REVIEW ARTICLE

Liposarcoma: A Pictorial and Literature Review

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ABSTRACT

Liposarcomas (LSs) are uncommon malignant mesenchymal tumors with adipose differentiation. There are different histological subtypes, and they can present in different anatomic regions. LSs are classified into five different categories: Well differentiated, dedifferentiated, myxoid, pleomorphic, and mixed type. The most common involved anatomical sites are the lower extremities, retroperitoneum, and trunk. It is important to understand that the anatomical distribution for LSs presentation is closely related to the histological subtype; however, there are some important differences regarding their presentation, radiological features, diagnosis, treatment, and prognosis.

Key words: Extremities, head and neck, liposarcoma, retroperitoneum, thoracic

INTRODUCTION

Sarcomas are rare soft tissue malignant tumors that originate from mesenchymal cells and they represent <1% from all malignant tumors. There are more than 50 histological subtypes, which differ in their presentation, diagnosis, treatment, and prognosis. The annual incidence of soft tissue sarcomas (STSs) is approximately 2–5/100,000/year. In the United States, 12,000 patients are diagnosed every year with STS, and nearly 5000 patients died annually.[1]

From all STS, undifferentiated pleomorphic sarcoma (formerly known as fibrohistiocytic sarcoma) and fibrous sarcomas are the most common. Liposarcoma (LS) represents the second most common and accounts for 10–35% of all STS. LSs are derived from primitive mesenchymal cells with adipose differentiation, and they are uncommon tumors, approximately 2.5 cases per million individuals.[2] They are predominant in males, with a male:female ratio of 1.23:1.00. LSs commonly present between 60th and 80th decade of life and they are more common in the white population.[3] In 90–95% of the cases, LSs occur in the lower extremities, retroperitoneum, and trunk; however, the lower extremities are more commonly affected, representing 72.9% of the cases (especially at the thigh in 67.7% of the cases).[4-6]

CLASSIFICATION

The World Health Organization has categorized LSs into five different subtypes:[7]

1. Atypical lipomatous tumor (ALT)/well-differentiated LS (WDL)
2. Dedifferentiated LS (DDLS)
3. Myxoid LS
4. Pleomorphic LS
5. Mixed-type LS.

According to some clinical trials and epidemiologic studies, WDL is the most common LS (40%), followed by myxoid LS (20%), DDLS, pleomorphic LS (5%), and, last, mixed-type LS.[3,6,8] There are crucial differences among each subtype regarding presentation, treatment, and prognosis.

WDL

WDL is the most common subtype, representing the 40–50% of all LSs. WDL is a low-grade tumor due to their highly lipomatous content. Histologically, they are composed of variable size mature adipocytes, with scattered lipoblast and large fibrous stroma, and in some cases, they may present sclerosing and inflammatory components.

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WDL is furthered classified due to their histological variability, into inflammatory, lipoleiomyosarcoma, lipoma-like, sclerosing, spindle cell, and mixed subtypes. The most common among these WDL subtypes is the lipoma-like subtype. Inflammatory subtype is characterized by the presence of lymphoid nodules in the cellular stroma and spindle cell type due to the presence of CD34+ spindle cells. The sclerosing subtype, characterized by collagenous fibrous components, is the subtype with the highest risk for dedifferentiation, therefore, is the version with the higher non-fatty component content.[9]

WDL frequently is intramuscular lesions, but more commonly arise in the deep soft tissues of extremities (65–75%). From all the cases of the extremities, 51% occur in the lower extremities, from which the majority originate in the thigh. The terminology WDL/ALT should be reserved for WDL liposarcoma situated in the subcutaneous tissue and in the extremities. The second most common region is the retroperitoneum, representing from 20% to 33% of the cases, followed by the trunk and last the head and neck. WDL terminology is reserved for lesions located in the retroperitoneum and/or mediastinum.[5,6]

WDL is a painless slow-growing tumor, which leads to their massive size at presentation. Only 10–15% of the cases present with pain and in some cases with abdominal symptomatology due to mass effect. Since lipomas can present similarly to low-grade LS, an adequate imaging and tissue biopsy assessments are crucial to establish a definite diagnosis. In some cases, it can be challenging to distinguish WDL from lipoma and patients commonly can be misdiagnosed. There have been reported that 30–40% of the time patients are radiologically misdiagnosed, and in 7–17% of the cases, the error was made in the histological evaluation.[1] However, there some factors and radiological features that have been reported to have statistical significance to differentiate WDL/ALT from lipomas, such as male gender, age >60 years, tumor size >10 cm, lower limb location, and the fat content >75% of the mass. Some imaging findings that are characteristic of WDL are as follows: Large mass with fatty content with non-lipomatous components, thick septa (>2 mm), and focal nodularity [Figure 1]. Tumor size >10 cm is an important factor that increases the odds to make a radiological diagnosis of WDL.[9]

In some lesions, calcifications had been described either by plain films or computed tomography (CT). In ultrasound (US) imaging, WDL is described as a heterogeneous, lobulated well-defined mass.[5] As for genetic biomarkers, gene amplification of the MDM2 gene, which is a negative regulator of p53 suppressor gene, is a complement tool for the pathological diagnosis, and it plays an important role in treatment decisions. Furthermore, MDM2 amplification by FISH method is the gold standard to differentiate WDL from lipomas. It has been described that 90% of WDL and ALT present amplified oncogenes MDM2 and CDK4.[6,10]

The management of LSs depends according to the localization, metastatic status, and subtype. The main treatment of LSs is surgical resection, and neoadjuvant therapies such as radiotherapy or chemotherapy may be utilized for high-grade and large tumors. In the case of WDL/ALTs due to their large size at presentation, primary surgical resection could be challenging in some situations. In these cases, retroperitoneal LSs are more difficult to resect than extremity localized tumors, due to their higher potential to involve visceral and vital organs. It is of great important regarding prognosis, to achieve a complete resection, since failure to achieve a complete resection can lead to increased local recurrence, metastatic, and dedifferentiation risk.[9]

ALTs more commonly are intramuscular lesions without osseous structures compromise, for this reason, surgical treatment does not represent a major challenge comparing to LS localized in the abdominal cavity or retroperitoneum. The primarily goal of surgical resection treatment is obtaining histologically negative margins, which is necessary to decrease the risk of local recurrence and metastatic disease.[6]

