Diagnostic Imaging of Pediatric Soft Tissue Sarcomas

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Learning Objectives

• Become familiar with common soft tissue sarcomas that occur in children
• Understand the role of appropriate imaging in the diagnosis, staging and management of pediatric soft tissue sarcomas
Introduction

• What is a sarcoma?
  – Malignant tumor arising from “solid” connective tissues of mesenchymal origin
  – 2 basic types: bone sarcomas and soft tissue sarcomas
  – <1% of all cancers
• C/W carcinoma:
  – Malignant tumor of epithelial origin
  – ~90% of all cancers
• Other cancers: leukemia, lymphoma, myeloma; mixed
Introduction

• ~11,000 new cases of STS per year in the U.S.
• Compared with:
  – ~3,000 new cases of bone sarcoma
  – ~50,000 new cases of leukemia*
  – ~70,000 new cases of non-Hodgkin lymphoma*
  – ~240,000 new cases of prostate carcinoma*

*Considered “common” cancers (>40,000 annual incidence) by the American Cancer Society

www.cancer.gov/cancertopics/types/commoncancers
Introduction

• Most STS are encountered in adults >20y of age
  – Most common soft tissue sarcomas in older adults:
    • Pleomorphic sarcoma ("malig. fibrous histiocytoma")
    • Liposarcoma
    • Leiomyosarcoma
• ~1 in 10 STS are encountered in patients <20y of age
  – ~5% of childhood malignancies (<leukemia, CNS tumors)
  – The common STS seen in older adult patients are relatively uncommon in children

www.cancer.gov/cancertopics/types/commoncancers
Classifying Pediatric Soft Tissue Sarcomas

“Pediatric Type” STS

• Median incidence in 1st two decades of life
• Commonly small round blue cell tumors (e.g., rhabdomyosarcoma, Ewing sarcoma family of tumors)
• High response rates to chemo (+ surgery and/or RT for local control)

“Adult Type” STS

• Occur most often beyond 3rd decade of life
• Spindle cell (or other) differentiation
• Surgery = mainstay of treatment +/- RT; chemoresistance often predominates
Classifying Pediatric Soft Tissue Sarcomas

• More “typical” classification:
  – **Rhabdomyosarcoma** (~50%): most children <6y of age; 2\textsuperscript{nd} peak between 15 & 19y
  – **Nonrhabdomyosarcomatous sarcomas** (~50%): most occur in adolescents and young adults
    • Synovial sarcoma
    • Fibrosarcoma
    • Malignant peripheral nerve sheath tumors (MPNST)
    • Ewing sarcoma family of tumors (ESFT)
Clinical Presentation and Evaluation

- Most common symptom: mass increasing in size; usually NOT painful
- Important: majority of soft tissue masses that present to physician are benign
  - Vascular lesions
  - Fibrous and fibrohistiocytic tumors
  - Pseudotumors
Clinical Presentation and Evaluation

- Is imaging necessary?
- Depends on H&P
- May observe lesion if <5 cm, soft, superficial, not enlarging
- Imaging should be considered in other cases
Role of Imaging

- Detection
  - Imaging not as important for detection of ST masses as for bone lesions
  - Exception: use of whole body imaging (MRI, PET) to detect “occult” primary soft tissue tumor in patients with disseminated disease

- Characterization of the mass
- Staging and post-treatment assessment
- Guiding biopsy
Role of Imaging

- Detection
- Characterization of the mass
  - Is it a neoplasm? If not, what is it?
  - If so, are there imaging features that suggest a particular diagnosis, and therefore suggest whether the mass is benign or malignant?
- Staging and post-treatment assessment
- Intervention (if necessary)
Imaging Studies

- Radiography
- Ultrasonography
- Computed Tomography
- Positron Emission Tomography (role developing)
- Magnetic Resonance Imaging
  - Technique of choice for evaluation of soft tissue masses due to excellent soft tissue contrast
Radiographs Remain an Important First Study!

