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Liposarcomas: Experience of the Oncology and Radiotherapy Department and the Anatomy-Pathology Department at the Mohammed VI University Hospital in Marrakech: 10-Year Retrospective Study from January 2010 to January 2020

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Abstract **Original Research Article**

Liposarcomas are rare soft tissue tumors that arise from adipose tissue. They account for 1% of all malignancies and 15% to 20% of soft tissue sarcomas. Between January 2010 and January 2020, we reported 21 cases of Liposarcomas detected at the university hospital Mohamed VI of Marrakech's anatomical pathology department. The average age is 50, with a male majority. The average length of consultation was two years. The most revealing indication is tumefaction of the soft tissue. Most of the lesions were concentrated in the lower extremity. The preferred seat for these malignancies is the thigh. The X-ray was used on 21 patients, the echography was used on 16 patients, and the computed tomography was used on 15 patients. There have been 12 cases of magnetic resonance imaging and two cases of Doppler echography for two patients. The well differentiated Liposarcoma is the most common histologic sub-type (52%), followed by myxoid Liposarcoma (28%). 95% of patients had surgery, 90% of which was conservative, and 17 patients were referred for radiation supplementation, with only one instance receiving chemotherapy. In five cases, there was a loco regional recurrence, and one incidence of metastasis was discovered.

Keywords: Liposarcoma, pathology, CDK4, MDM2, surgery, Radiotherapy.

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INTRODUCTION

The most prevalent soft tissue sarcomas, accounting for roughly 20% of all malignant mesenchymal neoplasms, are liposarcomas [1]. Atypical lipomatous tumor (ALT)/well-differentiated liposarcoma (WDL), dedifferentiated liposarcoma (DDL), myxoid/round cell liposarcoma (MRCL), and pleomorphic liposarcoma (PL) are the different forms of liposarcomas. Each subtype is classified based on different biologic, histologic, cytogenic, and molecular characteristics. Each liposarcoma subtype differs from the others in terms of clinical characteristics and prognosis [2].

Atypical lipomatous tumor/well-differentiated liposarcoma is a locally aggressive neoplasm with little chance of spreading to other parts of the body [3]. Despite its high-grade appearance, de-differentiated liposarcoma only metastasizes in 15–20 percent of patients, with uncontrolled local recurrences being the most common cause of death. Myxoid liposarcoma's clinical course is mostly dictated by histological grade (manifested by the degree of hypercellularity). Myxoid liposarcoma, often known as 'round cell' liposarcoma, has a remarkable proclivity for metastasizing to bone and soft tissues. Pleomorphic liposarcoma behaves similarly to other pleomorphic sarcomas in terms of clinical aggression [4, 5].

When deciding on the appropriate treatment and care for this condition, it's critical to appreciate the differences between each liposarcoma subtype [5].

We describe the natural history, pathology, clinical symptoms, and prognostic aspects of liposarcomas in this study, which includes 21 cases. It also compares our findings to previous research.

MATERIALS AND METHODS

A retrospective descriptive study of the anatomopathological profile of liposarcoma.

The data collection took place in the department of pathological anatomy and the department of oncology and radiotherapy of the CHU Mohammed 6 of Marrakech.

Our study was spread over a period of 10 years from January 2010 to January 2020.

They are included in our study, all patients diagnosed histologically in our department as liposarcoma. Our study did not include other histological types of mesenchymal tumors (especially common connective tissue tumors, vascular tumors, muscle and cartilage tumors or bone localizations); lipomas are also excluded.

Histo-pathological and immunohistochemical data were collected from the registers of the anatomical pathology department.

The clinical files were used to collect information about the patients, their clinical and radiological symptoms, the treatments they received, and their progression.

EXCEL software was used for data entry and analysis.

Quantitative factors are represented by numbers and percentages, while qualitative variables are represented by averages.

The records and data collected in our study were kept confidential.

RESULTS

Clinical Findings

Over a period of 10 years, we collected 21 patients with liposarcoma, which represented an average of 2 patients per year.

The average age of our patients was 50 years with extremes ranging from 19 to 80 years. And we noted a male predominance with a sex ratio calculated at 3.04.

For the site, our study found more liposarcomas in the extremities with a percentage of 71% predominantly in the limbs. Then we find the abdominal locations which are 4 in our study 2 retro peritoneal 1 case intra peritoneal and another case in the anterior abdominal wall.

We also note the presence of a case of inguinal liposarcoma and another cervical. Concerning the duration of the symptomatology, it varied between 5 months and 4 years.

