A Case of Malignant Transformation of Myositis Ossificans

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Abstract

A 49-year-old white man presented for evaluation of an enlarging left distal thigh mass with increasing pain over the last several months. The mass was first noticed 11 years prior to this presentation. During his initial examination, the patient was diagnosed with myositis ossificans and had a partial resection of the mass to improve knee function. His current examination revealed a low grade parosteal osteosarcoma arising from pre-existing mature heterotopic ossification. To our knowledge, no reported cases of secondary parosteal osteosarcoma arising from myositis ossificans have been reported in the literature; only a few reports of malignant transformation of myositis ossificans were found.

Myositis ossificans is typically described as a reactive, self-limiting process characterized by prominent heterotopic ossification.[1-3] It predominantly affects adolescents and active adults and typically develops at a site of previous trauma.[2-4] The classic form of myositis ossificans occurs in the soft-tissues without any involvement of the surrounding bone.[2] In parosteal myositis ossificans, its proximity to the underlying bone surface causes a periosteal reaction which contributes to its formation.[2]

Myositis ossificans proceeds through several ill-defined phases in an orderly sequence that reflects maturation and regression of the lesion.[2] These phases may be followed radiographically, with an ill-defined soft-tissue mass seen on initial radiographs. As Ackerman and colleagues[4] have pointed out, calcification is not present initially, but faint, irregular, floccular radiopacities sometimes described as a "dotted veil" may be seen at the end of the third week.[3] With time, a well-demarcated calcified mass is seen as the lesion matures with a characteristic zonal calcification pattern.[2,3] This is followed by a regressive phase that is marked by some reduction in the size of the lesion and increased mineralization at the periphery.[2]

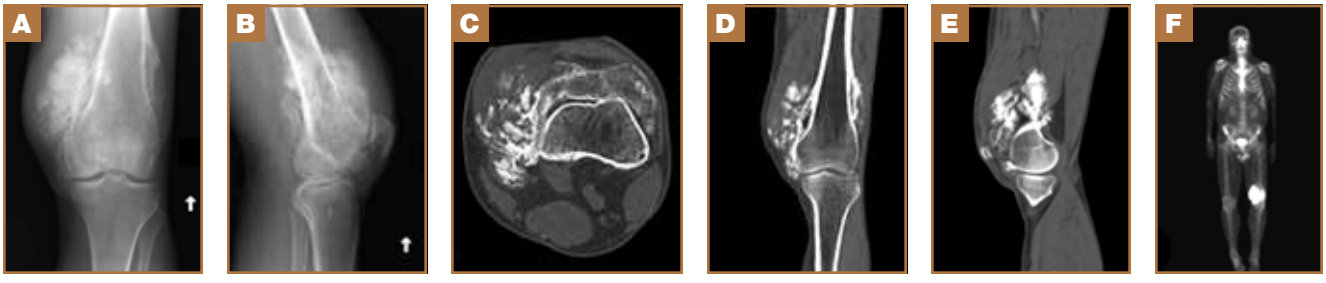
We report a case of malignant transformation of myositis ossificans. The patient provided written informed consent for print and electronic publication of this report.

Case Report

A 49-year-old white man presented for evaluation of a mass in the left distal thigh with increasing pain over the last several months. The mass was first noticed 11 years prior to this presentation. At that time he had been participating in martial arts and sustained an injury to his distal thigh. The mass arose several months after.

The patient originally sought medical evaluation several months after the mass first appeared because of discomfort. Initial magnetic resonance imaging (MRI) revealed a heterogeneous soft-tissue signal in the supra-patellar bursa concerning for a synovial hemorrhage versus a synovial based mass. A subsequent technetium-99 bone scan demonstrated focal increased uptake in the region of the supra-patellar bursa and

Figure 1. Radiographs reveal a large mineralized tumor projecting from the distal femur (A, B). Imaging shows areas of cortical thinning at the distal femur with a mineralized mass projecting from the cortex into the soft-tissues (C-E). Bone Scan reveals an area of high uptake at the anteromedial left distal femur (F).



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distal femur. Because of the concern for malignancy, the patient underwent an open biopsy. Histology was consistent with myositis ossificans of the left distal thigh involving the femur. Following this he had a partial resection of the mass to improve knee function.

After nearly a decade, the patient noticed an enlarging mass and increasing pain. During his current workup, laboratory studies, radiographs (**Figures 1A, 1B**), a computed tomography (CT) scan (**Figures 1C-1E**), and a bone scan (**Figure 1F**) were performed.

