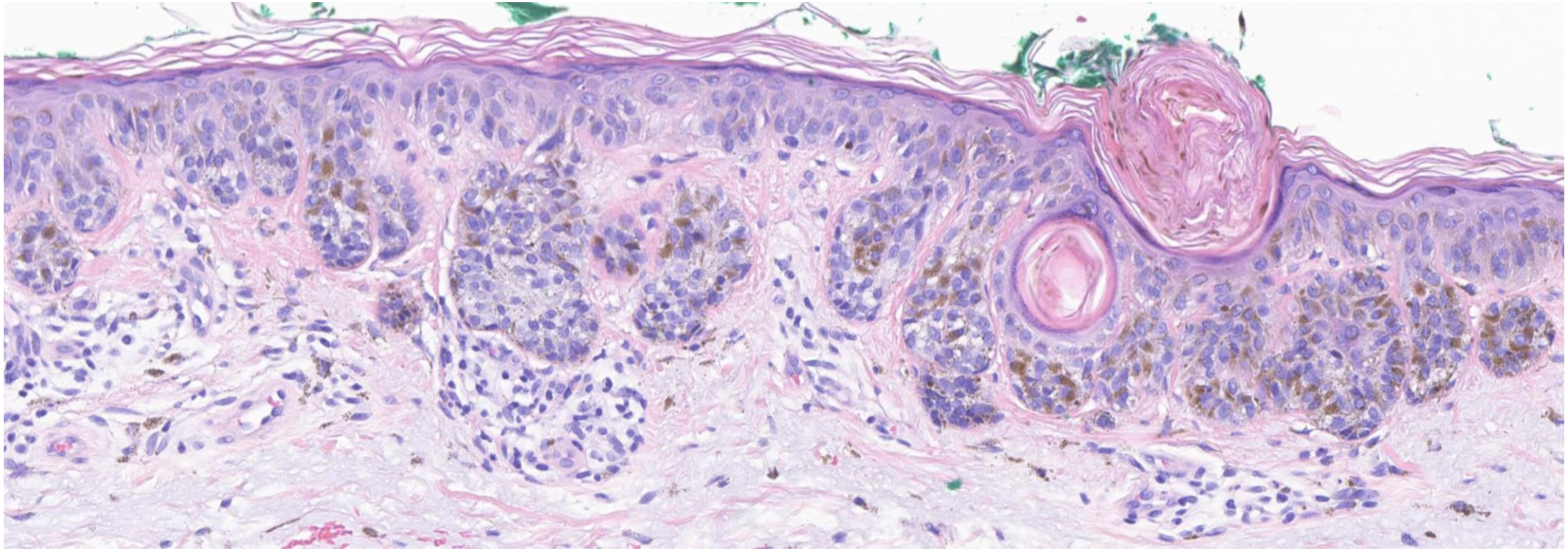
Memorial Sloan Kettering Cancer Center, NYC

New Jersey, USA

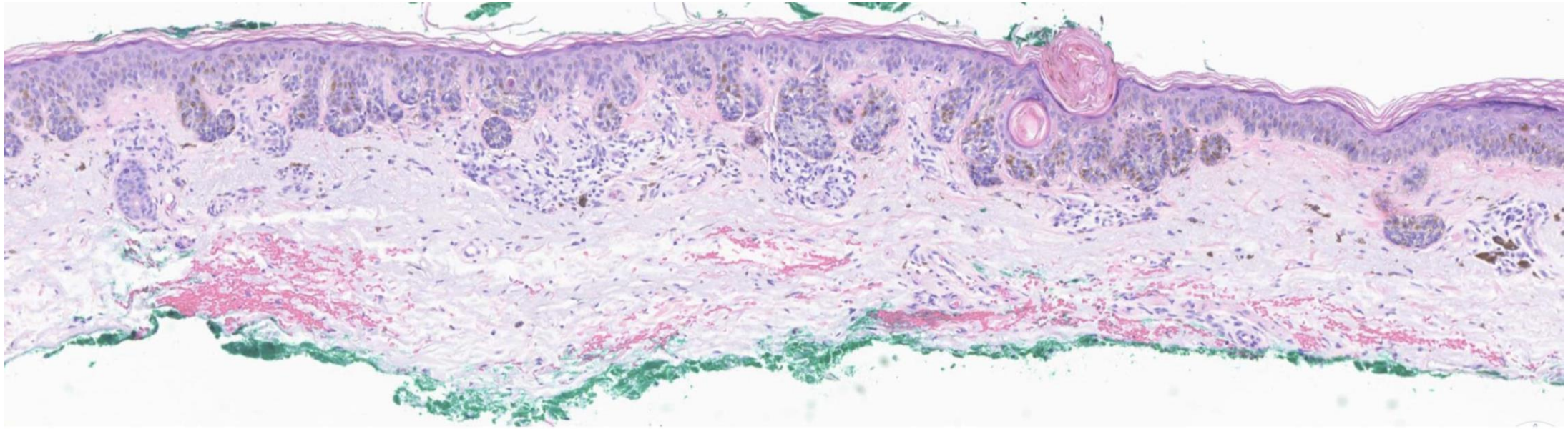
Melanocytic Tumors - Diagnostic Challenges

- Small partial view
- Primary or metastatic melanoma?
- Desmoplastic melanoma or not?
- Benign proliferative nodule or melanoma?

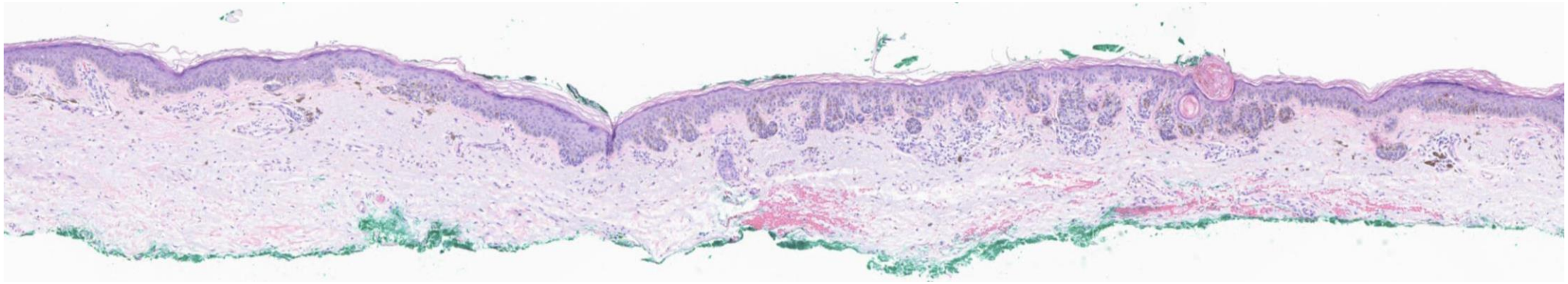
I. Melanoma in situ or junctional nevus?



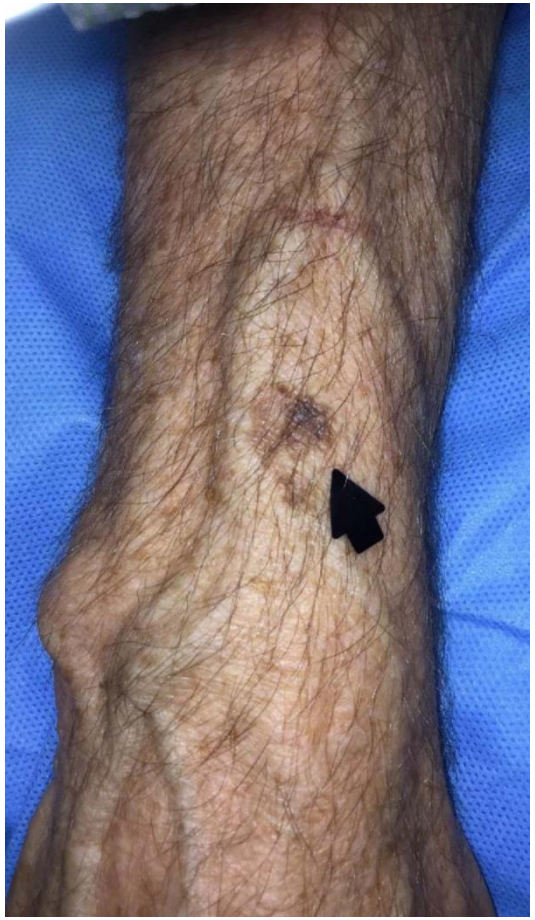
Melanoma in situ

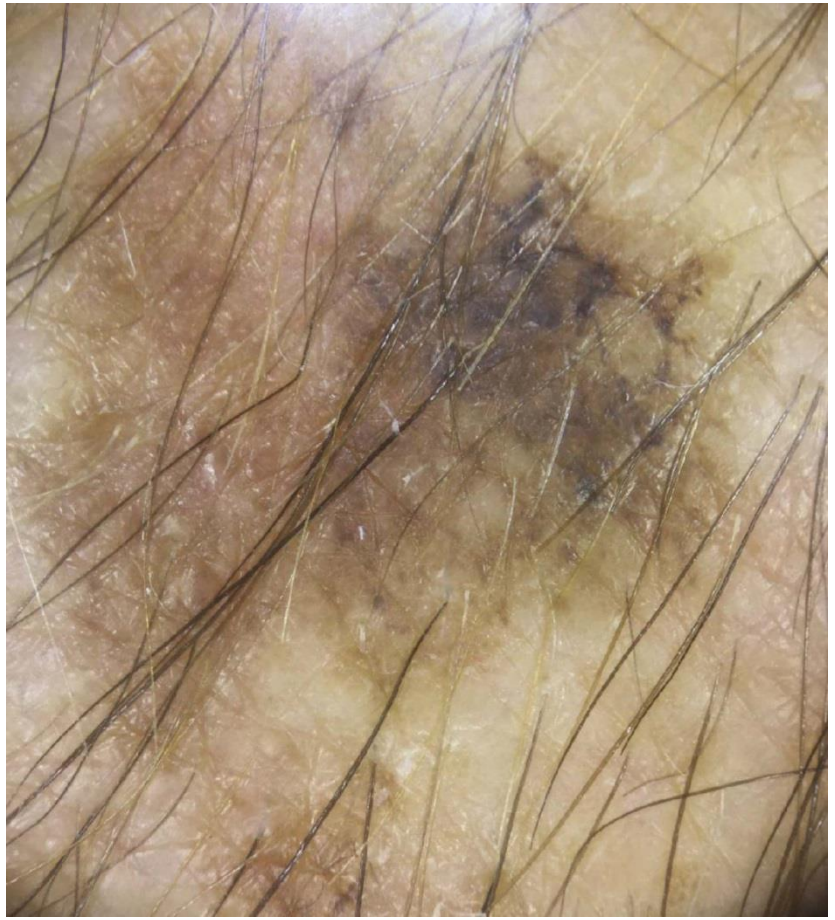


Melanoma in situ



Clinical Correlation: Melanoma in situ

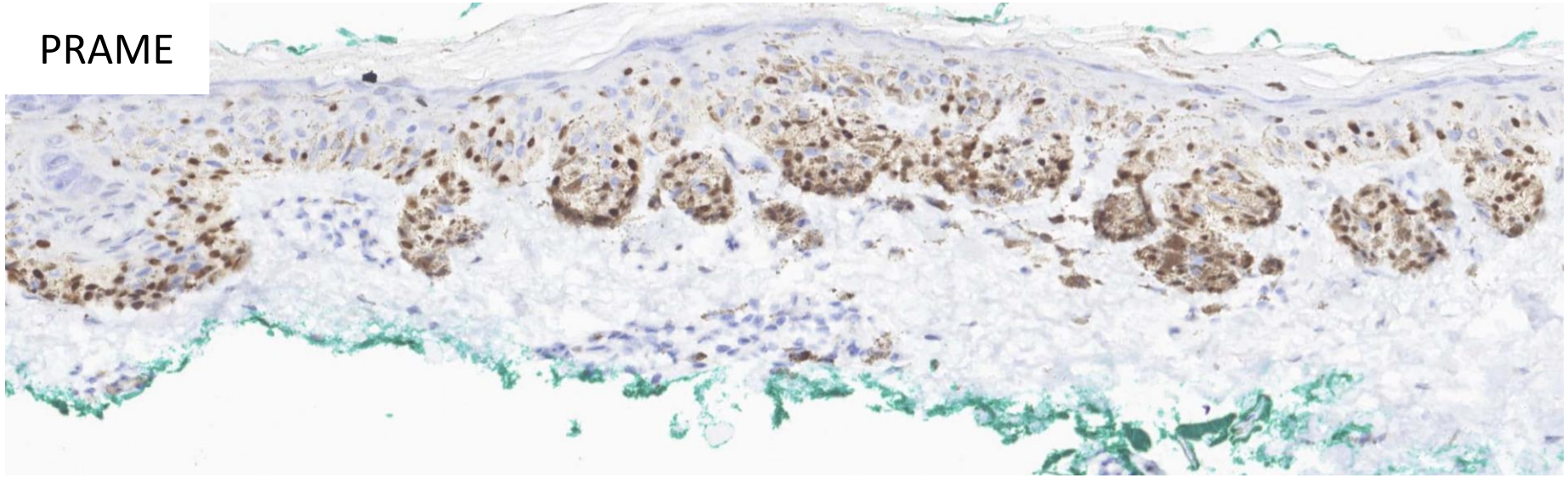




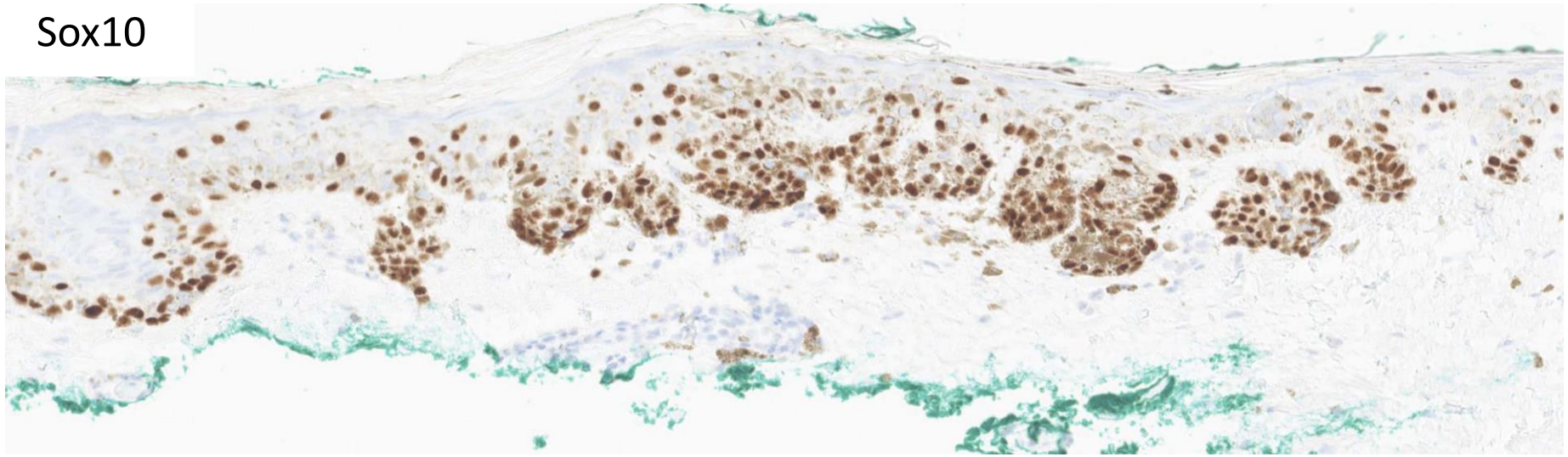
76M – changing lesion

Melanoma in situ

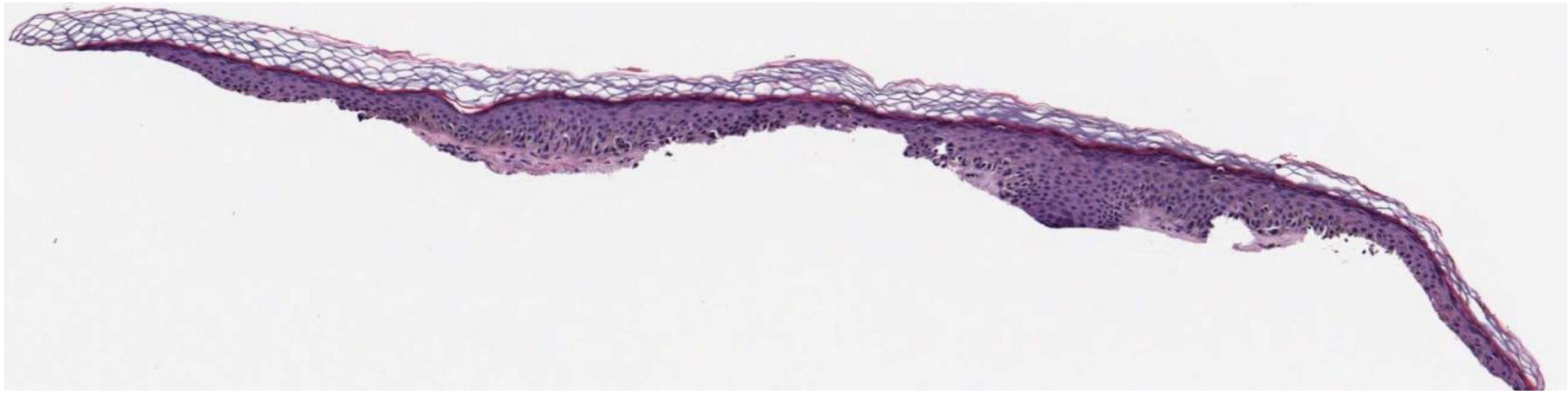
PRAME



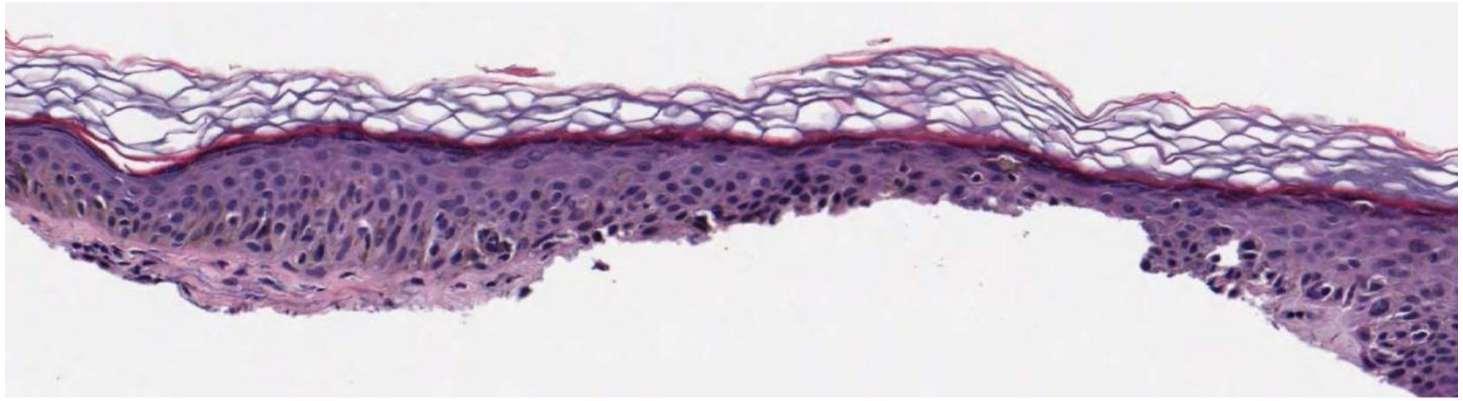
Sox10

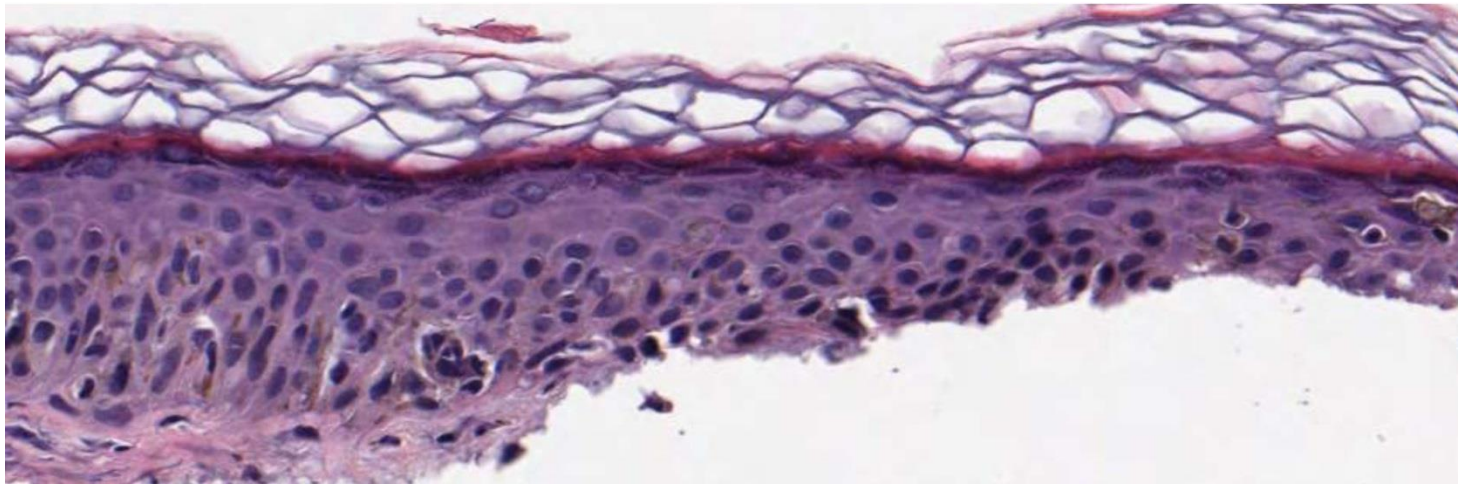


What is Your Diagnosis?

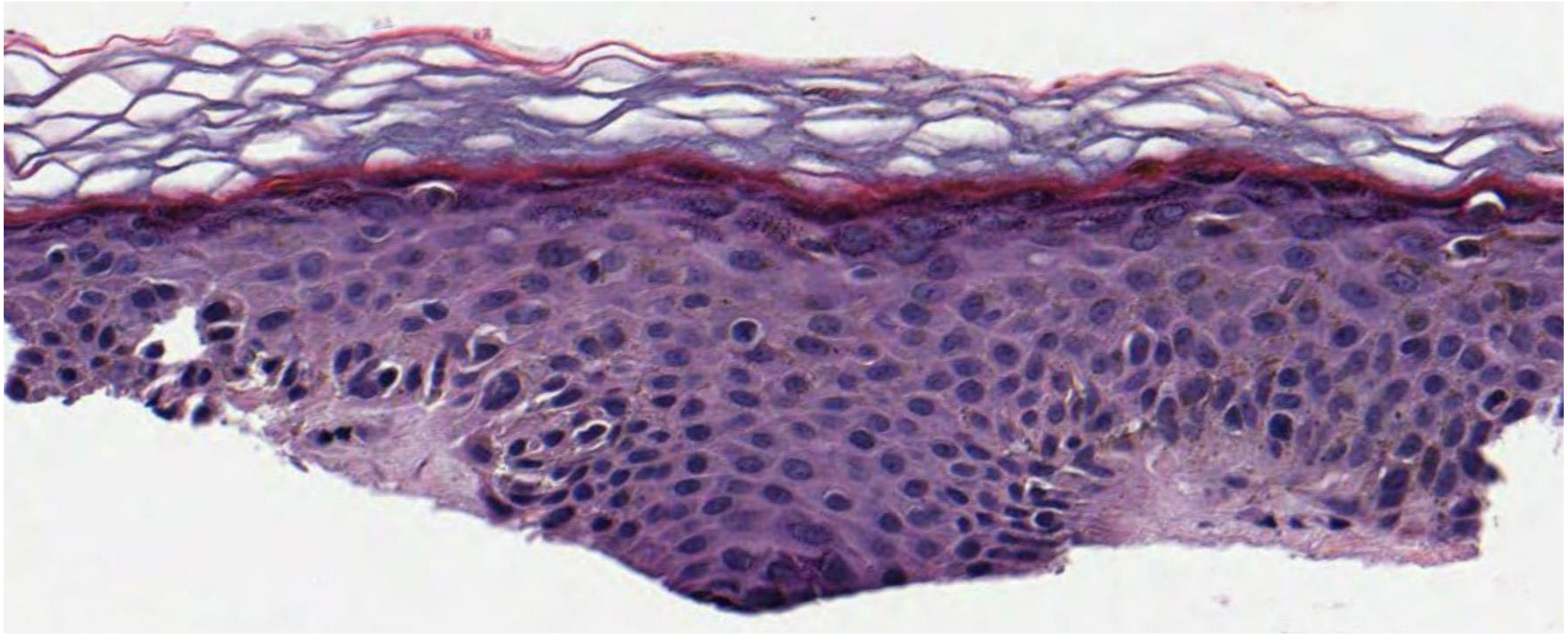


What is Your Diagnosis?





What is Your Diagnosis?



What is Your Diagnosis?

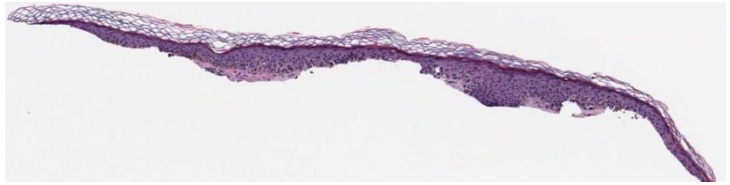
A. Melanoma in situ

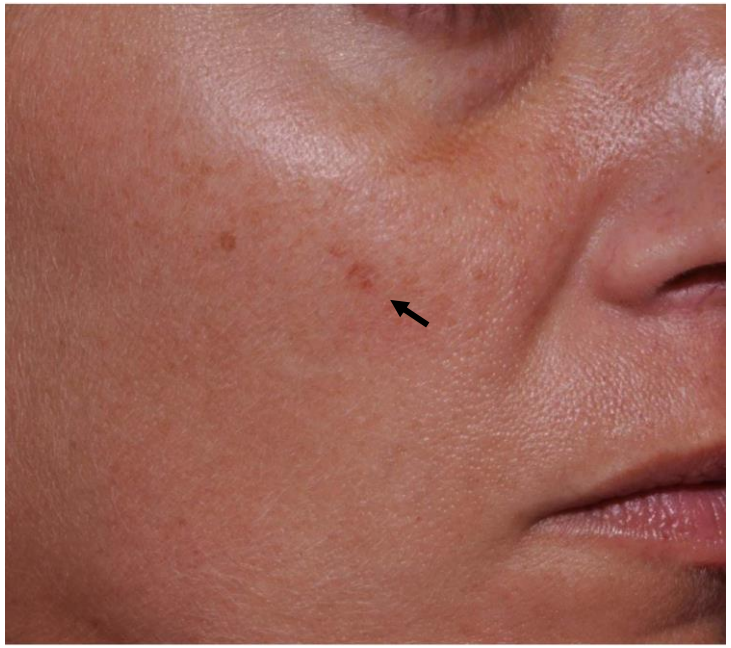
B. Melanoacanthoma

C. Melanocytic nevus

D. Don’t know yet (“intraepidermal melanocytic proliferation”)

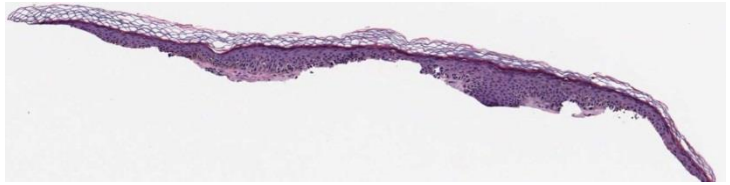
Diagnosis: Traumatized Melanocytic Nevus

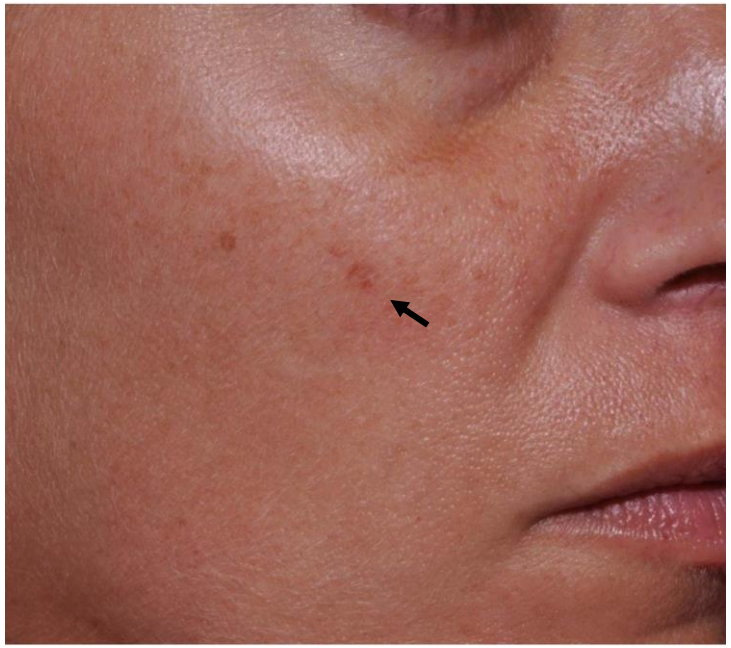


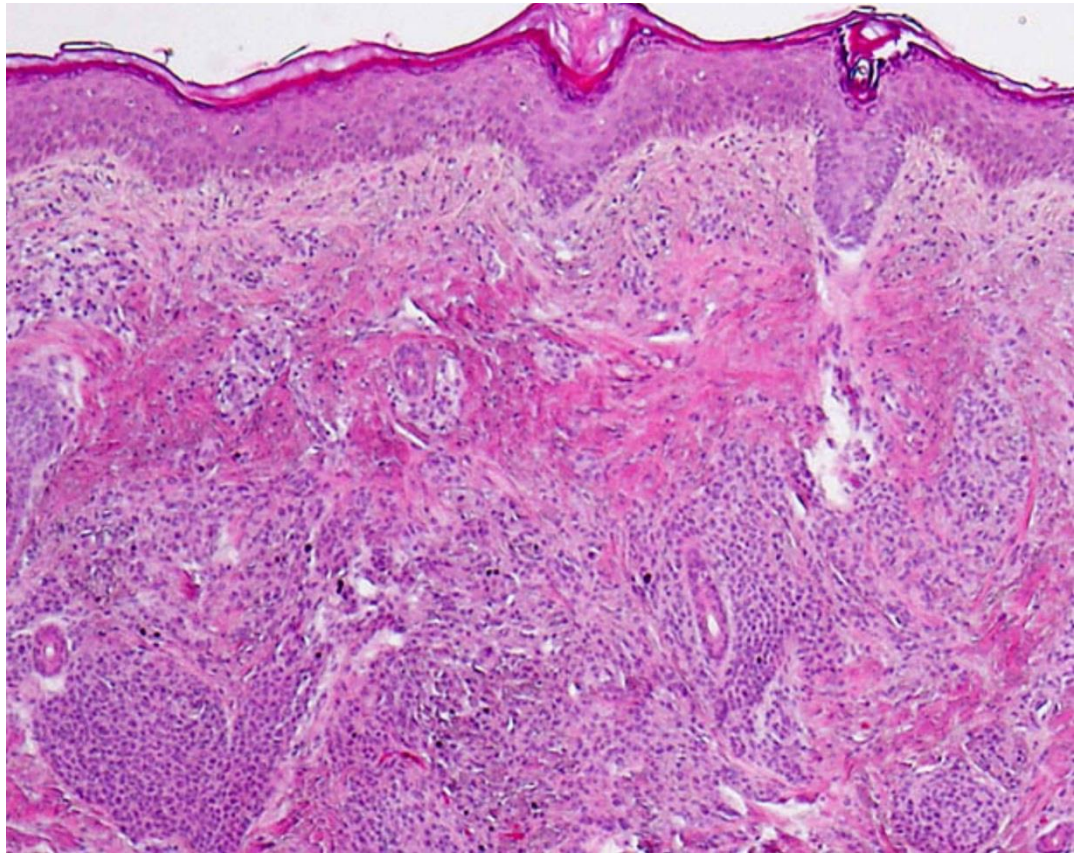


- Patient referred with a diagnosis “probable melanoma in situ”
- Clinical findings not typical for MIS
- Repeat biopsy for final diagnosis

Diagnosis: Traumatized Melanocytic Nevus







Ashbury Park, NJ

Stone Pony, Ashbury Park, NJ

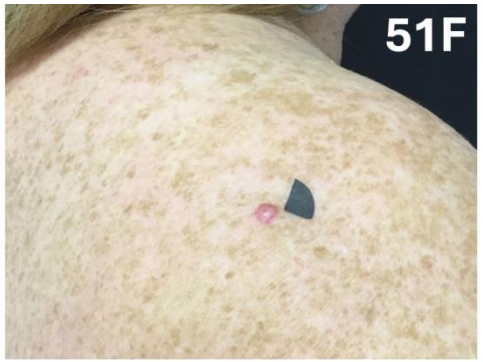
Ashbury Park, NJ

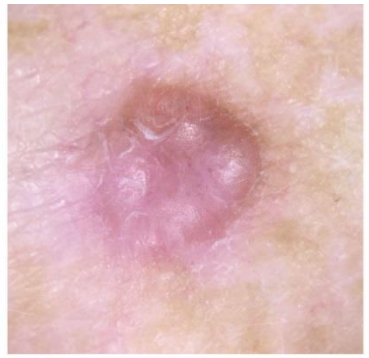
The Boss

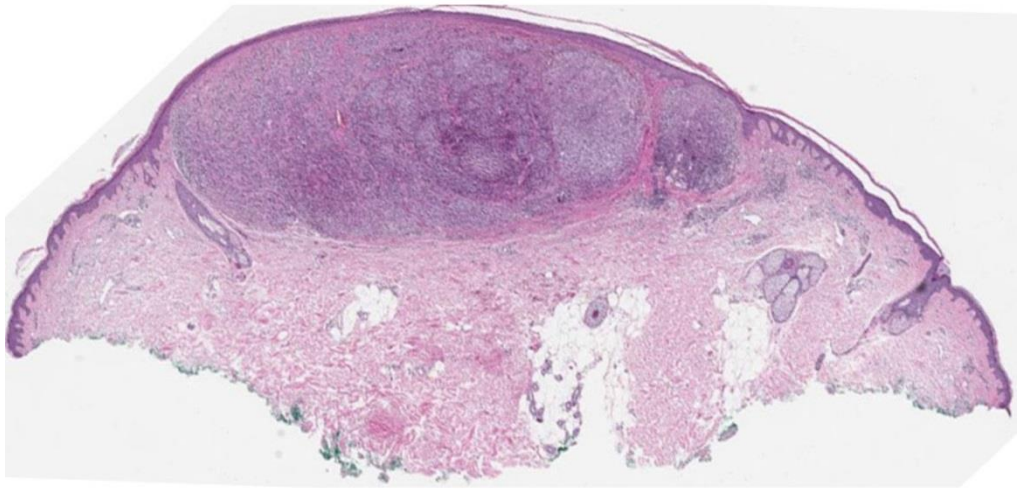
Watch Bruce Springsteen Join Southside Johnny Onstage in Asbury Park

