Bone Health Assessment of Patients with Mucopolysaccharidosis During Enzyme Replacement Therapy

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Synopsis:
In at risk populations, it is important to monitor bone development and indicators of bone health to prevent compromised bone strength and long-term complications. The mucopolysaccharidoses (MPS) are a group of lysosomal storage diseases in which glycosaminoglycans (GAG) are not degraded properly and as a result many systems, such as the skeletal system, are affected. Skeletal manifestations include growth retardation, gibbus deformity and dysostosis multiplex, which comprises a constellation of radiographic skeletal deformities such as dysplastic femoral heads and rib flaring. MPS patients also have poor bone health due to limited mobility from stiff joints and early onset of the disease before peak bone mass. Although treatments such as enzyme replacement therapy (ERT) address many aspects of MPS, the effects on bones are not well known. Our pilot study will evaluate bone growth and mineralization in MPS patients on ERT and examine the relationship between these parameters and inflammation induced by excess GAG storage. Inflammation could affect bone growth and mineralization directly by pro-inflammatory cytokine interactions between chondrocytes and osteoclasts, or indirectly through its affects on vitamin D levels, sex steroids and growth hormones.

The specific aims of our projects are:
1) To quantify the detrimental effects of MPS on bone growth and mineralization. Parameters to be assessed are:
   • bone mineral density and morphology via dual-energy x-ray absorptiometry (DXA) and peripheral quantitative computed tomography (pQCT)
   • markers of bone turnover in serum

2) To examine the relationship between inflammation stimulated by GAG storage with:
   • bone growth and mineralization
   • vitamin D levels and metabolism
   • pubertal development and endocrine function

3) To assess the long term effects of ERT in MPS patients by evaluating the same bone parameters at baseline assessment and biennially for four years.