In cases of unresectable or metastatic LSs, the treatment alternative is chemotherapy; however, it is important to mention that WDL is considered insensitive to chemotherapy.[11] Radiotherapy has an important role in

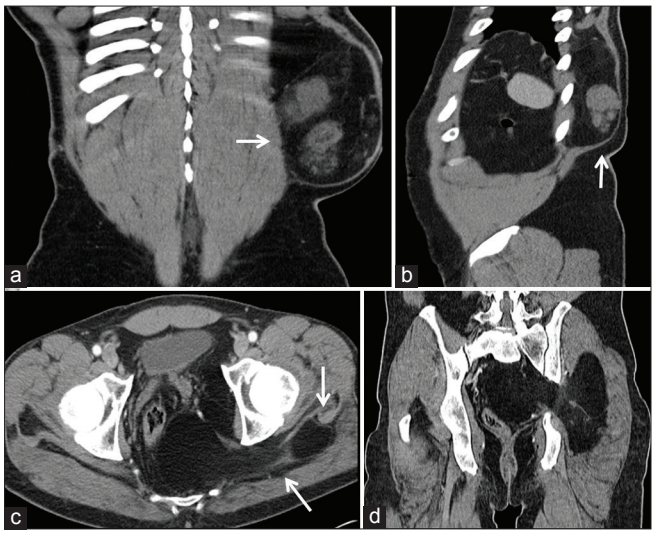

Figure 1: Well-differentiated liposarcoma (WDL). Contrast-enhanced coronal (a) and sagittal (b) computed tomography (CT) images showed a large, well-circumscribed mass in the subcutaneous tissue of the left back (arrows), composed mostly of fat and central areas of soft tissue density. The mass was surgically resected and the final histologic diagnosis was a WDL, lipoma-like variant with brown fat differentiation. Different case images (c and d) of a 53-year-old male with a pelvic mass found incidentally. Axial (c) and coronal (d) CT images of the pelvis showed a dense fatty mass arising in the left lower pelvis and protruding through the sciatic notch (arrows)

LS management, some studies had described favorable response and survival with adjuvant pre-operative radiation as compared with surgery alone for retroperitoneal tumors.[6]

The overall prognosis of WDL is favorable, and the 5-year survivorship is of 84%. WDLs are locally aggressive tumors, especially in the abdominal cavity; however, their recurrence risk is <10% and has no risk for metastatic disease.[3] The 5-year local recurrence rate for ATL is approximately 10% and 60% for retroperitoneal WDL according to recent studies. The mortality rates for ATL and retroperitoneal WDL differ in a meaningful way, being 0% and more than 80%, respectively.[9]

DDLS

DDLSs are a combination of WDL and non-lipomatous malignant tumors. The dedifferentiation can arise *de novo* in 90% of the cases or can arise from a pure ATL/WDLS at the time of local recurrence or represent a malignant progression in 10% of the cases.[6] Given the high rate of dedifferentiation, in ATL/WDLS cases, it always should be considered the possibility for dedifferentiation into high-grade tumor and the metastatic potential.

DDLSs are high-grade LSs with high risk of metastatic disease progression. Histologically, they have a high adipocyte well-differentiated portion well demarcated from a highly cellular, spindle cell-dedifferentiated portion.[8] The dedifferentiated components are high-grade fibrosarcoma or undifferentiated pleomorphic sarcoma in almost 90% of the cases. In other cases, the dedifferentiated components contain osteosarcoma, rhabdomyosarcoma, leiomyosarcoma, dermatofibrosarcoma protuberans, hemangiopericytoma, angiosarcoma, and meningioma.[12]

Since DDLSs more frequently arise from ATL/WDLS, usually, they present in the same anatomic regions of these tumors such as retroperitoneum, inguinal region, and extremities. The risk for dedifferentiation varies among different anatomic regions, in which lower extremity presents the highest rate (24%), then retroperitoneum (15%) and finally the upper extremity (4.5%).[9]

The diagnosis should be supported by imaging and biopsy. On CT or magnetic resonance imaging (MRI), visualization of a focal nodular non-lipomatous tissue in a WDLS suggests DDLS, and biopsy must be performed. The samples for histologic analysis must be taken from the fatty and the non-lipomatous mineralized components, since biopsy of the hemorrhagic or necrotic component can be not diagnostic. The histologic diagnosis is established with five or more mitoses per 10 high power fields. Histologically, the dedifferentiated element can resemble high-grade fibrosarcoma or undifferentiated pleomorphic sarcoma.[8,9]

For radiologic diagnosis, CT is preferred over MRI, since CT imaging can distinguish tumor ossification, which can be focal or extensive [Figure 2]. Furthermore, with CT it is possible to evaluate if there is bone damage involved. In the other hand, MRI is better to identify the fatty component from the dedifferentiated element, which will lack a fat signal intensity and in positron emission tomography (PET)-CT scan demonstrates an increased FDG-18 uptake.[9,12]

The management of DDLS is the same as WDLS, surgical resection is the mainstay of treatment and as well as WDL it has low chemotherapy response. Since 90% of DDLS cases has amplification of CDK4 oncogene, palbociclib, a potent *CDK4/CDK6* inhibitor, has a positive effect decreasing disease progression.[6]

DDLSs have an aggressive behavior that varies with tumor location and duration. The most important prognostic factor is anatomic localization, which retroperitoneal lesions have the worst clinical behavior, probably due to the silent and asymptomatic progression and the challenge to achieve a complete surgical resection.[12]

DDLSs have a local recurrence rate of 41%, and in most of the cases recur within the first 2 years after surgical resection. Their metastasis rate is of 17% and has a disease-related mortality of 28%. DDLS has survival rates of 57.2% and 40.1% for 5-and 10-year survivorship, respectively.[1]

