Intramedullary Fat Necrosis of Multiple Bones Associated with Pancreatitis

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We describe findings of intramedullary fat necrosis on five imaging studies in a patient with alcoholic pancreatitis. Radiography and CT of extremities showed multiple osteolytic lesions that were initially considered to be metastases. However, a 99mTc-methylene diphosphonate whole-body bone scan revealed abnormal areas of increased uptake in only the bones of extremities without involvement of the axial skeleton, a distribution quite unusual for metastatic disease. Furthermore, 99mTc-sestamibi scintigraphy was essentially normal. MRI revealed findings compatible with the diagnosis of fat necrosis/infarct. Findings from bone biopsy demonstrated necrotic bone marrow without malignant cells. It may not be necessary to perform all the imaging studies described in this report when clinical features suggesting metastatic fat necrosis are present. Appearance and distribution of abnormalities on the whole-body bone scan and MRI images show that necrosis/infarct of the marrow may obviate bone biopsy, which is often needed to confirm the diagnosis of intramedullary fat necrosis and to exclude neoplastic processes.

Key Words: pancreatitis; fat necrosis; radiography; scintigraphy


Pancreatic disorders can be complicated by fat necrosis at multiple distant sites, resulting in subcutaneous nodular lesions, polyarthritis and intramedullary fat necrosis (1). Although bone involvement of pancreatic disease had been believed to occur rarely, a necropsy study showed a relatively higher prevalence of bone lesion in postmortem samples with acute pancreatitis (2). The appearance of intramedullary fat necrosis on most imaging studies can be nonspecific, especially when an individual study is interpreted alone. We describe various radiologic and scintigraphic findings that led to the correct diagnosis in a patient with clinical features suggesting intramedullary fat necrosis.

CASE REPORT
A 69-yr-old man with pulmonary emphysema was admitted for pain in the extremities that had worsened over several weeks. He had been experiencing upper abdominal discomfort concurrent with the appearance of extremity pain that partly subsided after fasting. His medical history included smoking for 35 yr and alcoholism with multiple previous episodes of alcoholic pancreatitis. Three years earlier, the patient was found to have mesenteric fat necrosis associated with pancreatitis during emergency exploratory laparotomy that was performed because of suspicion of acute intestinal infarction.

On admission, physical examination of the patient showed an emaciated body habitus and a soft, nontender, subcutaneous mass.
(7 × 3 cm) in the left deltoid area (Fig. 1). There was a focal, reddish induration on the back of the right foot similar to erythema nodosum and nontender pitting edema in both pretibial areas. Laboratory tests showed serum amylase of 1349 U/liter (normal 60–160 U/liter) and lipase of 551 U/liter (normal <200 U/liter), both of which are consistent with acute pancreatitis. Serum levels of tumor markers were within normal limits. Ultrasonography and CT of the abdomen showed a pseudocyst at the pancreatic head adjacent to the portal vein and a slightly dilated pancreatic duct (Fig. 2). Plain radiographs of the extremities obtained to evaluate bone pain showed multiple focal osteolytic lesions with surrounding periosteal reaction in the right distal radius and both calcanei, suggesting metastases (Fig. 3). CT of the right forearm revealed an irregular osteolytic lesion, but the cortical margin was relatively intact (Fig. 3). A 99mTc-methylene diphosphonate (MDP) bone scan demonstrated multiple areas of intense, irregular tracer uptake in the long bones of both extremities, both calcanei and several other tarsal bones. However, the axial skeleton was spared (Fig. 4); a distribution quite unusual in metastatic bone involvement. Technetium-99m-sestamibi scintigraphy was performed and did not show any abnormal tracer uptake in areas corresponding to abnormal uptake on the bone scan (Fig. 4). Atypical hypertrophic pulmonary osteoarthropathy (HPO) was considered to be a possible cause of the bone scan findings, although the findings were also atypical for this diagnosis. However, findings on plain radiographs and CT were not compatible with a diagnosis of HPO. MRI of the tibia revealed findings compatible with the diagnosis of fat necrosis (Fig. 5). Results from the bone biopsy of the right distal radius demonstrated necrotic bone marrow without malignant cells (Fig. 6). Bone cells were found to be relatively well preserved despite extensive necrosis of the marrow.

The administration of parenteral analgesics while fasting relieved the patient’s abdominal pain and lowered the serum levels of pancreatic enzymes. The extremity pain and abdominal discomfort improved gradually over several days. One month later, the patient was almost free of symptoms and was discharged from the hospital despite persistent radiographic abnormalities.