- Often unrewarding, BUT…
- May reveal:
  - *Bone involvement by a soft tissue mass*
  - *Lesion projecting from bone* that presents as a deep soft tissue mass clinically
  - *Mineralization or fat* that assists diagnosis
Ultrasonography

• Simple first-line examination, esp. for young children
  – Cyst versus solid, non-vascular versus vascular, vessel density
  – Pseudotumors: synovial cyst, foreign body
  – Benign tumors: hemangioma, fibromatosis colli
  – Vascular malformations
Computed Tomography

- Largely replaced by MRI for evaluation of ST tumors
- Indications:
  - Patients with contraindication to MRI
  - Lesions of chest & anterior abdominal wall
  - Better characterization of mineralization

“Myositis Ossificans”

T2

T1+C
Positron Emission Tomography

• Role still developing:
  – High-grade malignancies → higher rates of glycolysis/FDG uptake (overlap)
  – Intensity of uptake and identification of necrosis on pre-treatment staging studies → prognostic markers
  – Direct biopsy to metabolically active area of tumor
MRI

• Accepted as modality of choice for evaluating ST masses
  – Superior soft tissue contrast
  – Lack of ionizing radiation
• Sedation usu. needed for young children
MRI

- Standard “anatomic” technique:
  - At least 2 orthogonal planes
  - T1W and fluid-sensitive images +/- fat suppression
  - Gd-enhanced imaging
    - Identifies viable tumor (versus necrosis) for biopsy, demonstrates enhancement in myxoid lesions with pseudocystic appearance
MRI

- Ability to predict histology limited
- Highest confidence in characterization occurs with benign masses
  - Lipomas/lipoblastomas (fat)
  - Vascular lesions (lobular structure)
  - Neurogenic tumors (nerve)
  - Cysts (nonenhancing fluid, location)
  - Hematomas (blood products)
  - Abscesses (pus + surrounding inflam.)
MRI

- Lesion characterization includes assessment of:
  - Signal intensity: often “nonspecific”; can detect fat, fluid, blood products, fibrous tissue
  - Morphology: fusiform, lobulated
  - Location
    - Subcutaneous v. deep
    - Intra- v. inter-muscular
    - Intra- v. juxta-articular
    - Adjacent structures
  - Size
  - *Patient age and lesion prevalence*
MRI

- Features favoring malignancy:
  - Large size
  - Deep location
  - Heterogeneous signal/enhancement (necrosis)
  - Bone/neurovascular involvement
MRI

- Pitfalls:
  - Both benign and malignant soft tissue tumors often have “well-defined margins”
  - Superficial sarcomas often appear less “aggressive” than deep sarcomas (smaller)
  - Gadolinium enhancement is seen in both benign & malignant tumors (overlap)
• Emerging techniques:
  – Dynamic contrast-enhanced MR imaging: evaluates enhancement patterns (wash in, wash out) over time
  – Diffusion-weighted MR imaging: evaluates random motion of water molecules (restricted diffusion implies higher cellularity)
  – MR spectroscopy: can characterize lesions based on metabolic constituents, including choline, a marker for membrane turnover

OVERLAP
Key Information From Imaging Studies that the Treatment Team Needs to Know

• Character of lesion (benign, malignant, indeterminate)
• Size of the lesion (+ reactive zone of edema)
• Location
  – Compartments
  – Relationship of lesion to neurovascular structures, joints
  – Relationship to palpable or fluoroscopically identifiable anatomic landmark
• Other lesions on field-of-view (lymph nodes, mets)
• Recommendation (orthopaedic oncology consultation versus biopsy)
Selected Sarcomas

- Rhabdomyosarcoma
- Synovial sarcoma
- Fibrosarcoma
- Dermatofibrosarcoma protuberans
- Malignant peripheral nerve sheath tumor
- Ewing sarcoma family of tumors
- Liposarcoma (myxoid)

