Case Report

A Rare Case Report of Primary Leiomyosarcoma of Distal Femur Bone in a Patient with Multiple Myeloma and Review of Literature

Xiaobing Jin, MD, PhD;[1] Adam L Chen;[2] Weiguo Liu, MD, PhD[3]*

[1] *Department of Pathology, State University of New York at Buffalo, Buffalo, NY*
[2] *City Honors School, Buffalo, NY*
[3] *Department of Pathology, New York University, New York, NY*

Primary leiomyosarcoma of bone is rare, with < 0.7% incidence of all primary malignant bone tumors. Here we report a primary leiomyosarcoma of bone arising in a patient with multiple myeloma. The patient is a 72-year-old male who was initially diagnosed with multiple myeloma (IgG Kappa) in 2007 which presented as a large plasmacytoma involving his thoracic vertebrae. He was treated with chemotherapy and eventually had a stem cell transplant in 2015. In 2017, a routine skeletal survey demonstrated a solitary lytic lesion in the right distal femur. The lesion grew fast and doubled in size to 7.9 cm within one year. The lesion was biopsied and proven to be a leiomyosarcoma. A total body PET/CT scan showed no evidence of other primary tumors or metastatic disease. The patient then underwent a distal femur resection. Grossly, majority of the tumor involved distal femur cortical bone and medullary cavity with focal extension into the surrounding soft tissue. Microscopically, the tumor consisted of fascicles of spindle cells with a focal storiform growth pattern. The tumor cells had eosinophilic cytoplasm and focally pleomorphic nuclei. The tumor cells were positive for SMA and Calponin and negative for Desmin, Myo-D1, Myogenin and S-100 immunohistochemical stains. The morphology and immunoprofile favored a diagnosis of pleomorphic leiomyosarcoma. Primary leiomyosarcoma of bone is a rare tumor and this patient's history of multiple myeloma made it even more challenging to make an early clinical diagnosis.
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Key Words: *primary leiomyosarcoma, femur, multiple myeloma*

INTRODUCTION

Primary leiomyosarcoma of bone is rare, with <0.7% incidence among all primary malignant bone tumors.[1] It was first described in 1965 by Evans.[2] The most frequent site is the lower extremity, especially around the knee joint. The craniofacial skeleton is the second most frequent location. Less common locations are the pelvic bones, clavicle and the vertebra.[3,4] Little is known about the biology and clinical behavior of primary bone leiomyosarcoma due to its extreme rarity. Herein we report a primary leiomyosarcoma of femur bone arising in a patient with multiple myeloma.

CASE REPORT

The patient is a 72-year-old male who was initially diagnosed in 2007 with IgG Kappa multiple myeloma which presented as a large plasmacytoma involving his thoracic vertebrae. He was treated systemically with chemotherapy. In 2013, the patient had palliative radiotherapy to sacrum. He eventually had an autologous stem cell transplant in 2015. In 2017, a routine skeletal survey demonstrated a large moth-eaten bone lesion in the right distal femur bone measuring 7.9 cm x 3.5 cm **(Figure 1A).** The lesion significantly increased in size since the prior examination confirmed on MRI. Biopsy of the lesion revealed leiomyosarcoma. A total body PET/CT scan was negative for metastatic disease. The patient then had the surgery of a distal femur resection.

Macroscopically, majority of the tumor involves distal femur cortical bone and medullary cavity with focal extension into the surrounding soft tissue **(Figure 1B)**. Microscopically, the tumor consists of fascicles of spindle cells with a focal storiform growth pattern. The tumor cells have eosinophilic cytoplasm and focally pleomorphic nuclei. Immunostains show that tumor cells are positive for SMA and Calponin and negative for Desmin, Myo-D1, Myogenin and S-100 **(Figure 2)**. The morphology and immunoprofile support a diagnosis of pleomorphic leiomyosarcoma.

