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Primary pleomorphic liposarcoma of the spine. Case report and review of the literature

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ABSTRACT

INTRODUCTION: To describe a single case, the fourth ever reported, of pleomorphic liposarcoma of the spine and to undertake a review of the literature.
PRESENTATION OF CASE: A 60 year old male patient had a bilateral lumbosciatica over a 3 month period. Imaging tests revealed a tumor mass in L1–L3 and a fracture in L2. Also, he had a mural thrombus both in the inferior vena cava and the left renal vein. The biopsy revealed a well-differentiated liposarcoma. En bloc resection of the lesion and stabilization was carried out. Due to the condition of the patient (hemodynamic instability, wound dehiscence and infection, and hypoproteinemia), a decision was made not to subject the patient to either radiation therapy or chemotherapy. The patient was subsequently found to suffer from myopathic paraparesis and a surgical wound infection. At three months, liver metastases were evident, as well as a recurrence of the lesion. A venous thrombosis that extended from the lower iliac vein to the right atrium was observed. The patient died from type I hepatorenal syndrome.
DISCUSSION: Pleomorphic liposarcoma of the spine is a rare occurrence. En bloc resection with wide margins is the treatment of choice. The use of radiotherapy in the spine is controversial. The role that should be played by chemotherapy is still unclear, although it has been employed in treatments.
CONCLUSION: In spite of treatment, these tumors lead to a poor prognosis, with high rates of recurrence, metastasis, and mortality.

1. Introduction

Liposarcomas are malignant tumors found in soft tissues. They are the most common sarcomas seen in adults [1]. The pleomorphic subtype is the rarest and the most aggressive subtype [2]. There are only three cases described in which the primary form of this variant was found in the backbone [3–5]. We report a case of pleomorphic liposarcoma of the lumbar spine.

2. Presentation of case

A 61 year old male with four-month history of a bilateral lumbosciatica. A physical examination showed that there was a weakness in the lower extremities at the level of the bilateral hallucis, which was graded at 4/5. Also, there was an associated hypoesthesia at the right L2 and L3 and left L1 and L2 dermatomes. There were no perturbations in the sphincters.

An MRI of the entire spine and a CT of the lumbar spine revealed a pathological fracture in L2 and that the prevertebral tumor extended into L1 and L3 (Fig. 1). CT scans of the chest, abdomen, and pelvis confirmed no evidence of metastatic disease. CT angiography revealed a thrombus in the yuxtarenal vena cava and the left renal vein (Fig. 2). A body PET-CT brought to light a tumor mass in L2 bordering L2 and L3. It also exposed a tumoral mural thrombus within the inferior vena cava. The CT-guided biopsy of the tumor mass led to an initial diagnosis of a well-differentiated liposarcoma.

The case was discussed by the hospital Tumor Committee. The large tumor mass, the chemoresistance of the well differentiated liposarcoma to adjuvant chemotherapy, and the patient's condition were taken into account. Placement of a vena cava filter followed by resection of the tumor was the course of action decided upon.

The surgery was performed in three stages. In the first stage, a right thoraco-phreno-laparotomy approach was used to perform a thrombectomy of the tumor inside the inferior vena cava and the left renal vein. After assessing the impact on the vascular wall, a vascular prosthesis (Gore-Tex) was implanted. The tumor in the right psoas was also removed. A discectomy of the L1–L2 of L3–L4 discs was performed. In the second stage of the surgery, tumor was removed at the level of the left psoas. In the immediate post-

