# Primary leiomyosarcoma of the distal fibula: A case report and review of the literature

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## Abstract

We describe a primary leiomyosarcoma of bone located in the distal fibula in a 67-year-old man. Plain radiographs and computer tomography scan revealed a lytic destructive lesion in the distal metaepiphyseal region of the left fibula with little involvement of the surrounding soft tissues. The lesion was composed of proliferating spindle-shaped cells with very slim cytoplasm and narrow oval cigar shaped nuclei. Immunohistochemistry studies demonstrated a strong positivity for actin and desmin, and weak positivity for caldesmon.

## Introduction

Leiomyosarcoma is one of the more frequent malignant mesenchymal tumors arising in soft tissues, the skin, the gastrointestinal tract, the uterus and rarely in the bone.[1-4] It is characterized by atypical spindle cells. The diagnosis of leiomyosarcoma is based essentially on histopathologic and immune-histochemical evidence.

## Case Report

A 67-year-old man was admitted to out hospital because of a 5-month history of pain in his left ankle. Physical examination revealed partial limitation of motion of the left ankle joint. On palpation, a tender, subtle swelling on the anterolateral lower third of the patient's left leg, just proximal to the ankle joint was noted. There was no palpable lymphadenopathy in the draining regional lymph nodes. The serum alkaline phosphatase, phosphorus, calcium, and uric acids levels were within normal limits. X-rays of the left leg with ankle revealed a poorly defined permeative osteolytic lesion in the distal third of the fibula. The tumor had mainly a metaphyseal location and extended into the epiphysis. This neoplasm occupied the medullary canal, breaking through the cortex and extending to surrounding soft tissue with slight periosteal new bone formation (Figure 1).

Computed tomography (CT) and Magnetic Resonance (MRI) confirmed the presence of an osteolytic fibular mass, which was expanding the medullary canal, destroying the lateral as well as the medial cortex and involving the surrounding soft tissue (Figure 1). A periosteal bone reaction was clearly Seen in CT. Magnetic resonance imaging of the lesion showed it to be hypointense on Tl-weighted image and heterogeneous on T2-weighted image with iso- and hyper-intense areas. The histological diagnosis of leiomyosarcoma was made on the basis of an open incisional biopsy. The most direct approach to the distal Fibula was selected, the skin incision was also planned to be included in the definitive resection. A 2-cm longitudinal incision was made under fluoroscopy from the tip of the lateral malleolus extending proximally over the posterolateral aspect of the fibula. The incision was then deepened through the subcutaneous tissue down to the periosteum, which was then incised. With the use of 2.5 mm drill bit, multiple cortical holes were performed in the form of a square. With the use of small osteotome, a cortical window was opened and bone curettage was done. Adequate specimen was taken followed by hemostasis to prevent the contamination of the surgical field with tumor cells. This was followed by closure of the different layers and Inserting a drain with the exit tract through the wound margin. A protective-weight bearing for was applied postoperatively. The routine oncological work-up revealed that the patient had no history of previous tumors. He denied any abdominal or pelvic pain. Abdominal and pelvic ultrasound revealed no evidence of tumors in gastrointestinal tract. Endoscopy demonstrated a completely normal oesophagogastric and doudenal mucosa. Thorax CT excluded pulmonary metastases. Since no primary tumor could be demonstrated at any other localization, an en bloc resection of the distal left fibula was performed. After presenting the results of the resection in the second tumor conference, neither radiotherapy nor chemotherapy were indicated. The surgical margins were free of tumor. The ankle was stabilized in a Vacuum Shoe. The patient was put on a program of physiotherapy. The patient is still on regular follow-up to check for recurrence or metastasis. The patient was informed that the data would be submitted for publication, to which he gave his consent.

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### Pathological findings

The *en-bloc* distal fibular resection yielded of a 15-cm segment including the distal fibula. Tumor tissue was predominantly confined to the bone (Figure 2).

The *en-bloc* resection included the distal fibula and a part from the neighboring distal tibia incisural cortex, the tumor Margins were free with complete resection of the biopsy canal. The histological evaluation (Figure 3) confirmed a moderate proliferative activity with mild nuclear atypia. Histologically, there was understructured cortical bone tissue. In the medullary canal, we found the formation of a mesenchymal tumor made of spindle cells with very slim cytoplasm and narrow oval cigar shaped nuclei, meanwhile, also sporadic tumor cells with hyperchromatic atypical nuclei. Active mitosis was almost undetectable. Immunohistochemically, the tumor cells were positive for actin and desmin, and weakly positive for caldesmon. Ten percent of the cell nuclei responded positively with the proliferation indicator ki-67.

