Name of Disorder: Gaucher Disease
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Molecular basis of Gaucher disease:

Gaucher disease (GD) is an autosomal, recessively inherited, lysosomal storage disease caused by a deficiency in the lysosomal enzyme β-glucocerebrosidase, which results in the accumulation of its substrate glucocerebroside. While the enzyme is deficient in all cells in the body, accumulation of glucocerebroside within lysosomes occurs only in macrophages referred to as Gaucher cells and are predominantly found in the spleen, liver and bone marrow. Evidently, hepatosplenomegaly, pancytopenia and bone complications can occur. Genetic studies have shown that the glucocerebrosidase gene (GBA) is located on chromosome 1q21, and more than 350 mutations of this gene have been reported as being associated with GD [1,2,3].

Symptoms of GD:

There is a broad spectrum of symptoms for GD and they may vary greatly among patients. The major clinical symptoms include enlargement of the liver and spleen, and attenuated red blood cell numbers. Attenuated platelet levels (thrombocytopenia) may also cause bruising. Skeletal abnormalities such as thinning of bones (osteopenia), bone pain and bone fractures and excessive fatigue may also be signs of GD [4,5].

Clinical features:

There are three major types of GD based on the clinical signs and symptoms. Type 1, which is the most common type of GD, often presents with abdominal pain and/or enlargement due to hepatosplenomegaly. A combination of anemia, leukocytopenia, and thrombocytopenia are also common clinical manifestations. Extensive skeletal disease, such as Erlenmeyer flask deformity of the distal femur, is the typical radiologic finding of GD. Additionally, a Pathologic fracture after falling or minor injury may be an initial presentation in some patients [4]. Clinical onset for Type 2 GD is between 3 and 6 months of age and accounts for less than 1% of cases [5]. This type of GD is the most severe, and patients exhibit systemic disorders, enlargement of the spleen and liver, and severe neurological manifestations. Type 3 is the most rare of GD and the neurological symptoms depicted are less severe than those present in Type 2 patients.

Epidemiology of GD:

Mutations in *GBA* are found at a high frequency amongst the Ashkenazi Jewish population, with an incidence of approximately 1/855 compared to 1/100,000 in other populations [6].

Prognosis and Treatment of GD:

In type 1 GD (adult form), the clinical features are extremely capricious in each patient, and within a family, various members can display diverse clinical problems. The infantile form (type 2) of GD may lead to early death. Sadly, most affected children die before the age of 5 years. Some individuals are mildly affected and can only be identified by screening or during evaluation for a chronic disease such as anemia. For others, GD can be a progressive condition. Close medical examinations and assessments are appropriate for those with GD during their lifetime [4].
Macrophage-targeted glucocerebrosidase is a specific treatment for GD. Enzyme replacement therapy with a recombinant glucocerebrosidase known as imiglucerase (Cerezyme) given intravenously is the mainstay of treatment for GD. While hepatosplenomegaly, anemia, and thrombocytopenia usually improve within 6 months, it is not effective on neurologic symptoms, as it does not cross the blood-brain barrier. In patients with severe manifestations, it is administered intravenously, typically in high doses at two-week intervals. The recommended starting dose is 60 u/kg intravenously every 2 weeks [7].

References:

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