Liposarcomas

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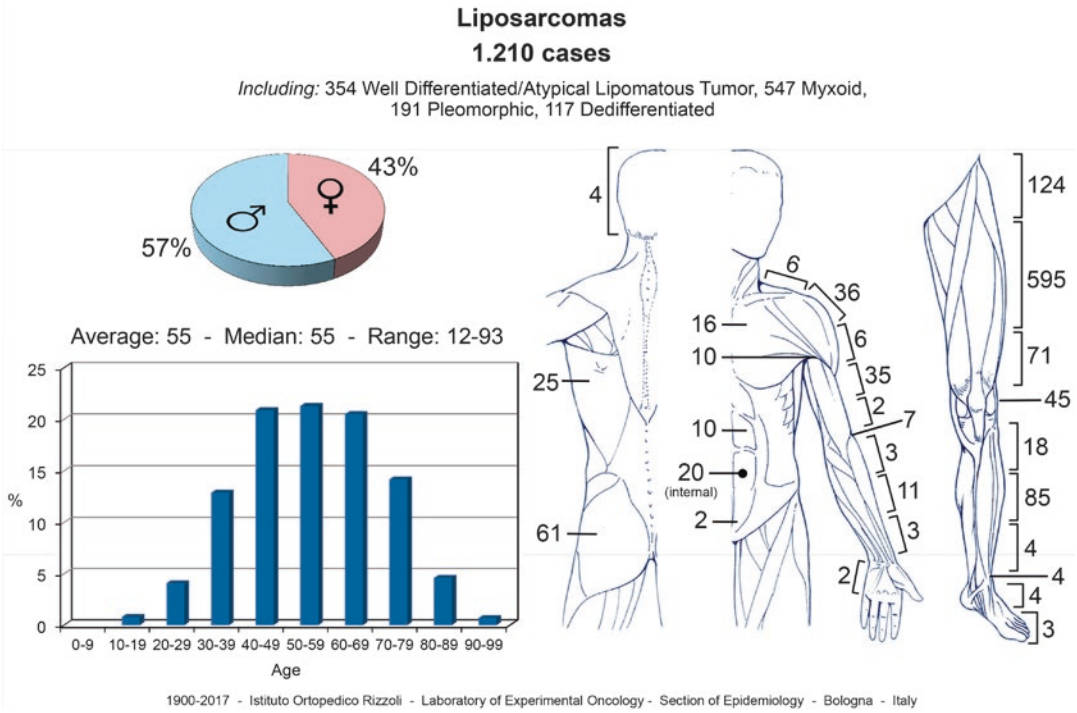
Definition: Malignant tumor featuring adipocytic differentiation.

Epidemiology: The most frequent sarcoma of the soft tissues. Prevails in males when it is localized in the limbs, but not when in retroperitoneum. Very rare prior to 20 years of age, whereas it is typical of adult and advanced age.



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Localization: Most common in thigh, retroperitoneum, inguinal region, and popliteal fossa. Rare in hands, feet, and neck.

Clinical: Insidiously growing, deep-seated, ill-defined mass that may attain a large size. Pain, tenderness, and functional disturbances occur in 10–15% of cases, but these are usually late complaints. Tumor may be painful due to compression on the nerve or cause edema of the limb due to venous occlusion. Retroperitoneal tumor may cause hydronephrosis, intestinal compression, inguinal hernia, and edema of the lower limbs.

Imaging: On X-ray: in more differentiated varieties, well-delineated radiolucency clearly distinguished from the surrounding muscles. Occasionally calcification, little vascularity. In more undifferentiated cases, less well defined masses with greater density. On CT scan: in lipoma-like type, well-marginated mass mimicking lipoma. Frequently, thickened linear, nodular septa that enhance after contrast. In myxoid type, encapsulated, septated, slightly heterogeneous mass mimicking a cyst. Density of water. On MRI, the myxoid type shows a homogeneous low signal intensity (dark) on T1 and high (white) on T2, strong enhancement, minute foci of fatty tissue, small bright streaks on T1 in an overall dark lesion are typical. Nonspecific appearances are displayed by the other varieties: heterogeneous signal intensity on T1, white and dark areas on T2, enhancement of all components. In dedifferentiated liposarcoma, a homogeneous mass of low signal intensity on T1 converts to a lesion with bright and intermediate areas on T2. Often the tumor is adherent or erodes adjacent cortical bone that responds with modest periosteal reaction. On bone scan, liposarcomas are inordinately hot in contrast to other malignant soft tissue tumors. On angiography: richly vascular with intense intra- and peritumoral neoangiogenesis.

Histopathology: Usually very large, multilobated, delimited by a thin reactive tissue (pseudocapsule) interrupted by some tumor nodules. Satellites are present.

