LIPOMATOUS TUMORS: DIFFERENTIATING BY A FAT MARGIN

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LEARNING OBJECTIVES

1. Recognize the different lipomatous tumors in their many presentations

2. Differentiate between benign, intermediate and malign lipomatous tumors

3. Explore the role of the imaging modality choice when diagnosing such lesions
Lipomatous Tumors (LT) represent a category of adipose tissue-originating neoplastic lesions that range from lipomas to high grade liposarcomas. They are the most common soft tissue tumors found in clinical practice and may occur in almost any site in the body.

There are some discrepancies related to the meaning of lipomatous tumor in the literature. Here, we consider it as synonym to adipocytic tumor.

**OVERVIEW**

**DEFINITION**

Lipomatous Tumors (LT) represent a category of adipose tissue-originating neoplastic lesions that range from lipomas to high grade liposarcomas. They are the most common soft tissue tumors found in clinical practice and may occur in almost any site in the body.

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**IMAGING**

**MR**

Is the ideal, gold standard, imaging modality for diagnosing soft tissue lesions such as LTs.

**CT**

Depending on tumor predilection, CTs are particularly important for evaluation of potential metastasis. Chest CTs play a relevant role since many liposarcomas have preference for lung tissue.

**US**

Best initial investigation for palpable masses.
The WHO 2020 Classification of Soft Tissue Tumors addresses adipocytic lesions as 15 entities divided in three groups:

**Benign**
- Lipoma & Lipomatosis;
- Lipomatosis of Nerve;
- Lipoblastoma;
- Angiolipoma;
- Myolipoma of Soft Parts;
- Chondroid Lipoma;
- Spindle Cell Lipoma;
- Atypical Spindle Cell Lipomatous Tumor;
- Hibernoma

**Intermediate**
- Atypical Lipomatous Tumor

Round cell liposarcoma is now grouped with Myxoid liposarcoma!

**Malignant**
- Well-Differentiated Liposarcoma;
- Dedifferentiated Liposarcoma;
- Myxoid Liposarcoma;
- Pleomorphic Liposarcoma;
- Myxoid Pleomorphic Liposarcoma
**LIPOMA**

Even being underreported due to its benign nature, lipoma remains the most common soft tissue tumor in adults. It presents itself as an often painless mass, with slow growth, that may be superficial and freely mobile, or deep and limited by muscle contraction.

US is a valuable initial assessment tool, revealing an:
- **Elliptical**, well-defined,
- Compressible, homogeneous
- Sometimes **Septated** mass

Clinical diagnosis is possible in most cases, however imaging may be required to evaluate deviations such as a mass bigger than 10cm in diameter (~5%)

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30 yo male with painless submandibular mobile mass

Case: Ammar Ashraf rID: 150849

US, axial and coronal non-contrast CT images show the classic features of a superficial lipoma.
LIPOMA

While US is particularly useful for characterizing superficial lipomas, the deeper forms of this tumor, which include intramuscular and intermuscular, may require further investigation.

On CT and MR, lipomas are homogeneous, encapsulated masses, sometimes **septated**, of Attenuation/Signal Intensity equal to that of subcutaneous tissue.

Intramuscular lipomas may show **Intermingling Muscle Fibers**

Lipomas may have unusual features such as calcifications, fat necrosis and mechanical edema, this possibility should be considered before assuming sarcomatous change. In fact, some of these are characteristic to some conditions - such as the cockade sign.
LIPOMATOSIS

Sometimes used interchangeably with infiltrating lipoma, lipomatosi is the diffuse accumulation of mature adipose tissue that can affect many organs and body cavities, differing from lipoma on CT and MRI by being Unencapsulated and less localized. It is associated with many risk factors:

- Obesity
- Steroid use
- Endocrine Disorders (mainly Cushing's Disease)
- HIV infection
- Recurrent UTIs (in the pelvic case)

Clinical presentation is mostly assymptomatic but can vary widely with the region affected, ranging from ureteric mass effect to dysphagia and dyspnea due to mediastinal displacement. Assymetry is an important sign.
Lipomatosis can occur in the:

- Heart
- Mediastinum
- Pelvis
- Retroperitoneum*
- Epidural Space
- Pancreas
- Kidney
- Ileocecal Valve
- Face, neck and extremities

There are also lipomatosis-related syndromes, such as Madelung's disease and Cowden syndrome.

