

# Primary Dedifferentiated Liposarcoma of the Axilla Arising in a Mixed, Well-differentiated and Myxoid Liposarcoma

Garth S. Campbell<sup>1\*</sup>, Thomas J. Lawrence<sup>2</sup>, Scott E. Porter<sup>3</sup>, Luminita Rezeanu<sup>2</sup>

1. Department of Radiology, University of Mississippi Medical Center, Jackson, MS, USA

2. Department of Pathology, University of Mississippi Medical Center, Jackson, MS, USA

3. Department of Orthopaedic Surgery, Greenville Hospital System, Greenville, SC, USA

\* Correspondence: Garth Campbell, Department of Radiology, University of Mississippi Medical Center, 2500 North State Street, Jackson, MS 39216-4505, USA  
(✉ [gcampbell@umc.edu](mailto:gcampbell@umc.edu))

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## ABSTRACT

We describe a case of mixed liposarcoma of the axilla presenting as a high grade undifferentiated sarcoma with areas of well-differentiated and myxoid liposarcoma. MRI demonstrated a lobulated, septated intermuscular mass with marked heterogeneous gadolinium enhancement. A small focus of the tumor demonstrated fat suppressed signal more characteristic of well-differentiated liposarcoma. Pathologic analysis following wide local excision revealed a large, high grade sarcomatous component with highly pleomorphic cells with a thin rim of well-differentiated and myxoid liposarcoma on histologic examination. Dedifferentiated liposarcomas arising outside of the retroperitoneum are very rare, as are dedifferentiated liposarcomas arising from a histologically mixed liposarcoma. In this regard, this case illustrates an unusual combination of tumor location and histology which, to our knowledge, has not previously been reported.

## CASE REPORT

### CASE REPORT

A 62 year-old African-American male presented with axillary discomfort and mild weakness of his right hand for approximately six months duration and was found to have an otherwise asymptomatic 8 cm right axillary mass. Apparently, he first noticed the mass seven months prior to presentation. On physical examination, the mass was firm and nontender, and it demonstrated mobility with respect to the surrounding soft tissues.

Magnetic resonance imaging (MRI) of the right upper extremity demonstrated an intermuscular mass in the posterior compartment of the right upper arm displacing the triceps laterally and the neurovascular structures medially. The largest portion of the mass demonstrated isointense signal in

comparison with adjacent muscle on T1-weighted (T1) imaging (Fig. 1A). There was marked heterogeneous enhancement with the administration of gadolinium on post-contrast T1 (Fig. 1B). Bone scintigraphy showed uptake of radiotracer contiguous with and equal to or greater than the adjacent bone in intensity (Fig. 2), anatomically corresponding to the area of contrast enhancement seen on MRI. There was moderately hyperintense signal to muscle on T2-weighted (T2) imaging throughout the majority of the mass (Fig. 3), although scattered foci of marked signal hyperintensity were identified consistent with necrotic or cystic areas. Hypointense septae and a hypointense rim were seen within and circumscribing the mass, respectively, on all sequences.

A 3-cm focus of the tumor with distinctly different MRI characteristics projected from its superior aspect. This

component was primarily hyperintense on T1 and T2 sequences and was suppressed on T2 spectral adiabatic inversion recovery (T2 SPAIR; Fig. 4). There were also nodular internal areas within this smaller focus of the tumor with signal and enhancement characteristics more typical of those seen in the adjacent larger component of the mass.

A computed tomography (CT)-guided biopsy was performed (Fig. 5) which revealed a spindle cell malignant neoplasm with a somewhat storiform architecture comprised of highly pleomorphic cells with large bizarre nuclei, prominent nucleoli, and abundant eosinophilic cytoplasm. The mitotic activity was brisk with numerous atypical mitotic figures whereas tumor necrosis was not identified (Fig. 6). Immunohistochemical studies for broad-spectrum cytokeratin, TTF-1, and CD45 were negative while vimentin was diffusely and strongly expressed throughout the neoplasm. Consequently, the biopsy was reported as spindle cell pleomorphic malignant neoplasm.

The surgical resection consisted of a 14.0 x 11.0 x 7.5 cm soft tissue specimen with attached skeletal muscle and fibroadipose tissue surrounding a 9.5 x 6.1 cm well-circumscribed multinodular mass (Fig 7). Grossly the mass was mostly yellow tan with scattered translucent foci. Microscopic examination revealed a proliferation of highly pleomorphic cells with large vesicular nuclei, numerous atypical mitoses, scattered floret-like giant cells and vague storiform architecture, these findings consistent with a pleomorphic sarcoma. There was a thin cuff of adipose tissue surrounding the high grade sarcomatous component where, as an incidental histologic finding, areas of well-differentiated (Fig. 8) as well as myxoid liposarcoma (Fig. 9) were identified.