Varieties

(a) **Well-differentiated Liposarcoma/Atypical Lipomatous Tumor (WDL/ALT)** 40% of all cases.
- Liposarcoma lipoma-like: The most common. Yellowish, soft, friable. Mature fat mixed with collagen. Variable number of lipoblasts (from many to none) and mature adipocytes. Hyperchromatic nuclei in both adipocytic and stromal cells most often within fibrous septa. Often confused with lipoma.
- Sclerosing liposarcoma: More frequent in retroperitoneum and spermatic cord. Whiter and firmer. Scattered bizarre stromal cells associated or not with multivacuolated lipoblasts set in abundant fibrillary collagen.
- Inflammatory: More frequent in retroperitoneum. Like liposarcoma lipoma-like and sclerosing liposarcoma but admixed with extensive chronic inflammation. Easily mistaken for an inflammatory process involving fat.

(b) **Myxoid Liposarcoma (ML):** Most frequent in the limbs (30–35%). Soft, pale yellow, mucoid and translucid or bright cherry red. Spindle cell proliferation set in a myxoid matrix and associated with a network of thin capillaries of uniform caliber organized in a plexiform pattern. Monovacuolated lipoblasts are most often seen at the periphery of the lesion. Mitotic activity is rare. Hypercellular areas > 5% fo the tumor, featuring ovoid-round hyperchromic cells with scanty cytoplasm and diminished intercellular myxoid matrix define the high-grade variant (formerly known as round cell liposarcoma). Genetics demonstrate characteristic chromosome translocations: t(12;16) that fuses the DDIT3 (CHOP) gene on 12q13 with the FUS gene on 16p11, and t(12;22) that fuses DDIT3 gene with EWSR1 gene on 22q12.

(c) **Pleomorphic Liposarcoma (PL):** Rare (5%). Softer, encephaloid. On high power pleomorphism is prominent. Pleomorphic lipoblasts with vacuolated cytoplasm are scattered amongst undifferentiated hyperchromatic neoplastic cells. Large atypical, multinucleated giant cells are scattered through the tissue. Myxoid change of the matrix is sometimes observed. One-third of cases features an epithelioid morphology associated with the presence of pleomorphic lipoblasts. Many atypical mitoses are observed. S-100 immunoreactivity may help highlight the presence of multivacuolated lipoblasts in those cases in whom adipocytic differentiation tends to be focal and, therefore, easily overlooked. Similar to most pleomorphic high-grade sarcomas, pleomorphic liposarcoma tends to exhibit complex karyotypes.

(d) **Dedifferentiated Liposarcoma (DL):** Relatively frequent (15%). Most cases occur in retroperitoneum. Abrupt (not always) transition for well-differentiated liposarcoma to high-grade non-lipogenic sarcoma. Sometimes dedifferentiation can show lipogenic features, with pleomorphic lipoblasts (homologous differentiation). Heterologous differentiation (myogenic, chondro-osteogenic) can be observed. On immunohistochemistry, overexpression of MDM2 and CDK4 is consistently observed in both components as a consequence of 12q13-15 chromosome region amplification.

Course and Staging: Type (a) are low-grade malignant tumors and present as stage IA. Type (b) purely myxoid liposarcomas are low-grade malignant tumors; they usually present as stage IA and seldom progress to higher stages. The presence of hypercellularity is associated with worsening of prognosis and these lesions should be considered stage II. Type (c) are high-grade malignant tumors and present as stage IIB. Type (d) are high-grade malignant tumors and present as stage IIB. Type (a and b) recur also many years after excision, whereas in type (c and d) local recurrence occurs rapidly. Metastases are exceptional in type (a), rare in type (b), frequent and early in type (c and d).

Treatment: in type (a and b) wide excision, while in type (c and d) radical removal. Radiotherapy is useful in type (c and d), and particularly effective in type (b). Conventional ifosfamide-based chemotherapy is preferred in type (c). Trabectedin (ET743) has shown to be effective in myxoid liposarcoma.

WDLPS/DDLPS (Well-differentiated liposarcoma/ Dedifferentiated liposarcoma)