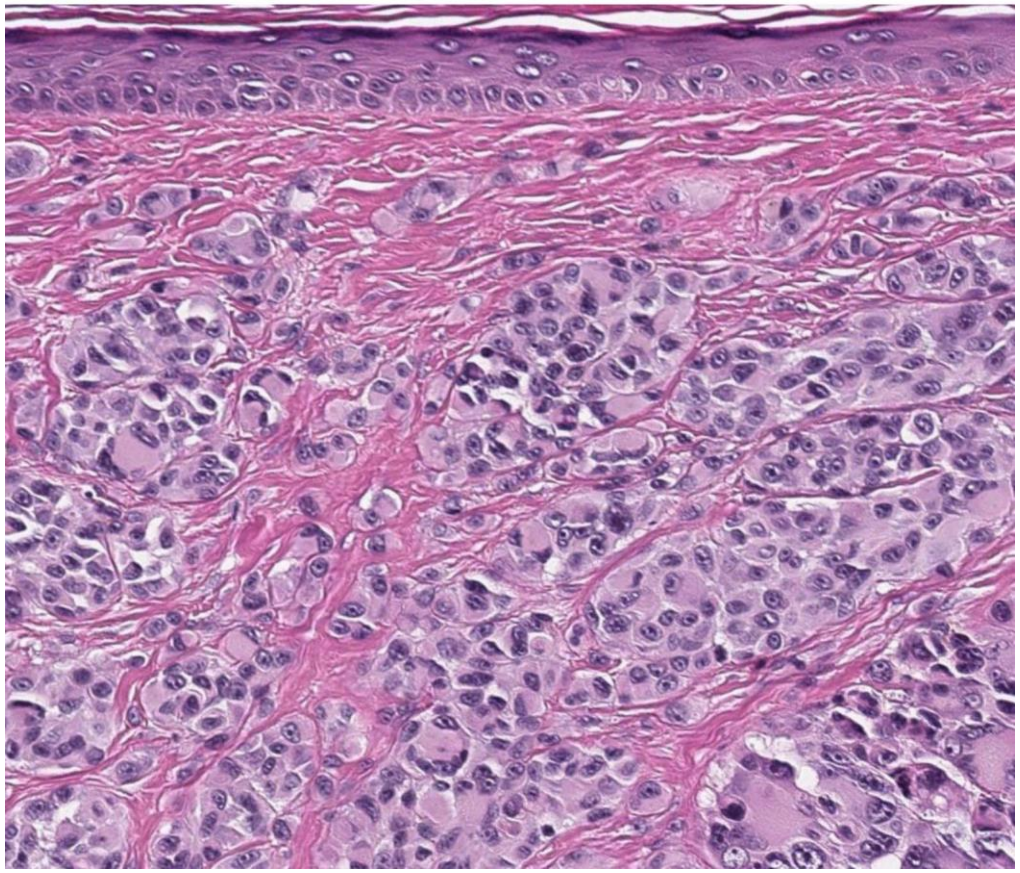
By MICHELE AMABILE ANGERMILLER

II. Primary or Metastatic?



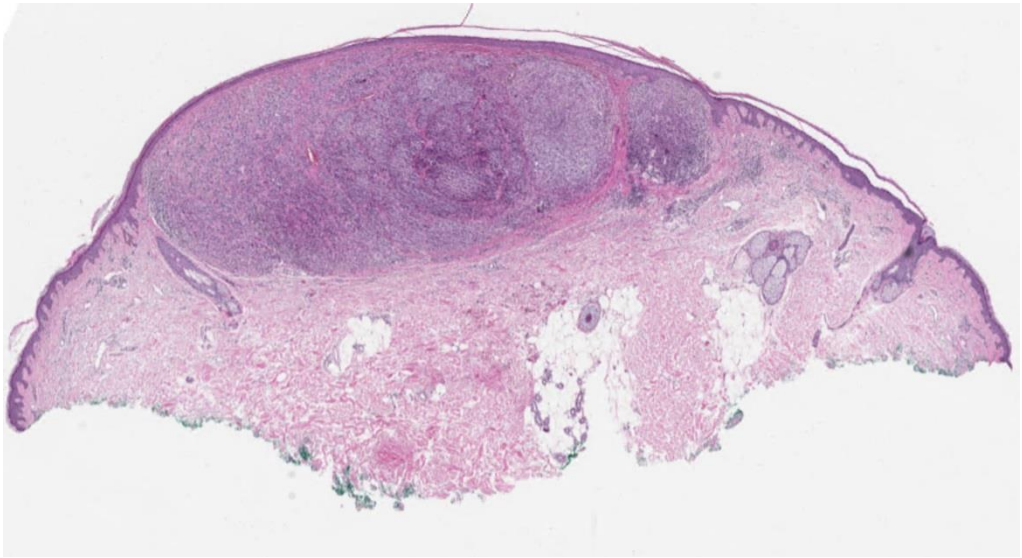


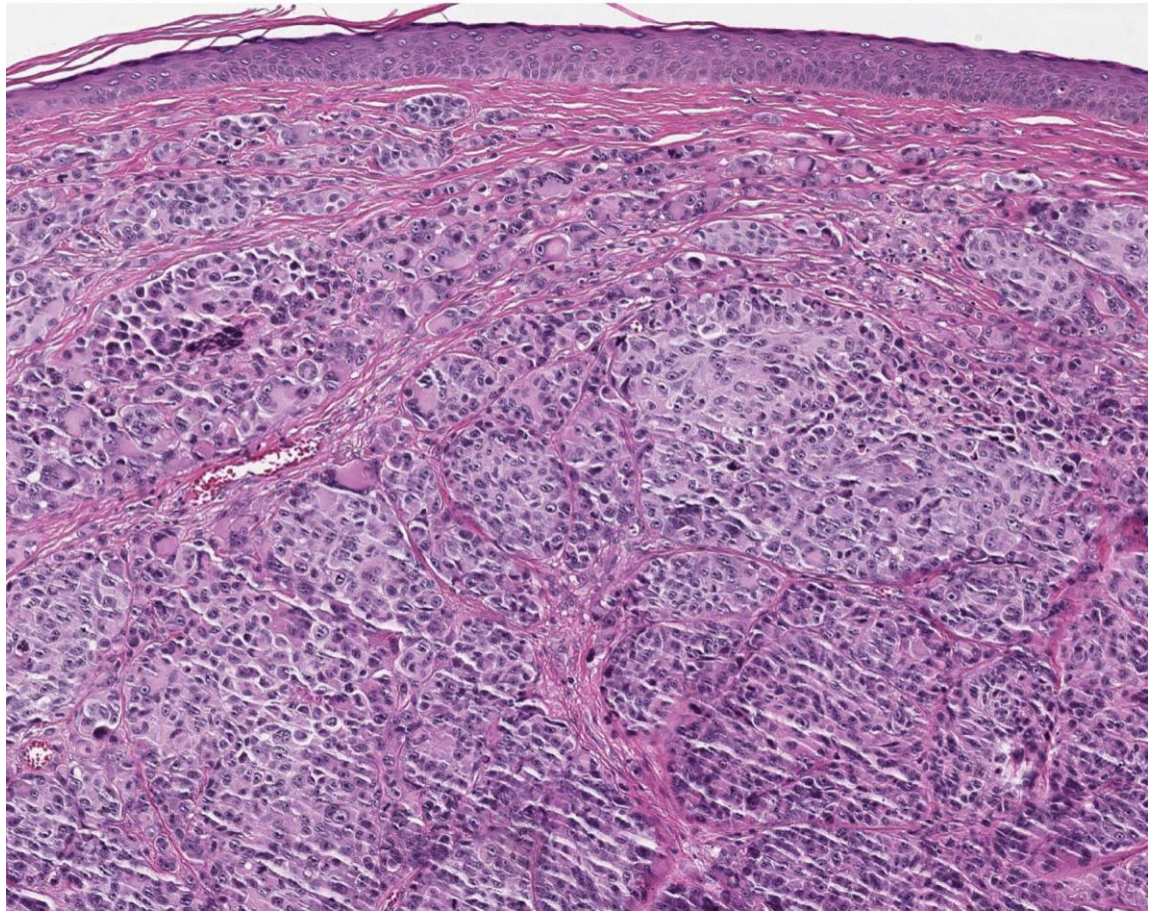




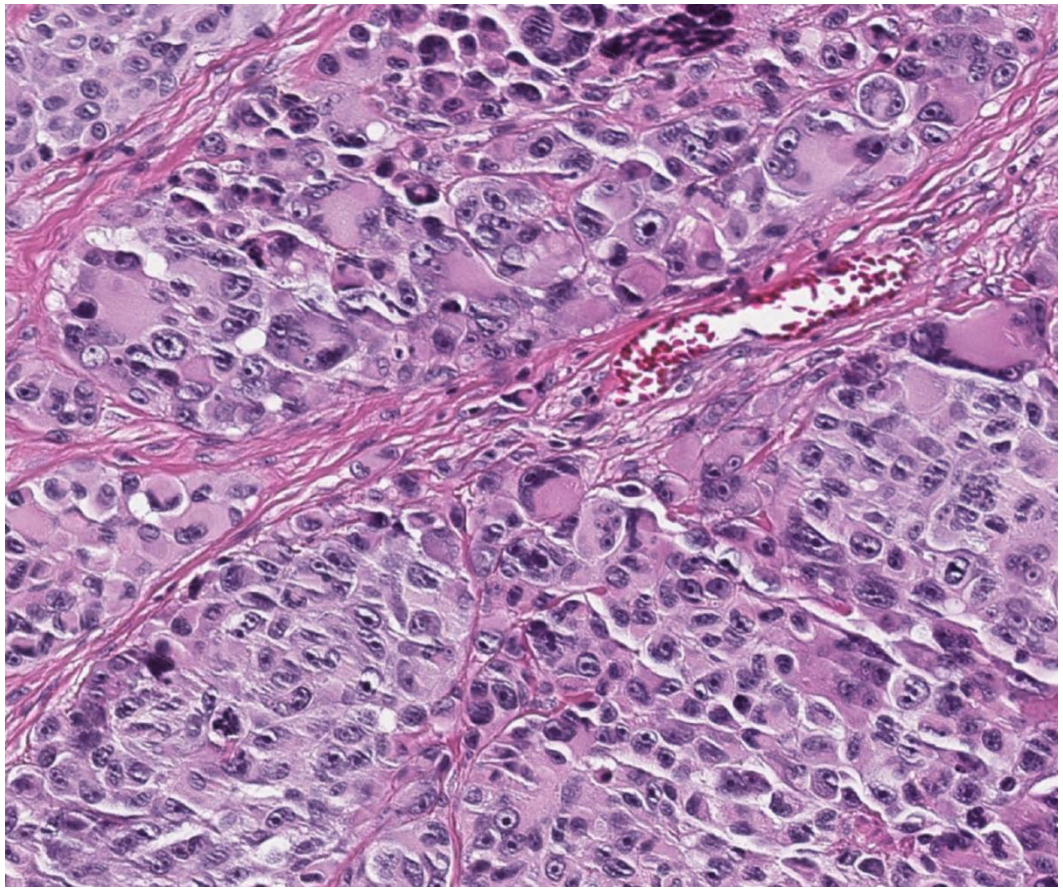
What is Your Diagnosis?

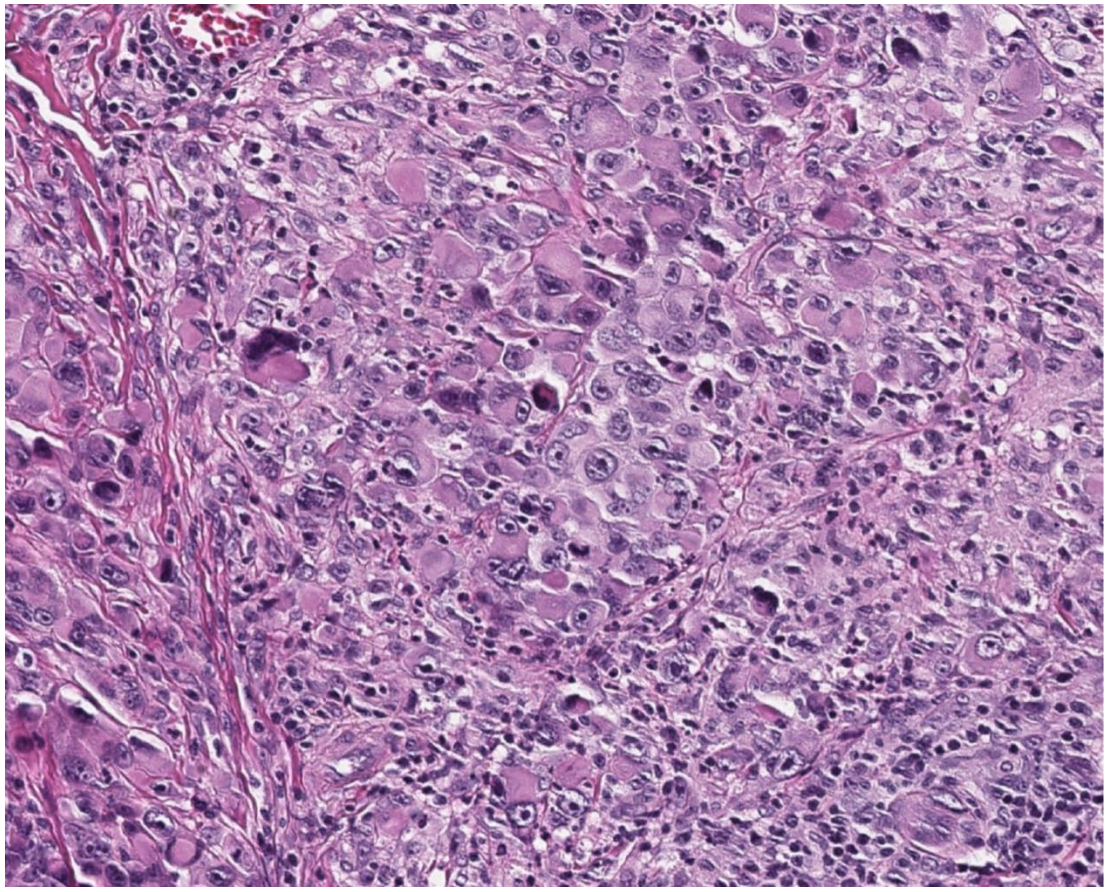
- 51 F with h/o metastatic melanoma





Cytology of tumor cells





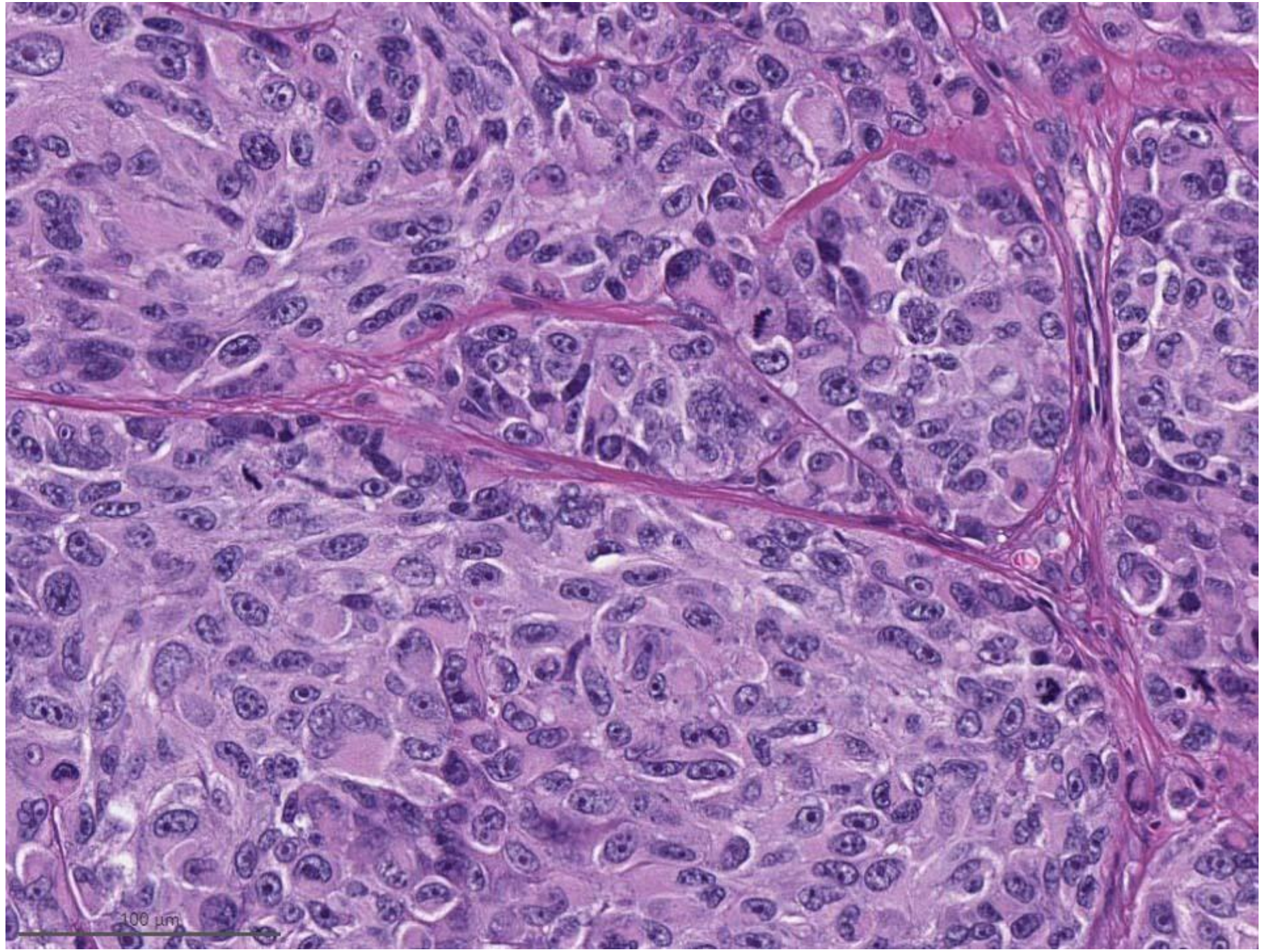
What is Your Diagnosis?

A. Bap1-inactivated melanocytoma

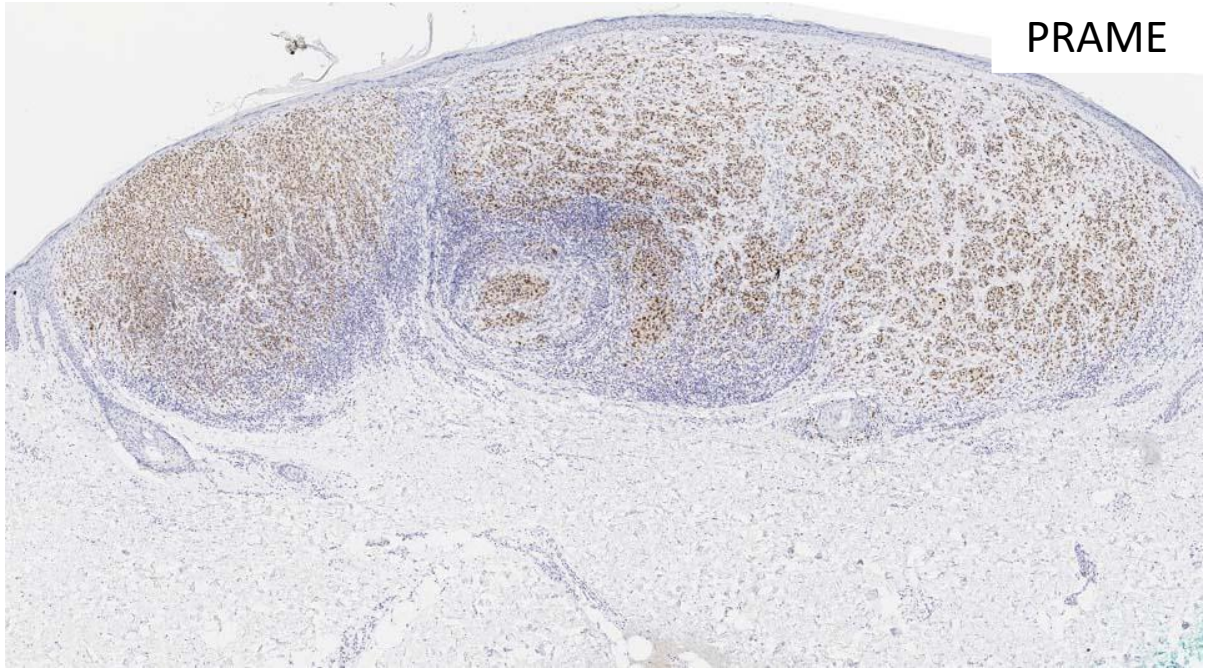
B. Primary nodular/dermal melanoma

C. Metastatic melanoma

D. Other

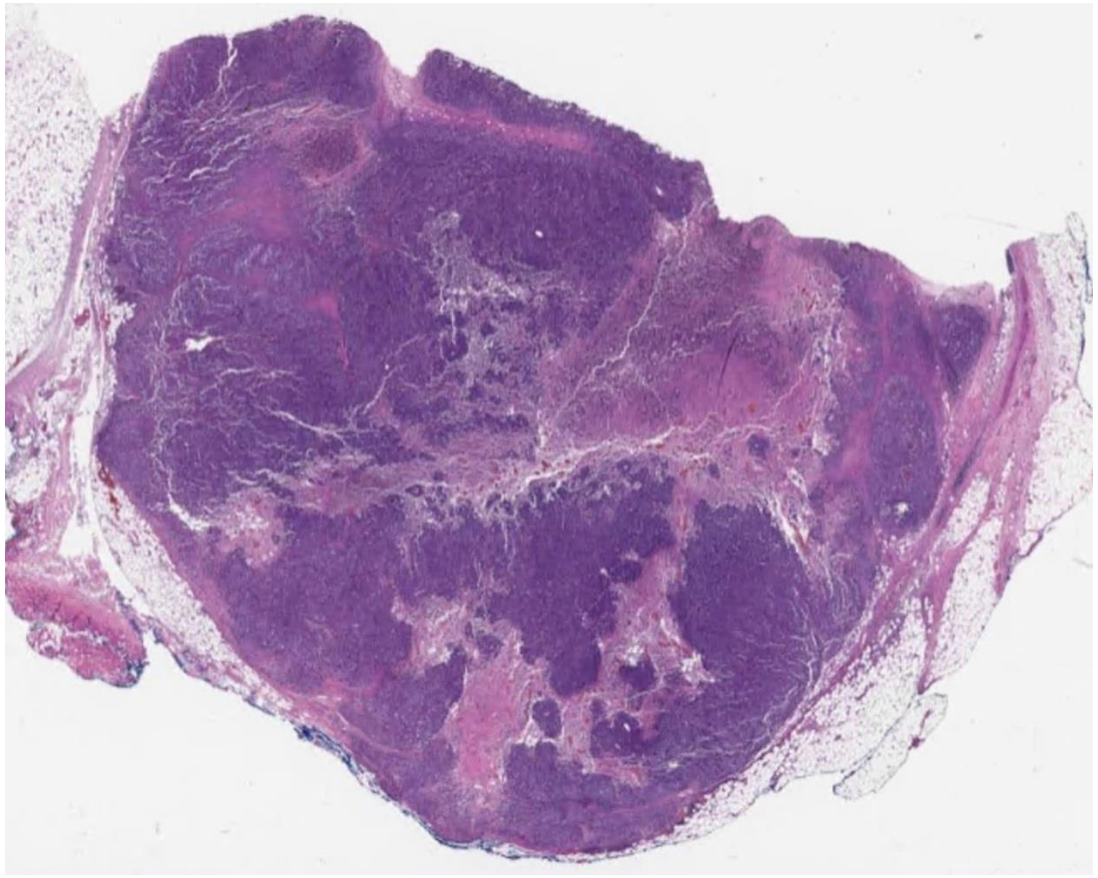

100 µm

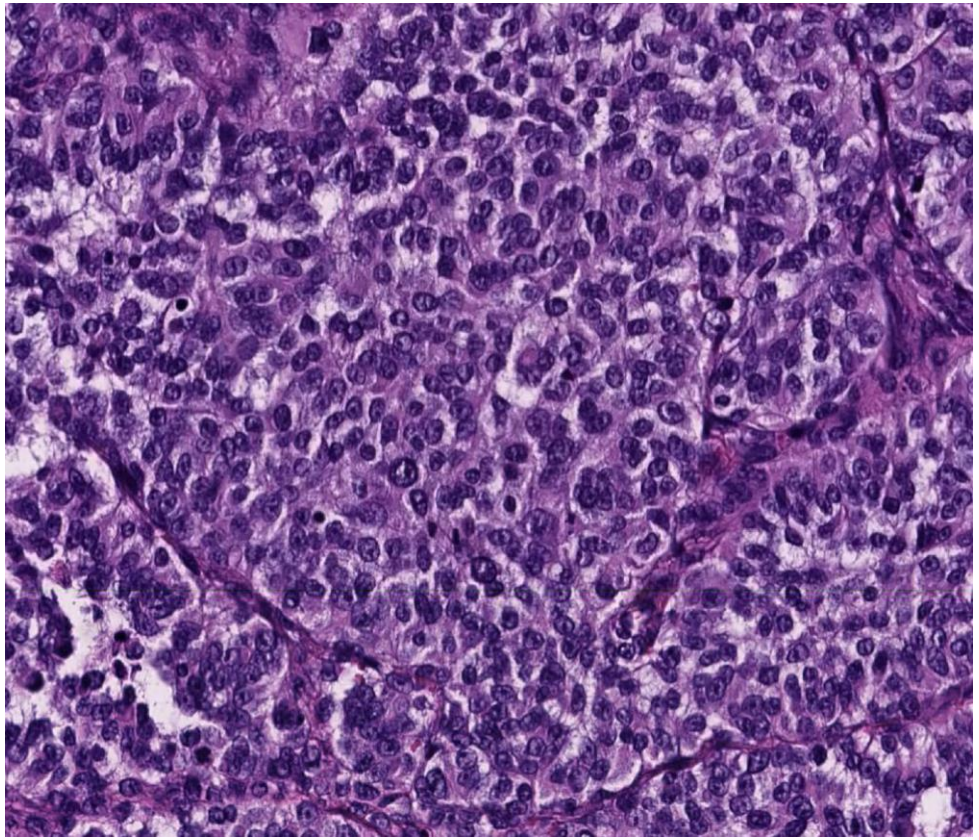
Diagnosis: Melanoma



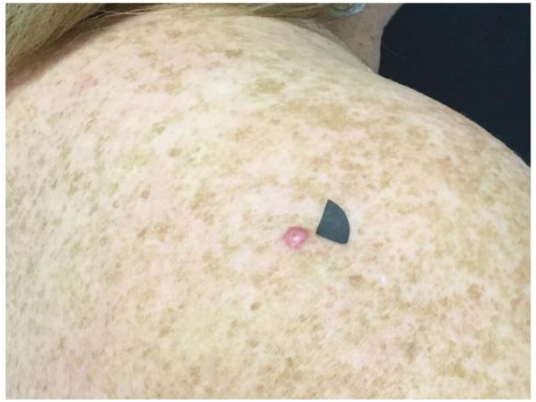
- BAP1 retained (no loss)
- Atypia and no maturation
- TMR: 6/mm2
- 4+ PRAME

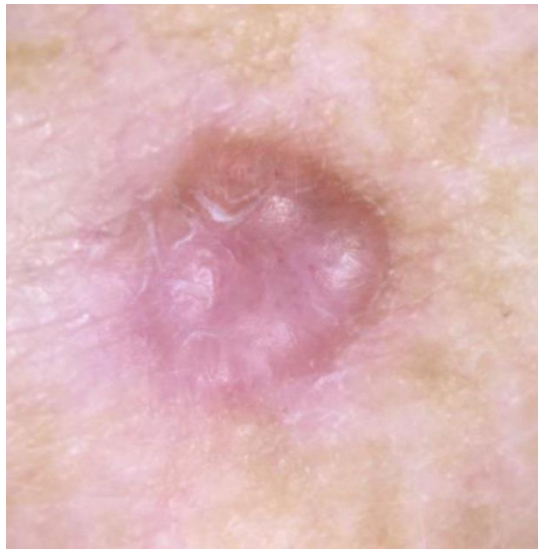
Metastatic melanoma of unknown primary





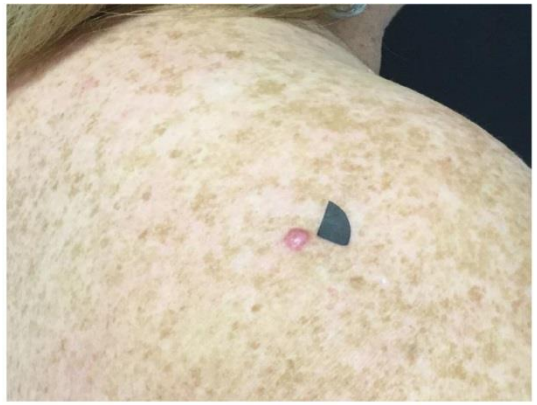
Clinical History

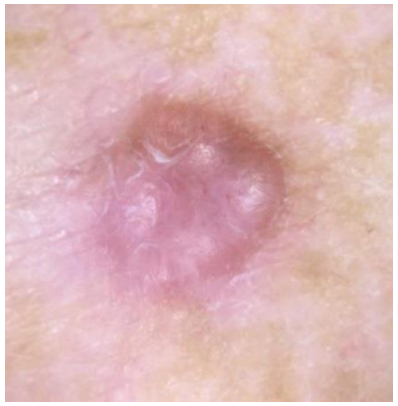


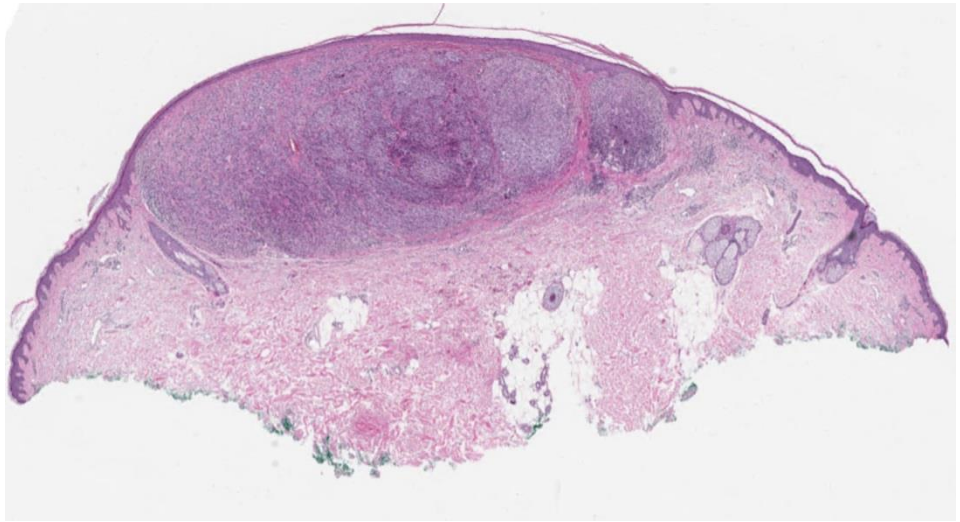


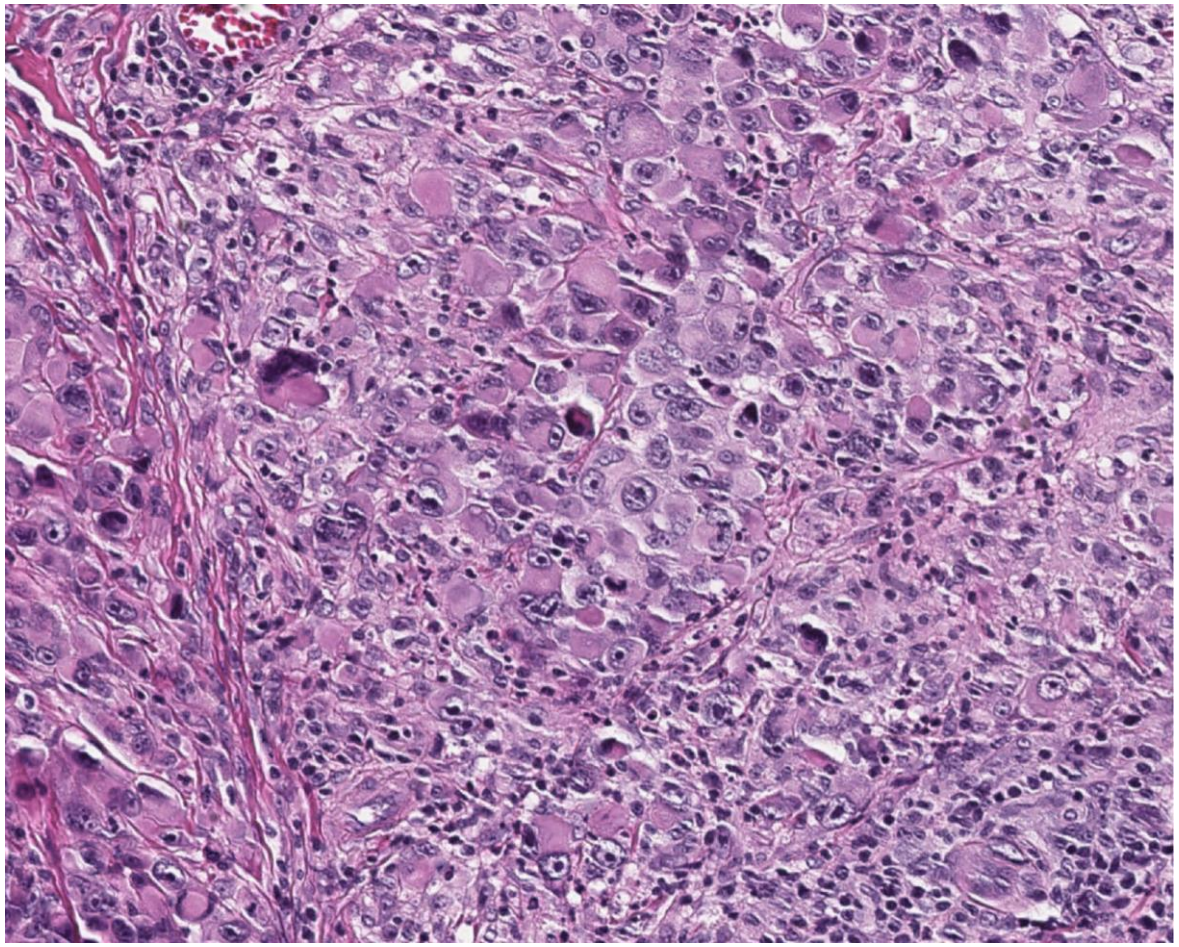
- Skin nodule present 3 years prior to metastasis
- Treated as probable DF with liquid N2 (not at MSKCC)
- Metastasis at site of lymphatic drainage

Diagnosis: Primary Dermal Melanoma









PDM – a diagnostic challenge for staging

dermatopathology

MDPI

Case Report

Primary Dermal Melanoma: A Rare Clinicopathological Variant Mimicking Metastatic Melanoma

Oriana Simonetti [1,*,†], Elisa Molinelli [1,†], Valerio Brisigotti [1], Donatella Brancorsini [2], Davide Talevi [3] and Annamaria Offidani [1]

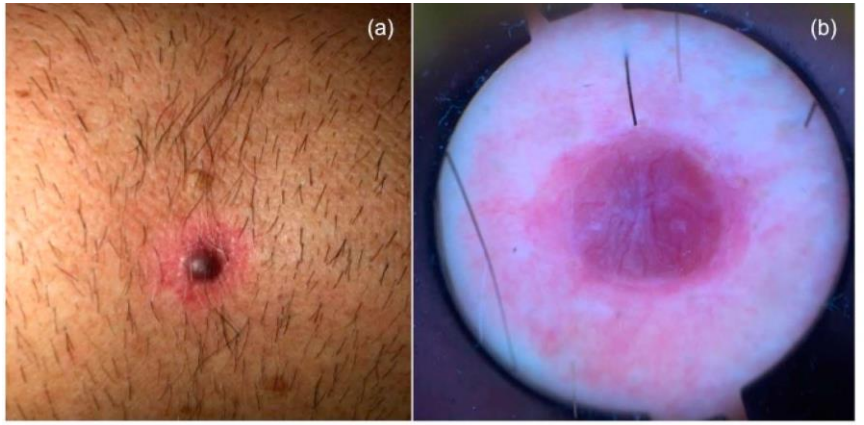
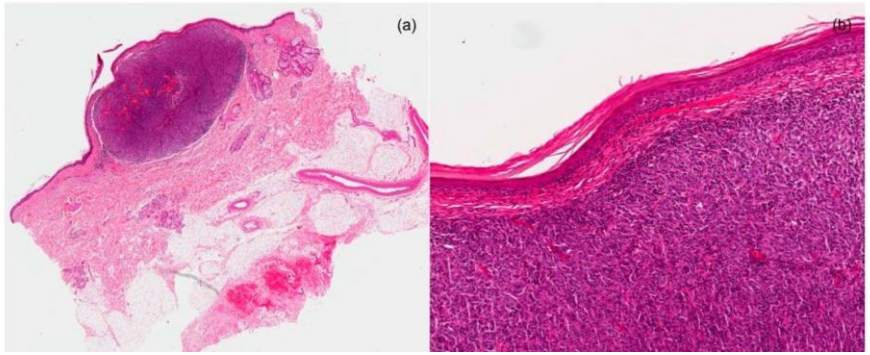


Figure 1. (**a**) Pink nodule with a peripheral erythematous halo of the chest. (**b**) Dermoscopic pattern of nodular lesion: reddish-purplish homogeneous pattern, with atypical vessels.



Primary Dermal Melanoma

OBSERVATION

Solitary Melanoma Confined to the Dermal and/or Subcutaneous Tissue

Evidence for Revisiting the Staging Classification

Glen M. Bowen, MD; Alfred E. Chang, MD; Lori Lowe, MD; Ted Hamilton, MS; Rupa Patel, BA; Timothy M. Johnson, MD

Background: Several patients presented with a single focus of presumed cutaneous metastatic melanoma with an unknown primary tumor based on clinical and histologic staging criteria of the American Joint Committee on Cancer (AJCC). This population is classified as having stage IV disease by the current AJCC staging system, which carries a dismal prognosis (5%-18% 5-year survival). Our clinical observation was that these patients had a higher survival rate than would be expected for stage IV disease. We believe this population represents a subgroup of primary dermal- and/or subcutaneously-derived melanoma that simulates cutaneous metastatic melanoma in histologic and clinical presentation but may differ in behavior.

Observations: The database records of 1800 patients from the University of Michigan Melanoma Clinic, Ann Arbor, were retrospectively reviewed to identify the prevalence and survival for patients diagnosed with a single focus of presumed metastatic melanoma to the skin based on accepted histologic and clinical parameters. The prevalence of this population was 0.61% (11 of 1800 patients). The Kaplan-Meier 8-year survival estimate was 83% (95% confidence interval, 58%-100%).

Conclusions: By AJCC convention, these cases are classified as stage IV metastatic disease. Our data suggest that these presumed metastatic tumors do not behave like stage IV metastatic disease to the skin via lymphatic or hematogenous spread from an unknown primary site; rather they are behaving like primary tumors originating in the dermal and/or subcutaneous tissue.

Arch Dermatol. 2000;136:1397-1399

- 11 of 1800 melanoma patients presented with solitary nodule and no associated precursor
- Initially thought to be metastatic
- Unusual high survival rate suggests that they may be primary tumors

Primary Dermal Melanoma

OBSERVATION

Primary Dermal Melanoma

A Distinct Subtype of Melanoma

Susan M. Swetter, MD; Phillip M. Ecker, BA; Denise L. Johnson, MD; Jeff D. Harvell, MD

Background: The term *primary dermal melanoma* has been used to describe a subtype of melanoma confined to the dermis and/or subcutaneous fat that histologically simulates metastasis but is associated with an unexpectedly prolonged survival. We report 7 cases of primary dermal melanoma diagnosed from 1998 to 2002 with no identifiable junctional or epidermal component or nevoid precursor. Histopathologic and immunohistochemical features were compared with known cases of cutaneous metastasis and nodular melanoma in an attempt to differentiate this entity from clinical and pathologic mimics.

Observations: Seven patients had a single dermal and/or subcutaneous focus of melanoma. Metastatic staging workup findings were negative, including results from sentinel node and imaging studies. Mean Breslow depth was 7.0 mm, and mean maximum tumor diameter was 6.2 mm. The study cohort showed 100% survival at mean follow-up of 41 months (range, 10-64 months). Immunohistochemical analysis with S100, HMB-45, Ki-67, CD34, and p75 antibodies showed no significant staining patterns compared with metastatic and nodular melanomas.

Conclusions: Primary dermal melanoma appears to be a distinct subtype of melanoma based on the excellent prognosis associated with this case series and others. Additional research focusing on cause, appropriate staging, and outcome of previously identified solitary dermal metastasis is warranted to further delineate this entity.