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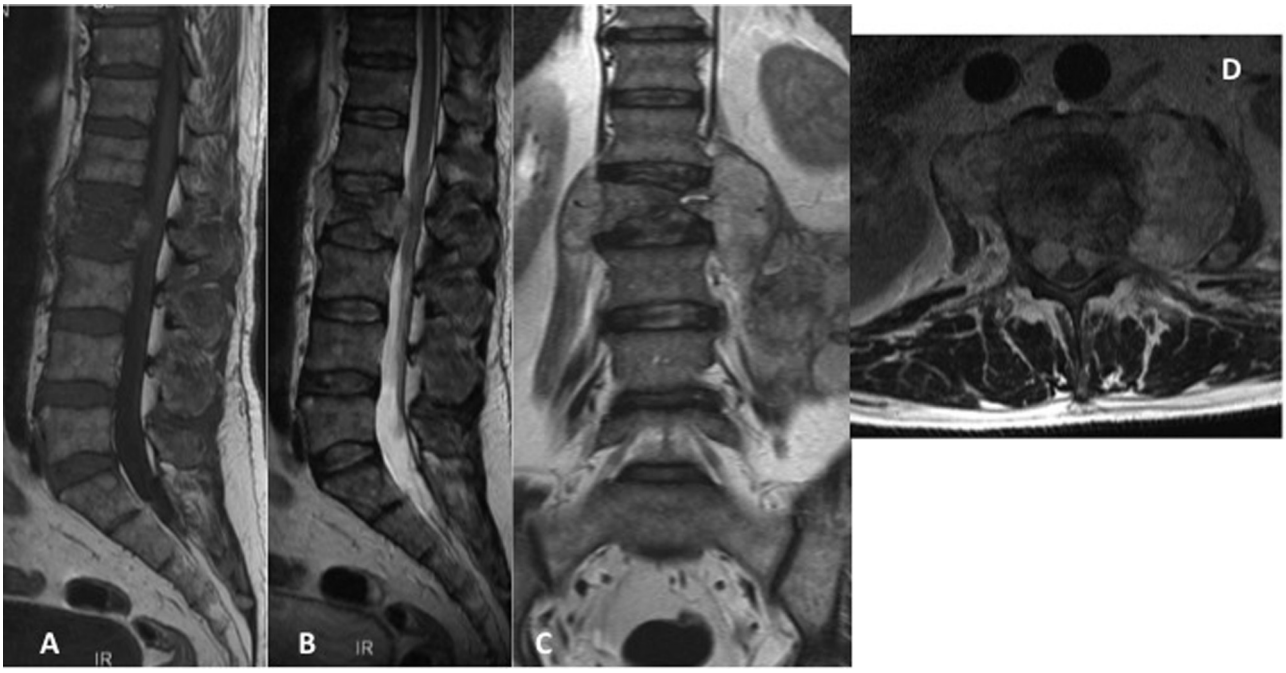

Fig. 1. MRI of the lumbar spine.
(A) A sagittal T1-weighted image which shows a hypointense signal, a fracture at the level of L2, and a prevertebral extension at the lower third of L1 and upper L3. Also seen is an anterior epidural component which contacts the L1–L2 disc and extends caudally, especially on the left side, a few millimeters from the L3 to L4 disc.
(B) A sagittal T2-weighted image showing a hyperintense signal of the bone marrow at the affected levels.
(C) A coronal T2-weighted image reveals paravertebral extension that appears predominantly on the left side of the tumor. The right paravertebral component extends from the L1 to L2 disk psoas and has a longitudinal diameter of 6.6 cm. The left paravertebral extends from the T12 to L1 disk to L3 to L4. The rest of the impact on the left psoas is appears to be due to a hematoma.
(D) An axial T2-weighted image.

operative period the patient had a pulmonary thromboembolism. Moreover, he had a retroperitoneal hematoma with a size greater than 25 cm which had to be surgically drained the next day. During the third stage of operation, an en bloc resection of tumor was performed through a posterior approach. In addition, reconstruction at T10–T12, L4, and L5 was carried out with pedicle instrumentation and at the stackable boxes of T12 to L3 with a structural allograft (Fig. 3). Tumor growth in the epidural venous plexus was monitored during this final stage of surgery.

Histological analysis tumor specimen showed that it had the features of a pleomorphic liposarcoma (Figs. 4 and 5). The maximum diameter of the tumor was 10 cm. 8 Mitoses were observed per high-powered field and tumor necrosis was observed in 50% of the total tumor area. Lymphovascular invasion was observed. The tumor impacted the right edge of the mass. Histological analysis of the mural thrombus also confirmed that its tumoral origin.