## Discussion

Our patient sought in the summer of 2013 medical advice because of persistent pain and swelling in the left lateral malleo-

lus. The Initial workup showed an osteolytic lesion in the distal fibula. At first we have done the necessary imaging work-up. A biopsy procedure was then carried out on 12/07/2013, which confirmed the diagnosis of primary leiomyosarcoma of the bone.

After the usual preoperative preparation and patient consent, we carried out an en bloc resection of the left distal fibula on 16/08/2013. Here, a 15 cm piece en bloc has been resected at the distal fibula. With the marker pen the skin Access was planned so as to include the old scar of the biopsy. Then followed under fluoroscopic control the determination of the safe zone about 4 cm cranial to the old biopsy Scar. The skin incision was elliptical around the old scar. The tissues were then prepared to expose the lateral leg compartment. The fibula was sawed with the oscillating saw 6 cm above the tumor and then enucleated after that the attaching distal ligaments have been discontinued (syndesmosis and lateral collateral ligaments). After Resection of the distal fibula appeared a bony-erosion in the tibia in the incisural fossa just above the Joint line. It was unclear to the naked eye whether if that was Tumor infiltration or not. The preoperative Magnetic resonance imaging and CT showed no evidence of tumor extension into the tibia. It was then decided to remove this eroded bone island with the oscillating saw. Postoperatively the patient was mobilized with landscaped Vacoped boots (Figure 4). The postoperatively performed radiographs showed an orthograde position of the tibia in the mortise. Now and after almost 80 months after the Index surgery, the patient does well, has good ankle mobility, and had no recurrence (Figures 5 and 6).

Primary leiomyosarcoma of bone is an extremely uncommon malignant condition first described by Evans and Sanerkin.[5] In the Literature, there are only about 97 cases of reported primary bony leiomyosarcomas. On the other hand these lesions are well documented in the gastrointestinal and female genital tracts.

According to their location, leiomyosarcomas can be subdivided into three groups with different clinical behaviors. The most common and aggressive group of leiomyosarcomas arises in deep soft tissues (*e.g.* the retroperitoneum and abdominal cavity) and female genital tract. The second group is represented by cutaneous and subcutaneous tumors. The third Group consists of rare cases of vascular and primary bony leiomyosarcomas. Prognosis is generally poor for the retroperitoneal and subcutaneous tumors, variable for the bony type, and best for the cutaneousleiomyosarcomas.[3,5-29]

Seventy-three of the 97 primary leiomyosarcomas of bone reported in the literature were located in the long bones of the extremities and involved mainly the meta- epiphyseal area. The femur is the long bone most frequently involved (42%), followed by the tibia (38%) and the humerus (15%).

A leiomyosarcoma of the bone is a rare occurrence. Adelani *et al.*[1] In 2009 reviewed 107 skeletal leiomyosarcomas that had been previously reported in the English literature. According to their review, the patients' age widely ranged from 9- to 87-year-old with a median age of 47 years. Twenty-nine prozent of tumors arose in the distal femur, followed by proximal tibia (26%). The locations of skeletal lesions (Figure 7) were femur in 46 patients (distal 27, proximal 8, diaphysis 7, unknown 4), tibia in 27 (proximal 16, distal 5, diaphysis 2, unknown 4), pelvis in 14, humerus in 8 (proximal 7, diaphysis 1), mandible in 8, fibula in 4 (distal 4), maxilla

