Background

Gaucher Disease, Treatment, and Bone Involvement

Gaucher Disease (GD) is a rare, autosomal recessive, heterogeneous, inborn error of metabolism caused by a deficiency of the lysosomal enzyme acid β-glucosidase, leading to accumulation of glucosylceramide within/somes of tissue macrophages in multiple organs. Patients may present with a variety of clinical manifestations, including hepatosplenomegaly, mucocutaneous and include splenomegaly, hyperpigmentation, anemia, thrombocytopenia, diverse skeletal lesions, bone pain, and bone crises.

Enzyme replacement therapy (ERT) with exogenous acid β-glucosidase is standard of care. However, there is limited information on the long-term outcome of patients treated with ERT. This may be due to the rarity of the disease, the difficulty in maintaining long-term participation in clinical trials, and the heterogeneity of the disease.

Methods

Patient Population (N=3554)

All pediatric and adult GD1 patients enrolled in the ICGG Gaucher Registry (ClinicalTrials.gov NCT00358943) as of 07 August 2015 who:

• Had a recorded diagnosis date,
• Were imiglucerase/alpha-glucosidase-treated with a recorded treatment start date,
• Had no fractures prior to treatment and excluding imiglucerase/alpha-glucosidase discontinuation, and
• Had known splenectomy status

Analysis Strategy

Risk for first fracture (all fracture sites) was analysed using multivariable logistic regression with forward selection for all patients. Evaluated predictors were based on published research and included:

• Sex
• Time between diagnosis and imiglucerase/alpha-glucosidase treatment initiation (per 5-year increase)
• Splenectomy status
• Bone pain
• Year of GD1 diagnosis
• Bone crises
• Age at imiglucerase/alpha-glucosidase treatment initiation (per 5-year increase)
• Chitotriosidase activity

Results

Table 2: Site of first fracture for pediatric and adult patients (n=293)

For adults, spinal fractures (41%) are the most common fractures followed by femur/hip fractures (20%).

Table 3: Risk factors for total fracture among pediatric adult GD1 patients

Five factors (listed in Table 3) were significant (p<0.05) predictors of first fracture among imiglucerase/alpha-glucosidase treated GD1 patients.

Table 4: Risk factors for subset analyses: spinal fractures (all patients), all fractures (adult patients), spinal fractures (adult patients)

For adults, spinal fractures are the most common fractures followed by femur/hip fractures.

Discussion

The following set of clinical predictors have been identified for fracture risk for imiglucerase/alpha-glucosidase treated GD1 patients, particularly in adult patients:

• Splenectomy
• Longer duration between diagnosis and treatment
• Earlier age at treatment initiation
• Elevated chitotriosidase activity
• Bone pain

Can the identified predictors be combined into an overall meaningful fracture-risk score?

Are GD1 pediatric patients fractures similar to fractures in the healthy pediatric population?

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References