CASE REPORT – OPEN ACCESS

International Journal of Surgery Case Reports 39 (2017) 332–338

Contents lists available at ScienceDirect

International Journal of Surgery Case Reports

journal homepage: www.casereports.com

Free disease long-term survival in primary thoracic spine leiomyosarcoma after total en bloc spondylectomy: A case report

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ARTICLE INFO

Article history:
Received 4 July 2017
Received in revised form 27 August 2017
Accepted 27 August 2017
Available online 1 September 2017

Keywords:
Case report
Leiomyosarcoma
Thoracic spine
Total en bloc spondylectomy

ABSTRACT

INTRODUCTION: To describe an unusual primary vertebral leiomyosarcoma in thoracic spine.
PRESENTATION OF CASE: An isolated lesion of the T11 vertebra in a 62-year-old woman with no neurologic deficit is reported. Imaging findings indicated a nonspecific high-grade malignant lesion. TC-guided biopsy failed thus open incisional biopsy was needed. A diagnosis of low-intermediate mesenchymal sarcoma was made. A total en bloc spondylectomy of T11 was performed with three-column reconstruction. The histology and immunostaining showed the appearance of leiomyosarcoma. After diagnosis, post-operative radiation therapy was performed. Metastatic lesion was ruled out by CT scans of the chest, abdomen and pelvis, in addition to total body radionuclide scanning and 18-F-FDG-PET. After five years of follow-up, no signs of local recurrence, metastasis or distant lesions suggesting a primary lesion were observed.
DISCUSSION: Vertebral primary leiomyosarcoma is exceedingly rare. Primary vertebral leiomyosarcoma diagnosis must be performed when the metastatic origin is excluded. For the treatment of primary tumors, total en bloc spondylectomy (TES) is the technique of choice to achieve marginal or wide tumor resection, decrease the risk of local recurrence and remote lesions and increase survival.
CONCLUSIONS: A well-planned pre-operative study and a wide surgical excision can result in local tumor control and long-term survival. This case presents the longest disease-free survival period of a primary leiomyosarcoma in spinal location after total en bloc spondylectomy.

1. Introduction

Primary spinal tumors are uncommon, representing approximately 5% of all spinal tumors. Leiomyosarcoma, a malignant soft tissue sarcoma originating from smooth-muscle cells and typically arising in the uterus, retroperitoneal space, abdominal viscera, skin or soft tissues of the extremities, accounts for 7% of soft tissue sarcomas, with an estimated overall incidence of 0.7 cases per 100,000 persons per year [1,2]. Primary leiomyosarcoma of the bone is a rare primary bone malignancy, with only 90 cases described since 1965 [3,4], and very few cases reported with a primary spine location [5]. Moreover, existing imaging techniques support a diagnosis in some cases with an alleged primary bone location as a metastasis that originated somewhere else [2]. Conventional imaging techniques such as X-Ray, computed tomography (CT) and magnetic resonance (MR) are needed to describe the morphology of the injury pattern, however, the findings are nonspecific. Recently fluordeoxyglucose positron emission tomography (18F-FDG-PET) has shown to be useful to define origin, behavior and recurrence after treatment [6].

A definitive diagnosis is made by biopsy and the preferred technique is a puncture-needle aspiration or transpedicular biopsy guided by imaging. If results from these techniques do not show any malignant cells, an open incisional biopsy is needed, and in this case, a careful approach must be used to reduce the risk of contamination. Because the diagnosis impacts the treatment, planning and prognosis, a second opinion to confirm it is often recommended [7].

The most widely accepted classification staging system is Weinstein, Boriani and Biagini (WBB) [8]. For the treatment of primary tumors, total en bloc spondylectomy (TES) is the technique of

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http://dx.doi.org/10.1016/j.ijscr.2017.08.045