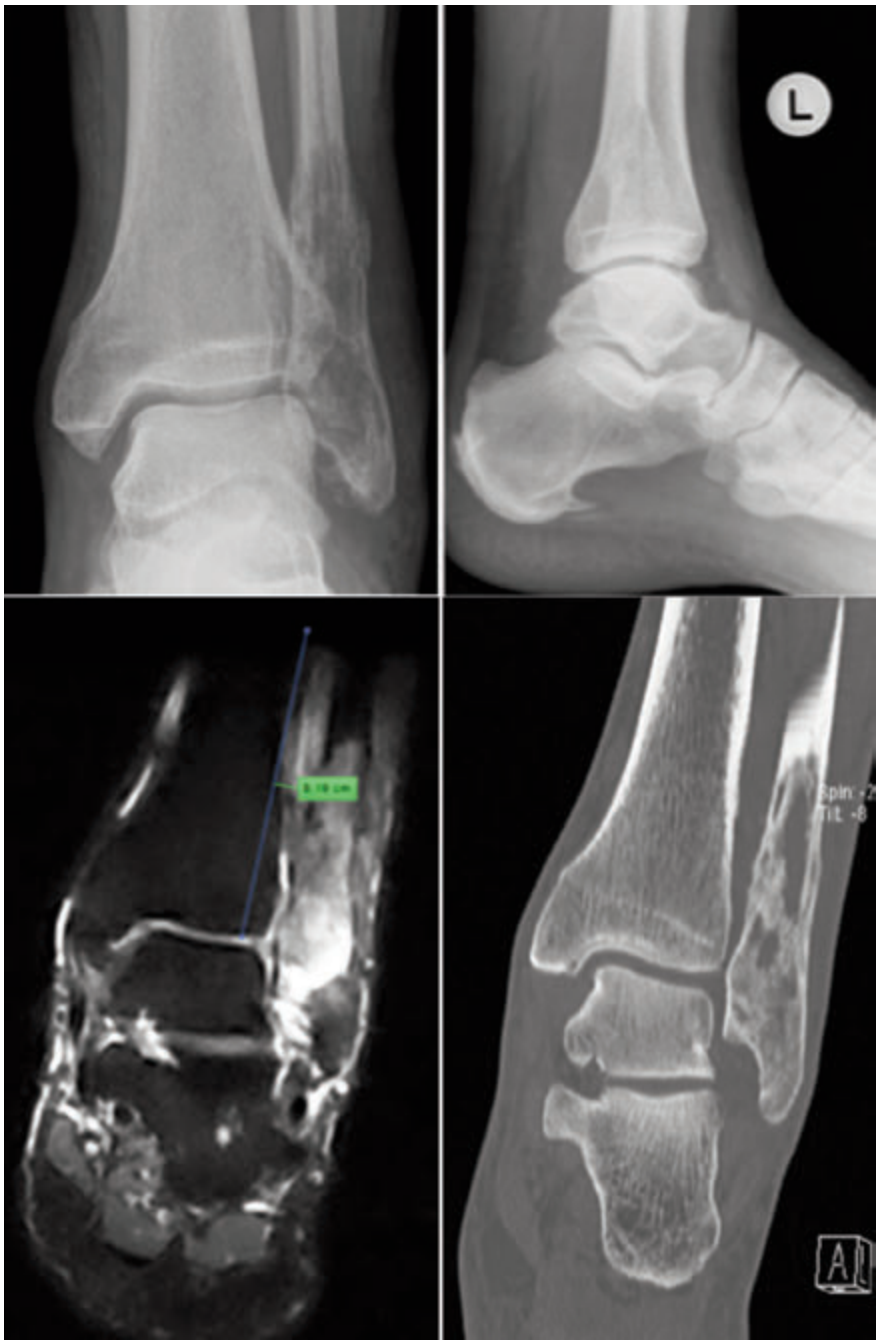


**Figure 1. Preoperative anteroposterior radiographs, lateral radiographs, CT and MRI of the left ankle revealing a metaphyseal fibular lesion with lytic destruction of the cortex.**

in 3, rib in 3, clavicle in 2, scapula in 1, sternum in 1, distal phalanx in 1, thoracic vertebrae in 1, sacrum in 1, talus in 1. Most of the leiomyosarcomas arising in long bones involved the metaphyses.[1]

The present case was located in the meta-epiphyseal region of the left distal fibula. There have been a few isolated cases in the literature where the tumor has involved the bones of the foot and ankle. The primary leiomyosarcoma involving the fibula has been, to our knowledge, four times previously reported in the literature. Radiologically, this tumor and most of the reported primary leiomyosarcoma of long bones show similar findings: they are usually osteolytic and may exhibit aggressive characteristics, such as permeation of the cortical bone and extension to surrounding soft tissue. However, generally speaking, Primary leiomyosarcoma of the bone does not have a typical radiographic appearance and can mimic any other primary or secondary malignant tumor. High-grade leiomyosarcomas show an ill-defined, irregular osteolytic appearance with a moth-eaten or permeative pattern. On the other hand, low-grade tumors exhibit a geographic pattern of bone destruction with in a sclerotic rim, a thing that can simulate a benign process.[8,30]

