Journal of Orthopedic Surgery and traumatology

Review article

Lipomas: much more than a "bump of fat"

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Abstract: Lipomatous tumors are a common group of mesenchymal lesions. Over the 5 years, major changes in the classification of lipomatous tumors included the 6 addition of several new lipoma variants, the use of the term atypical lipoma for well-differentiated liposarcoma 7 of subcutaneous tissue, and the recognition of the entity liposarcoma. 8 dedifferentiated. Lipomas, the most common lipomatous tumor, account for almost half of all 9 benign lesions.
In their typical form, they rarely present diagnostic problems for the pathologist. However, lipomas that are in deep locations (eg, intramuscular lipoma 11) or those that have unusual features (eg, chondroid lipoma, angiolipoma 12 cell, spindle cell/pleomorphic lipoma) may be confused with a liposarcoma.
13 Recent cytogenetic studies have reaffirmed the separate nature of many of the 14 lipoma variants.

Keywords: Lipoma; liposarcoma; atypical lipoma; lipomatous tumor

1. Introduction

Lipomas are benign tumors of adipose tissue and are the 19 most frequent soft tissue tumors in adults. Most are solitary lesions, since multiple lipomas 20 usually suggest the presence of rare autosomal dominant syndromes 21 (called lipomatosis). Most lipomas are painless, mobile, and slow-growing masses, and complete resection is usually the curative treatment of choice. Nerve compression 23 by lipomas is rare, but when it occurs it is a reason for 24 surgical resection.

Its malignant cousin, liposarcoma, is the most common soft tissue sarcoma in adults. It rarely arises from subcutaneous tissues or from pre-existing lipomas, and it is rarely found in children. The hallmark of liposarcoma is the immature fat cell or 28 lipoblast.

However, not everything is black or white, and we will see that there are lipomas that present 30 confounding factors and make it difficult for us to classify between benign and malignant.

2. Diagnosis

It is usually done clinically by physical examination. However, if there are 34
If malignancy is suspected, diagnostic imaging, MRI, or CT (computed tomography) scans may be performed if it is large, has unusual features, or appears to go deeper than fatty tissue.

Ultrasound and MRI have been used with some success to differentiate lipomas from liposarcomas, but are not yet a reliable diagnostic route. Many studies have 39 performed an MRI examination to clarify the characteristics of lipomas. The signal intensity is the same between the conventional (benign) lipoma and the

Atypical lipoma (which we will talk about later). The tumor margins of ALT and benign lipoma are well defined and smooth in almost all cases. However, Gaskin et al. analyzed MRI in patients with tumors derived from adipocytes, and the atypical lipoma showed low intensity on T1 and high intensity on T2 with septal structures greater than 2 mm in diameter with a sensitivity of 100% and specificity of 86%.

Even so, fine needle aspiration is the extraction of a tissue sample (biopsy) for laboratory analysis, with which we would have a confirmatory diagnosis of the 49 histological type of the lesion.

Warning signs of malignancy are rapid and excessive growth of the tumor, a size greater than 5 cm in diameter, located in the extremities, retroperitoneally, in the groin, in the scrotum or on the abdominal wall, which is deep (below or attached to the superficial fascia) or invade nerve or bone.

In the following image we observe the histological differences between a conventional lipoma (Figure 1, image above) and a liposarcoma (Figure 1, image below) with cellularity with fat vacuoles and lipoblasts. The middle term that we will see later, 57 the atypical lipoma, corresponds to figure 2.

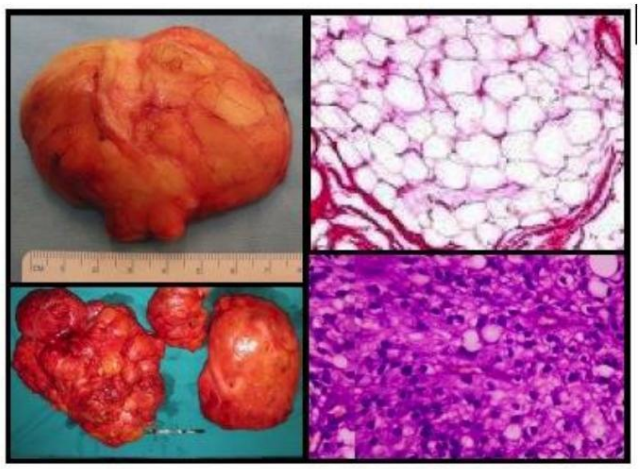

Figure 1

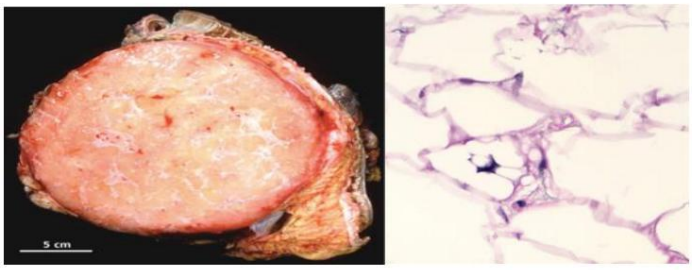

Figure 2

3. Classification

Lipomas can be classified according to particular morphological features in: lipoma conventional, intramuscular lipoma, fibrolipoma, myxolipoma, angiolipoma, spindle cell (spindle cell) lipoma, myelolipoma, and pleomorphic lipoma. They can also be classified by their chromosome rearrangements.

