

Intraosseous lipoma. A clinical, radiologic, and pathologic study of 5 cases

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Abstract

Intraosseous lipoma is an uncommon tumor of bone with indistinct radiologic features that makes it diagnostically challenging to radiologists and pathologists. There is a need to familiarize these physicians with the radiographic and pathologic features of this lesion for the correct diagnosis. We described the radiologic and pathologic features of intraosseous lipoma in 5 women. In 4 patients, the tumors occurred in long bones, whereas in the fifth patient, the skull was involved. Patients' age ranged from 50 to 63 years. Plain radiographs of the long bones revealed well-circumscribed benign-appearing osteolytic lesions with sclerotic margins, whereas in the skull, a poorly defined lytic aggressive-looking lesion was observed. In the long bones, the lesions showed remodeling of the affected bone with matrix calcification, simulating bone infarcts. Microscopically, mature adipose tissue with fat necrosis, absence of hematopoietic elements, and dystrophic calcification corresponding to the calcified matrix seen on the plain radiographs were seen. The osteolytic skull lesion had large caliber thin-walled vasculature with occasional fibrin thrombi mimicking intramuscular hemangiomas of soft tissue. On plain radiographs, an intraosseous lipoma is usually seen as a rather benign-appearing osteolytic bone lesion with well-defined margins and a heavily calcified/ossified dense matrix. Plain radiographs alone cannot establish the diagnosis of intraosseous lipoma as it mimics several other benign and malignant bone lesions. Intraosseous lipoma often contains calcified necrotic fat with little mature adipose tissue and characteristically induces expansion/remodeling of the affected bone.

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1. Introduction

Although intraosseous lipomas are considered rare benign lesions of bone accounting for less than 0.1% of primary bone tumors [1-3], in recent years, an increasing number of cases of this disease have been reported, and the real incidence of the disease seems higher than previously recognized [4-7]. However, most of the present knowledge about this distinct entity is based on single-case reports. In addition, the histopathologic findings of this disease have been infrequently described in most of the published series.

Intraosseous lipomas are composed of mature adipose tissue devoid of hematopoietic elements with variable quantities of fibrous and vascular tissue, often showing areas of fat necrosis and calcification. Because of its significant histologic variations, due to variable stages of involution as proposed by Milgram [8], intraosseous lipoma is frequently confused histologically or radiologically with fibrous dysplasia, enchondroma, osteoblastoma, chondrosarcoma, bone cyst, and bone infarct [4,8-10]. Plain film radiography may suggest the diagnosis of intraosseous lipoma, but it can be nonspecific and would not discriminate other entities [11]. In contrast, either magnetic resonance imaging (MRI) or computed tomography (CT) can establish the diagnosis; thereby, the correct management can be planned with certainty [7,11-13].

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Table 1
Summary of clinical and radiologic data

Case	Age/sex	Presenting symptoms	Radiologic finding	Radiologic impression	Treatment	Follow-up
1	50 F	Incidental finding	Right parietal bone lytic lesion with poorly defined margins	Osteomyelitis, metastasis, or eosinophilic granuloma	Excision	Well—4 years
2	59 F	Right leg pain	Right proximal femur well-circumscribed radiolucency with sclerotic edges	Fibrous dysplasia	Curettage	Well—7 years
3	63 F	Right ankle pain	Right distal tibia well-circumscribed radiolucency. Mild expansion of the bone. Areas of calcification	Intraosseous lipoma	Curettage	Well—5 years
4	57 F	Incidental finding	Well-defined radiolucency in diaphysis of left tibia	Bone infarct, chondroid neoplasm	Curettage	Well—3 years
5	63 F	Incidental finding	Well-defined radiolucency in left proximal fibula	Bone infarct, chondroid neoplasm	Curettage	Well—4 years

We describe clinical, radiologic, and pathologic features of 5 patients presenting with intraosseous lipoma, involving the long bones in 4 cases and the skull in 1, the latter with an unusual radiologic presentation.

2. Materials and methods

Five cases of intraosseous lipoma were found after searching the surgical pathology files at the Department of Pathology at MD Anderson Cancer Center, Houston, TX (n = 2), and the Department of Pathology at the University of Texas Medical Branch at Galveston, Tex (n = 3). Patients' age, sex, symptoms, site of involvement, and treatment were obtained from the patients' medical record. Imaging studies were reviewed and evaluated for lesion location, size, marginal sclerosis, calcification, and bone expansion. The diagnosis of intraosseous lipoma was made by the combination of characteristic radiologic and histopathologic findings.