Immunohistochemical studies failed to highlight any type of differentiation of the high-grade sarcomatous component which showed positive expression solely for vimentin while broad-spectrum cytokeratin, desmin, myogenin, smooth muscle actin, S-100, CD30, CD45, and ALK-1 immunostains were negative. Cytogenetic studies revealed non-specific, complex karyotype abnormalities. The lack of cytogenetic aberrations specific to either well differentiated or myxoid liposarcoma, i.e. supernumerary circular or giant rod chromosomes and t (12;16)(q13;p11) respectively, is explained by the fact that only the dedifferentiated, high grade sarcomatous part was submitted for analysis.

Following surgical excision, the patient was treated with external beam radiation therapy over a period of two months and subsequently with 6 cycles of dacarbazine and adriamycin systemic chemotherapy. The patient did experience shoulder pain following radiation and chemotherapy, although this improved on subsequent clinical visits to mild residual discomfort localized to the site of the surgical scar. At last clinical visit, 26 months after surgery, he exhibited no residual neurologic deficit, and no recurrent mass or adenopathy was identified on physical exam. However, as of now, no follow-up imaging has been performed, apparently due to the patient's claustrophobia.

## DISCUSSION

Liposarcoma is arguably the most common malignant mesenchymal neoplasm accounting for 20% of all soft tissue sarcomas in adults [1]. Currently, liposarcoma is classified into several subtypes based on morphology and malignant behavior. The World Health Organization (2002) describes five subtypes of liposarcoma, including well-differentiated, dedifferentiated, myxoid, pleomorphic (these four representing histologically distinct entities) and mixed liposarcoma (a combination of pleomorphic and myxoid or of dedifferentiated and myxoid subtypes) [2]. It is helpful to think of liposarcomas in three main groups based on a biologic continuum which include: well differentiated to dedifferentiated liposarcomas, myxoid to round cell liposarcomas, and pleomorphic liposarcoma [3].

Dedifferentiated liposarcoma represents the transition of a well-differentiated liposarcoma to a non-lipogenic sarcoma. Round cell liposarcoma is considered to be a subtype of the myxoid variety; myxoid subtypes exhibit prominent areas of myxoid stroma. Pleomorphic liposarcoma is defined by the presence of pleomorphic lipoblasts and, in contrast with dedifferentiated liposarcoma, does not include a well-differentiated lipomatous component. In terms of prevalence, well-differentiated liposarcomas are the most common (slightly less than half of liposarcomas) followed by the myxoid subtypes (about one third) and dedifferentiated liposarcomas (dedifferentiation occurs in up to 10% of well-differentiated liposarcomas). The pleomorphic variety represents the rarest individual subtype (about 5% of liposarcomas) [2].

Prognosis of liposarcoma varies with location, subtype and histologic grade [2]. In general, high grade sarcomas of the extremities are now treated with a combination of limb-sparing surgery, radiotherapy, and systemic chemotherapy; a recent single-institution study estimated a 5-year survival of 80% in patients with high grade extremity sarcomas receiving neoadjuvant chemotherapy and radiation [4]

With regard to dedifferentiated liposarcoma, it is thought to exist as a biphasic neoplasm with juxtaposed elements of low grade and high grade sarcoma [5]. Although dedifferentiated liposarcomas can occur in many locations within the soft tissues, the retroperitoneum is by far the most commonly involved site [6], with only an estimated 4.5% arising in the upper extremity [7].

Imaging features of dedifferentiated liposarcoma arising in the lower extremity have previously been characterized [8, 9]. In accordance with those previous findings our case also demonstrated a lobulated, multiseptated mass with marked contrast enhancement and prolonged T1 and T2 relaxation times. Radiotracer uptake corresponding to the areas of gadolinium enhancement was identified at bone scintigraphy which has been previously described not only in dedifferentiated tumors [8], but as a feature of liposarcomas in general distinguishing them from benign lipomas [10], although this was not a dilemma in our case.

The smaller adjacent focus with both fatty characteristics (T1 and T2 hyperintensity with decreased intensity on fat saturated images) and internal enhancing nodules likely represents a well-differentiated liposarcoma component of the tumor in this case, and its relatively diminutive size in comparison to the high grade corresponds with previous generalizations that such lesions typically contain less than 25% identifiable fat on MRI, and often contain no identifiable fat on MRI, in which case they are indistinguishable by imaging from other types of soft tissue sarcoma [8].