Case: Prashant Mudgal  rID: 67434

* The identification of a retroperitoneal fatty mass is often accompanied by some degree of wariness, since that is the most common presentation of Well Differentiated Liposarcoma, however, optimistically, it could also be a case of retroperitoneal lipomatosis.

Case: Matt Skalski  rID: 30219

50 yo female with left flank pain and increased creatinine - non-contrast axial CT

Renal lipomatosis with total left kidney replacement by fat

Presence of large coral calculi, which may be the cause of the atrophy seen

Madelung's Disease in a 50 yo female with enlarging neck - coronal and sagittal T1W
Although named lipoma, Lipoma Arborescens (LA) is actually a form of lipomatoses - Diffuse Articular Lipomatosis - representing the rare, benign, hyperplastic replacement of subsynovial tissue by mature adipocytes. It is frequently accompanied by effusions that outline a Frond-like pattern, supporting the current idea that it is caused by chronic synovial irritation, being a nonspecific reaction, and not a neoplasm.

MRI and CT images should always be interpreted together with plain radiographs, since the presence of mineralization may not be indicated by the former and can be invaluable in the differential diagnosis. In the case of LA, the presence of calcifications is the main feature to differentiate it from Primary Synovial Chondromatosis.
LIPOMATOSIS OF NERVE (LN)

Marked by the proliferation of fatty and fibrous tissue along thickened nerve bundles, with infiltration of both perineurium and epineurium, LN, also known as Neural Fibrolipoma, is a rare Lipomatous Tumor.

Radiologic features include:
- Typical "chocolate cookie" finding on US images.
- Mixed SI due to fatty, fibrous and neural components.
- On axial T1W images, these might show a "cable-like" appearance.
- Only indirect signs can be seen on plain radiographs, such as osseous enlargement.

Mainly affects children and young adults

Bone hypertrophy and Nerve territory overgrowth can occur

Surgical treatment is controversial, since even after excision, trophic factors may persist and contribute to tumor progression

Given its pathognomonic features, biopsy should be avoided

The median nerve is the most frequently affected nerve
LIPOMATOSIS OF NERVE (LN)

The upper limb (78-96%), especially the volar aspect of the wrist, is more frequently affected than the lower limb, as reported by the Archives from the AFIP - Armed Forces Institute of Pathology.

Patients present with a slowly growing soft tissue mass, with or without neurologic deficit.

Onset of symptoms often happens many years after the soft tissue mass's appearance.

Another pathognomonic MR finding is the "spaghetti-like" appearance on coronal planes.

Up to 66% of LN cases are associated with macrodystrophia lipomatosa.

Case: Samir Bernoudina
rID: 82735

Enlargement of 2º, 3º and 4º digits

7 yo male with left hand enlargement - Plain Film

Classic "spaghetti-like" pattern

Case: Khalid Alhusseiny
rID: 93542

5 yo female with right wrist swelling - T2W FS
LIPOMATOSIS

Lipoblastoma

Angiolipoma

ML. of S. Parts

Chondroid L.

Spindle Cell L.

LIPOBLASTOMA (LB)

LB is a lesion composed by adipocytes, lipoblasts and poorly differentiated mesenchymal cells, with varying degrees of each cell type. It tends to be well encapsulated, confined to the subcutaneous tissue and have fibrovascular septations. More profound location characterizes Diffuse Lipoblastoma or Lipoblastomatosis.

Imaging modalities reveal:

- US: Mixed echogenicity, mostly hyperechogenic.
- CT: Fat density mass with scattered soft tissue density foci.
- MR: On T1W images there is heterogeneous SI, with areas of high SI interspersed by low SI strands, which may be hyperintense on T2W images. There may also be cystic areas and nodular enhancement.