Most of these tumors have no specific imaging features (hypointense on T1WI, hyperintense on T2WI)
Rhabdomyosarcoma

- **Most common soft tissue sarcoma in children**
- Tumor with cells showing features of skeletal muscle, but does not necessarily arise from skeletal muscle
Rhabdomyosarcoma

- Three subtypes
  - Embryonal
  - Alveolar
  - Pleomorphic (almost exclusively in adults; rare in children)
Rhabdomyosarcoma

- Three subtypes
  - Embryonal
    - 2/3 of cases
    - Children typically <10y of age
    - ~50% in the head and neck, followed by GU system (~30%); <10% arise within skeletal musculature of extremities
  - Alveolar
  - Pleomorphic
Rhabdomyosarcoma

- Three subtypes
  - Embryonal
  - Alveolar
    - 1/3 of cases
    - More common in adolescents and young adults
    -Usu. intramuscular
    -Lesions in extremities are typically alveolar
    -Worse prognosis than embryonal type (esp. if assoc. w/ translocation)
- Pleomorphic
Rhabdomyosarcoma

- Radiographs: no specific features (mass, occ. bone involvement)
- MRI: no specific features
  - T1WI: usually isointense to muscle
  - T2WI: usually hyperintense
  - Enhancement with Gd
  - Intraloesional hemorrhage not unusual
  - High-flow vessels described with alveolar subtype
Rhabdomyosarcoma

- Metastases detectable in 10-20% of patients at dx (most common to lungs and pleura; also: bone & bone marrow)
- **Lymph node involvement** not uncommon; frequency dependent on site (GU>extremity>orbit)
Synovial Sarcoma

- Common NRSTS in children
- Most common STS of lower extremity in patients 6-35y of age (most common b/t 15 & 35y)
- Upper extremity, head and neck, and other sites may be involved
- Microscopic resemblance to developing synovial tissue
  BUT
  - Does NOT arise from nor differentiate toward synovium
  - Rarely originates within a joint or bursa
  - “Tumor of uncertain differentiation” (WHO)
Synovial Sarcoma

• Radiographs
  – Normal in 50%
  – When abnormal:
    • Mass
    • **Calcifications** in up to 1/3 (relatively rare in other STS)
    • Adjacent bone involvement in 20%
Synovial Sarcoma

- **MRI**
  -Usu. nonspecific large heterogeneous deep mass arising near joint capsules, tendon sheaths or bursae
  -**Hemorrhage** in up to ¾: high SI on T1WI, cyst-like appearance, fluid levels
  -“**Triple signal**” on T2WI in up to 1/3: hyperintense, isointense and hypointense areas relative to fat due to necrosis, hemorrhage, solid elements
Synovial Sarcoma

- MRI
  - Smaller lesions may be encountered
    - May be homogeneous
    - Notorious mimics of benign lesions
Synovial Sarcoma

- Mets in up to 25% at presentation (most commonly lung); may develop many yrs after dx
- Lymph node involvement in 5-15%
- Local recurrence common; may be late
Epithelioid Sarcoma*

- Most common malignant STS of hand and wrist in adolescents/young adults
- “Proximal” variant – more aggressive
- MRI spectrum: sm. subq. nodule to large infiltrative mass
- Tends to grow slowly in nodular manner along fascia/tendons, often w/ ulceration
- Lymph node involvement common
- Lung metastases common (up to 40%)
- Recurrence/mets can occur up to 25yrs after resection

* “Tumor of uncertain differentiation”
Alveolar Soft Part Sarcoma*

- Rare; usu. affects thigh, buttock, head & neck of adolescents/young adults
- Slow growing, hypervascular (may be pulsatile w/ bruit)
- MRI: signal intensity often greater than that of skeletal muscle on T1WI; flow voids particularly at periphery
- Mets in up to 20% of patients (lung, brain, bone) at dx, with late recurrences