The diagnosis of primary leiomyosarcoma of bone was established by its characteristic histological appearance and supported by the positive immunohistochemical staining. So far, all the leiomyosarcomas described in bone have shown the same features, consisting of a sheet-like proliferation of spindle cells arranged in intersecting fascicles with focal malignant fibrous histiocytoma-like areas.[8,31,22]

In any case of leiomyosarcoma involving bone, a metastatic lesion must be ruled out before the lesion can be designated as a primary tumor. The differential diagnosis includes malignant haemangiopericytoma, epithelioid angiosarcoma and epithelioid haemangioendothelioma.[32,33] Malignant haemangiopericytoma of bone, although rare,[34] may be difficult to differentiate from leiomyosarcomas. However, hemangiopericytoma does not show immunoreactivity for actin antibodies[2,35] and does not display a complete ultrastructural smooth muscle differentiation. The most common misdiagnosis of leiomyosarcomas across the literature was the malignant fibrous histocytoma. Other differential diagnoses include lymphoma, malignant fibrous histiocytoma, plasmacytoma, fibrosarcoma, Ewing's sarcoma, osteolytic osteogenic sarcoma and metastatic carcinoma. Sundaram *et al.* reported two characteristics of primary bone leiomyosarcoma that may be helpful

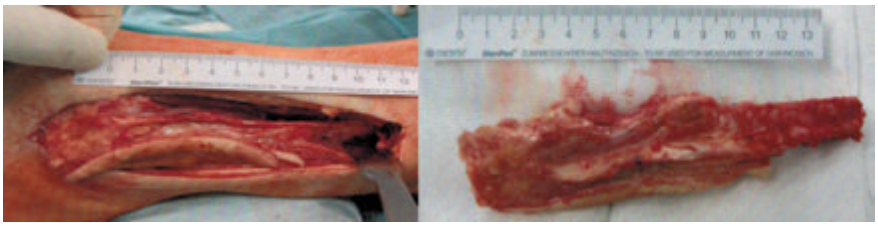

**Figure 2. The resected part with the safe-zone.**

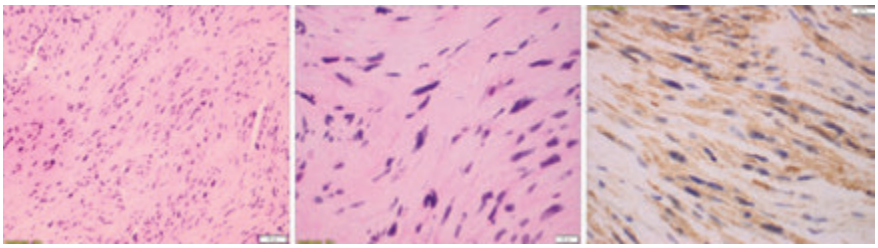

**Figure 3. Microscopic view of the lesion H&E: 1. Spindle shaped tumor cells with fascicular muster, tumor cells with eosinophilic cytoplasm and cigar shaped nuclei with atypia. 2. Nuclear atypia with hyperchromatosis. 3. Positive cytoplasmic actin expression in the tumor cells.**