Plain radiographs (**Figures 1A, 1B**) revealed a large mineralized tumor projecting from the distal femur into the soft-tissue with areas of mature bone formation and associated cloud-like opacities of various sizes medially. CT imaging (**Figures 1C-1E**) showed a mineralized mass at the distal femur with focal areas of cortical thinning. The technicetium-99 bone scan (**Figure 1F**) had increased uptake in the location of this mass.

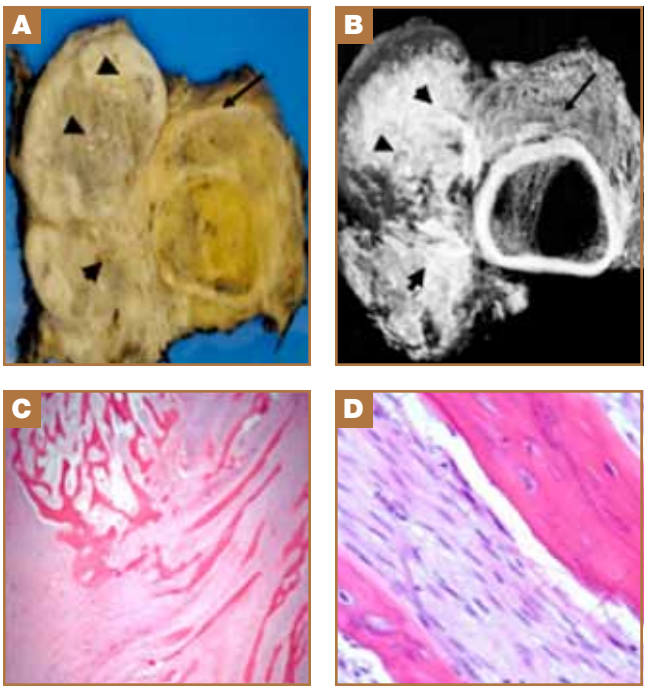
A CT guided biopsy was performed and the resultant histologic specimen showed bony trabeculae with an intervening fibrocellular stroma. The bone trabeculae were irregular with cement lines and suggested parallel array arrangement. The intervening stroma showed a modest spindled cellularity with fibrous tissue. No cellular anaplasia or high grade sarcoma were evident. A small peripheral cap of cartilage was present. The diagnosis of a low-grade parosteal osteosarcoma was made.

After a discussion of the differential diagnosis and treatment options, the patient decided to proceed with surgical resection of his distal femur with surgical reconstruction using a modular distal femoral implant.

Grossly, a large parosteal (juxtacortical) bony mass (12.5 cm x 9 cm x 6 cm) was present on the medial aspect of the distal femur end. Serial sectioning and specimen radiography revealed an irregular area of heterotopic ossification of up to 1.5 cm thickness surrounding the anterior and lateral side of the distal femur (**Figures 2A, 2B; arrows**) with a morphologically different overlying lobulated bony tumor measuring 12.1 cm x 9 cm x 5.8 cm (**Figures 2A, 2B, arrowheads**). Microscopically, the tumor was formed of parallel well-formed bony trabeculae separated by a modestly cellular stroma (**Figure 2C**) with bland appearing spindle cells (**Figure 2D**). No cartilaginous differentiation or areas of dedifferentiation (anaplasia) were seen within the tumor. Some areas rich in collagen without bone resembling desmoplastic fibroma were present. The heterotopic ossification was, at a late stage, formed of mature mineralized trabeculae attached to the bone condyle.

The final diagnosis was that of a parosteal osteosarcoma arising from pre-existing myositis ossificans.

Figure 2. Sectioning/Radiograph of gross surgical specimen (A, B); arrows show irregular area of heterotopic ossification surrounding the anterior/anterior-lateral side of the femur; arrowheads show a morphologically different overlying lobulated bony tumor over the anteromedial femur. (C,D) Histologic slides of the tumor show bony trabeculae separated by a modest cellular stroma with bland appearing spindle cells. No cartilaginous differentiation or anaplasia was seen.