* “Tumor of uncertain differentiation”
Fibrosarcoma

• 2 histologically identical forms:
  – Infantile fibrosarcoma (a.k.a. “congenital” fibrosarcoma)
    • Infants and young children
    • Favorable prognosis (5-year survival rate ~85%)
  – Adult fibrosarcoma
    • Usu. in middle-aged/older adults; but occ. encountered in childhood (peaks in 10-15-year-olds)
    • Unfavorable prognosis (5-year survival rate 40-55%)
Infantile Fibrosarcoma

- Almost always occurs in 1st 2 years of life (congenital in 40-80%)
- Location: extremities (50-70%) > trunk, head/neck
- Tends to be large, grows rapidly
- Overlying skin discoloration may lead to misdiagnosis of hemangioma; analysis of translocation t(12;15)(p13;q25) important
- Complete resection curative
- Local recurrence common, but metastases rare
Infantile Fibrosarcoma

- Nonspecific ST mass on imaging studies
  - Bone deformity/erosion > destruction
  - Heterogeneous on MRI (hemorrhage/necrosis)
  - High-flow vascular structures (may mimic vascular lesion)
Infantile Fibrosarcoma

- DDx soft tissue malignancies in infancy
  - Infantile fibrosarcoma
  - Rhabdomyosarcoma (5-10% diagnosed in 1st year)
  - Rarely MPNST, PNET
  - Undifferentiated

- Benign etiologies
  - Vascular tumors (most common ST/subq. neoplasms in infants)
  - Infantile myofibromatosis (most common fibrous tumor of infancy)
Dermatofibrosarcoma Protuberans

- Arises from dermis, typically trunk, proximal extremities, head/neck
-Usu. occurs in 3rd-5th decades of life; pediatric involvement not uncommon
- Local recurrence common (up to 50%; less w/ Mohs resection)
- Rate of distant mets low (~5%)
- May have areas of transformation to higher-grade tumor
Dermatofibrosarcoma Protuberans

- Unmineralized protuberant mass involving skin & subcut. tissue
- MRI:
  - Nonspecific signal
  - Hypervascular
  - Linear extensions along skin surface
  - Satellite nodules
Malignant Peripheral Nerve Sheath Tumor

• Usu. affects adults but can occur as early as infancy
• **May be assoc. w/ NF1**
  – Mets (usually lung) more common
• May arise in pre-existent plexiform neurofibromas or de novo
• Prognosis generally poor, although better with extremity lesions
Peripheral Nerve Sheath Tumors

• MRI of PNSTs (benign & malignant)
  – Nonspecific mass
  – Fusiform mass with entering/exiting nerve
  – “Split fat” sign (intermuscular location)
  – Target sign on T2WI, fascicular sign (more typical of BPNSTs)
Malignant Peripheral Nerve Sheath Tumor

- MRI features suggestive of MALIGNANT PNST:
  - Large (5-10cm) w/ rapid growth
  - Heterogeneity w/ central necrosis
  - Prominent peripheral/patchy enhancement
  - Infiltrative margins & perilesional edema

- PET: may offer some utility in distinction of MPNSTs in patients with NF (cutoff SUV\textsubscript{max} \sim 3.5)
Ewing Sarcoma Family of Tumors

• Includes ES of bone, extraskeletal ES, PNET, Askin tumor
  • Previously considered distinct neoplasms
  • Most are associated with a chromosomal translocation (usually t(11;22))
• Common locations: paravertebral, chest wall (Askin tumor), retroperitoneum, lower extremities
• Mets (lung/bone) & local recurrence common
Ewing Sarcoma Family of Tumors

- Imaging findings nonspecific
  - Intermediate signal intensity on long TR images due to high cellularity
  - Heterogeneous enhancement
  - High-flow vascular channels described
Liposarcoma

- Common in adults, rare in children
- Most fatty tumors in children >3y of age are lipomas
- Most fatty tumors in children <3y of age are lipoblastomas
Liposarcoma