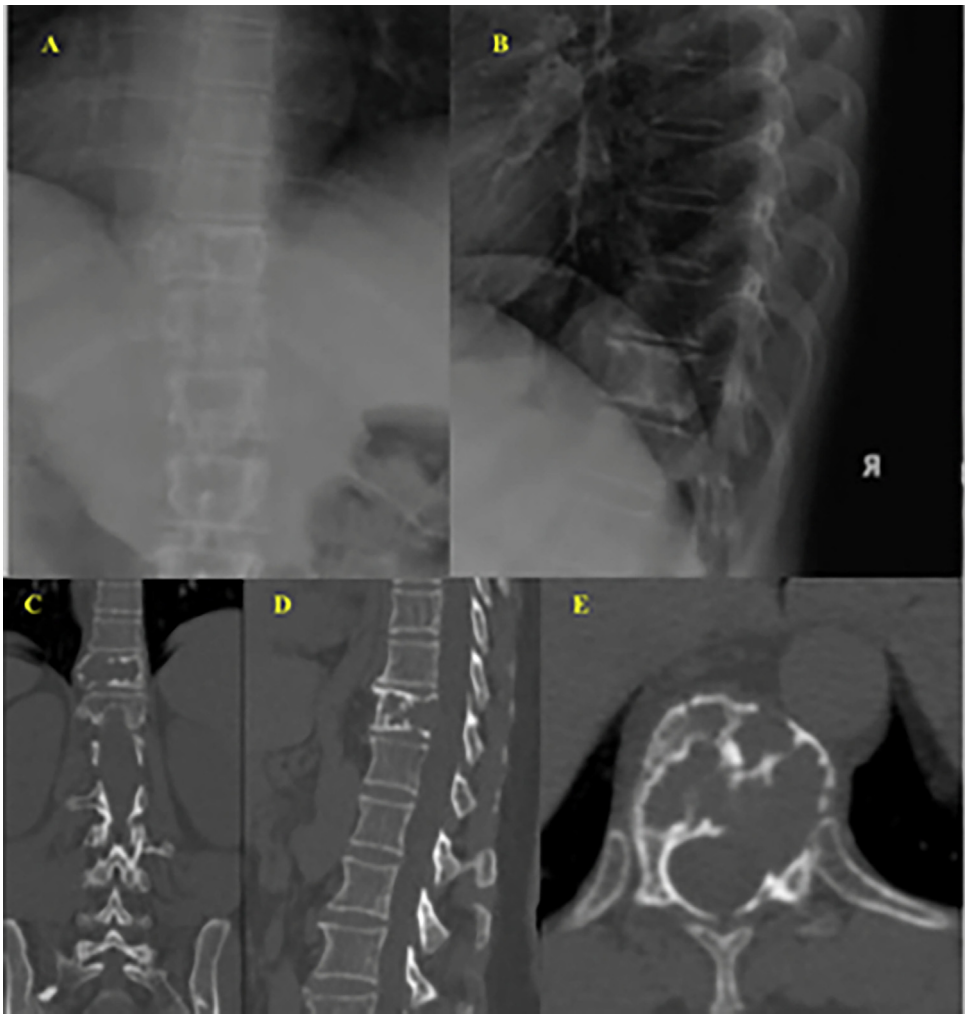

Fig. 1. A,B) Anteroposterior and lateral radiograph showed a discrete loss of height and asymmetry of the T11 vertebral body and as well as cortical expansion, effacement of the left pedicle and sclerosis. C–D) CT showed an expanded lobular lytic lesion boundary, partial sclerotic borders of the T11 vertebral body and thinning with anterior cortical and posterior wall rupture.

choice to achieve marginal or wide tumor resection, decrease the risk of local recurrence and remote lesions, and increase survival [9]. After diagnosing a leiomyosarcoma, periodic follow-up must be done to detect a possible primary origin and local recurrence.

To date, this case report describes a case of primary vertebral leiomyosarcoma in the thoracic vertebra treated by total en bloc spondylectomy with the longest follow-up period. This report is in line with the SCARE criteria [10].

