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Sarcomatoid Dedifferentiated Melanoma arising in a melanoma-in situ

Pennsylvania Academy of Dermatology and Dermatologic Surgery

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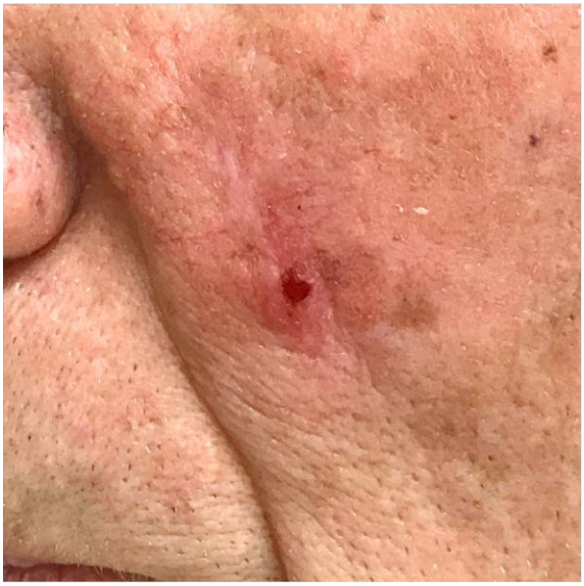
Clinical History

A 78-year-old man with a history of numerous non-melanoma skin cancers and melanoma in-situ presented with a 2 month history of an ulcerating papule on the cheek at the edge of his previous melanoma in-situ excision scar that was diagnosed and treated five years prior.