1 yo male with a right flank mass - CT. There was suspicion of sarcoma

CT shows a fat containing mass with mildly thickened septa, displacing the liver and right kidney

Case: Michael P Hartung rID: 67022

LB occurs almost exclusively in early childhood and infancy, with 75-90% of cases in patients less than 3 yo.
2 yo male with soft perineal mass, growing slowly since first weeks of life - Axial T1W water-only DIXON sequence, US, and Sagittal SPAIR

MR images reveal a well-defined, high SI lesion on DIXON; suppressed on SPAIR sequence. US shows homogeneity.

Case: Frank Gaillard  rid: 81126

The extremities are the most commonly affected regions

The male to female ratio is 2:1

Although there is excellent prognosis after excision, diffuse LB may recur.

Clinical presentation is usually that of a rapid growing, painless mass

In some rare cases, imaging features may not allow for differentiation from Myxoid Liposarcoma, however, Liposarcomas are exceedingly rare in children less than 5 years old, making age a vital information to consider in this differential diagnosis.
Lipoma

Lipomatosis

Ls. of Nerve

Lipoblastoma

Angiolipoma

ML. of S. Parts

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**Angiolipoma**

Marked by mature adipocytes and an intertwining network of capillaries, Angiolipoma is a relatively common tumor divided in two types: Infiltrating and non-Infiltrating. It usually occurs in young adults, with **wrist preference**.

**Non-Infiltrating**: Most cases, encapsulated and subcutaneous. Imaging is often unnecessary.

**Infiltrating**: Rare, unencapsulated and locally aggressive. May have phleboliths. **Mass Effect** possible.

Its most frequent presentation is that of multiple, small (<2cm) nodules in the subcutaneous tissue. Occasionally painful. The treatment, complete resection, can be difficult in the infiltrating type, which tends to recur.

**Case**: Frank Gaillard  **rID: 28242**

40 yo male with lower limb weakness - Sagital T1W, T2W, T1W C+ FS and Axial T2W show an extradural thoracic lesion

- Epidural heterogeneous SI lesion
- High SI, showing vascularity
- Posterior spinal Mass effect
- Marked enhancement
Although it presents as a single, large (10-25cm) mass in the retroperitoneum, abdominal or pelvic cavities, it is often asymptomatic. The female to male ratio is 2:1. Due to the presence of non-fatty elements, and possible calcification, radiologic findings may not allow for differentiation from WDLS, although presence of a partial capsule favors a benign diagnosis.

Despite its size and deep location, Myolipoma of Soft Tissue follows a benign clinical course, with no reported recurrence after surgical excision.
CL is a rare benign lipomatous tumor with features that can be difficult to distinguish from myxoid liposarcoma. Composed by mature and immature fat cells, and a chondroid-like matrix, which is frequently **calcified**, CL has a female predilection and a good prognosis. Excision is usually curative.

On MRI, its components show:
- High SI on T1W and Signal Suppression on FS images: **Adipose tissue**
- High SI on T2W and Low SI on T1W: **Chondroid tissue**

- It is encapsulated, lobulated and usually arises in the proximal limbs.
- As imaging **cannot definitively differentiate** between malignant and benign nature, biopsy is often required for the final diagnosis.

A heterogeneous, predominantly myxoid lesion with high SI on T2W, completely **suppressed** on T2W FS and **enhancing** on post contrast sequences is seen. Radiographs showed no calcifications.
SPINDLE CELL LIPOMA (SCL)

SCL is marked by the replacement of adipose tissue by collagen forming spindle cells. It is known as a Pleomorphic Lipoma subtype when the degree of cellular pleomorphism is high. Differentiation from a Liposarcoma depends mainly on clinical features, since there is significant radiologic feature overlap.

**Clinical Presentation**

- Painless, single, 3-5 cm slowly growing, well-defined lesion
- Men aged 45-60 years (~90%)
- Posterior neck, shoulders and back.

