Chapter 76
Synovial Sarcoma (SS)

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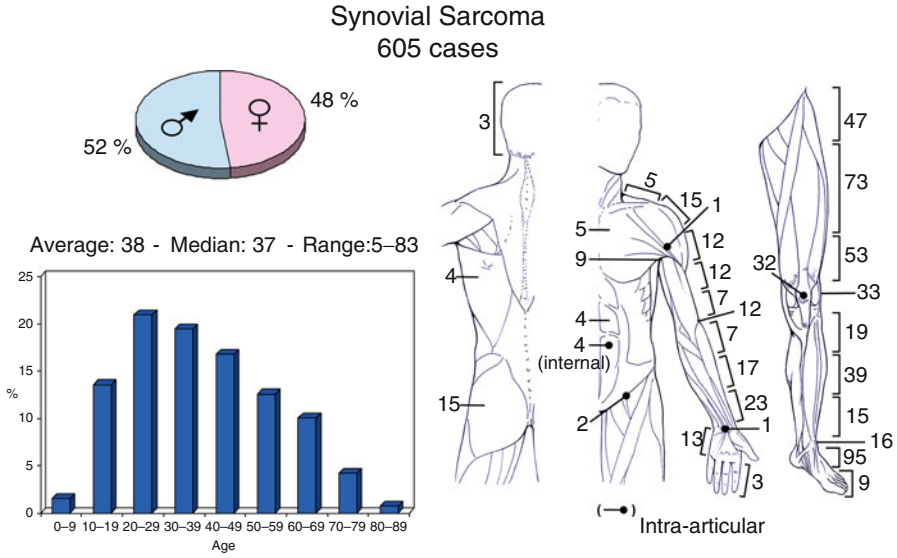
Definition: Malignant mesenchymal tumor which displays a variable degree of epithelial differentiation and a specific translocation t(X;18).
Epidemiology: 5–10 % of all sarcomas of soft tissues. Males. 15–40 years old.



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Location: 80 % extremities. Lower limb (60 %: thigh, knee, foot, ankle) and upper limb (23 %: forearm, wrist, shoulder). Only 10 % within a joint. Usually, close to a major joint, intimately related to tendons, tendon sheaths, bursae, and beyond the confines of the joint capsule.
Clinical: A palpable deep-seated mass with pain. Pain may be the first symptom of the disease. Tumor grows slowly and insidiously, and the duration of symptoms ranges from 2 to 4 years, although in some cases they have been noted for as long as 20 years.
Imaging: On x-ray: a round or oval, lobulated swelling of moderate density near a joint. Usually, bone is uninvolved. Periosteal reaction, bone erosion, or bone invasion (15–20 %). Multiple, small and spotty calcifications, or cloudy and faded shadow or massive and dense radiopacities of bone formation (40 %). Radiopacities more frequent in the periphery. On angiography: richly hypervascularized. On CT: infiltrating ST mass with slightly higher density than muscle, markedly enhanced, with easily detected calcifications, cortical erosion, and joint invasion when tendons or ligaments are involved. On MRI: 90 % hypointense on T1, hyperintense on T2. Fluid levels (15 %). Marked inhomogeneity, enhancement, and septation on T2. A triple-signal pattern on T2 (30 %): white-like fluid, gray-like fat, and dark-like fibrous tissue. Small high signal areas on T1 (45 %) are foci of hemorrhage. This and the triple pattern are suggestive of SS.
Histopathology: 1–20 cm. Slow-growing lesions are a firm, lobular mass fairly well circumscribed, attached to surrounding tissues, from yellow to gray-white. More rapidly growing lesions are a soft, globose mass poorly encapsulated, with a variegated, friable, or shaggy appearance, from mottled pink-yellow to light brown, with frequent necrosis, hemorrhage, and cystic areas. Calcifications can be seen. Two different types of cells: epithelial and spindle cells. (1) Biphasic type: two cellular components; (2) monophasic fibrous type: only spindle cells; (3) rare monophasic epithelial type: only epithelioid cells; and (4) poorly differentiated type (20 %). In type (1), there is a balanced distribution of the two components. Epithelioid cells are globose, cubic, or cylindrical, with large vesicular nuclei, abundant pale cytoplasm, and with well-defined limits. They are disposed in solid cords, whorls, nests, islands, and border irregular pseudoglandular, cleft-like or cyst-like spaces with granular or homogeneous secretions. Fibrous cells are well-oriented, plump, and spindle-shaped and have a uniform appearance, with scant and indistinct cytoplasm and oval, dark nuclei. They form solid, compact masses with irregular nodular arrangement. A fine net of collagen fibers surrounds the single cells of the fibrous component. Mitotic figure infrequent. In type (2), spindle cells are often arranged in a herringbone or HPC-like pattern. In type (3), a pseudoglandular feature with a poorly developed spindle cells pattern prevails. In type (4), hypercellular areas with round (similar to Ewing's sarcoma) or spindle or epithelioid cells with severe nuclear atypia and high mitotic activity.