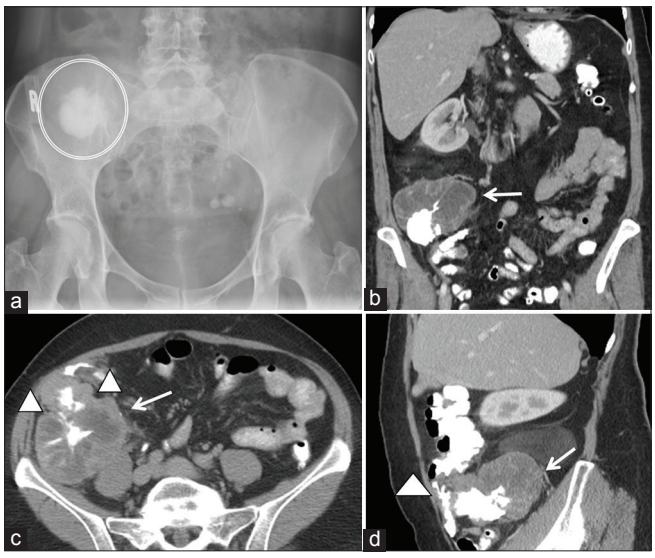

Figure 2: Dedifferentiated liposarcoma with osteosarcoma differentiation. Abdominal plain film (a) demonstrates a large round calcification in the right lower quadrant (circle). Contrast-enhanced computed tomography coronal (b), axial (c), and sagittal (d) images demonstrate a complex mass composed of low attenuation areas, a coarse spiculated calcification, and fatty components located in the right lower fossa (arrows). Note that in some areas, the mass is inseparable from the ascending colon (arrowheads)

Myxoid round cell liposarcoma

Myxoid round cell liposarcoma (MRCL) is the second most frequent subtype, which represents about 20% of liposarcomas. It is a malignant intermediate-grade tumor. MRCL is characterized by a t(12;16) chromosomal translocation between CHOP and FUS genes, which is present in 95% of the cases.[11] Another translocation fusion but less frequent is the EWS-CHOP oncogene t(12;21) (q13;q12). These chromosomal translocations contribute to lipogenic arrest and are pathognomonic for MRCL.[6]

Histologically, it is composed by abundant highly cellular myxoid material, a sparse cellular component with mature adipocytes, immature adipocytes, plexiform capillary network, and hemorrhage can be present in some cases. The round cell components are seen as small blue uniform cells with paucity of intercellular myxoid stroma and must compromise more than 5% of the tumor mass. It has been suggested that tumors with a round cell component >25% indicate a high-grade neoplasm and worst prognosis.[9]

MRCL most commonly arises in the lower extremities, which represent 30–40% of all extremity liposarcomas. The most affected lower extremities regions are the proximal region, the medial thigh, and the popliteal fossa.[9] Furthermore, MRCL is one of the most common liposarcomas localized in the thoracic cavity. MRCL metastasis has metastatic spread potential risk of 10–20%, which has an anatomical predilection to visceral organs, fat-bearing regions, skeletal structures in the chest wall, spine and ribs, paraspinal musculature, retroperitoneum, and lungs.[4,11]

Mentioning this, abdominal, pelvic, skeletal, and pulmonary imaging staging, and surveillance, is important in MRCL management. In contrast to WDL/ALT, in MRCL, the fatty component usually is <10% of the mass. The high water myxoid content seen at pathologic analysis and constituting most of the lesion is reflected at sonography, CT, and MRI.[5] In MRI, a low T1 signal intensity and a high T2 signal intensity demonstrate the high water content of the myxoid stroma component. Furthermore, it is important to take in consideration that myxoid LS can have a round cell component that decreases the tumor water content; this will result in a low-to-intermediate T1 and T2 signal intensity. The round cell tumor component demonstrates focal areas of contrast enhancement, which is directly proportional with overall worse prognosis [Figure 3].[9]

Surgical wide resection is also the treatment of choice for MRCL. Higher grade subtypes such as MRCL and pleomorphic liposarcoma (PLS), depending on the extent and invasiveness of the mass, may require resections of entire muscle subgroups to get adequate margins.[6] In cases in which tumors with size >5 cm, with more than 5% round cell component or that are intramuscular localized, neoadjuvant radiation and/or chemotherapy may be considered. MRCL

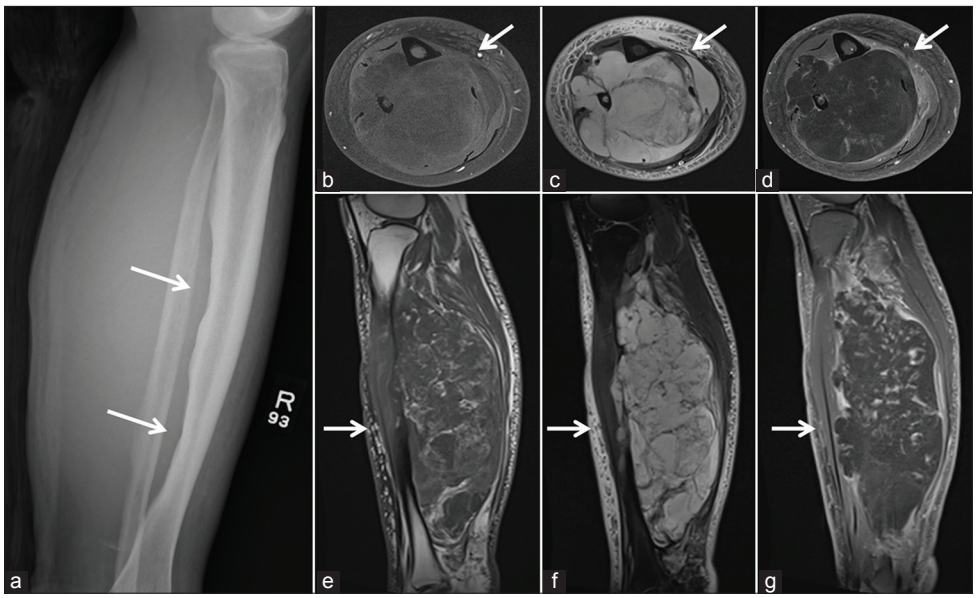

Figure 3: Myxoid liposarcoma in the calf region. Lateral plain film of the right lower extremity (a) demonstrates hyperostosis with changes consistent with chronic bone remodeling of the tibia. There is associated increased density of the soft tissue related to significant leg edema. T1 fast spin echo (T1FSE) (b and c), T2FSE (d and e), and short inversion time inversion-recovery (f and g) axial and coronal images demonstrate a heterogeneous soft tissue mass with the epicenter located in the deep posterior compartment (arrows). Note the associated tumor invasion into the anterior and lateral compartments. On T1-weighted (T1WI), there is high signal intensity suggesting fat content, and the high signal on T2WI suggests high cellularity. The soft tissue mass encases all the major regional neurovascular bundles and abuts the tibial cortex with chronic cortical thickening and remodeling of the tibial diaphysis without cortical infiltration or intramedullary extension

has a high chemotherapy response. The front-line therapy consists of doxorubicin and ifosfamide or doxorubicin compounds, and the second-line therapies generally consist of gemcitabine/docetaxel.[9,11] In metastatic disease, a traditional regimen containing doublets of doxorubicin/ifosfamide or gemcitabine/docetaxel result in response rates of 25–35% and survival of 12–18 months. Furthermore, for patients with metastatic disease, both trabectedin and eribulin have received recent FDA approval. The responsiveness of myxoid liposarcoma makes this tumor amenable to pre-operative radiation therapy.