Postoperatively, the patient developed significant hemodynamic instability. This called for the transfusion of 18 red blood cell concentrates and the infusion of vasoactive drugs. The patient displayed dehiscence and surgical wounds that were infected with Acinetobacter baumannii and Staphylococcus haemolyticus. These issues were rectified in the operating room through antibiotic treatment and VAC (Vacuum Assisted Closure) therapy. The clinical outcome of these interventions was good. Regarding neurological elements, sagging was observed in the lower limbs and muscular strength was graded 0/5. Non-responsive tendon reflexes were observed in all four limbs, as were incontinence of the bladder and anal sphincters. The electromyogram was consistent with an inflammatory polymyopathy in the context of the myopathy of the critically ill patient. In light of the patient's clinical situation and its complications, adjuvant treatment options were not considered.

Over the course of treatment, the patient completely recovered muscular strength in his upper limbs while recovering only partial strength in his lower limbs. Also, he regained control of his sphincters.

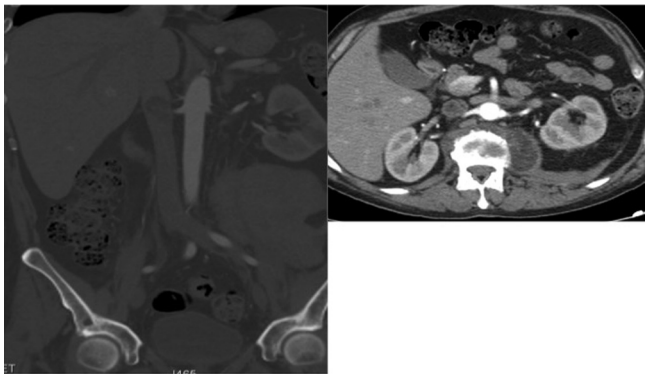

Fig. 2. A coronal and an axial CT angiogram in which thrombi are seen in the yuxtrarrenal vena cava and the left renal vein.

Two months after surgery, the patient progressively developed lower limb edema, kidney failure, ascites, coagulation disorder, and jaundice followed by encephalopathy. Upon revising the image study, the disease was shown to develop locally as a mass in the *para*-aortic area and in the area of the hematoma in the iliopsoas. There was also a single liver metastasis. Also observed was an extensive thrombosis spreading from the femoral, and external and common iliac veins to the vena cava and the right atrium. This thrombosis caused hepatic deterioration and the patient died.

3. Discussion

Liposarcoma is a malignant soft tissue tumor that originates from primitive mesenchymal cells. 20% of all adult sarcomas are