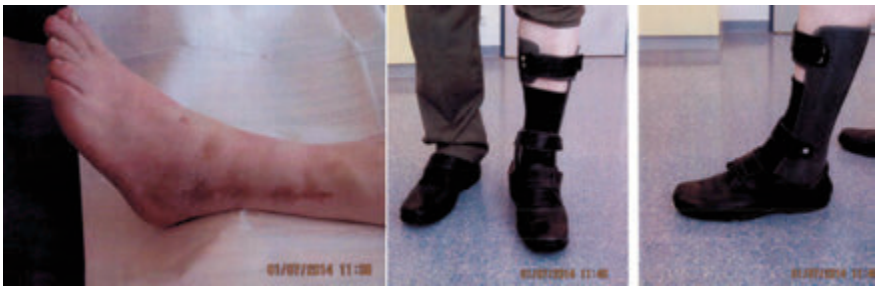

**Figure 4. clinical follow-up photos one year postoperatively and rehabilitation with vacoped Boots.**

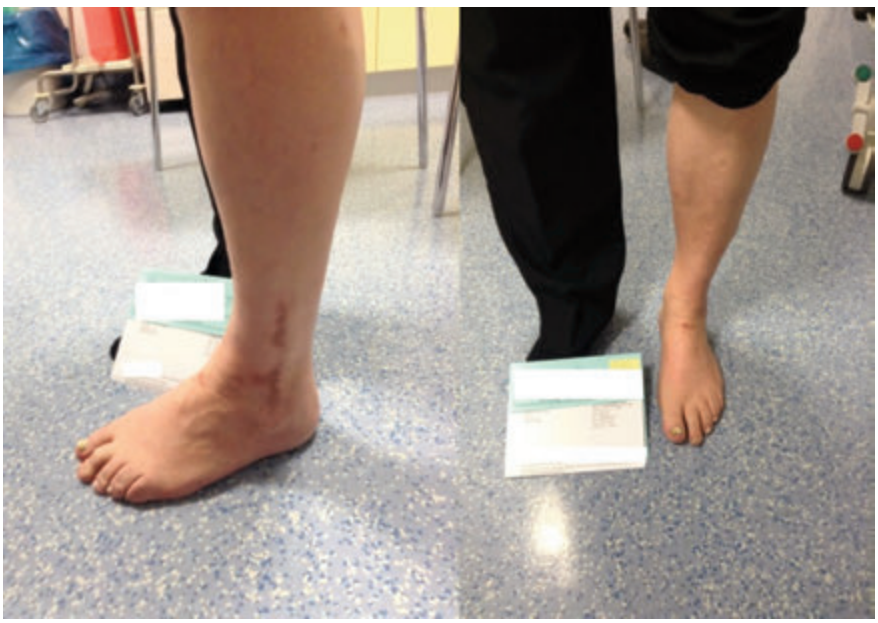

**Figure 5. Clinical follow-up 3 years after the index operation.**

in differentiating these from other aggressive osteolytic lesions. First, lesions had a considerable length, extending along the longitudinal axis of the bone, and second, the signal intensity of these lesions on T2-weighted MR images is intermediate to low (decreased signal intensity with respect to normal bone marrow), whereas most osteolytic lesions are hyperintense on T2-weighted images.[36]

The pathogenesis of the primary leiomyosarcoma of bone is unclear. Most opinions consider that it arises from the smooth muscle cells of blood vessels, although an origin in perivascular myofibroblasts or mesenchymal fibroblasts cannot be ruled out.[6,5,13,23] Potential risk factors were identified in 10% of the cases across the literature and included chemotherapy, Paget disease of the bone, and orthopedic implants, previous bone infarction and

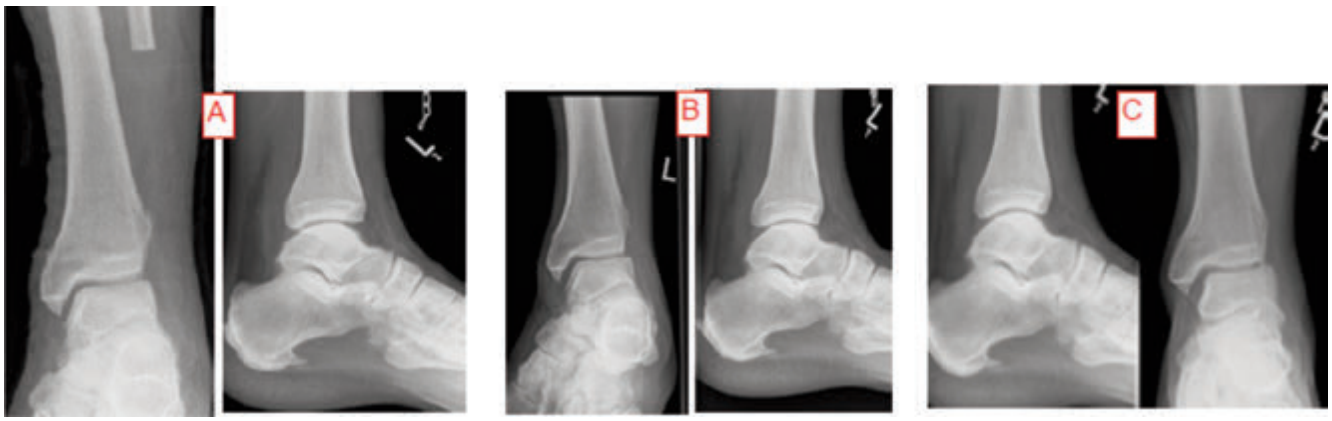


**Figure 6. Radiological findings: A, immediately postoperative. B, one year postoperative. C, three years after the index operation.**

