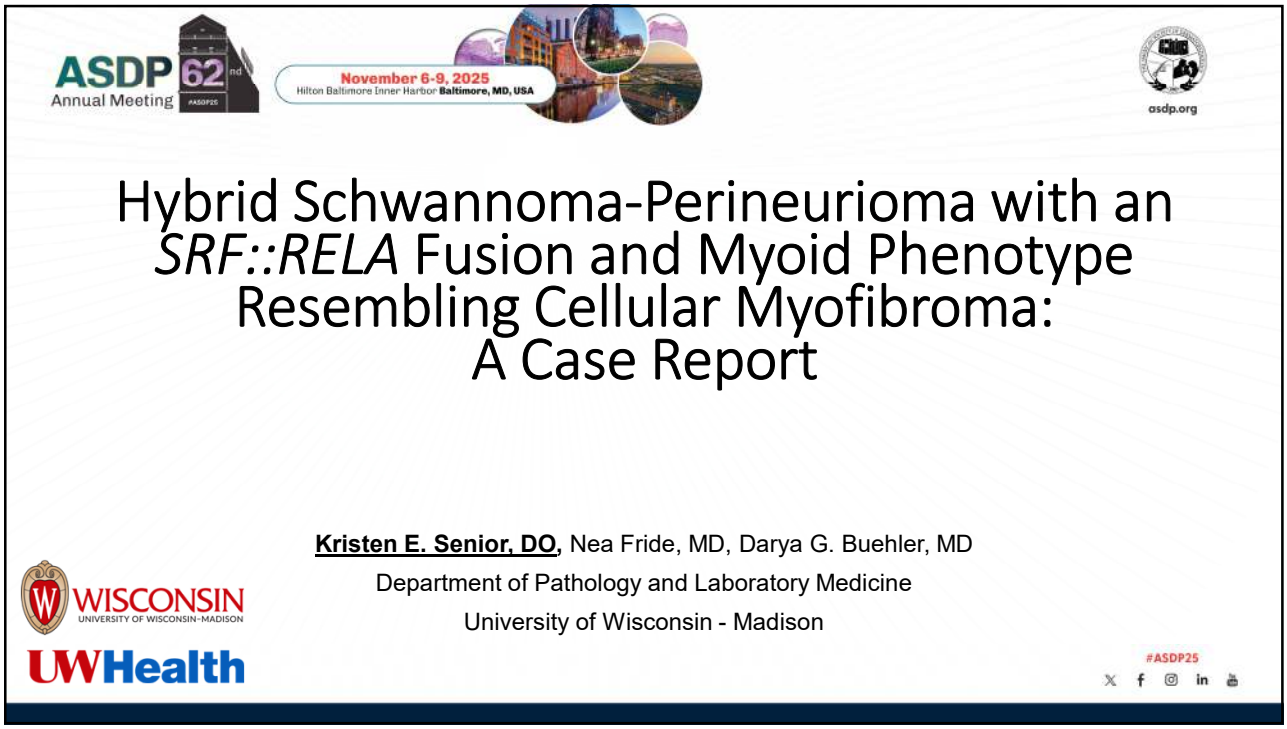
ASDP 62nd Annual Meeting
November 6-9, 2025
Hilton Baltimore Inner Harbor Baltimore, MD, USA
asdp.org
Hybrid Schwannoma-Perineurioma with an *SRF::RELA* Fusion and Myoid Phenotype Resembling Cellular Myofibroma: A Case Report
Kristen E. Senior, DO, Nea Fride, MD, Darya G. Buehler, MD
Department of Pathology and Laboratory Medicine
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WISCONSIN
UNIVERSITY OF WISCONSIN-MADISON
UWHealth
#ASDP25

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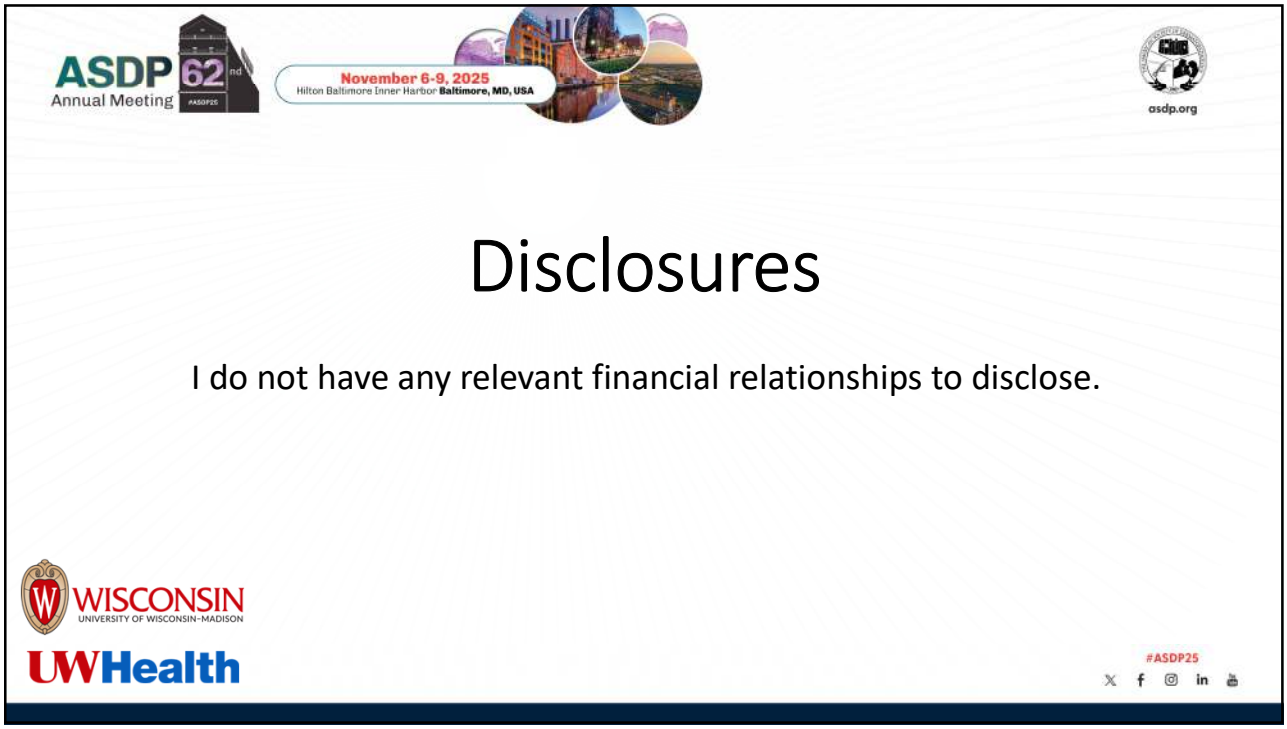
ASDP 62nd Annual Meeting
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Disclosures
I do not have any relevant financial relationships to disclose.
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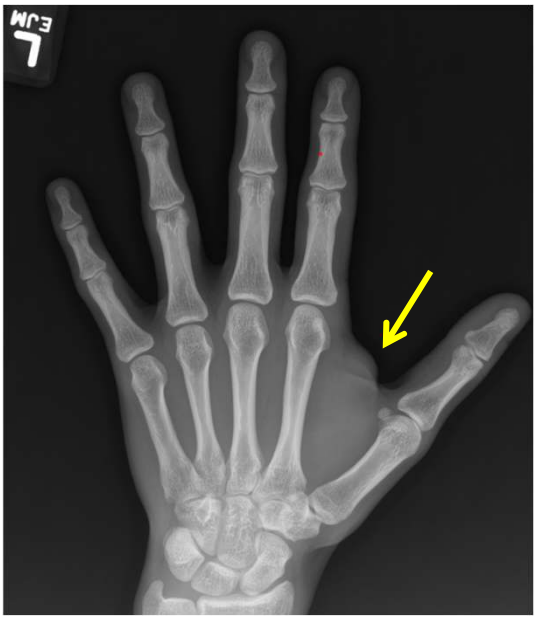
Clinical presentation