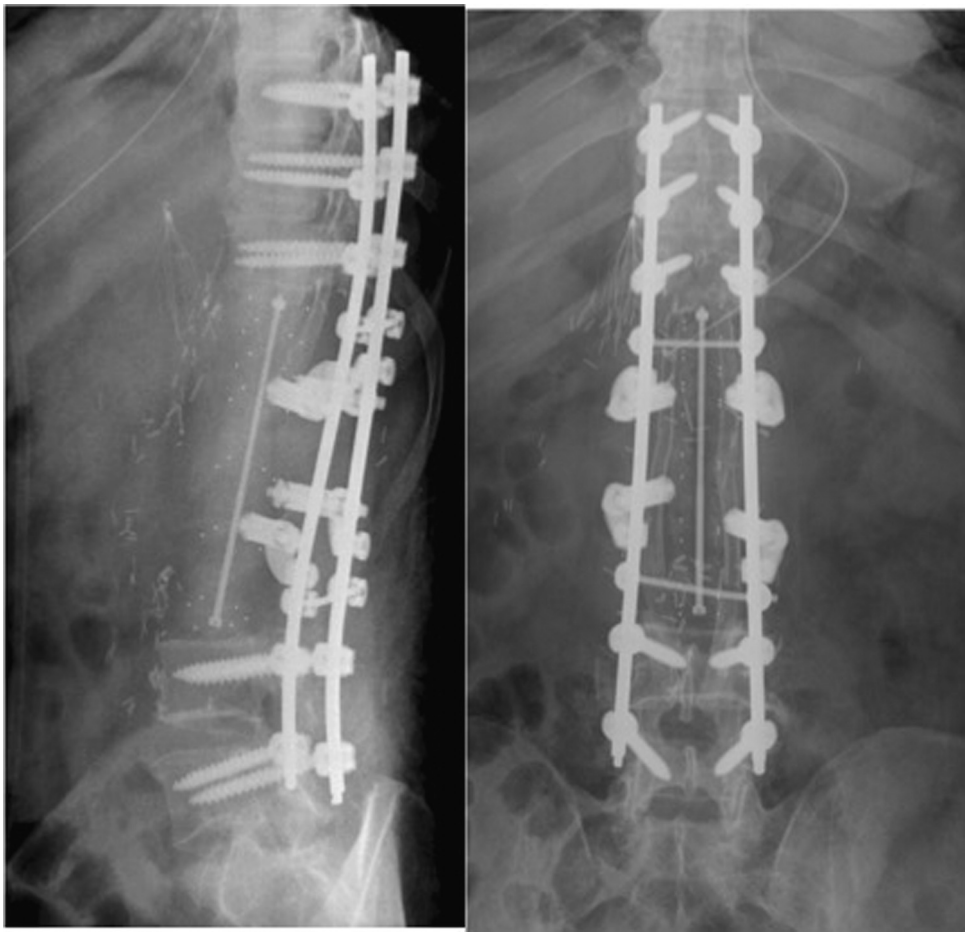

Fig. 3. An anteroposterior radiograph and profile of the postoperative lumbar spine.

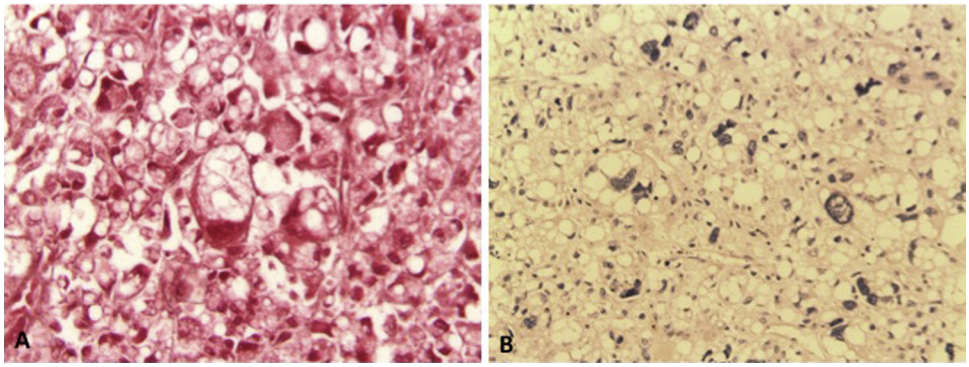

Fig. 4. Optical microscopy images.
(A) Pleomorphic multivacuolated lipoblasts with hyperchromatic nuclei, and elongated cells, fusiforms (100 × hematoxylin and eosin stain)
(B) Immunohistochemical studies which reveal a negative immunoexpression for cytokeratin (CAM 5.2, AE1/3), CD 34, specific active muscle, and S100

of this type [1,6]. Although this variety of tumor can be found in bone, it is rarely found in primary form in the backbone: only six such cases have been reported in the literature [1,3–5,7,8]. Pleomorphic liposarcoma is the least common subtype: it only accounts for 5% of all liposarcomas. It is defined as a high-grade sarcoma composed of a variable number of pleomorphic lipoblasts with a complex genomic profile. This subtype appears more often later in life: the peak incidence is in the seventh decade. It is slightly more predominant in males. In most cases, it occurs in the extremities (mostly in the lower limbs). We came across only three reported instances of pleomorphic liposarcoma of the spine when reviewing the literature (Table 1) [3–5].