The tissues received from the surgical operations were routinely fixed in neutral buffered formalin, decalcified in diluted formic acid, and stained with hematoxylin and eosin.

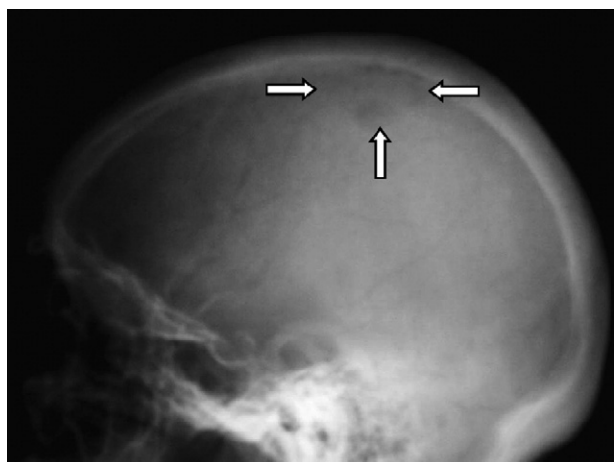


Fig. 1. Patient 1. Radiograph of the skull. A poorly defined lytic lesion involving the right parietal bone is seen (arrows). This lesion mimics an aggressive disease such as osteomyelitis, metastasis, or eosinophilic granuloma.

Immunostains for CD31 (clone JC70A; Dako, Carpinteria, CA) was performed on case 1 using the avidin-biotin peroxidase complex amplification/detection system with diaminobenzidine as the chromogen. A weak hematoxylin counterstain was further used. Follow-up information was obtained directly from the medical records, patients, or relatives.

3. Results

The clinical and radiologic features are summarized in Table 1. The patients' age ranged from 50 to 63 years, and



Fig. 2. Patient 3. Lateral radiograph showing a well-circumscribed radiolucency in the right distal tibia with prominent and extensive central calcification.



Fig. 3. Patient 3. Magnetic resonance imaging study displaying a large well-demarcated lipoma involving the right distal tibia with prominent calcification.

all 5 patients were female. Two patients presented with bone pain, whereas 3 were asymptomatic, and the lesions were detected incidentally. None of the 5 patients had any diseases known to be associated with bone infarction such as irradiation, storage disease, occlusive vascular disease, collagen diseases, infections, lymphoproliferative disorders, and corticosteroid therapy. Four cases occurred in the lower

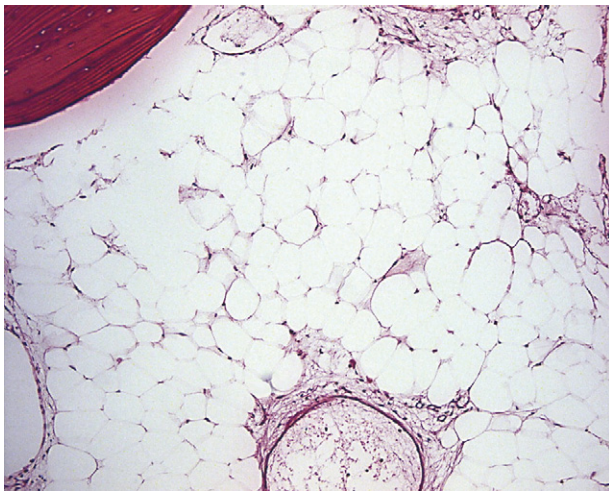


Fig. 4. Patient 1. Mature adipose tissue devoid of hematopoietic elements with prominent large caliber capillary-like vessels (hematoxylin and eosin, original magnification $\times 400$).

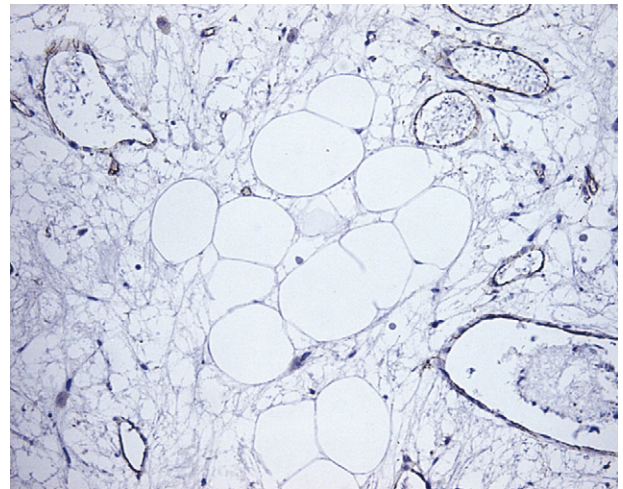


Fig. 5. Immunohistochemical staining of case 1. The capillary-like vessels stain with antibodies against CD31 (original magnification $\times 400$).

limbs (right proximal femur, right distal tibia, left tibial diaphysis, and left proximal fibula), and 1 case presented in the skull (right parietal bone).