In general, well-differentiated lesions closely simulate the appearance of adipose tissue. Conversely, the dedifferentiated, myxoid and pleomorphic varieties are predominantly non-fatty on MRI or CT [7]. However, distinguishing characteristics include the presence of a T2-hyperintense cyst-like mucinous component in myxoid lesions or the presence of hemorrhage or necrosis in pleomorphic liposarcoma [7, 11].

In the absence of an identifiable fat component on imaging, other entities may mimic the appearance of a high grade liposarcoma. These include malignant fibrous histiocytoma (also a heterogenous, enhancing lesion which may also manifest as a myxoid tumor), malignant peripheral nerve sheath tumor (may have an intermuscular location as in our case), and dermatofibrosarcoma protuberans (heterogenous, enhancing lesion involving deeper soft tissues distinguished by its abutment to the dermis) [12].

In more recent years, a new category of liposarcoma, "mixed liposarcoma" has emerged, although sporadic cases have been previously described by Stout and Evans but not identified as such [5, 13]. Mixed liposarcomas are defined by the WHO as liposarcomas showing features of combined myxoid/round cell and well-differentiated liposarcoma or of myxoid / round cell and pleomorphic liposarcoma and account for only 4% of all malignant adipose tissue tumors [3, 14]. Molecular evidence of true mixed liposarcomas was reported in 2001, including in particular a tumor of the thigh with well-differentiated areas expressing the ring chromosomes and giant markers associated with well-differentiated liposarcoma and myxoid areas expressing the characteristic t(12;16) associated with myxoid liposarcoma [15]. Mixed-type liposarcoma has been reported in the thigh with amplification of MDM2 and CDK4 corresponding to the well-differentiated component and fusion of CHOP and FUS genes corresponding to the myxoid component [16]. Similar cases have also been reported since which document the biphasic appearance of such tumors on MRI as well as histology [17].

Until recently, dedifferentiation was considered to occur only in association with well-differentiated liposarcomas. However, three cases were reported in 1997 of "dedifferentiated myxoid liposarcoma", two cases in the retroperitoneum and one in the inguinal region [18]. The first retroperitoneal case consisted of myxoid liposarcoma adjacent to non-lipogenic dedifferentiated sarcoma with focal areas of well-differentiated liposarcoma. The case arising in the inguinal area consisted of typical myxoid liposarcoma with myxofibrosarcoma-like areas and focal areas of well-differentiated liposarcoma. Another case series of

dedifferentiated liposarcomas of the extremities did remark on "areas of myxoid change identified histologically" in one case involving the lower extremity, although it was not classified as a mixed tumor per se [8]. No liposarcoma with combined mixed and dedifferentiated histology has yet been reported in the extremity to our knowledge, and the origination of the tumor in this case from the upper extremity is particularly peculiar.

#### TEACHING POINT

Although dedifferentiated liposarcomas are relatively rare in the extremities, small areas of macroscopic fat and areas of myxoid change in a predominantly solid soft tissue tumor may prospectively characterize a lesion as a liposarcoma; otherwise a nonspecific sarcomatous appearance is exhibited which may not be easily distinguishable on imaging from other types of soft tissue sarcoma. Definitive characterization can be performed with tissue histology; molecular and genetic markers, if available, are highly sensitive and specific.

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## FIGURES



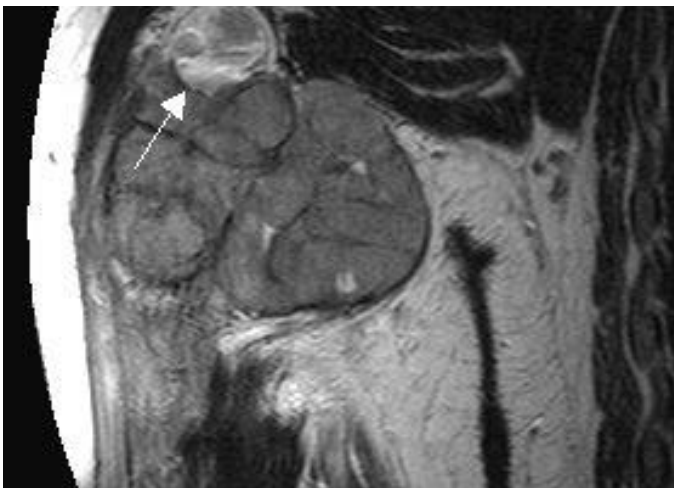
**Figure 1:** 62 year-old male with right axillary primary dedifferentiated liposarcoma. T1-weighted MRI prior to (A, top) and following (B, bottom) the administration of intravenous gadolinium. Axial T1-weighted MR images demonstrate an intermuscular mass with intrinsic T1 signal isointense to adjacent skeletal muscle (a) and intense, heterogeneous enhancement with contrast (b). Contrast agent: Magnevist 20 mL, TR = 659, TE = 10, Magnet Strength: 1.5 Tesla