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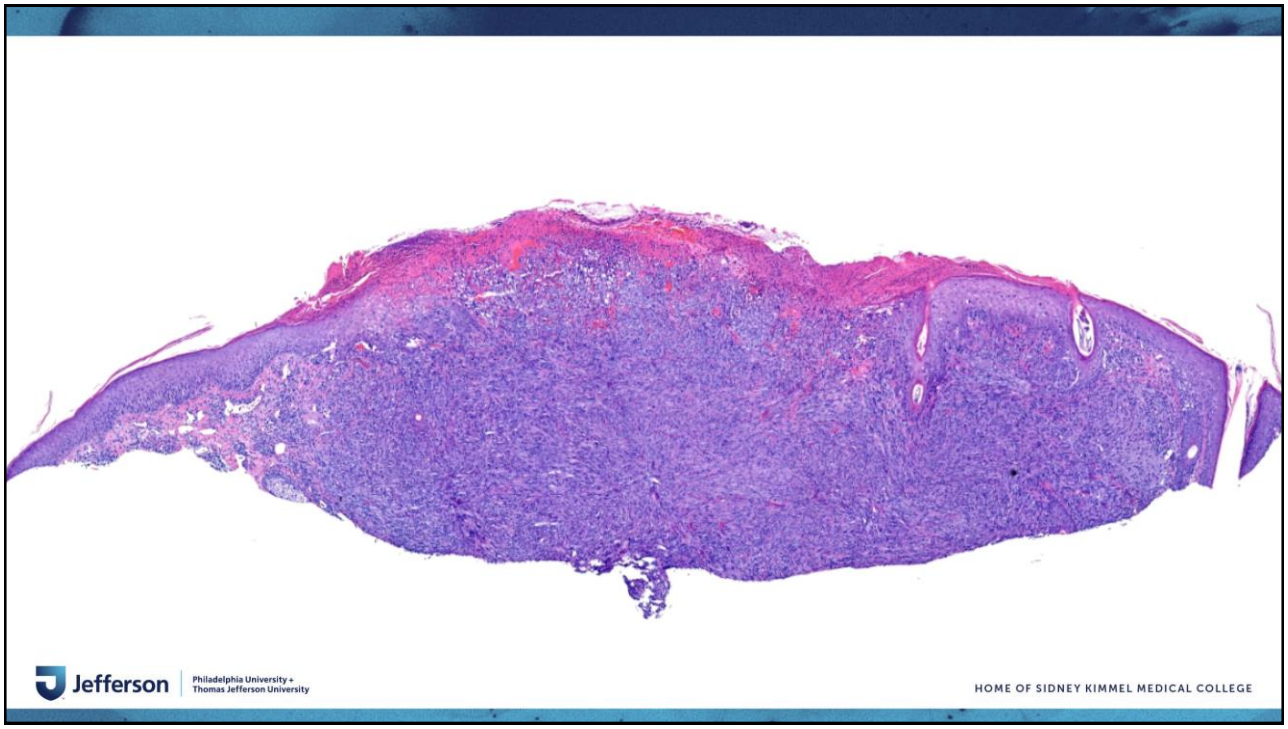
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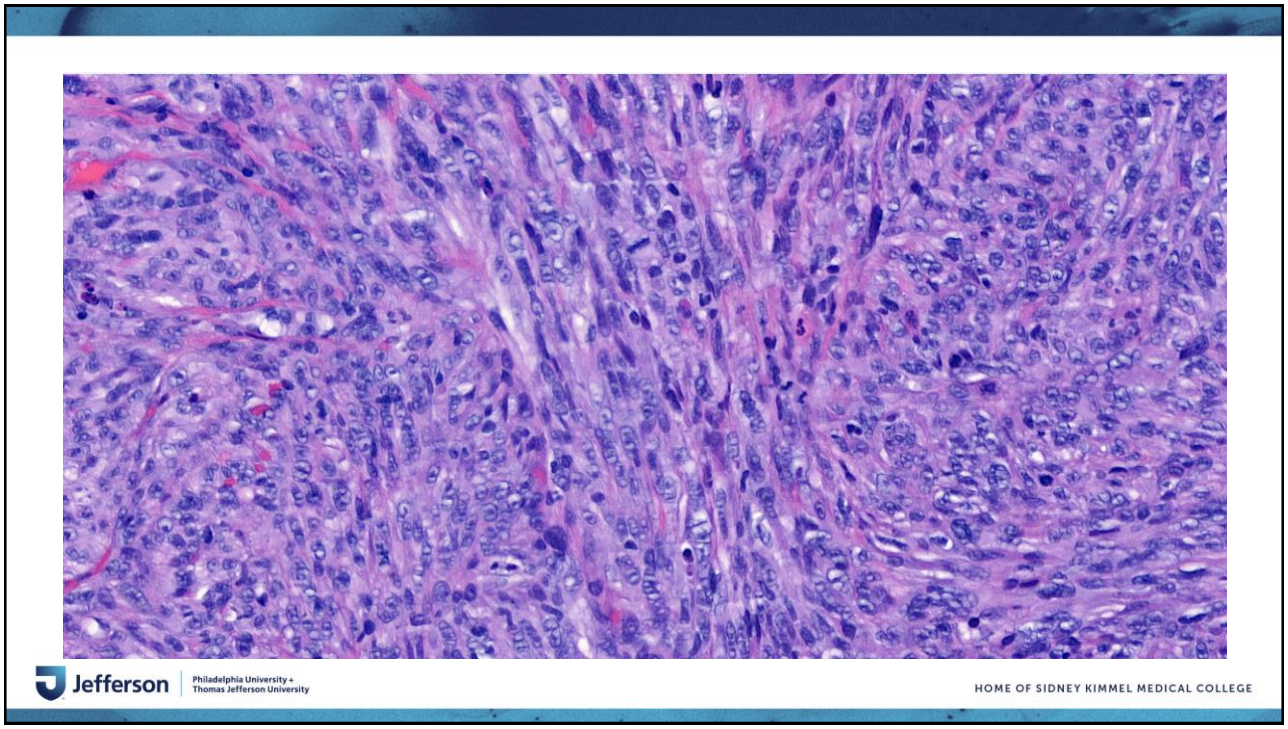
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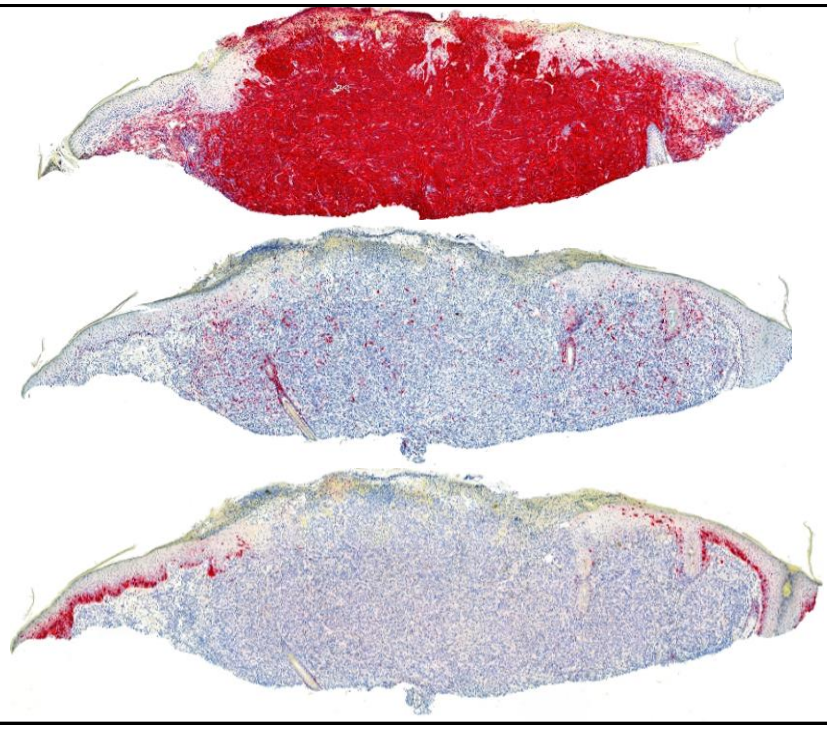
CD10