Pleomorphic sarcomas are very aggressive. A rate of 30–50% of metastasis and a tumor-related mortality of 40–50% have been reported [6,9,10]. Most metastases occur in the lung [10–12]. In the series of Hornick et al., 57 patients were analyzed [13]. Here, there was a 5 year survival rate of 63%. The rate of local recurrence and metastases was 42%. The disease-free survival rate was 39%.

In the case of our patient, the disease progressed rapidly. The onset of liver metastases and recurrence of the tumor occurred 3

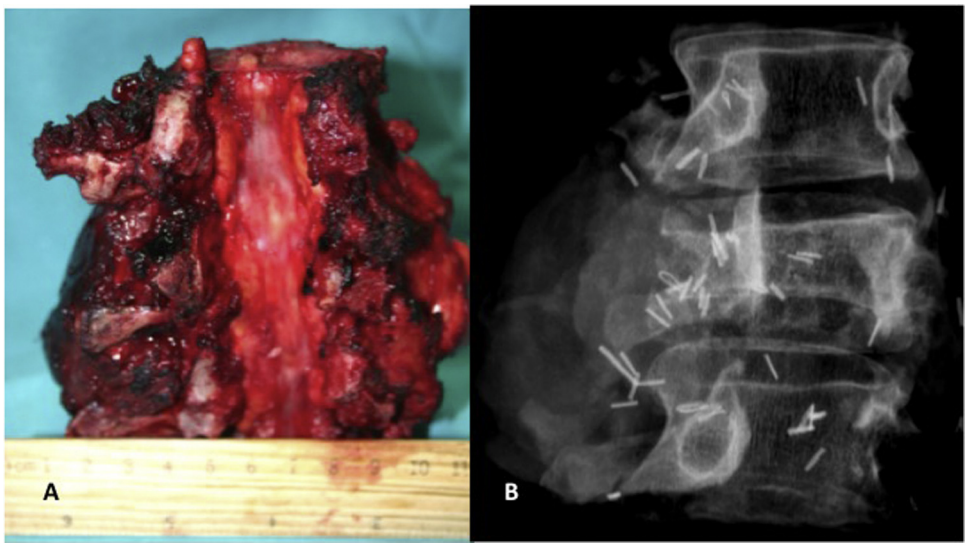

Fig. 5. (A) Macroscopic image of the specimen; (B) Simple radiograph of the specimen.

Table 1
Clinical and demographic characteristics of the present case as well as the 3 cases of liposarcoma already documented in the literature.

Study	Age (years)	Sex	Localization	Clinical data
Lmejjati[1]	45	Male	L4 and L5	Bilateral lumbosciatica. Gait abnormality. Cauda equina syndrome. No alteration in the sphincters. 2 month term.
Abderrahmane Hamlat[2]	45	Female	T7 and T8.	Backache. Paraplegia. Sensory level at T4. Clonus and bilateral extensor plantar reflex.
Frederico Barra de Moraes[3]	60	Female	L4 .	Lumbosciatica on the left side. No motor or sensory deficit. 6 month term.
Case presented here.	61	Male	L1–L3.	Bilateral lumbosciatica. Motor deficit in the lower limbs. Hypoesthesia in L1, L2, and L3. No alteration in the sphincters. Change in gait. 4 month term.

[1] Ref. [1].
[2] Ref. [2].
[3] Ref. [3].

Table 2
Comparison of treatments applied in each case.

Study	Initial treatment	Result	Follow-up
Lmejjati[1]	Surgical decompression + 45 Gy Radiation therapy	Neurological recovery. Death at 6 months.	3 months. Death
Abderrahmane Hamlat[2]	laminectomy + instrumentation + 45 Gy Radiation therapy	No neurological improvement (paraplegia). Lung and costal area were irradiated.	13 months. Physical deterioration. Alive.
Frederico Barra de Moraes[3]	Resection of L4, L3 to L5 arthrodesis. Radiation therapy,chemotherapy.	At 18 months, neither pain, nor neurologic deficit, nor recurrence, nor metastases.	3 years. Lung metastasis.
Case presented here.	En bloc resection in L1, L2 and L3 + instrumentation	Dehiscence and a deep wound infection. Inflammatory polymyopathy.	2 months. Local recurrence. Hepatic metastasis. Extensive thrombosis. Type I hepatorenal syndrome. Death.