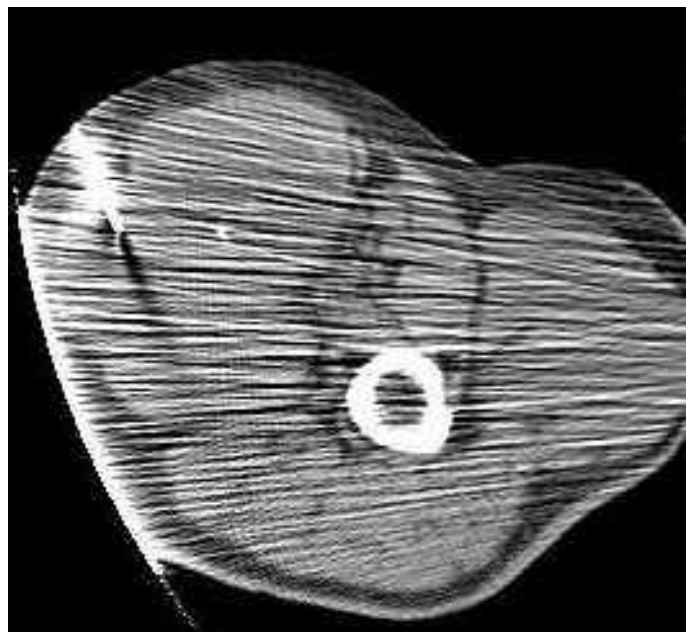
**Figure 2:** 62 year-old male with right axillary primary dedifferentiated liposarcoma. Technetium-99m radiolabeled MDP. Intense focal radiotracer uptake is seen overlying the proximal right upper extremity and humerus, corresponding to the soft tissue mass. Technetium-99m MDP dose: 20.1 mCi



**Figure 4:** 62 year-old male with right axillary primary dedifferentiated liposarcoma. T2-weighted MRI. Coronal T2-SPAIR (spectral adiabatic inversion recovery) MR image demonstrates T2-hyperintense mass with areas of suppressed signal in the round focus at the superior extent of the tumor, consistent with macroscopic fat. TR = 4490, TE = 60, Magnet Strength: 1.5 Tesla

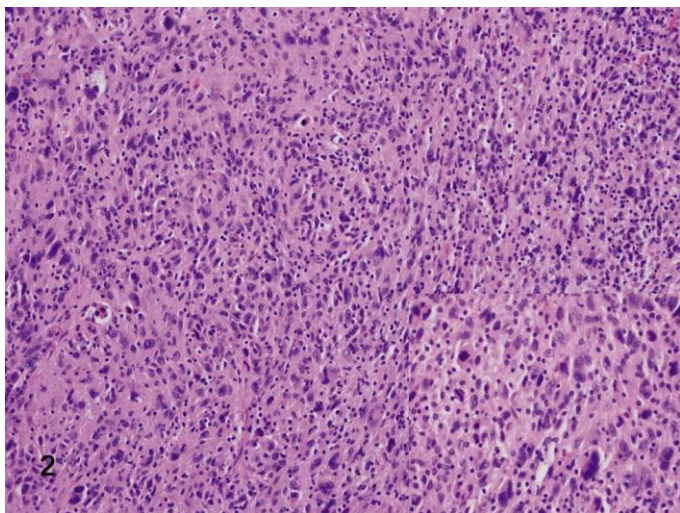


**Figure 3:** 62 year-old male with right axillary primary dedifferentiated liposarcoma. T2-weighted MRI. Coronal T2-weighted MR image demonstrates the mass to be generally moderately hyperintense to adjacent skeletal muscle with small areas of marked hyperintensity. In correlation with fat suppressed sequence, these areas within the main portion of the tumor correspond to fluid. The round focus at the superior extent (arrow) appears to contain a small amount of macroscopic fat. Thin, linear T2-hypointense capsule-like rim and internal septa around and within the mass, respectively, are demonstrated on this sequence. TR = 4107, TE = 100, Magnet Strength: 1.5 Tesla