For the reason of consultation, swelling was the main reason of consultation found in 90% of our patients. This swelling was associated with pain in 38%.

Digestive disorders such as pain, vomiting and abdominal bloating were revealing in 14% of patients.

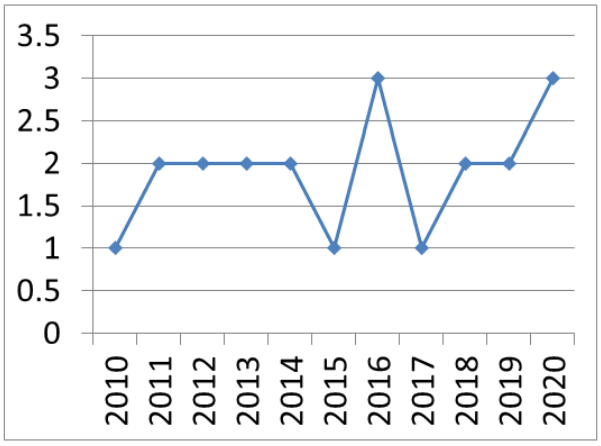

Figure 1: Number of liposarcoma cases detected per year

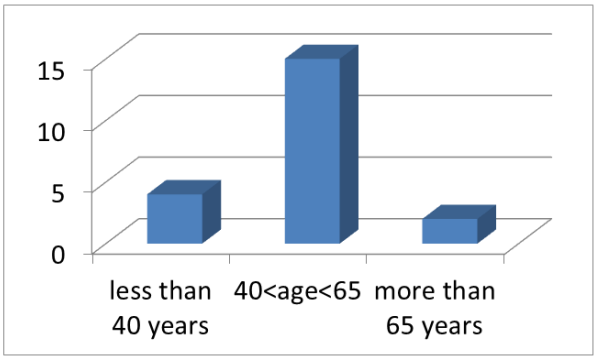

Figure 2: Number of Patients by Age Range

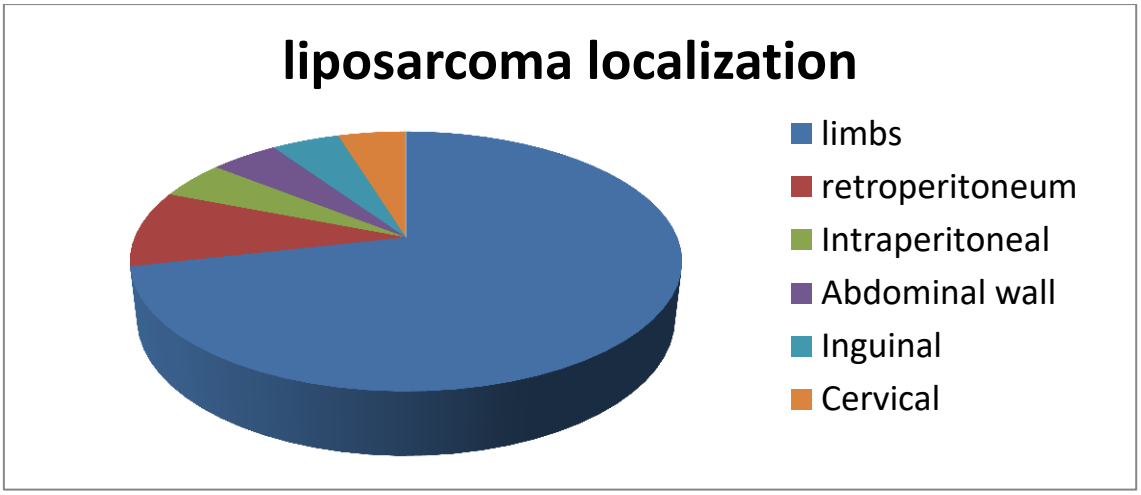

Figure 3: Liposarcoma Localization

Radiological features

On the radiological level, Standard radiography was requested in 52% of patients: it showed thickening of the soft tissues without bone involvement in 81% of cases, Bone erosions in contact with the lesion in 20% of patients.

Ultrasound was requested in 16 patients whose appearance depended mainly on the degree of tumor differentiation and the abundance of adipose tissue.

CT scans were used in 15 patients (71%), contributing to the identification of liposarcomas of the abdomen (intra and retroperitoneal).

Pathological Findings

Macroscopically the size of the specimens varied from 2 cm to 30 cm and their Weight from 5 grams to 4 kg 700 g. The tumors were well circumscribed nodular firm and hard sometimes friable yellowish whitish or brownish color seat of hemorrhagic and necrotic myxoid reworking.