Synovial sarcoma shows cytokeratin and/or EMA expression, although it can be quite focal and confined to only rare cells in an entire section. There is nuclear expression of TLE-1 protein. The balanced reciprocal translocation t(X;18)(p11.2;q11.2) is found in more than 95 % resulting in fusion of the SYT gene on chromosome 18 with the SSX1, SSX2, or rarely SSX4 gene on the X chromosome.

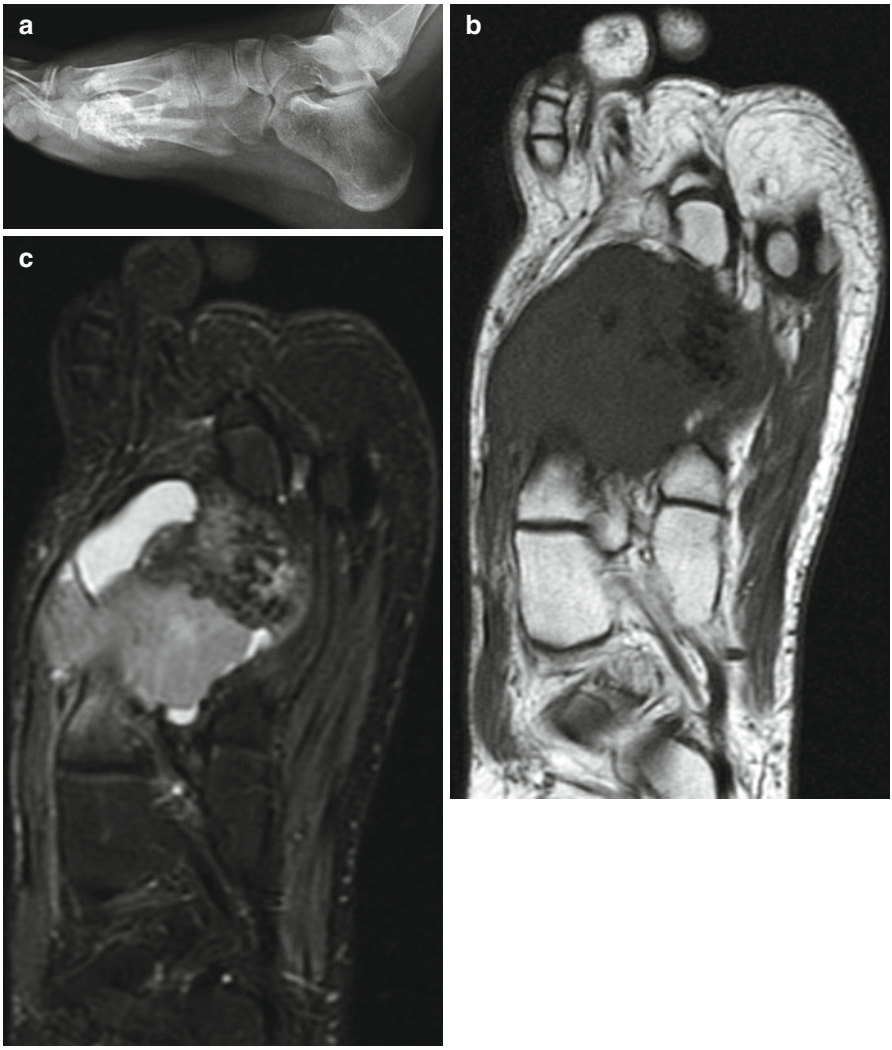
Course and Staging: Usually, it grows between and adheres to the tendons, joint capsules, bursae mucosae, fasciae, skeleton, muscles, and interosseous membranes. It pushes its growth along these multiple planes, infiltrating these structures and creating intravascular plugs. Local recurrence is common also 10 years after inadequate surgery. Metastases develop in about 50 % of cases. Usually, stage IIB.
Treatment: Surgery aims at obtaining wide margins, also sacrificing functionally important structures or amputating the limb. Wide conservative surgery may be difficult for the characteristic growth of the tumor. It may be useful to associate adjuvant chemotherapy and pre- or postoperative radiation therapy. Excision of the regional lymph nodes is appropriate for the high rate of metastases in this site. Overall 10-year survival varies from 15 to 35 %. Favorable prognostic factors are <5 cm, youth, women, distal extremities, calcifications, <15 mits/10HPF, degree of glandular differentiation, and no intravascular plugs.

