Case Report

Multifocal Xanthoma of Bone

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ABSTRACT

We report a case of a 40-year-old woman with hyperlipidemia and associated multifocal xanthoma of bone requiring prophylactic fixation of her bilateral femurs. Although xanthomas of bone are themselves a benign process, their presence may indicate that the patient has poorly controlled lipids and is at an increased risk of cardiovascular disease. Lytic lesions may require prophylactic fixation to prevent pathologic fracture.

Xanthoma of the bone is a rare form of xanthoma involving the axial and appendicular skeleton in association with aberrant lipid metabolism. These xanthomas are rarely reported in the literature with predominant involvement of the craniofacial regions. A characteristic of xanthomas of the bone includes inflammatory cell infiltrates including lipid-laden histiocytes and scattered multinucleated giant cells. Non-specific clinical manifestations and non-specific imaging including cystic parenchymal enhancement on magnetic resonance imaging (MRI) and CT make the differential diagnosis difficult (Figure 1, A–D). A presumptive diagnosis is based on serum-lipid panels displaying characteristics of dyslipidemia with an associated clinical bone involvement on imaging. In addition, bone biopsy remains the standard when confirming the diagnosis of xanthoma of bone. In this report, we describe a woman with an impending femoral shaft fracture leading to the diagnosis of xanthoma of the bone secondary to hypertriglyceridemia. Informed verbal consent was obtained from this patient before completion of this case report.

Case Report

A 40-year-old woman with a history of type II diabetes mellitus and peripheral neuropathy presents to the emergency department with an insidious onset of throbbing and stabbing left thigh pain. She was complaining of back pain for 7 months, right thigh pain for 8 weeks, and left thigh pain for 6 weeks prior to admission. She reported that her pain progressively worsened without any relief from analgesics. In addition, she had a weight loss of 65 lbs in the past year. Although she reported her initial 20 lbs of weight loss was intentional, she continued to lose weight without additional effort. She also reported of night sweats. Osseous radiographic evaluation revealed bilateral impending pathologic femoral shaft fractures secondary to multiple lytic lesions. Radiographs also demonstrated bilateral humeral shaft lesions. The lesion in the right femur extended from the greater trochanter at the level of the
Figure 1

A. Radiograph showing the coronal T1 magnetic resonance imaging of the left femur demonstrating approximately 13-cm lesion in the proximal femoral shaft and associated endosteal scalloping. B. Coronal T2 magnetic resonance imaging of the left femur demonstrating approximately 13-cm lesion in the proximal femoral shaft and associated endosteal scalloping. C. Coronal fat suppression MRI of the left femur demonstrating approximately 13-cm lesion in the proximal femoral shaft and associated endosteal scalloping. D. Coronal CT image of the left femur demonstrating the fairly uniformly hypoattenuating lesion with no evidence of internal matrix and scalloping of the cortex present. E. AP radiograph of the lesion in the right femur extended from the greater trochanter at the level of the midshaft and measured approximately 21.2 cm in length causing a thinning of the inner cortex. F. AP radiograph of the lesion in the left femoral shaft with an approximate length of 9.7 cm.
midshaft and measured approximately 21.2 cm in length causing a thinning of the inner cortex (Figure 1, E). Similar characteristic lesions were also seen in the left femoral shaft with an approximate length of 9.7 cm (Figure 1, F). CT scan of her chest/abdomen/pelvis demonstrated no obvious source of malignancy. Based on radiograph, CT scan, and MRI of the left femur, no conclusive diagnosis could be made, and the differential diagnosis remained broad.

Routine inpatient laboratory serum biochemistry was predominantly normal; however, it did did reveal hypertriglyceridemia of >2,100 mg/dL, a fasting triglyceride of greater than 600 mg/dL, cholesterol of 540 mg/dL (normal < 200 mg/dL), an A1C of 11% (normal < 6.5%), and the endocrinology service was consulted to assist with management. The patient was prescribed 160 mg/day of fenofibrate, 2 g BID of fish oil, and tight glycemic control subject was prioritized.