- 24 y.o. female with a firm mass in the first webspace that slowly grew over 6 months
- No pain, numbness, or tingling
- Simple excision was performed
- The mass was somewhat infiltrative and adherent to surrounding subcutaneous tissue



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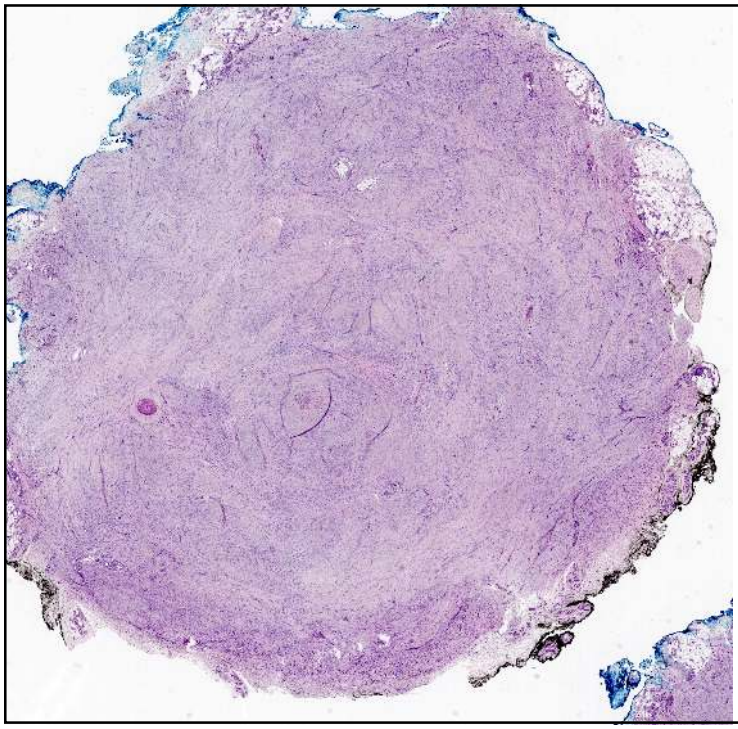

Gross exam showed a 1.8 x 1.3 x 1.3 cm tan-white, firm and homogeneous mass

Circumscribed but unencapsulated

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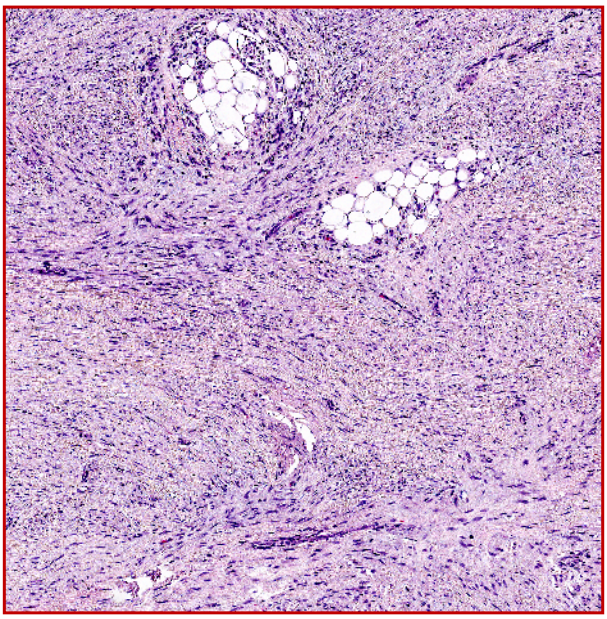

