A 24-year-old male presented with a 5-day history of pain above the left knee with extreme tenderness to palpation. The patient's temperature is 100°F. Labs are normal except for an erythrocyte sedimentation rate of 47 and H/H of 12.5/37. Plain films (Fig. 1) of the left distal femur and magnetic resonance images (Fig. 2A, B) of both distal femurs were obtained. A bone scan was negative. *Your diagnosis?* 

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Gaucher’s Disease

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The patient was treated with supportive measures. After a few days, the temperature returned to normal and the pain resolved over a period of seven to ten days. The patient was diagnosed to have Gaucher’s disease in 1974 and has had multiple hospitalizations for bilateral thigh and knee pain.

General Features

Gaucher’s disease is a rare familial disorder characterized by an abnormal accumulation of lipid in the reticuloendothelial system. The disease affects both sexes equally and although it may occur at any age, it is particularly frequent in childhood and early adult life. The disease is most prevalent among Ashkenazi Jews, however, all other ethnic groups and races may be affected. The basis of the disease is a genetically induced (autosomal recessive) relative deficiency of glucocerebrosidase which results in accumulation of glucocerebrosides, a complex lipid.

Three forms of Gaucher’s disease are recognized. A rare infantile form is characterized by severe involvement of the central nervous system and usually terminates fatally within 18 months. The most common type spares the central nervous system and is characterized by chronic, slowly progressive visceral and osseous involvement. The disease is usually present at birth. The third type is uncommon and has its onset in childhood, with visceral and osseous involvement and mild to moderate neurological disturbances.

Clinical Features

The chronic form of Gaucher’s disease may appear at any age from childhood onward, causing variable degrees of morbidity. The manifestations of Gaucher’s disease are attributed to the accumulation and proliferation of Gaucher cells in various organs and within the bone marrow. Clinical findings include splenomegaly, less prominent hepatomegaly, weakness, fatigue, and jaundice due to anemia and hemolysis. Pancytopenia, anemia, thrombocytopenia, or leukopenia are found in varying combinations. Thrombocytopenia may cause significant, recurrent bleeding episodes. Abnormal conjunctival and skin pigmentation may be evident. Orthopedic complications include bone or joint pain, aseptic necrosis, pathologic fracture, vertebral collapse leading to kyphoscoliosis, unstable gait and skeletal deformity.

Non-specific bone pain is common and often described as a deep-seated, persistent dull ache in both thighs. Recurrent episodes lasting one to three days resolve spontaneously or following treatment with simple analgesics. Attacks resembling osteomyelitis are common. Localized tenderness, redness, swelling, and warmth are found on physical examination and fever, elevated erythrocyte sedimentation rate and polymorphonuclear leukocytosis are often present. Differentiation from osteomyelitis is difficult and episodes may last a few days or several weeks. These episodes are probably due to ongoing bone infarction. Bouts of pain and limitation of motion of joints most often occur in the hips, knees, and glenohumeral joints and reflect degenerative joint disease secondary to adjacent epiphyseal osteonecrosis and osteolysis. Diagnosis is usually established by demonstration of typical Gaucher cells on bone marrow or liver biopsy.

Radiographic Features

Radiographic findings predominate in the axial skeleton, proximal long bones and distal femur. A bilateral, symmetric distribution is frequent. Marrow infiltration by Gaucher cells results in cellular necrosis, fibrous proliferation, resorption of spongy trabeculae, and endosteal cortical erosion. Diffuse osteopenia and coarsening of the trabecular pattern represent radiographic counterparts to these histologic changes. Isolated, focal destructive lesions resembling myeloma or metastasis can also occur.
In the spine, osteopenia, accentuation of vertical trabeculae and multiple compression fractures may be evident. Kyphoscoliosis or another deformity may ensue. Other frequent sites of pathologic fracture include the proximal femora, ribs, and tibiae.3,6

Osteonecrosis of epiphyses and diaphyses is a well known complication of Gaucher’s disease. Episodes of bone crisis may simulate osteomyelitis. Areas of diaphyseal infarction are often surrounded by a subcortical layer of reactive new bone formation creating a “bone within a bone” appearance as is commonly seen in sickle cell anemia.3 Epiphyseal bone necrosis commonly involves the femoral head, humeral head, or tibial plateaus. Collapse of the articular surface leads to secondary degenerative joint disease.

Gaucher’s disease characteristically causes modeling deformities of the appendicular skeleton. In the distal femur, the Erlenmeyer flask deformity results from expansion of the bony contour, especially medially, with cortical thinning and formation of a convex, rather than concave, bony outline (Fig. 3). This deformity may be encountered in other conditions, but when it is associated with epiphyseal osteonecrosis, the diagnosis of Gaucher’s disease is strongly suggested.5

Growth disturbance at the chondro-osseous junction of the vertebral end plate is suggested as the cause of “H-shaped” vertebrae in Gaucher’s disease.7 These step-like depressions of the superior and inferior vertebral margins are also found in sickle cell anemia and other hemoglobinopathies.