**DISCUSSION**

Disseminated (metastatic) fat necrosis is a syndrome in which patients with pancreatitis (two-thirds) or carcinoma of the pancreas (one-third) develop lesions that have a similar or identical appearance with nodular panniculitis (1). The exact pathogenesis of pancreatic-disseminated fat necrosis remains obscure, but it might be related to the release of lipase and other enzymes from the diseased pancreas into the bloodstream through venous or lymphatic channels (2–4). When a pseudocyst erodes into major vessels, it can allow a large amount of pancreatic enzymes into the vascular space (5). This results in direct damage to the fat cells located in subcutaneous tissue, bone marrow, peritoneum, brain,
kidney, mesentery and other distant sites reached by blood flow. Based on the identification of IgG and C3 in the affected areas, immune-mediated injury also has been implicated in the pathogenesis of fat necrosis (6). In our case, the presence of a pseudocyst in close proximity to the portal vein may explain the pathogenesis of the fat necrosis in the long bones distant from the pancreas.

The diagnosis of fat necrosis in acutely ill patients is not easy. Jackson et al. (7) proposed the following six features as those that suggest metastatic fat necrosis: (a) skin lesions resembling erythema nodosum or Bazin’s disease; (b) subcutaneous nodules tending to break down and become sterile abscesses; (c) limb pain and a tendency for the necrotic process to involve the joints; (d) tendency for eosinophilia; (e) malaise, high fever and wasting; and (f) duration of illness measured in months. Our patient had all of these features except eosinophilia.

Skeletal involvement may occur as an isolated phenomenon or simultaneously with subcutaneous nodules and polyarthritus. A necropsy study showed a relatively higher prevalence (approximately 10%) of intramedullary fat necrosis in postmortem samples obtained from 67 acute pancreatitis patients (2). However, intramedullary fat necrosis is essentially a radiologic entity and largely has been found incidentally in patients with acute or chronic pancreatitis (8). Radiographic findings of intramedullary fat necrosis include osteolytic lesions with moth-eaten bone destruction, periostitis of the tubular bones of the extremities and calcification of medullary cavities (9–13). In the carpal and tarsal bones, cystic defects and a coarse trabecular pattern can be apparent, whereas the epiphyses may be unaffected.

Bone scintigraphy of our patient revealed numerous lesions that were not apparent on the plain radiographs, as in a previously reported case (14). The appearance of individual abnormalities associated with intramedullary fat necrosis on radiographs, CT or bone scanning is nonspecific and is similar to that of malignant metastatic lesions, osteomyelitis and osteonecrosis. However, metastatic deposits typically affect axial bones containing hematopoietic marrow (15), whereas the osseous changes associated with intramedullary fat necrosis are seen predominantly in limb bones probably because distal long bones contain primarily fatty marrow. The whole-body bone scan in our patient clearly showed the distribution of the lesions; making metastatic disease unlikely.

The exclusive long-bone involvement in our patient raised the possibility of secondary hypertrophic osteoarthropathy that is commonly associated with lung cancer, chronic pulmonary  

\[ \text{FIGURE 4. Bone scan (left) demonstrates multiple areas of intense, irregular tracer uptake in the long bones of all extremities and feet. A } ^{99m} \text{Tc-sestamibi scan (right) shows normal findings.} \]

\[ \text{FIGURE 5. Coronal MR images. (Top) T1-weighted MR image shows diminished signal intensity. (Bottom) T2-weighted MR image shows areas of decreased signal intensity within a region of overall increased signal intensity in diaphysis and metaphysis of both tibias.} \]

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disease and gastrointestinal disorders. The radiographic findings did not support this diagnosis, and the appearance on the bone scan was atypical.

Technetium-99m-sestamibi has shown promise in identifying malignant bone disease and in assessing tumor response to therapy (16). In our patient, none of the numerous areas of abnormal uptake on the bone scan showed 99mTc-sestamibi uptake, which also made malignant bone disease unlikely.

MRI is sensitive for identifying early marrow changes. MRI in our patient showed diminished signal intensity on T1-weighted images and areas of decreased signal intensity within a region of overall increased signal intensity involving the medullary space of the tibiae on T2-weighted images. These findings are characteristic of intramedullary necrosis/infarct (17).

CONCLUSION

We have described findings of intramedullary fat necrosis on five imaging studies in a patient with alcoholic pancreatitis. In a patient with clinical features that suggest metastatic fat necrosis, performing all the imaging studies described in this report may not be necessary. Awareness of findings on the whole-body bone scan, including the absence of axial bone involvement, and MR images show that necrosis/infarct of the marrow may obviate bone biopsy, which is often needed to confirm the diagnosis of intramedullary fat necrosis and to exclude neoplastic processes.

REFERENCES