**Radiologic findings include:** On T1W, non-adipose components tend to be isointense to muscle and there is variable T2W signal characteristics

**Local recurrence is uncommon, even with incomplete resection**
Chondroid L.

The radiological and even histological diagnosis of ASCLT can be very challenging or even impossible. Highly variant cellular, fibrous, vascular and myxoid components delineate a broad microscopic morphological spectrum for this tumor.

A.S.C.L.T.

Lipoma

Lipomatosis

Ls. of Nerve

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A.S.C.L.T.

ATYPICAL SPINDLE CELL LIPOMATOUS TUMOR (ASCLT)

Having been described in the WHO 2020 Classification of Soft Tissue Tumors only recently, ASCLT is considered a benign neoplasm, with no metastatic potential, but a 10-15% recurrence rate after incomplete resection.

Radiologic findings:

Probably include variable signal characteristics on MRI, being an intermediate of SCL and other subtypes of lipoma

Imaging of ASCLT has been only scarcely described in the literature, given its recent definition as a separate entity.

The most effective tool to establish an accurate diagnosis of ASCLT seems to be the cytogenetic evaluation of MDM2 and CDK4 amplification, by Fluorescence in Situ Hybridization (FISH)

The previous WHO Classification considered ASCLT as a subtype of Atypical Lipomatous Tumor

The radiological and even histological diagnosis of ASCLT can be very challenging or even impossible. Highly variant cellular, fibrous, vascular and myxoid components delineate a broad microscopic morphological spectrum for this tumor.
Fat suppression techniques may not suppress classic hibernomas due to high brown adipose tissue content.

Inconspicuously named, Hibernoma is a rare benign tumor of brown adipose tissue. It presents as a soft, septated and encapsulated mass that is warm to the touch due to its highly vascular stroma. Young adults are more frequently affected. There are four histologic variations:

**Classic:** composed primarily of brown fat, being slightly hypointense to subcutaneous fat. (82%)

**Myxoid:** high water content imaging features. (8%)

**Lipoma-like:** lower brown to white fat ratio. (7%)

**Spindle cell:** mixed features from SCL and hibernoma. (2%)

Tumor high vascularity might make core needle biopsy an inadequate option, especially in sites of difficult blood control. Image-guided fine needle aspiration, avoiding areas of prominent vasculature, may be a better choice.

Hibernomas are highly $^{18}$FDG avid, often being identified as an incidental finding on PET scans.

Further MR imaging revealed a well defined mass, slightly hyperintense on T1W FS, with lateral flow voids.

25 yo female underwent CT for an abdominal pain, incidentally finding a right gluteal intramuscular mass.
Categorized as an intermediate lesion, only locally aggressive, ATLs are histologically identical to Well-Differentiated Liposarcomas. These entities may be best understood as precancerous, with recurrence rate and risk of malignant change depending on anatomical location. ATLs are almost always deep to fascia, show preference for thigh and have a similar presentation as lipoma.

Important differential MRI characteristics are the presence of **Thick Fibrous Septa** (>2mm), Size of >10cm and **Enhancement** on Post-Contrast sequences.

Although ATLs have a very good prognosis, large lipomatous masses should be sent to a Sarcoma Referral Center (SRC) for definitive treatment.
WELL DIFFERENTIATED LIPOSARCOMA (WDLS)

Considered by the previous WHO classification as an intermediate lipomatous tumor, WDLS is currently included in the malignant category and represents ATLs arising in the retroperitoneum, mediastinum and spermatic cord. WDLSs have a much worse prognosis, being in some cases essentially incurable.

65 yo male with 2 month history of throat tightness and mild dysphagia

Although there is no metastatic potential, these tumors show high recurrence rates due to complete resection difficulty. Retroperitoneal lesions have a 10 to 20-year mortality rate of 80% and demonstrate close to 100% recurrence rate. Also, there is a 10-15% risk of progression into a dedifferentiated LS. Surgical treatment is expansive and may lead to significant morbidity.
Clinical presentation only becomes symptomatic when the tumor has reached a significant volume, and may include pain, neurologic dysfunction and occasionally gastrointestinal bleeding. WDLS is the most common type of liposarcoma, accounting for approximately 50%.