Arch Dermatol. 2004;140:99-103

Definition:

- Melanoma in dermis and/or subcutis
- No associated in situ melanoma or nevus

Study:

- 7 cases with mean thickness of 7 mm
- 100% survival (mean FU of 41 months)

Primary Dermal Melanoma

Primary dermal melanoma: clinical behaviour, prognosis and treatment

Christopher G. Harris [a, b], Serigne Lo [a, c], Tasnia Ahmed [a], Richard A. Scolyer [a, b, c, d], Peter M. Ferguson [a, b, c, d], Rooshdiya Z. Karim [b, c, d], Tai Khoa Lam [b], Kenneth K. Lee [a], Kerwin F. Shannon [a, b, c], Andrew J. Spillane [a, c, e], Jonathan R. Stretch [a, b, c], John F. Thompson [a, b, c], Robyn PM. Saw [a, b, c, *]

Eur J Surg Oncol 2020; 2131 - 39

- 62 PDM (MIA 1978 – 2013)
- Disease-free survival similar to stage I-II controls
- Prognosis much better than for stage IV M1a controls

PDM – Genetically Heterogeneous

Human Pathology (2020) 106, 32–38

ELSEVIER

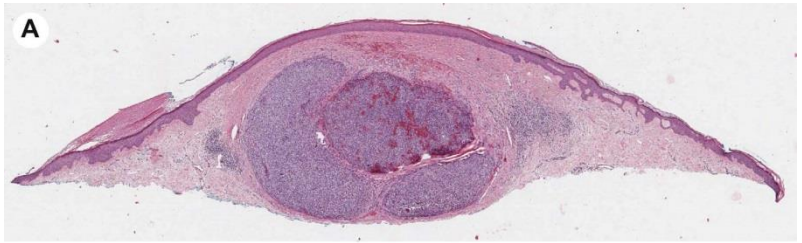
Human PATHOLOGY

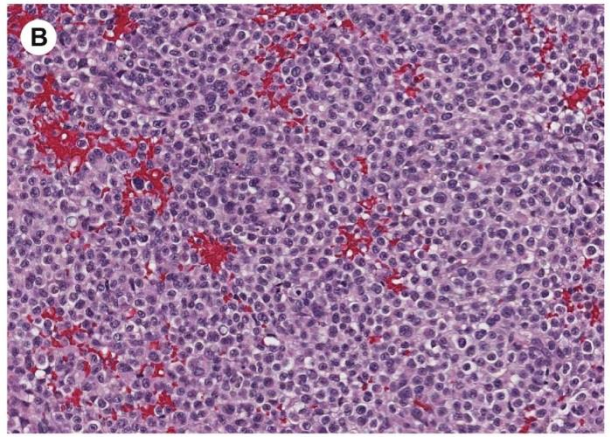
www.elsevier.com/locate/humpath

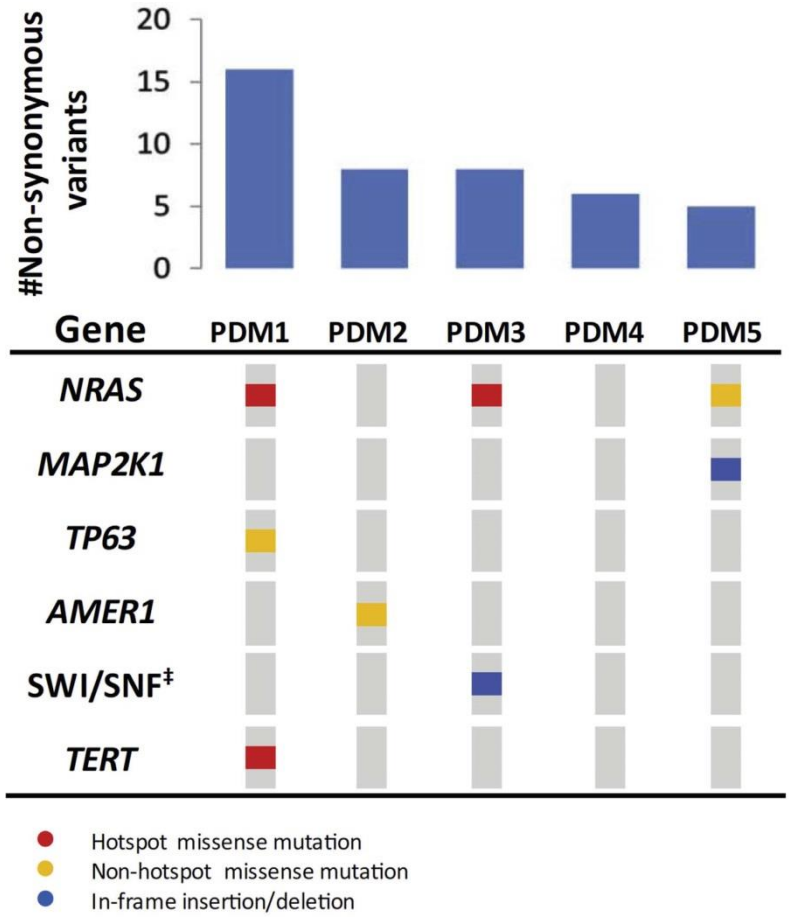
Original contribution

Lack of distinct molecular profile of Primary Dermal Melanoma☆

Sheila Shaigany MD[a,1], Basile Tessier-Cloutier MD[b,1], Klaus J. Busam MD[c], Basil A. Horst MD[a,b,*]



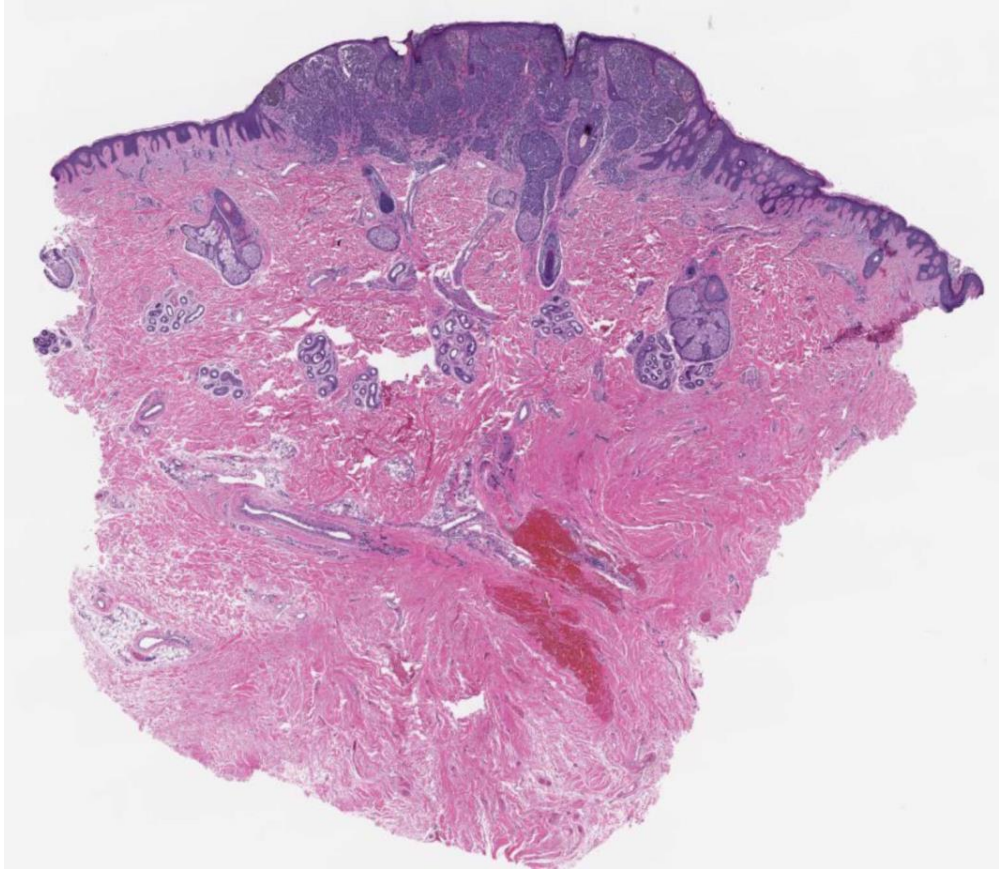




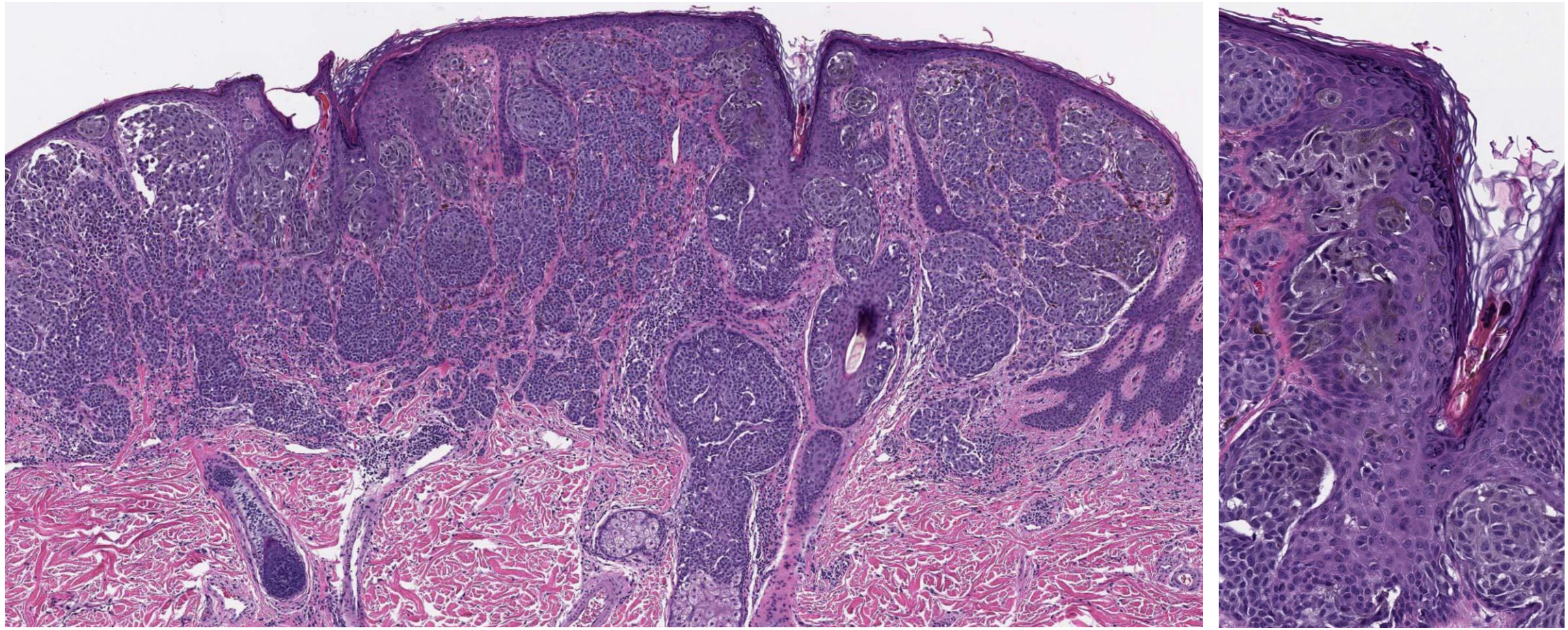
Primary Dermal Melanoma

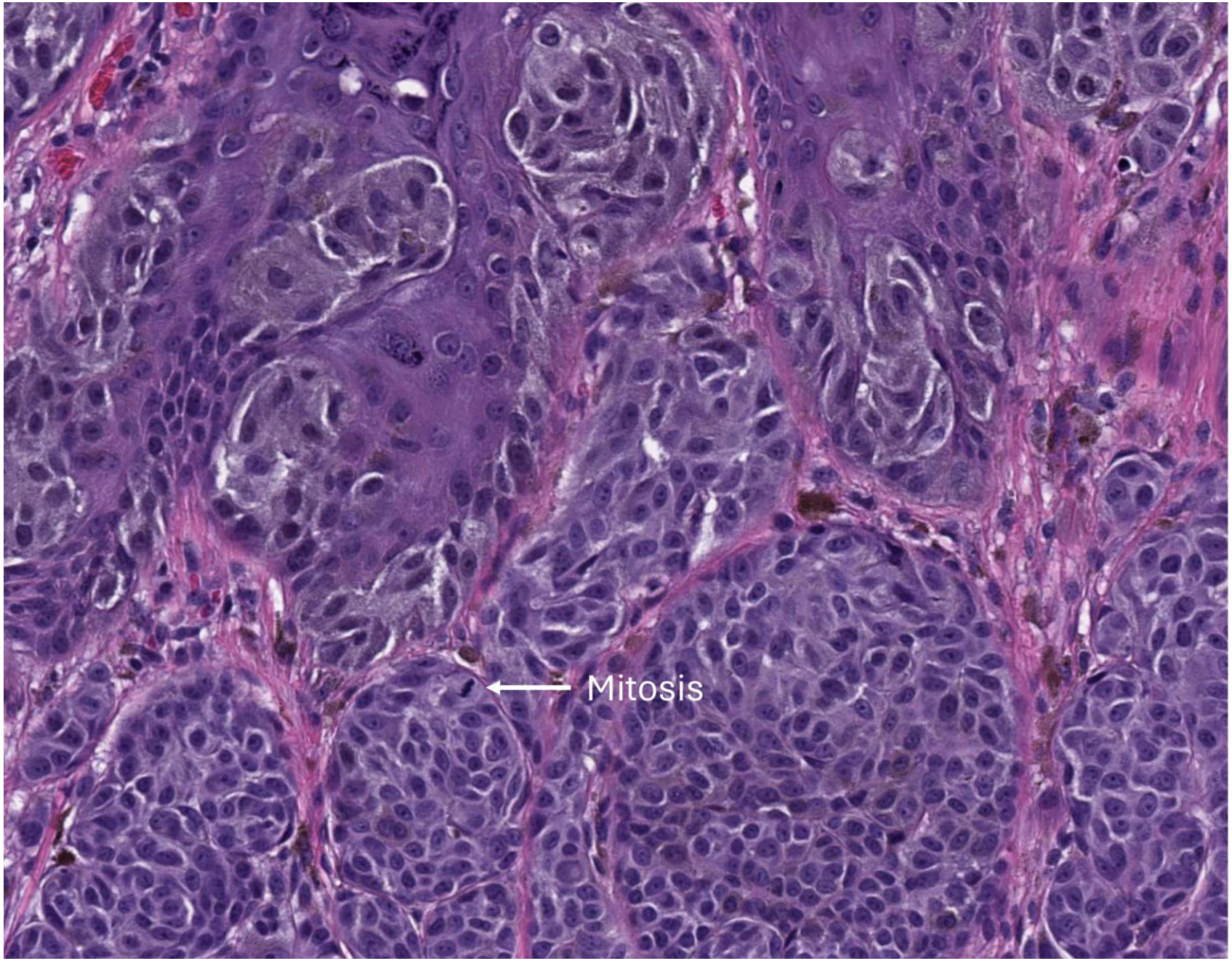
A solitary dermal melanoma nodule is most likely primary, unless there is a known history or other concurrent evidence of melanoma

What is Your Diagnosis?

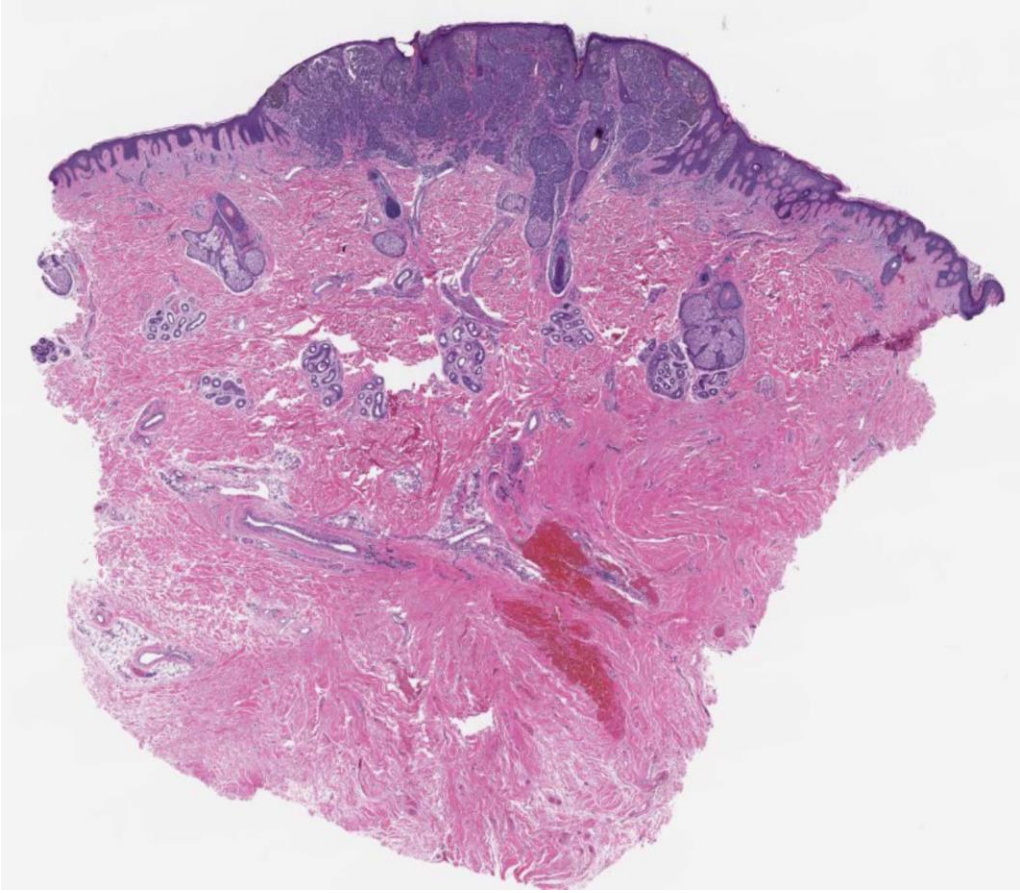


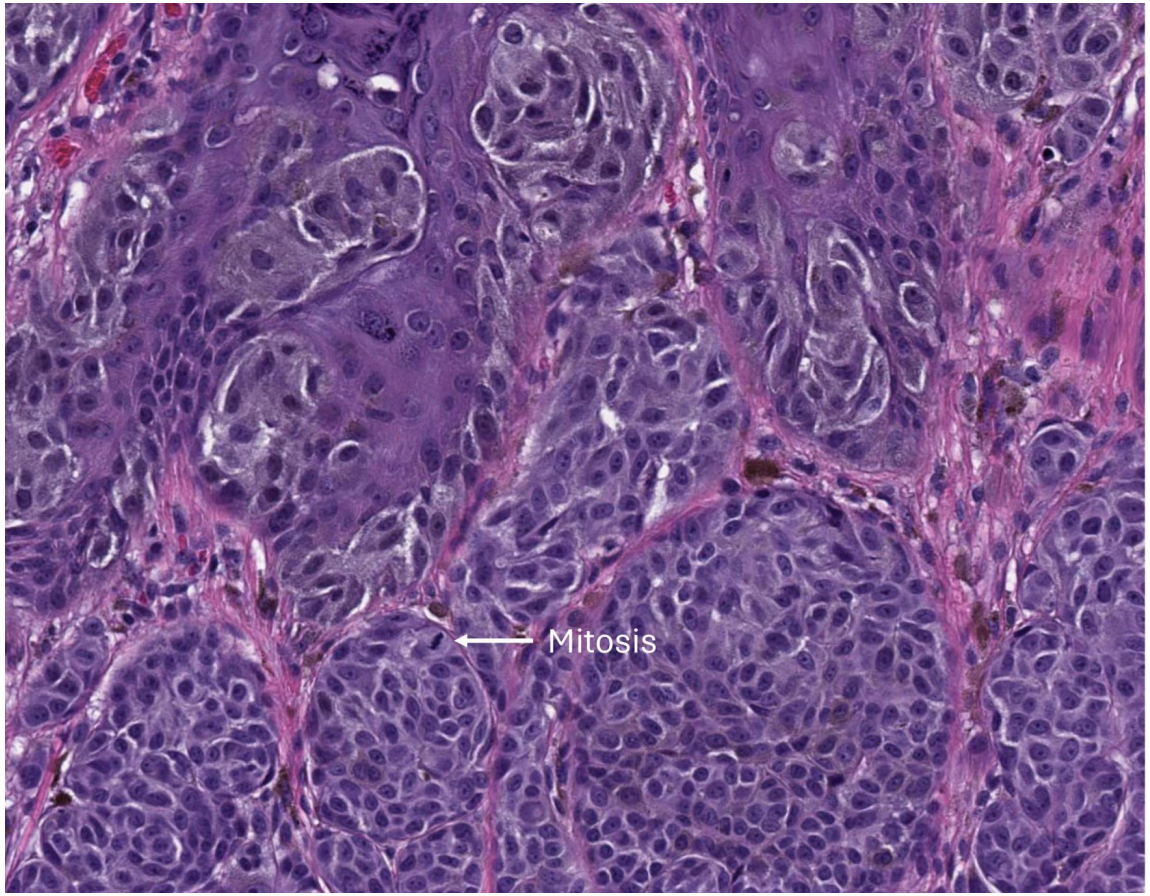
- 26 M with nodule on temple



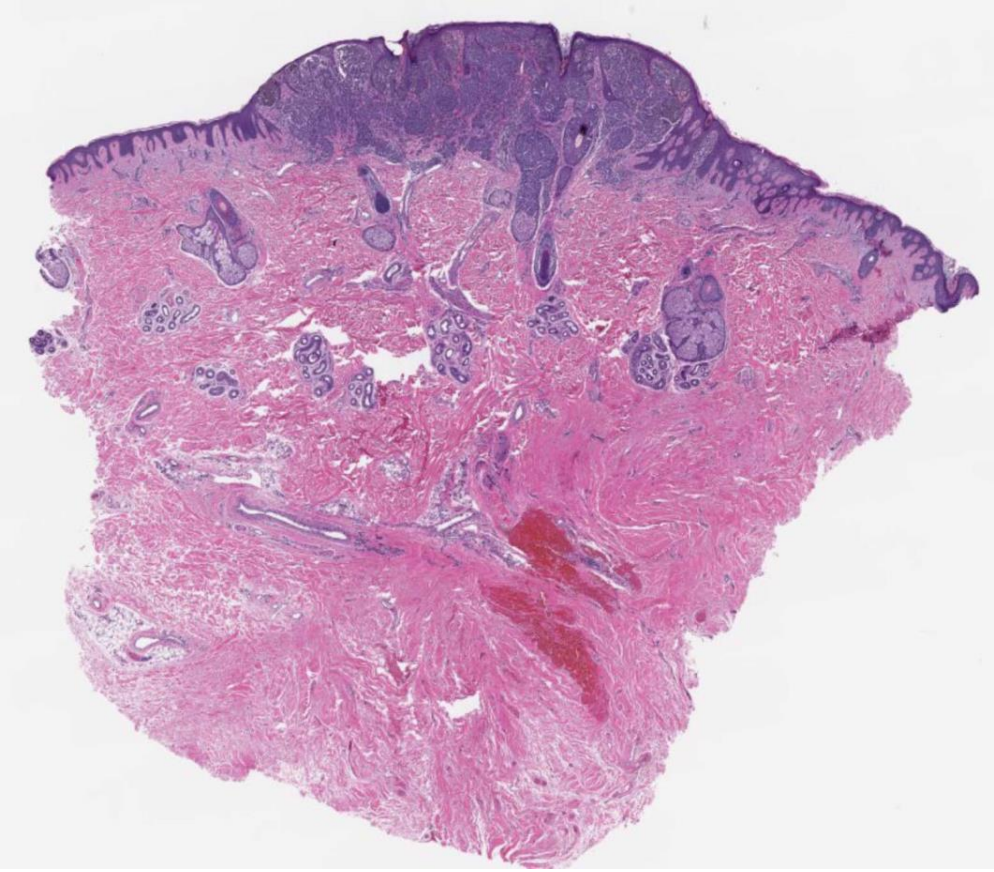

Mitosis

Nevus or Melanoma?



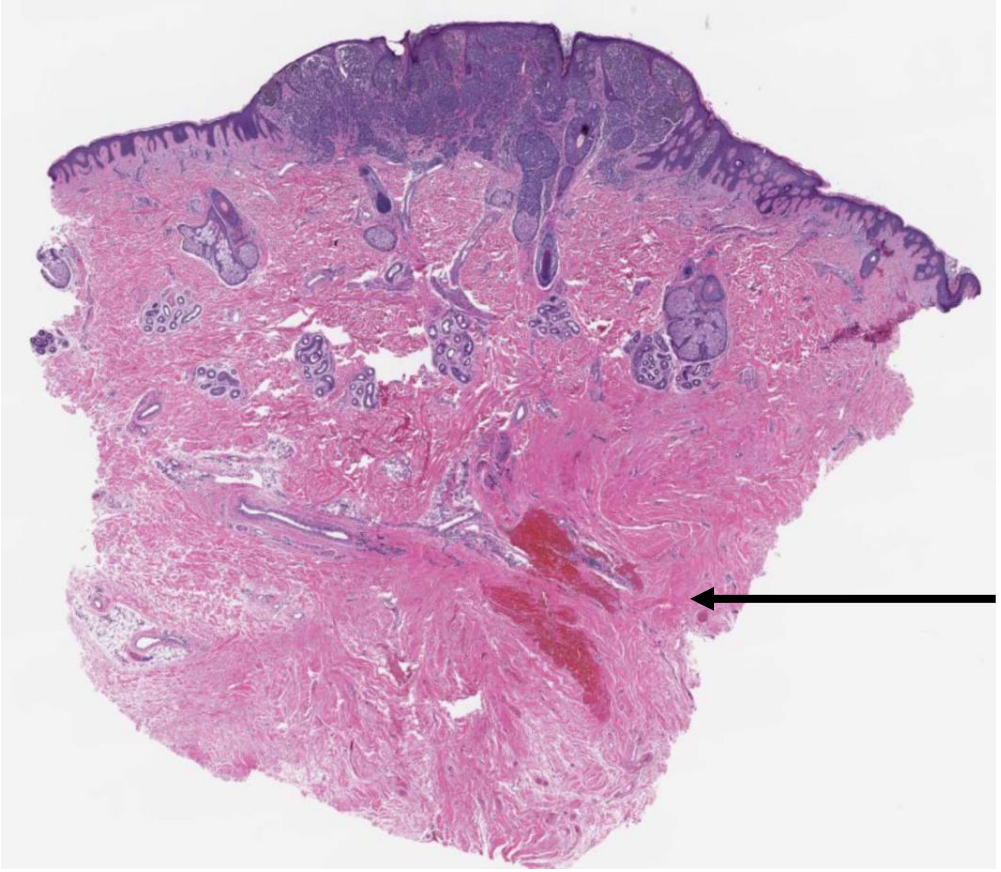


Diagnosis - Melanoma

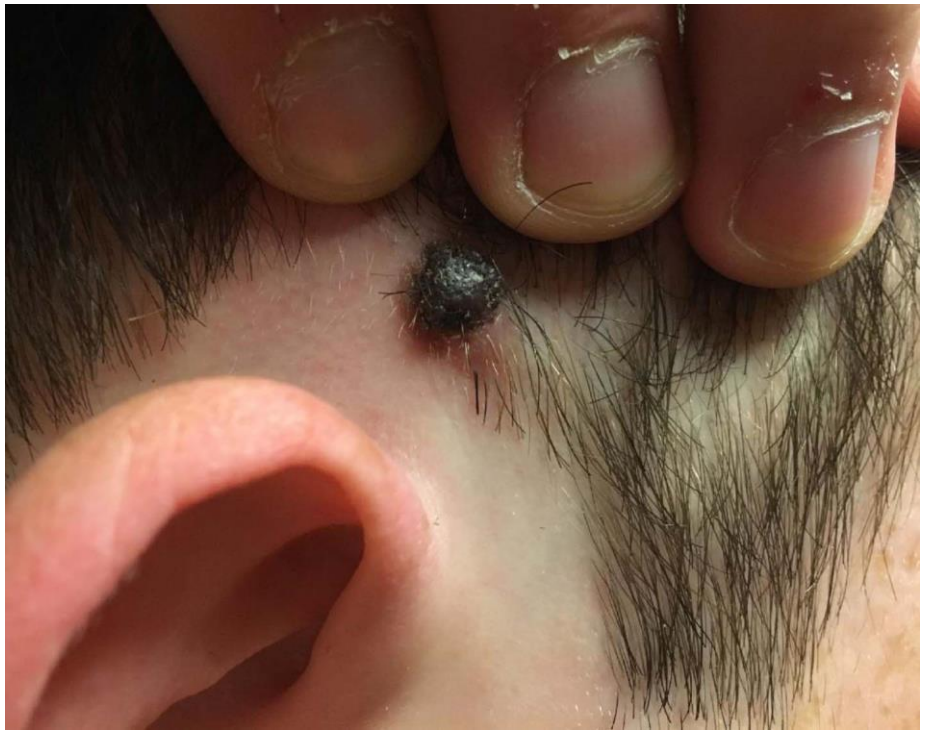


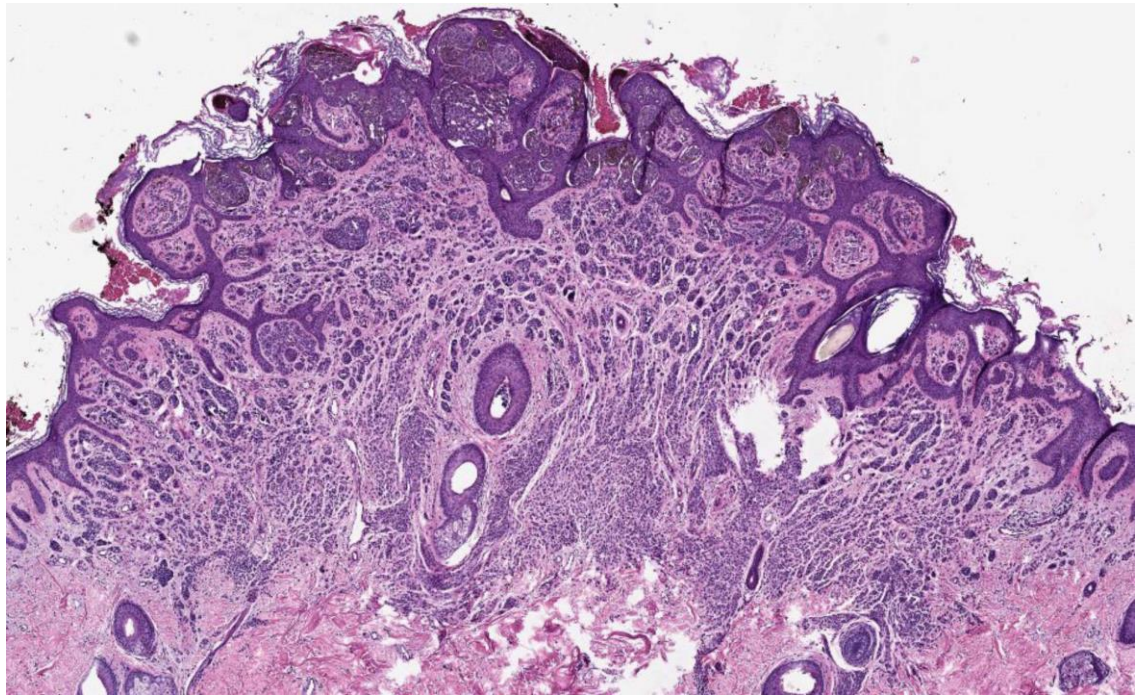
- Asymmetric pigmentation
- Focal pagetosis
- Cytologic atypia
- Mitoses
- 4+ Labeling for PRAME