2. Presentation of case

A 60-year-old female referred to our spine unit had been experiencing pain over a three-month period, without any improvement after medical treatment with analgesics, AINES and physical therapy. No neurological deficit was shown after examination. The patient did not refer any genetic disorder, drug or psychosocial history. In the X-Ray study (Fig. 1), an injury at the T11 vertebral body level with discrete loss of the T11 vertebral body height and asymmetry of the vertebral body was observed, in addition to cortical expansion, effacement of the left pedicle and sclerosis. Laboratory findings showed an erythrocyte sedimentation rating (ESR) of 67 mm/h and β-2 microglobulin, albumin (Alb) and IgG levels of 4.5 mg/dl, 4.8 g/dl, and 790 m g/dl, respectively. Bone marrow aspiration (BMA) showed 6% of plasma cells, and puncture bone marrow biopsy (PBMB) revealed 8% of plasma cells with lambda chain expression and monoclonal gammopathy of undetermined significance (MGUS). CT showed an expanded lobular lytic lesion boundary, partial sclerotic borders of the T11 vertebral body and thinning with anterior cortical and posterior wall rupture (Fig. 1). By MR, a solitary lesion in T11, diffuse hypointense on T1-weighted and heterogeneous hyperintense on T2-weighted were observed (Fig. 2). In addition, a small mass of prevertebral soft tissue and anterior epidural and contrast enhancement were detected. Total body scan and scintigraphy with TC^{99} showed low osteoblastic activity at the lower thoracic spine. 18F-FGD PET-CT showed hyper-metabolic pathological activity at the T11 level (standard uptake value (SUV) 5.4 uCi/ml) and at the gastric wall without significant malignancy (SUV 4.2 uCi/ml). CT-guided biopsy carried out by the department of radiology showed an absence of malignant cells. An open transpedicular biopsy was performed and was guided by radioscopy through the left pedicle. Histologically, there was a highly cellular, spindle cell proliferation with mainly a fascicular growth pattern and the presence of atypical and pleomorphic cells without evidence of mitosis or necrosis. Immunostaining showed positivity for smooth muscle actin and focal positivity for caldesmon, while desmin, S-100, CKAE/AE3 and CD34 were neg-

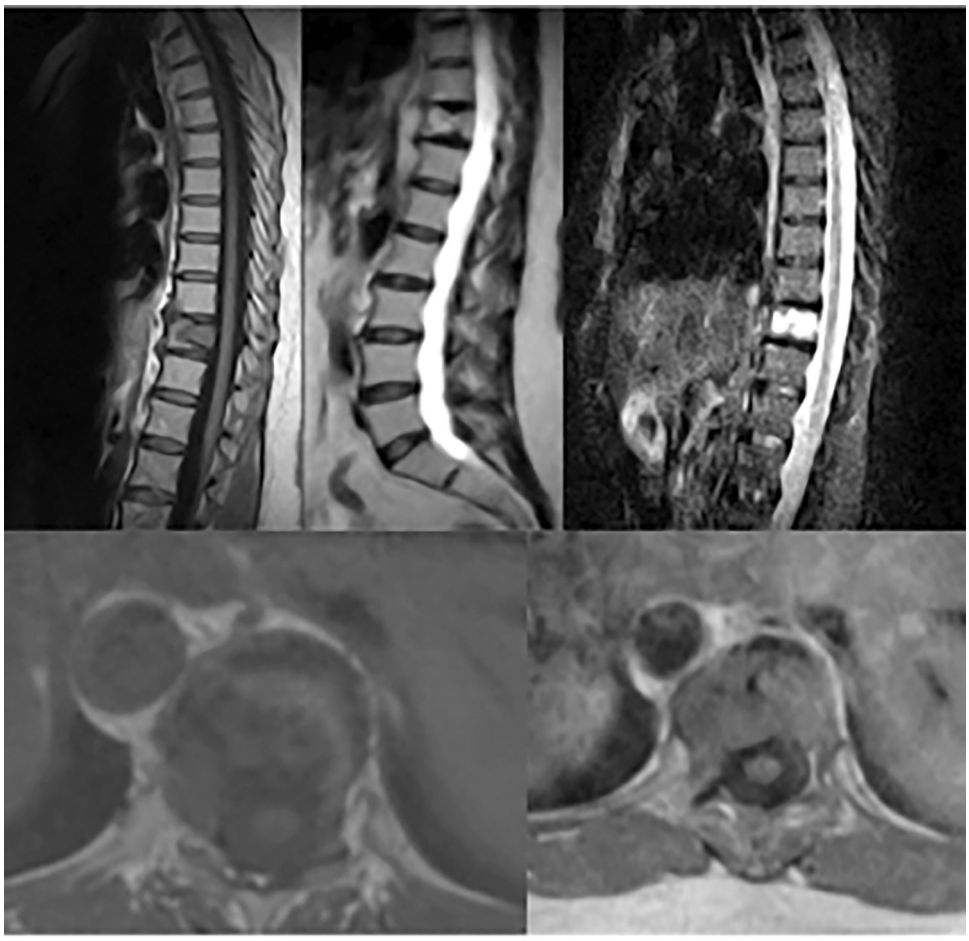

Fig. 2. MR showed a solitary lesion in T11 while diffuse hypointense on T1-weighted and heterogeneously hyperintense on T2-weighted were observed. Furthermore, a small mass of pre-vertebral soft tissue and anterior epidural and contrast enhancement were detected.

