DISCLOSURES

▶ Nothing to Disclose
What immunohistochemical marker is seen in nerve sheath myxoma?

- S100
- HMB-45
- EMA
- Melan-A
What immunohistochemical marker is seen in nerve sheath myxoma?

- S100
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INTRODUCTION

- Uncommon neoplasia of peripheral nerves
- Signs and symptoms due to mass effect on surrounding tissue or direct nerve invasion
- Categorized according to cell type
- Most present as dermal or subcutaneous nodules
- Symptomatic if compresses nerve
NERVE SHEATH ANATOMY

- Epineurium
- Endoneurium
- Perineurium
- Schwann cells
- Axons
- Nerve fiber
- Nerve fascicles

- Perineuroma
- Neurofibroma
- Schwannoma
- Dermal Nerve Sheath Myxoma

Bologna 4th Edition
CELLULAR MARKERS

- S100, SOX 10 - Neural crest derivatives (Schwann cells, melanocytes)
- Synaptophysin - Presynaptic vesicles (neuronal and neuroendocrine cells)
- Epithelial membrane antigen (EMA) - Epitheloid cells (including perineurial cells)
- NF - Neuron cytoskeleton
- CD34 - Hematopoietic cells (fibroblasts)
- Glial fibrillary acidic protein (GFAP) - Non myelinating schwann cells (function as astrocytes in PNS)
SCHWANNOMA

- Proliferation of Schwann cells
- Neurilemoma = Nerve sheath tumor
- Majority are solitary, some associated with NF2
- Most common in large nerve on flexor surfaces > head and neck
  - Deep dermis or subcutis
- More frequent in adults, female predilection
- Likely deleterious mutation in NF2 (merlin protein)
  - Tumor supressor, multiple acoustic Schwannomas in neurofibromatosis type 2
SCHWANNOMA
SCHWANNOMA

HISTOLOGY

- Encapsulated by perinerium
- Hypercellular tissue (Antoni A-type)
  - Proliferation of spindle cells, haphazardly arranged
  - Indistinct cytoplasmic contours
  - Verocay Body - elongated palisaded nuclei in two parallel lines, alternating with hyaline areas void of nuclei (cytoplasmic processes)
- Hypocellular tissue (Antoni B-type)
  - Variable degree of degeneration (cystic, edematous, mucinous, fibrotic, vascular)
  - Thin wispy cells
  - Possible ancient cell changes - atypia
- + S100, + SOX10, + EMA (capsule), - synaptophysin, + collagen IV

Joshi 2012
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NEUROFIBROMA

- Proliferation of Schwann cells triggers proliferation of other components of peripheral nerve (neuromesenchymal tissue)
  - Perineurial cells, endoneurial fibroblasts, mast cells, undifferentiated cells
  - Residual axons intermixed in tumor, helps differentiate from schwannoma

- Solitary cutaneous neurofibroma - common
  - No gender predilection, more frequent in adults

- Easily invaginated - ‘Buttonhole’ sign
NEUROFIBROMA

McKee’s Pathology of the Skin 4th Edition
NEUROFIBROMA

- Neurofibromatosis - consider if multiple neurofibromas on exam
  - Plexiform neurofibroma highly suggestive (not pathognomonic)
    - Involves multiple nerve fascicles
    - Only neurofibroma with risk of malignant transformation (~2-13%)
- Plexiform neurofibroma almost always indicative of Neurofibromatosis type 1
Neurofibroma

Plexiform Neurofibroma

Donner et al 1994
NEUROFIBROMA

HISTOLOGY

- Superficial - non encapsulated
  - Usually in upper dermis
  - Haphazard spindled Schwann cells with wavy nuclei,
  - Fibroblasts form shredded carrot collagen in myxoid stroma
  - Mast cells common
- Deep - encapsulated by perineurium or epineurium
  - More likely location of plexiform neurofibroma
    - Fascicles surrounded by diffuse neurofibroma
  - Rare scattered axons
- + S100, + SOX10, + EMA, + CD34, + NF
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PERINEURIOMA

▶ Proliferation of perineurial cells (epitheloid myofibroblast)
▶ May be intraneural or extraneural (isolated in soft tissue / skin)
▶ Extraneural
  ▶ Cutaneous type - relatively frequent, most commonly on extremities of females
  ▶ Soft tissue type - Most commonly in subcutis of trunk or extremities
  ▶ Sclerosing type - Most common on hand of young male
▶ No sex or age predilection
PERINEURIOMA

HISTOLOGY

- Elongated spindle cell with wavy nucleus
- Well circumscribed, cells may be epithelioid
- Soft tissue perineuroma
  - Form fascicles, surrounding stroma may be hyalinized or myxoid
- Sclerosing perineuroma
  - Form cords, surrounded by think collagen bundles
- + EMA, - S100

Macarenco et al 2007
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HISTOLOGY

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Macarenco et al 2007
DERMAL NERVE SHEATH MYXOMA

- Schwann cell differentiation
- Originally though on spectrum with cellular neurothekeoma
- Wide range of ages (5 months - 84 years old)
  - Average = 36 years old
- No gender predilection
- Most common dermal sites: fingers, knee, pretibial
  - May be found in oral cavity, paranasal sinuses, intraspinal, paravertebral
DERMAL NERVE SHEATH MYXOMA

HISTOLOGY

- Multiple myxoid hypocellular nodules
  - Cord / cluster of epitheloid Schwann cells aggregates
  - Separated by fibrous connective tissue bands
  - Stains with acidic mucopolysaccharides
- + S100, + SOX-10, + GFAP
MALIGNANT PERIPHERAL NERVE SHEATH TUMORS

- Most commonly arise from plexiform neurofibroma (2-13%)
  - Half of MPNST arise from plexiform neurofibroma
  - Rapid enlargement of neurofibroma
- Most commonly found on extremities and trunk > head and neck
- Sporadic - no gender predilection, most frequent in 40 - 50 years old
- NF1 Associated - More common in males 30 - 40 years old
- Loss of NF1 + tumor suppressors (p53, p16)
- Fibroblasts often form majority of tumor (Perineurial or Endoneurial fibroblasts)
MALIGNANT PERIPHERAL NERVE SHEATH TUMORS

HISTOLOGY

- Proliferation of spindle cells
- Hypercellular
- Intersecting fascicles (‘herring bone’)
- Cells often uniform
  - Hyperchromatic nuclei
- Mitoses
- Areas of necrosis
- Partial + S100
- Possible inactivation of NF1 or CDKN2A

Elston 3rd Edition
HISTOLOGY

- Proliferation of spindle cells
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  - Mitoses
  - Areas of necrosis
- Partial + S100
- Possible inactivation of NF1 or CDKN2A
TREATMENT

- Observation
- Biopsy may be therapeutic
- Symptomatic - Excision
  - Malignant peripheral nerve sheath tumor - Treated as soft tissue sarcoma
    - Wide local excision + adjuvant radiotherapy
- Margins not well defined
QUESTION

▸ What histologic characteristic distinguishes NSM from neurothekeoma?

▸ Well Circumscribed

▸ Multinodular

▸ Hypocellularity

▸ Fibrous Connective Tissue
What histologic characteristic distinguishes NSM from neurothekeoma?

- Well Circumscribed
- Multinodular
- Hypocellularity
- Fibrous Connective Tissue