The prognosis for MRCL depends on the round cell component proportion, which is directly proportional to the metastatic and mortality rates. As mentioned before, tumors with more than 5% round cell component are considered to have better prognosis. The 10-year mortality rate in tumors with a round cell component of 5–25% is about 30% and nearly 60% for patients with >25% of round cell component. MRCL progresses to metastatic disease in 23% and 56% of the cases with 0–5% and >25% of round cell component, respectively. The 5-year survivorship in the myxoid subtype is about 77%.[6,9]

PLS

PLS is the least common subtype representing about 5% of all liposarcomas. Both genders are equally affected and it is more frequently after the 5th decade. It is a malignant high-grade neoplasm with poor prognosis. The pleomorphic variant demonstrates a diverse mix of chromosomal rearrangements, and the most common mutations are found in p53.[6]

Histologically, PLS is characterized by pleomorphic lipoblast and can resemble undifferentiated pleomorphic sarcoma, myxofibrosarcoma, poorly differentiated carcinoma, and melanoma.

In most of the cases (56%), PLSs involve lower extremity and it presents as a deep firm painless soft tissue mass with rapid growth rate.[9]

PLSs typically appear as heterogeneous soft tissue masses, secondary to scattered necrosis, and hemorrhages areas. In MRI, there are seen small amounts of fat in 62–75% of the cases, these findings suggest the diagnosis of PLS [Figure 4].[5] PLS may require resections of entire muscle subgroups, and in some cases, amputation may be required. Post-surgical radiation decreases the local recurrence rate, which is about 35%. Furthermore, patients with PLS may benefit from neoadjuvant chemotherapy, which can improve survival rates.[9,11] PLSs have poor prognosis and a high risk for metastases; some factors associated with a poorer prognosis are non-extremity lesions and a lesion size >5 cm. PLSs have an overall survivorship of 50% and 5-year survival rate of 63%.[1,6]

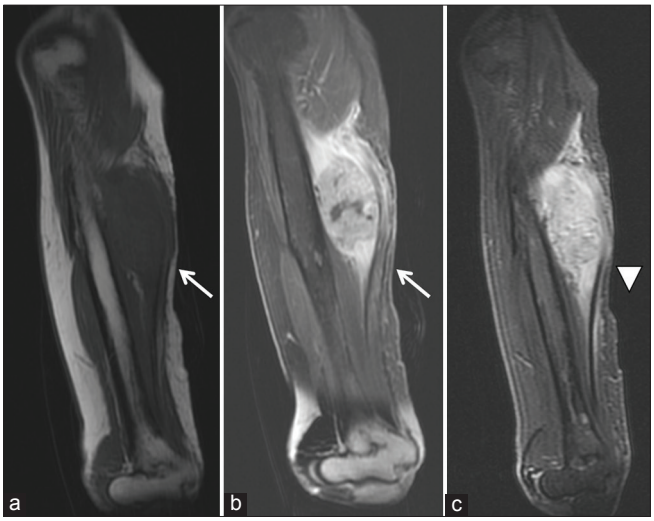

Figure 4: Pleomorphic liposarcoma with infiltration into skeletal muscle. Coronal T1-weighted (a) and short inversion time inversion-recovery (b) images demonstrate a heterogeneous enhancing mass partially necrotic in the medial upper third of the left arm and the lateral head of the triceps muscle surrounded by edema (arrows). There is mild enhancement after contrast administration (c) (arrowhead)

Mixed-Type Liposarcoma

Mixed-type liposarcomas have features representing a combination of the other liposarcomas subtypes, and it accounts for 5–12% of all liposarcomas. Mixed-type liposarcoma usually affects older patients. Common anatomical sites of involvement are the retroperitoneum and abdominal cavity, and less commonly, the mediastinum and extremities. The clinical, pathologic, and imaging features, as well as the treatment and prognosis of mixed-type liposarcoma, are a combination of the specific components of the lesion.[5]

LIPOSARCOMAS ANATOMICAL PRESENTATIONS

Liposarcomas can originate basically in any anatomic location; however, the anatomical distribution for liposarcoma presentation is closely related to the histological subtype. We decided to describe each of the most common anatomical presentations of liposarcomas to provide a more segmental focused review regarding presentation, diagnosis, treatment, and prognosis.

Head and Neck Liposarcomas

Liposarcomas from head and neck are not very common, and they represent up to 9% of all liposarcomas. From these LSs, the most affected anatomical region is the neck, which is affected in 19% of the cases, these LSs are developed from the neck's soft tissue [Figure 5]. Other common locations are the face (13%), larynx (6%), pharynx (6%), dura (6%), the

orbit (6%), and oral cavity (5%), other anatomical regions are less common.[13]

Liposarcomas from the hypopharynx, which are very rare and <28 cases had been reported until 2016, arise from the piriform sinus, they present clinically with progressive dysphagia and weight loss due to mass effect.[14] Liposarcomas from the head and neck commonly are <10 cm in size and they can be polypoid and pedunculated, giving them a very similar gross appearance to benign polyps, which can delay the diagnosis.[13] In MRI, which is the imaging modality of choice, WDLs of the hypopharynx can be misdiagnosed with other benign lipomatous tumors, for this reason, an histologic diagnosis is necessary.[15] The gold standard for diagnosis is biopsy, which can be obtained endoscopically or with open surgery. The surgical treatment, due to the anatomic location in some cases, can lead to considerable sequelae and complications. Resection can be achieved endoscopically with laser or scalpel and with open surgery lateral pharyngotomy. For non-operable lesions or incomplete resections, radiotherapy may be the best treatment option.[14]