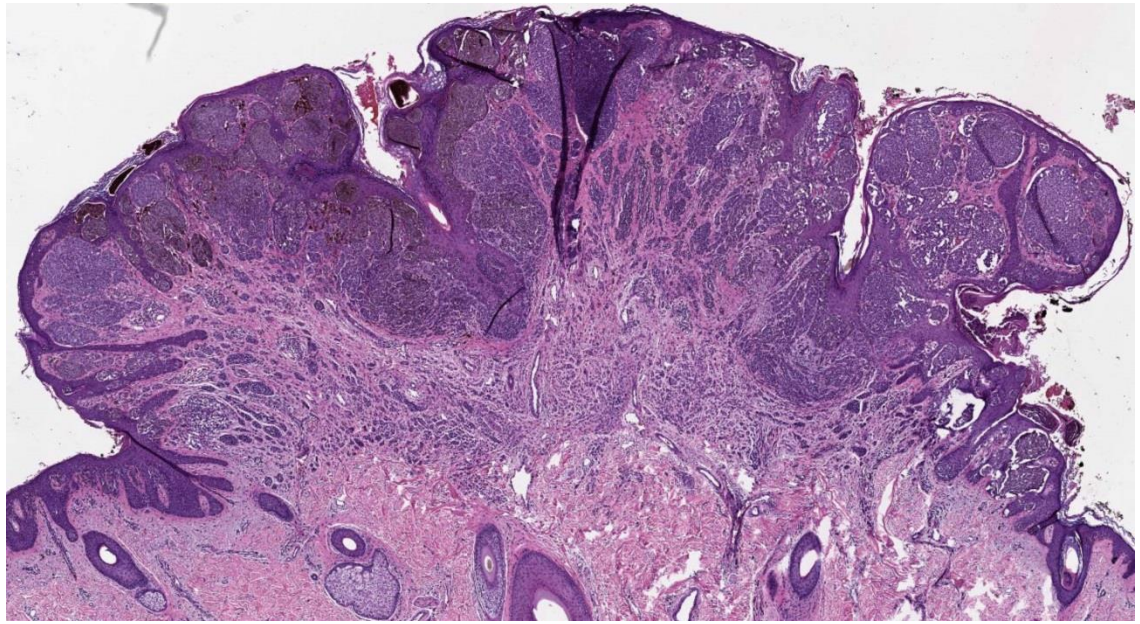
Additional Diagnostic Clue



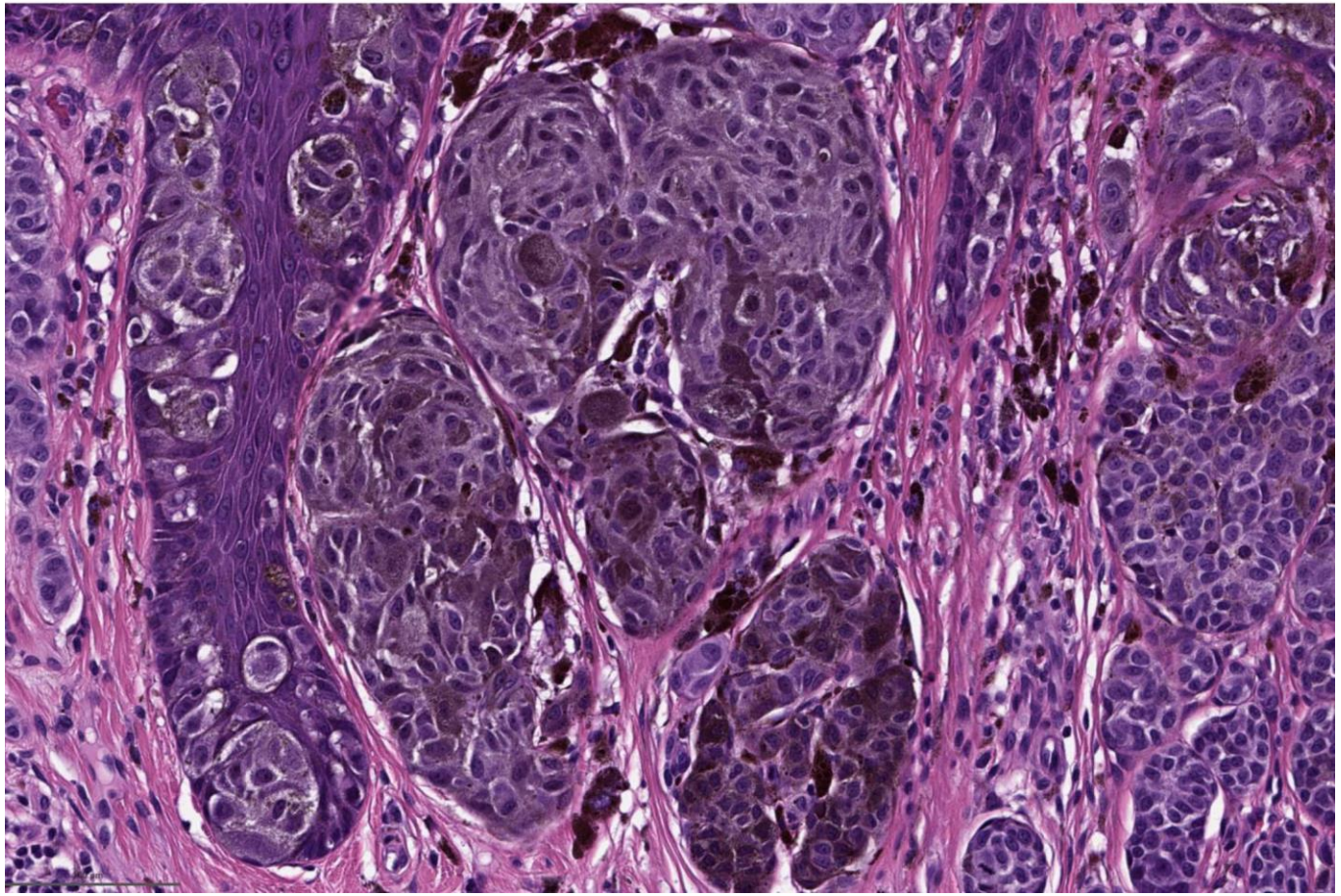
16 months earlier…

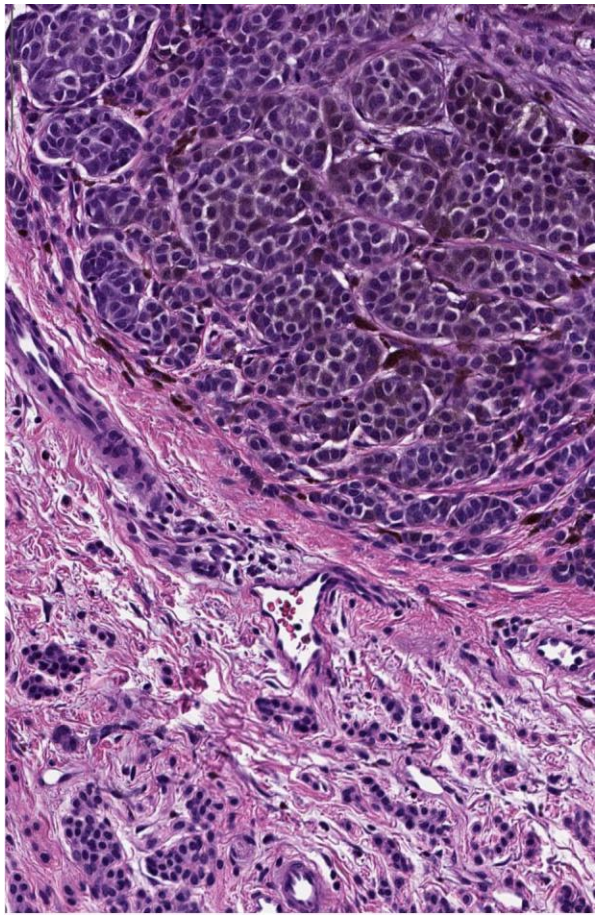




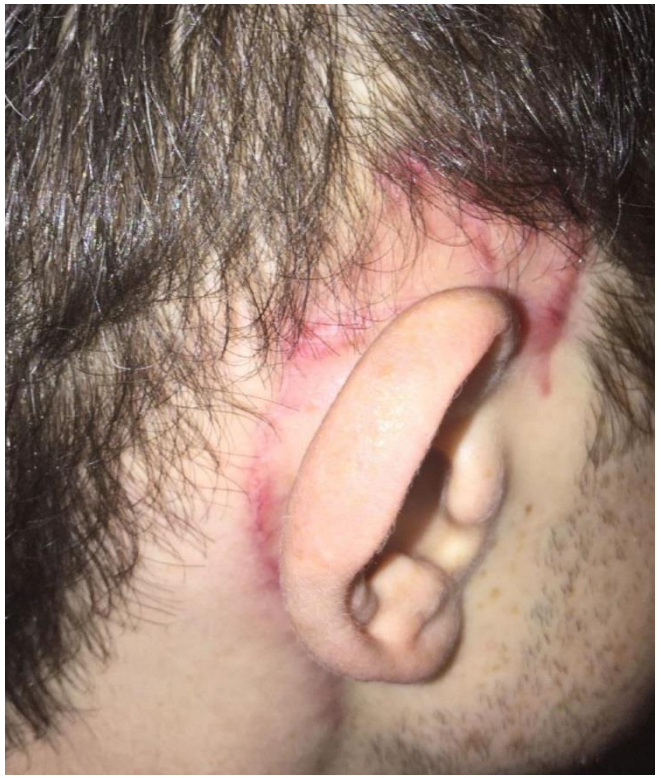


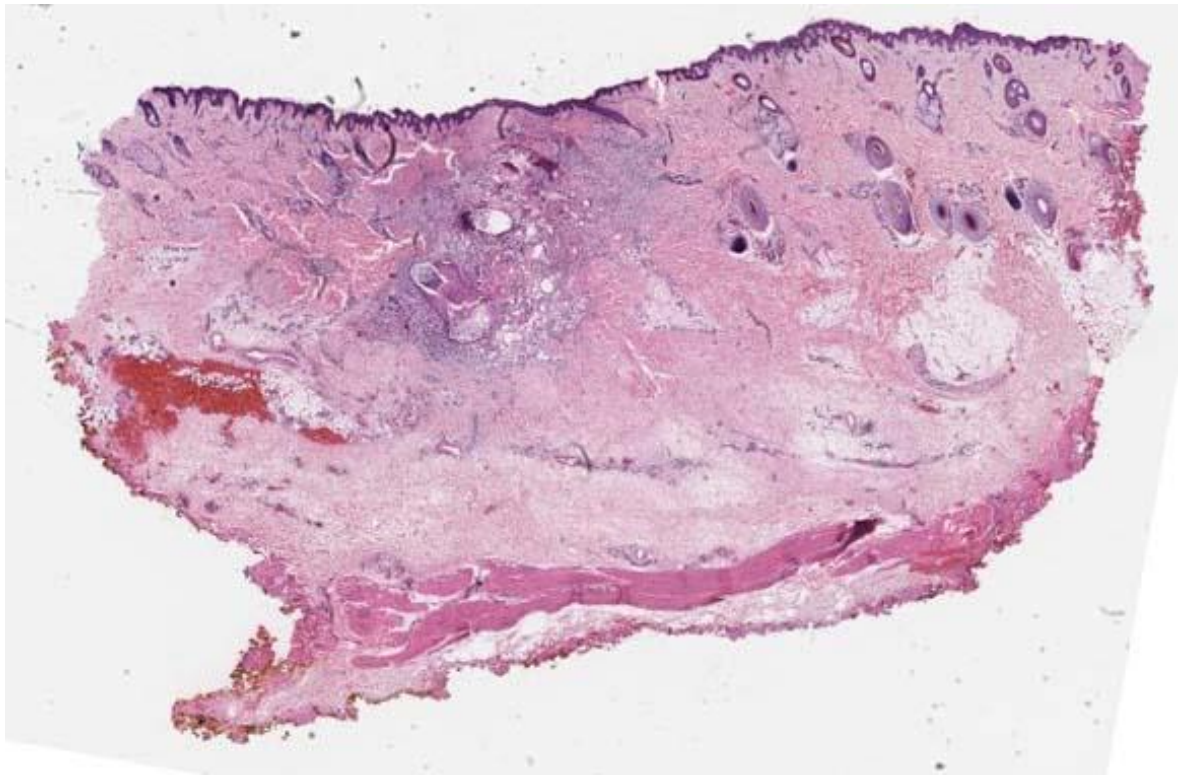
Melanoma associated with a nevus



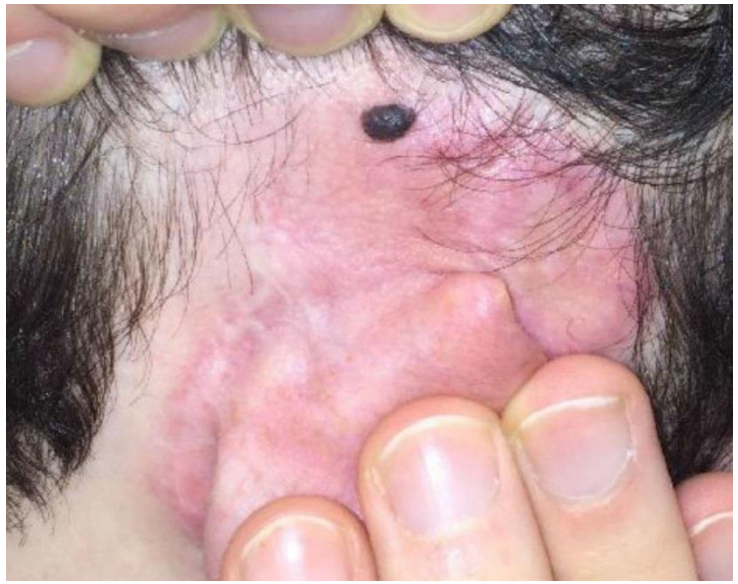


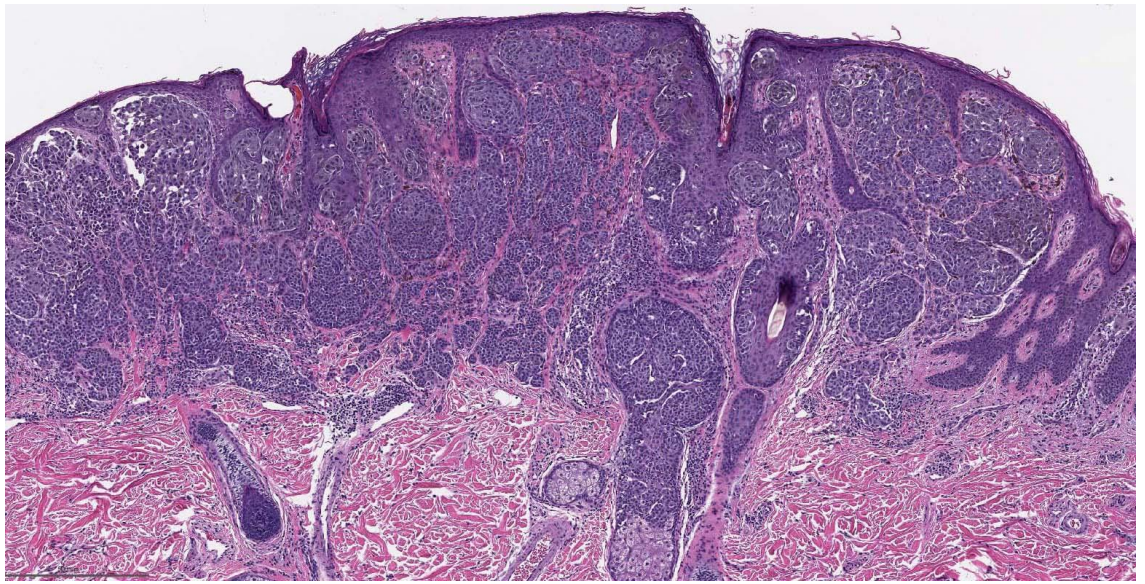
Excision with neg margins



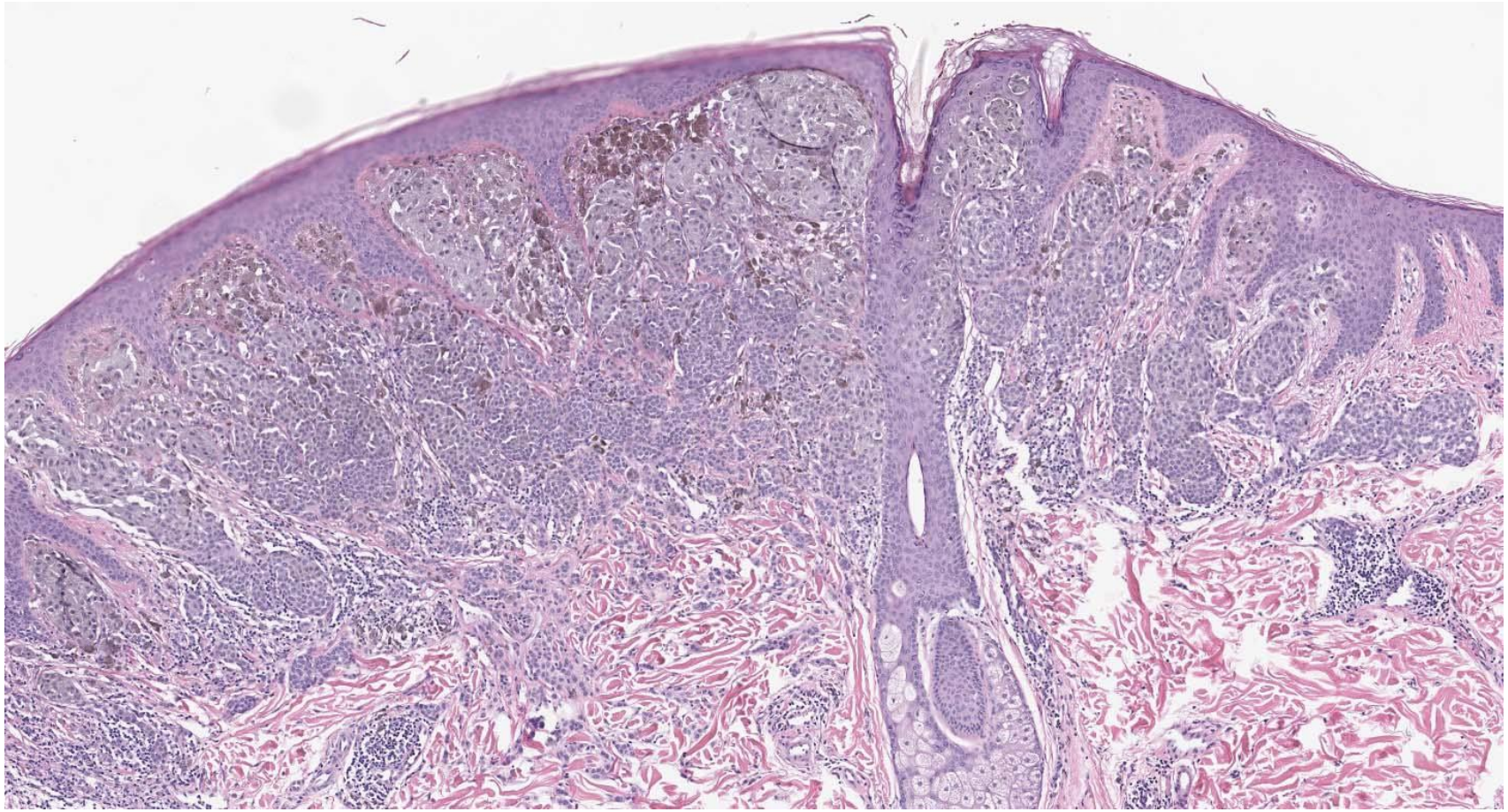


Current Tumor: Metastatic Melanoma





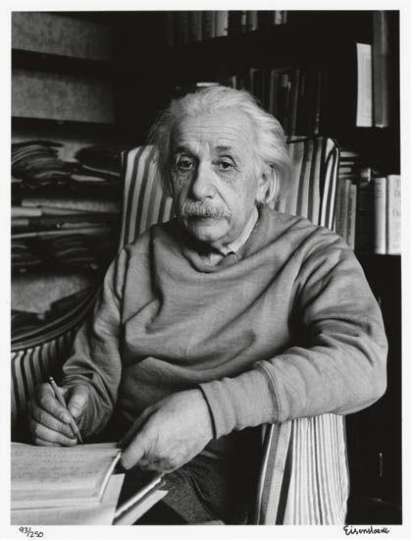
Metastatic Melanoma



Staging of melanoma – Clinical context matters

- Prior history of melanoma
- Clinical presentation of tumor
- Evidence from other clinical studies and follow-up
- Evidence from ancillary tests, especially molecular studies

Princeton University, Princeton, NJ




VOTES FOR WOMEN
Chatham Historical Society
VOTE
CHATHAM
GIRL SCOUTS
FX4


EXPRESS
SERVICE

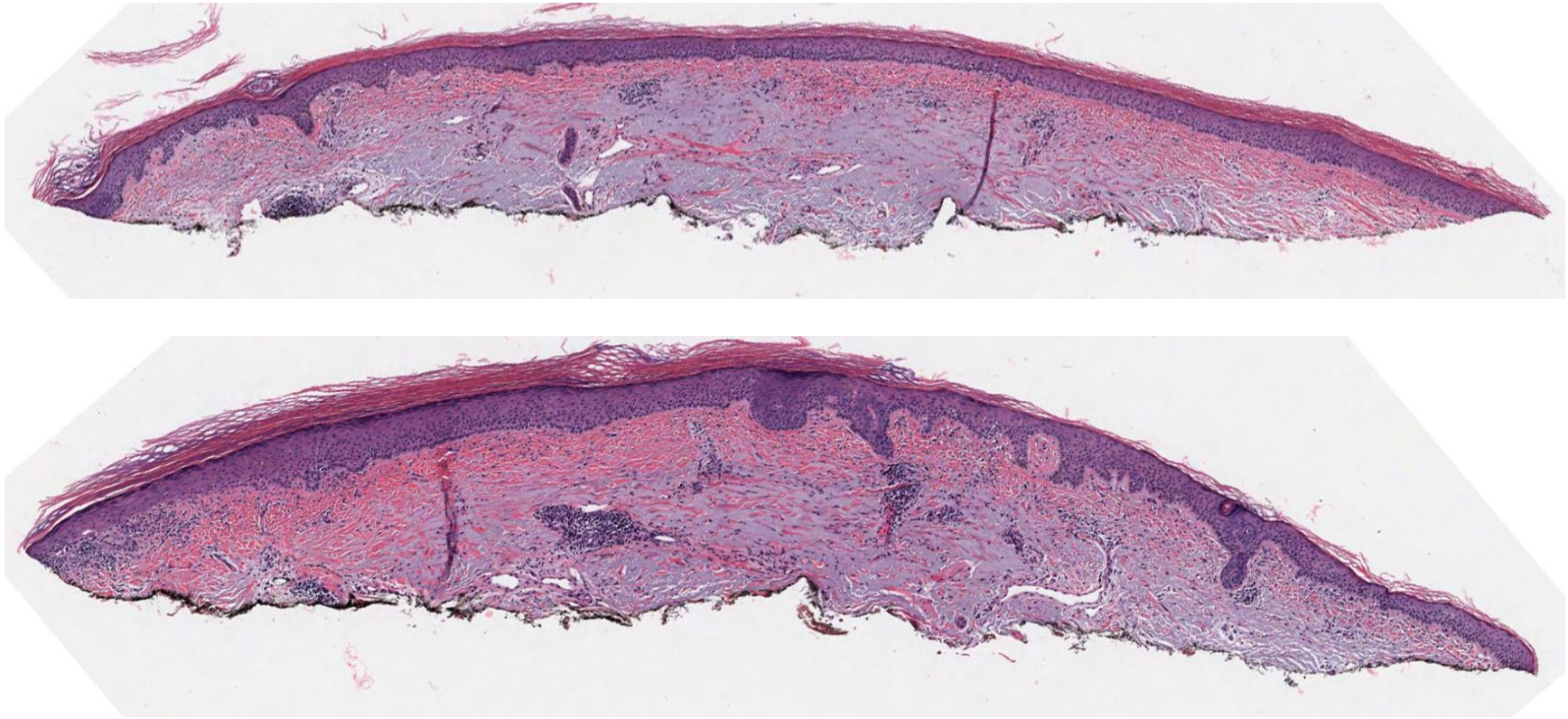
III: Desmoplastic Melanoma

- **Diagnostic Pitfall**
  - Difficult to diagnose clinically
  - Risk for misdiagnosis by pathologist
- **Distinct Variant of Melanoma**
  - Distinct pathologic features
  - Distinct clinical behavior

DM Pathology – Differential Diagnosis

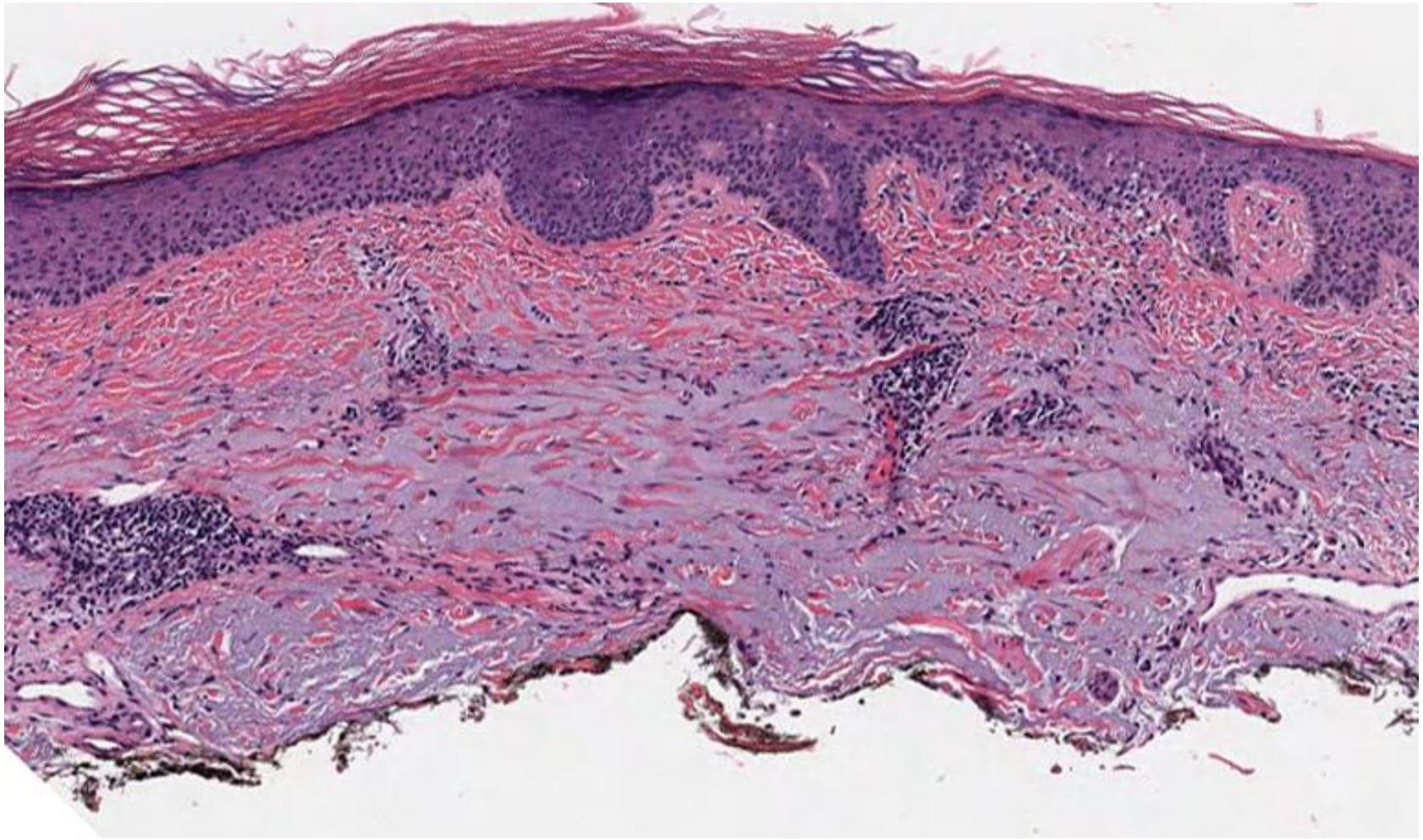
- DM vs benign fibrosing lesion
  - DM vs scar
  - DM vs dermato- or neurofibroma or other benign nerve sheath tumor
  - DM vs desmoplastic melanocytic nevus (acquired or congenital)
- DM vs non-melanocytic malignant tumor
  - Spindle cell sarcoma with desmoplasia
  - Desmoplastic carcinoma (usually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

What is Your Diagnosis?



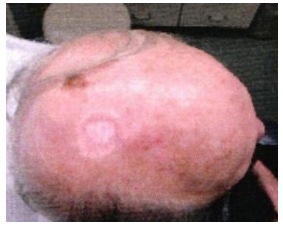
86 yo man with pink papule on scalp

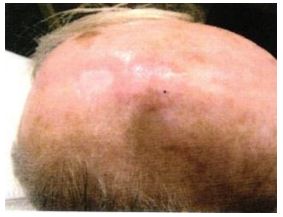
What is Your Diagnosis?