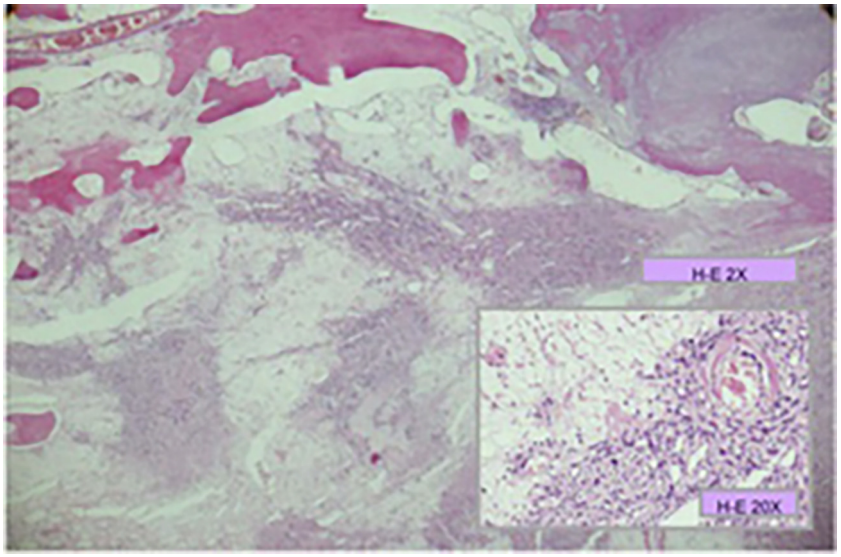

Fig. 3. H/E staining. Spindle cell proliferation: highly cellular, cigar-shaped nuclei with marked atypia and pleomorphism, without mitosis or necrosis and with areas of lower cellularity and hyalinized foci.

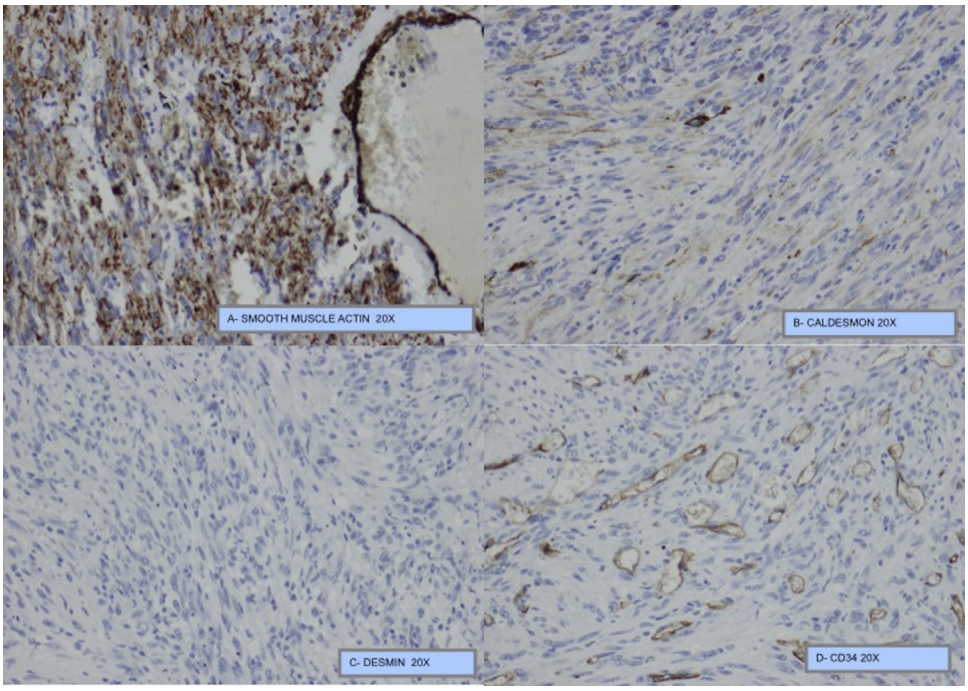

Fig. 4. Inmunostaining: A) Smooth muscle actin: diffuse positivity B) Caldesmon: focal positivity C–D) Desmin and CD34: negative.

ative. A diagnosis of mesenchymal neoplasm of low-intermediate malignancy grade was made with these findings.