The most frequent histological type found was well-differentiated/dedifferentiated liposarcoma in 14 patients, (66% of cases) distributed as follows: Well-differentiated liposarcoma in 11 cases (52%). The dedifferentiated liposarcoma in 3 cases (14%). Followed by myxoid/round cell liposarcoma in 6 cases (28%). Pleomorphic liposarcoma was found in only one case in our series.

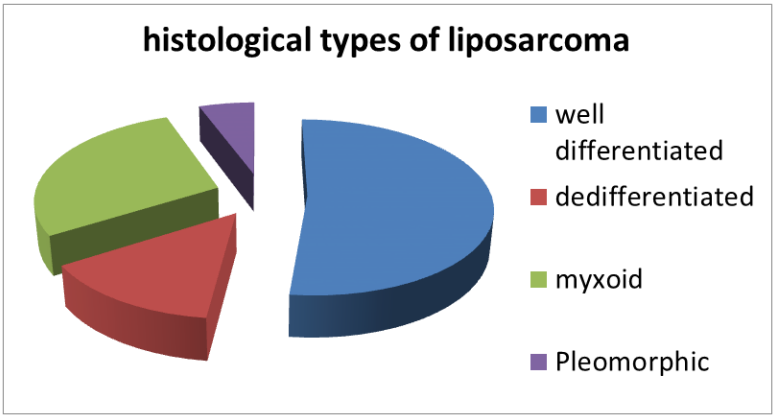

Figure 4: Histological types of liposarcoma

In our series, 15 specimens were labeled with CDK4 and MDM2.

The detection of CDK4 protein in immunohistochemistry with the anti CDK4 antibody shows positive immuno reactivity in 51% of the cases, negative in 11% of the cases and not precise in 38% of the cases.

The study of the detection of the MDM2 protein in immunohistochemistry shows a positive immuno reactivity in 40% of the cases, negative in 9% of the cases and unspecified in 51% of the cases

The distribution according to the FISH technique shows an amplified MDM2 in 32% of the cases, not amplified in 57% of the cases and not precise in 11%.