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***Corresponding Author:** Department of Pathology, New York University, 550 1st Avenue, Suite TH461, New York, NY 10016. Tel: 212-263-5470. (Email: liuwg21@hotmail.com)

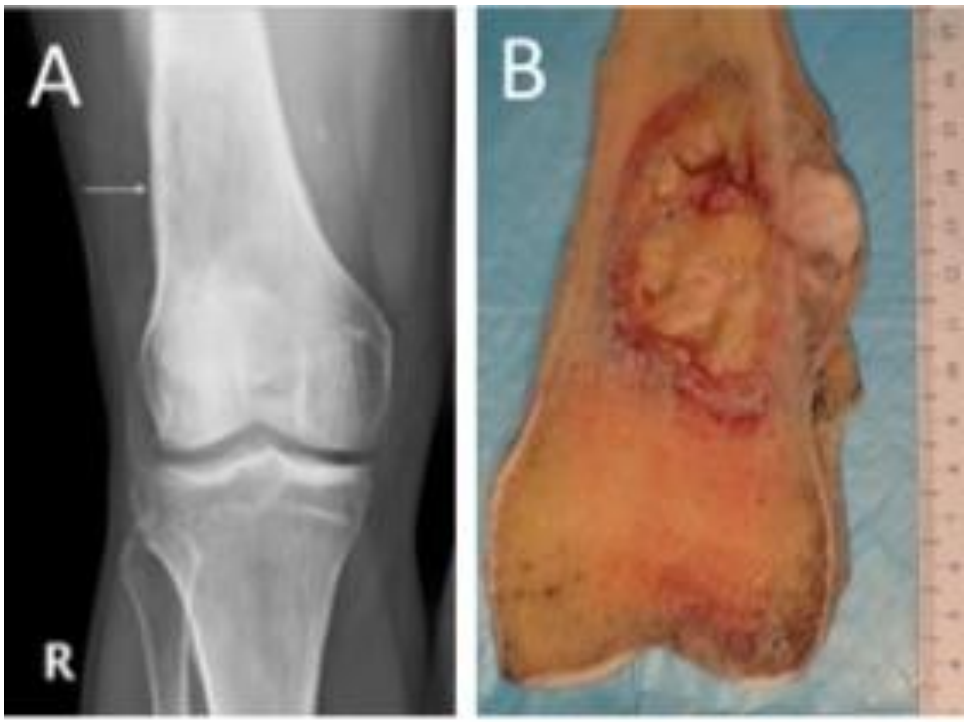

Figure 1. Radiology and gross examination of the tumor. X ray shows a large osteolytic lesion with moth-eaten pattern **(A)**. Grossly, majority of the tumor involve the distal femur cortical bone and medullary cavity with focal extension into the surrounding soft tissue with diffuse necrosis **(B)**.

