SOFT TISSUE SARCOMAS: AN UPDATE FOR THE ABDOMINAL RADIOLOGIST

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OBJECTIVES

• Describe the revised 2013 WHO classification of soft tissue sarcomas with emphasis on molecular genetics and updates that affect abdominal radiologists.¹

• Review the common soft tissue sarcomas of the torso based on patient demographics, imaging features and metastatic patterns in the context of the revised classification.

• Discuss the role of the abdominal radiologist in sarcoma management, follow-up, and assessing response to therapy.

* NO DISCLOSURES
The WHO classification of soft tissue sarcomas (STS) was updated in 2013, with several major changes based on immunohistochemistry and a better understanding of molecular mechanisms of pathogenesis.

The new classification includes gastrointestinal stromal tumors (GISTs) and nerve sheath tumors (previously included in tumors of digestive tract and tumors of the nervous system or skin, respectively).

STS represent approximately 1% of adult and 12% of pediatric malignancies. Extremities are the most common site of involvement (approximately 60%).

The torso accounts for 20-30% of STS. With GISTs included in the revised classification of STS, this proportion is now probably higher.
REVISED WHO 2013 CLASSIFICATION

STS are classified into four main subtypes:

- **Benign**: usually don’t recur, and if it does, it is in a non-destructive fashion; does not metastasize (e.g. lipoma)

- **Intermediate (locally aggressive)**: often recur, are locally infiltrative and destructive (e.g. desmoid, well-differentiated liposarcoma)

- **Intermediate (rarely metastasizing)**: locally aggressive, but can also metastasize in <2% cases (e.g. dermatofibrosarcoma protuberans)

- **Malignant (most common subtype)**: recurs with high risk of metastasis (e.g. GIST, leiomyosarcoma, dedifferentiated liposarcoma)
REVISED WHO 2013 CLASSIFICATION

Based on tissue of origin, STS are classified into several categories. The common ones (yellow font) are discussed further.

- Adipocytic tumors
- Fibroblastic/myofibroblastic tumors
- So-called fibrohistiocytic tumors
- Skeletal muscle tumors
- Smooth muscle tumors
- Pericytic/perivascular tumors
- Vascular tumors
- Chondo-osseous tumors
- GIST
- Nerve sheath tumors
- Tumors of uncertain differentiation
- Undifferentiated/unclassified tumors
**REVISED WHO 2013 CLASSIFICATION**

Multiple major and minor changes have been made, including the introduction of **three new categories** of tumors.

<table>
<thead>
<tr>
<th>2002 Classification</th>
<th>2013 Classification</th>
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<tr>
<td>Liposarcoma</td>
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<td>Well-differentiated</td>
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<td>Dedifferentiated</td>
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<td>Myxoid</td>
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<td>Round cell</td>
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<td>Pleomorphic</td>
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- Pleomorphic sarcoma (classified under ‘So-called fibrohistiocytic tumors’)  
  - GIST (NEW)  
  - Nerve sheath tumors (NEW)  
  - Undifferentiated/ unclassified tumors (NEW)  
  - Pleomorphic sarcoma
**ADIPOCYTIC TUMORS**

- True (benign) lipomas are less common in the torso apart from the abdominal/chest wall, although they can be seen involving the viscera too.

- They can be differentiated from well-differentiated liposarcoma (LPS) by the absence of 12q13-15 amplification in the lipomas.\(^2\) 12q13-15 amplification is present in well-differentiated and dedifferentiated LPS.
ADIPOCYTIC TUMORS

- Well-differentiated LPS (intermediate-locally aggressive) commonly occur in the retroperitoneum or mediastinum, where margin-negative resection is almost impossible, and cause significant morbidity.

- The term ‘atypical lipomatous tumor’ is reserved for similar tumors in locations like the abdominal wall, where complete resection is feasible (as in the abdominal wall) (A).

- Well-differentiated LPS is seen on CT as a predominantly fatty mass with thick septations (>2 mm) or nodular non-lipomatous elements that are <1 cm in size (B).³
ADIPOCYTIC TUMORS

- Dedifferentiated (most common), myxoid, pleomorphic LPS and LPS (not otherwise specified) are the subtypes of ‘malignant’ LPS. ‘Mixed LPS’ described in the previous 2002 classification has been removed, and is now considered an atypical form of dedifferentiated LPS.

- Dedifferentiated LPS is characterized by an adipocytic mass with >1 cm sized non-lipomatous elements.³
  - The non-lipomatous element can be (most commonly) soft tissue density, fluid density or mixed density.
  - Fluid density elements have been reported to grow faster than soft tissue density elements.³

- It is useful to look at the non-lipomatous elements on restaging scans to assess interval growth.
ADIPOCYTIC TUMORS

A. Baseline tumor with fatty (dashed arrow), soft tissue density (arrowhead), and mixed density (dotted arrow) elements.

B. Recurrent tumor with soft tissue density (arrowhead) and fluid density (arrow) elements.
ADIPOCYTIC TUMORS

- Myxoid LPS is characterized by the \( t(12;16)(q13p11) \) translocation. The previously described ‘round cell LPS’ demonstrates the same, and is no longer a separate entity in the revised classification.