Discussion and Treatment

It can be difficult to differentiate parosteal myositis ossificans from osteosarcomas.[2,3] However, the zonal architecture seen with myositis ossificans can be helpful in distinguishing these lesions from malignant bone forming tumors such as parosteal and periosteal osteosarcoma.[2-5] Classically, the mineralization pattern seen in parosteal osteosarcoma differs from myositis ossificans, in that the former has a heavily mineralized central portion fused with the underlying cortex.[2,3] Twenty percent of parosteal osteosarcomas are more cellular with obvious features of anaplasia that can help differentiate the two.[3]

Most parosteal osteosarcomas are a low-grade malignant tumor, first described in 1951, that grows predominantly on the surface of long bones in an exophytic pattern.[5-10] These rare tumors have a predilection for the posterior aspect of the distal femur with a peak incidence occurring during the third and fourth decades.[6,11] Patients with these tumors usually present with an enlarging mass, with or without dull pain, and there is often a history of a previous biopsy or attempt at resection of a benign, reactive process, as was the case with our patient.[6,8,10]

The average delay from the onset of symptoms to the correct diagnosis is approximately 15 weeks.[11] This is in contrast to a study from the Mayo Clinic[7] with 168 patients, where 49 patients had symptoms for 1 to 5 years and 44 patients had symptoms for over 5 years before receiving the correct diagnosis.

While overall, parosteal osteosarcomas are low-grade malignant lesions with a relatively good prognosis (5-year survival rates from 85% to 90%), this delay in diagnosis is not inconsequential.[6,7] Studies have shown that these tumors have a tendency to become more anaplastic with local recurrence after incomplete excision, and overall have a 20% incidence of dedifferentiation into high grade lesions.[5,8] The interval from the onset of symptoms to the time of dedifferentiation in one study ranged from 31 to 396 months.[8]

The survival of patients with dedifferentiated parosteal osteosarcoma has been found to be worse than survival of patients with low-grade parosteal osteosarcoma.[8] This can be explained by the significant association that dedifferentiation has with the development of metastasis.[7] In one study from the Mayo Clinic,[7] 11 patients died as a result of the tumor, and 10 of the 11 patients had dedifferentiated tumors.[7]

While most cases of parosteal osteosarcoma are considered primary osteosarcomas, secondary parosteal osteosarcomas have been reported to occur after previous radiation exposure.[6,12] However, no reported cases of secondary parosteal osteosarcoma arising from myositis ossificans were found after a review of the literature.

Likewise, a review of the literature shows only a few reports of malignant transformation of myositis ossificans.[3,13] But most of these reports lack biopsy results to confirm an original diagnosis of myositis ossificans or are complicated by other causative factors, such as radiation exposure.[1,13] According to Dorfman and Czerniak,[6] several of these cases are not convincing and were likely originally misdiagnosed.[6]

However, Konishi and colleagues[13] described a case of malignant transformation of myositis ossificans in a 53-year-old woman that had a mass on the volar aspect of her wrist for 4 years. Though the patient had no previous biopsy, the specimen and radiographic findings were consistent with a diagnosis of mature myositis ossificans associated with a high-grade extra-skeletal osteosarcoma. The patient underwent neoadjuvant chemotherapy followed by surgical excision of the tumor, and distal radius and adjuvant chemotherapy. The patient was well and without disease 5 years after her diagnosis.

Malignant transformation of myositis ossificans was also reported by Aboulafia and colleagues.[1] The patient sustained an electrical burn to his forearm and over the course of a few months slowly developed flexion contractures of the upper extremity. Imaging studies revealed diffuse heterotopic ossification of the forearm which remained stable for 9 years, until the patient noticed an enlarging soft-tissue mass. Biopsy revealed a high-grade telangiectatic osteosarcoma arising from the site of heterotopic ossification. The patient underwent a transhumeral amputation, because of the functional status of the limb and involvement of the neurovascular structures. During the first course of chemotherapy, the patient developed neutropenia and an infection associated with a central venous catheter, and refused any further chemotherapy treatment. Twelve months after the amputation the patient was diagnosed with multiple pulmonary metastases and died from respiratory failure 1 month later.

The case of our patient involved malignant transformation of heterotopic bone, which developed after trauma during martial arts training. Initial biopsy results were consistent with myositis ossificans. Clinically, the lesion was stable for some years before beginning to slowly increase in size and cause discomfort. After resection of the distal femur, sectioning of the mass was consistent with transformation of myositis ossificans into parosteal osteosarcoma.

We believe that the cases described in the literature and our case is an example of malignant transformation of myositis ossificans. The paucity of convincing reports in the literature is testament to the rarity of this event.

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This paper will be judged for the Resident Writer's Award.