S100

Melan-A



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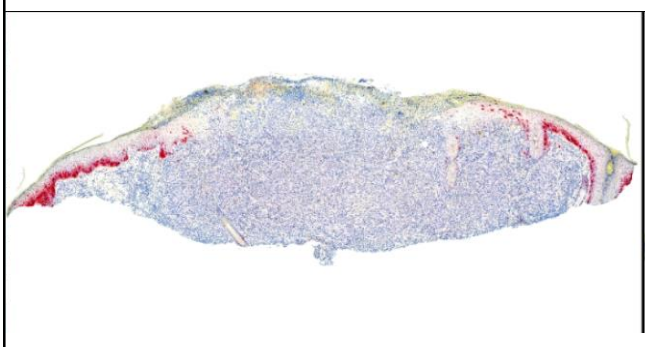

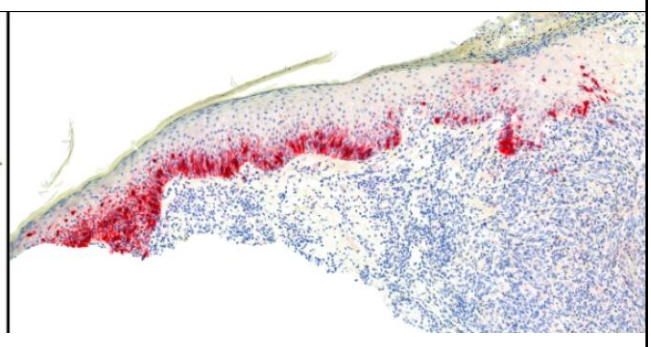

Melan-A

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Molecular analysis – next generation sequencing

NF1, CDKN2A, TP53, and TSC1 mutations detected in the spindle cell component

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Pathology

Diagnosis: Malignant Spindle Cell Neoplasm, Ulcerated and Melanoma In-Situ

Consistent with sarcomatoid dedifferentiated melanoma arising in a melanoma in-situ