- The myxoid element is seen as enhancing fluid density on CT and T2 hyperintensity on MRI. Macroscopic fat need not be always seen on imaging. **Round cell component >5% is the most adverse prognostic factor** for myxoid LPS. It appears as a non-fatty non-myxoid enhancing component on imaging.\(^4\)

CT and MRI show myxoid LPS with fluid density T2 hyperintense myxoid element (arrows) along with fat (arrowhead). Note the pleural-based metastases.
Aggressive fibromatosis (desmoid tumor) is an intermediate-locally aggressive tumor. Dermatofibrosarcoma protuberans and solitary fibrous tumor are examples of intermediate-rarely metastasizing tumors.

Desmoids occur most commonly in females between 15-40 years of age. They are sporadic in half the cases, but may be related to trauma, pregnancy or FAP (familial adenomatous polyposis).

- Abdomen is involved approximately half the time. Pregnancy-associated desmoid commonly involves the anterior abdominal wall.
- They present as homogeneous or heterogeneous soft tissue masses on imaging. MRI is the modality of choice as it best demonstrates the disease activity and extent of infiltration. Enhancing linear extensions may be seen along the fascial planes, indicating infiltration (fascial tail sign).
- T2 hyperintense lesions are more ‘active’ and tend to progress while T2 hypointense lesions are more ‘burnt out’ (fibrous) and remain stable.\(^5\)
FIBROBLASTIC/MYOFIBROBLASTIC TUMORS

34-year-old female with sporadic desmoid: Enhancing left pelvic side wall soft tissue (arrow, B) with corresponding T2 hyperintensity (arrow, A), consistent with active desmoid tumor

Restaging MRI reveals the tumor to now be T2 hypointense, burnt-out & fibrotic (solid arrows). New enhancing, T2 hyperintense paraspinal active component has developed (dashed arrows)
Pregnancy-associated desmoid: Non-contrast axial T2W MRI shows a well-defined T2 hyperintense lesion involving the anterior abdominal wall (arrow), consistent with an active desmoid tumor.

Dermatofibrosarcoma protuberans: Commonly seen in the 2nd-5th decades, it presents as a subcutaneous soft tissue mass which often protrudes out, and can involve deeper tissue.
S M O O T H  M U S C L E  T U M O R S

- Leiomyosarcoma (LMS) (malignant) commonly arises from the uterus, retroperitoneum, and large vessels.
- Uterine LMS (mean age 50 years) mimics a fibroid clinically and radiologically; incidentally found in 0.2% patients operated for presumed fibroids.
- FDG uptake, T2 hyperintense signal and areas of necrosis can be seen in both degenerating fibroids and LMS, with the lack of calcification being the only relatively consistent finding seen in LMS.\(^6\)
- Suspect LMS in older patients with the above imaging findings.

Two patients with heterogeneous uterine lesions (arrows). Patient A had fibroids and patient B had LMS on pathology.
SMOOTH MUSCLE TUMORS

- Retroperitoneal LMS presents as a large heterogeneous soft tissue mass, although smaller lesions may be homogeneous.

- Tumors may also arise from large vessels like the IVC, presenting as well-defined intra or extraluminal soft tissue masses.

- The liver and lungs are the most common sites of metastases.
VASCULAR TUMORS

- Angiosarcoma (AS) is the most common malignant vascular sarcoma. It can primarily involve solid organs (commonly spleen and liver), arise from large vessels, or be radiation-induced (breast).
- Splenic AS presents as single or multiple enhancing lesions and may undergo hemorrhage and present with left upper quadrant pain/ hemoperitoneum. Liver and bone metastases are common.
- Breast AS presents as variably enhancing ill-defined infiltrative or large soft tissue lesions involving the chest wall at the site of prior radiation therapy.
GIST

- GIST is the most common gastrointestinal sarcoma, occurring in the 5\textsuperscript{th}-8\textsuperscript{th} decades of life. It is characterized by activating mutations in the receptor tyrosine kinase (TRK) KIT.

- It most commonly occurs in the stomach and small bowel, and presents as a circumscribed enhancing soft tissue mass, which may be endo- or exophytic.

- Targeted therapy with TRK inhibitors like imatinib has revolutionized GIST management. Biologic changes do not always manifest with decreased size.
  - Response to TRK inhibitors classically results in decreased attenuation and lesions becoming more well-defined.
  - To reflect the CT findings, alternative response criteria (Choi et al) incorporating attenuation changes have been developed and better correlate with response for GISTs on targeted therapy. 15% decrease in CT attenuation or 10% decrease in unidimensional size constitutes partial response as per the Choi criteria.
60-year-old man with gastric GIST and hepatic metastases at baseline (arrows, A). Restaging scan after 6 months of imatinib (B) demonstrates decreased size and attenuation of the primary mass with development of internal foci of gas (dashed arrow), consistent with a tumor-bowel fistula. The hepatic metastases (solid arrows) appear more well-defined and hypoenhancing than prior, consistent with response by Choi criteria.
A. **Duodenal GIST**: Heterogeneously enhancing exophytic mass (arrow) arising from the 2nd part of the duodenum.