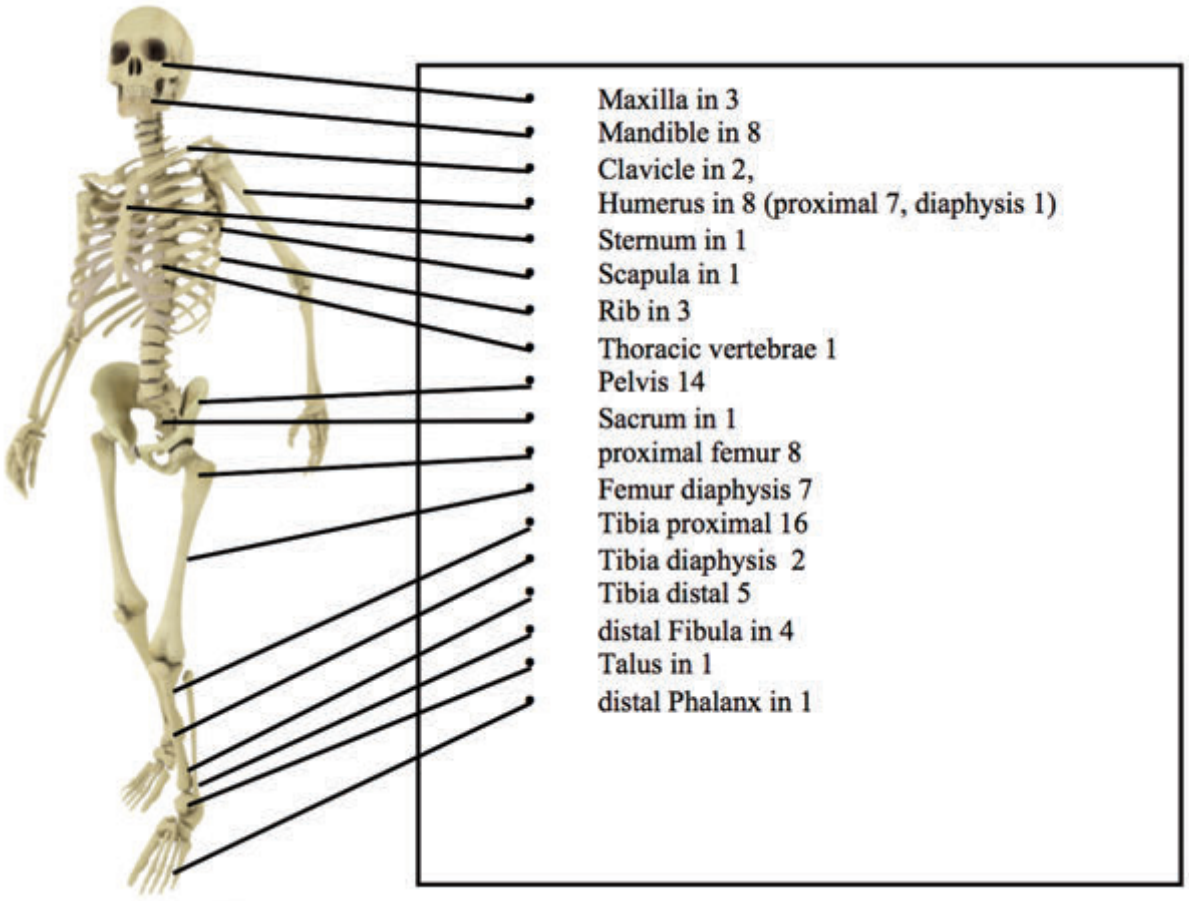


**Figure 7. Distribution of the primary leiomyosarcoma of the bone following the review of Adelani *et al.* (2009).**

Epstein Barr Virus (EBV) infection.[9,25,29,35]