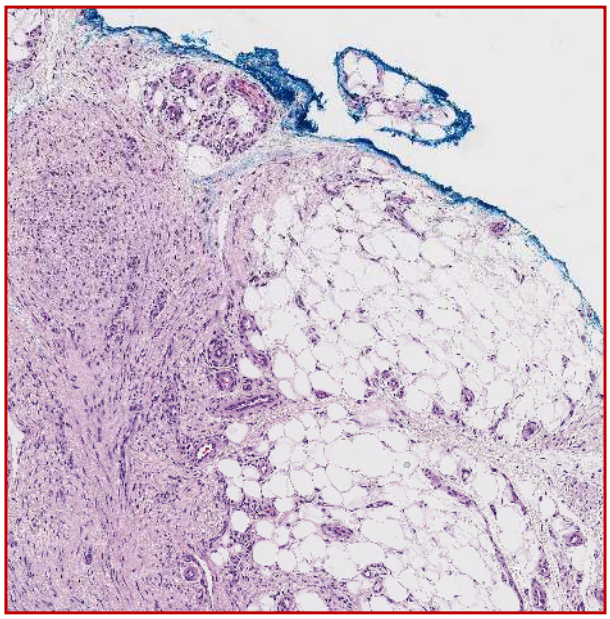

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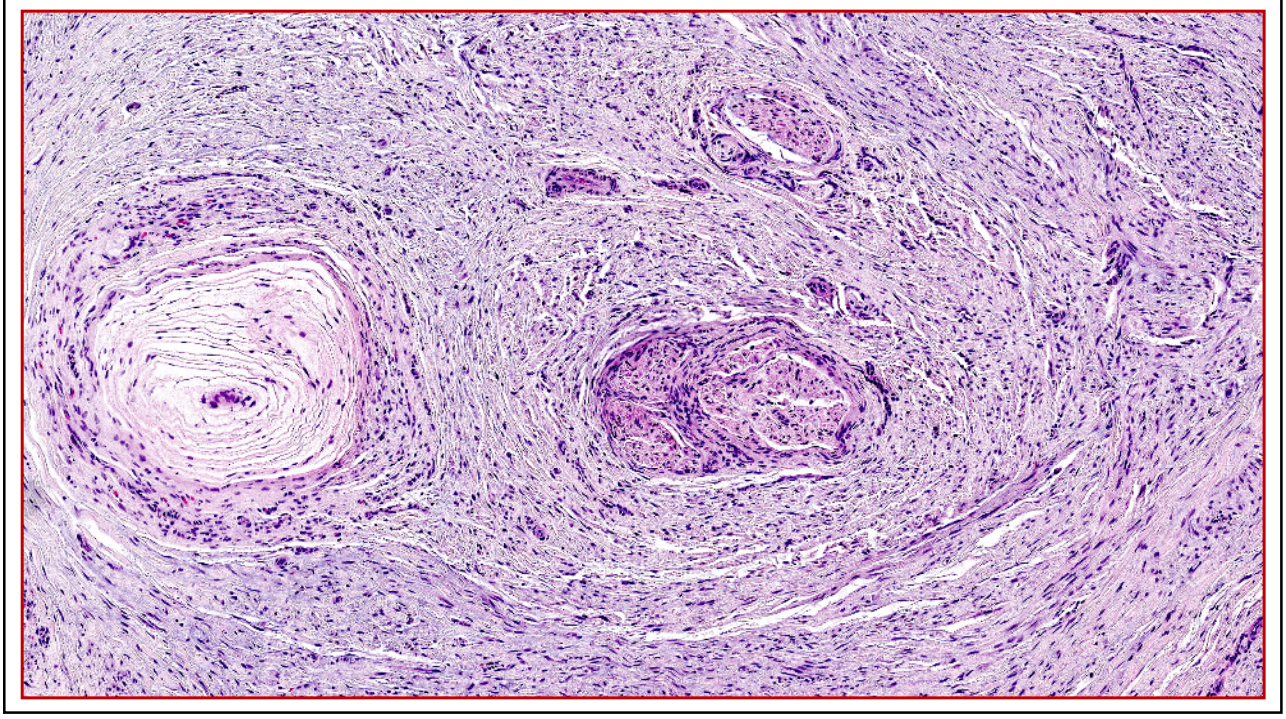

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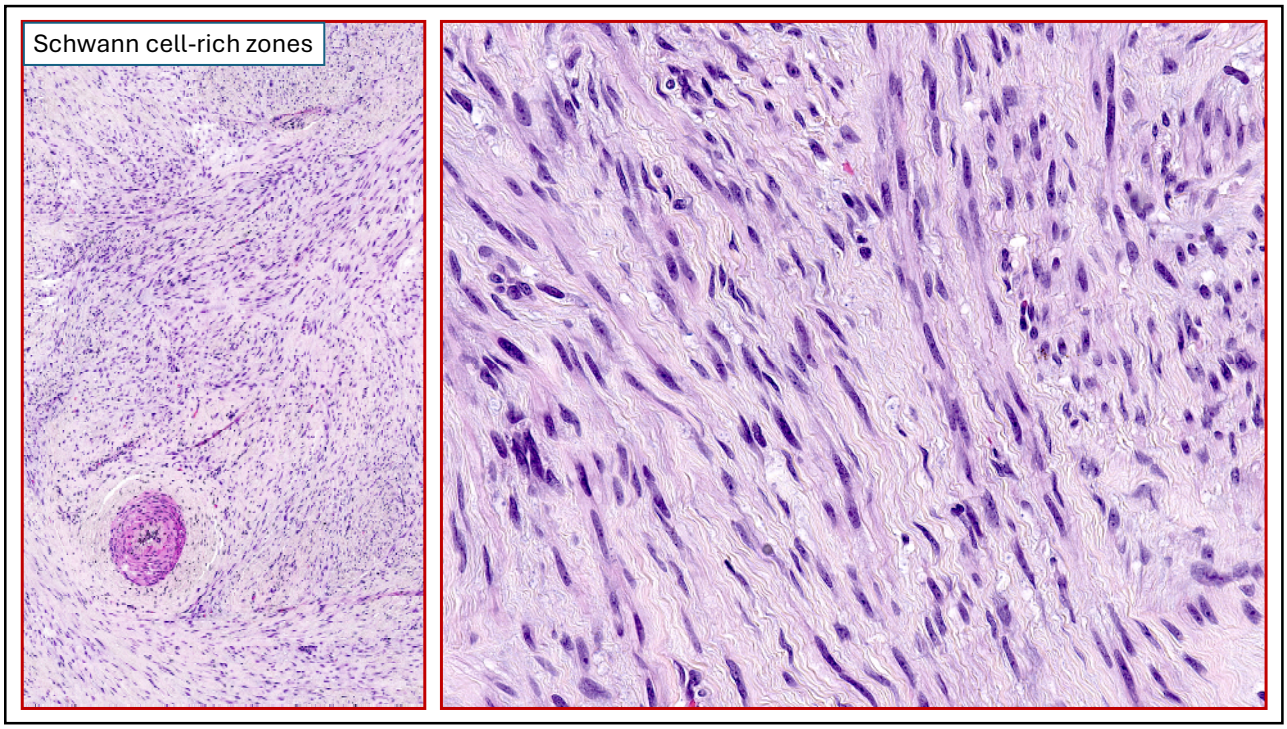