Laryngeal liposarcoma (LLS) is also a rare LS, it is more common in males with a reported male-to-female ratio of 8:1 and a mean age of 55 years. The most common region affected in the larynx is the supraglottic area, and it can present with symptoms related to obstruction such as snoring, dysphagia, weight loss, and hoarseness. Most of LLS cases are low-grade histologic subtypes, their overall prognosis is good, with a low-risk potential for distant metastases and local lymph nodes involvement. However, LLS is locally aggressive. As other LSs, the treatment of choice is wide surgical resection, and it has been reported that adjuvant chemotherapy or radiotherapy do not achieve better results compared to surgery alone.[16]

Liposarcoma from the esophagus is an extremely rare tumor, representing only 0.5% of all esophageal tumors,[17] and there are only a few cases that have been reported since the first case reported 34 years ago.[18] Among the histological subtypes, WDL is present in 68% of the cases, myxoid LS in 20%, DDL in 6%, and pleomorphic LS also in 6% of the cases.[17]

There is a male predominance and the mean age has been reported to be about 58.4 years. In most cases, they present as an intraluminal polypoid mass and less commonly transmural, and the mean lesion greater dimension is about 13 cm. In about 80% of the cases, they arise in the upper third of the esophagus and less commonly in the distal region.[19]

Esophageal liposarcoma (ELS) presents with progressive dysphagia, odynophagia, weight loss, foreign body or globus sensation, cough, emesis, and nauseas.[18] The diagnosis can be made with barium study, CT scan, MRI, and endoscopy.[17] Due to the rarity of ELS and the unspecific clinical symptoms, we must consider other entities as differential diagnosis such as GIS tumor, leiomyosarcoma, giant fibroepithelial polyp, pleomorphic undifferentiated sarcoma, and last anaplastic carcinoma [Figure 6].[18]

The resection can be achieved endoscopically which is less invasive or surgically with transcervical, transthoracic, or transabdominal approach.[19] Furthermore, radiotherapy and chemotherapy can be considered as they have been demonstrated a positive response, so this can be a treatment possibility, especially in non-surgical candidates.[20]

Thoracic/Mediastinal Liposarcomas

Primary intrathoracic liposarcoma is a very uncommon tumor, only a few cases have been reported. Most reported cases of LS involving the mediastinum are secondary in relation to metastatic disease. Most of LS arising in the thoracic cavity are WDL and myxoid LS histologic subtypes. Mediastinal liposarcomas are extremely rare, making up from 0.1% to 0.75% of all mediastinal tumors, within these tumors, pleural, and pulmonary liposarcoma are less common.[4,15]

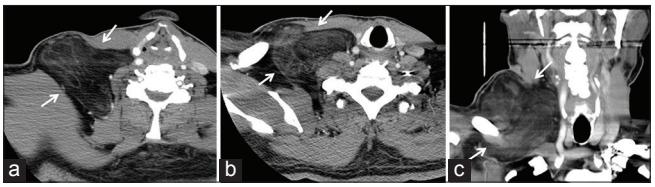

Figure 5: Large supraclavicular mass in a 73-year-old man. Contrast computed tomography, axial (a and b) and coronal (c) images showed a large heterogeneous low-density fatty mass in the right supraclavicular region (arrows). After surgical resection, the final pathology reported atypical lipomatous tumor

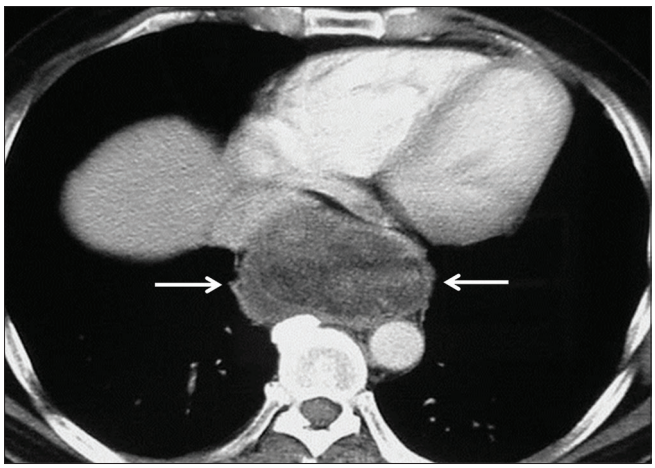

Figure 6: Esophageal pleomorphic liposarcoma. Contrast-enhanced computed tomography axial images demonstrated a large well-circumscribed heterogeneous solid ovoid mass in the distal esophagus with some areas of fatty density (arrows)

Primary lung LS is very uncommon, most of the reported cases are myxoid, pleomorphic, and unclassified subtypes and less commonly dedifferentiated subtype.[21] In liposarcomas of the lung and mediastinum, it is important to differentiate them from pleural LS if there is chest wall or mediastinal invasion. This must be made clinically, with imaging evaluation or surgically [Figure 7].[4]

The clinical presentation is usually due to respiratory compromise including chest pain, cough, and shortness of breath. Regarding imaging, MRI represents the gold standard for diagnostic and preoperative evaluation due to its superior definition of tumor invasion of vessels and thoracic structures. Contrast-enhanced chest CT scans aid in determine the complete extent, size, and localization of the mass lesion in pre- and post-surgical resection evaluation.[4]

The treatment of choice is complete surgical resection, although this could be challenging due the anatomic region complexity. For intrathoracic liposarcoma, radiotherapy and chemotherapy are believed to be ineffective therapeutic modalities for survival. However, for chemotherapy management, doxorubicin and ifosfamide are the most frequently used chemotherapeutic agents for these cases. Metastasis to various structures including lung, pleura, liver, and bone are described, especially in the poor differentiated varieties.[4]