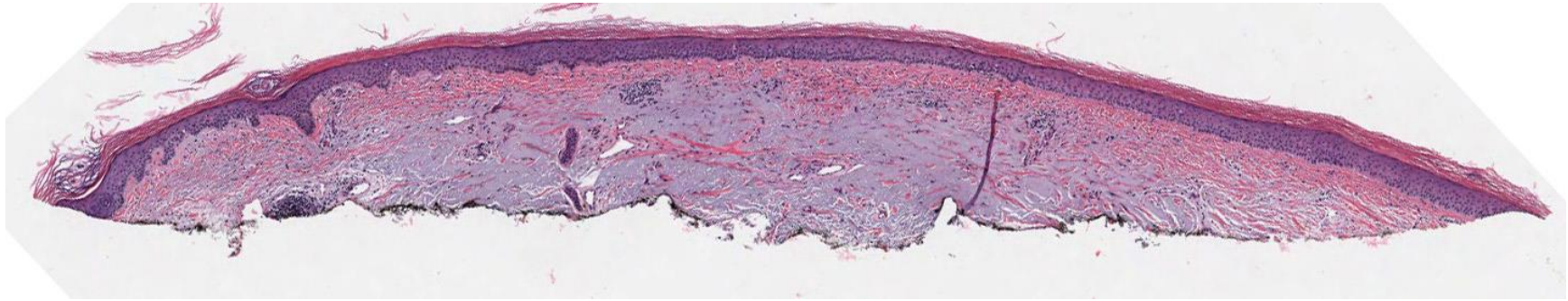
86 yo man with pink papule on scalp

Clinical context: Near surgical scar for lentigo maligna

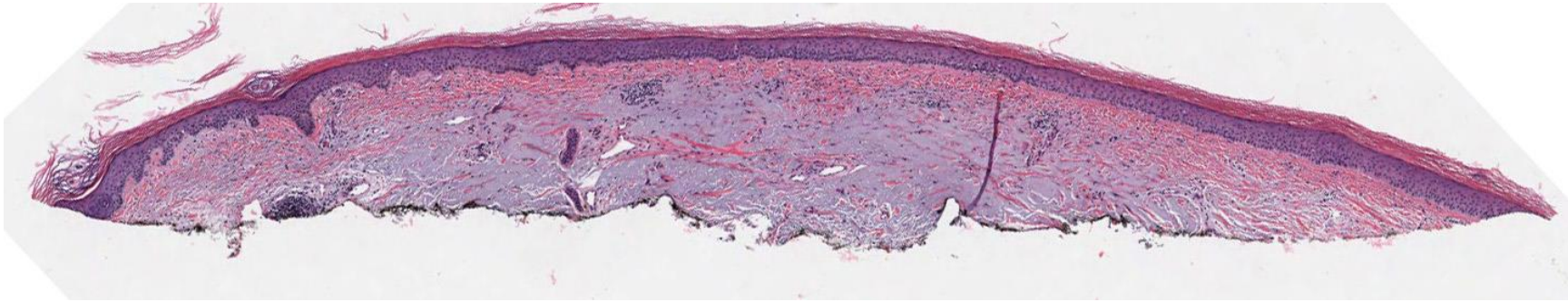




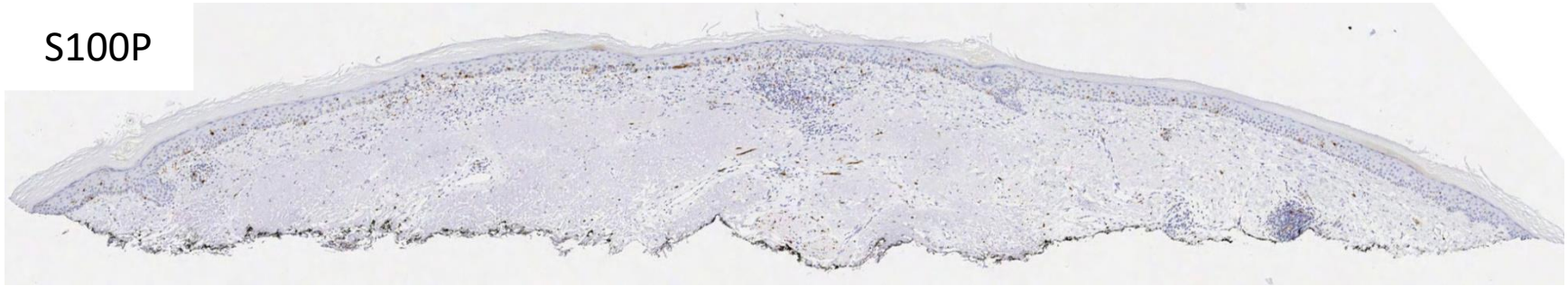
86 yo man with pink papule on scalp

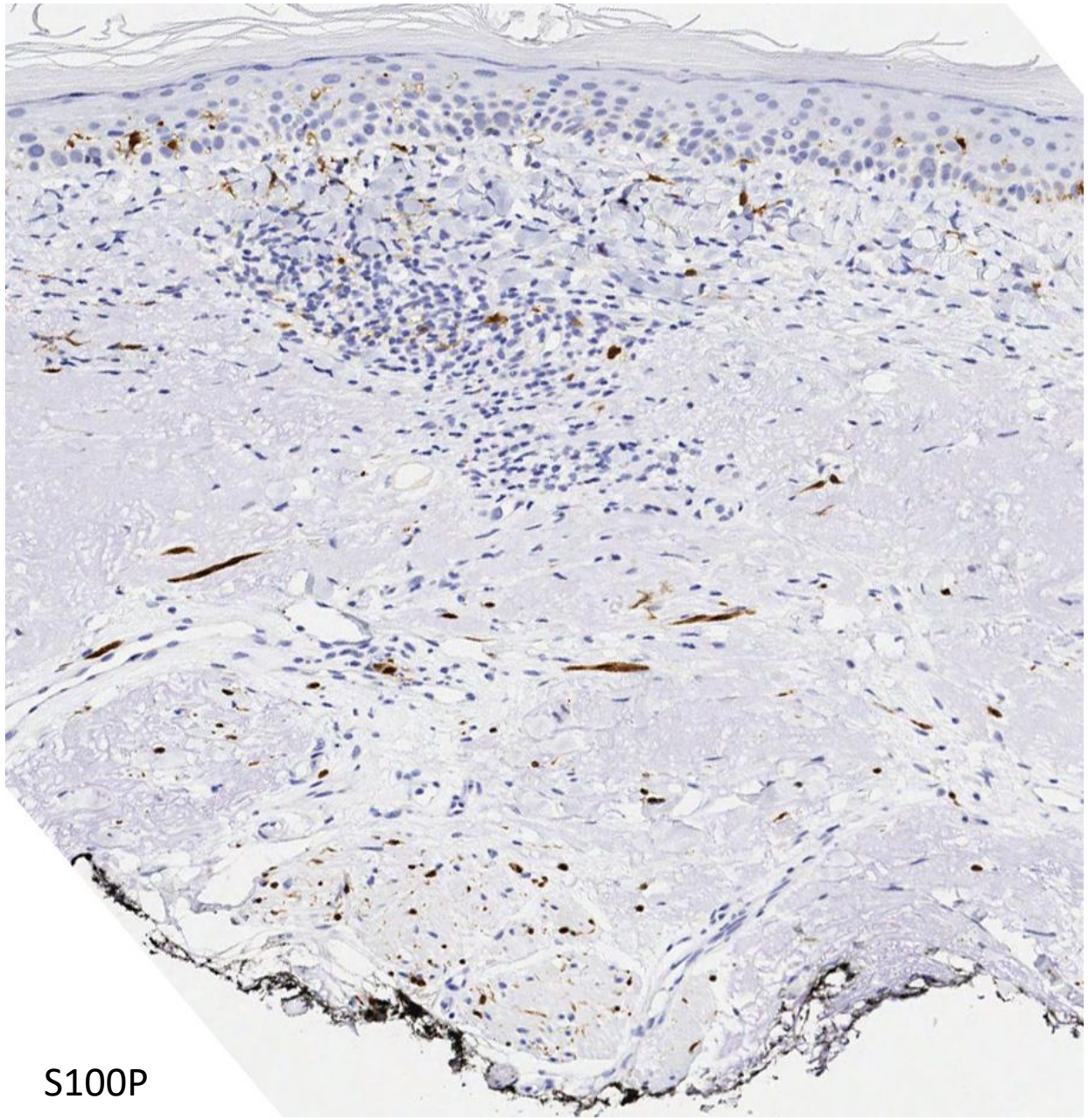


86 yo man with pink papule on scalp



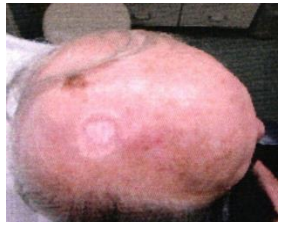
S100P

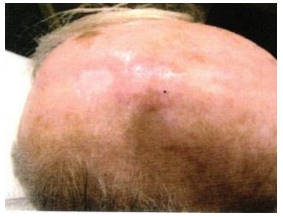




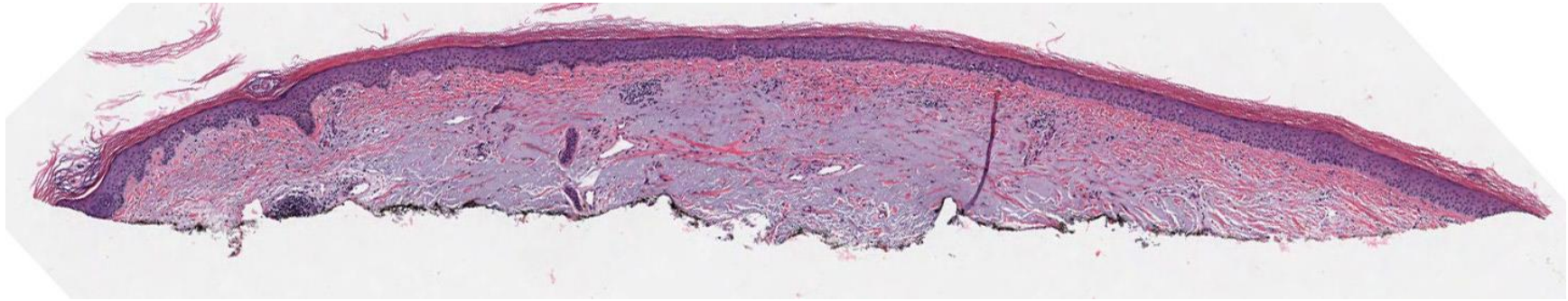
S100P

Clinical context: Near surgical scar for lentigo maligna

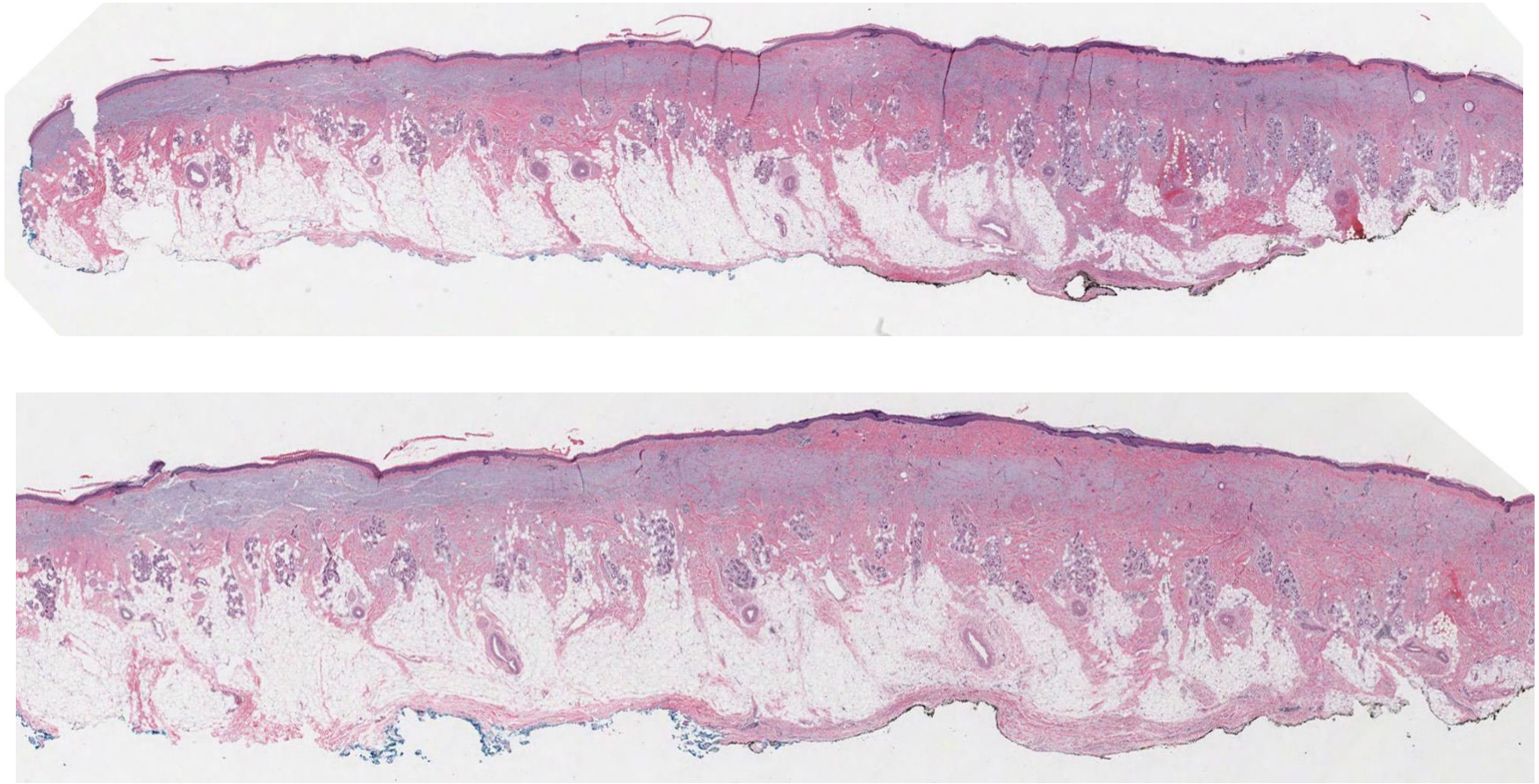




86 yo man with pink papule on scalp

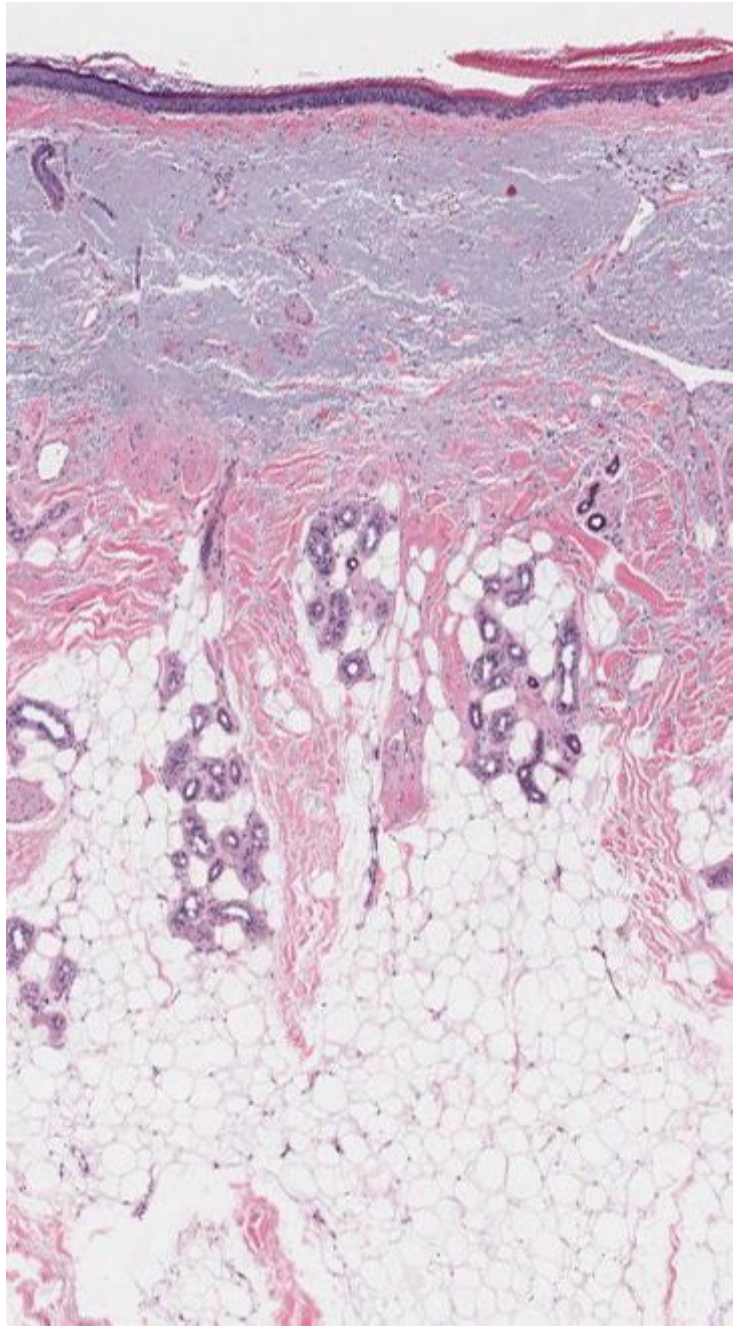


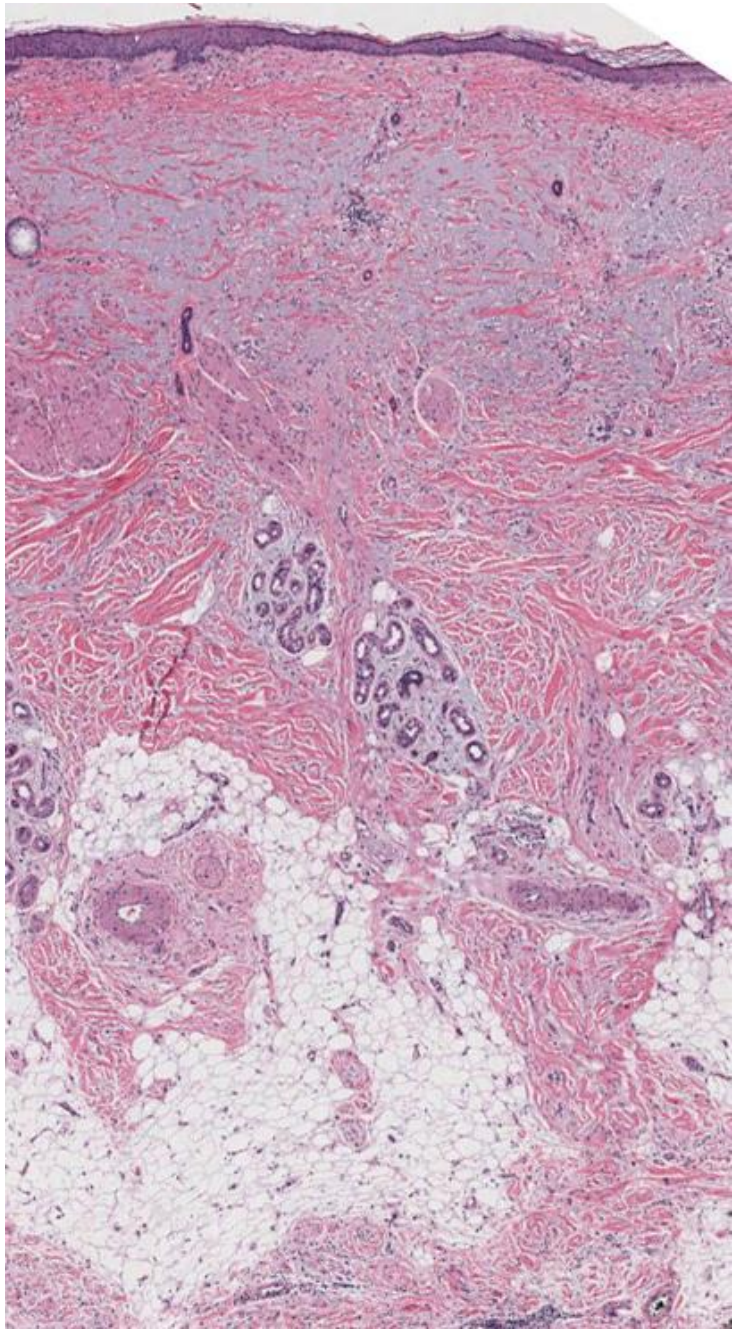
Desmoplastic Melanoma



86 yo man with pink papule on scalp

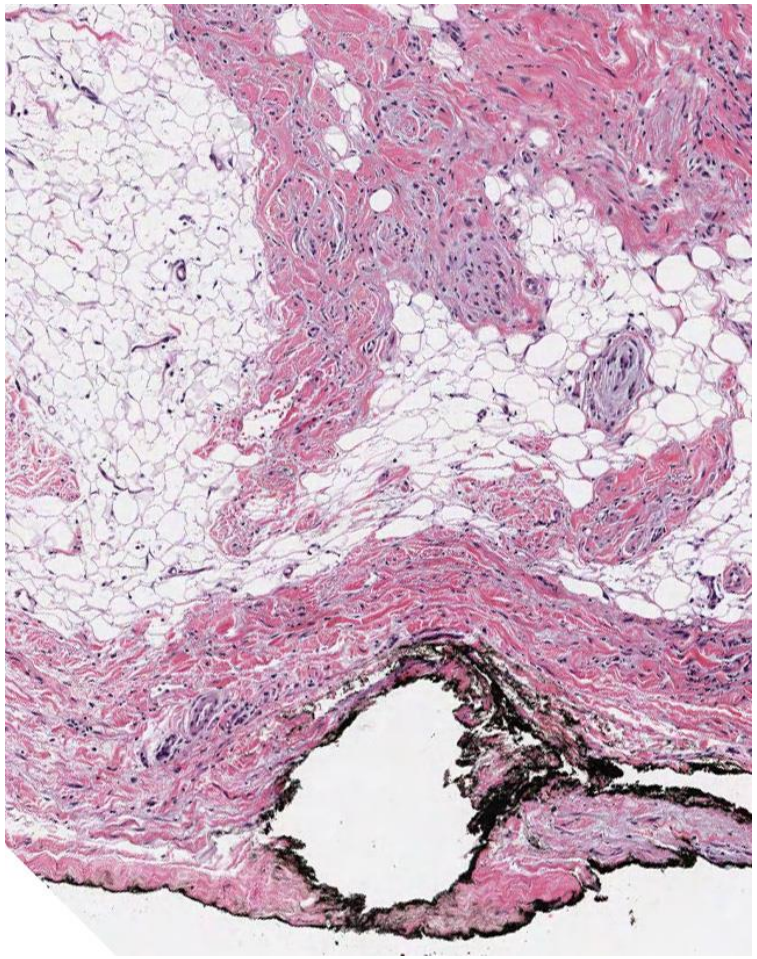
Normal

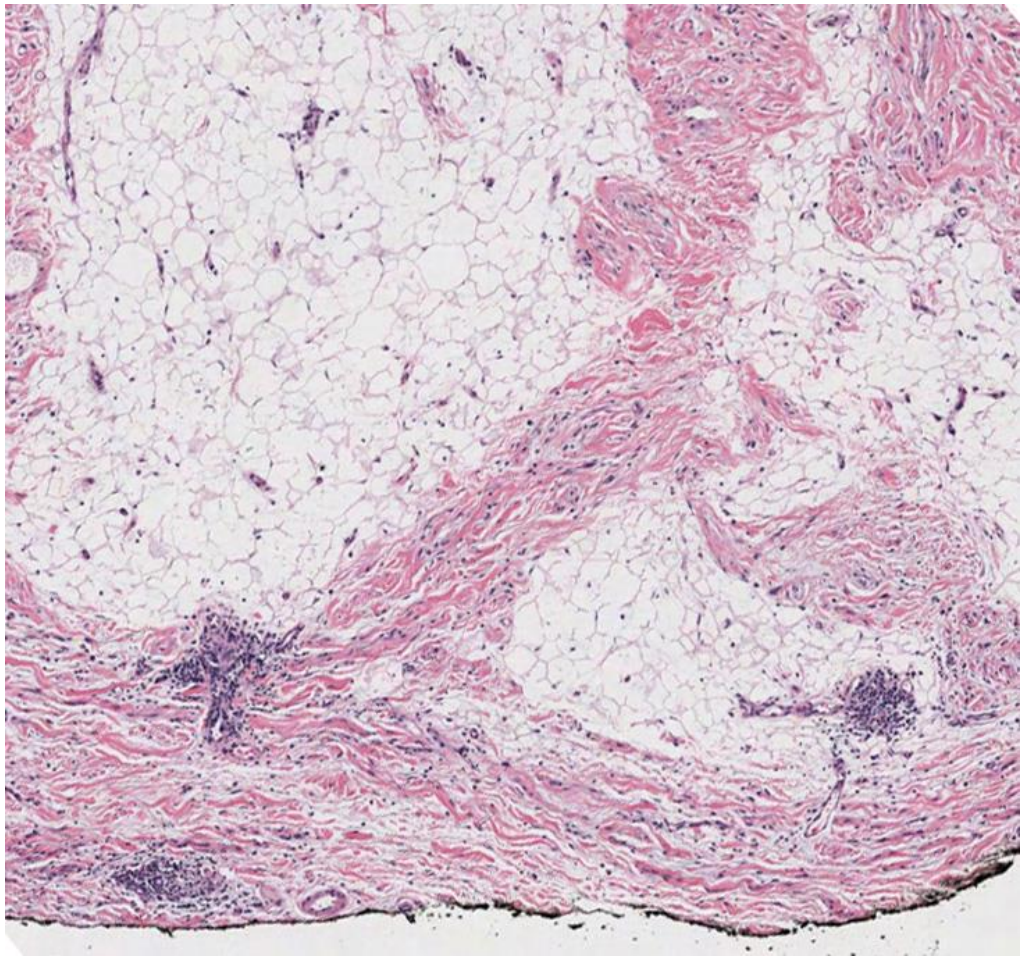




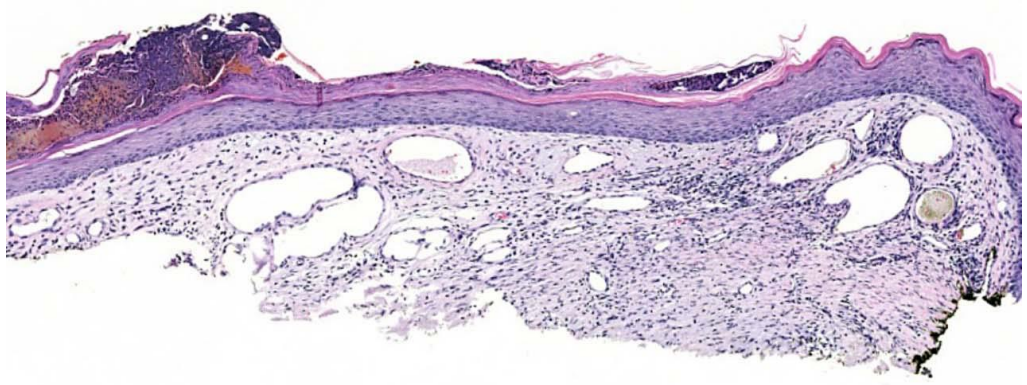
Tumor

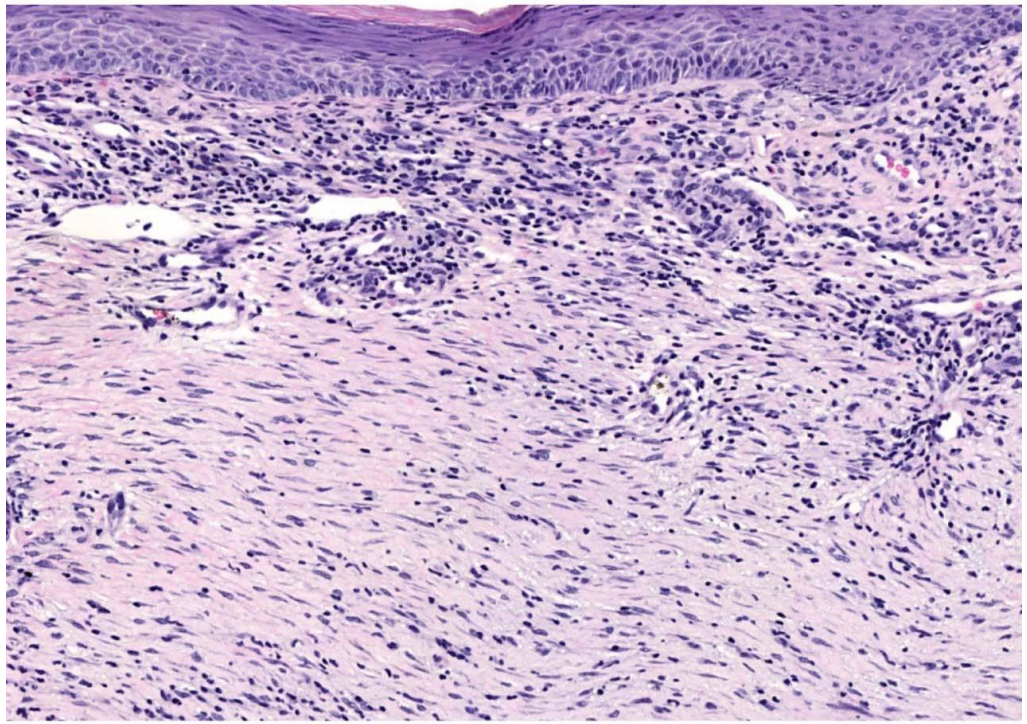
Desmoplastic Melanoma



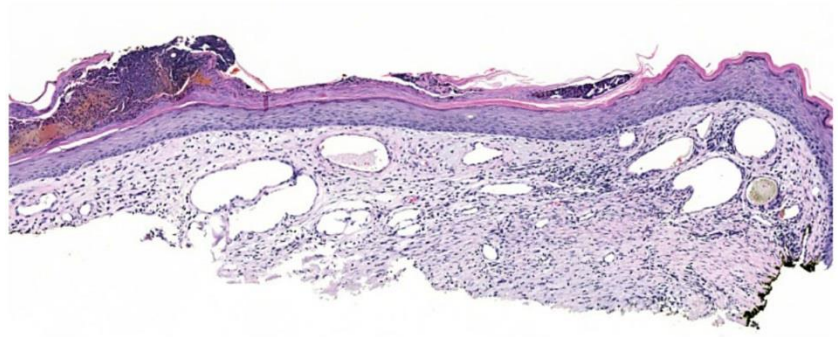
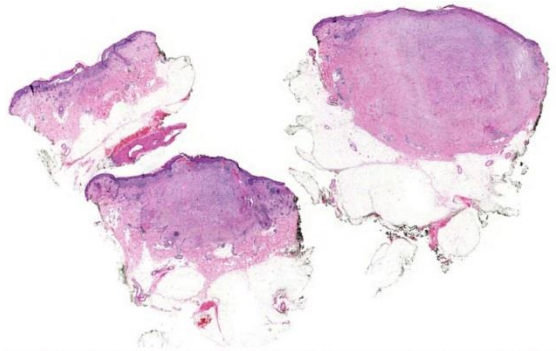
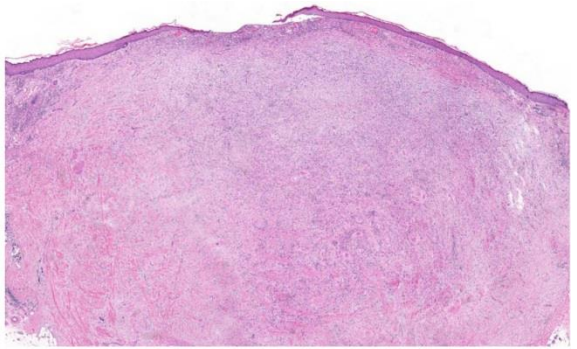
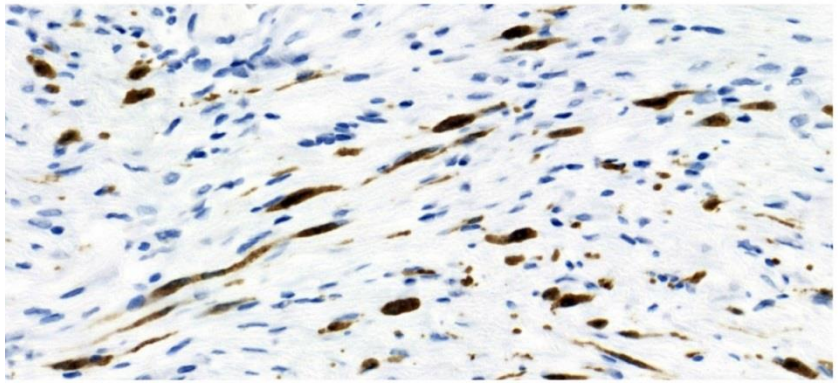
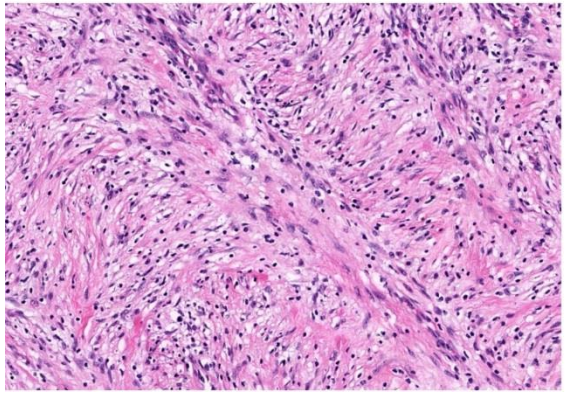
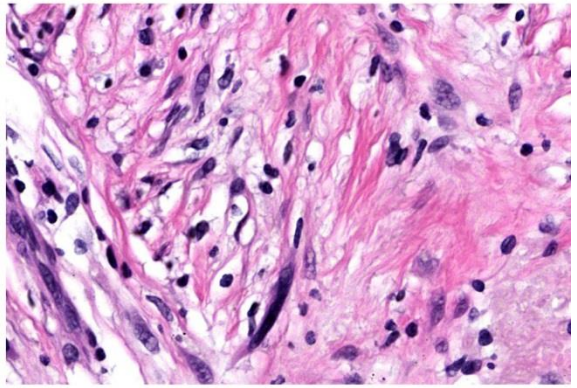


DM –Confusion with a scar



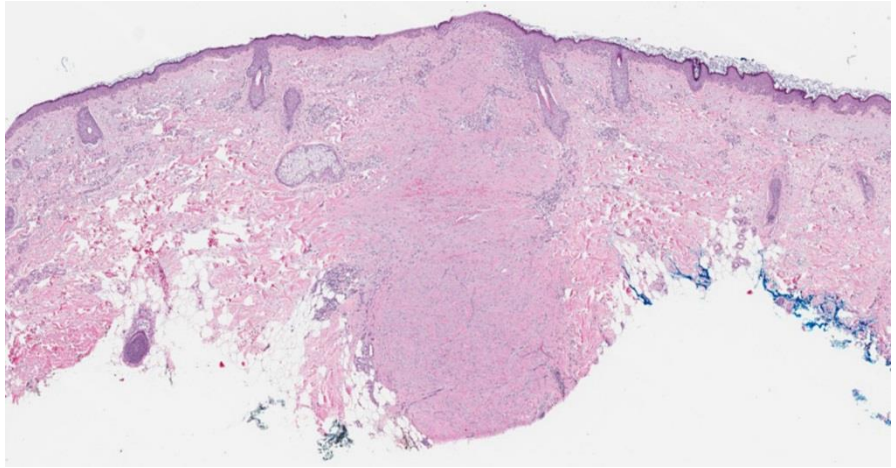


Desmoplastic Melanoma

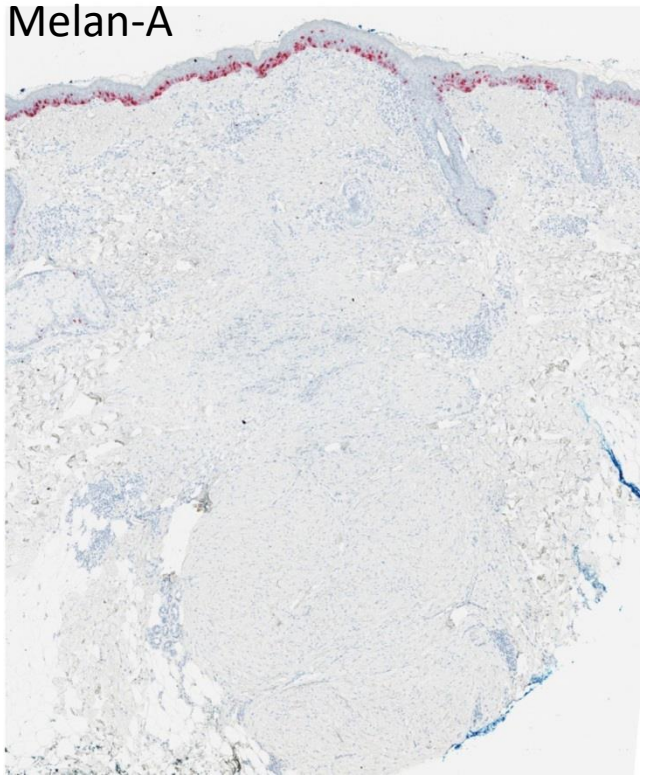







What is Your Diagnosis?

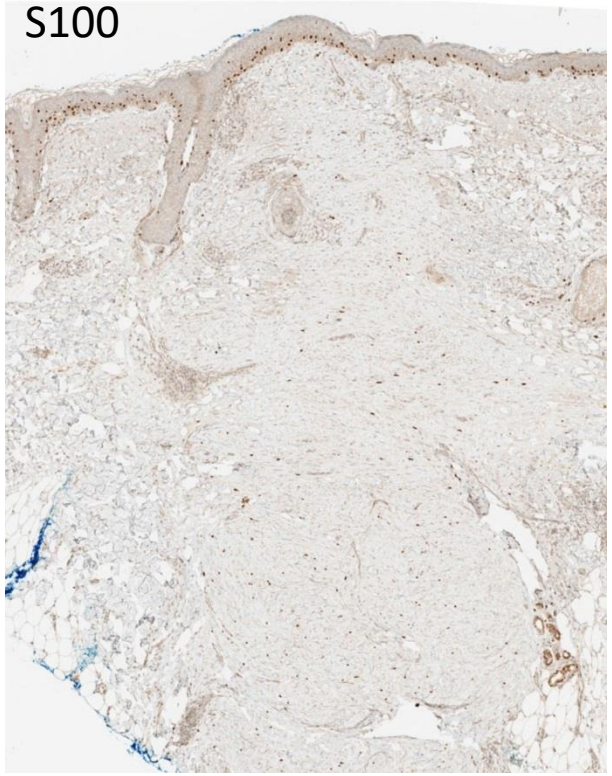
Re-excision for melanoma in situ



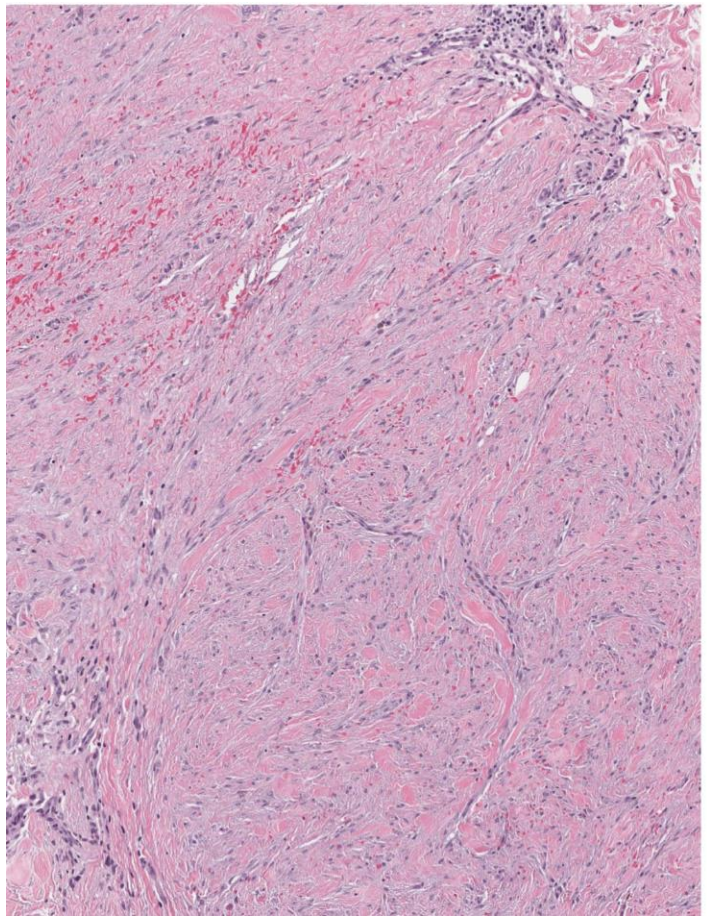
Melan-A



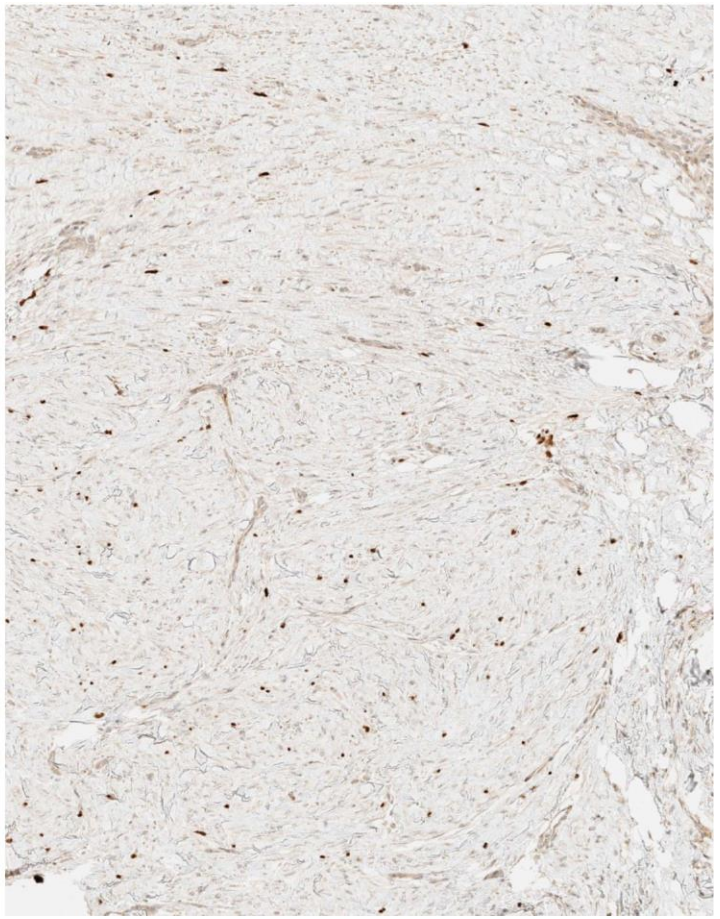
S100



What is Your Diagnosis?



Sox10



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

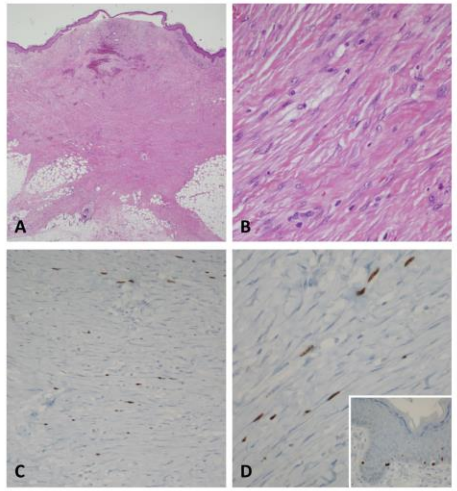


Fig. 1 (A) Low power view of scar (H&E). (B) High power view of scar (H&E). (C) High power view of scar showing distribution of sparse SOX10 positive cells (SOX10). (D) High power view of SOX10 positive cells. The SOX10 positive cells probably represent schwannian cells (SOX10). Inset: Basal melanocytes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

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

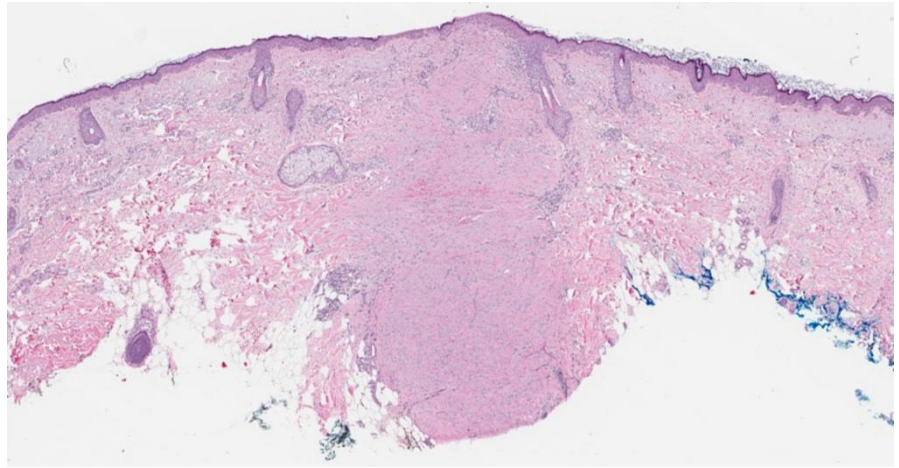
The American Journal of Dermatopathology *24(4): 309–312, 2002*

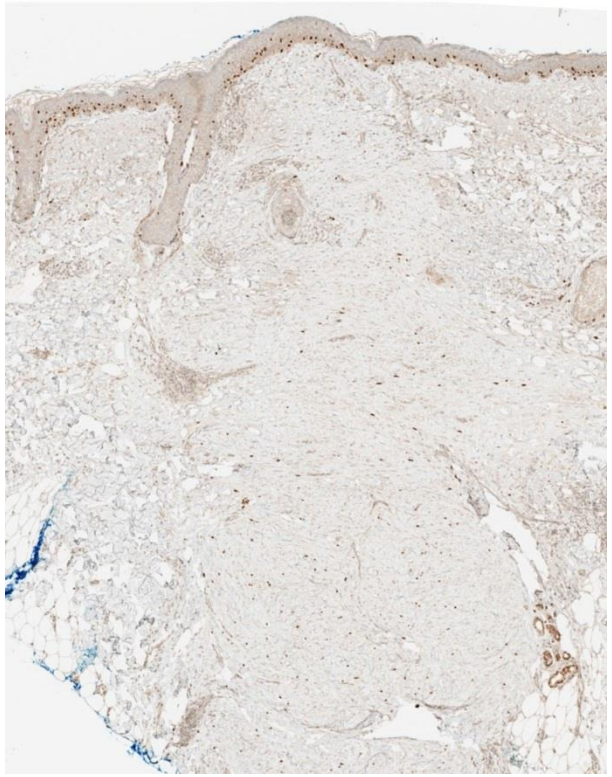
S100-Positive Spindle Cells in Scars

A Diagnostic Pitfall in the Re-Excision of Desmoplastic Melanoma

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

Scar with Sox10/S100-positive cells – not DM





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 vs Nerve Sheath Tumors

- Neurofibroma
- Schwannoma
- Hybrid Nerve Sheath Tumor

Neurofibroma vs Melanoma

- Histologic Clues for NF-like Melanoma
  - Atypical junctional melanocytic proliferation
  - Lymphoid aggregates
  - Fascicles of spindle cells
  - Nuclear atypia
  - Deep infiltrative growth
  - Involvement of papillary dermis

- Beware of collision scenarios
  - Nevus or melanoma colliding with a neurofibroma

DM vs Desmoplastic Nevus

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

Findings favoring a desmoplastic nevus

- Clinical
  - Small papule, younger individual, sun-protected site
- Histopathology
  - Small, symmetric, with evidence of maturation
  - Cytology
- Ancillary Studies
  - IHC: Melan-A, p16
  - Molecular: mutation profile

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.

DM – Clinical Behavior

- Local persistence/recurrence more common
- Regional node metastasis less common
- Survival advantage among thick melanomas

DM – Local Recurrence

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

Desmoplastic Melanoma: SLN Biopsy

Excerpta Medica

The American Journal of Surgery

The American Journal of Surgery 182 (2001) 590–595
Scientific paper

The clinical behavior of desmoplastic melanoma

Dawn E. Jaroszewski, M.D.[a], Barbara A. Pockaj, M.D.[a,*], David J. DiCaudo, M.D.[a], Uldis Bite, M.D.[b]

[a]*Department of General Surgery, Mayo Clinic Scottsdale, 13400 E. Shea Blvd., Scottsdale, AZ 85259, USA*
[b]*Mayo Clinic Rochester, Rochester, MN, USA*

Manuscript received July 31, 2001; revised manuscript September 24, 2001
Presented at the 53rd Annual Meeting of the Southwestern Surgical Congress, Cancun, Mexico, April 29–May 2, 2001.

- 12 patients with desmoplastic melanoma
- SLN biopsies negative

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

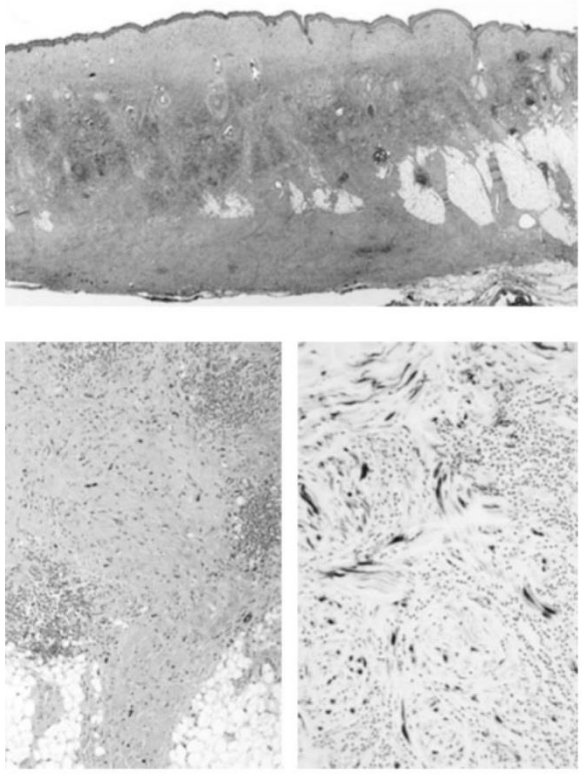


FIG. 1. Desmoplastic melanoma. (**A**) Scanning magnification shows a fibrosing tumor infiltrating the dermis and subcutis. (**B**) The tumor is composed of hyperchromatic spindle cells in a collagen-rich stroma and is focally associated with lymphoid aggregates. (**C**) The tumor cells are homogenously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

Lyndon D. Su, M.D.[1,2]
Douglas R. Fullen, M.D.[1,2]
Lori Lowe, M.D.[1,2]
Timothy S. Wang, M.D.[2]
Jennifer L. Schwartz, M.D.[2]
Vincent M. Cimmino, M.D.[3]
Vernon K. Sondak, M.D.[3]
Timothy M. Johnson, M.D.[2–4]

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[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…

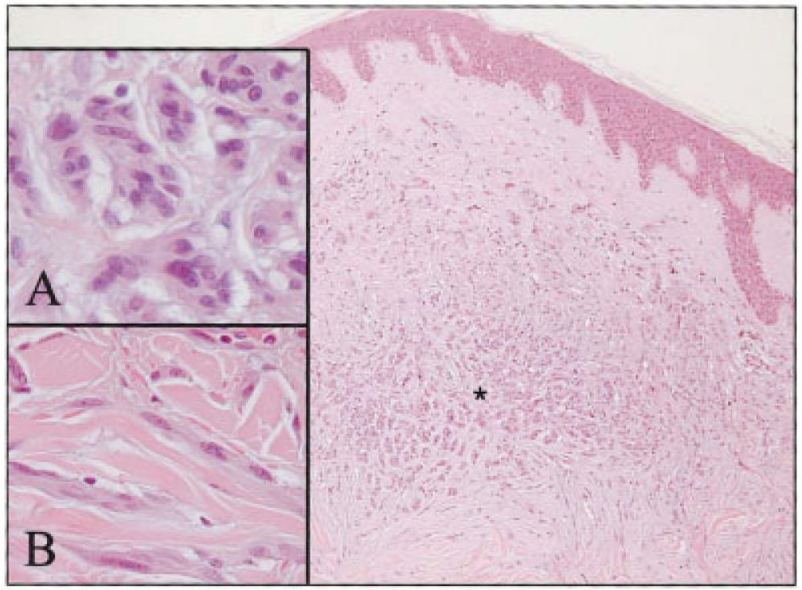


FIGURE 5. Desmoplastic and neurotropic melanoma from Patient 3 showed a small population of conventional epithelioid melanoma cells (asterisk and *inset A*) in the upper part of the tumor and atypical spindle cells invading the deep dermis accompanied by prominent desmoplasia (*inset B*).