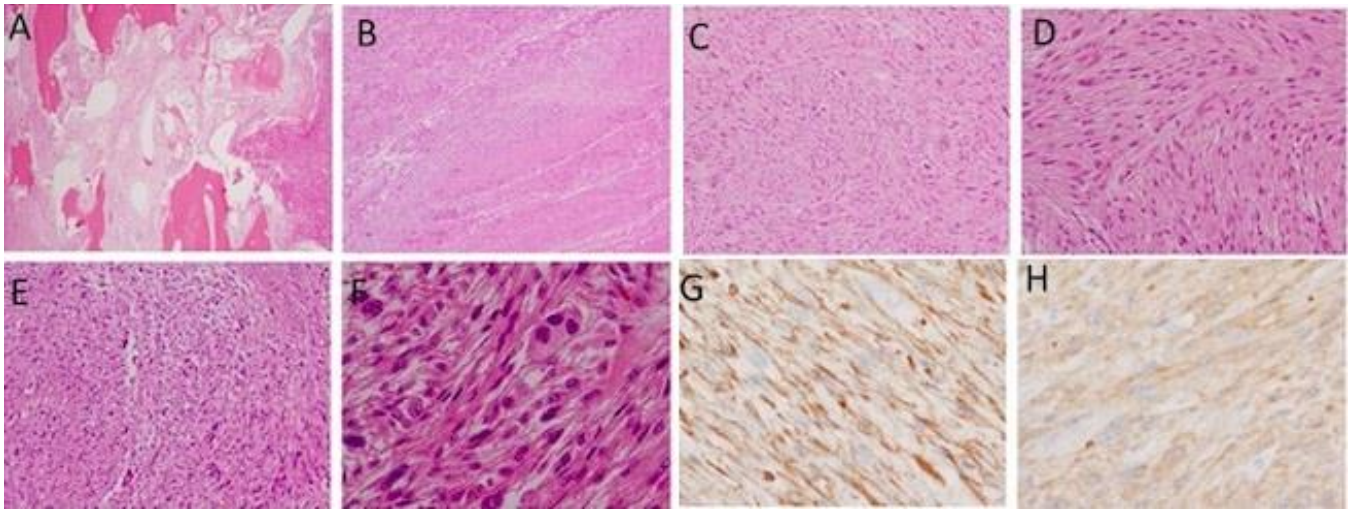

Figure 2. Histology and immunohistochemistry examination. The site of tumor breaks through the cortical bone (**A** x2). Microscopically, the tumor consists of fascicles of spindle cells with a focal storiform growth pattern (**C** x10 and **D** x20). Large area of necrosis is present (**B** x10). The tumor cells have eosinophilic cytoplasm and focally pleomorphic nuclei (**E** x10 and **F** x40). Immunostains show that tumor cells are positive for SMA (**G** x40) and Calponin (**H** x40), and negative for Desmin, Myo-D1, Myogenin and S-100 (data not shown). No chondroid and osteoid matrix are identified in the tumor tissue.

DISCUSSION

Primary leiomyosarcoma of bone is a very rare malignant tumor. Since being first described by Evans [2] in 1965, about130 cases have been reported in the literature.[3-6] It commonly occurs in men and usually affects the long bones particularly distal femur and proximal tibia. Patients usually presents with pain and swelling. Due to its aggressive clinical behavior, it is important to recognize the presence of this rare entity and make the accurate diagnosis.

Most of the primary bone leiomyosarcomas are de novo cases. About 15% of the cases are associated with prior radiation exposure according to one report.[3] And chemotherapy is also regarded as a definite risk factor of developing primary leiomyosarcoma of bone. Antonescu et al[3] reported two cases in their study with high-grade bone leiomyosarcoma developing after intensive chemotherapy for hairy cell leukemia/Hodgkin's malignant lymphoma. The latency period were 15 years and 8 years respectively. In our case, the patient initially presented with a large plasmacytoma involving thoracic vertebrae and diagnosed with multiple myeloma. He was then treated with several cycles of multiple chemotherapy regimens and a palliative radiotherapy to sacrum followed by autologous peripheral stem cell transplant. Nine years later, a routine skeletal survey demonstrated a solitary lytic lesion in the right distal femur. This radiographic presentation is not specific. Malignant fibrous histiocytoma, fibrosarcoma, chondrosarcoma and metastatic carcinomas, all can have the similar moth-eaten pattern of osseous destruction. Based on the history of multiple myeloma, this initially was interpreted as a recurrent myelomatous lesion. A total body PET/CT scan showed no evidence of other primary tumors or metastatic disease. The lesion was then biopsied and proven to be a leiomyosarcoma. To the best of our knowledge, this report is the first description of bone leiomyosarcoma arising in a patient with history of multiple myeloma.

