Case Presentations 17-20
Case Presentations 17
Case 17

- 2 year old boy with history of urinary retention and prostate biopsy.
- After biopsy and chemotherapy, child regains urine flow but the mass does not shrink on imaging.
- A total prostatectomy was performed.
Case 17: Prostatic neoplasm: capsule

Geographic necrosis

Viable neoplasm
Case 17. Undifferentiated neoplasm
Case 17. Moderately pleomorphic primitive cells

Lymphs, mits, karyo
Case 17. Anaplasia
Case 17. Anaplasia
IHC

- Desmin: strongly positive
- MyoD1: strongly positive
- SOX-9: strongly positive [by report]
- Myogenin: focally positive
Cytogenetics

• FISH for FOXO1 (13q14.1) gene rearrangement: negative (performed at two institutions)
Case 17
Diagnosis: Treated embryonal rhabdomyosarcoma, with diffuse anaplasia, fusion-negative
Anaplastic rhabdomyosarcoma (RMS)

• Original concepts
  – Seen in both forms of RMS, embryonal and alveolar
  – Builds on concepts of anaplastic Wilms tumor
    • Nucleomegaly (>3X size of adjacent cells)
    • Hyperchromasia
    • Atypical multipolar mitoses
  – Diffuse and focal forms
    • Diffuse = clonal
    • Focal = occasional isolated cell
Anaplastic RMS: prognosis

• Persists with chemotherapy (marker of chemoresistance)
• Proven marker of bad outcome in embryonal RMS in prospective and retrospective studies
  – No effect on alveolar RMS outcome
• Did not make level of significance in multivariate analysis
• Has not been used to make protocol-based treatment decisions

- Nine per cent of embryonal RMS (23/223 cases)
- Eight per cent of alveolar RMS (12/139 cases)
- Two of 17 spindle cell RMS cases
- One of 36 botryoid RMS cases
- Total 7% of RMS cases (39/463)
Qualman et al: Outcome analysis of embryonal RMS

- No difference between diffuse and focal anaplasia
- Univariate analysis: 5 year survivals
  - With anaplasia: 68%
  - Without anaplasia: 82%
  - Only predictive with intermediate risk disease
- Multivariate analysis
  - Demonstrated a statistical trend (p = 0.08)
  - Was not a significant factor compared to proven factors like metastasis, age, stage, site, group, etc.
Anaplastic RMS: Genetics

- Qualman: Double minutes (gene amplification) found in 6 of 9 karyotypes
- Bridge: Genomic amplification frequent on comparative genomic hybridization
  - All but one of 6 ERMS with amplicons showed anaplasia
  - These 6 involved 15q, 18q, 11q, and 12q.
Case 18

- 15 month-old male infant with large buttock mass
- Pulmonary metastasis found on imaging.
- Wide excision of soft tissue mass was performed.
- Slides courtesy of Dr. Denise Malicki, Rady Children’s Hospital, San Diego.
Case 18. Fibrosarcoma-like spindle cell tumor
Case 18: Permeation of adjacent fat
Case 18: Permeation of adjacent fat
Focal myxoid change
Focal myxoid change
Herring bone pattern
Other IHC

- Glut 1: negative
- CD31: negative
- D2-40: negative
- Factor XIIIa: negative
Cytogenetics

- **ETV6-PDGFB RT-PCR:**
  - negative for fusion
- **SS18 FISH:**
  - negative for 18q11.2 rearrangement
- **NTRKC FISH:**
  - negative for rearrangement
Diagnosis:
CD34 positive fibrosarcoma, most consistent with fibrosarcoma ex dermatofibrosarcoma protuberans
Comment: Cannot absolutely exclude extra-pleural solitary fibrous tumor. STAT6 testing may be helpful.
Differential diagnosis of pediatric fibrosarcoma

• Infantile fibrosarcoma: t(12;15), \textit{ETV6-NTRK3} fusion
• Low grade fibromyxoid sarcoma: MUC4, alternating pattern, large collagenous rosettes, \textit{FUS-CREB3L1/FUS-CREBL2} fusions
• Synovial sarcoma: EMA/CK/TLE1 positivity, \textit{SSX-SS18} fusions
• MPNST: involvement of nerve or neurofibroma, NF1 history, S100 positivity
• Fibroma-like epithelioid sarcoma: EMA/CK positivity, INI1 negativity
Differential diagnosis of pediatric fibrosarcoma

- Dermatofibrosarcoma protuberans
- Solitary fibrous tumor
Dermatofibrosarcoma protuberans (DFSP) in children

- Relatively uncommon in children but being increasingly recognized
- Congenital lesions may appear innocuous
- Slowly progressive lesion most often in trunk
- May be associated with immunodeficiency
- May be multifocal
DFSP: pathology

- Classic, giant cell, myxoid, fibrosarcomatous, and pigmented forms
- Permeation of fat
- CD34 positive, Factor XIIIa negative (beware intermediate lesions in spectrum of dermatofibroma)
  - CD34 expression often lost in fibrosarcomatous areas
- Has t(17;22) translocation, COL1A1-PDGFB fusion
  - Two of seven RT-PCR negative in one study
DFSP: Differential diagnosis