55 yo male had a right spermatic cord mass found during hydrocele surgery.

The lesion has cystic, solid and adipose components, infiltrates the epididymis and shows enhancement.

It is vital that clinical team members use agreed-upon terminology to promote universal comprehension and appropriate treatment.

Main prognostic factors
- Tumor Resectability
- Histologic Subtype*

*Histologic subtypes include lipoma-like, sclerosing and inflammatory

Imaging reveals
- Predominantly fatty, large mass
- Irregularly thick (>2mm), enhancing septa
- Non-adipose elements
- Calcification in 10-32% of cases
Highly malignant, DDLS is composed of a well-differentiated adipose region that abruptly transitions into a dedifferentiated, nonfatty area. Most arise as de novo lesions, but about 10% of cases are late complications of WDLS. Metastasis occurs in up to 20% of patients, mainly to lungs, bones, and liver.

Case: Muhammad Aminuddin Bin Ashari
ID: 90070

70 yo male with weight loss and a feeling of right sided fullness

Axial C+ portal venous phase CT shows a mass isodense to muscle with involvement of the right kidney lower lobe, IVC and psoas major.

This patient had undergone excision of a large retroperitoneal lesion 3 years before this presentation.

Most common location is the retroperitoneum

Biopsy should be directed at the nonlipomatous component

5-year mortality rate is ~30%

A multidisciplinary treatment plan should be delineated for each case, preferably in a SRC.
Encompassing a spectrum of low-grade to high-grade tumors, MLS is the second most common subtype of liposarcoma. It is composed of uniform ovoid cells, lacking atypia, set in a myxoid matrix. The most common clinical presentation is that of a large, painless mass in the deep thigh.

Unlike most sarcomas, MLS has a tendency to metastasize to other soft tissue (particularly serosal surfaces) and bone, with lung being less common (14%).

Imaging reveals less than 10% of fat composition in a nodular, well defined myxoid lesion with high SI on T2W and some linear, internal foci of adipose tissue. US is particularly useful to distinguish it from cystic lesions and intramuscular myxoma.

40 yo male with progressive right calf painless swelling

- Intense and heterogeneous enhancement can be seen

Negative prognostic factors
- High cellularity (thus higher-grade);
- Absence of pseudocapsule;
- Spontaneous necrosis; >10cm.

MLS is extremely sensitive to radiotherapy

Most common type of liposarcoma in children

High-grade lesions have a 35% metastasis and mortality rate.

Case: Ammar Haouimi
rID: 95054
Hibernoma

Pathologically proven epithelioid variant of PLS

W. D. LS.

Pleomorphic LS.

Myxoid LS.

Before recognition of the myxoid pleomorphic subtype, PLS was considered the rarest yet most aggressive type of liposarcoma, with recurrence and metastasis rates ranging from 30 to 50%, and lung predilection. It requires identification of pleomorphic lipoblasts on microscopy for diagnosis and differentiation from an undifferentiated pleomorphic sarcoma.

A. L. Tumor

Dedifferentiated LS.

Myxoid LS.

Pleomorphic LS.

Peak incidence in the seventh decade of life

Extremities are most frequently affected

Rapidly growing mass, sometimes associated with pain and swelling

50 yo male with scapular region swelling for 6 years

Radiologic features on MRI include very low intraläsional fat signal, in a relatively well-defined nonspecific soft tissue mass. Heterogeneous SI may be seen due to necrosis and hemorrhage, for distinction of which fat suppression sequences are useful. Absence of fat hinders the imaging diagnosis.

A well-defined, elliptical, subcutaneous mass of about 3,4 cm with central hyperechogenicity and peripheral hypoechoic areas can be seen. This heterogeneous sonographic image is suggestive of malignant change.