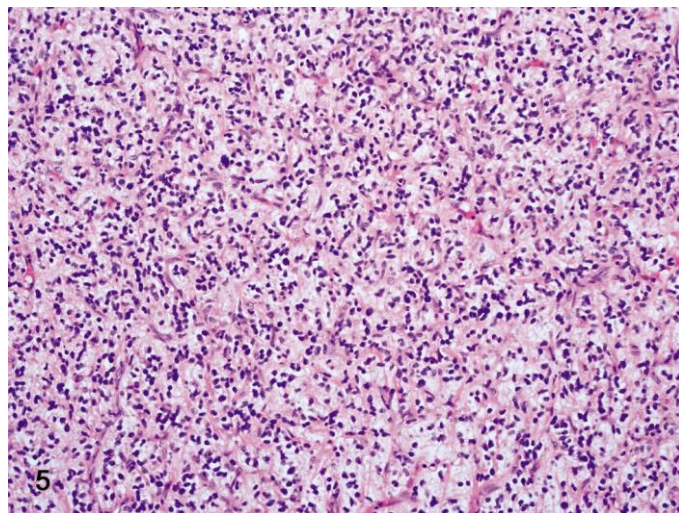


**Figure 5:** 62 year-old male with right axillary primary dedifferentiated liposarcoma. Computed Tomography. Axial noncontrast CT-guided biopsy image demonstrates needle position within the soft tissue mass which has similar attenuation to adjacent muscles. GE Lightspeed CT scanner. kVp = 120, mAs = 180, slice thickness = 5 mm.

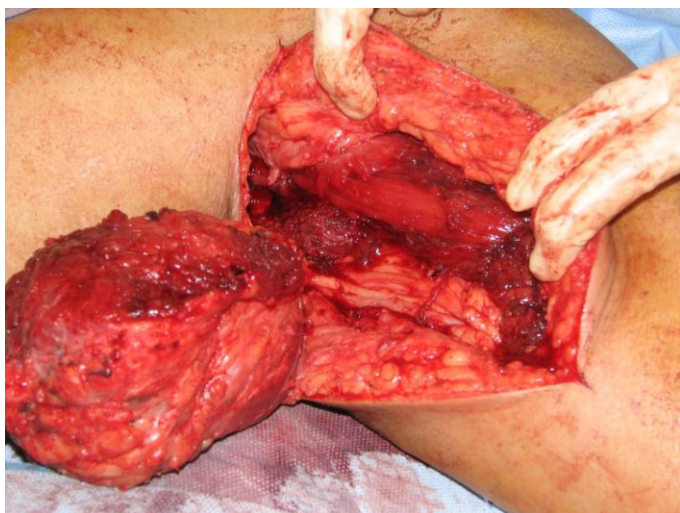




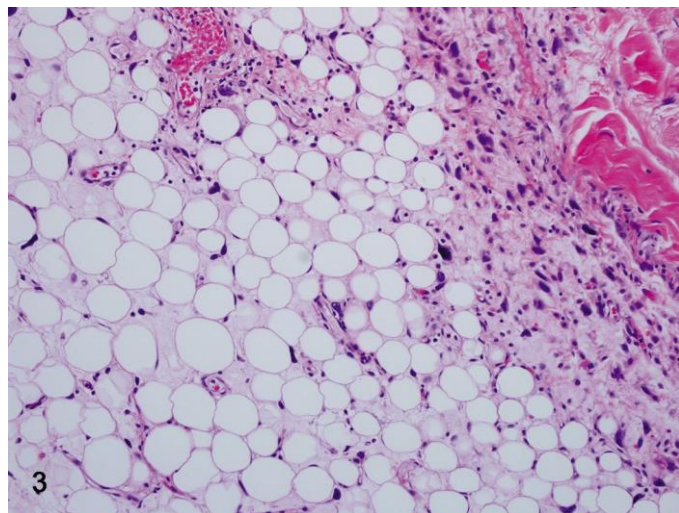
**Figure 6:** 62 year-old male with right axillary primary dedifferentiated liposarcoma. Histopathology Specimen, Dedifferentiated Component. Hematoxylin and eosin (H&E) stain. Magnification 200X, Inset Magnification 600X. Pleomorphic cells with large nuclei, prominent nucleoli and abundant eosinophilic cytoplasm.