Immunohistochemical Panel

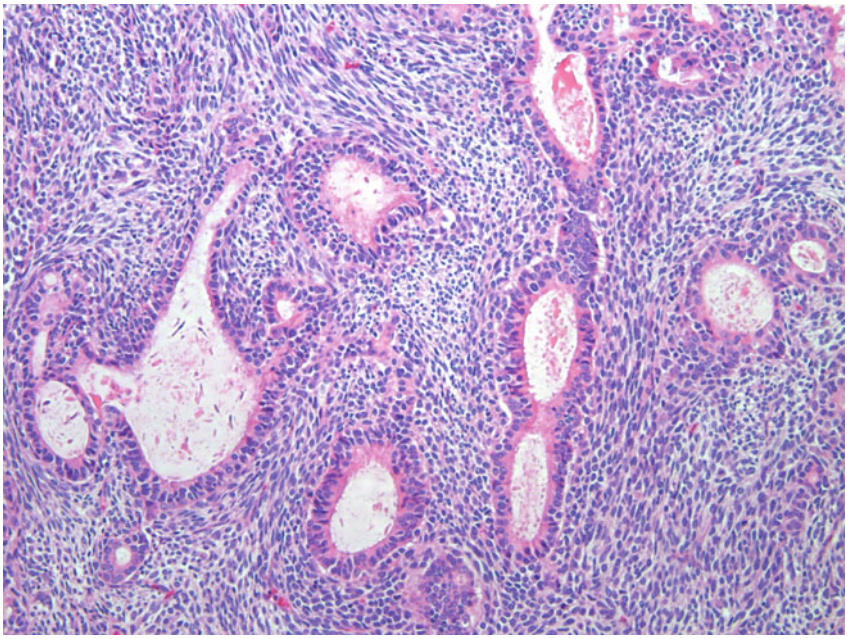
VIM	+
CK	+/–
EMA	+/–
TLE1	+
CD99	+/–
S100	+/–
Bcl2	+/–

Chromosomal Translocations

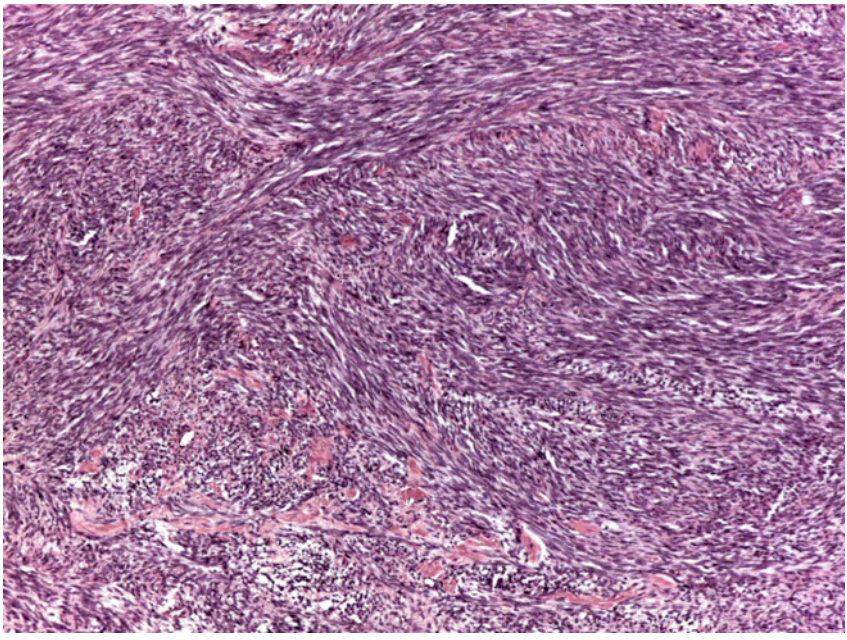
t(X;18) (p11;q11)	SYT-SSX (ssx1 e ssx2)	95 %
	SYT-ssx4	<1 %



Radiograph, axial and sagittal T1 and T2 FS MR images. The mass is calcified, displaces the bones, and has an heterogeneous signal on MR



Biphasic synovial sarcoma: glandular component and spindle cell component intermixed in the same tumor



Monophasic type: spindle cell sarcoma with variable grade of malignancy organized in a herring-bone pattern or HPC-like pattern

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