Following the diagnosis of an isolated malignant mesenchymal vertebral lesion, the WBB vertebral staging system and surgical classification of Tomita was used to stage the spinal tumor. According to WBB and Tomita, for zones 5–9 and intra-compartmental type 3 respectively, TES has been established [8,11]. The TES was conducted by the first author in this case report according to the technique described by Stener/Tomita [9]. This was done under general anesthesia, with prophylactic antibiotics (cephalosporin) and neurophysiological monitoring. A single posterior approach was used and two-above and two-below levels were instrumented with pedicle screws at the affected level. Three proximal centimeters of the ribs at the T11 level were cut and removed bilaterally, with extra-pleural exposure of the lateral walls of the vertebral body and ligation of segmental vessels. Two T11 roots were cut and a rod was placed to the right side to prevent instability. Using a Tomita saw (T-saw), we proceeded to cut through each of the pedicles to remove the posterior arch. After cutting the left pedicle, bone wax was used to prevent tumor spread. Following the anterior dissection, we proceeded to cut the superior and inferior discs and the vertebral body was removed. In the empty space, carbon fiber stackable cages were placed and filled with heterologous bone. The cages were connected to the posterior instrumentation to achieve three-column spinal stability.

Histological examination of the surgical specimen showed remnant tissue of cancerous bone and a lesion with ill-defined margins that had replaced most of the vertebral body. The bone consisted of highly cellular areas, arranged in bundles with an irregular distribution, intermixed with areas of low cellularity that had an intensely eosinophilic and hyaline appearance. This was accompanied by many vascular structures, both ectasic and congestive. The cellularity of the bundles was spindle-shaped with marked atypia, prominent nucleoli and striking pleomorphism. There were no mitotic images or necrosis (Fig. 3). Immunostaining showed intense and diffuse positivity for smooth muscle actin (1A4) with focal positivity for caldesmon; S100, desmin, actin (HHF35), CKAE1/AE3 and CD34 were negative (Fig. 4). Because of the rarity of the findings, a second opinion was requested and the specimen was submitted to another department, which reported that the appearance of the lesion was typical of leiomyosarcoma, suggesting a possible metastatic origin. Examination by gastroscopy, trans-vaginal ultrasound, and FDG-PET ruled out gastric, uterine and retroperitoneal origins of the primary tumor lesions. Post-operative external beam radiation therapy (EBRT) was used with fractionated doses and 45 Gy was administered.

For the post-operative process, the patient was advised to be cautious when walking, to avoid falling both by using crutches and carrying heavy weights. During the five years of follow-up, the patient reported no pain of the surgical wound without neurological deficit in the lower limbs. The imaging assessment for the developmental follow-up using X-ray shows adequate coronal and sagittal balance. In the MR and CT-body image studies, a free medullary canal without changes of local recurrence in the adjacent vertebral bodies, solid fusion and no distant lesions suggesting a primary lesion were observed (Fig. 5). The FDG-PET showed no pathological metabolic activity increase. The patient was pleased with the information provided prior to the surgery, the nature and complexity of the procedure and the expected result.

3. Discussion

Primary leiomyosarcoma of bone is a rare location. The cellular origin in bone locations is attributed to smooth muscle cells of the vascular wall, mesenchymal stem cells or intermediate cellular forms, such as myofibroblasts that are capable of differentiating into smooth muscle cells [3,4]. A vertebral leiomyosarcoma is generally a secondary tumor caused by metastasis and typically represents a late manifestation of the disease [12–14]. Primary paraspinal cervical [5] and thoracic leiomyosarcoma [14] have also been described. A primary vertebral location is extremely rare and few cases have been described in a spinal location [2,3,15–21] with thoracic predominance and mostly in female**s**, as in our case.