- Nodular fasciitis (positive for USP6 fusions)
- Infantile myofibroma (actin positive)
- Deep dermatofibroma/intermediate lesions (may be Factor XIIIa and CD34 positive)
- Spindle cell melanoma (check epidermis, melanocytic markers)
Solitary fibrous tumor in children

- Extremely rare, limited to isolated case reports
- Pleural or extrapleural
- Patternless and hemangiopericytomatous patterns
- CD34, CD99, BCL2 positive (may be actin positive)
- A new marker: STAT6 (has gene fusion and overexpression)
Case 19
Case 19

- 12 year old girl with tumor involving metaphysis of distal radius.
- Periosteal elevation and soft tissue extension found on radiographs.
- The patient was treated with chemotherapy.
- An *en bloc* resection was performed afterwards.
Case 18. malignant cartilage
Case 19. Cartilage with osteoid
Case 19. Lacy osteoid, no cartilage
Case 19. Small cell pattern
Diagnosis: Conventional osteosarcoma, high grade, chondroblastic variant
Differential diagnosis: malignant chondroblastic neoplasms in children

• Primary chondrosarcoma
  – Rare but may occur in spine and head and neck
  – Usually mesenchymal variant

• High grade chondroblastic osteosarcoma (more common in kids)
  – Differentiate from osteoid producing mesenchymal chondrosarcoma

• Intermediate grade chondroblastic periosteal osteosarcoma

• Teratomatous lesions (look for other elements)

• Heterologous differentiation in dedifferentiated liposarcoma, Sertoli-Leydig tumor, PNET, RMS (other elements)

• Chordoma (location and cytokeratin/brachyury expression)
Primary pediatric chondrosarcoma

- Age range of 16 months-81 years in one large metaanalysis, with mean of 34-39 years and peak between 30-50 years
  - Includes mesenchymal chondrosarcoma (covered in another lecture)
- Genetic predisposition
  - Ollier's disease
  - Maffucci's disease
  - Hereditary exostosis ($EXT1, EXT2, EXT3$ mutations)
  - Even rarer osteodysplasias ($PTPN11, ACP5$ mutations)
- Acquired mutations in $IDH1, IDH2$ frequent overall
  - Isocitrate dehydrogenase genes in Kreb cycle
Chondroblastic osteosarcoma

• One of multiple other variants
  – Osteoblastic/sclerosing
  – Fibroblastic
  – Anaplastic
    • Fibrohisticytic or epithelioid (beware cytokeratin positivity)
  – Telangiectatic
  – Round cell (covered in another lecture)
Case 20
Case 20

• 19 year old male who develops swelling and increasing pain of lower jaw
• Follows wisdom teeth extraction.
• CT shows a destructive lytic and sclerotic lesion of mandible.
• A biopsy was performed.
Case 20: irregular bony trabeculae
Case 20. Collagenous intertrabecular region
Case 20: Sparse lymphocytes
Variable osteoid seam
Case 20. dense cortical bone
Case 20. Dense collagenous zones, with osteoid transition
Dense collagen
Diagnosis:
Chronic sclerosing osteomyelitis
Differential diagnosis: non-neoplastic bony lesions

• Fracture callus (hemorrhage, organization, chondroid matrix)
• Osteomyelitis (inflammation, osteonecrosis, reactive bone)
• Fibrous dysplasia of bone (woven bone, non-osteoblastic)
• Osteofibrous dysplasia (tibia, cytokeratin)
• Osteitis fibrosa cystica (hyperparathyroidism, high serum Ca)
• In soft tissue, consider myositis ossificans, dermatomyositis, heterotopic bone, trauma, periostitis ossificans
Garré's sclerosing osteomyelitis

• First described by Carl Garré in 1893
• Non-suppurative chronic osteomyelitis form of periostitis ossificans
• Proliferative periosteum
• Peripheral subperiosteal bone formation
• Mild but prolonged infection or irritation, without necrosis or exudate
• Particularly common in tibia, jaws
Garré's sclerosing osteomyelitis
Clinical features

- Facial assymetry, bony assymetry
- Progressive swelling
- Variable pain, malaise, trismus
- Unilateral induration with normal overlying skin or mucosa
Garré's sclerosing osteomyelitis

• May or may not respond to antibiotics
  – Resolution of pain, bony changes
• May require multiple CT scans, with relatively high dose of irradiation
• Rarely progresses to secondary osteosarcoma
• May occur with multifocal recurrent osteomyelitis, an autoimmune disease with a genetic basis
Garré's sclerosing osteomyelitis: histology

- Fibrous dysplasia-like pattern ("ground glass" appearance on imaging)
- Retiform pattern (lace-like)
- Paralled (lamellated) pattern - do not confuse with parosteal osteosarcoma
- Overlapping features with Caffey's disease (cortical hyperostosis), seen in infants
Other diseases to consider

- Low grade, osteoblastic-like osteosarcoma
- Parosteal osteosarcoma
- Hypertrophic osteoarthropathy
  - History of heart or lung disease
- Congenital syphilis
- Cherubism (bilateral, extensive)