



POSNA

The Core Curriculum

Gaucher's disease

Objectives

1. Describe the pathophysiology of Gaucher's disease
2. Describe the most frequent orthopaedic problems associated with Gaucher's disease
3. Describe radiographic features of Gaucher's disease
4. Discuss the prognosis for Gaucher's disease

Discussion

Gaucher's disease is a lysosomal storage disease, characterized by intracellular accumulation of glucocerebroside, an important component of cell wall membranes. The accumulation of cerebroside occurs in macrophages, found primarily in the spleen, liver, and bone marrow. The enzymatic defect is a deficiency of glucocerebrosidase, and results from one or several common mutation sites, some producing more severe deficiency than others. The genetic pattern is autosomal recessive. Type I, the most common, is particularly prevalent among descendants of Ashkenazi Jews. Effects are most evident in the spleen, liver, and bones. This type has also been reported in Japanese. Type II, the acute neuronopathic type generally causes death by age 2. Type III, the chronic neuronopathic type, has features of group I with slowly progressive neurologic dysfunction.

Age of diagnosis is quite variable, and appears related to the genetic focus of the enzymatic deficiency. Common presenting symptoms are related to coagulation problems, with splenomegaly. Bone pain or fracture is an uncommon (13%) presenting symptom.

Skeletal changes have been well described, and include the classic "Erlenmeyer flask" shape of the metaphyses, especially in the distal femora; but also osteopenia, cortical thinning, avascular necrosis, and pathologic fracture. Gaucher crises are common, similar to sickle cell crisis, and also mimic osteomyelitis. They result from sudden bleeds into the marrow space, with sudden rise in marrow pressure. As a result, bone scintigraphy often reveals decreased uptake initially, followed by increased uptake during the repair phase. Steroids have been reported to alleviate symptomatology during crises. Pathologic fractures are prevalent in the lower extremities and spine, with occasional kyphosis resulting, sometimes threatening neurologic function. Osteonecrosis of the femoral heads does not appear to be as debilitating as in sickle cell disease. Favorable reports have been reported with enzyme therapy with aglucerase, with reversal of skeletal

changes reported. There presently is a Gaucher registry to better accumulate data on the condition and response to treatment, which at this point appears to be promising.

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