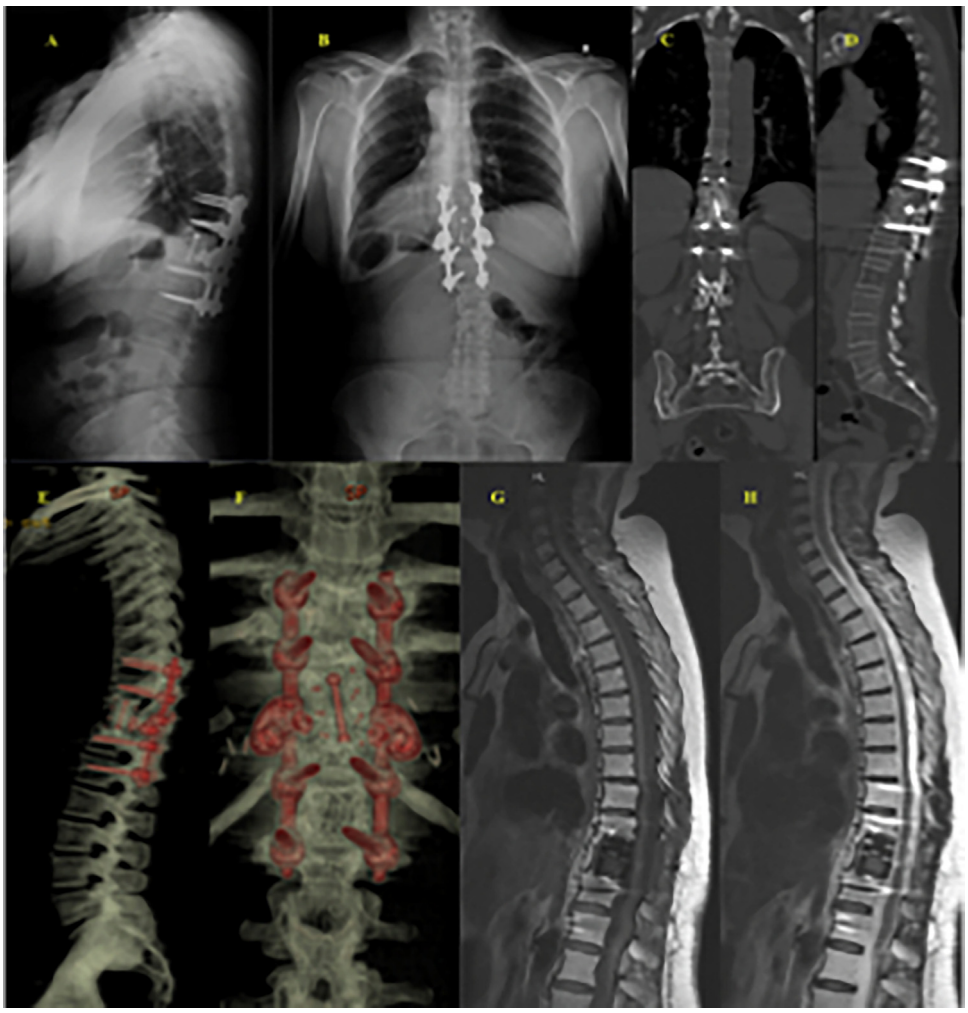

Fig. 5. After 60 months of follow-up, an anteroposterior and lateral radiograph showing adequate coronal and sagittal balance (A, B). In the CT-body (C–F) and MR images studies (G, H), a free medullary canal without changes of local recurrence in the adjacent vertebral bodies, solid fusion and no distant lesions suggesting a primary lesion were observed.

Clinical signs vary, but generally, there is pain reported with pathological fracture and an occasional neurologic deficit secondary to medullar compression. Although laboratory studies of the blood and serum do not contribute much to the diagnosis of primary tumors of the musculoskeletal system, in this case the presence of monoclonal gammopathy should rule out the presence of solitary plasmacytoma or multiple myeloma. BMA showed 6% of plasma cells, and PBMB revealed 8% of plasma cells with lambda chain expression and monoclonal gammopathy of undetermined significance (MGUS).

X-Ray images showed a permeated appearance characteristic of long bones; however, there are no specific radiographic features that allow diagnosing of leiomyosarcoma by radiography alone. A sclerotic rim may be seen, and occasionally, cortical expansion can be identified in slow-growing cases with a secondary metastatic vertebral location [12]. CT images appear as poorly defined lytic lesions and sclerosis with erosion or bulge and cortical rupture. MR exhibits low signal intensity on T1-weighted images and isointense/hyperintense homogenous or heterogeneous signals on T2-weighted images. Scintigraphy Tc^{99} can show different degrees of intensity according to the osteoclastic activity.