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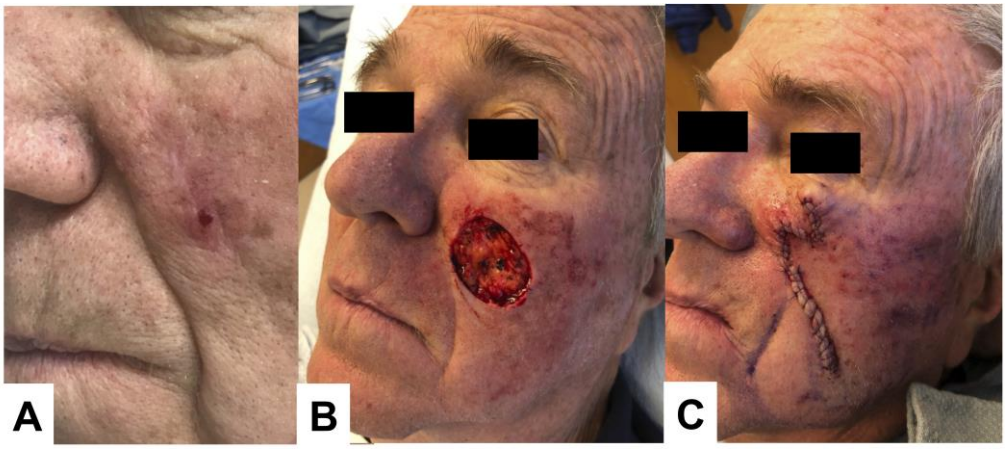
Treatment: Mohs micrographic surgery



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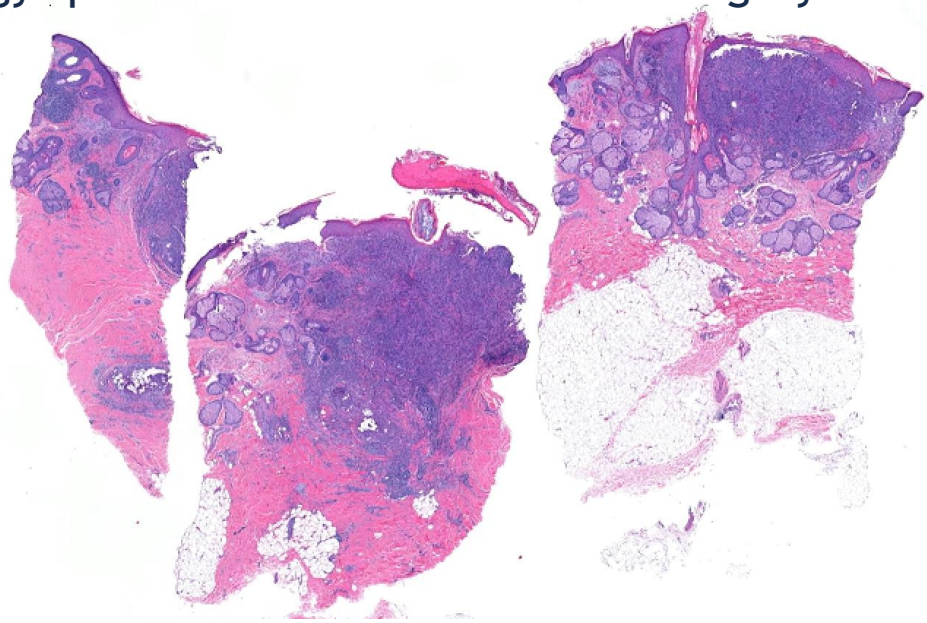
Pathology: permanent section of Mohs surgery debulk