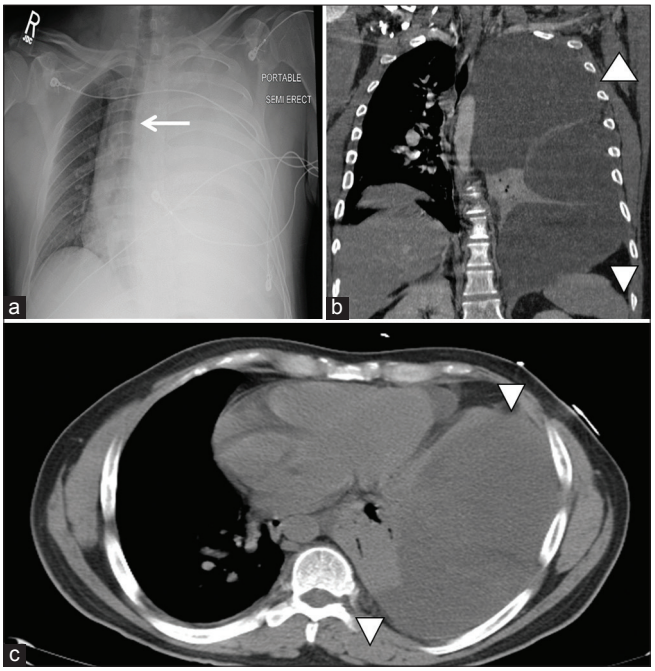

Figure 7: Pleomorphic intrathoracic liposarcoma in a 45-year-old male complaining of shortness of breath, chest pain, and cough. Chest plain film (a) showed a whiteout left hemithorax with mediastinal shift to the right (arrow). Coronal (b) and axial (c) computed tomography images of the chest demonstrated a large low-attenuation mass occupying most of the left hemithorax, associated with the complete collapse of the left lung (arrowhead). Note that the mass mimics a huge pleural effusion. Patient underwent left lung decortication and removal of multiple masses

Retroperitoneal/Abdominal Liposarcoma

Liposarcoma is the most common mesenchymal tumor arising in the abdominal cavity, they can affect the retroperitoneum, mesentery, gastrointestinal wall, or even any organ within the abdominal cavity.[22] The most common site is the retroperitoneum, and LS represents about the 50% of all retroperitoneum sarcomas. The can present at any age, but the mean age of presentation is at 56 years, and it affects males and females equally. The most frequently histologic LS subtype in the retroperitoneum is WDL and DDLS.[23] DDLS is much more common in the retroperitoneum than in lower extremities, where WDL is usually more frequent.[24]

Diagnosis of retroperitoneal LS is challenging because the symptomatology is vague and non- specific, and usually manifest until the lesion becomes very large in size, about 20–50% have a diameter >20 cm.[23] Imaging evaluation is important to determine the source and extension of the lesion, both CT and MRI are useful for retroperitoneal evaluation [Figure 8]. However, CT scan is the modality of choice, since it is less sensitive to motion artifact comparing to MRI; therefore, it is better for anatomical relationship and metastatic disease identification.[25]

When making the diagnosis, some other sarcomas should be in the differential diagnosis, such as leiomyosarcoma, which represent about 28% of retroperitoneal sarcomas, pleomorphic undifferentiated sarcoma (7%), fibrosarcoma (6%), and malignant peripheral nerve sheath tumor (3%). For definitive diagnosis of retroperitoneal LS, surgical exploration may be required, since obtaining non-surgically samples can be more challenging for achieving a histological diagnosis.[25]

Wide surgical resection is also the treatment of choice for retroperitoneal LS, and it is curative in most cases.[25] It is often necessary *en bloc* removal of adjacent anatomical structures such as the abdominal wall, psoas, or paravertebral muscles. This surgical approach diminishes the risk or recurrence, which is the main cause of death.[24] Regarding recurrence, DDLS is more common to recur and frequently an extensive, or multiple organ resection is necessary.[22] Adjuvant radiation therapy may be considered in high-grade or unresectable tumors to reduce the risk of recurrent disease. Furthermore, pre-operative radiotherapy is a treatment option; however, a positive impact in the survival rate has not been proved yet.[23]

Liposarcoma arising in the mesentery is another uncommon tumor, most often present during age of 50th to 70th and males

are more frequently affected [Figure 9].[26] Symptomatology usually is non-specific, and it can present as an abdominal mass, abdominal distension, postprandial pain, weight loss, and mass effect symptoms.[24,26] Abdominal imaging evaluation is important for diagnosis and surgical management; mesenteric angiography is a useful tool for localize the lesion before surgical resection. It is important to consider and rule out GIST as differential diagnosis in LS of the mesentery due to its anatomical relationship to the bowel. This differentiation could be made molecularly with CD117 (c-kit) and CD34 which are usually expressed in GIST.[24]

The mainstay of treatment is wide surgical resection with negative margins and sometimes should be followed by radiation or adjuvant systemic therapy with doxorubicin.[26] In some cases, other structures must be resected with the tumor and debulking surgery may be performed. The most common post-operative complications are anastomotic leak, effusion, and infection.[22]

Pelvic and Inguinal Liposarcoma

The retroperitoneum cavity extends superiorly from the diaphragm to the pelvic brim inferiorly; therefore, most of pelvic liposarcomas are retroperitoneal liposarcomas that grow longitudinally to extend into the pelvis.[27] Even though liposarcomas arise commonly in the retroperitoneum, pelvic involvement is very rare.[28] Liposarcomas that extend retroperitoneally into the pelvis in female patients can be misdiagnosed as adnexal masses, so gynecologist should consider LS as a differential diagnosis.[29] Conversely, most liposarcomas from the spermatic cord (LSC) arise from the spermatic cord and less frequently extend from the retroperitoneum to the inguinal region.[30] LSC represents about 5–7% from all paratesticular malignant tumors. WDL and myxoid LS are the most common subtypes of LSC, accounting for 48.7% and 25.6%, respectively [Figure 10]. It presents more commonly in adults with a mean age of presentation of 61 years and an increased incidence in the Japanese male population has been reported.[30]

Liposarcomas from the pelvis at the time of identification present as large masses given their silent growth, and they produce symptomatology until they are compressing or invading pelvic organs.[27] In the inguinal region, presents as slow-growing inguinal painless mass, LSC is commonly misdiagnosed as an inguinal hernia, hydrocele or spermatocele, or even confused with a testicular or epididymal tumor.[30] For radiological evaluation of pelvic liposarcomas or LSC, ultrasonography, contrast CT, and MRI are useful imaging modalities; however, CT scan and MRI are preferred for structure involvement and lipomatous nature identification of these masses.[27,30]

The treatment of pelvic liposarcomas can be difficult in some cases; this because its proximity to important organs and