A biopsy is mandatory if the isolated lesion is unknown, being CT-guided biopsy the method of choice, and can lead to a diagnosis in 46–76% of cases, higher in lytic than in osteoblastic lesions [22]. In this case, no malignant cells were observed and an incisional biopsy was needed. Although no evidence has been shown to prevent the spread of tumor cells, the biopsy area can be covered with bone wax or acrylic cement. Poorly planned biopsies increase the local recurrence of a tumor by allowing it to disseminate along the biopsy tracts.

In this case, the unusual findings in a vertebral location caused doubts about the diagnosis, and another opinion was requested [23]. Histologically, leiomyosarcoma appearance will vary according to the degree of differentiation. However, a minimum requirement is the presence, at least focally, of fascicles of brightly eosinophilic spindle cells with vesicular, ovoid to cigar-shaped nuclei and showing uniform strong positivity for smooth muscle actin and/or desmin, and/or convincing ultrastructural evidence of leiomyogenic differentiation, specifically longitudinal filaments with focal densities, prominent, almost continuous, external lamina, and pinocytotic vesicles.

Nevertheless, primary vertebral leiomyosarcoma is exceedingly uncommon, and ruling out a primary lesion with metastasis must be done. Conventional radiologic staging before surgery generally includes MR and CT scan evaluations of the chest, abdomen, and pelvis, in addition to total body radionuclide scanning. Gastroscopy and trans-vaginal ultrasound can be useful to exclude primary tumor. 18-FDG-PET may play an important role in diag-

nosis and may prove particularly useful in evaluating patients who have undergone surgery and when looking for local disease recurrence or searching for metastatic lesions. Although not specific to an osseous location of leiomyosarcoma, the SUV_{max} is correlated with tumor grade and tumor size at the greatest dimension and is a likely predictor of tumor behavior [6].

For primary and metastatic vertebral tumors, the WBB staging and Tomita scoring systems describe the localization into the vertebral body and the outside extension and involvement of other regions (intra- or extra-compartmental or multiple) [8,9]. TES is a technically demanding and risky surgical procedure that allows for the attainment of wide to marginal resections of primary tumors and solitary metastatic lesions of the spine. The rationale for en bloc resection is to allow for the removal of the tumor in one piece, together with a layer of healthy tissue (marginal or wide resection), thus improving long-term survival and providing better local tumor control than intra-lesion resection [24]. In this case, en bloc resection was achieved but the cut performed through the affected left pedicle is defined as intralesional surgical margin. However, a low potential for regrowth has been proved when T-saw is used [25]. Moreover, adjuvant radiation therapy was used as an additional treatment for improving the rates of local control, although the benefits have not been proven in bone location [3].

Although image studies, low osteoclastic and metabolic activity and histological findings can be compatible with a low-grade leiomyosarcoma, the same predicted outcome is expected as in a high-grade tumor and should be treated in the same manner because they share the same prognosis by definition of tumor grade [6]. Patients with these tumors have an approximately five-year survival, and a lack of leiomyosarcoma research continues to result in poor patient prognosis [2,5,8].

In previous reports in spinal location the follow-up ranges from 4 to 24 months. After five years of follow-up without evidence of a metastatic origin, this case presents the longest disease-free survival period of a primary leiomyosarcoma in spinal location after total bloc in spondylectomy.

4. Conclusions

Primary vertebral leiomyosarcoma diagnosis must be performed when the metastatic origin is excluded. Although this is an individual case study, it is the case with the longest disease-free survival period presented with a primary spinal leiomyosarcoma. Given the satisfactory results obtained here, and providing that a well-planned pre-operative assessment and wide surgical excision are carried out, this can result in local tumor control and long-term survival.

Conflicts of interest

The authors have nothing to disclose.

Funding

This research did no receive and specific grant form funding agencies in the public, commercial, or not-for-profit sectors.

Ethical approval

The paper is a case report, and therefore does not require ethics approval.

Consent

Informed consent has been obtained from the patient, and all identifying details have been omitted.

Authors contribution

José Ramírez-Villaescusa – Conception of study, acquisition and analysis of data

Adriana Canosa-Fernández – Acquisition of data, management of case and histological analysis.

Antonio Martín-Benlloch and Jesús López-Torres Hidalgo – Revision of article.

David Ruiz-Picazo – Revision of the article.

Guarantor

The guarantor of this article is Dr. Ramírez-Villaescusa.

Acknowledgments

The authors thank Dr. Chistopher D. Fletcher for his support and comments on the histological analysis.

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