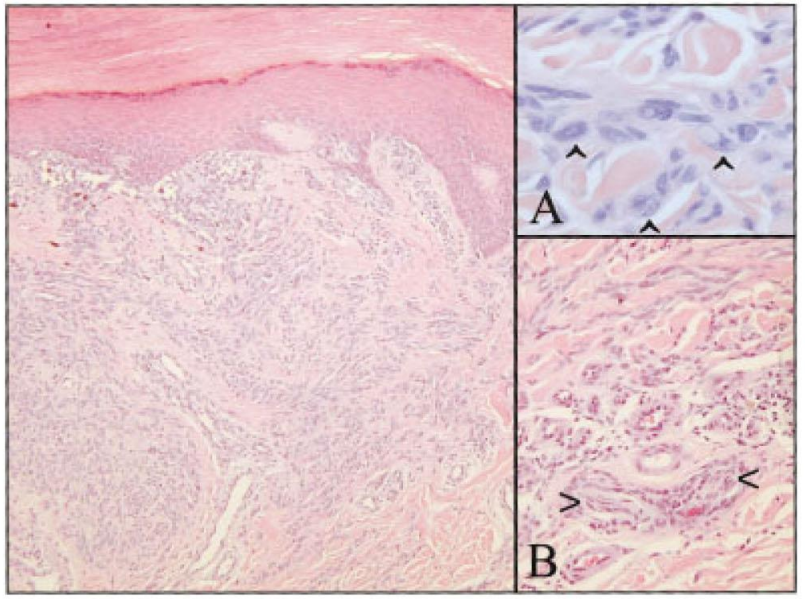
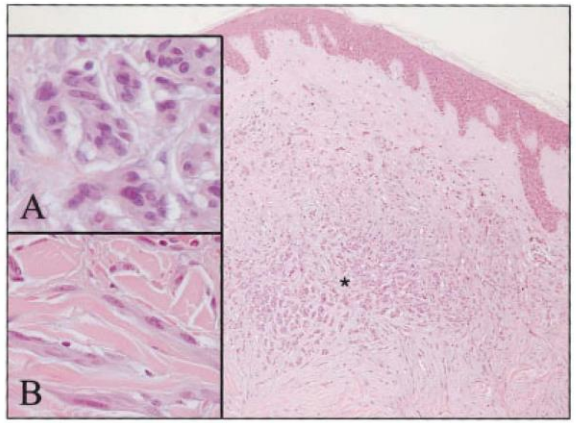


FIGURE 6. Desmoplastic and neurotropic melanoma arising in acral lentiginous melanoma from the foot of Patient 4 showed highly atypical spindle melanocytes infiltrating the dermis (arrowheads in inset A). Tumor cells displayed neurotropism surrounding and invading nerve twigs in deep dermis (arrowheads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

Metastases with Melan-A-positive epithelioid cells



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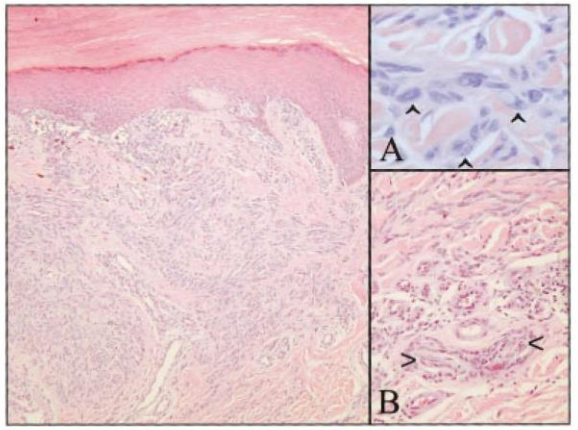


FIGURE 6. Desmoplastic and neurotropic melanoma arising in acral lentiginous melanoma from the foot of Patient 4 showed highly atypical spindle melanocytes infiltrating the dermis (arrowheads in inset A). Tumor cells displayed neurotropism surrounding and invading nerve twigs in deep dermis (arrowheads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

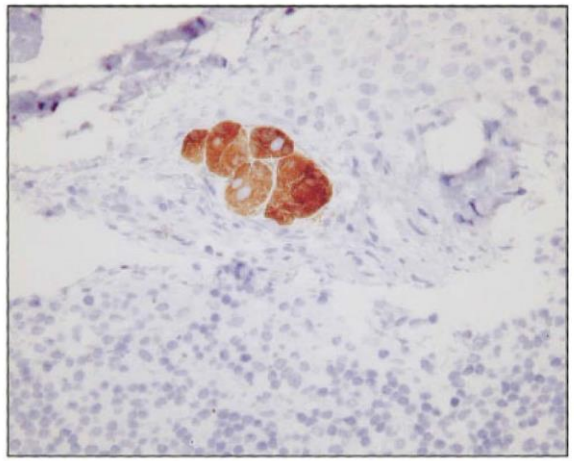


FIGURE 7. One of a few clusters of metastatic epithelioid melanoma in the lymph node parenchyma from Patient 3 was found to express melan-A.

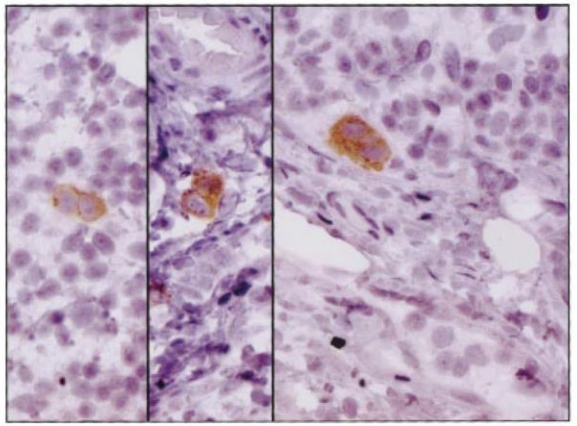
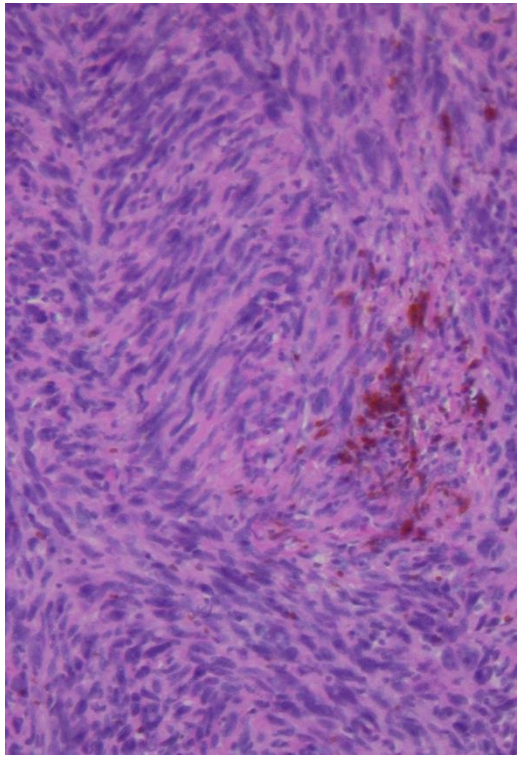
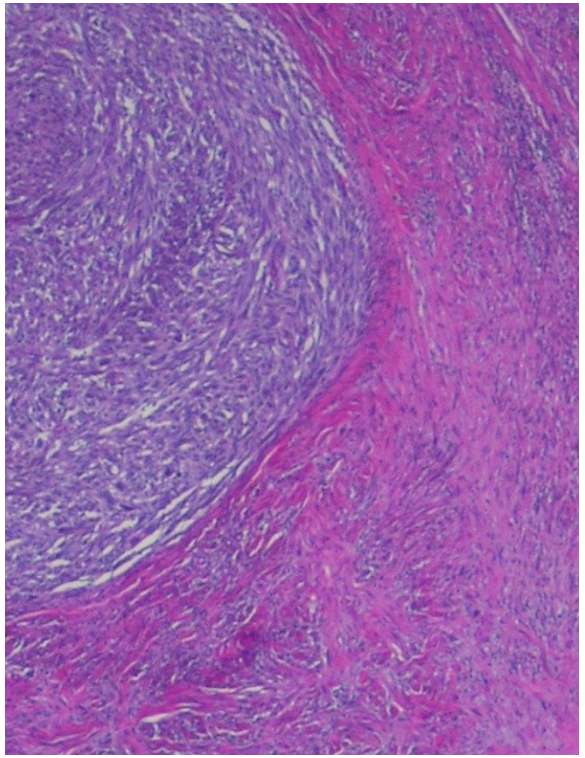


FIGURE 8. In the sentinel lymph node from Patient 4, a few clusters of melan-A positive, atypical epithelioid cells were identified in the parenchyma and peritrabecular areas, consistent with metastatic melanoma.

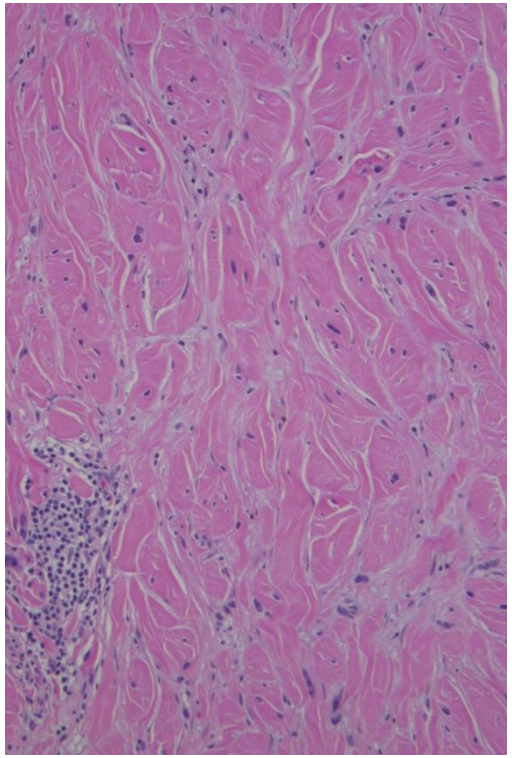
Pure vs mixed vs non-desmoplastic Melanoma



Solid spindle cell

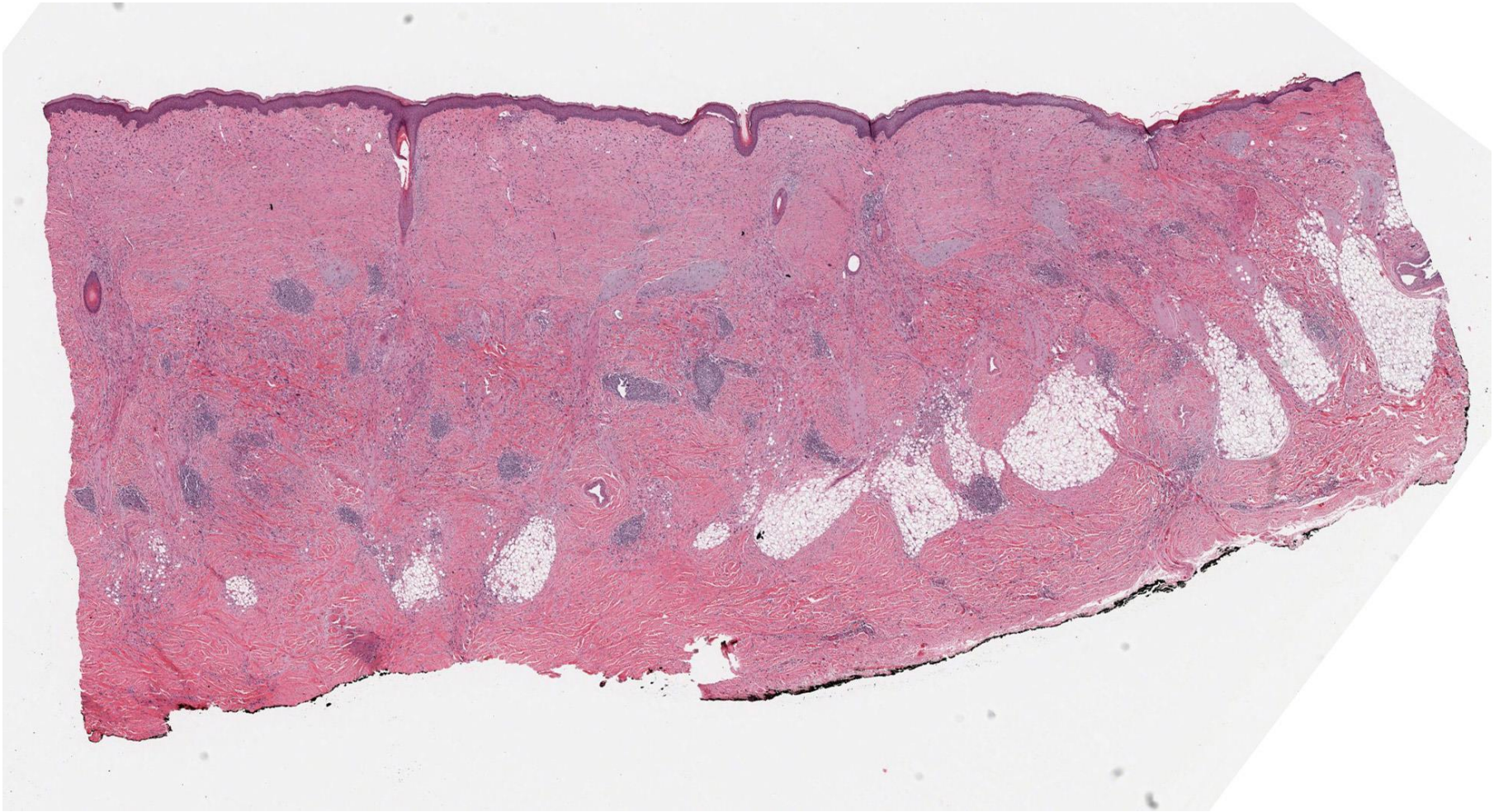


Combined (mixed) DM

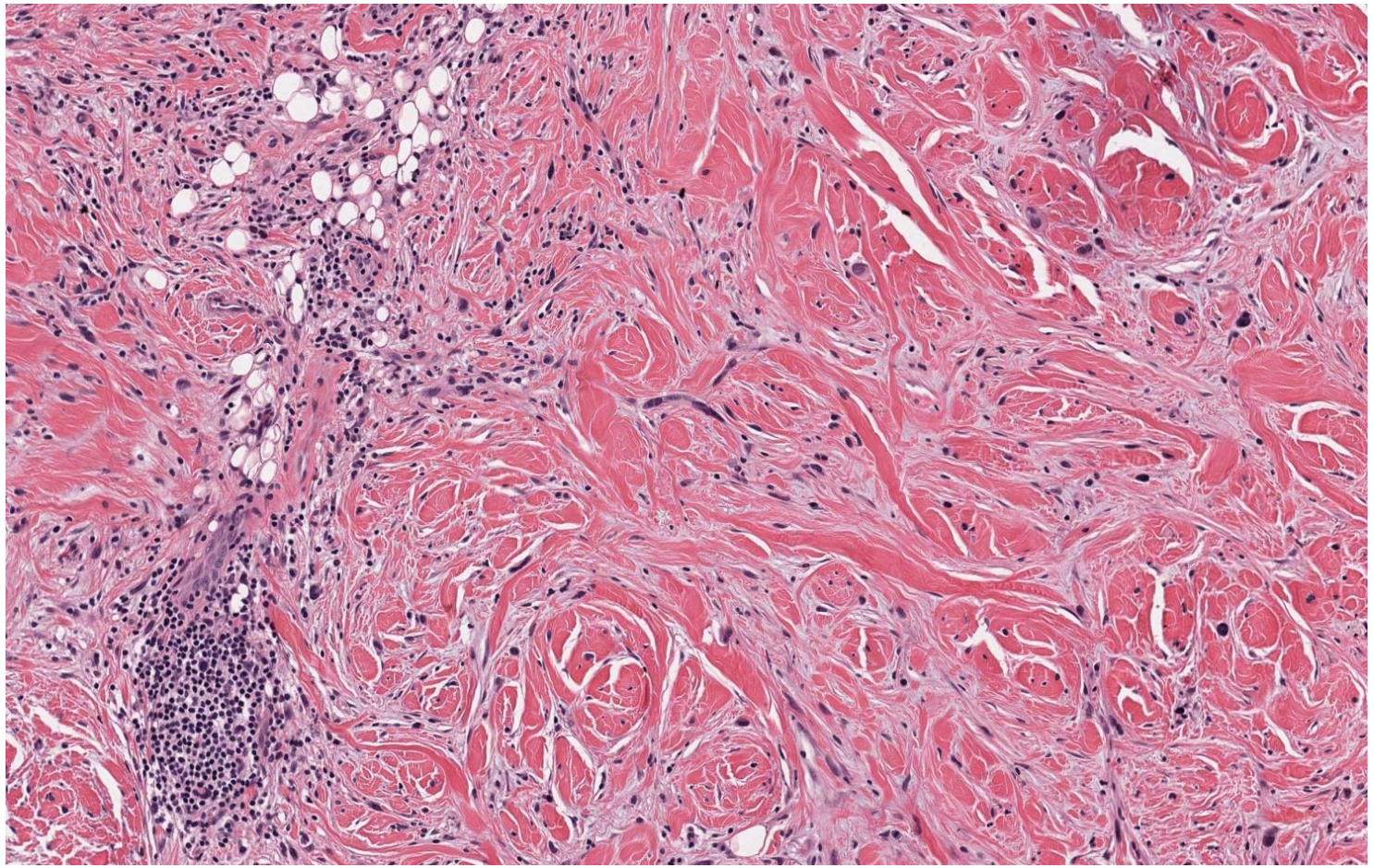


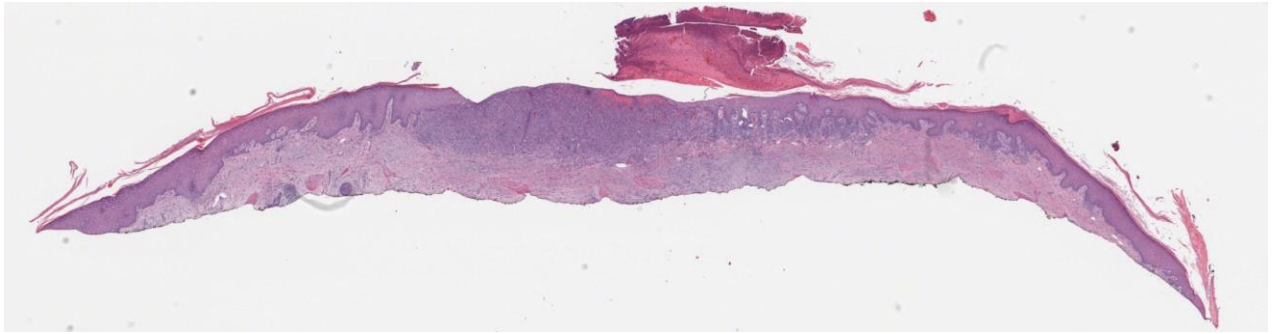
Pure DM

Pure Desmoplastic Melanoma

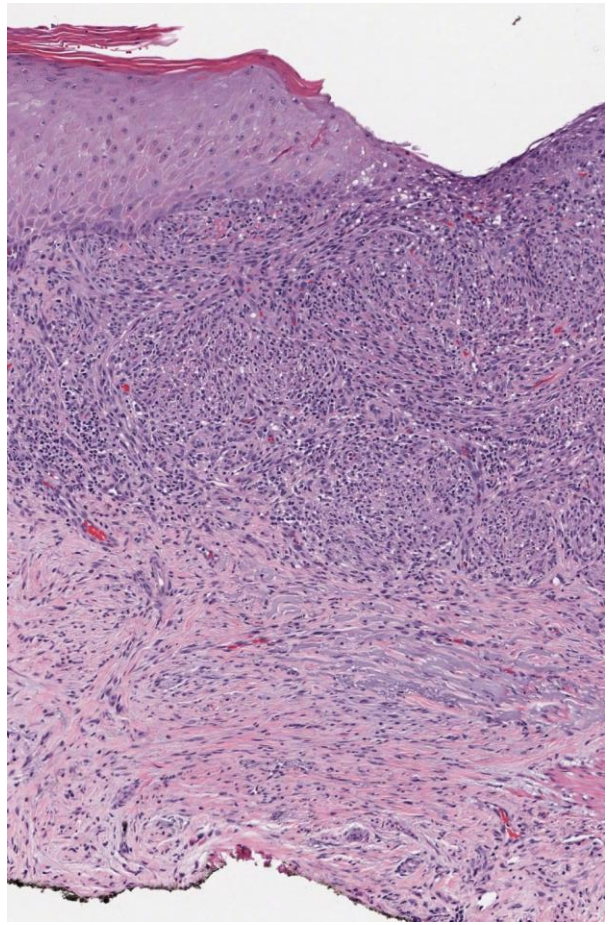


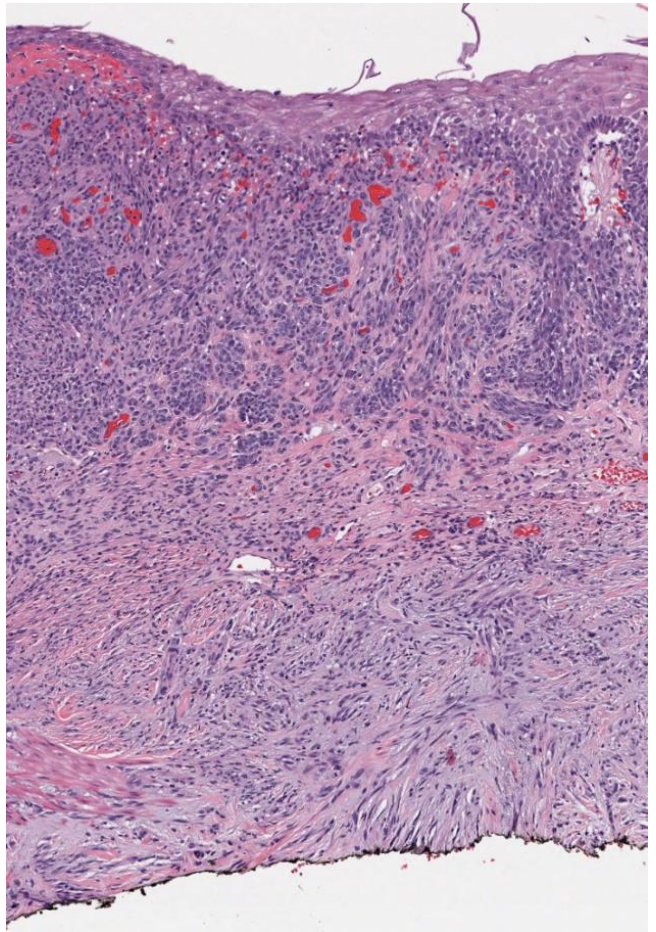
Pure Desmoplastic Melanoma





Mixed Desmoplastic Melanoma

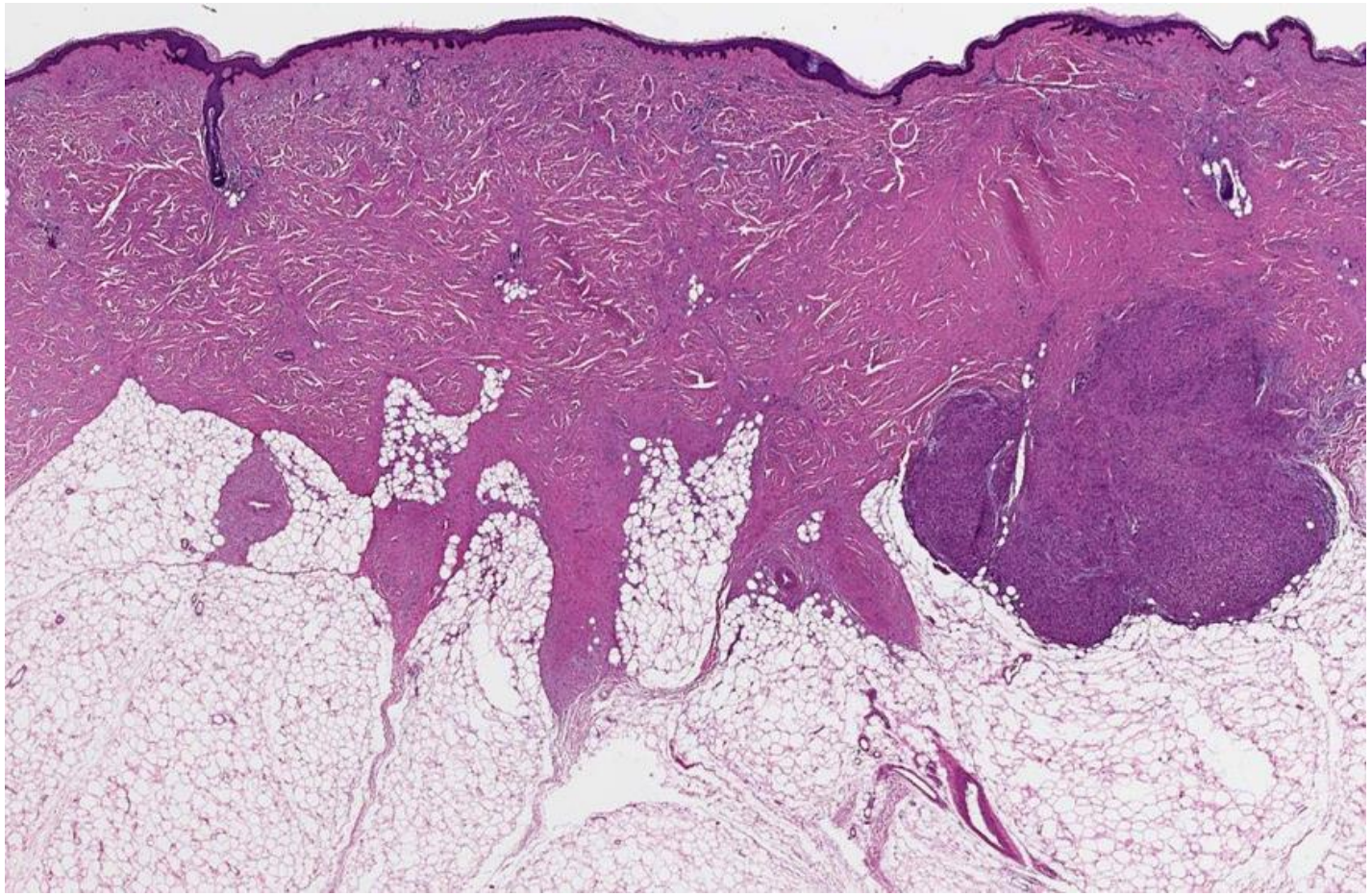




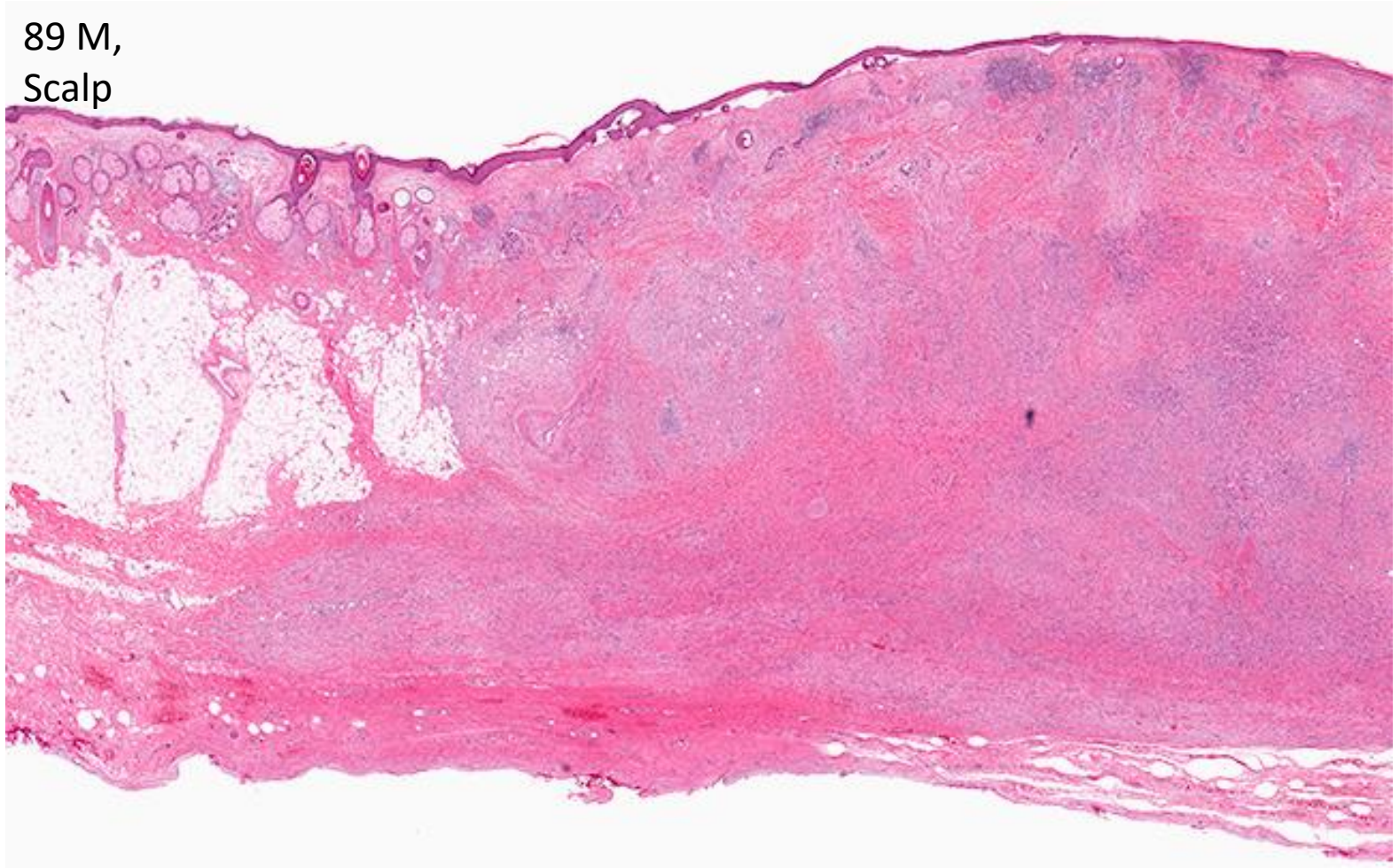
Non-desmoplastic

Desmoplastic

Mixed Desmoplastic Melanoma

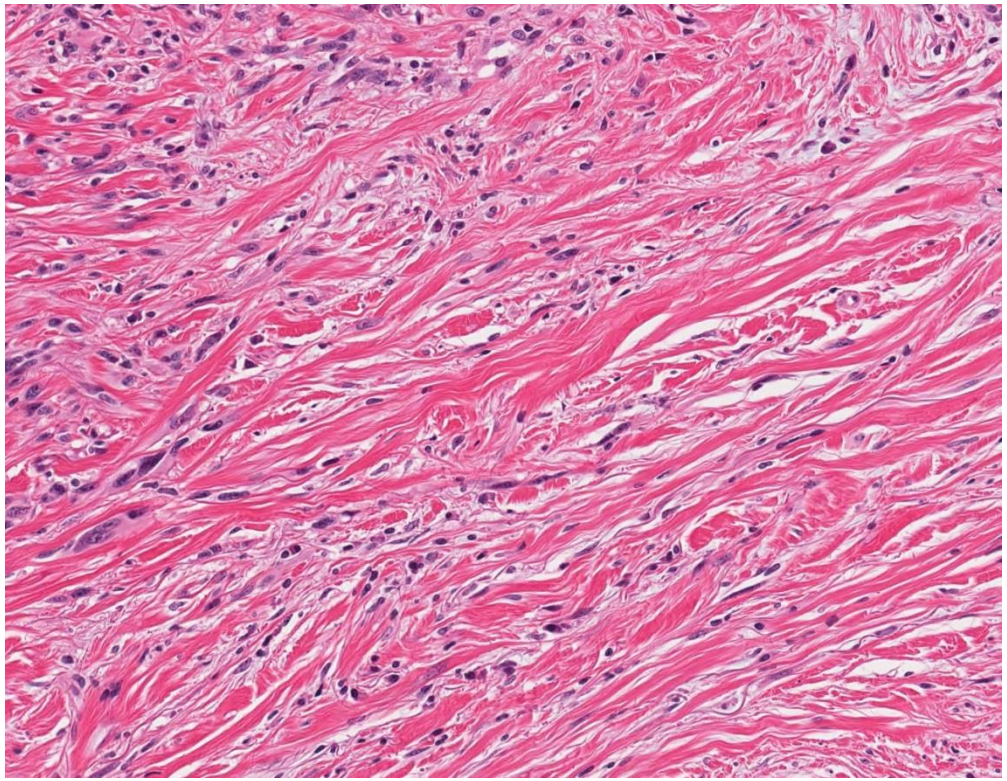


Mixed Desmoplastic Melanoma



Mixed Desmoplastic Melanoma

Cell-poor stroma-rich



Cell-rich stroma-poor

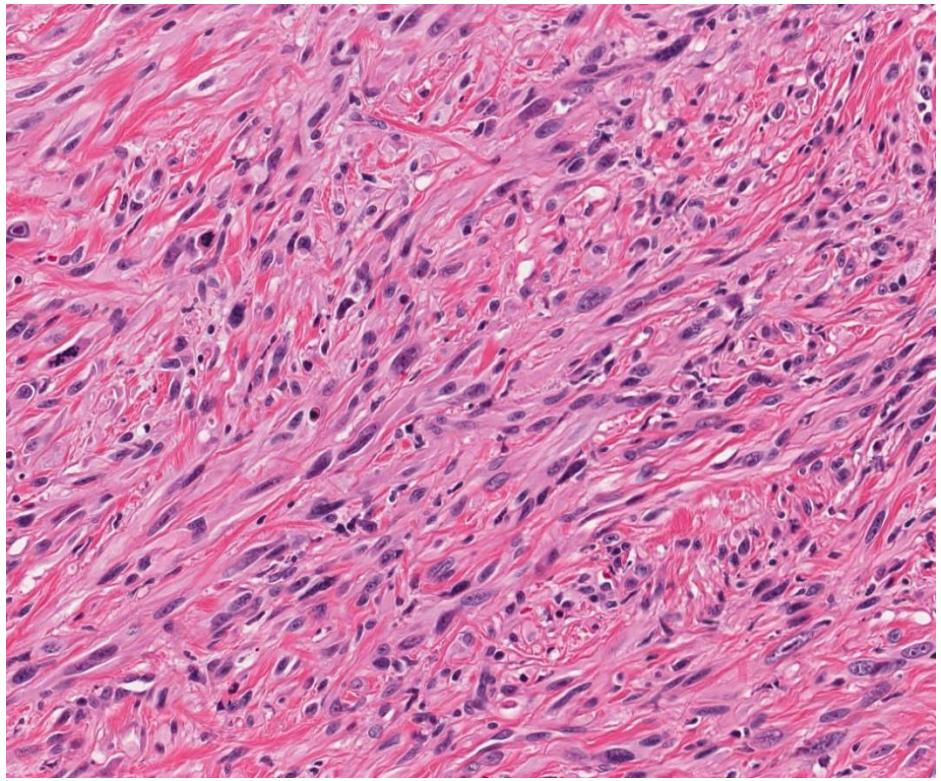


Table 2 SLNB outcomes for included studies.