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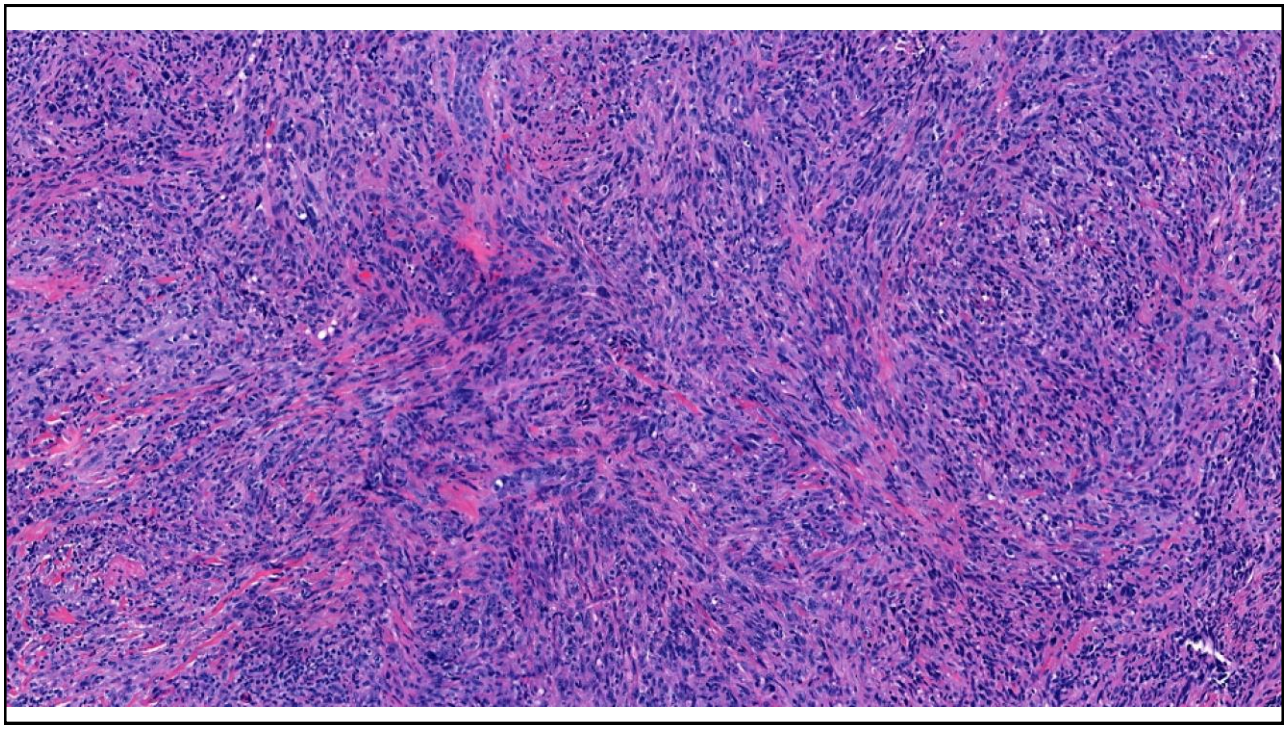