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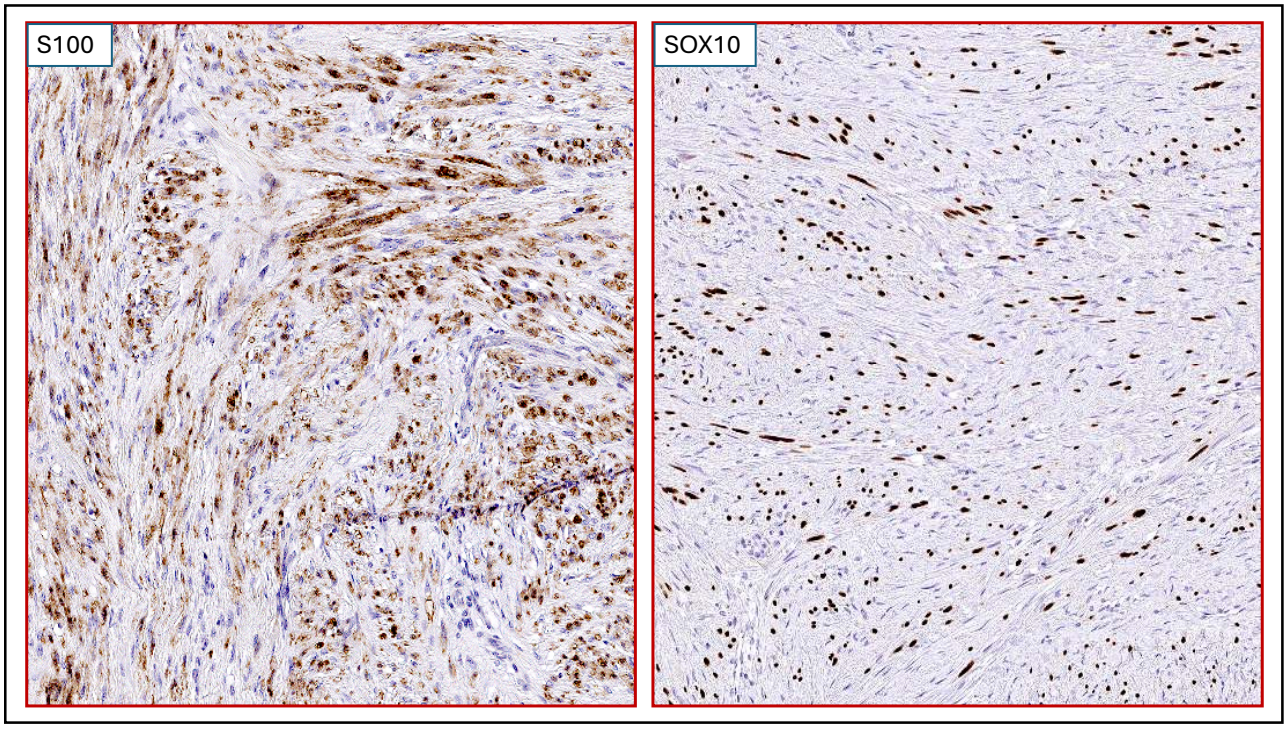

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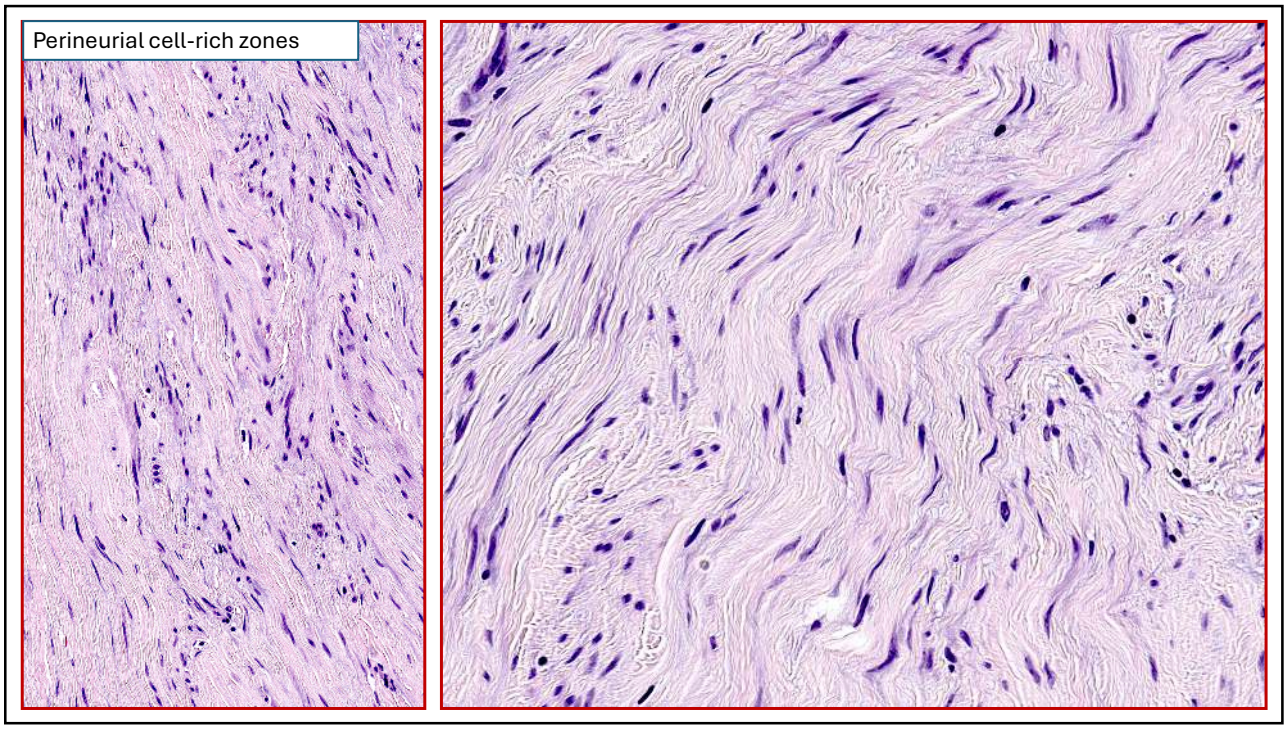

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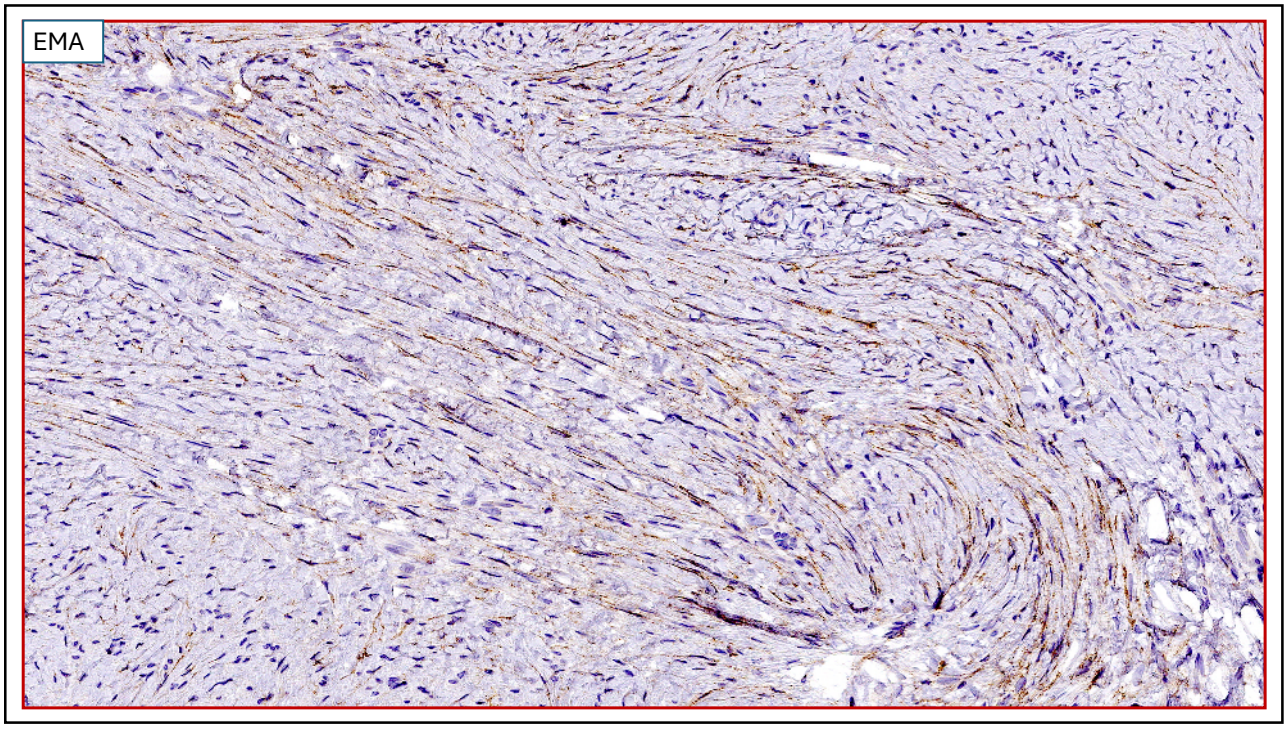