B. **Small bowel GIST**: Enhancing endophytic lesion in the proximal small bowel (arrow), incidentally seen on the CT.
TUMORS OF UNCERTAIN DIFFERENTIATION

- Heterogeneous group including synovial sarcoma (SS), desmoplastic small round cell tumor (DSRCT), alveolar soft part sarcoma (ASPS), extraskeletal myxoid chondrosarcoma, PEComas etc.\(^1\)

- Generally present as indeterminate soft tissue masses. Tumor location and patient demographics may give a hint.

- SS occurs in young-to-middle aged patients and are pleuropulmonary in location, presenting as a large heterogeneous pleural-based mass without adenopathy.

Pleuropulmonary SS: Two patients with large heterogeneous pleural-based masses (arrows).
TUMORS OF UNCERTAIN DIFFERENTIATION

- **DSRCT** is a rare tumor but has a classic presentation as a pelvic soft tissue mass in an adolescent male (15-25 years).

- **Alveolar soft part sarcoma (ASPS)** is a rare hypervascular soft tissue sarcoma affecting young adults (15-35 years) and can affect any organ.

- **Extraskeletal myxoid chondrosarcoma (EMC)** (mean age 52 years) presents as a large heterogeneous soft tissue mass with T2 hyperintense enhancing component, consistent with myxoid matrix. Calcification is rare.
**UNDIFFERENTIATED/UNCLASSIFIED SARCOMAS**

- Pleomorphic sarcoma (formerly malignant fibrous histiocytoma) is the most common example in this new category.

- It affects **older patients** (50-70 years), most commonly arising in the extremities, followed by the retroperitoneum.

- Imaging features are non-specific:
  - Smaller lesions present as homogeneous soft tissue masses
  - Larger masses are **heterogeneous** with hypodense areas, which may represent necrotic or myxoid changes.

*Pleomorphic sarcoma: Axial CT in two different patients showing right axillary and retroperitoneal heterogeneous large soft tissue masses (arrows)*
Metastatic Patterns

- Sarcomas disseminate hematogenously, with the lungs and bones being the most common sites of metastases.
- Peritoneal involvement is common in certain abdominal sarcomas like GIST, uterine leiomyosarcoma and DSRCT.
- Nodal involvement is rare overall. However, certain sarcomas are known to spread to LN, albeit uncommonly (e.g. synovial, clear cell, ASPS, rhabdomyosarcoma, DSRCT, and epitheloid sarcoma).
- SS often demonstrates pleural-based metastases.
**Metastatic Patterns**

- ASPS has the highest propensity for brain metastases amongst all sarcomas.
- Myxoid LPS has a predilection for extrapulmonary metastases, which precede pulmonary involvement.
- CT can be insensitive for detection of osseous myxoid metastases, thus MRI with STIR sequences is often used for surveillance.

Myxoid metastasis: Patient with low back pain. The sacrum appears normal on the axial CT (A). MRI (B) demonstrates the STIR hyperintense myxoid metastasis (arrow).
CHEMOTHERAPY-ASSOCIATED TOXICITIES

- Various chemo-toxicities may be encountered on restaging scans.
- TKIs cause a variable degree of fluid retention (subcutaneous edema, effusions, ascites). Patients may also develop tumor-bowel fistulas (previous slide on GIST).
- Patients on molecular targeted therapy like VEGF inhibitors may develop enteritis/colitis (fluid-filled bowel loops, bowel wall thickening, hyperemia), pneumato-rosis, pneumonitis and tumor-bowel fistula.
- Patients on mTOR inhibitors may develop enterocolitis, pneumonitis and cholecystitis.
The majority of STS present as indeterminate soft tissue masses and require a biopsy for definitive diagnosis. However, certain features are important when interpreting baseline and follow-up examinations.

Baseline scan:

- The main role of the radiologist is to identify the mass, with detailed description of the location and extent (involvement of vessels and adjacent structures) for both biopsy and surgical planning. Detecting metastases at baseline is also crucial as it typically alters management.
- Even though biopsy is usually required, certain features can suggest the diagnosis –
  - morphology (presence of fat or myxoid stroma),
  - site (e.g. LMS arising from a large vessel, GIST arising from bowel, DSRCT presenting as a pelvic mass in a young male).
  - typical history (desmoid developing after surgery or pregnancy, breast angiosarcoma after h/o radiation)
**APPROACH**

**Surveillance scan (following resection):**
- Screen for *local recurrence and common sites of metastases*. Myxoid tumors may be screened using MRI.
- Radiation-induced secondary cancers should be considered in the appropriate setting.

**Restaging scan:**
- Response to chemotherapy based on *conventional and alternate* (if applicable) response criteria.
- *Evaluation for therapy-related toxicities* is important in order to account for symptoms or complications.
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THANK YOU