	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"

Check for updates

Received: 14 April 2023 | Revised: 18 September 2023 | Accepted: 24 September 2023

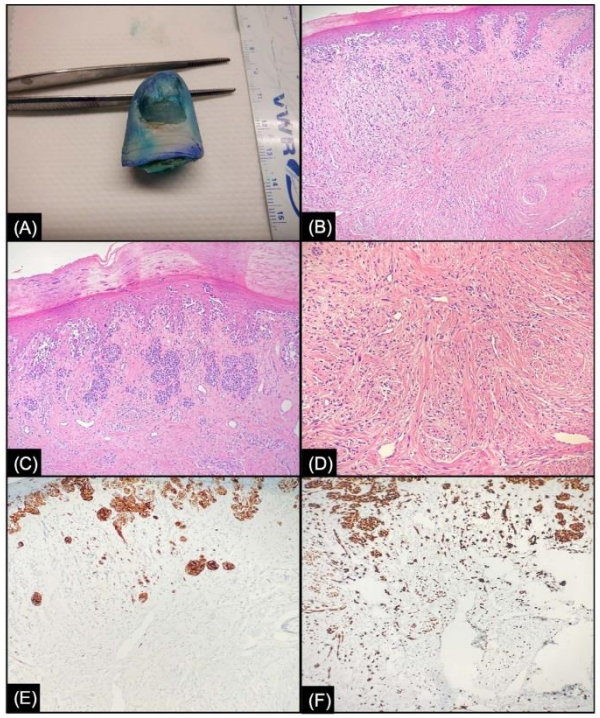
DOI: 10.1111/cup.14542

CASE STUDY

JCP JOURNAL OF CUTANEOUS PATHOLOGY WILEY

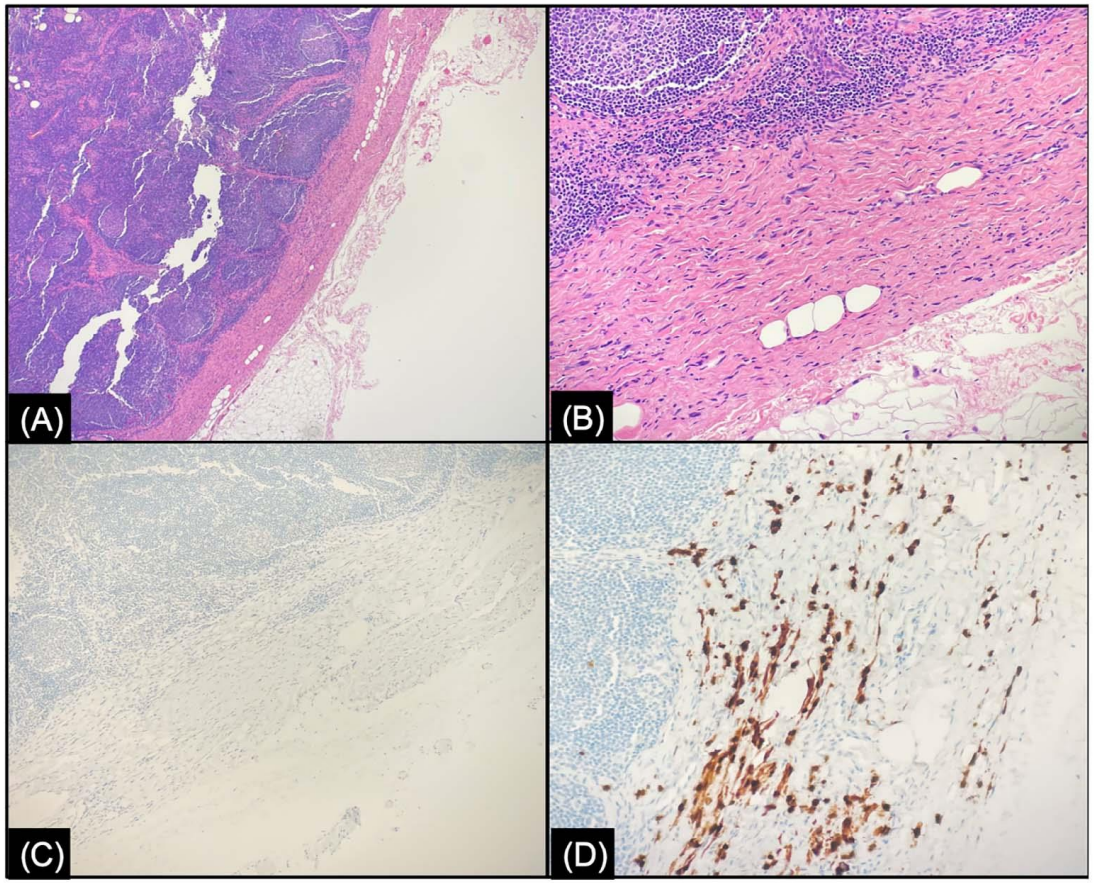
The utility of SOX10 in mixed type desmoplastic melanoma with lymph node metastasis of the spindle cell component: A cautionary tale of inattentional blindness

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

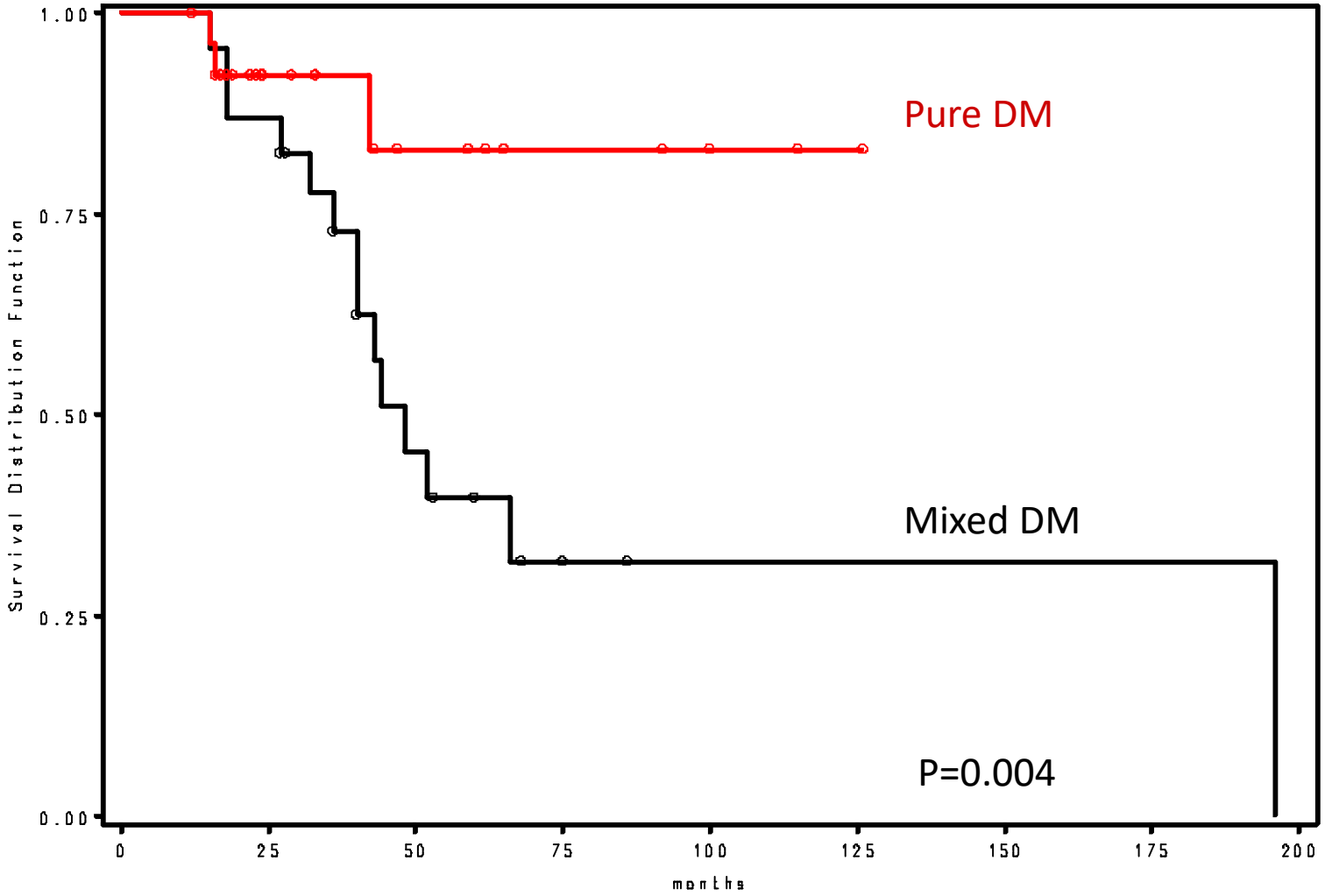


CAUTION!

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.15759 JEADV

ORIGINAL ARTICLE

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

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[1]Victorian Melanoma Service, Alfred Hospital, Melbourne, Vic., Australia
[2]School of Public Health and Preventive Medicine, Monash University, Melbourne, Vic., Australia
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*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”

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

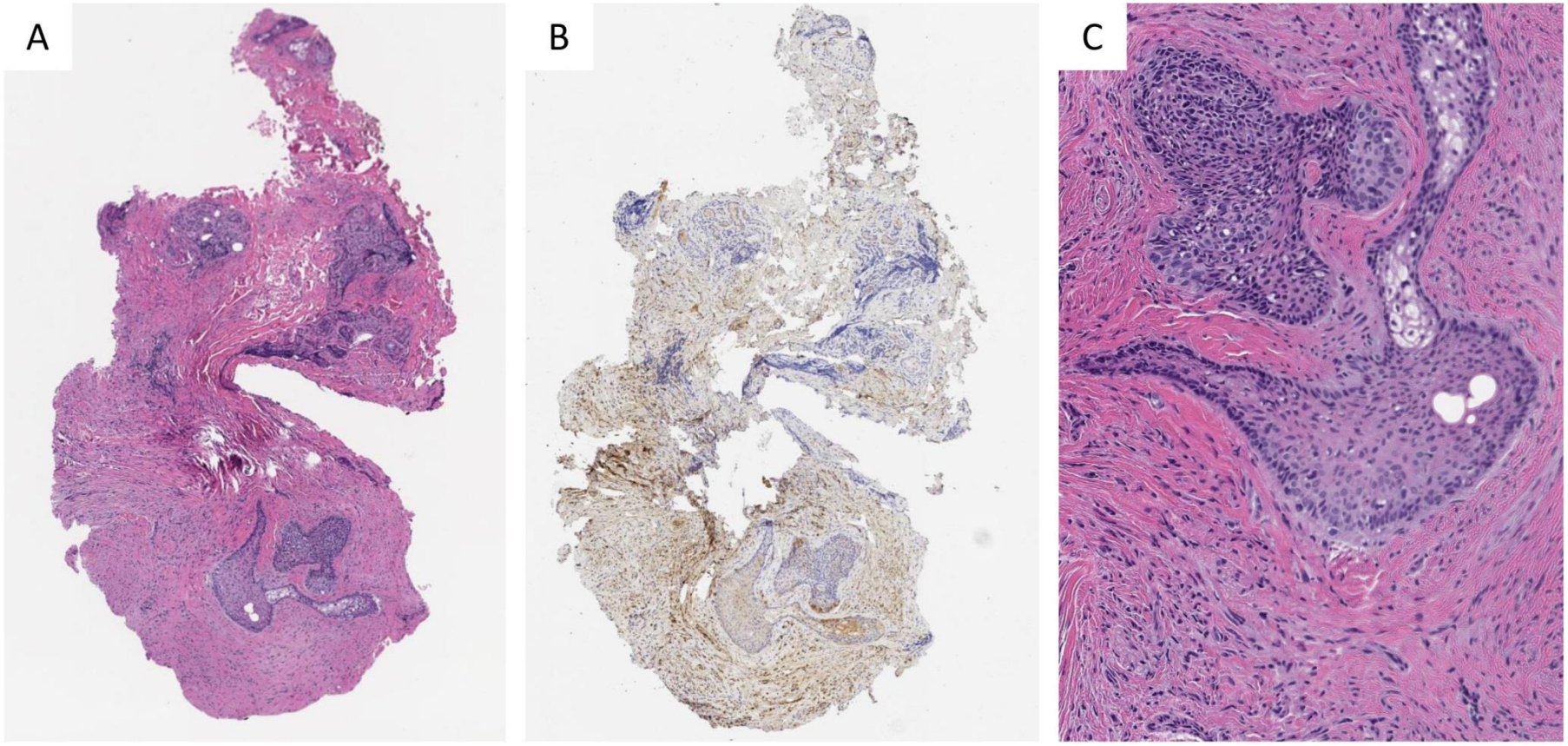
MELANOCYTIC TUMOUR PATHOLOGY

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]

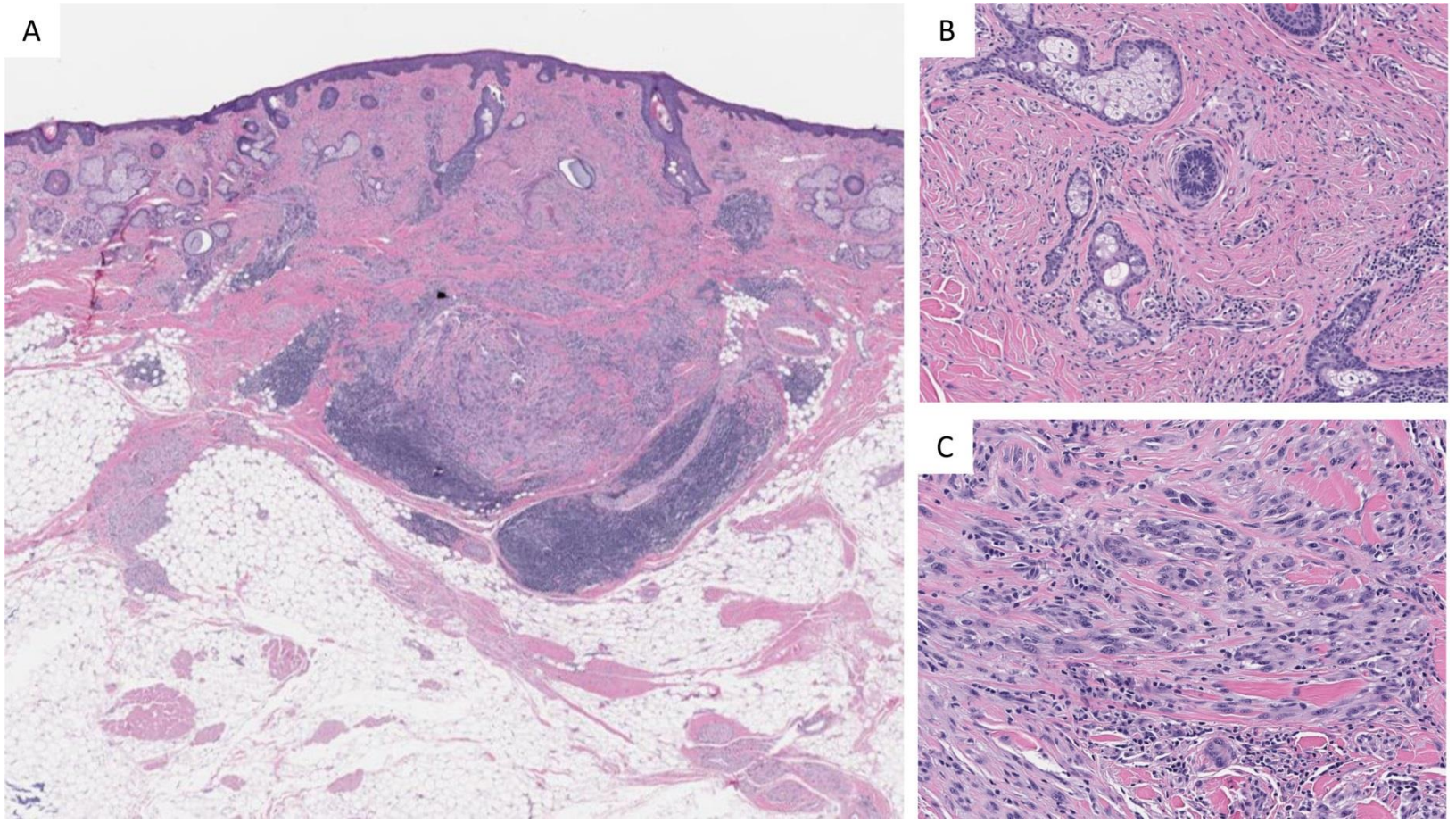
- 91/101: Biopsy and excision concordant for pure DM
- 10/101: Changed to mixed DM upon review of excision

What is your diagnosis?



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

Mixed Desmoplastic Melanoma



CANCER DISCOVERY

News in Brief

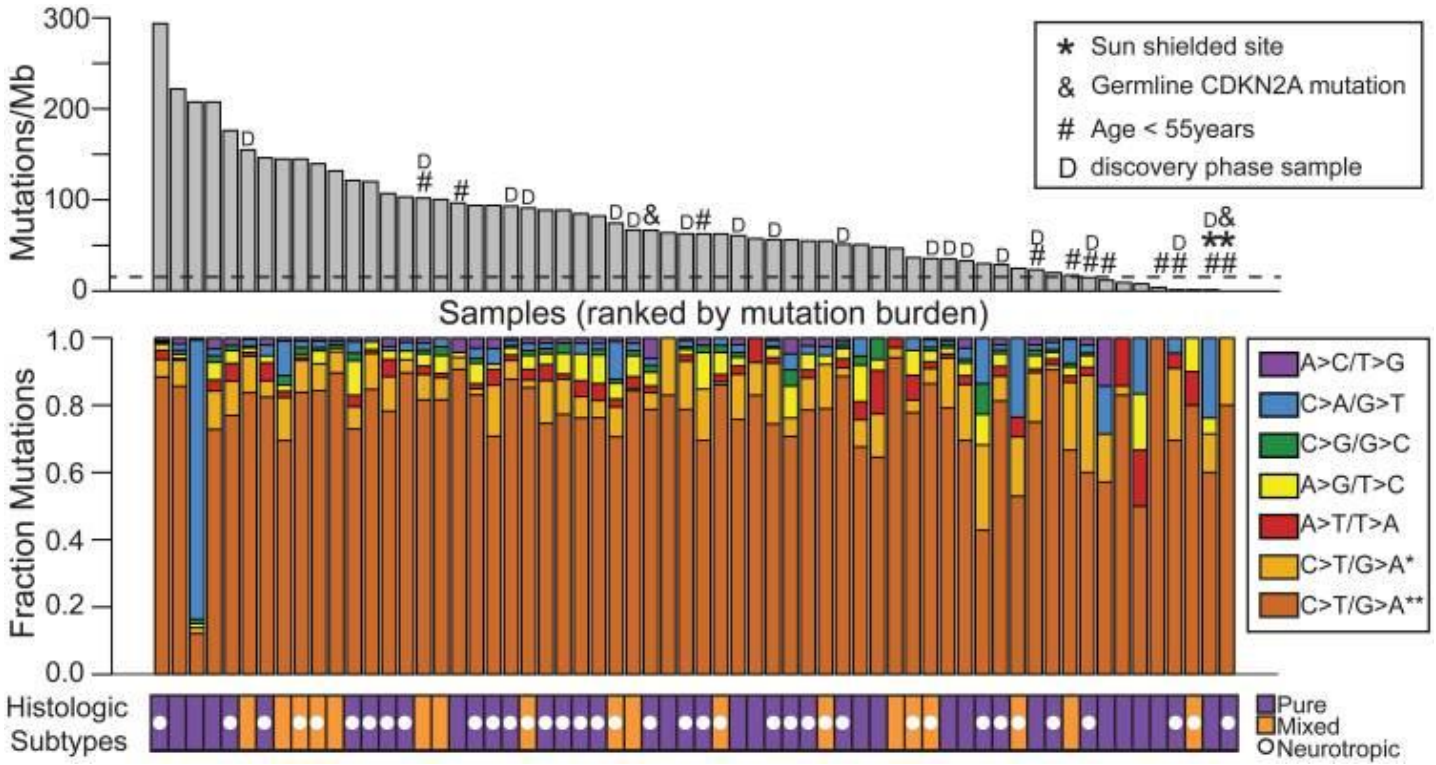
Desmoplastic Melanoma Carries High Mutation Burden

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]



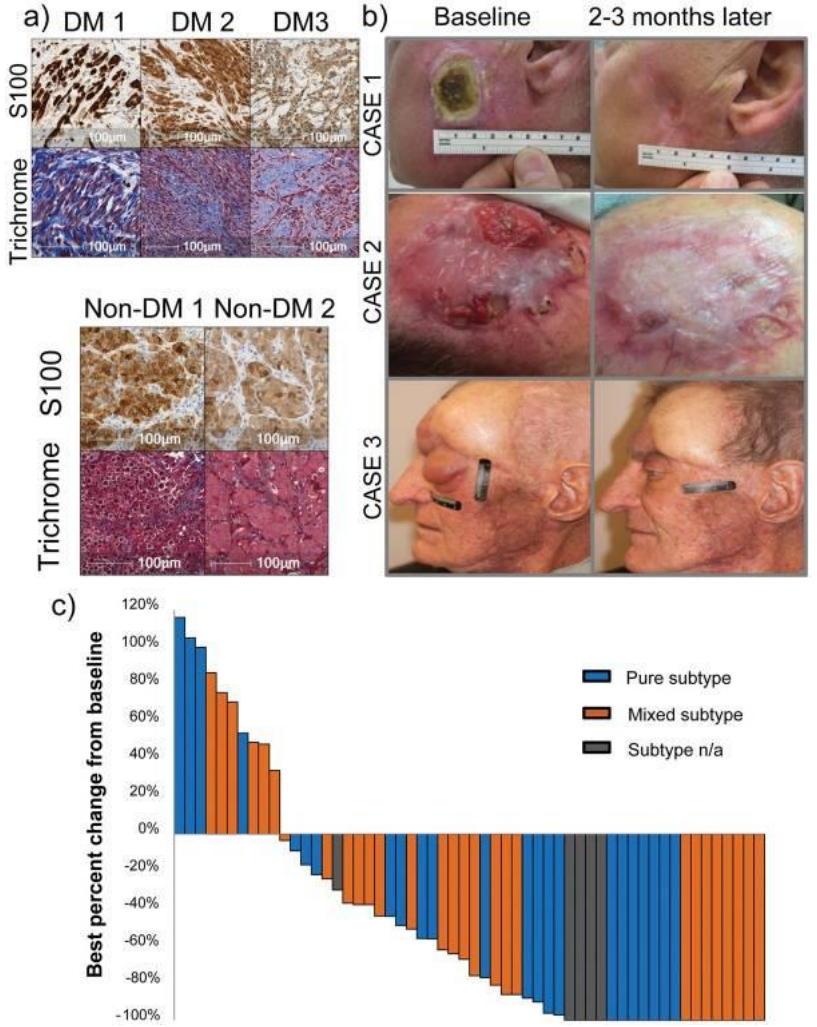
LETTER

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



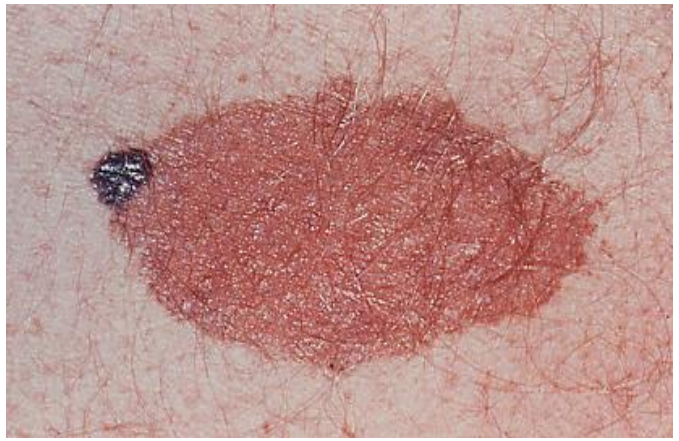
Nature 2018; 553: 347 - 350

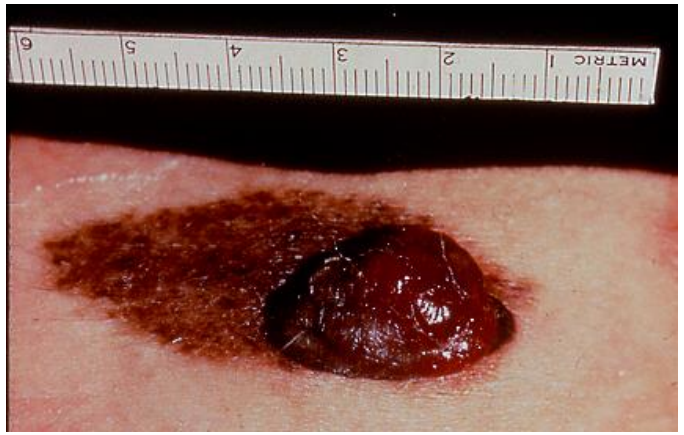

THE BAKERY TABLE
HOME MADE
AT HACKLEBARNEY FARM
PIES
ORDERS TAKEN
fresh pies baked daily

IV: Melanoma associated with congenital nevi

- Risk for melanoma: approx 1%
- Risk for melanoma in giant congenital nevus: 10 %

Melanoma of small/medium congenital nevus

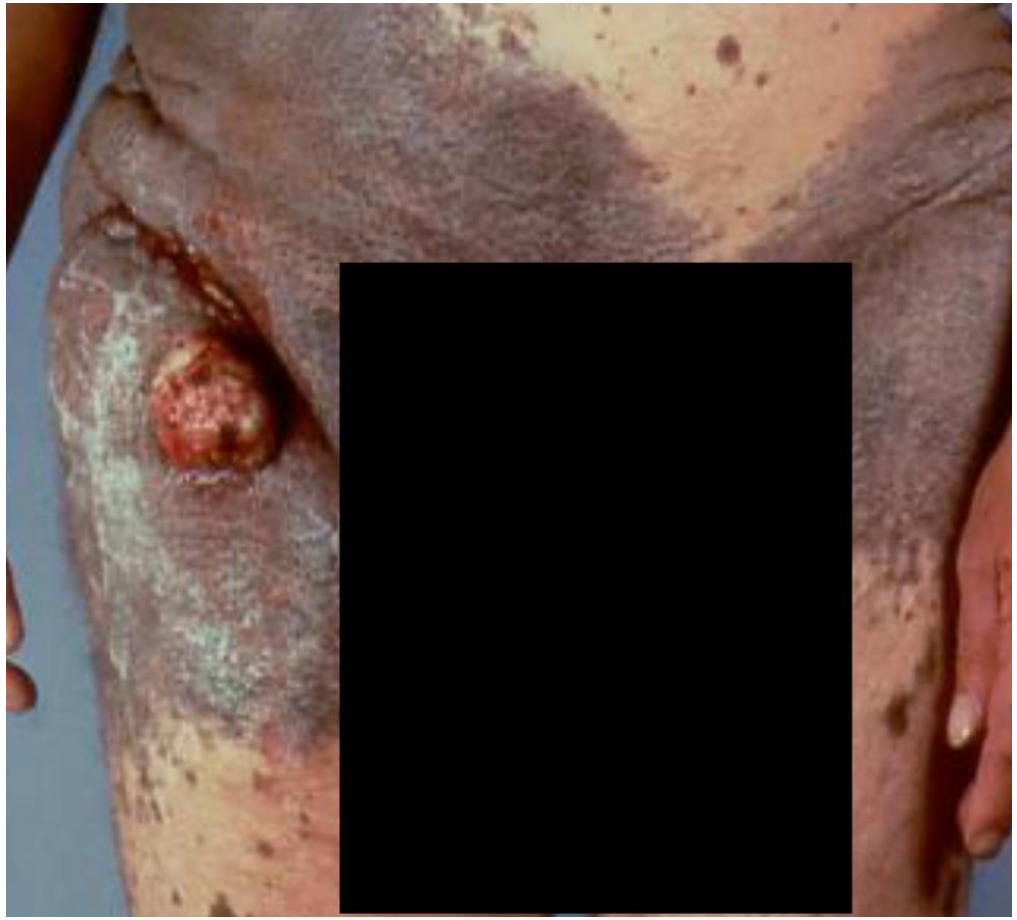




- Usually after puberty
- Often at edge of CMN
- Usually a/w melanoma in situ

Betti et al. J of Dermatol 2000;27:583-590 (mean age when MM develop = 41)

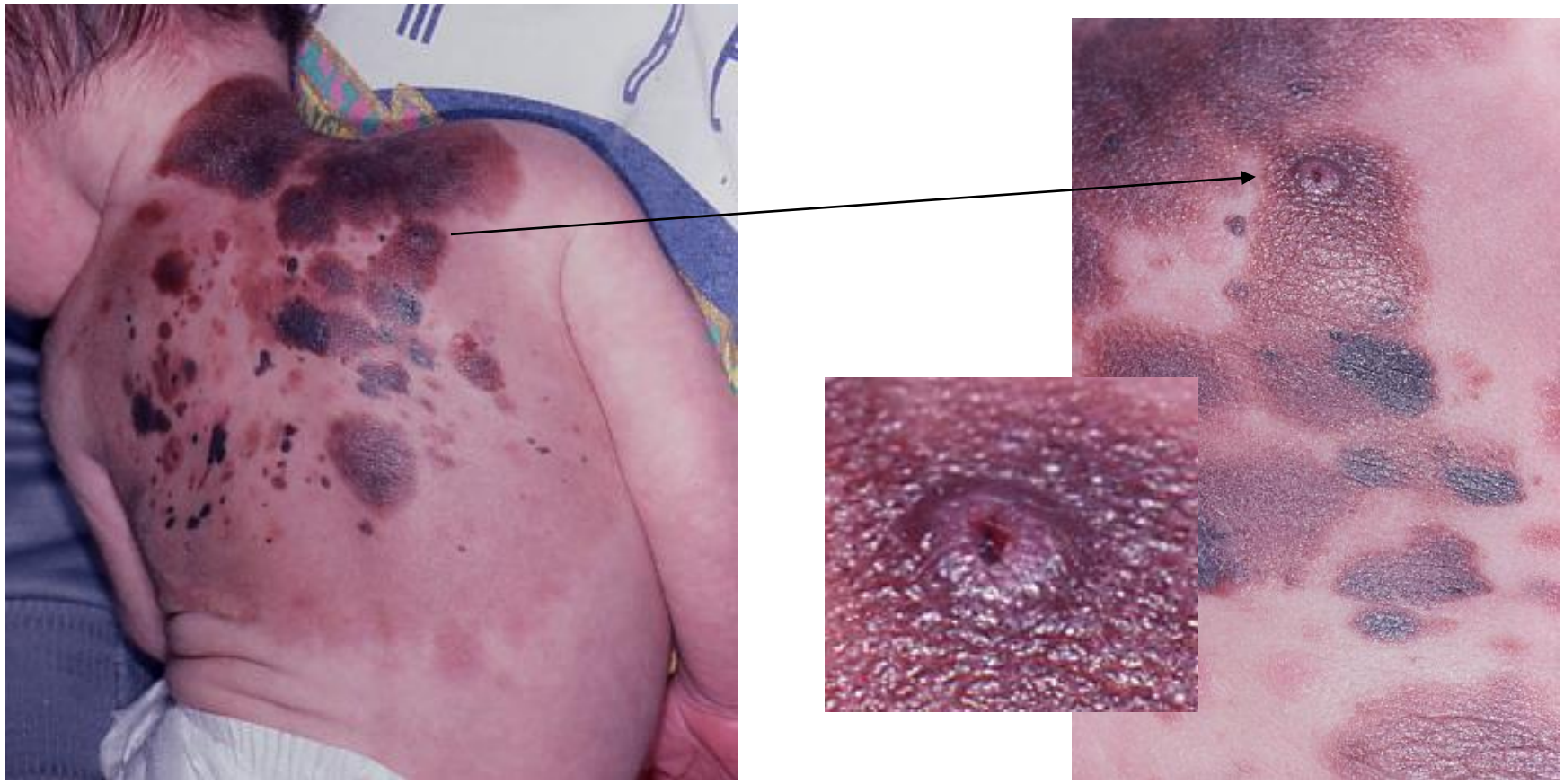
Melanoma of giant congenital nevus



- Often large
- Typically unassociated with epithelia (no melanoma in situ)

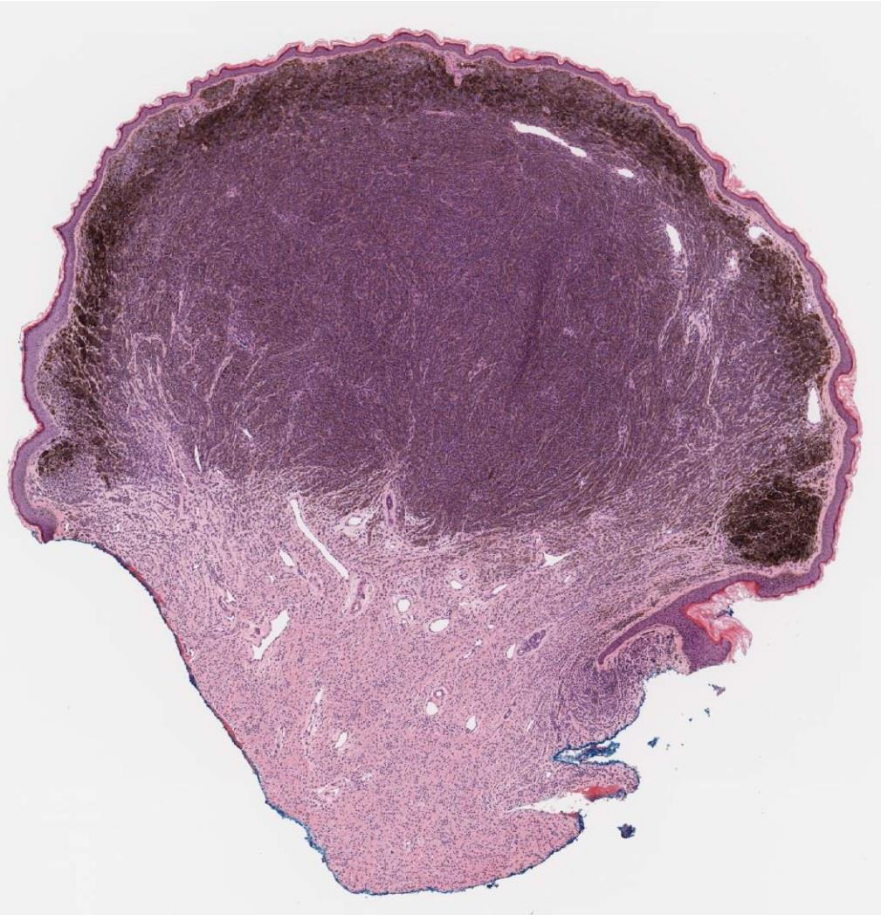
Diagnostic Challenge: Proliferative Nodules

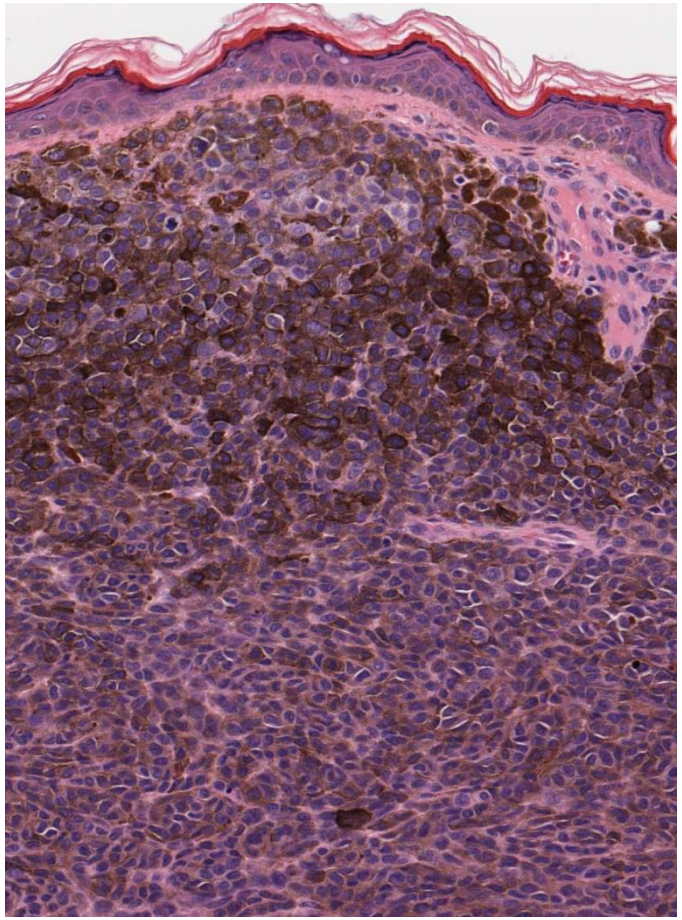
- Often appear in the neonatal period
- They can be large & atypical



Kerl et al. Mel Res 2001;11:S56)

Benign Proliferative Nodule

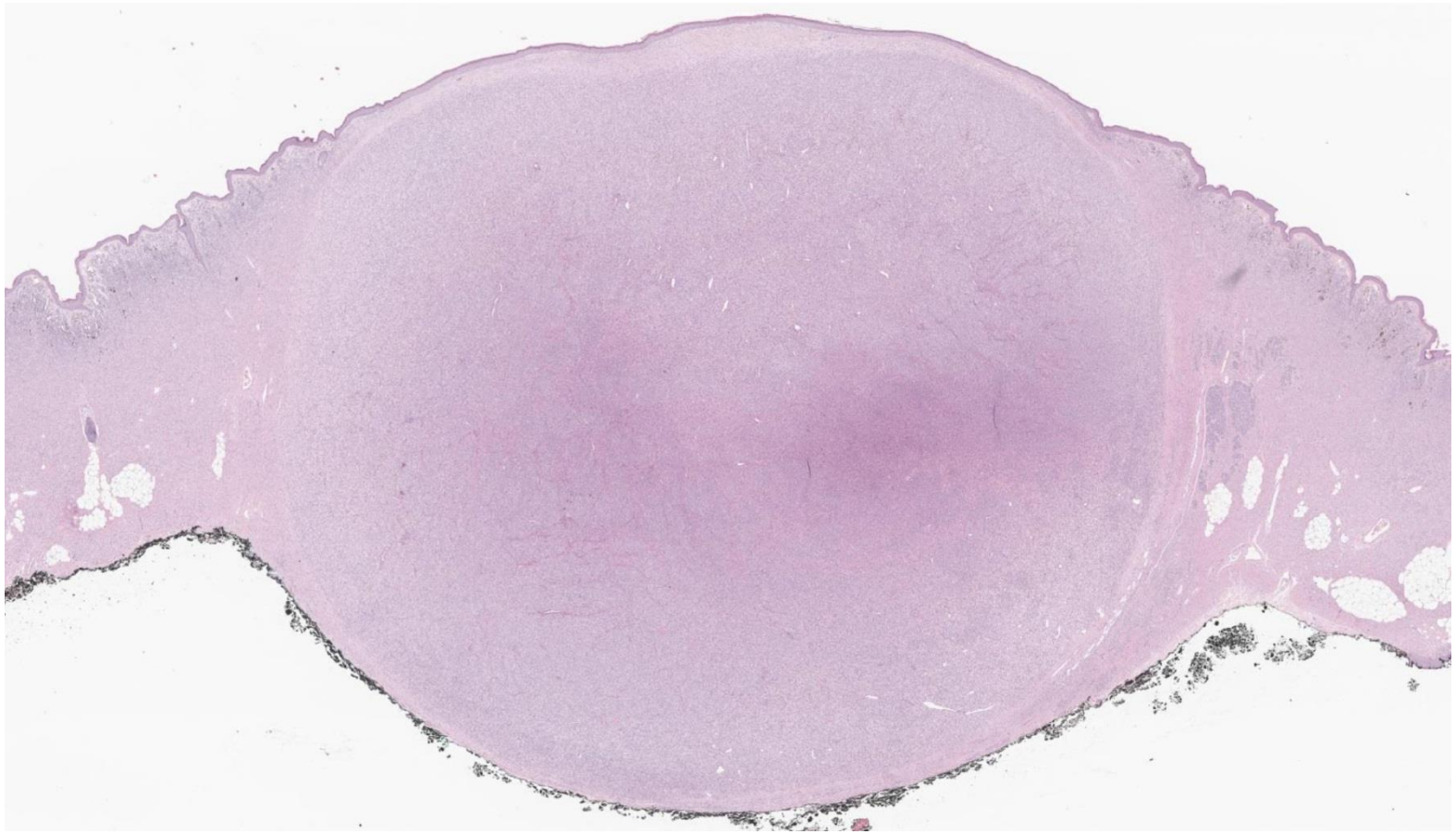




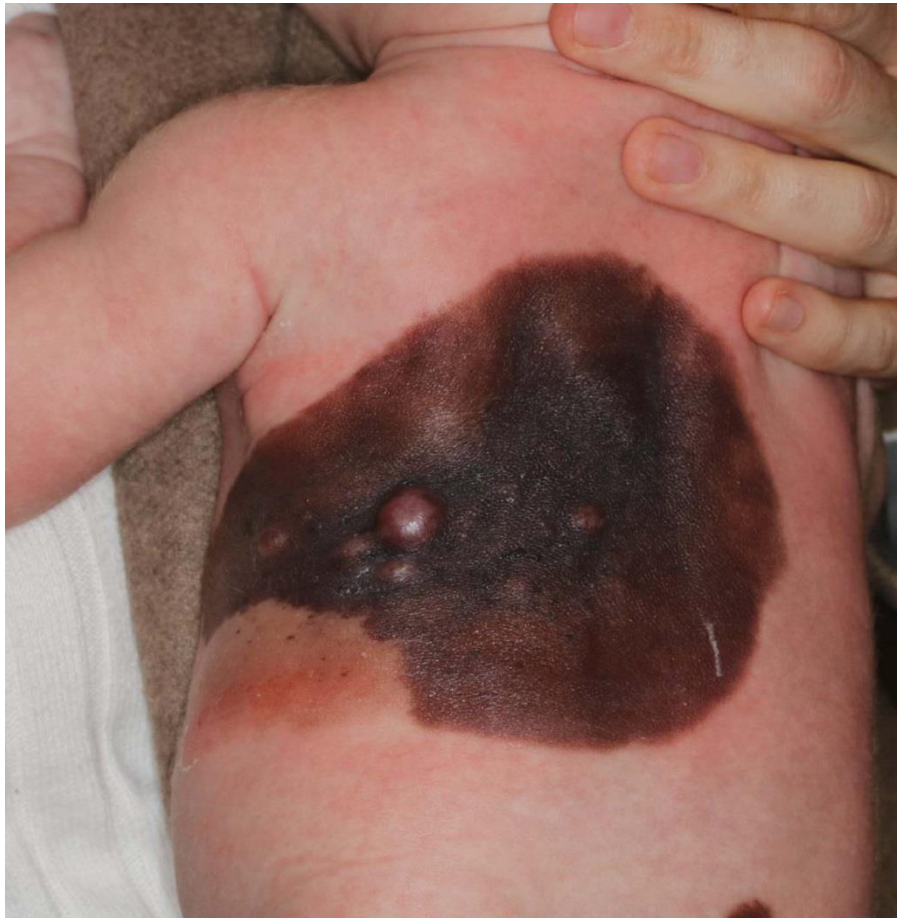
Phenotypes of proliferative nodule

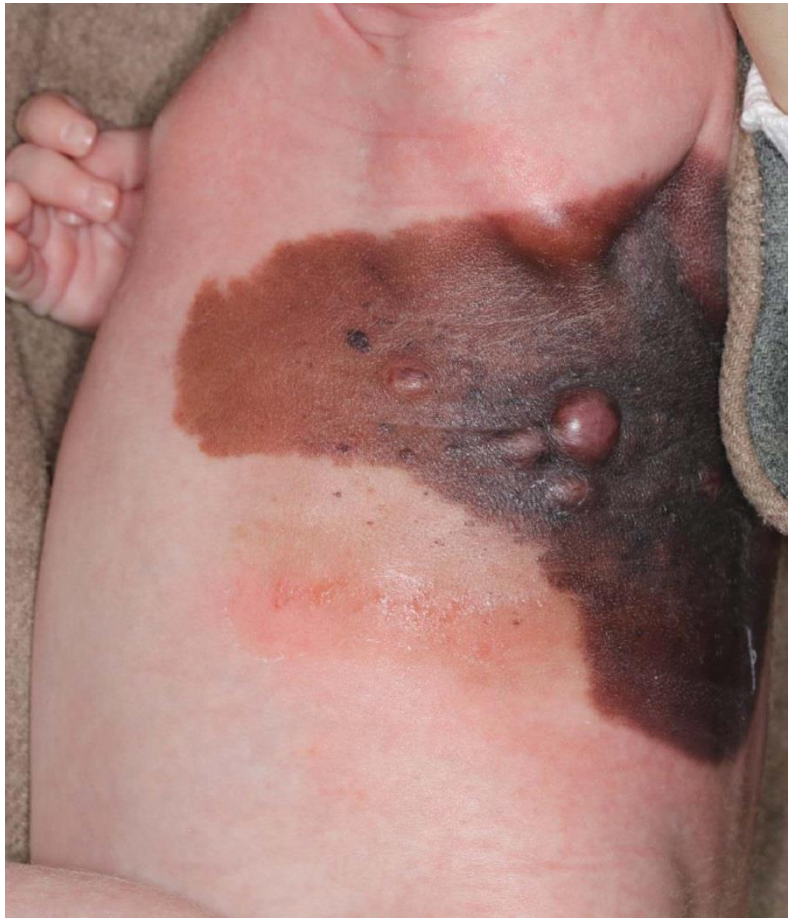
- Nevoid melanoma-like
- Blue Nevus/PEM-like
- Spitzoid/Bapoma-like
- Small cell/blastic features
- Mesenchymal

Proliferative Nodule or Melanoma?