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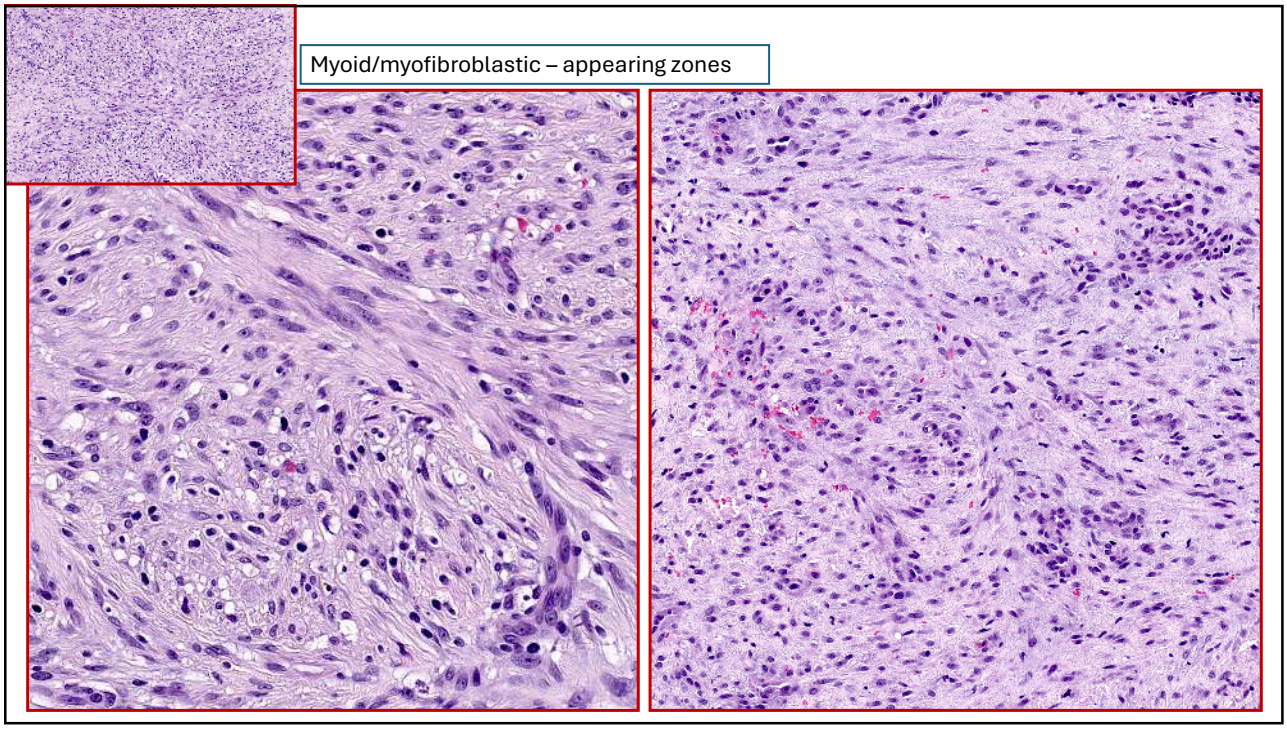
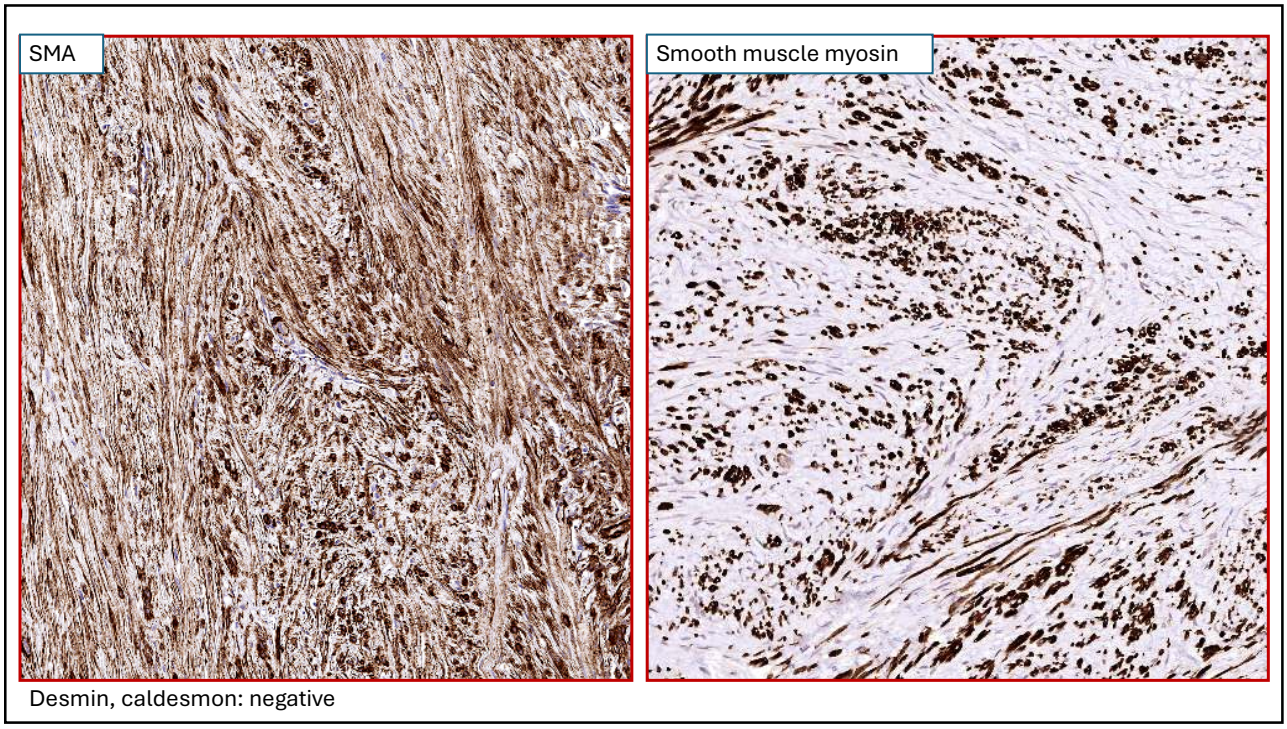