- 4 subtypes: well-differentiated, dedifferentiated, myxoid, pleomorphic
- Almost all cases in children are of the *myxoid* subtype
  - Usu. late childhood/teen years
  - Usually extremities
  - Mets unusual in children
Liposarcoma

- Myxoid liposarcoma
  - May simulate cyst on nonenhanced MRI
  - Foci of amorphous or lacy fat in most cases (may be small)
  - Complete or heterogeneous enhancement in most cases
Role of Imaging

• Detection
• Characterization of the mass
• Staging and post-treatment assessment
• Guiding biopsy
Staging

- No well-accepted staging system applicable to all childhood sarcomas
- American Joint Committee on Cancer (AJCC) system used for adults not validated in pediatric studies

www.cancer.gov/cancertopics/pdq/treatment/child-soft-tissue-sarcoma
Rhabdomyosarcoma

- Staging is complex
- Involves several variables:

<table>
<thead>
<tr>
<th>Risk Group</th>
<th>Histology</th>
<th>Stage</th>
<th>Group</th>
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<tbody>
<tr>
<td>Low risk</td>
<td>Embryonal, Embryonal</td>
<td>1, 2, 3</td>
<td>I, II, III</td>
</tr>
<tr>
<td>Intermediate risk</td>
<td>Embryonal, Alveolar</td>
<td>2, 3, 1, 2, 3</td>
<td>III, I, II, III</td>
</tr>
<tr>
<td>High risk</td>
<td>Embryonal or alveolar</td>
<td>4</td>
<td>IV</td>
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Soft Tissue Sarcoma Committee of the Children's Oncology Group: Rhabdomyosarcoma Risk Group Classification

PRE-treatment staging
TNM-based

POST-surgical group based on completeness of resection

http://www.cancer.gov/cancertopics/pdq/treatment/child/rhabdomyosarcoma/HealthProfessional/page3
Rhabdomyosarcoma

- **Features of importance for radiologists:**
  - Location: favorable site (e.g., orbit) or unfavorable site (e.g., extremity)
  - Invasiveness of tumor (confined or not confined to anatomic site)
  - Size (greater than or less than 5cm)
  - Regional lymph node involvement
  - Metastatic disease $\rightarrow$ Stage 4
Rhabdomyosarcoma

- Accepted workup of patients with RMS includes:
  - Clinical examination
  - MRI or CT of 1° tumor w/ local-regional nodal basin
  - CT lungs
  - Bone scan
  - Bilateral bone marrow aspirates & biopsies
  - Lumbar puncture / lymph node biopsy (select patients)

- PET-CT performs better than conventional imaging in identifying nodal, bone, marrow & soft tissue disease (may replace bone scan, help direct lymph node biopsies)
Nonrhabdomyosarcoma Soft Tissue Sarcomas

- No pediatric NRSTS staging system validated
- Staging workup more variable than with RMS
  - MRI (or CT) of the primary tumor
  - CT of chest
  - In select patients:
    - Bone scan
    - FDG-PET
    - Roberge et. al.: routine use of FDG-PET/CT as part of the initial staging of adult soft tissue sarcomas unlikely to alter management

www.cancer.gov/cancertopics/pdq/treatment/child-soft-tissue-sarcoma
Post-Treatment Assessment

• Determination of extent of lesion and treatment response after neoadjuvant chemotherapy and/or radiation therapy (e.g., before surgery)
• Assessment of postsurgical site for recurrent/residual disease
• Post-treatment assessment of metastases
Treatment Response Before Surgery

- MRI – Anatomic techniques
  - Size of tumor not necessarily a robust measure of treatment necrosis:
    - Stable: unknown response
    - Increase in size: nonresponse, hemorrhage
  - Static contrast-enhanced MRI may not be able to differentiate enhancing viable tumor from fibrosis and granulation tissue
Treatment Response Before Surgery

- MRI – Functional techniques may help predict response (require further investigation)
  - Dynamic contrast-enhanced MRI: use change in enhancement patterns (slope)
  - MR spectroscopy: use decline in choline levels
  - DWI: use diffusion properties (minimum ADC changes)

