Immunohistochemistry of soft tissue tumors
Immunohistochemistry

• Major advances:
  → antigen retrieval techniques (HIER)
  → sensitive detection systems
  → numerous antibodies of good quality

• Standardization:
  → automated immunostainers
  → quality assurance programs

• Impressive amount of new information:
  → 12 000 papers/year
  → internet (Pubmed, Immunoquery, …)
Immunohistochemistry

- Future of IHC is promising
- Tissue microarray
- cDNA microarray
Immunohistochemistry of soft tissue tumors

- STT: several lines of differentiation
- Numerous pseudosarcomatous benign lesions
- Non-mesenchymal malignant tumors
Soft tissue tumors
Immunohistochemistry

Conditions of use

- Complementary to H and E
- Quality of technique
- Panel of markers
- Quality of interpretation
Basic panel of antibodies for soft tissue tumors

- Cytokeratin
- EMA
- S100 protein
- Desmin
- Smooth muscle actin
- CD34

Sarcomatoid carcinoma

Synovial sarcoma, ...

Nervous and melanocytic T

Muscle tumors

Myofibroblastic lesions

Numerous tumors
Immunohistochemistry of soft tissue tumors
Basic panel

- AE1/AE3
- EMA
- S100 protein
- SMA
- Desmin
- CD34

- CD99
- CD31
- HMB45/Melan A
- CD20/CD3/CD30
- Chromogranin A
Immunohistochemistry of soft tissue tumors
New antibodies

- Myogenin
- H-caldesmon
- CD117 (c-kit)
- HHV8
- MDM2/CDK4
- CD163
Immunohistochemistry of soft tissue tumors

Useful antibodies

- Vimentin
- BCL2
- Antichymotrypsin
- Myoglobin
- NSE
Soft tissue tumors
Immunohistochemistry

Interpretation

• Quality of technique
• Type of positivity
• Expected positivities
• Unexpected positivities
Soft tissue tumors
Immunohistochemistry

Type of positivity

ERMS - myogenin

PNET – CD99

SFT- CD99
Poorly specific markers

• CD34
• CD99
• EMA
• S100 protein
• SMA
Soft tissue tumors which are CD34 positive

- Vascular tumors
- DFSP
- Solitary fibrous tumor
- GIST
- Spindle cell/pleomorphic lipomas
- Some nervous tumors
- Epithelioid sarcoma
Soft tissue tumors which are CD99 positive

- PNET
- Synovial sarcoma
- Solitary fibrous tumor
- Mesenchymal chondrosarcoma
- Neuroendocrine carcinoma
- Lymphoblastic lymphoma
- Alveolar rhabdomyosarcoma
Markers with unexpected positivities

- Cytokeratin
- Desmin
- CD31
- CD117
- Fli-1
Unexpected positivity for cytokeratin

- Leiomyosarcoma
- Rhabdomyosarcoma
- PNET
- Epithelioid vascular tumors
- Melanoma
PNET and cytokeratin
Tenosynovial tumor and desmin
Histiocytes and CD31
Soft tissue tumors
Immunohistochemistry

*Practical interests*

- Identification of a benign lesion
- Nature of an undifferentiated malignant tumor
- Classification of a sarcoma
Soft tissue tumors
Immunohistochemistry

*Benign vs malignant*

- Major and frequent problem
- Solution: - clinical context
  - H and E
- *Usefulness of IHC*
Soft tissue tumors
Immunohistochemistry

Rare/atypical benign lesions

• Nerve sheath tumors
• Histiocytic lesions
• Rare tumors: (paraganglioma, glomus T, SFT, angiomyolipoma, myoepithelioma)
• Myofibroblastic lesions
Atypical/rare benign nerve sheath tumors - *S100 protein*

- Ancient schwannoma
- Cellular schwannoma
- Myxoid neurofibroma
- Neurofibroma with nuclear atypia
- Diffuse neurofibroma
- Granular cell tumor
Cellular schwannoma
Benign histiocytosisfibroma

CD34
Rare benign tumors

- **Paraganglioma**: chromogranin A, S100+
- **Glomus T**: SMA, caldesmon +
- **SFT**: CD 34 +
- **Myoepithelioma**: AE1/AE3, PS100+
- **Perineurioma**: EMA+
Rare benign tumors

- Paraganglioma:
  - S100 and Chromogranin A +
Soft tissue tumors
Immunohistochemistry

*Practical interests*

• Identification of a benign lesion
• **Nature of an undifferentiated malignant tumor**
• Classification of a sarcoma
Non-mesenchymal malignant tumors

• Carcinoma
• Melanoma
• Lymphomas

Be careful if:
• Previous history of cancer
• Some localisations
• Non-specific pattern
Non-mesenchymal malignant tumors

Localisations at risk

- Skin and mucosae
- Lymph node areas
- In the vicinity of some viscera (lung, kidney, thyroid, breast...
Non-mesenchymal malignant tumors

Solutions

• If previous history: compare both tumors
• Correct sampling
• IHC : AE1/AE3, S100, CD20,....
Sarcomatoid carcinoma

