This 20-year-old Jewish student came to the university medical center with complaints of tenderness over the right supraclavicular fossa and bilateral pain in his upper extremities. Findings of a limited physical examination included a liver and spleen palpable below the thoracic outlet; temperature, 98.0°F; blood pressure, 130/80 mm Hg; and respiratory rate, 19 breaths per minute. His hemoglobin was 11 mg/dL and hematocrit, 30%. A bone marrow biopsy detected Gaucher cells in the macrophage-monocyte system. He had a history of abdominal pain; swollen, painful joints; and fractures after minor trauma. Although he knew he had Gaucher’s disease, the student health service did not.

He said he had fallen on his left arm and shoulder 5 days earlier, and now reported pain over his right clavicle and humerus. Radiographs revealed a transverse fracture of the proximal third of the right humerus; multiple discrete lytic lucencies and honeycombing in the medullary bone; cortical thinning, irregular margins, and endosteal scalloping; and an expanded amorphous head of the right clavicle (Figure 1). Follow-up radiographs of the left humerus 2 months later revealed sclerotic changes and a large callus that was evidence of a healed fracture (Figure 2, page 14).

Some 6 months after we first saw him, he came in with severe cramping abdominal pain. An upper gastrointestinal barium examination revealed a paucity of bowel gas and a greatly enlarged spleen and liver causing medial and near vertical displacement of the stomach and small bowel. The hepatic and splenic flexures were positioned no more than a few centimeters above the iliac crests (Figure 3, page 14).

A month after that, he started experiencing pain in his right femur. Radiographs disclosed distal medullary expansion in a so-called Erlenmeyer flask deformity, a large lucency, thinning cortex, and infarcted bone with fractured segments in the soft tissue (Figure 4, page 15). The pain grew extreme over the next month, and pelvic radiographs revealed asymmetrical right and left femurs with diffuse, irregular medullary osteoporosis; multiple, discrete, lytic lesions without sclerotic margins; honeycombing in the remaining medullary bone; and endosteal scalloping in cortical and periosteal bone (Figure 5, available at FPRonline.com).
He had a right hip replacement 4 years later, and radiographs of the resected femoral head indicated changes of aseptic necrosis (Figure 6, available at FPRonline.com). He was confined to a wheelchair and thereafter lost to follow up.

Discussion

Gaucher’s disease, the most common inherited lysosomal storage disease, is caused by a deficiency of glucocerebrosidase. This enzyme works to cleave glucose from ceramide, a by-product of cell wall destruction and normal blood cell turnover. Without it, glucocerebroside accumulates in the lysosomes of macrophages in the spleen, liver, lungs, bone and bone marrow, and sometimes the brain to form characteristic Gaucher cells. The disorder is transmitted in an autosomal recessive manner so both parents must carry the genetic mutation to transmit disease to their offspring. Genetic testing can determine whether or not a person is a carrier.

Of the three major clinical types of Gaucher’s disease, type 1, or nonneuropathic, is the most common. It is also most prevalent in persons of Ashkenazi Jewish descent, but it occurs in all ethnic groups. Estimated prevalence is 1 in 40,000-60,000 worldwide.\(^1\)\(^-\)\(^3\) Distinguishing characteristics include splenomegaly, hepatomegaly, anemia, thrombocytopenia, and bone involvement, including pathologic fractures. Bone pain is the typical presenting symptom, which may sometimes occur as a bone crisis with severe pain, swelling, and fever. Ecchymoses and fatigue suggest thrombocytopenia and anemia. Bony involvement, the greatest source of disability in type 1 disease, occurs in the vast majority (94%) of patients.\(^1\)\(^-\)\(^3\) It can include abnormal remodeling (often manifest in the distal femurs as Erlenmeyer flask deformities), osteoporosis with decreased bone density, cortical thinning, and osteonecrosis. The vertebrae are also frequently involved, with proliferating cells that destroy the trabeculae and cause pathologic compression fractures. A skeletal survey is appropriate when the disease is doc-
Documented or suspected. The classic method of diagnosis was to detect Gaucher cells in a bone marrow specimen. Today, a glucocerebrosidase assay or DNA analysis is preferred, especially since pseudo-Gaucher cells can be found in other hematologic diseases. Type 1 is sometimes called the adult or chronic form of the disease, but symptoms may appear at any age. Life span of affected persons is close to normal.

Type 2, the acute neuropathic form of Gaucher’s disease, may be apparent as early as 3 months of age and progresses rapidly. Symptoms include hepatosplenomegaly, extensive and progressive brain damage, spasticity, seizures, and the inability to suck and swallow. It has no ethnic prevalence. These patients usually die between 1 and 2 years of age. Type 3 is also neuropathic but milder, less rapidly lethal, and more variable than type 2.

Until about 15 years ago, the only treatment for Gaucher’s disease was supportive and symptomatic such as splenectomy and hip replacement. Today, enzyme replacement therapy is safe and effective treatment for most patients with type 1 disease, and it also appears to have some benefit for those with type 2 disease. It has been shown to increase hemoglobin concentrations to normal or near normal within a year; improve thrombocytopenia within 2 years; decrease hepatomegaly by 30%-40% and splenomegaly by 50%-60% in 6-12 months; and reduce bone pain and crises in most patients within 2 years. Patients also report improved energy levels and quality of life. Responses appear to be sustained after 3-5 years of treatment. Another recent study found an encouraging response in bone marrow, as measured by magnetic resonance imaging, within the first year of enzyme replacement therapy. The major drawback of this therapy is its cost—upwards of $100,000-$400,000 per patient per year. There is no effective treatment for severe neurologic involvement in types 2 and 3.

**Take-home message**

Gaucher’s disease is an inherited autosomal recessive deficiency of glucocerebrosidase that causes glucocerebroside to accumulate in the spleen, liver, lungs, bone marrow, and sometimes the brain. Clinical manifestations include severe splenomegaly, hepatomegaly, anemia, thrombocytopenia, and bone involvement, which is often the most debilitating for the patient. Medullary expansion and pathologic fractures of the long bones may lead to wheelchair confinement. Although the clavicle does not contain marrow, it was involved in this patient.

### REFERENCES


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**Figure 4** This anteroposterior radiograph of the distal right femur (F) displays a large lucent infarcted area (L) of the diaphyseal-metaphyseal region, fractured medullary bone (X) displaced into the soft tissues, irregular coarse trabeculae (2 arrows) marginating multiple asymmetrical lucencies. Observe the marked thinning of the cortex (C) in the medial condyle and the Erlenmeyer flask deformity of the distal femur. T = tibia.