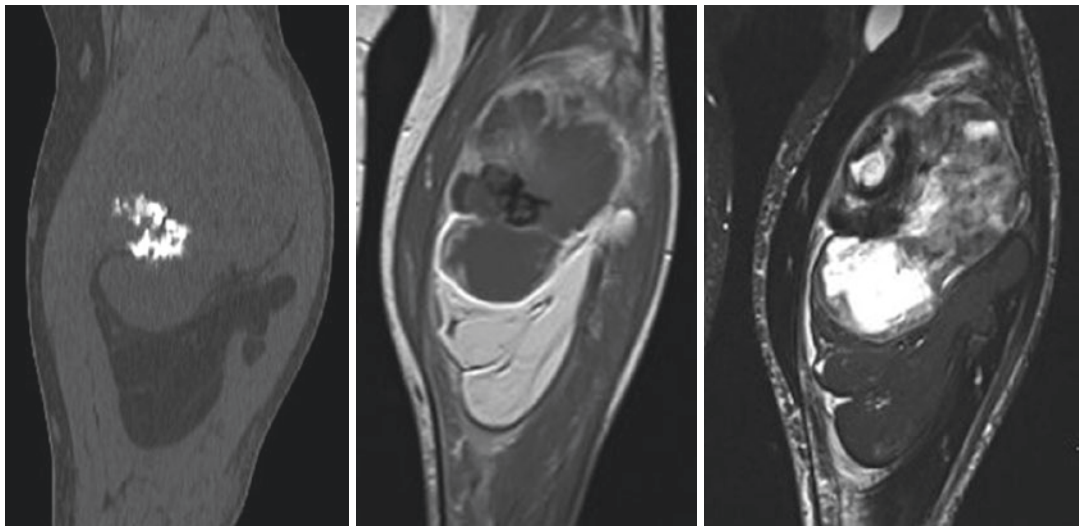
Immunohistochemical panel	
• S100	+
• MDM2	+
• CDK4	+

Atypical lipomatous tumor/well-differentiated LPS/ dedifferentiated LPS

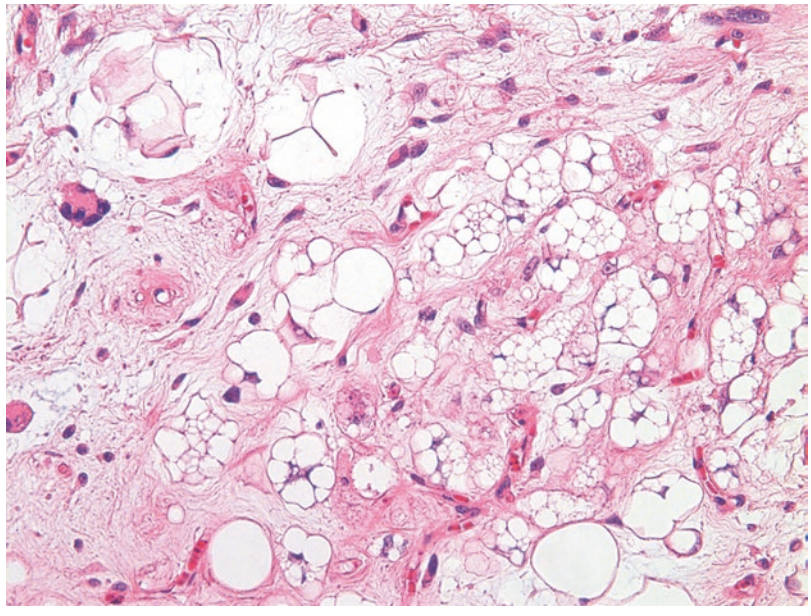
Genetic aberrations	
• MDM2	Amplification
• CDK4	Amplification

Myxoid/round cell liposarcoma

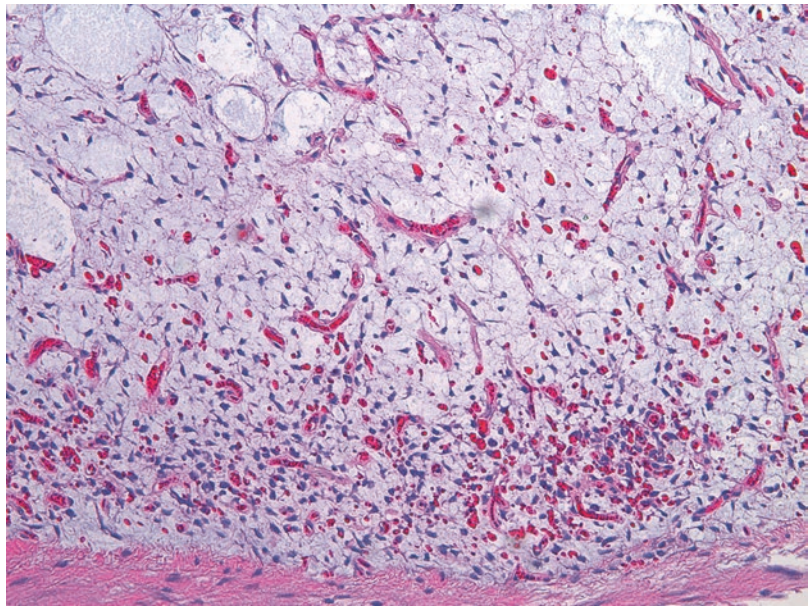
Chromosomal translocations		
• t(12;16) (q13;p11)	TLS(FUS)-DDIT3 (type 1, type 2)	95%
	TLS(FUS)-DDIT3 (type 3)	
• t(12;22) (q13;q12)	EWSR1-DDIT3 (type 1)	1–5%
	EWSR1-DDIT3 (type 2, type 3)	