Plain films of the long bones in 4 patients revealed well-circumscribed lytic lesions with mild bony expansion in 1 case. In 3 cases, peripheral rims of sclerosis were noted and 1 case contained areas of calcification. In 1 case (case 1), a lytic lesion with poorly defined margins was observed in the skull (Fig. 1). The lesions in the long bones showed remodeling with variable matrix calcification/ossification, simulating bone infarcts (Fig. 2). Computed tomography revealed a well-circumscribed radiolucency with sclerotic margins and no recognizable matrix in the intertrochanteric region of the right femur in case 2. Magnetic resonance imaging in this case showed low to intermediate magnetic resonance signal intensity of the T1-weighted sequence and a high magnetic resonance signal intensity of the T2-weighted

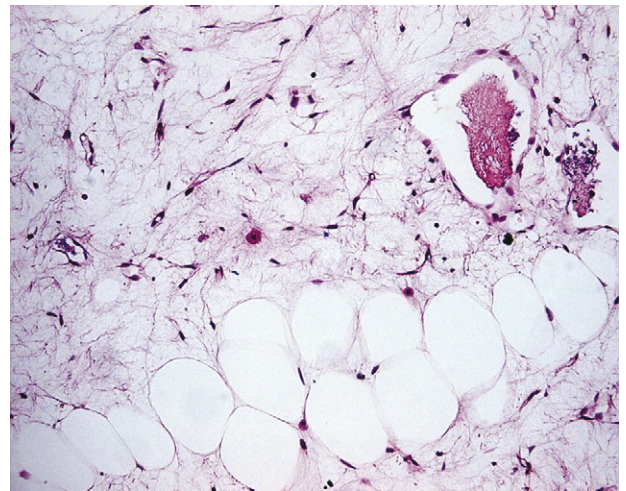


Fig. 6. Patient 1. Some of the vessels contain eosinophilic fibrin-like material. They appear as fibrin thrombus on hematoxylin and eosin sections (original magnification $\times 400$).

sequence, which were interpreted as nonspecific. No extra osseous extension to this lesion was documented. One patient (case 3) had a history of endometrial cancer. A radionuclide bone scan performed on this patient demonstrated no increased uptake of radiotracer in the tibia at the site of intraosseous lipoma. Magnetic resonance imaging of this patient revealed mostly fat signal on all pulse sequences with minimal amount of enhancement in the center of the lesion, possibly representing inflammatory changes due to necrosis (Fig. 3). No involvement of the cortex or the overlying soft tissues was present. Radiologic differential diagnoses included fibrous dysplasia, lipoma, chondrosarcoma, and bone infarct. In case 1, the lesion in the right parietal bone on plain radiographs was purely lytic with poorly defined margins suggesting an aggressive lesion, such as osteomyelitis, metastasis, or eosinophilic granuloma. A radionuclide bone scan revealed no increase in uptake of the radiotracer in the lesion.

3.1. Pathology

Macroscopic examination of the resected specimen from case 1 showed a 4.6-cm yellow, lobulated, well-circumscribed mass of adipose tissue. The remainder of the specimens was the product of curettages.

Histopathologic examination of the resected and/or curetted lesions in the long bones of these patients revealed a spectrum of morphological changes. The lesion from the skull (case 1) consisted of sheets of mature adipocytes with prominent thin-walled, large caliber, capillary-like vessels (Fig. 4) and focal areas of myxoid degeneration. Immunohistochemical stain for CD31 confirmed that these were indeed thin-walled vessels (Fig. 5). Some of the vessels contained eosinophilic fibrin-like material that appeared as fibrin thrombus on hematoxylin and eosin sections (Fig. 6). At the periphery of the lesion, there were areas of calcification