Conventional lipoma, the most common subtype, is a well-encapsulated mass of mature adipocytes of widely varying sizes. It appears in the subcutaneous tissue of the proximal region of the extremities and trunk, more frequently in people of

middle age. They are usually very well defined. Macroscopically it is yellowish and microscopically it is made up of unilocular mature adipocytes.

Intramuscular lipomas are deep lipomas that arise within or between skeletal muscle fibers. Angiolipomas present vessels and adipocytes and can sometimes cause pain. Myolipomas contain smooth muscle fibers and adipocytes.
Chondroid lipoma has adipocytes with a chondral-like cellularity. The spindle cell and pleomorphic lipoma have few adipocytes and the proliferation of spindle cells, with cellular atypia, is striking. Lipoblastomas are an almost exclusive lesion of childhood that morphologically can be totally overlapping with myxoid liposarcoma. In myelolipoma adipocytes are mixed with bone marrow cells. Hibernoma is made up of multilocular brown fat.

3.1. So how do we know when they are good or bad?

The vast majority of benign lipomatous lesions do not present diagnostic problems and are easily recognized. However, there is a small group that can confuse us with different types of liposarcoma. These are intramuscular lipoma, chondroid, lipoblastomatosis, spindle cell lipoma, myxolipoma, and dendritic cell fibromyxolipoma.

3.1.1. intramuscular lipoma

As a general rule, it is noted that the larger and deeper an adipocytic lesion is, more likely to be malignant. The exception to this rule is presented by intramuscular lipoma. This lesion is easily confused with the atypical lipoma that we will discuss later. Intramuscular lipomas are typical adult lesions (30-60 years); when they are discovered in children, their distinction from lipoblastomatosis can be almost impossible. The places most commonly affected are the large muscles of the extremities, especially the thigh, buttock, girdle, and arm. They show slow growth, not painful, which is well manifested during muscular contraction.

Macroscopically they are yellowish masses of fat within the muscle tissue. in the histological study the muscle tissue appears infiltrated by sheets of adipocytes that cause dispersion and atrophy of the trapped muscle fibers. The adipocytes do not present nuclear atypia or variations in their size and, in addition, lipoblasts or stromal pleomorphic cells are not observed. Another important piece of information for the differential diagnosis with atypical lipomas is the contour of the lesion. The intramuscular lipoma has an infiltrating contour, while the other tends to be circumscribed and tends to compress but not infiltrate the adjacent muscle tissue. In extreme cases of doubt, immunohistochemistry with the MDM2 antibody can be of great help, since this protein appears amplified in atypical lipoma/myxoid liposarcoma and not in intramuscular lipoma.

3.1.2. Chondroid lipoma

This is an unusual lesion that preferentially affects women and is located in the subcutaneous tissue of the limbs and waists. Because it shows some histological resemblance to myxoid liposarcomas or extraskeletal myxoid chondrosarcomas, deep or large lesions are easily confused with these sarcomas. In general, they are well-defined and encapsulated tumors, with white-yellowish coloration, and a tendency to lobulate. Within the lobules, the cells are arranged to form cords and nests immersed in a myxoid or myxohyaline matrix.
The cells are round, lack nuclear pleomorphism, and their cytoplasms may be dense and eosinophilic or vacuolated; the latter correspond to lipoblasts in various maturational stages. Cells often dominate

vacuolized, but there are cases where the opposite occurs. In general, mitosis is not observed and there may be mature adipose tissue to a greater or lesser extent. Cytogenetics has revealed a rather characteristic translocation t(11;16)(q13;p12-13).

3.1.3. Spindle cell lipoma, myxolipoma, and dendritic cell fibromyxolipoma.

These three types of lesions are closely related and can be confused mainly with myxoid liposarcomas. Spindle cell lipomas 125 are located in the posterior region of the neck and in the shoulder girdle (>80%). Generally 126 are single lesions, but multiple familial cases have been described. Because recurrences are exceptional, this term should be restricted to superficial lesions 128 located in the hypodermis or, more rarely, the dermis. Histologically identical lesions located in deeper tissues should be called atypical lipomatous tumors since they show a greater tendency to local recurrence. In the same way, those located 131 in unusual locations would be better considered as suspicious. In the histological study, 132 they are well-circumscribed lesions, delimited by a fine or lobulated capsule, showing a variable proportion of adipocytes, spindle cells, collagen, and myxoid matrix. Spindle cells tend to be arranged in bundles or scattered and contain scant cytoplasm and a pale, uniform nuclei.