Since primary bone leiomyosarcoma is very rare. Metastasis from uterus, gastrointestinal tract and other sites should be excluded by clinical and radiological findings, especially when dealing with female patient. Various imaging studies such as X-ray, CT scan, MRI, abdominal ultrasonography and PET/CT scan are recommended before rendering the diagnosis of primary leiomyosarcoma of bone. Similar to its soft tissue counterpart, histologically primary bone leiomyosarcoma demonstrates spindle cells containing oval, blunt-ended nuclei and distinct eosinophilic cytoplasm. Other histologic variants including myxoid, epithelioid, giant-cell rich and inflammatory also exist. Judicious application of immunohistochemical markers especially SMA and Desmin is very helpful in differentiating leiomyosarcoma from other rare primary sarcomas such as undifferentiated pleomorphic sarcoma, myxofibrosarcoma, synovial sarcoma and solitary fibrous tumor et al.[7] In our case, the tumor cells have typical fascicles of spindles cells which have eosinophilic cytoplasm. Focal pleomorphic nuclei and necrosis suggest high-grade malignancy. Immunostains show tumor cells are positive for SMA and Calponin and negative for Desmin, Myo-D1, Myogenin and S-100. It is reported only about 50% of the primary bone leiomyosarcoma cases are negative for desmin and thus should not be regarded as the primary screening antibody.[4,5] Variable aberrant keratin staining can be present in some cases.[5,8] Electron microscopy may be a useful method to establish the diagnosis in that situation.[3,9] Typical ultrastructural findings include parallel arrangement of actin microfilaments, dense bodies and attachment plaques. Dystrophic or non-neoplastic calcification represents another pitfall. According to the report of Rekhi[10] and Bush,[11] about 20% of the primary bone leiomyosarcoma cases show focal dystrophic calcification. This may be mistakenly interpreted as fibroblastic osteosarcoma. However, lack of myogenic differentiation and presence of malignant osteoid/bone formation are helpful in differentiating fibroblastic osteosarcoma from leiomyosarcoma. In Summary, diagnosis of primary leiomyosarcoma of bone is based on the combination of clinical information, histology and ancillary studies. Absence of Desmin staining and focal cytokeratin expression should not deter one from making the diagnosis.

Data for optimal treatment plan of bone primary leiomyosaroma is limited due to its low prevalence. Overall the prognosis depends on the grade and stage of the tumor. According to the study of Adelani et al.[5] The low-grade malignancies have 100% 5-year survival rate compared with 60% of high-grade cases. Stage I and IIA patients have 90% and 60% 5-year survival rates respectively, however, the number decreases to 29% and 0% in patients with stage IIB and III/V tumors.[5] Surgical excision with wide margin is regarded as the gold standard for curative management. Patients with negative surgical margins had significantly longer overall survival and disease- free survival rates.[4] Adjuvant radiation therapy has been used to augment surgery for local control in Antonescu's study.[3] However, there is no significant survival rates difference between the patients who had surgery alone and patients who received surgery and adjuvant radiation therapy. Unlike primary osteosarcoma which is generally sensitive to chemotherapy, primary leimyosarcoma of bone unfortunately appears resistant to chemotherapy, which has minimal impact on overall survive.[3] There is no significant difference of local recurrence rate between low-grade and high-grade tumors. In contrast, the high-grade tumor has a higher 5-year metastatic rate (58%) than that of the low-grade tumor (33%). Lung is the most common site of metastasis, followed by axial skeleton and liver.[5] In the study by Rekhi, all metastatic cases happened in the first year of diagnosis.[10] In our case, the patient did not have adjuvant chemo or radiation therapy after surgical resection. Multiple lung masses were identified 28 months after surgery. The mass was biopsied and proven to be metastatic leiomyosarcoma.

Bone marrow multipotential mesenchymal stem cells which are capable of smooth muscle differentiation are regarded as the cell of origin for primary leiomysarcoma of bone.[12-14] Other studies have suggested a possible vascular smooth muscle cell origin based on the observation that these neoplasms are highly vascular and even recapitulate a hemangiopericytoma like pattern.[3,15]

In conclusion. Herein we report clinicopathologic features of primary leiomyosarcoma in the proximal femur bone of a 72-year-old male patient with multiple myeloma. Diagnostic challenges and clinical treatment are discussed. A primary leiomyosarcoma should be considered in the differential diagnoses if an osteolytic lesion is present especially in a long tubular bone.

CONFLICT OF INTEREST

The authors have no conflict of interest to disclose.

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