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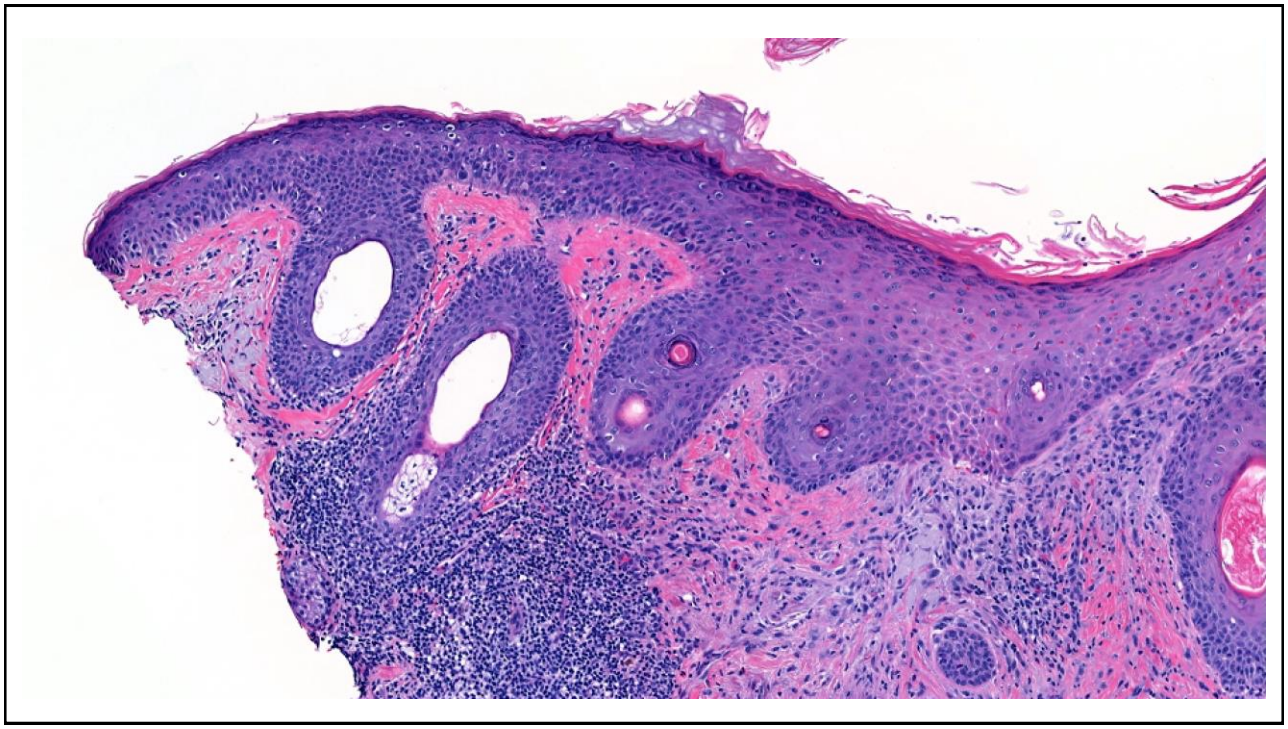

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Treatment and Outcome

- Sentinel lymph node biopsy: negative
- PET scan: negative

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Proposed diagnostic criteria for dedifferentiated/undifferentiated melanomas

TABLE 5 - Criteria Proposed to Diagnose Undifferentiated Metastatic Malignant Melanoma

Our patient

- Histologically and/or immunohistochemically proven primary cutaneous or mucosal melanoma

OR

- At least 1 histologically and/or immunohistochemically proven differentiated melanoma MUP
- Exploration of the remote clinical history (primary tumor might have been excised decades ago)
- Review of previously excised melanocytic lesion/s to exclude melanoma before adopting a diagnosis of MUP
- Undifferentiated histology in the metastasis (UPS) with multiple cytologic (epithelioid, rhabdoid, spindled and pleomorphic cells) patterns
- Inconclusive immunophenotyping with either vimentin-only immunophenotype or phenotypes/patterns of limited specificity, eg, pleomorphic rhabdomyoblastic, smooth muscle–like, myofibroblast-like, osteocartilaginous, primitive small cell or multiple patterns
- Lack of histologic patterns that are known to be associated with specific or defining genetic alterations/etiology such as synovial sarcoma, EWSR1-positive Ewing sarcoma, conventional leiomyosarcoma, etc.
- Undifferentiated metastasis not epicentered at a site of previous irradiation (otherwise postradiation sarcoma should be considered)
- Demonstration of a melanoma-compatible or melanoma-typical genotype or of a mutation known to have occurred in the primary melanoma, eg, *BRAF*, *NRAS*, *KIT*, or *NF1* mutation*
- In the very exceptional cases with frankly epithelial differentiation, eg, adenocarcinoma-like, exclude another primary, eg, *BRAF* mutated colorectal carcinoma, etc. by appropriate clinical examination/imaging
- Exclude undifferentiated neoplasms with possible *BRAF* mutation such as anaplastic thyroid carcinoma by appropriate immunohistochemistry and/or clinical examination/imaging

Agaimy A, Stoehr R, Hornung A, et al. Dedifferentiated and undifferentiated melanomas: report of 35 new cases with literature review and proposal of diagnostic criteria. Am J Surg Pathol. 2021;45:240–254.