Myoid/myofibroblastic – appearing zones

11


SMA
Smooth muscle myosin
Desmin, caldesmon: negative

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Preliminary diagnosis:

- **Hybrid schwannoma/perineurioma** based on the clear presence of schwannian and perineurial components
- An unusual third, myofibroblastic/myoid phenotype that resembled cellular myofibroma, nodular fasciitis or another myofibroblastic or smooth muscle neoplasm

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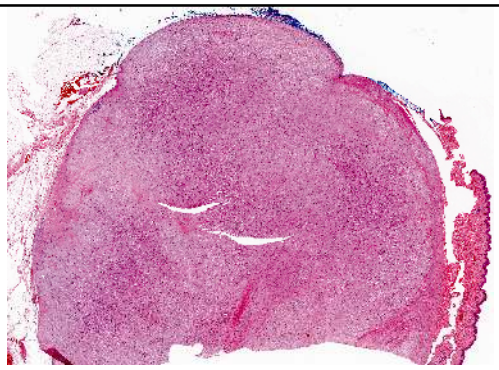
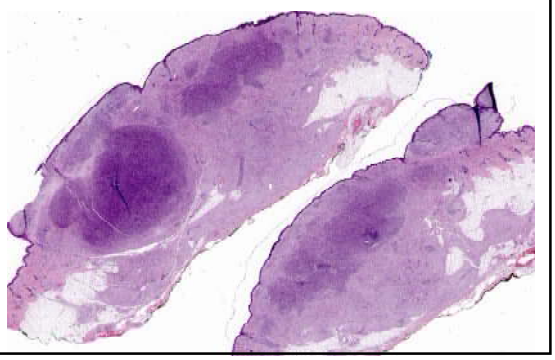
Classic Hybrid Schwannoma/Perineurioma

- Benign hybrid peripheral nerve sheath tumor (hPNST) with varying combinations of schwannian and perineurial components
- Sporadic, indolent tumors with a small risk of local recurrence and very rare metastasis, usually with histologic progression
- Gene fusion driven tumors:
  - Most cases show *VGLL3* fusion, either with *CHD7*, *CHD9* or *MAMLD1*
  - Approximately 20% show alternative fusions including *TEAD1*, *NCOA2*, *BRAF* and others
- Dermal/subcutaneous masses, unencapsulated, circumscribed or infiltrative





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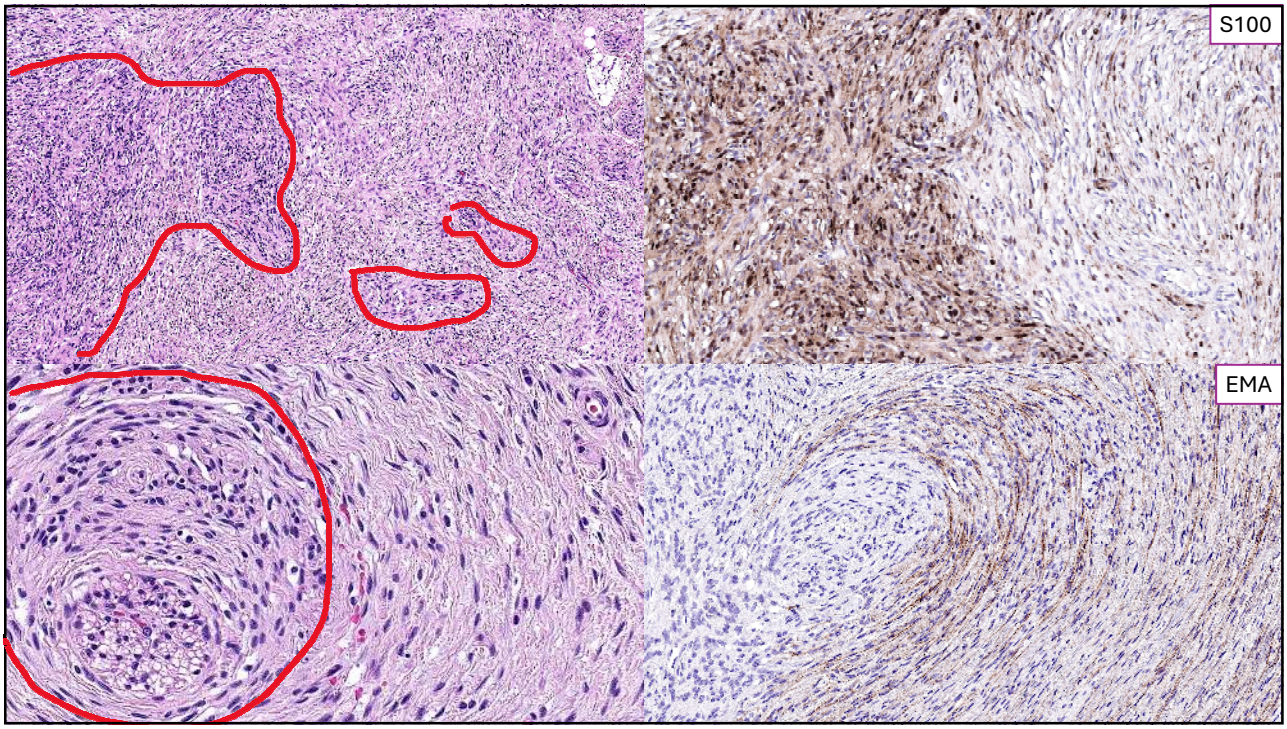