According to Young and Freemont, the risk of early recurrence and metastasis is small if the original tumor is adequately excised at the time of diagnosis. In a review by Myers et al, the mortality in primary bone leiomyosarcoma was 18%, with a mean survival rate of 75% 3.4 years after the diagnosis when the tumor is surgically adequately treated. Theo recurrence rate was roughly 25%. The metastasis rate is 25 %. The lungs were the main site of metastasis.9,29

Most of the studies have indicated that primary bony leiomyosarcomas are aggressive. Antonescu *et al*. attempted to stratify their prognosis based upon grade; however, no significant differences were noted in disease-free or overall survival rates between low- and high-grade tumors.[8]

Wide excision with Safe zone is the mainstay of treatment for leiomyosarcoma. The best scenario would be when a low-grade tumor is widely excised in the absence of metastasis. However, obtaining a wide surgical margin may be difficult, and amputation may be necessary for high-grade tumors in the extremities specially when there is soft tissue infiltration or when the neurovascular bundle is infiltrated with the tumor. Neoadjuvant and adjuvant chemotherapy have in several reports not provided an improved prognosis. However, chemotherapy should be considered in case of a diffuse metastatic disease to the lungs or large pelvic masses with neurovascular involvement that preclude safe resection.[29,30] Few reports in the literature have used chemotherapy as a way to debulk the tumor in order to facilitate the surgical excision. The indications for radiotherapy are on the other hand controversial, this includes mainly the cases in which a contaminated resection bed was left over or in which a wide resection cannot be carried on. The operative treatment is the gold standard. The early wide resection of the primary lesion and secondary reconstruction is standard of care in localized disease. A clean surgical margin is an important goal of the surgical resection.[10,27]

## Conclusions

Primary leiomyosarcoma of the bone is rare and should be kept in the differential diagnosis of primary malignant osteolytic neoplasms. Histopathological evaluation with immunohistochemistry analysis is the mainstay in reaching the accurate diagnosis. Treatment is primarily surgical with limited benefit from neoadjuvant and adjuvant therapies.