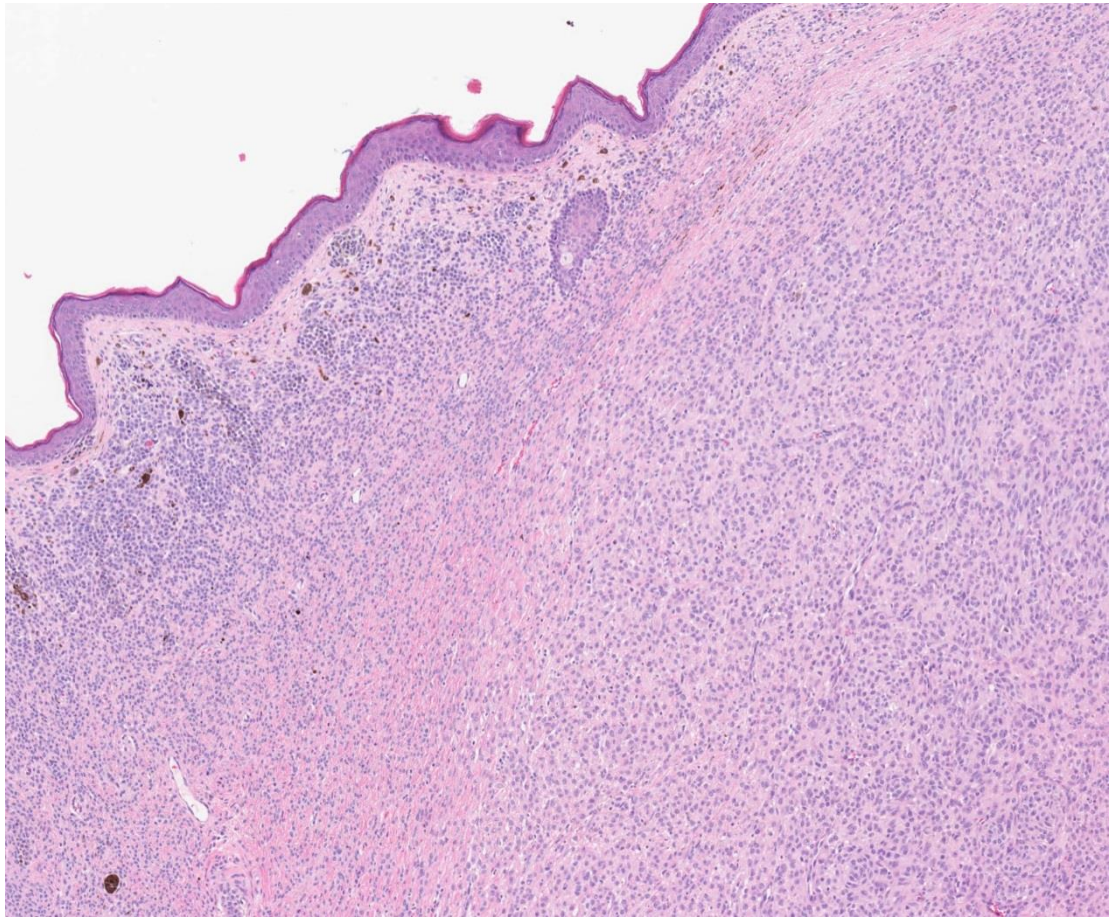


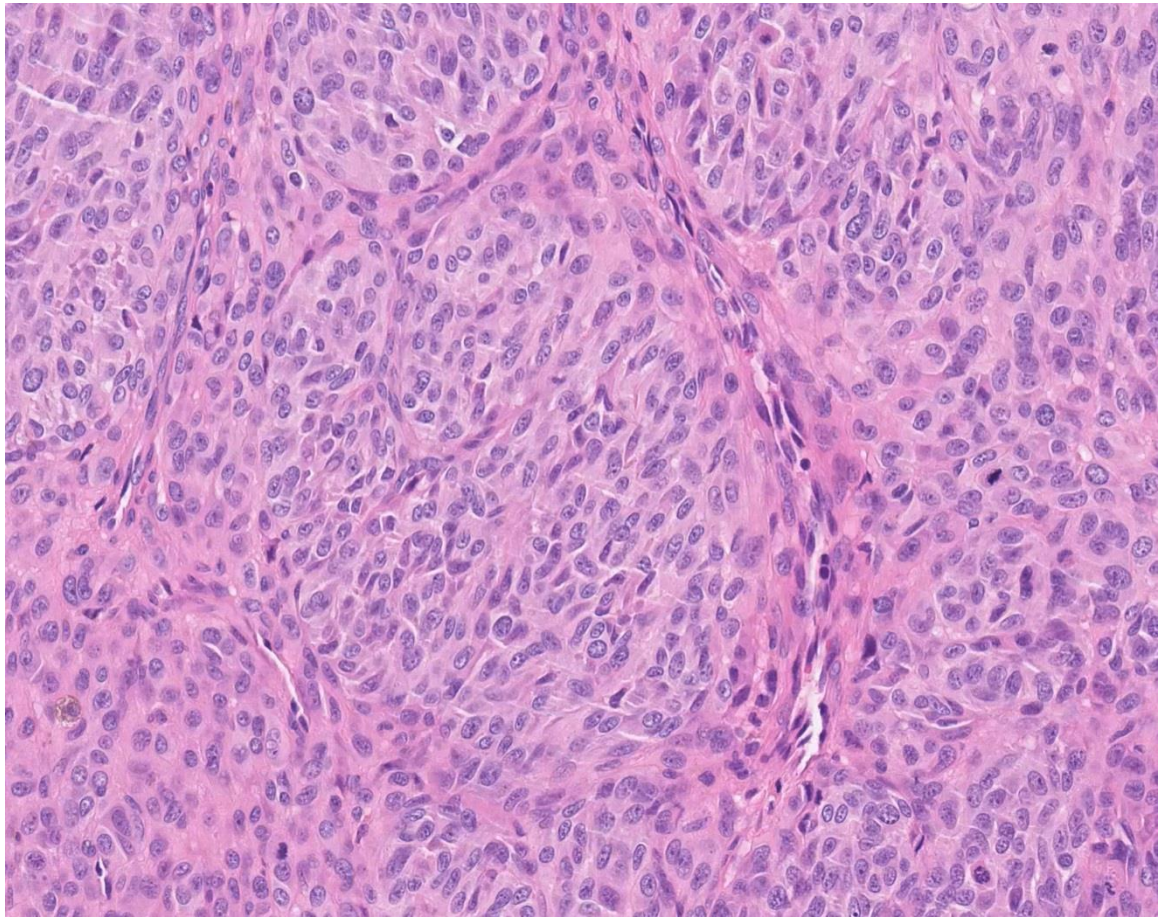
6 wk Baby with nodules in CMN



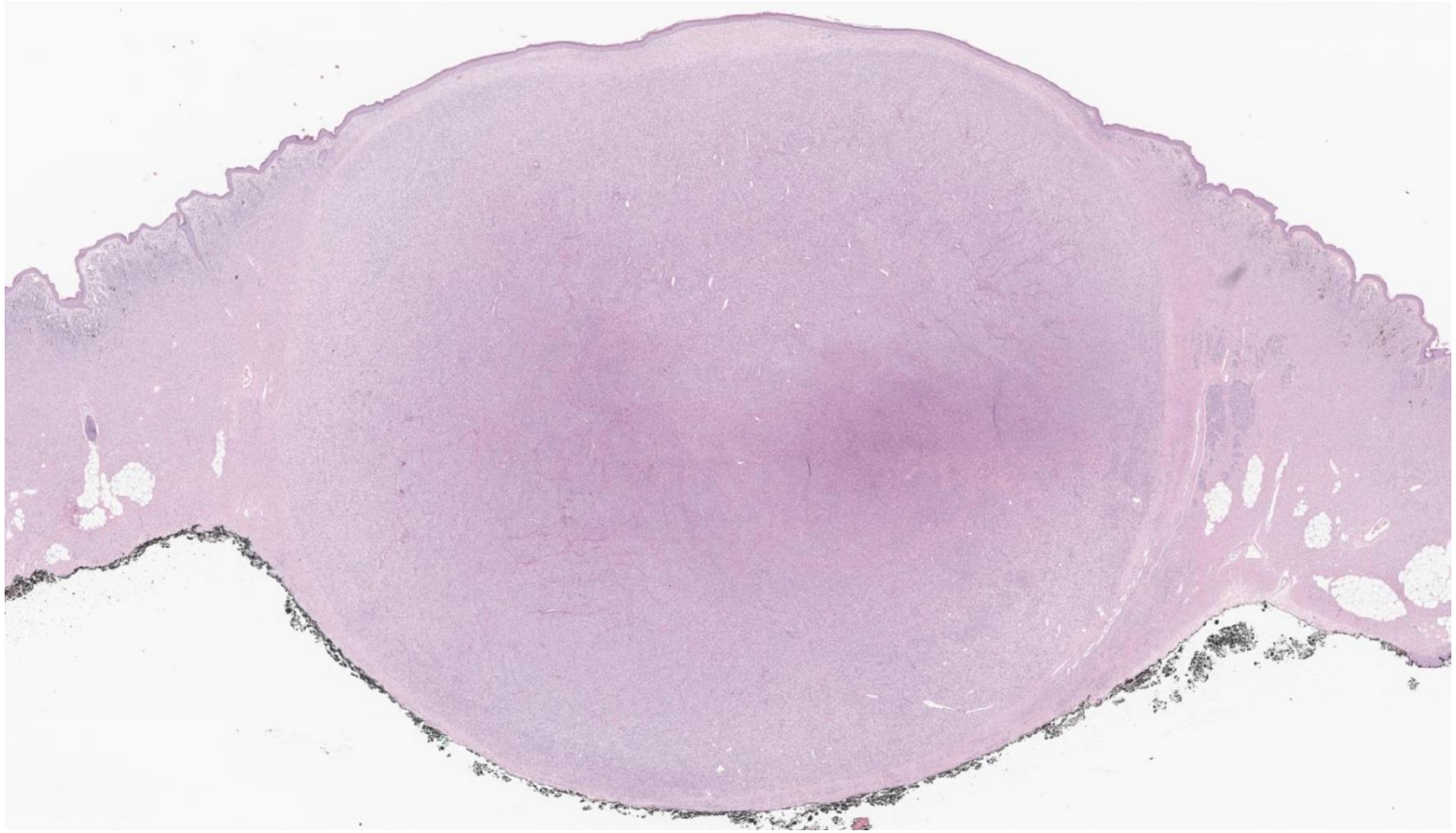


Histopathology

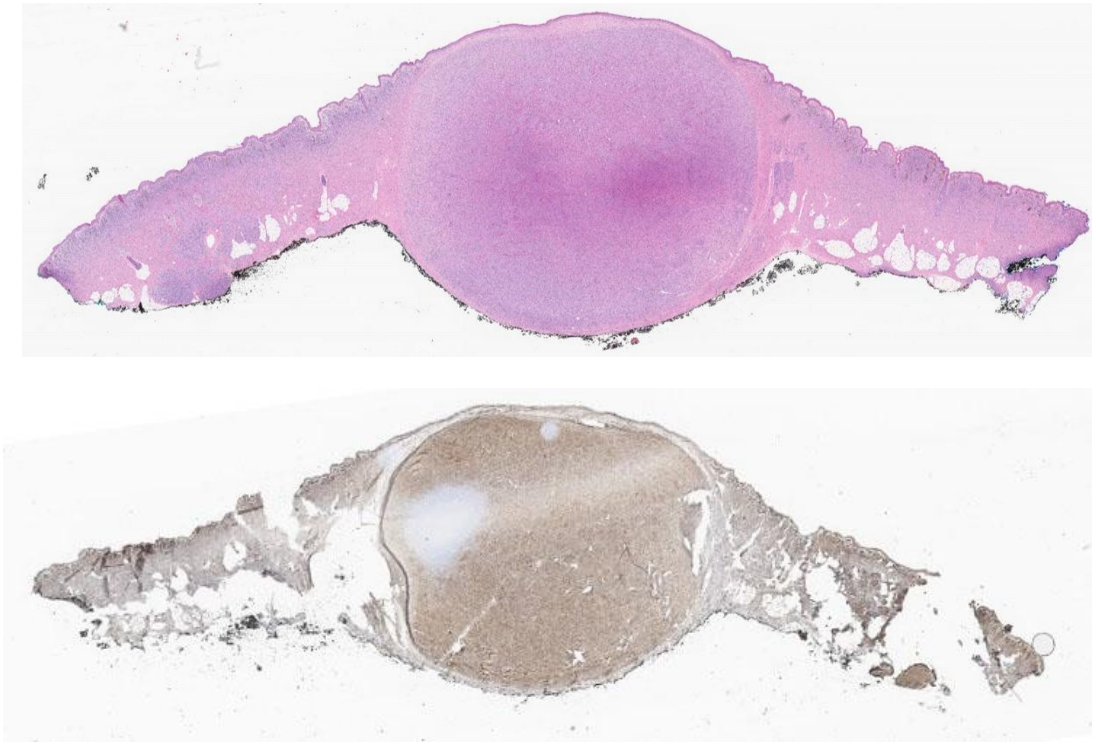


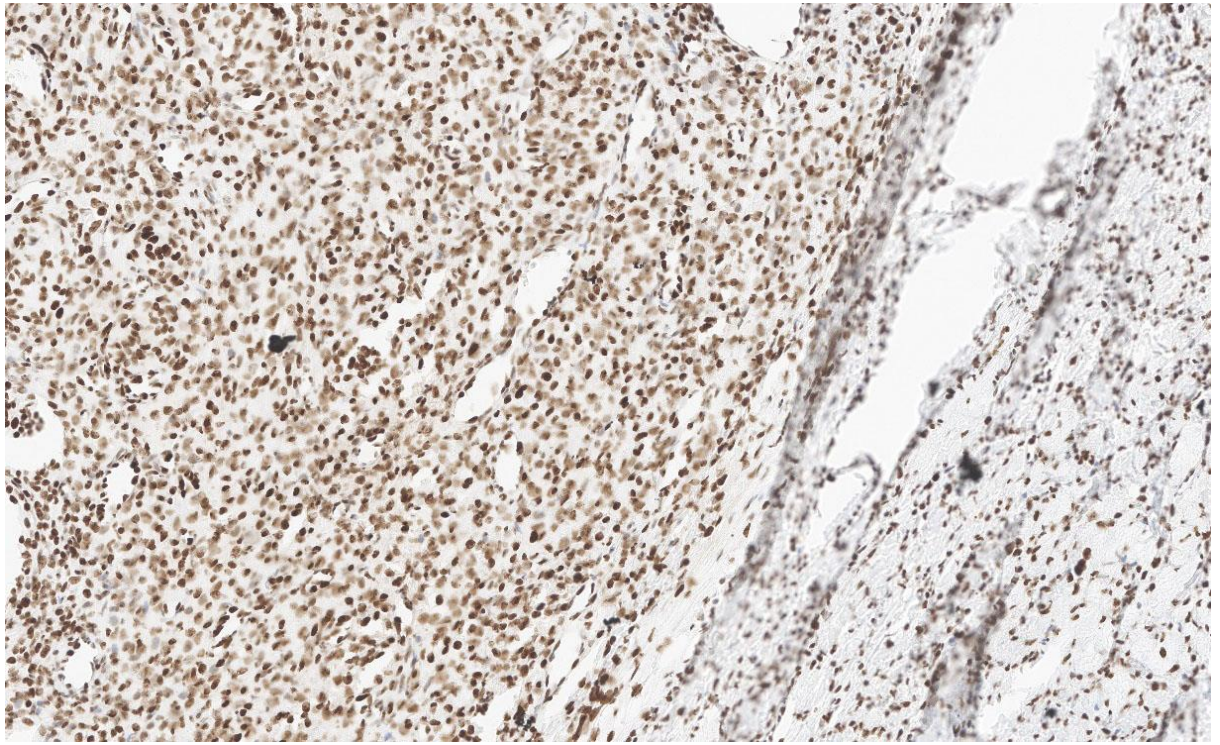


Benign Proliferative Nodule



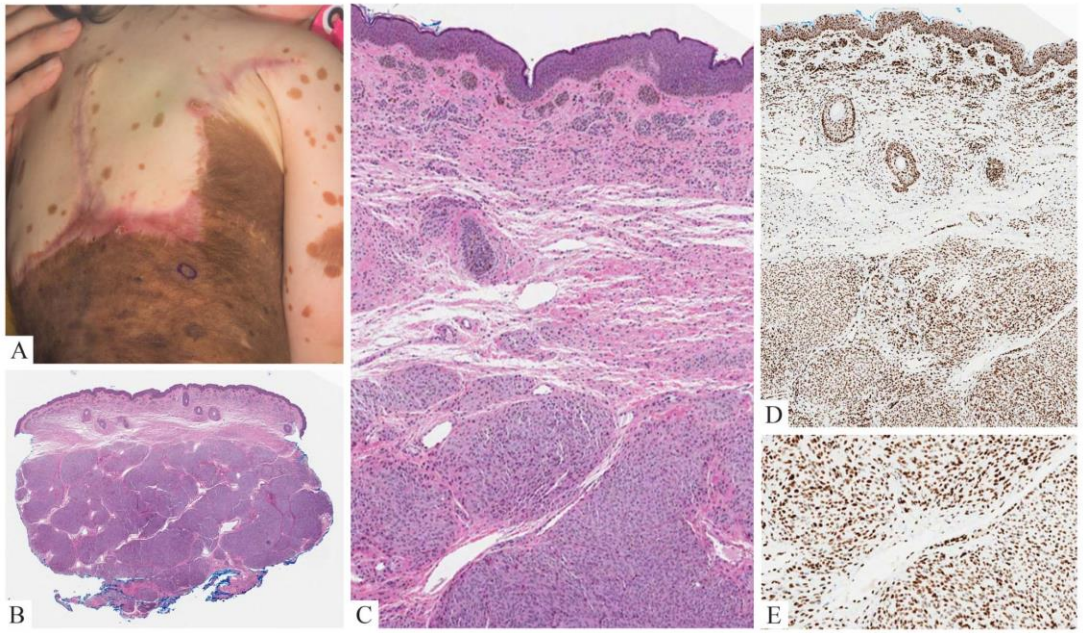
IHC for H3K27me3



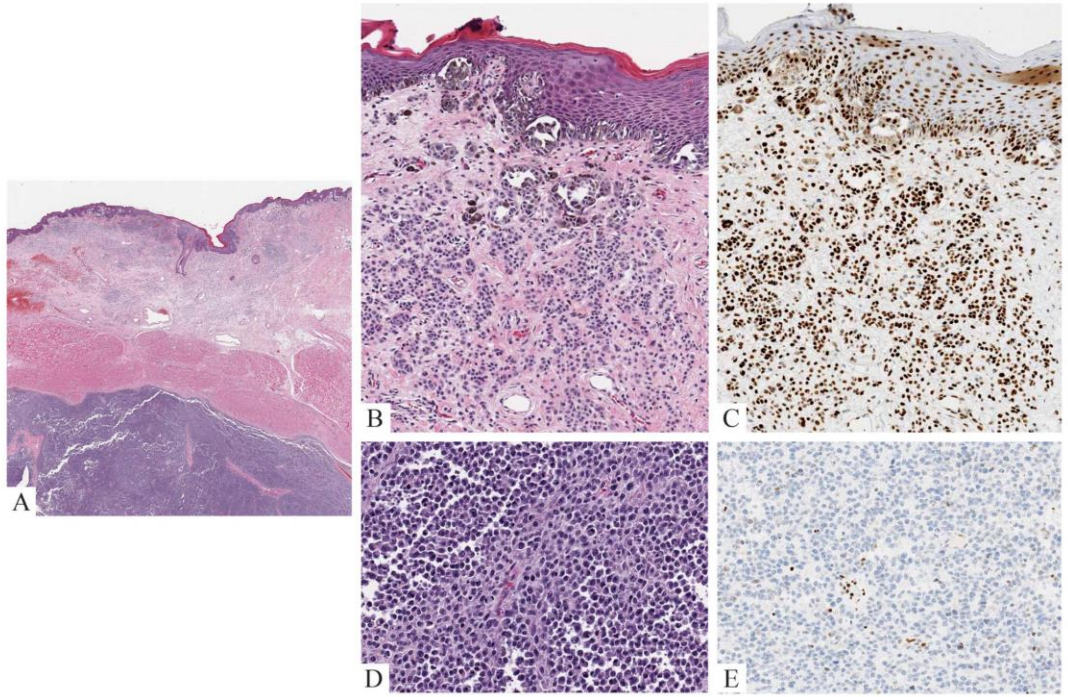


IHC for H3K27me3

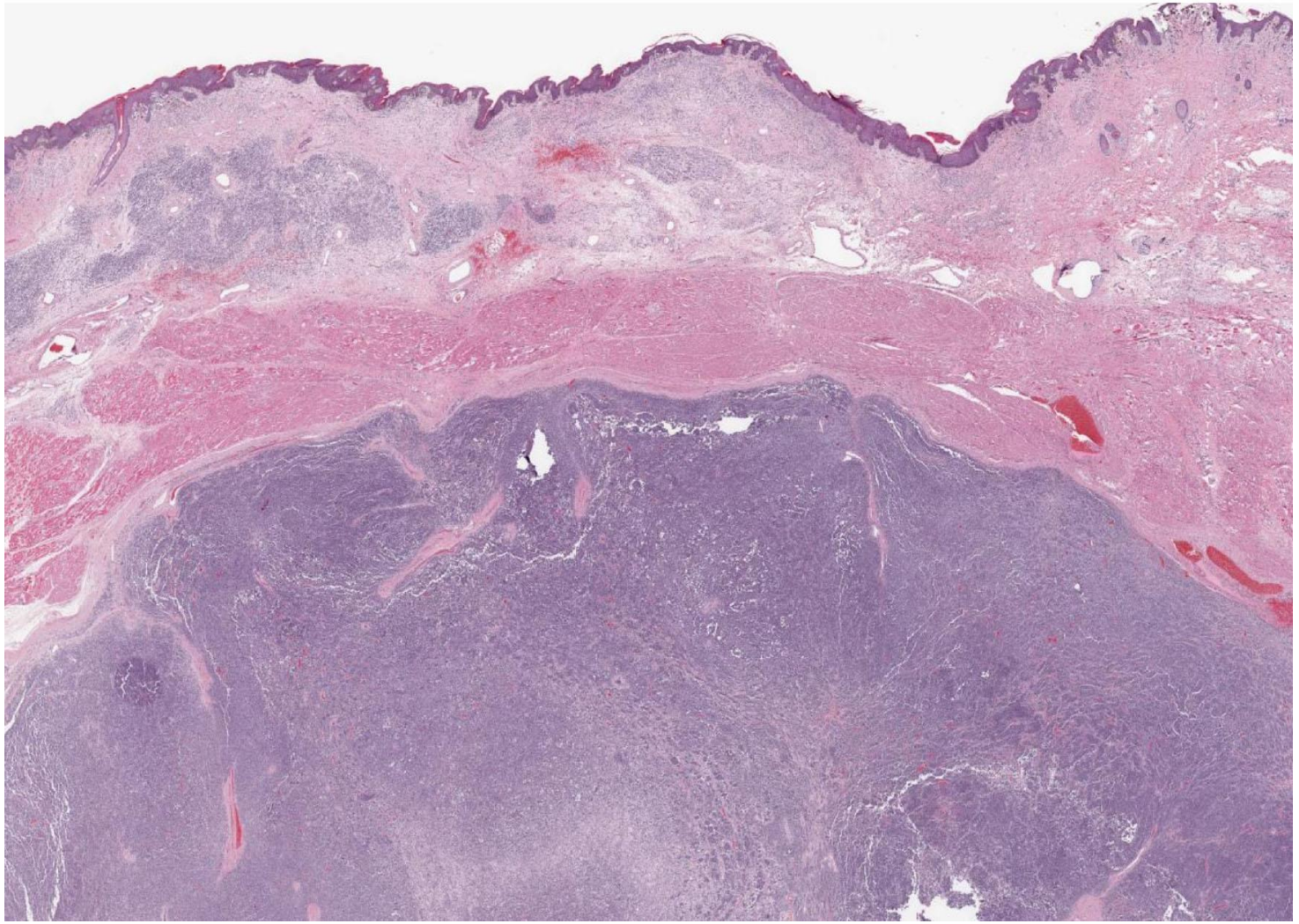
Proliferative Nodule



Melanoma

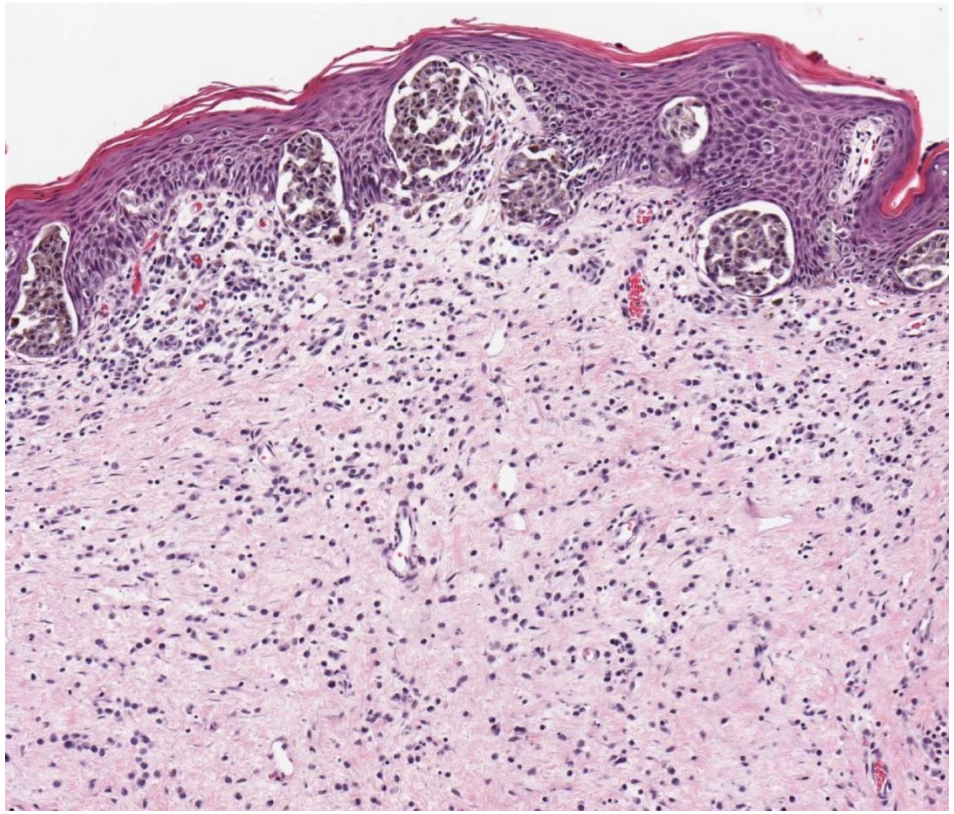


Melanoma arising in a large CMN

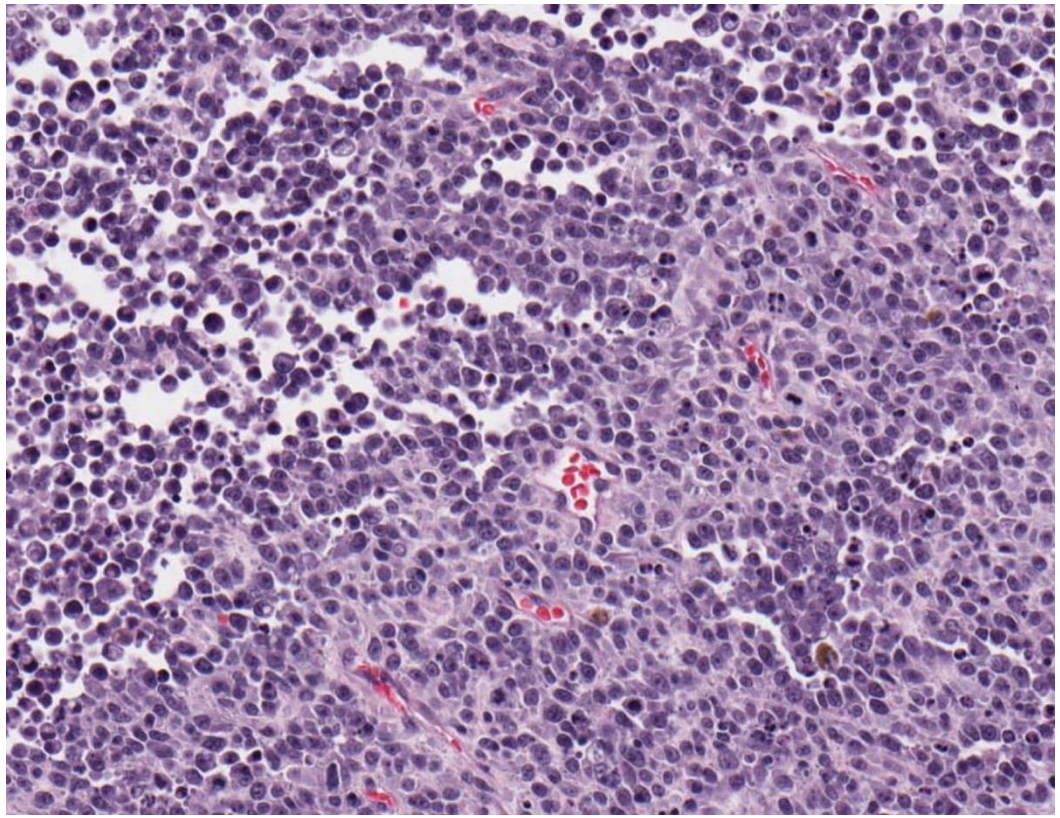


Melanoma arising in a large CMN

Nevus



Melanoma



Proliferative Nodule vs Melanoma

Proliferative Nodule

- Clinical
  - Relatively small, non-ulcerated
- Pathology
  - Organized, differentiated
  - Circumscribed
  - Atypia and mitoses variable
  - Tends to blend with nevus
- Ancillary Studies
  - No or whole chromosome aberrations
  - IHC for H3K27me3 (positive)

Melanoma

- Clinical
  - Large, ulcerated
- Pathology
  - Infiltrative
  - Malignant cytology, frequent mitoses
  - Undifferentiated, transdifferentiated
  - Tends to be very different from nevus
- Ancillary Studies
  - Segmental copy number aberrations
  - IHC for H3K27me3 (negative)

Ancillary Studies for Diagnosis: Cytogenetics

American Journal of Pathology, Vol. 161, No. 4, October 2002

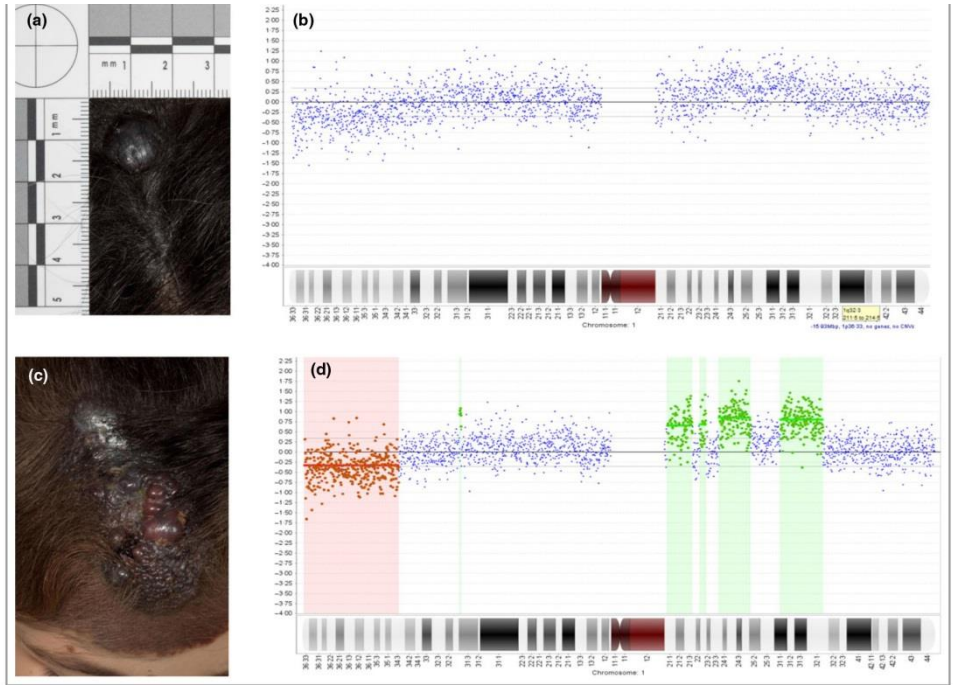
Genetic Changes in Neoplasms Arising in Congenital Melanocytic Nevi

Differences Between Nodular Proliferations and Melanomas

Boris C. Bastian,*†‡ Jessie Xiong,† Ilona J. Frieden,* Mary L. Williams,* Pauline Chou,§ Klaus Busam,¶ Dan Pinkel,‡ and Philip E. LeBoit*†‡

From the Departments of Dermatology and Pathology,† and the University of California at San Francisco Comprehensive Cancer Center,‡ University of California at San Francisco, San Francisco, California; the Department of Pathology,§ Children's*

quent numerical chromosomal aberrations in atypical nodular proliferations arising in CMN identifies these as clonal neoplasms with a genomic instability consistent with a mitotic spindle checkpoint defect. This difference compared to the aberration pattern found in melanoma might explain their more benign clinical behavior and may be of diagnostic value in ambiguous cases. ***(Am J Pathol 2002, 161:1163–1169)***



Kinsler et al BJD 2017;176:1143

Test Limitations

EXTRAORDINARY CASE REPORT

Metastatic Melanoma in Association With a Giant Congenital Melanocytic Nevus in an Adult: Controversial CGH Findings

Salma Machan, MD, Ana M. Molina-Ruiz, MD,* Maria J. Fernández-Aceñero, MD,† Beatriz Encabo, MD,† Philip LeBoit, MD,‡ Boris C. Bastian, MD,‡ and Luis Requena, MD**

Am J Dermatopathol 2015; 37: 487 - 94

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- My family

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Thank You!