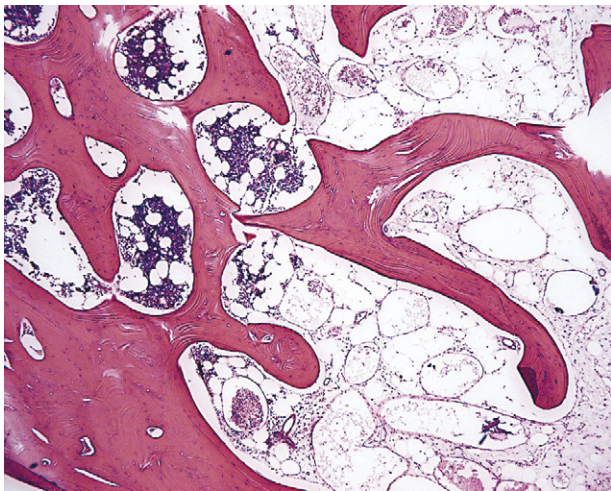


Fig. 7. Patient 1. At the periphery of the lesion, normal-appearing bone marrow elements form an interdigitating zone with the fat lobules of the tumor among thin trabeculae of lamellar bone (hematoxylin and eosin, original magnification $\times 200$).

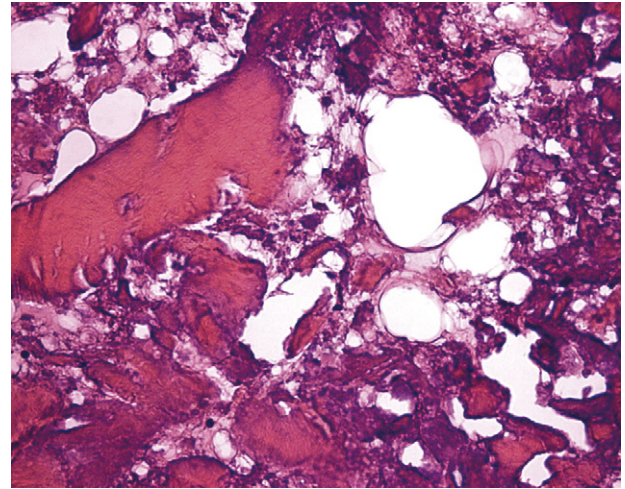


Fig. 8. Curretted lesion reveals an area of dense dystrophic calcification with ghost outlines of necrotic adipose tissue, aggregates of eosinophilic material, and absence of hematopoietic elements (hematoxylin and eosin, original magnification $\times 400$).

mixed with necrotic tissue, but with little or no adipocytes. No reactive new bone formation or sclerosis was present. However, at the periphery of the lesion, normal-appearing bone marrow elements were noted forming an interdigitating zone with the fat lobules of the tumor among thin and atrophic trabeculae of lamellar bone (Fig. 7). These changes corresponded to stage 1 of Milgram's classification [8].

In the long bones, the curretted lesions showed similar histopathologic features consisting of occasional mature adipose tissue with extensive fat necrosis, dystrophic calcification, aggregates of eosinophilic material, and absence of hematopoietic elements (Fig. 8). The areas of fat necrosis contained trabeculae of viable bone and secondary calcification/ossification corresponding to the calcified matrix of these lesions observed on radiographs.

4. Discussion

Intraosseous lipoma is regarded as a rare benign lesion of bone, accounting for less than 0.1% of primary bone tumors. However, Chow and Lee [4] have reported a higher incidence in their institution (2.5%). This difference in incidence can be partially explained by an increased awareness of this disease. Although males are reported to be more frequently affected than females with a ratio of approximately 1.6:1 [8], this difference in sex incidence of intraosseous lipomas is controversial, with some series reporting no sex predilection. Interestingly, all our 5 cases were females. This is probably due to the small number of cases in our study, because large series recently published showed nearly equal sex distribution of the intraosseous lipomas [7]. Most of the intraosseous lipomas are asymptomatic being incidental findings during radiologic evaluation for other complaints. Localized mild pain may be present in some patients. It is not unusual for pain to be referred to the adjacent joint. Three of our patients were