## References


1. Adelani MA, Schultenover SJ, Holt GE, Cates JMM. Primary leiomyosarcoma of extragnathic bonclinicopathologic features and reevaluation of prognosis. Arch Pathol Lab Med 2009;133:1448-56.
2. Enzinger FM, Weiss SW. Soft tissue tumours. St Louis: Mosby; 1995. pp 713-25.
3. Suster S. Epithelioid leiomyosarcoma of the skin and subcutaneous tissue. Clinicopathologic and ultrastructural study of five cases. Am J Surg Pathol 1996;18:232-40.
4. Suster S, Huszar M. Epithelioid leiomyosarcoma of the stomach. A case study of the intermediate filaments. Am J Surg Pathol 1987;11:575-80.
5. Evans DMD, Sanerkin NG. Primary leiomyosarcoma of bone. J Pathol Bacteriol 1965;90:348-50.
6. Abdelwahab IF, Hermann G, Kenan S, et al. Case report 794: primary leiomyosarcomas of the right femur. Skeletal Radiol 1993;22:379-81.
7. Abdin HA, Prabhu SR. Leiomyosarcoma of mandible in a Sudanese female. Int J Oral Surg 1985; 14:85-8.
8. Antonescu CR, Erlandson RA, Huvos AG. Primary leiomyosarcoma of bone: a clinicopathologic, immunohistochemical, and ultrastructural study of 33 patients and a literature review. Am J Surg Pathol 1997;11:1281-94.
9. Berlin O, Angervall L, Kindlom LG, et al. Primary leiomyosarcoma of bone. A clinical, radio- graphic, pathologic-anatomic, and prognostic study of 16 cases. Skeletal Radiol 1987;16:364-76.
10. Da Silva LF, Mejjad O, Vittecoq O, et al. Leiomyosarcoma of the tibia. Report of a case. Rev Rhum 1997;64:835-8.
11. Delsman BM, Hagena FW, Nerlich A, et al. Das primäre Leiomyosarkom des Knochen. Z Orthop 1996;134:435-40.
12. Eady JL, McKinney JD, McDonald EC. Primary leiomyosarcoma of bone: a case report and review of the literature. J Bone Joint Surg Am 1987;69:287-9.
13. Fornasier VL, Paley D. Leiomyosarcoma in bone: primary or secondary? A case report and review of the literature. Skeletal Radiol 1983; 10:147-53.
14. Hochstetter AR, Eberle, Ruttner JR. Primary leiomyosarcoma of extragnatic bones. Cancer 1984;53:2194-200.
15. Jundt G, Moll C, Nidecker A, et al. Primary leiomyosarcoma of bone. Hum Pathol 1994;25:1205-12.
16. Kawai T, Suzuki M, Mukai M, et al. Primary leiomyosarcoma of bone: an immunohistochemical and ultrastructural study. Arch Pathol Lab Med 1983;107:433-7.
17. Khoddami M, Bédard YC, Bell RS, Kandel RA. Primary leiomyosarcoma of bone. Report of seven cases and review of the literature. Arch Pathol Lab Med 1996;120:671-5.
18. Kratochvil FJ III, MacGregor SD, Budnik SD, et al. Leiomyosarcoma of the maxilla. Report of a case and review of the literature. Oral Surg Oral Med Oral Pathol 1982;54:647-55.
19. Loizaga JM. Leiomiosarcoma primario de hueso. Informe de un caso. Patología 1976;9:247-54.
20. Meister P, Konrad E, Gokel JM, Remberger K. Case report 59: leiomyosarcoma of the humerus. Skeletal Radiol 1978;2:265-7.
21. Mirra JM. Bone tumours. Clinical, radiologic, and pathologic correlations. Philadelphia: Lea & Febiger; 1989. pp 874-886.
22. Myers JL, Arocho J, Bernreuter W, et al. () Leiomyosarcoma of bone. A clinicopathologic, immu- nohistochemical, and ultrastructural study of five cases. Cancer 1991;67:1051-6.
23. Overgaard J, Frederiksen P, Helmig O, Jensen OM () Primary leiomyosarcoma of bone. Cancer 1977;39:1664-71.
24. Peoch M, Vitetta F, Girard MH, et al. Le léiomyosarcome osseous primitif. Une observation anatomoclinique avec étude immunohistochimique et revue de la littérature. Arch Anat Cytol Pathol 1997;45:28-36
25. Sanerkin NG. Primary leiomyosarcoma of the bone and its comparison with fibrosarcoma: a cytological, histological and ultrastructural study. Cancer 1979;44:1375-87.
26. Shamsuddin AK, Reyes F, Harvey JW, Toker C. Prima- ry leiomyosarcoma of bone. Hum Pathol 1980;11:581-3.
27. Wang TIE, Erlandson RA, Marcove RC, Huvos AG. Primary leiomyosarcoma of bone. Arch Pathol Lab Med 1980;104:100-4.
28. Wendum D, Sautet A, Prévot S, et al. Léiomyosarcomes primitifs de l'os: étude an- atomoclinique et immunohistochimique de 3 observations. Ann Pathol 1996;16:115-9.
29. Young MP, Freemont AJ. Primary leiomyosarcoma of bone. Histopathology 1991;19:257-62.
30. Singh D, Kumar R, Kamau GG, et al. Primary leiomyosarcoma of the first metatarsal bone: A case report. SA Orthop J 2017;16:45-8.

31. Schürch W, Skalli O, Seemayer TA, Gabbiani G. Intermediate filament proteins and actin isoform as markers for soft tissue tumour differentiation and origin. Smooth muscle tumours. Am J Pathol 1987;128:91-103.
32. Kleer CG, Unni KK, McLeod RA. Epithelioid hemangioendothelioma of bone. Am J Surg Pathol 1996 20:1301-11.
33. Tsuneyoshi M, Dorfman HD, Bauer TW. Epithelioid hemangioendothelioma of bone. A clinicopathologic, ultrastructural, and immunohistochemical study. Am J Surg Pathol 1986;11:754-64.
34. Tang JSH, Gold RH, Mirra JH, Eckardt J. Hemangiopericytoma of bone. Cancer 1988;62:848-59.
35. Schürch W, Skalli O, Lagacé R, Seemayer TA, Gabbiani G. Intermediate filament proteins and actin isoforms as marker for soft tissue tumour differentiation and origin. III. Hemangiopericytomas and glomus tumours. Am J Pathol 1990;136:771-86.
36. Sundaram M, Akduman I, White LM, et al. Primary leiomyosarcoma of bone. AJR Am J Roentgenol 1999;172:771-6.