Patients with Gaucher’s disease have an increased susceptibility to infection.8 The pathogenesis is unclear but it is suggested that devitalized bone with areas of hemorrhage and lipid-laden marrow elements produces an ideal environment for bacterial proliferation.5

**Differential Diagnosis**

The radiographic findings of Gaucher’s disease are encountered in many other disorders but most closely overlap those associated with the hemoglobinopathies. Diffuse osteopenia may be found in a variety of metabolic, hematologic and neoplastic disorders. Localized areas of osteolysis may resemble metastasis, plasma cell myeloma, and amyloidosis. Osteonecrosis and a coarsened trabecular pattern may be seen in sickle cell anemia and other hemoglobinopathies. Epiphyseal and/or diaphyseal osteonecrosis may be found in hemoglobinopathies, hypercortisolism, pancreatitis, caisson disease, Cushing’s syndrome, and collagen vascular disease. An Erlenmeyer flask deformity may be seen in Niemann-Pick disease, certain anemias, fibrous dysplasia, osteopetrosis, Pyle’s disease, and heavy metal poisoning.9 The combination of hepatosplenomegaly, widespread osteopenia and trabecular coarsening, ischemic necrosis, and Erlenmeyer flask deformity of the distal femurs represents the classic radiographic findings and suggests the diagnosis of Gaucher’s disease.5

**Imaging of Marrow Disease**

It is apparent that magnetic resonance imaging (MRI) will have broad application in the evaluation of musculoskeletal disorders.9 In particular, MRI is uniquely suited for the evaluation of bone marrow disease.10,11 This is due to its inherently high contrast resolution and lack of streak
artifact from thick cortical bone (which hampers evaluation by computed tomography). Normal bone marrow gives a strong signal and is clearly visualized on MRI because of its high fat content (Fig. 4). Infiltrating neoplasms of the marrow, such as leukemia and lymphoma, or disorders which result in marrow replacement with cellular material, such as Gaucher’s disease or myelofibrosis, cause a reduction in the signal. Because these cell populations contain more water than marrow fat, areas of infiltration appear darker than normal marrow. Conversely, processes that cause a decrease in the hematopoietic component of bone marrow with replacement by fat, such as aplastic anemia or radiation (Fig. 5), result in a marrow signal that may appear brighter than normal.12

In general, T1-weighted spin echo sequences are the most useful for routine evaluation of marrow.11 Such sequences produce images with higher contrast between normal marrow and infiltrating lesions than T2-weighted sequences. Moreover, T1-weighted sequences can be obtained more rapidly than T2-weighted sequences. However, in patients with marrow disorders who present with acute bone pain, T2-weighted images may be particularly useful. A recent report describes the MR evaluation of patients with painful sickle cell crisis.13 In most painful joints, focal areas that demonstrated low signal intensity on T1-weighted images, converted to high signal intensity on T2-weighted images. This was probably due to edema and suggests acute marrow infarction. Areas of old infarction or fibrosis present with low signal intensity on both T1-weighted and T2-weighted images.

The utility of MRI in the evaluation of the extent and severity of marrow involvement in Gaucher’s disease has been recently demonstrated.14 In this study, MRI revealed distinct patterns of marrow involvement in the lower extremities. The more proximal regions were affected more frequently than the distal regions and a tendency toward sparing of the epiphyseal and apophyseal regions was identified. Patients with a history of fracture or osteonecrosis revealed more extensive involvement without epiphyseal sparing and, on average, were older than...
patients without these complications.

Plain film evaluation of marrow-based disorders is limited because lesions cannot be detected unless there is extensive osteolysis of cortical or trabecular bone. This is especially true in long bones where thick cortical bone accounts for a large portion of the radiodensity. Moreover, significant bone destruction often occurs as a late manifestation of marrow-based disorders.

Radionuclide bone scans using Tc-99m methylene diphosphonate and bone marrow scanning using Tc-99m sulfur colloid may be useful in the early detection of bone infarction and in differentiating infarction from osteomyelitis. Bone marrow scans are useful in detecting changes in the distribution of hematopoietic marrow and in the diagnosis of bone marrow infarction. However, uptake of the labeled sulfur colloid is limited to the hematopoietic marrow and, therefore, in the absence of significant marrow expansion, evaluation of peripheral marrow is incomplete by this technique.

CT has found limited application in the workup of marrow disorders. It may be difficult to appreciate the difference in x-ray attenuation produced by an infiltrating process from that produced by normal marrow. A disease such as leukemia, which often produces a diffuse and symmetric pattern of marrow infiltration poses significant problems. Moreover, because of beam hardening and streak artifacts caused by surrounding dense cortical bone, evaluation of marrow in long bones by CT is often unrewarding.

References