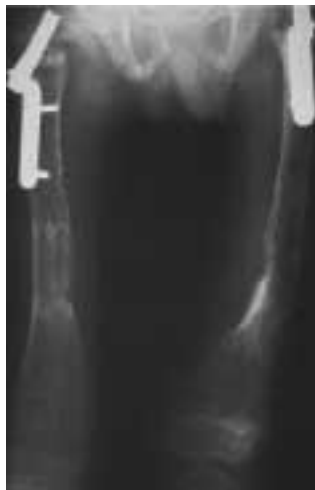


Bone Disease in Adults with Type 1 Gaucher Disease

Published in the Journal of Bone and Mineral Research, 2007 data from the International Collaborative Gaucher Group (ICGG) reveals the impact of treatment on bone disease. In this report Dr Suyash Prasad Senior Associate Medical Director, Genzyme Therapeutics, UK summarises the full clinical paper;

'This X ray picture is of the legs and hips of an adult with Gaucher Disease Type 1.

'It demonstrates the weakened structure and deformities of the thigh bones characteristic of Gauchers disease, along with surgical repair of the heads of both femur bones, where the hip joint is formed.



'Complications of the bones and joints are

common in Type 1 Gaucher disease. There is often a reduction in bone mineral density which increases the risk for bone fractures and osteoporosis in such patients. A study by Wenstrup and colleagues¹ published recently in the Journal of Bone and Mineral Research, found that therapy with imiglucerase (Cerezyme[®]) significantly increases the bone density of adults with type 1 Gaucher disease. There is some thought therefore, that achieving a normal bone density should be a therapeutic goal for people with type 1 Gaucher disease as this may prevent serious and irreversible bone complications.

'Bone disease occurs frequently amongst individuals with type 1 Gaucher disease. This occurs as a result of Gaucher cells infiltrating the bone marrow. Bone disease in Gaucher, is a considerable cause of poor health and long-term disability. Indeed skeletal manifestations may be the chief complaint in some patients, and can have greater impact on quality of life than other features of Gaucher. Common complications of bone in Gauchers include bone pain, pathological fractures (ie fractures secondary to underlying disease) and joint collapse. In children with Gaucher, bone disease may result in poor growth and delayed development.

'The infiltration of bone marrow by Gaucher cells, results in a reduction of bone

mineral density (BMD - an indicator of the strength of bone); this reduced BMD is a typical finding in Gaucher Disease. This leads to a weakening of the bone structure, and an inability of the bony skeleton to perform its anatomical and physiological functions optimally. A technique known as dual-energy x-ray absorptiometry (DXA) is the

most widely used method for assessing bone density. It is a simple technique that involves an individual receiving an extremely small dose of radioactive isotope (less than one tenth the dose of radiation of a chest x ray); the individual then lies on a firm couch, whilst a mechanical arm passes over the body and takes an image of the hips and spine.

'To determine the effect of enzyme replacement therapy, imiglucerase, on bone density in people with type 1 Gaucher disease, Wenstrup and colleagues¹ analysed data from all type 1 Gaucher adults enrolled in the International Collaborative Gaucher Group Registry, who had bone density measurements determined by DXA. Included in the study were 342 people who received imiglucerase, and 160 people who did not receive imiglucerase therapy for Gaucher disease. The analysis found that adults with type 1 Gaucher disease have an increased risk of osteoporosis compared to a healthy population. If left untreated, this risk of osteoporosis among people with Gaucher disease ranged from approximately 10 to 30% in women and 10 to 25% in men.

'In both groups (ie those that did, and those that did not receive imiglucerase therapy), at baseline, bone density was significantly lower than the normal population. In patients not treated with imiglucerase, the BMD showed no

improvement or a slight decline over time. In those treated with imiglucerase, bone density improved over time as treatment continued. This improvement appeared to be dose-dependent. That is, those people receiving the highest doses of therapy, for the longest periods, experienced the greatest increases in BMD. The results of the analysis demonstrated that those treated with imiglucerase 60 units per kg every 2 weeks (in keeping with UK licensing recommendations³), achieved a normal bone density after approximately 8 years of treatment.

'Since imiglucerase increases bone density in people with Gaucher Disease, which may lead to a decreased risk of bone complications, achieving and maintaining a normal value might be considered an appropriate therapeutic goal for adults with type 1 Gaucher disease. In contrast to other tissues in the body, bone takes much longer to grow and the turnover of cells that make up bone is much longer. Therefore, it is reasonable to assume that improvements in bone pathology and associated symptoms, may take much longer than other manifestations of Gaucher disease.

'In the management of such patients, it would be important to perform an initial assessment of skeletal involvement by DXA and/or MRI² and annual monitoring of the effects of treatment on such parameters. As always, it is appropriate to tailor therapy on an individualised patient basis, with due consideration to all aspects of disease.'

References

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2. Weinreb NJ, Aggio MC, Andersson HC, et al. Gaucher Disease Type 1: Revised Recommendations on Evaluations and Monitoring in Adult Patients. *Seminars in Hematology*. 2004; 41(4 Suppl 5):15-22.
3. Cerezyme Summary of Product Characteristics