asymptomatic, and 2 of the 5 cases presented with pain at the site of the lesion. Most often, intraosseous lipoma appears as a benign well-defined osteolytic lesion on plain radiographs with sclerotic borders in almost all cases [3,5-8]. The intramedullary lesion may, at times, mildly expand/remodel the original contours of the bone with resorption of the endosteal cortical surface. Areas of heavy calcification and ossification within its matrix are often seen [3,5-8]. The radiologic differential diagnosis is extensive and includes bone infarct, fibrous dysplasia, enchondroma, osteoblastoma, chondrosarcoma, and simple bone cyst [4,8]. Rarely, the lesion may appear aggressive as purely lytic with ill-defined margins, mimicking osteomyelitis, metastasis, or eosinophilic granuloma, and rare cases with extraosseous extension of the lesion have also been described [14]. A radionuclide bone scan is usually negative or may be mildly positive, and is nondiagnostic [11]. Although the diagnosis of intraosseous lipoma may be difficult on plain radiographs alone, either CT or MRI is useful in detection of fat within the lesion, allowing for a more accurate diagnosis. However, in the presence of heavy calcification and ossification within the tumor (Milgram's stage 3 lesions), difficulty may arise to correctly diagnose these lesions even on CT and MRI because most of the normal fat within the lesion is replaced with dystrophic changes [6]. Computed tomography and MRI can show the extent of the lesion and delineate the tumor matrix. These imaging modalities can also detect any cortical involvement and soft tissue extension. Most of the intraosseous lipomas are solitary lesions involving most frequently the calcaneus and the metaphysis of long bones (especially, the femoral neck) [4-8]. They have also been described involving other sites, such as skull, vertebrae, maxilla, pelvis, and ribs [15-19]. Only a few cases of multiple intraosseous lipomas have been reported [20,21].

Intraosseous lipoma in the skull is especially rare, and only 5 such cases have been reported in the literature [8,15,22]. Our current case had a unique radiologic appearance that suggested an aggressive lesion and leads to its surgical resection. The normal bone marrow and the degenerated areas at the periphery of the lesion form an interdigitating zone on histopathology, accounting for the ill-defined border of the lesion on the plain radiographs. Although a delicate fibrovascular pattern may be seen in intraosseous lipomas, the presence of large caliber capillary-like vessels within this skull lesion was quite unique. Some of these vessels contained eosinophilic material, which appeared as fibrin thrombi. How this change contributed to the involution of the intraosseous lipoma is not known. Interestingly, this lesion was histologically more reminiscent of an angioliipoma arising in soft tissues with secondary calcification and/or ossification and with little mature adipose tissue.

The exact nature of intraosseous lipomas is still controversial. Many authors have regarded these lesions as benign tumors of the medullary adipose tissue [1,4,10]. Other authors have proposed that intraosseous lipomas are reactive changes secondary to infarcts, infections, or the

result of healed bony infarcts secondary to trauma [23]. However, none of these theories explains adequately the genesis of intraosseous lipomas. Future cytogenetic studies may resolve these issues because lipomatous neoplasms are characteristically associated with specific chromosomal abnormalities [24]. Recently, several authors have demonstrated that parosteal lipomas and lipomas of soft tissue share similar genetic findings, including the translocation $t(3;12)(q28;q14)$ [25,26].

The paucity of specific histopathologic features of an intraosseous lipoma usually poses a challenge to pathologists. Milgram proposed that the histopathologic features of intraosseous lipomas are due to involutional changes, and he subdivided intraosseous lipomas into 3 stages according to their histologic appearances: In stage 1, the lesions consist of sheets of adipocytes without distinctive abnormal cytologic features (normal fat). In stage 2, the lesions are composed partly of viable adipocytes and partly of fat necrosis and calcification. In stage 3, the lesions exhibit extensive fat necrosis, calcification, cyst formation, and reactive peripheral or intralesional ossification, with occasional aggregates of viable fat cells [8]. Thus, the stages 2 and 3 lesions are most frequently confused with bone infarct histologically. Recently, Chow and Lee [4] suggested that the involutional changes in intraosseous lipomas are secondary to a state of ischemia caused by increased intramedullary pressure and the growth of the tumor with compromise of blood supply at the capillary level [11].

In conclusion, intraosseous lipoma is a rare benign bone lesion that is difficult to diagnose on plain film imaging alone because it may be confused with a bone infarct, cartilaginous neoplasm, fibrous dysplasia, or other benign conditions. However, both CT and MRI are quite useful in diagnosing these lesions by their ability to show presence of fat within the tumor. Intraosseous lipomas often contain necrotic fat with little mature adipose tissue along with secondary calcification/ossification within it and, characteristically, induce enlargement/remodeling of the affected bone. Rarely, an intraosseous lipoma may present as a poorly defined lytic lesion radiologically and mimic an aggressive lesion such as metastasis, osteomyelitis, and eosinophilic granuloma.

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