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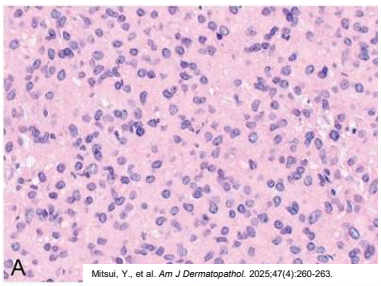
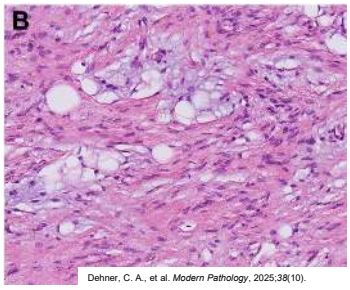
Phenotypic Variations in Hybrid Schwannoma/Perineurioma:

Epithelioid schwannoma component



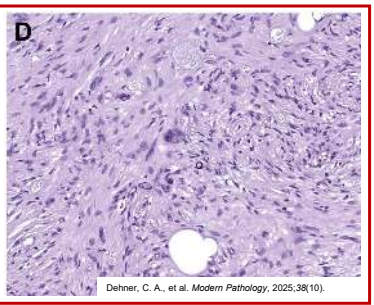
Mitsui, Y., et al. *Am J Dermatopathol.* 2025;47(4):260-263.

Myxoid stroma with pseudo-lipoblasts



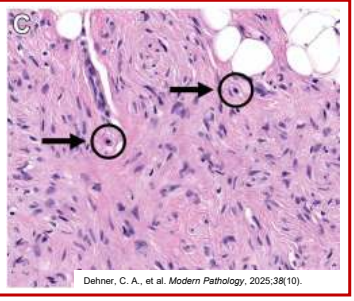
Dehner, C. A., et al. *Modern Pathology*, 2025;*38*(10).

Degenerative nuclear atypia



Dehner, C. A., et al. *Modern Pathology*, 2025;*38*(10).

Abundant peripheral fat with numerous mast cells



Dehner, C. A., et al. *Modern Pathology*, 2025;*38*(10).

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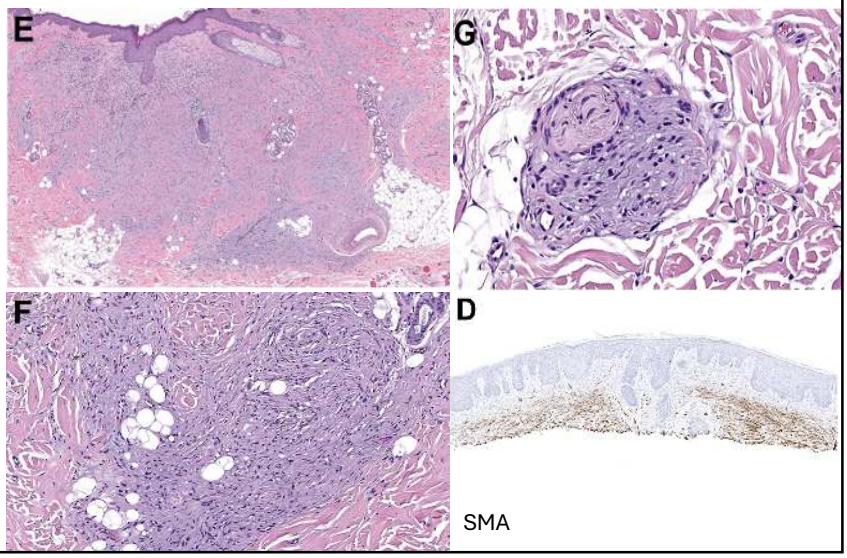
Does myoid/smooth muscle differentiation occur in hPNSTs?

MODERN PATHOLOGY
USCAP
Journal homepage: https://modernpathology.org/
Research Article

Beyond Hybrid Morphology: A Large Series of Fusion-Driven Benign Peripheral Nerve Sheath Tumors Including 5 Tumors With Novel Fusions

Carina A. Dehner[a], Tania Platero-Portillo[b], George Jour[c], Carla Saoud[d], Yanming Zhang[d], Darya Buehler[e], Meera Hameed[d], Michael Michal[f,g], Darcy Kerr[h], Klaus J. Busam[d], Abbas Agaimy[i], Jorge Torres-Mora[a], Cristina R. Antonescu[d], Konstantinos Linos[b,*]

- 1 case of hPNST with expression of SMA is reported
  - *Novel SRF::MYOCD* fusion, a know driver of myoid differentiation
  - Combined neural and smooth muscle phenotype by IHC but not by morphology
  - Bland fibroblastic cells resembling desmoplastic melanoma
- Fully developed myoid phenotype in hPNST does not usually occur



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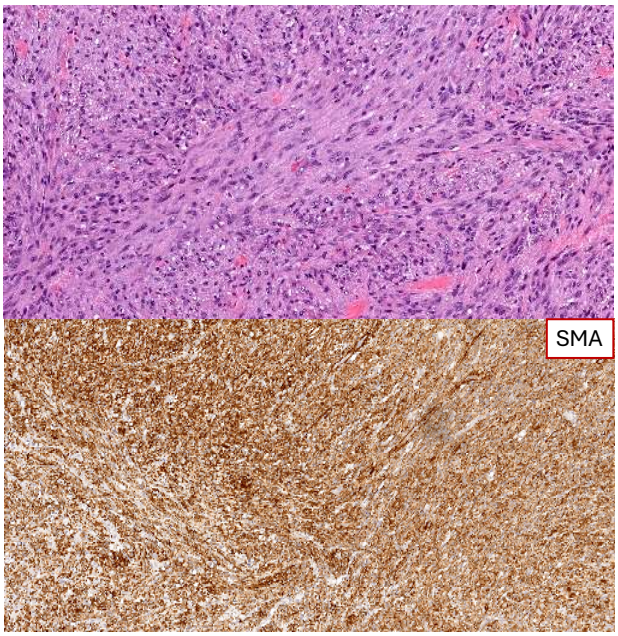
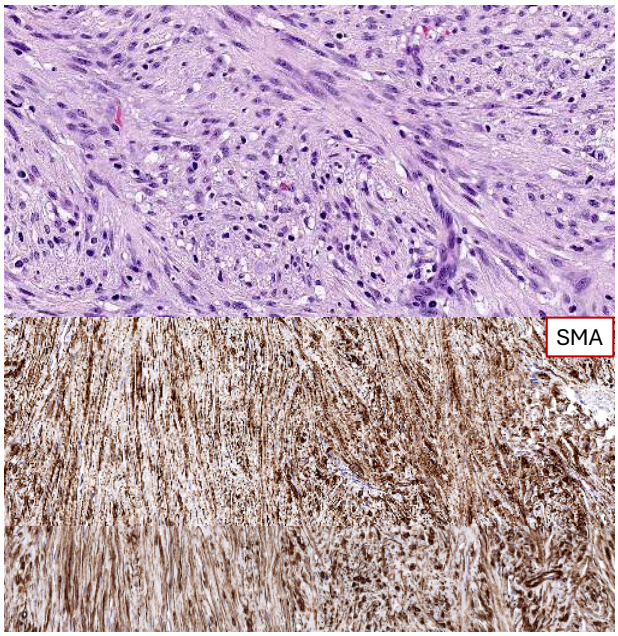
Cellular myofibroma