The term myxolipoma is used to designate lipomas with extensive myxoid change. 137 In general, this finding has been considered simply as a secondary phenomenon in a conventional lipoma. However, when studied more closely, certain common features with spindle cell lipomas are noted, such as a predilection for the posterior region of the neck and back, good delineation, presence of cord-like collagen, spindle cells with CD34 immunoreactivity, and sometimes even mature adipocytes; Furthermore, cytogenetic studies have revealed the 13q and/or 16q rearrangement, characteristic of this type of lipoma. Myxolipoma differs from myxoid liposarcoma in that it is a small, well-defined superficial lesion that lacks plexiform vascularization and 146 usually does not contain lipoblasts; Furthermore, their cells present immunoreaction to CD34 instead of to the S-100 protein. Dendritic cell myxofibrolipoma is the name 148 coined by Suster and Morán in 1997 to signify a benign lesion that is easily 149 confused with sarcoma and is currently considered a variant of spindle cell lipoma with marked myxoid change. Macroscopically, they are well-circumscribed neoplasms, not encapsulated, with a lobulated pattern, bright yellowish-white coloration, and a mucoid appearance. Histologically, it combines several elements in different proportions: myxoid matrix, spindle and dendritic cells, mature adipose tissue, and mature collagen. With IHC techniques, they present reactivity to CD34, bcl-2 and negativity to S-100, AML, desmin and CK. Although pleomorphic lipoma was initially described by 156 Enzinger as an independent lesion, 157 it is currently considered to be part of the same lesion spectrum as spindle cell lipoma based on the existence of mixed morphological pictures, the same anatomical location, and cytogenetic abnormalities. common. These lesions may appear as single pure forms or interspersed with spindle cells and may be confused with pleomorphic liposarcomas, since they contain lipoblasts and occasionally atypical mitoses.

4. The atypical lipoma, between benign and malignant

The WHO defines an atypical lipoma or atypical lipomatous tumor as an intermediate malignancy mesenchymal neoplasm composed entirely or in part of mature adipocytes with variation in size and at least focal nuclear atypia in adipocytes and stromal cells. Molecular biology has revealed that most of

these lesions show amplification of the 12q14-15 segment, with formation of giant or ring chromosome 12. The terms atypical lipomatous tumor (ALT) and atypical lipoma (AL) refer to lesions that, due to their location in the extremities and trunk (superficial and intramuscular), surgery is potentially curative. On the other hand, the well-differentiated liposarcoma (LPS BD) is used for morphologically identical lesions but located deep (retroperitoneum, mediastinum and groin) where surgery is hardly curative. TLA/LPS BD would indeed be considered a malignant type and is the most common liposarcoma variant, representing 40-50% of all liposarcomas. They are typical tumors of adults, without sexual differences, and maximum incidence in the 6th decade of life. Preferential locations in order of frequency are: extremities (70%), especially thigh, retroperitoneum (RP) (20%), paratesticular area, mediastinum, and others (10%).

Macroscopically, they are voluminous, well-circumscribed, yellow lesions with a variable proportion of fibrous or myxoid tissue. In the histological study, 4 subtypes have been recognized (lipoma, sclerosing, inflammatory, and spindle cell type), if 183 well frequently in the same lesion two or more of them can coexist, the first two being the most frequent. The lipoma type is constituted by relatively mature adipocytes. Interspersed with these cells, and widely scattered, are bizarre, often multinucleated stromal cells, as well as fibrous or myxoid septa with hyperchromatic spindle cells. It should be noted that the presence of lipoblasts is not a necessary requirement. Foci of necrosis are especially common in long-standing lesions.
evolution.

Cytogenetic studies have been particularly important to understand this 191 tumor group, since in 93% of cases there are clonal 192 chromosome alterations and, in 60%, the defining finding is the presence of giant or ring chromosome 12. which is related to the amplification of the 12q14-15 segment. The MDM2 gene is found in this region, which is always amplified in this type of tumor.
Using IHC techniques it is possible to demonstrate the amplification of the MDM2 and CDK4 genes in LPS BD/TLA cells, in contrast to lipomas that are negative.

5. Prognosis and treatment

Treatment of a lipoma is usually not necessary, unless the tumor is painful or interferes with movement. They are predominantly withdrawn for reasons 200

aesthetic. They are removed when they are very large, there is compression of surrounding structures 201 or the diagnosis is uncertain. Deeper tumors may recur if 202 are incompletely excised. Surgical excision is usually curative.

Regarding the atypical lipoma/LPS BD, the most important prognostic factor is the time 204 of evolution, even more than the anatomical location itself. Regarding the rate of 205 local recurrence of atypical lipoma, Weiss SW et al. reported that 91% of patients with 206 retroperitoneal disease had high local recurrence and unfavorable 207 clinical behavior.
On the other hand, the rate of local ALT recurrence in the muscle layer 208 of the extremities was 43%. Therefore, the principle of treatment is an extended surgical 209 resection for deep-type ALT because repeated local recurrence 210 could increase the risk of tumor dedifferentiation. It is important to note that 211 LPS BD does not metastasize until it has dedifferentiated.

6. Conclusions

We can conclude that, although lipomas are benign tumors in their immense 215
Most of us cannot forget to rule out warning signs that could indicate the 216 presence of a liposarcoma or a lipoma of intermediate malignancy. For this, the IHC 217

it has shown great efficacy and more ways of molecular identification are under development.

The author declares no conflicts of interest.
The author declares no external funding.

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9. Images are from the Robbin Pathology textbook.