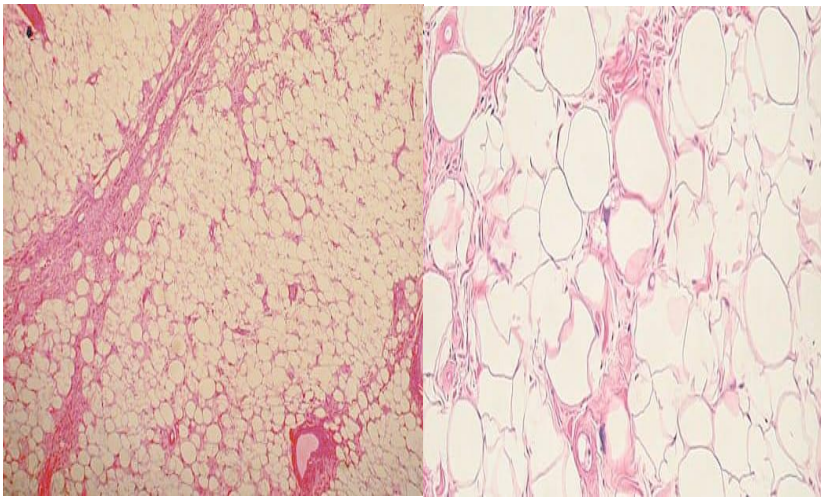

Figure 5: Histological appearance of well-differentiated liposarcoma

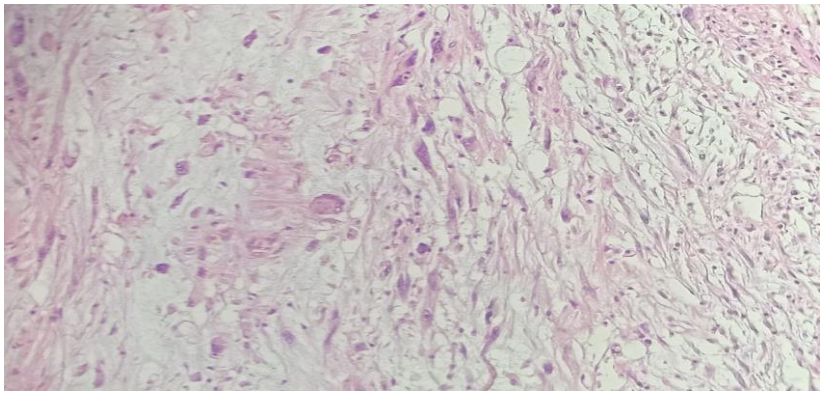

Figure 6: Histological appearance of myxoid liposarcoma

DISCUSSION

Liposarcoma is one of the most common soft tissue sarcomas; it represents nearly a quarter of soft tissue neoplasms. After malignant fibrous histiocytoma, it is the second most frequent sarcoma [6]. It is, however, an uncommon cancer because it affects just a few people. It is, nevertheless, a rare disease, accounting for just around 1% of all malignancies in humans [7]. It is a malignant soft tissue tumor of mesenchymal origin, according to histogenetic criteria. The presence of lipoblasts at various stages of development characterizes the origin [8].

Our study was retrospective and included all the biopsies and tumor removal specimens sent to the pathology laboratory of the Mohammed VI University Center in Marrakech over a period of 10 years.

In the 21 patients included in our study, the average age was 50 years with extremes ranging from 19 to 80 years. Our results are consistent with other studies; Indeed Khin Thway and Jayson Wang (2017) have shown that the age of occurrence of differentiated and dedifferentiated liposarcoma in London varies with age ranging from 12 to 95 and with an average age of 59 years [1]. Another study conducted by Kossivi Dantey and Karen Schoedel (2017) in the University of Pittsburgh, USA also shows that the age of patients varies between 44 and 92, with an average age of 69 years [9].

The distribution of patients according to age groups in our study shows a single peak of frequency located between 40 and 65 years of age.

According to the literature and in the same studies already cited above (Khin Thway 2015 and Kossivi Dantey 2017), there is a slight male predominance of liposarcoma with a strong male predominance, 61.7% of men and 38.3% of women, in the London study (Khin Thway 2015); while in the study done in Pittsburgh USA (kossivi Dantey 2017) the male/female distribution is balanced with a sex ratio of 1. Our results also show a male predominance of 66.6%, which is quite consistent with the literature.

Liposarcomas can be seen anywhere, but unlike lipomas most develop in deep structures and are very rare in subcutaneous tissues with a predilection for the extremities [10].

The proximal part of the limbs predominates over the distal part, and the lower limbs predominate over the upper limbs [11].

The most affected regions are therefore in order of frequency:

- Lower extremities,
- The retro peritoneum and mediastinum,
- The shoulders,
- Political fossa,
- The mesenteric region.

It can also be located exceptionally in:

- The epidural space
- The breast
- The spermatic cord
- The mandible.

Primary pleural liposarcoma was reported by Ackerman and Wheeler in 1942.

Less than 20 cases of primary pleural liposarcoma have been described in the literature [12].

The distribution of our liposarcomas is similar to the literature with a predilection for the thigh.

Liposarcoma often has an insidious evolution, which explains the delay of consultation which explains the delay in consultation, especially in the case of liposarcoma of the abdominal cavity; this delay varies from a few months to a few years according to the cases reported in the literature [13].

In our study, the average delay was 20 months.

As for the clinical signs, as in our study and in the bibliography, they are mainly represented by tumefaction and pain.

And for the abdominal localizations, they can be manifested by signs of digestive or urinary of digestive or urinary compression.

The other signs are indirect signs:

- Weight loss,
- Inflammatory syndrome,
- Abnormalities of the blood formula (hyperleukocytosis),
- Hypoglycemia.

With regard to hypoglycemia, the mechanism of which is excessive glucose consumption in the tumor, the symptoms are most often discrete (easily reduced by diet), but can sometimes be very severe: sweating, mental and behavioral disorders, seizures and coma [14].

In practice, standard radiography remains valuable for the study of calcifications and still remains the first imaging examination requested in soft tissue tumors mainly to study the underlying skeletal behavior [15].

In our study, standard radiography was used in 11 cases, and it showed thickening of the soft tissues without bone involvement in 81% of cases, Bone erosions in contact with the lesion in 20% of patients.

The diagnosis of liposarcoma is based primarily on histological and anatomical histological basis and anatomopathological informations. All liposarcomatous tumors are graded according to the criteria established by the FNCLCC taking into consideration three parameters: tumor differentiation, mitotic index and tumor necrosis.

The different parameters of the FNCLCC provide information on the activity and evolution of the tumor, on its proliferative extension and the appearance or not of metastases and all this is in favor of an adequate treatment and a good management of the patient and then an evaluation of the prognosis, adequate treatment and good management of the patient [15].