Pre-chemo DWI (b=800)
Post-chemo DWI (b=800)
Post-chemo ADC map

Tumor necrosis → loss of cell membrane integrity → greater diffusion
Treatment Response Before Surgery

- PET: can evaluate response to chemotherapy by evaluating changes in glucose tumor metabolism (more accurate than size decrease in assessment of response)
Assessment of Postsurgical Site

- No controlled studies
- Most sarcomas recur w/in 2yrs of primary treatment
- ACR recommendation:
  - MRI +/- contrast
  - Alternatively: baseline US + MRI, follow-up with US (MRI if US inconclusive)
  - FDG-PET/CT: as a problem-solving tool
    - Detect local recurrence in cases where MR is equivocal
    - Distant metastases (vs. whole body MRI)
Assessment of Postsurgical Site

- MRI – Anatomic techniques
  - T2WI:
    - No high signal intensity or mass $\rightarrow$ usually not tumor
    - High signal intensity mass $\rightarrow$ tumor (or seroma, hematoma, postoperative inflammation or RT changes)
  - T1WI: architectural distortion (mass) vs. normal muscle; blood
  - Contrast-enhanced images: smaller/subtle recurrences; tumor versus seroma
  - Postoperative inflammation/fibrosis may appear masslike
Assessment of Postsurgical Site

- MRI – Functional techniques (need further exploration)
  - MR spectroscopy: can analyze choline content (no choline if no recurrent tumor is present)
  - Dynamic contrast-enhanced MRI: tumor enhances early/rapidly; inflammation/fibrosis enhances gradually
  - DWI: characterize diffusion properties for confirmation/exclusion of recurrent tumor (low ADC)
Post-Treatment Assessment of Metastases

• ACR recommendation:
  – Surveillance for pulmonary metastases:
    • CT scan of the chest without contrast q3-6 months
  – Osseous metastatic disease
    • Image only if symptomatic
Role of Imaging

- Detection
- Characterization of the mass
- Staging and post-treatment assessment
- Guiding biopsy
  - Planning is important!
  - Poor biopsy planning may lead to:
    - Errors in diagnosis
    - Limitations in treatment options
    - Unnecessary amputation
Intervention - Biopsy

- Imaging should be performed before biopsy
- Enhancing or metabolically active areas of the tumor should be targeted (nonenhancing or metabolically inactive areas are more likely to yield nondiagnostic specimens)
Intervention - Biopsy

• If surgical resection of the tumor is definite or even a possibility, then communication with the orthopaedic oncologist who will be primarily responsible for the definitive surgical resection of the neoplasm is key.

• Biopsy should be directed so that the potentially contaminated/seeded biopsy tract may be removed at definitive surgery.

• Compartments uninvolved by neoplasm should not be violated; avoid neurovascular bundles.

• *Simplest/most direct route not necessarily the most appropriate route!*
Intervention - Biopsy

- Adequate tissue needed for diagnostic pathology as well as molecular testing by fluorescence in situ hybridization or reverse transcription-polymerase chain reaction for specific translocations
  - Open biopsy or core biopsy (18-14G)
  - FNA may not yield sufficient tissue for histology, cytogenetics, & molecular testing; however:
    - May be obtained prior to planning a biopsy
    - Can be considered for highly vascularized lesions (hemangioma versus highly vascularized sarcomas)
Conclusions

• Accurate diagnosis of pediatric soft tissue sarcomas requires a fundamental knowledge of relative tumor prevalence by age
• Imaging plays multiple roles, including characterization, staging and post-therapy assessment of soft tissue sarcomas
• The management of soft tissue sarcomas, particularly in pediatric patients, is challenging, and patients should be referred to tertiary centers with multidisciplinary teams experienced in the diagnosis and treatment of these tumors
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Thank You!

Handout available at:
radiology.uchicago.edu/page/faculty-lectures