Owing to the diffuse nature of her disease, the patient was scheduled for a needle biopsy with interventional radiology. Initial pathology report demonstrated reactive histiocytes with no obvious malignancy. It was then decided to proceed with incisional biopsy to obtain a larger specimen before fixation. The incisional biopsy was sent as a frozen specimen intraoperatively, which again demonstrated predominant histiocytic proliferation with reactive foci and no evidence of malignancy (Figure 2, A and B). Although the presentation of this patient was unusual, the needle biopsy and incisional biopsy each demonstrated similar features including predominant histiocytic proliferation with reactive foci and no evidence of malignancy. Both nonsurgical and surgical management was considered in the treatment of these lesions. A Mirel score of 11 was calculated for both the right and left femurs. As such, surgical intervention was pursued. Prophylactic intramedullary nailing of the bilateral femurs was deemed safe, based on the initial pathology, and subsequently performed before the final pathologic specimen testing (Figure 3). The lesions in her bilateral humeri were not impending fracture, and conservative management was chosen.

After the final pathologic specimen testing, a diagnosis of xanthoma of the bone secondary to hypertriglyceridemia was confirmed. She was then continued on her medication for hypertriglyceridemia and elevated A1C. After several days, the patient was discharged in good condition to an acute rehab facility. On follow-up in clinic, her triglycerides have decreased to 471 mg/dL, and cholesterol has decreased to 253 mg/dL. Radiograph obtained in clinic 6 weeks after initial presentation demonstrated some increased bony...
deploitation within the bilateral humeri. Bilateral femur radiographs demonstrated stable hardware with no change in the size of the lesions. She continues to see the hematology and endocrinology services regularly in clinic and, at the time of this report, is approximately 6 months from initial presentation.

Discussion

Xanthomas of bone are rarely reported in the literature. The lack of literature and the nonspecific presentation of this condition complicate the diagnosis. On initial presentation, the differential diagnosis for this patient included several conditions more commonly seen in an orthopaedic oncology setting. Based on the involvement of multiple bones and the radiograph appearance, polyostotic fibrous dysplasia and multiple myeloma were considered. In addition, multifocal benign fibrous histiocytoma and the more common fibroxanthoma (nonossifying fibroma) were included in the differential. CT of the left femur demonstrated a central intramedullary lesion with minimal endosteal scalloping, but no cortical breakthrough, periosteal reaction, or distinct internal matrix suggesting a benign process such as a unicameral bone cyst or an intramedullary lipoma in an atypical location. MRI examination of the left femur favored polyostotic fibrous dysplasia, although multiple myeloma and lymphoma were also suggested. Serum and urine protein electrophoresis were normal as was immunoglobulin evaluation, eliminating multiple myeloma from the differential.

Although serum biochemistry demonstrated poorly regulated lipids and diabetes mellitus, these were initially thought to be independent and without relation to the bony lesions. From the initial interventional radiology biopsy, the presence of histiocytes brought Langerhans cell histiocytosis and Rosai-Dorfman disease near the top of the differential. Again, multifocal benign fibrous histiocytoma and nonossifying fibroma were considered; however, the absence of fibroblastic spindle cells in whirled or storiform pattern and the lack of a fibroblastic connective tissue background made this a less likely diagnosis. Ultimately, it was the final pathology evaluation that allowed for confirmation of the diagnosis of xanthoma of bone. The sections showed trabecular bone with sheets of foamy macrophages and scattered multinucleated giant cells. The cells of interest were positive for CD163 (Figure 4) and negative for CD1a and S100, which strongly argued against the diagnosis of Rosai-Dorfman disease and Langerhans cell histiocytosis. The patient’s lipid profile, radiological findings, and pathological features are those of xanthoma of bone.

Although the xanthomas of bone are themselves a benign process, the presence of the associated poorly controlled lipids indicate that the patient is at an increased risk of cardiovascular disease. Although the xanthomas themselves do not increase the risk of cardiovascular disease, it is the presence of the xanthomas that should raise suspicion for notable hyperlipidemia, which is a known risk factor for cardiovascular disease.

The presence of xanthomas of bone is often associated with a history of familial hyperlipidemia, which proved to be true for our patient. Lesions, as in the discussed patient, may also present in a location and with enough cortical bone compromise that prophylactic fixation is necessary to prevent pathologic fracture. Curettage and grafting of painful lesions and tight control subject of lipids are also options for the management of this rare condition.

References