Our case



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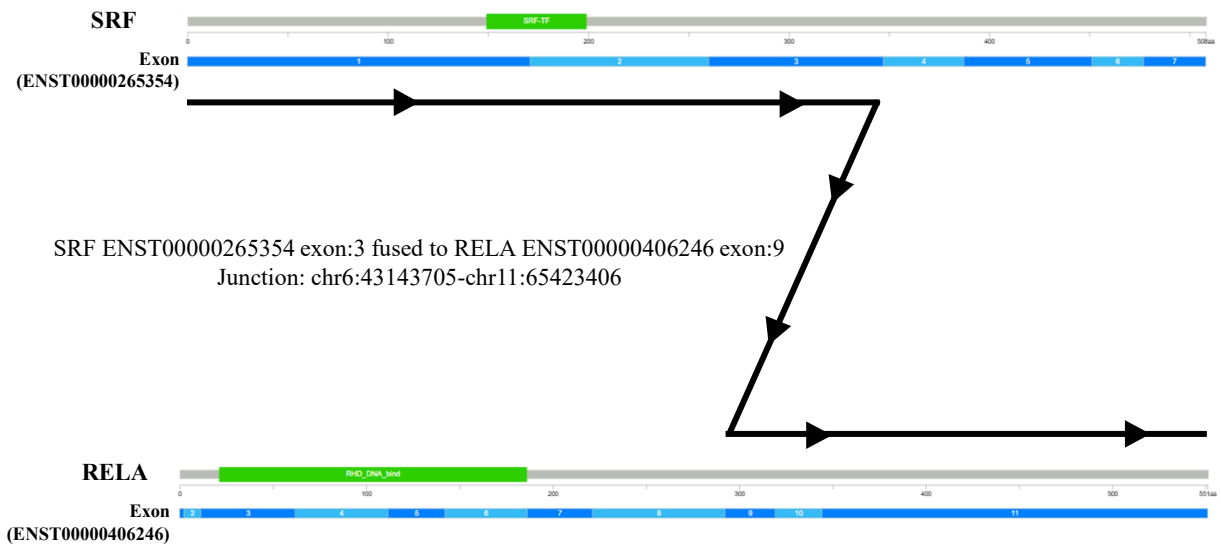
DNA and RNA sequencing by NGS: *SRF::RELA* Fusion



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Serum response factor (SRF) 6p21.1

- A transcription factor regulating all aspects of muscle development
- SRF fusions drive tumors by aberrantly activating smooth and skeletal muscle gene programs through chimeric SRF fusion oncoproteins
- SRF fusions are only found in tumors expressing muscle phenotype:
  - Cellular myoid neoplasms:
    - cellular myofibromas
    - some myopericytomas/perivascular tumors
  - A subset of inflammatory myofibroblastic tumors
  - A subset of rhabdomyosarcomas with favorable outcomes

Antonescu, C. R., et al. *Am J Surg Pathol.* 2017;41(5):677-684.
Costa, A., et al. *Biomolecules.* 2022;12, 1678
Suurmeijer, A.J., et al. *Am J Surg Pathol.* 2020;44:55-60

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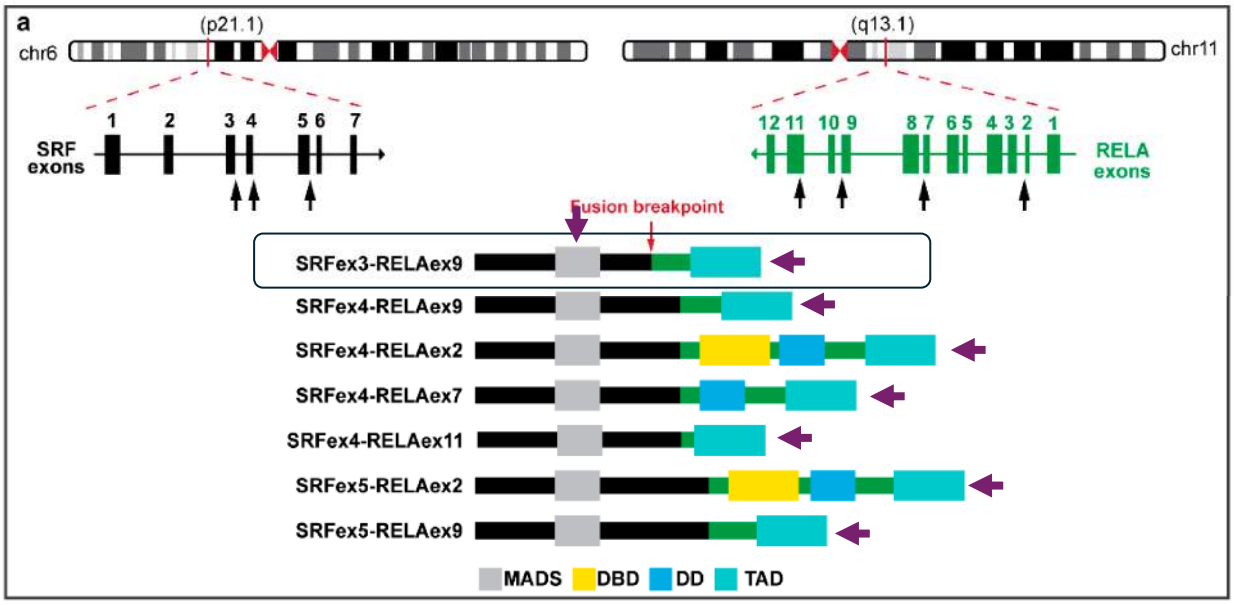

Costa, A., et al. *Biomolecules.* 2022;12, 1678

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Takeaways

- We report a triphasic hPNST, consisting of schwannian, perineurial, and cellular myofibroma-like components
  - The myoid phenotype is a result of *SRF::RELA* fusion
- This is a second case of hPNST with an *SRF* fusion, expanding the histologic spectrum of this entity and showing a fusion-dependent true myoid/smooth muscle phenotype
- The diversity within hybrid peripheral nerve sheath tumors and prognostic impact of various gene fusions, including SRF-driven tumorigenesis, requires further study
- So far (6 months), this tumor has behaved in a benign fashion – no recurrence or metastasis

22

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Thank You!

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