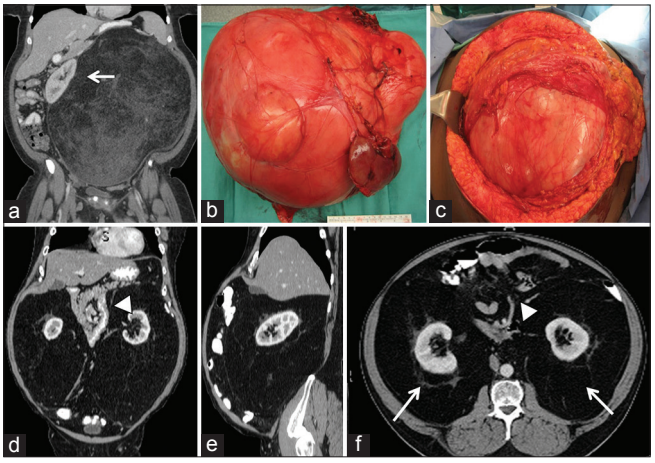

Figure 8: Retroperitoneal well-differentiated liposarcoma (WDL) in a 34-year-old female with increased abdominal girth over 1 year. Contrast computed tomography (CT) coronal image (a) of the abdomen and pelvis showed a large well-circumscribed mass with fatty density arising in the left side of the retroperitoneum with displacement of the right kidney, bowel and mesentery to the right of the midline (arrow). Intraoperative photographs (b) and photograph of the gross specimen (c) showed a large lobulated yellow mass with smooth walls. Different case (d and f) of a WDL in a 63-year-old male complaining of weight gain. Contrast CT coronal (d), sagittal (e), and axial (f) images demonstrated symmetrical increase of the retroperitoneal fat with anterior displacement of both kidneys (arrows) and central displacement of the root of the mesentery (arrowheads)

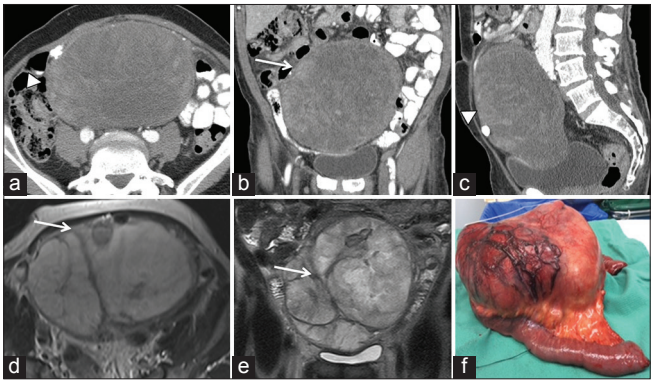

Figure 9: Contrast-enhanced computed tomography axial (a), coronal (b), and sagittal (c) images showed a large ovoid mass with heterogeneous enhancement and with a peripheral coarse calcification (arrowhead) located in the mesentery and displacing the small bowel and colon laterally. Note this mass is abutting the bladder dome. Photograph of the surgical specimen (d) demonstrated a large lobulated mass with peripheral vascularity and smooth contours with the epicenter in the mesentery of the small bowel

structures, the anatomical characteristics of the region, and the usually large tumor size. These factors can compromise the complete surgical resection or achievement of negative margins.[28] In the cases of LSC, the treatment of choice is

radical orchiectomy with wide local excision and high ligation of the spermatic cord.[30] There is a high risk for local recurrence of pelvic soft tissue sarcomas, which has been reported to be about 35–44%. Pelvic liposarcomas have an increased risk of intralesional margins, and patients with high-grade subtype and local recurrence have very poor prognosis.[28] In LSC, the local recurrence rate is about 55–70%, despite this, the prognosis is good after radical orchiectomy with complete clearance and negative margins.[30]

Extremity Liposarcoma

Liposarcomas in the extremities are not an uncommon presentation, about 80% of liposarcomas involve the lower extremities.[31] From liposarcomas in the extremities, 40–65% present in the thigh. Furthermore, they commonly arise in the upper arm, shoulder, popliteal fossa, lower leg, buttocks, and the forearm.[32] Liposarcomas from the foot are a very rare entity, only a few cases had been reported, some of the reported cases were one WDL and three PLSs. The WDL was from the plantar region of the 4th metatarsal and was treated by amputation. From the pleomorphic subtypes, one of them was from the left great toe and presented as a persistent ingrown toenail, the other cases presented from sole arised from a burn scar, and finally, the third one affected the dorsum of the right foot.[33]

From all the liposarcomas histologic subtypes, myxoid LS is the most common subtype that affects the extremity.[32] Myxoid and pleomorphic subtypes represent about 29% and 12% of liposarcomas, respectively, and both subtypes are more common in the extremities.[31]

As we mentioned before, in the case of WDL, when it presents in the lower extremities, we called it "ALT," a term that was first proposed in 1975 by Kindblom *et al*.[34] This term differentiation was proposed due to the clinical presentation variation to the retroperitoneal presentation. WDL of the extremity presents as slow-growing painless mass, with no metastatic potential; however, they are locally aggressive tumors.[35] The metastatic disease risk increases if dedifferentiation occurs; however, this is very rare, contrary to retroperitoneal WDL. Previous studies had reported a dedifferentiation rate about 1–4% in liposarcomas from the extremity.[35]

Imaging evaluation is preferred with MRI, it is more specific than CT scan since it can distinguish more accurately neurovascular structures and delineate the soft tissue tumor [Figure 11].[31] Furthermore, we must consider other fat-containing heterogeneous tumors in the extremities as differential diagnosis such as lipoblastoma, hibernoma, hemangioma, and angiolipoma.[32] However, in some cases, radiological findings with CT scan or MRI can suggest and correlate with the histologic diagnosis.[36]

In the past, extremity amputation was considered the treatment of choice due it basically eliminates the recurrence risk. Today, with a 1 cm margin circumferentially surgery, negative margins and minimal recurrence rates can be achieved.[36] Furthermore, a wide margin surgical resection over a marginal excision is preferred for better local control, hence, less recurrence risk.[35] In cases with poorer prognosis, such as patients with neurovascular invasion, amputation is indicated.[32] Furthermore, the histologic type and grade of the lesion take part in this decision; in low-grade LS (WDL and myxoid), limb-sparing surgery is adequate, conversely, high-grade LS (Dedifferentiated and pleomorphic) amputation is the indicated treatment.[32]