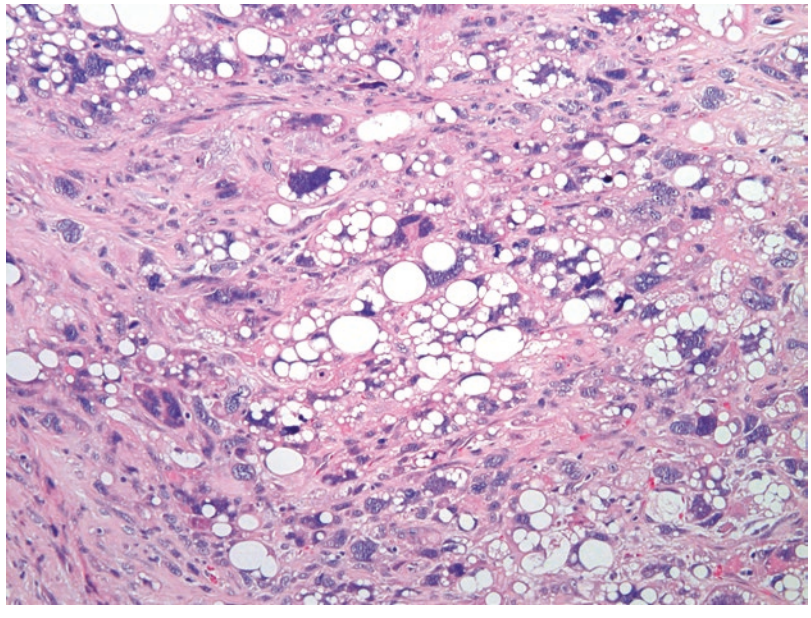
Well-limited mass of the thigh. On CT, the mass is ossified. On T1 and T2W FS coronal images, the lesion is made of two components. One is fat, corresponding to a well-differentiated liposarcoma, the second mainly fluid, is partially ossified, and corresponds to a myxoid component



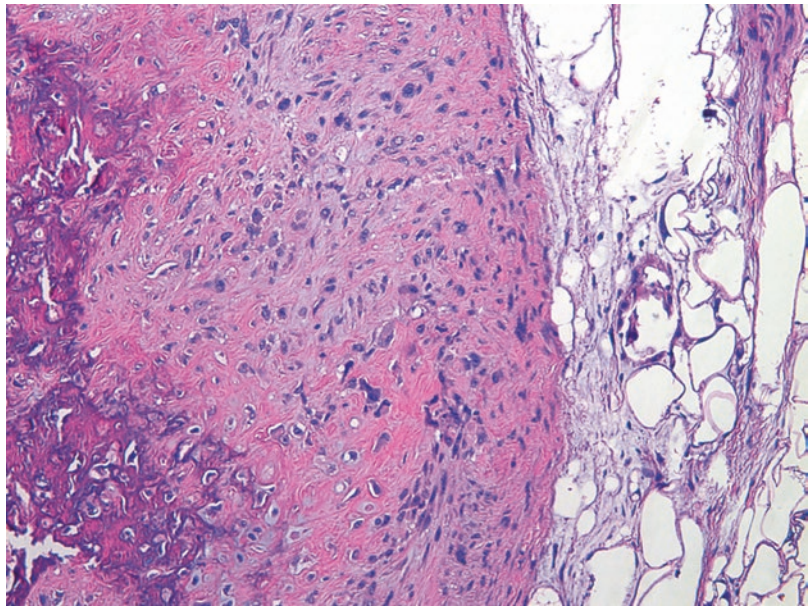
Well-differentiated liposarcoma/atypical lipomatous tumor. Mature adipocytic cells and scattered atypical adipocytes with hyperchromic nuclei and rare lipoblasts (unnecessary for diagnosis)



Myxoid liposarcoma. Oval to stellate cells embedded in a myxoid matrix with typical arborizing vascular pattern. Variable presence of an hypercellular component



Pleomorphic liposarcoma. Undifferentiated pleomorphic sarcoma-like high-grade sarcoma with scattered pleomorphic lipoblasts



Dedifferentiated liposarcoma. Lipoma-like liposarcoma that abruptly turns into a high-grade spindle cell and/or pleomorphic sarcoma; osteosarcomatous heterologous differentiation is evident in this case

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