Immunohistochemistry in Bone and Soft Tissue Tumors

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Introduction

• Bone tumors represent a wide variety of tumors of various origins and malignant potentials.

• These different tumor entities may display strong morphological resemblance to each other, thereby resulting in
  – Profound difficulties in differential diagnosis
Introduction

• Since determining the best course of treatment for sarcomas of the bone and soft tissues is a complex process.

• Making an accurate diagnosis in those tumors is essential to have effective personalized treatment strategies.

• Besides appropriate radiographic imaging and histological findings, immunohistochemical studies can be important adjuncts to make an accurate diagnosis.
Primary Bone Tumors

- Although the diagnosis is based primarily on clinical, radiological and histological findings, the role of immunohistochemistry continues to be investigated for diagnostic and prognostic implications.
Most commonly used IHC stains in primary bone tumors

- Vimentine: mesenchymal benign and malignant
- Alkaline phosphatase: bone forming tumors
- S100: cartilage forming tumors
- SMA: some cases of high grade osteosarcoma

- **Ki67 and P53**
  - *usually considered as indicators of malignant potentiel*
  - *have been highly studied in bone tumors (benign vs malignant)*

- **MDM2 and CDK4**:
  - Can distinguish low grade osteosarcoma (positive) from benign fibrous and fibro-osseous lesion (negative)

- **Her2 neu**: prognostic issue
Osteoblastoma

- subclassified:
  - **Classical**
  - **Atypical**
    - Based on histological parameters (in atypical osteoblastoma: high cellularity, prominent blue osteoid, and epithelioid osteoblasts).
Atypical osteoblastomas and osteosarcoma
Ki67

- Osteosarcoma
- Atypical osteoblastoma
P53

Osteosarcoma

Atypical osteoblastoma

Figure 6 - Atypical osteoblastoma. Immunohistochemical detection of the p53 protein with DO7. A distinct nuclear reaction is seen the majority of the tumor cells (Case 26, immunohistochemistry, X 400)
Ki67 and P53 in bone tumors

- Ki67 and P53 don't have a significant role in distinguishing osteosarcomas from atypical osteoblastomas.
- However, Ki67 and p53 can be used as predictors of recurrence in atypical osteoblastomas.
MDM2 in low grade osteosarcoma and fibrous dysplasia
CDK4 in low grade osteosarcoma
MDM2 and CDK4 in bone tumors

*Immunohistochemical staining for MDM2 and CDK4 is not very sensitive on biopsy specimens!!*

- *Can be misinterpreted as false negative*
Recent studies show that over-expression of \textbf{Her2/neu} by osteosarcoma is correlated with a significantly worse response to pre-operative chemotherapy and shorter survival.
IHC in Anaplastic/poorly differentiated Osteosarcoma

- Micro description
  Bizarre and undifferentiated tumor cells with malignant osteoid.
- Foci carcinoma-like.
- Foci of undifferentiated sarcoma.
Osteosarcoma vs Metastasis

1- Osteosarcoma

[Image of histological slides showing different staining techniques for osteosarcoma]
Epithelioid osteosarcoma

Cytokeratin and EMA usually negative in osteosarcoma but positive cases exist. Some rare osteosarcomas show strong positivity.
Osteosarcoma v/s poorly differentiated metastatic carcinoma

- **Osteoid formation is the KEY feature** in the differentiation of osteosarcoma from metastatic poorly differentiated carcinoma and pleomorphic sarcoma.

- Special techniques are of little diagnostic help.
IHC in cartilage forming tumors

- Enchondroma and well differentiated chondrosarcoma can have similar morphology due to hypercellularity, binucleation, myxoid changes, erosion of cortex.
  - Studies have shown that there is no reliable immunohistochemical panel for distinction between benign and malignant counterparts.
IHC plays a major role in differentiating the various entities of round cell tumors in contrast to bone and cartilage forming tumors.
Round cell tumor bone and soft tissue

- Ewing sarcoma/PNET
  - Terms usually used interchangeably; some suggest to call Ewing if undifferentiated or a bone tumor and PNET if neural morphologically or a soft tissue tumor

- Lymphoma
- Multiple myeloma
- Metastatic small cell carcinoma
- Small cell osteosarcoma
- Embryonal rhabdomyosarcoma
- Metastatic neuroblastoma
- Malignant melanoma
- Desmoplastic round cell tumor
• Lymphoma (CD20)

• Multiple Myeloma (CD138)

• Ewing Sarcoma (CD99, Vimentin)
• Immunohistochemistry is not only essential but mandatory in the differential diagnosis of round cell tumors.
Metastatic carcinomas IHC is useful to target the primary

- PSA IN METAS PROSTATE
CK7 and TTF1 in lung adenocarcinoma metastatic to bone
Metastatic clear renal cell carcinoma
Metastatic malignant melanoma
Synovial sarcoma

Cytokeratin, VIMENTIN, EMA, Bcl2
In Summary

• The role of immunohistochemistry in primary bone tumors is limited

• However, it is mandatory in round cell, biphasic, spindle cell tumors and melanomas to obtain a definitive diagnosis

• It is also essential in identifying and targeting the primary site in metastatic tumors
• Thank you