55 year-old male

Polypoid tumor of the tongue
Soft tissue tumors
Immunohistochemistry

Practical interests

• Identification of a benign lesion
• Nature of an undifferentiated malignant tumor
• Classification of a sarcoma
Classification of a sarcoma

Immunohistochemistry usefulness

- Sarcomas with specific IHC
- Sarcomas with useful markers
- Sarcomas with no specific markers
Sarcomas with specific IHC

- Rhabdomyosarcoma
- Vascular sarcomas
- GIST
- Dedifferentiated liposarcoma
- Epithelioid sarcoma
- Clear cell sarcoma
- Intra-abdominal desmoplastic tumor
Myogenic transcription factors

Myogenin and MyoD1
Immature skeletal muscle
Specific marker:
  myogenin > myoD1
  nuclear positivity
  regenerative muscle
Sensitivity and histologic types
Alveolar rhabdomyosarcoma

myogenin
Embryonal rhabdomyosarcoma

myogenin
Pleomorphic rhabdomyosarcoma

myogenin
Vascular sarcomas

- Spindle cell angiosarcoma
- Epithelioid angiosarcoma
- Kaposi sarcoma
- Epithelioid hemangioendothelioma
Vascular sarcomas

Useful markers

- CD 31 +
- CD 34 +
- Factor 8 +
- FLI1 +
- HHV8 +/-
- cytokeratin +/-
- EMA +/-
- C-Kit +/-
Vascular sarcomas

Useful markers

• Epithelioid angiosarcoma: CD31, CD34 +
Vascular sarcomas

Useful markers

• Kaposi sarcoma: CD34, CD31 and HHV8+
Human Herpes Virus 8 (HHV8)

- Kaposi sarcoma
- Effusion lymphoma
- Castleman disease
- Nuclear positivity
Kaposi sarcoma

HHV8
CD117 (c-kit)

- C-kit $\rightarrow$ tyrosine kinase receptor
  (mast cells, melanocytes, germ cells, interstitial cells of Cajal)
- GIST : mutation of c-kit $\rightarrow$ permanent TK activity
- CD117 positive in 95 % of GIST
- CD117 positivity is required for imatinib treatment
CD117 - c-kit
CD117 positivity

- GIST
- Mast cell disease
- Seminoma
- Melanoma
- CML
- Angiosarcoma
- PNET
- Chondrosarcoma
- Synovial sarcoma
- Carcinomas
Immunohistochemistry of GIST

- CD117: 95%
- CD34: 60-70%
- H-caldesmon: 80%
- SMA: 15-60%
- S100 protein: 5-10%
• MDM2: Inhibitor of P53 protein
• MDM2/CDK4 amplification in well diff/dediff liposarcomas
• IHC with IF2 antibody for MDM2
• Diagnosis of dediff. liposarcoma
Epithelioid sarcoma

- Useful markers: CytoK, EMA, CD34+ and CD31-
Clear cell sarcoma/Soft tissue melanoma

- Useful markers: S100, HMB45, MELAN A, MART1 +
Classification of a sarcoma

Immunohistochemistry usefulness

- Sarcomas with specific IHC
- **Sarcomas with useful markers**
- Sarcomas with no specific markers
Sarcomas with useful markers

- Synovial sarcoma
- Leiomyosarcoma
- PNET
- DFSP
- MPNST
- Extra-skeletal myxoid chondrosarcoma
Synovial sarcoma

Useful markers

- AE1/AE3 + (65%)
- EMA + (95%)
- CD34 - (+ 5%)
- S100 + (30%)
- CD99 + (>50%)
Spindle cell synovial sarcoma

- Useful markers:
  EMA,
  AE1-AE3, CD34
Leiomyosarcoma

*Useful markers*

- H-caldesmon (40-70%)
- SMA (70%)
- Desmin (50%)
**H-caldesmon**

- Regulator of smooth muscle contraction
- Positivity in: - smooth muscle tumors
  - glomus tumor
  - GIST
  - angiomyolipomas
- Negative in: - myofibroblastic proliferations
  - skeletal muscle tumors
Pleomorphic leiomyosarcoma

SMA

desmin

caldesmon
Muscular markers

• Desmin: smooth muscle and skeletal muscle
• Smooth muscle actin: smooth muscle and myofibroblasts
• Myogenin: immature skeletal muscle
• H-caldesmon: smooth muscle
Sarcomas with useful markers

- Synovial sarcoma
- Leiomyosarcoma
- PNET
- DFSP
- MPNST
- Extra-skeletal myxoid chondrosarcoma
Tumors with no specific marker

- Fibrosarcoma
- Myxofibrosarcoma
- Low-grade fibromyxoid tumor
- Osteosarcoma
- Myxoid/round cell liposarcoma
- Pleomorphic liposarcoma
- Pleomorphic MFH
Immunohistochemistry of soft tissue tumors

Conclusions

• Major tool for soft tissue tumors
• Quality of technique
• Panel of markers depending on H and E
• Global interpretation