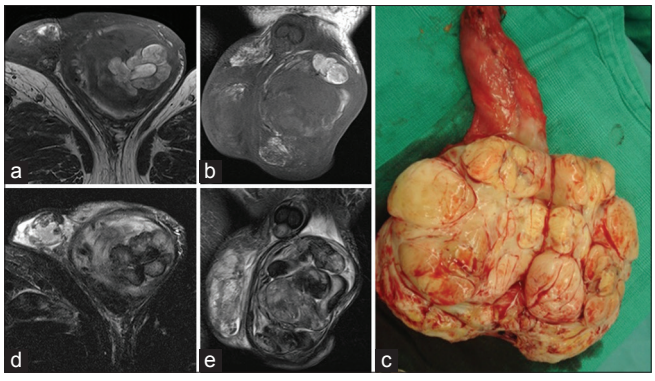

Figure 10: Well-differentiated liposarcoma of the spermatic cord in a 90-year-old male presenting with a large distended scrotum. T1FSE axial (a) and coronal (b) and T2FSE axial (c) and coronal (d) images showed a large heterogeneous, lobulated mass in the right scrotum composed of fat and soft tissue. Photographs of the gross specimen (e) showed a lobulated, fleshy, and yellow mass

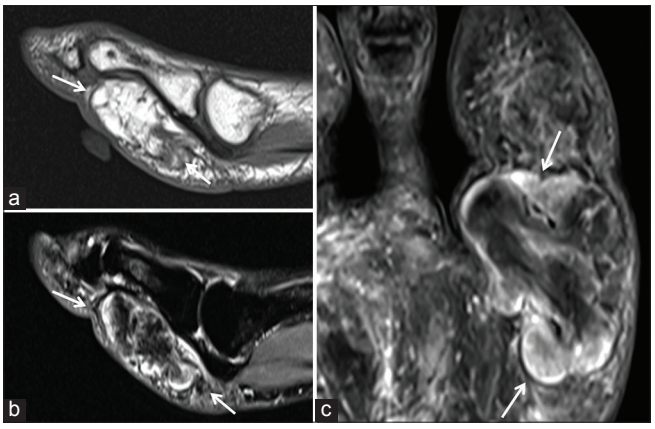

Figure 11: Atypical lipomatous tumor of the great toe in a 30-year-old female presenting with toe swelling and pain. T2FSE (a), short inversion time inversion-recovery (b) axial, and T1WIFS post-gadolinium coronal (c) images showed a 4 cm mass in the deep soft tissues underlying the first proximal phalanx containing internal septations and containing areas of both fat suppression and non-fat suppression (arrows)

Table 1: Imaging workup for sarcomas according to anatomic region

Workup guidelines	
Head and neck, superficial trunk, and extremity sarcomas	Retroperitoneal and intra-abdominal sarcomas
MRI±contrast CT of primary tumor *Angiogram and plain X-rays may be required in certain cases Chest X-ray or non-contrast CT (preferred) Additional imaging PET/CT scan (staging, prognosis, grading) Abdominal/pelvic CT (myxoid/round cell liposarcoma) Spine MRI (myxoid/round cell liposarcoma)	Chest/abdominal/pelvic CT±Abdominal/pelvic MRI

*National comprehensive cancer network (NCCN) clinical practice guidelines in oncology. Soft tissue sarcoma NCCN. MRI: Magnetic resonance imaging, CT: Computed tomography, PET: Positron emission tomography, US: Ultrasound

Table 2: Imaging follow-up for sarcomas according to anatomic region

Follow-up guidelines	
Stage	Head and neck, superficial trunk, and extremity sarcomas
Stage IA and IB	Chest X-ray or CT every 6–12 months (use contrast if abdomen/pelvis imaging) Consider post-operative baseline and periodic imaging MRI±CT US (small superficial lesion)
Stage II and III	PET/CT scan for>3 cm lesions to evaluate neoadjuvant chemotherapy response Post-operative MRI or contrast CT for primary tumor and to rule out metastatic disease Chest X-ray or CT every 3–6 months for 2–3 years, then every 6 months for next 2 years, then annually Consider post-operative baseline and periodic imaging MRI±CT US (small superficial lesion)
Stage IV	Chest and metastases sites X-ray or CT every 3–6 months for 2–3 years, then every 6 months for next 2 years, then annually Consider post-operative baseline and periodic imaging MRI±CT US (small superficial lesion)
Stage	Retroperitoneal and intra-abdominal sarcomas
Resectable R0, R1, R2	Post-operative abdominal/pelvic CT or MRI every 3–6 months for 2–3 years, then every 6 months for next 2 years, then annually Chest X-ray or CT (preferred)
Unresectable or stage IV	Imaging to assess treatment response Chest/abdominal/pelvic CT or chest non-contrast CT and abdominal/pelvic MRI

*National comprehensive cancer network (NCCN) clinical practice guidelines in oncology. Soft tissue sarcoma NCCN. MRI: Magnetic resonance imaging, CT: Computed tomography, PET: Positron emission tomography, US: Ultrasound

Tumors with low risk of recurrence may be treated with surgery alone.[36] On the other hand, for high risk patient's, surgical resection and adjuvant radiotherapy are the mainstay treatment. Systemic chemotherapy is indicated in patients with metastatic disease.[31]

Liposarcomas from the extremity have a local recurrence rate from 8% to 52% and the median time of recurrence is from 38 to 56 months after the primary surgery. Furthermore, it has been reported that deep tumors have greater risk of recurrence.[35] In general, liposarcomas from the extremity have good prognosis, its risk of recurrence and metastatic disease are related to the histologic type and tumor size, and if they invade neurovascular structures or not.[31]

CONCLUSION

Liposarcomas are malignant mesenchymal tumors and the second most common soft tissue neoplasms. They present more commonly after the 60th decade and can originate in any anatomic site, in the majority of the cases arises in the lower extremities, retroperitoneum, and trunk. However, the most common site is the lower extremities, specifically the thigh. WDL is the most common subtype

and has the greatest survival rate; nevertheless, its local recurrence rate is the highest, especially when develops in the retroperitoneum. PLS is the least common subtype and has the worst prognosis.

All liposarcomas subtypes have key clinical, radiological, pathological, and genetic distinctions; moreover, their diagnostic and follow-up approach varies and it depends on their site of origin and their clinical stage [Tables 1 and 2].

Therefore, it is crucial to become acquainted with the differences among the liposarcomas subtypes and their diverse anatomical presentations and imaging characteristics; since this differentiation will impact in their management and prognosis.

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