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Sarcomatoid Dedifferentiated Melanoma (SDDM)

- Rare aggressive spindle cell subtype of melanoma that simulates a sarcoma
- Clinical presentation:
  - Large, thick hemorrhagic and ulcerated nodule
  - Usually diagnosed at late stage with significant depth or once already metastasized
- All reported cases show a biphasic morphology: conventional melanoma + pleomorphic spindle cell component
- Diagnostic challenge:
  - Absence of specific clinical features
  - Spindle cells lack expression of the usual melanocytic markers including S100, SOX10, MITF, and Melan A
  - Stains diffusely for CD10 - can mimic atypical fibroxanthoma (AFX) and pleomorphic dermal sarcoma (PDS)

Next Generation Sequencing (NGS)

- Mutational profiling through NGS assays can help to establish the correct diagnosis when staining is ambiguous
- Mutational analysis by NGS on cases of SDDM can be performed on microdissected sections of the sarcomatoid and conventional melanoma components.

TABLE 1. - Summary of Shared Mutations Between Conventional Melanoma and the Sarcomatoid Component in Cases of SDDM Described in the Literature (Adapted From Chung et al[5])

Author and year	Age/Sex	Site/Clinical Information	Breslow Depth/Stage	Shared Mutation
Kiuri et al (2014)[1]	66/M	Scalp hemorrhagic nodule	Not provided	† ***TP53*** —p.R248Q, p.P219L, p.V147A ***CDKN2A*** —p.E26 *
				TSC2 —p.G1367S
				NF1 —p.R2179C *
Erstine et al (2017)[2]	65/F	Right inframammary 1.8 cm polypoid ulcerated lesion	9 mm, Stage III	***BRAF*** —wild type
	62/M	Left heel ulcerated pedunculated mass	4.5 mm, Stage III	***BRAF*** —wild type
				NRAS —wild type
				KIT —wild type
Lefferts et al (2020)[3]	73/M	Left thigh 6 × 5 × 3 cm pedunculated nodule	7.9 mm, Stage III	***TP53*** —p.P278S
				NRAS —p.Q61L
Chung et al (2021)[5]	72/M	Left cheek ulcerated nodule	1.8 mm, Stage IIA	§ ***TP53***
				CDKN2A
				TSC1 *
				NF1
Agaimy et al (2021)[4]	74/M	Lower rectum lesion	Not provided	¶ ***KIT*** —p.L576P
Current case*,‡	65/M	Right medial knee crusted nodule	3.3 mm, Stage IIIC	***TP53*** —p.R213
				NRAS —p.Q61K
				TERT —c.-139_-138delinsTT
				JAK2 —p.V617F

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Valiga AA, Fuller CG, Doyle JA, Lee JB. Sarcomatoid Dedifferentiated Melanoma: The Diagnostic Role of Next-Generation Sequencing. Am J Dermatopathol. 2022 Apr 1;44(4):282-286. doi: 10.1097/DAD.0000000000002092. PMID: 34726188.

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Conclusions

- SDDM is a rare diagnosis and serves as a diagnostic challenge as it lacks characteristic melanocytic staining
- Recognition of an associated conventional melanoma is an essential clue in diagnosis of SDDM
- Molecular mutational analysis can aid is accurate diagnosis
- Can consider Moh's micrographic surgery as treatment

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2- Lefferts JA et al., *J Cutan Pathol*. 2020 Jun;47(6):541-547.

3- Kiuru M et al., *Am J Surg Pathol*. 2014 Jun;38(6):864-70.

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5- Valiga AA et al., *Am J Dermatopathol*. 2022 Apr 1;44(4):282-286.

6- Kooper-Johnson S et al., *Am J Dermatopathol*. 2020 Sep;42(9):697-699

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8- Massey RA et al., *Dermatol Surg*. 1998 Sep;24(9):995-8.

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