[1] Ref. [1].
[2] Ref. [2].
[3] Ref. [3].

months after resection, leading to the death of the patient. Tumor resection had only been attempted in one of the three previously reported cases [5]. Pulmonary metastases were observed 18 months later. In the other two reported cases [3,4], palliative surgery was employed; the result was tumor recurrence and an early death (Table 2).

The definitive diagnosis of pleomorphic liposarcoma is made histopathologically [4]. They are non-encapsulated and formed by a variable number of pleomorphic lipoblasts. There are two distinct and interrelated histological forms. The main difference between the two patterns is in cytoplasmic lipid content. The most common histological pattern is similar to that of malignant fibrous histiocytoma. However, this pattern contains gigantic lipoblasts with bizarre, hyperchromatic nuclei. The other, less common, pattern is similar to that of an adrenal carcinoma. It is formed by the growth of gigantic pleomorphic cells and of smaller mononuclear cells, in sheets. In both cell types, atypical pleomorphic lipoblasts are frequently observed. Miettienen and Enzinger [9] reported a third variant known as the epithelioid type.

Immunohistochemical techniques contribute very little to differential diagnoses. These tumors expresses vimentin, however a specific immunoreactivity to the S-100 protein is observed in less than less than 50% of cases, despite lipogenic differentiation [14], as seen in the present case. The epithelioid variant may present epithelial markers [9]. MDM2 and CD4 staining are typically negative [15]. The few cytogenetic and molecular studies that have been carried out have revealed complex changes in chromosomes 8, 12, and 17 [16,17].

The differential diagnoses of liposarcoma include any high-grade pleomorphic sarcoma, spinal tuberculosis, metastasis, multiple myeloma, and lymphoma [3].

Whenever possible, the treatment of choice for all forms of localized liposarcoma is complete surgical resection. High grade forms, including the pleomorphic type, require wider margins (2 cm of normal tissue). However, as in this case, margins are limited according to localization. Staged multilevel en bloc spondylectomy may provide good oncological outcomes in difficult cases [18].

Treatment with adjuvant radiation therapy is a controversial option. Local radiotherapy is generally assumed to reduce the risk of the local recurrence of lesions in the extremities. There are no data justifying the use of this treatment in other localizations.

In the case of adjuvant chemotherapy, sensitivity profiles specific for each subtype of liposarcoma in its metastatic or unresectable form have yet to be determined. It is generally recommended that each case be assessed individually. In the case of pleomorphic liposarcomas, responses to the treatment with a combination of gemcitabine and docetaxel have been described [19]. The activity of trabectedin is less pronounced [20].

4. Conclusions

In conclusion, pleomorphic liposarcoma in the spine is rare. The treatment of choice is en bloc resection with wide margins. Employing neoadjuvant radiation therapy in the spine is controversial. The role that should be played by chemotherapy is still unclear, although it has been employed in treatments. These tumors have a poor prognosis, with high rates of recurrence, metastasis, and mortality.

Conflicts of interest

None of the authors has any potential conflict of interest in relation with this work.

Sources of funding

None.

Ethical approval

Not required.

Consent

Written informed consent was obtained from the patient for publication of this case reportand accompanying images.

Author contribution

All three authors were directly involved in the patients' management and treatment. A.M. Morales-Codina and J.A. Martín-Benlloch reviewed the literature and wrote the manuscript. M. Corbellas Aparicio analysed and reviewed the manuscript.

Guarantor

Morales-Codina, Ana María, Martín-Benlloch, Juan Antonio, Corbellas Aparicio, Miguel.

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