**Figure 8:** 62 year-old male with right axillary primary dedifferentiated liposarcoma. Histopathology Specimen, Myxoid Component. H&E stain. Magnification 200X. Prominent branching vasculature and bland ovoid mesenchymal cells consistent with myxoid histology.



**Figure 7:** 62 year-old male with right axillary primary dedifferentiated liposarcoma. Intraoperative Gross Specimen. The soft tissue mass gross specimen is seen adjacent to the surgical bed.



**Figure 9:** 62 year-old male with right axillary primary dedifferentiated liposarcoma. Histopathology Specimen, Well-Differentiated Component. H&E stain. Magnification 200X. Atypical stromal cells adjacent to and intermixed with mature adipose tissue, characteristic of well-differentiated liposarcoma.

Diagnosis	General	CT	MRI T1	MRI T2	Enhancement
<b>Liposarcoma</b>	Spectrum of malignancy, ranging from well-differentiated to dedifferentiated	Attenuation characteristics depend on the components; the more fat, the lower attenuation. Calcific ossification is seen in some tumors.	Fat-containing components are hyperintense. Generally, other components are isointense to hypointense.	Fat-containing components will lose signal with fat-suppression. Myxoid components will remain bright. Soft tissue will remain intermediate.	Generally, the soft tissue component will enhance whereas the remainder will not.
<b>Lipoma/Atypical Lipomatous Lesion</b>	Atypical lipomatous lesions must be subcutaneous, or else they are considered well-differentiated liposarcomas.	Fat-density lesions with little or no soft tissue component	Fat-containing components are hyperintense.	Predominantly fat-containing lesions are hyperintense on fast spin-echo, but with signal loss on fat suppression imaging.	None for lipoma; atypical lipomatous lesion may show mild enhancement.
<b>Malignant Fibrous Histiocytoma or Fibrosarcoma</b>	Aggressive sarcomas which are distinguishable at histology. These tumors lack a fatty component, but may be indistinguishable from pleomorphic liposarcomas.	Soft tissue attenuation mass, often poorly marginated. Dystrophic calcification may be present.	Generally isointense to muscle; lacks fatty components	Heterogeneous hyperintense signal; may contain areas of myxoid change.	Heterogeneous enhancement
<b>Dermato-fibrosarcoma Protuberans</b>	Slow growing sarcoma common in the axilla	Usually superficial soft tissue lesions extending from the dermis, although deep lesions have been described.	Generally isointense to slightly hypo- or hyper-intense.	Hyperintense to muscle	Enhancement may be uniform or patchy
<b>Malignant Schwannoma</b>	Malignant nerve sheath tumor	Deep soft tissue mass with fusiform shape, associated with a large nerve; distal muscular atrophy	Isointense to slightly hyperintense	Hyperintense to muscle; may occasionally display the "target sign" with hyperintense rim and hypointense center	Even mildly heterogeneous enhancement and irregular margins may suggest malignant rather than benign schwannoma.

**Table 1:** Differential table of liposarcoma

<b>Etiology</b>	Malignant tumor of lipomatous origin
<b>Incidence</b>	Most common (or second-most common, depending on source) malignant tumor of mesenchymal origin
<b>Gender Ratio</b>	Essentially equal male:female ratio
<b>Age Predilection</b>	Generally, patients are > 30 years of age
<b>Risk Factors</b>	No specific risk factors
<b>Treatment</b>	Wide local excision, frequently with adjunctive chemotherapy and radiation in the case of poorly-differentiated, myxoid, or pleomorphic tumors
<b>Prognosis</b>	Highly variable, depending on the location and type of tumor. However, prognosis is generally better for subcutaneous extremity lesions and uniformly well-differentiated tumors.
<b>Imaging Findings</b>	Variable, depending on the type of tumor. Well-differentiated liposarcomas are predominantly fatty tumors. Myxoid liposarcomas may show fluid-like areas of myxoid change or necrosis. Poorly differentiated liposarcomas may possess larger nodular foci of non-lipomatous tissue.

**Table 2:** Summary table of liposarcoma

**ABBREVIATIONS**

- CT = Computed Tomography
- H&E = Hematoxylin and Eosin
- MR = Magnetic Resonance
- MRI = Magnetic Resonance Imaging
- SPAIR = Spectral Adiabatic Inversion Recovery
- T1 = T1-weighted
- T2 = T2-weighted

**KEYWORDS**

Liposarcoma; myxoid; upper extremity; axilla; magnetic resonance imaging

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