For example, Jours *et al*., (2015) reported in their study that there are more cases of metastasis and recurrence in Grade III liposarcoma compared to Grades I and II. Naofumi Asano and Akihiko Yoshida (2017) also showed, in a study of 56 patients in Japan, that more than 50% of liposarcomas, both well-differentiated and undifferentiated, are grade III, followed by grade II with a percentage of 33%, while grade I liposarcoma is only represented by 17%. According to Kossivi Dantey and Karen Schoedel (2017) liposarcomas grade I and II combined are represented with a percentage of 25.4% and 74.5% are Grade III.

On the other side, F. Hammedi and A. Trabelsi (2011), in their study on the anatomoclinical and evolutionary particularities of liposarcomatous tumors originating from sousse in Tunisia, have shown that there is not a very significant difference between the percentages of the different grades; 33.3% of liposarcomas are grade I, 30% are grade II and 36.6% are grade III [16].

Our study showed results that are not quite similar to those in the literature. Most of the patients in this study have grade I liposarcoma with a percentage of 66 %, followed by grade II with a percentage of 23% and only 12% of liposarcomas grade III.

The highest percentage of this study is represented by the group of grade I patients, this can probably be explained by the low recruitment of patients or by the discordance of histological interpretation.

The knowledge of the modes of extension of soft tissue sarcomas of the extremities allows us to

understand the surgical management of these tumors [14].

The growth of soft tissue sarcomas of the limbs is centrifugal against adjacent tissues and results in the formation of a pseudocapsule, which may contain tumor cells. These tumors tend to spread along a longitudinal axis, respecting the anatomical barriers (fascias, aponeurosis, and muscle partitions). These are invaded late and the tumor often stays within limited in an anatomical compartment [14].

Enneking and all defined the notion of compartment including the agonist muscles limited by a common partition. This makes it possible to differentiate intra-compartmental tumors from extra-compartmental tumors. The tendon insertions tendon insertions, bone and periosteum are rarely invaded by this type of tumor unlike the vascular-nervous axes, which are a frequent route of extension [17].

The lymph node curage is systematically performed as well as the drainages are systematically placed in the axis and close to the cicatrice in case of recurrence and to limit the postoperative radiation fields.

The surgical specimen should ideally be sent as a fresh specimen to the laboratory with a schematic illustration to help orientate the specimen, while marking the minimal margins with threads. The storage (tumorotheque) is highly recommended [13].

In our serie: 86% of liposarcomas of the limbs benefited from conservative surgery. Liposarcomas of abdominal locations benefited from extended surgery except for one case of metastatic liposarcoma where surgical abstention was indicated for the cervical liposarcoma: cervicotomy and removal of the tumor.

Radiotherapy has a central role in the therapeutic strategy of soft tissue sarcomas, as well as conservative surgery. Radiotherapy can be performed pre-, per- (brachytherapy) and postoperatively [11].

Radiation therapy alone achieves local control in only 33% of patients at the cost of significant radiation-induced residual damage [5].

In Europe, it tends to be reserved for patients with inadequate margins, medium or high grade tumors and tumors larger than 5 cm.

The start of irradiation should be as close as possible to surgery but should not be too early in order not to interfere with the healing process. The delay varies from 5 to 8 weeks.

The application of radiotherapy to the retro peritoneum faces difficulties related to the often large size of the field to be irradiated and the limited tolerance of the surrounding structures. The association of high dose radiotherapy with a complete removal of the tumor has allowed to improve the local control without gain in survival [7].

In our series, all cases were referred to the radiotherapy department for additional radiotherapy.

Chemotherapy has limited place in the treatment of liposarcoma which are malignant tumors known to have low chemo sensitivity.

However, chemotherapy is proposed in the case of metastases, advanced tumors or to sterilize possible micro metastatic dissemination. Three products have clearly demonstrated some efficacy: Adriamycin Ifosfamide and Doxorubicin [2].

In our series 5 patients presented a local recurrence and benefited from adjuvant chemotherapy. It was proposed as a palliative treatment in only one case of metastatic liposarcoma

Finally, LPS is one of the most prevalent varieties of STS, despite the fact that it is divided into three groups: WDLS/DDLS, MLS/RCLS, and pleomorphic LPS. Detailed analysis have identified the best surgical and adjuvant methods to various diseases, as well as commonalities and differences in treatment response and genetic causes [17].

Declaration of Conflicting Interests

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