Pathologically proven epithelioid variant of PLS

Only few flow signals are noted, indicating almost no increase in vascularity

Case: Maulik S Patel rID: 26654
**MYXOID PLEOMORPHIC LIPOSARCOMA (MPLS)**

MPLS is an exceedingly rare malignancy that shows features of myxoid and pleomorphic liposarcoma. Although being genetically and morphologically linked to conventional PLS, clinical differences justify a separate classification. It has significantly worse survival than other liposarcomas.

**1 yo male with insidious onset of respiratory distress**

Axial C+ CT displays a large, heterogeneous, enhancing mass that occupies the entirety of the left hemithorax, displacing the heart and great vessels to the right.

Recurrence of MPLS is expected. Chemotherapy and irradiation may decrease recurrence rates.

- MPLS tends to affect children and adolescents, with female predominance, albeit cases in older patients have been reported.

Early lung and bone metastasis may occur.

One marked characteristic of MPLS is its tendency to affect the mediastinal region.
There are multiple subtypes of benign, intermediate and malign lipomatous tumors, many with overlapping MRI features.

Lipomas are the most common benign adipocytic tumor, while WDLS is the most common malignant fatty lesion.

The differentiation between lipoma and WDLS relies on irregularly thickened septa, nonfatty elements, size and location; better characterized on MRI, the gold standard.

Lipomas might show atypical features, which don't necessarily mean malignant change.

Clinical presentation is extremely determinant in the radiologic diagnosis of LTs, thus ample communication between radiologists and assistant physicians is required to improve outcomes and should be done in all cases.
Lipomatosis of nerve has highly characteristic MRI findings and biopsy should be avoided.

Lipoma Arborescens is actually a type of lipomatosis and has a very interesting MRI fractal frond-like pattern.

Atypical Lipomatous Tumor has an excellent prognosis and similar presentation as lipoma, but tend to be larger and show post-contrast enhancement.

In a lesion without MRI characteristics of a benign adipocytic tumor, image-guided biopsy is indicated.

Unlike most sarcomas, Myxoid Liposarcoma tends to metastasize to other soft tissue sites, such as serosal membranes. It is also extremely sensitive to radiotherapy.

Pleomorphic Liposarcoma is the most aggressive type of liposarcoma.

It is important to keep in mind that some non-lipomatous tumors may also contain fatty components. These entities, fortunately, will usually have other very characteristic findings that permit a confident diagnosis by imaging.

The use of fat suppression is an important imaging tool in adipocytic lesion characterization.

The finding of an uncharacteristic lipomatous mass in a very young patient should raise the possibility of a lipoblastoma. Liposarcomas almost never occur in children under 5 years old.

Lipomas may show mesenchymal components, edema and calcifications, although hard to differentiate from WDLS and ATL, malignancy shouldn't be presumed in those cases.
Biopsy is helpful and necessary in many situations, however, its execution should be carefully planned since it **might compromise further imaging** examination.

Highly vascular areas should be avoided - in a hibernoma, for example - and the biopsy should focus on the nonadipose areas.

Biopsies should also avoid **tumor seeding**, that is, the needle pathway should be completely inside the pre-planned resection margins.

MR and CT for assessment of MSK lesions should always be interpreted together with a plain radiograph. Calcifications are key in some differential diagnosis.

Large lipomatous masses should be sent to a Sarcoma Referral Center (SRC) for definitive treatment.

**THE BOTTOM LINE**

The diagnosis of adipocytic soft tissue tumors can be challenging at times, and the continuous updates on the WHO Classification represent one of the many joint efforts between pathologists, radiologists and clinicians to make these cell proliferation disorders more recognizable, manageable and curable.
Franz M. Enzinger (1923-2006) was a pioneer in the field of soft tissue tumors, being the first to describe many of the entities discussed here. During his work at the AFIP, he lectured extensively and outlined the foundation without which current pathology would be impossible.

A special thanks to all case contributors!

REFERENCES


