Gauchers Disease

Gaucher’s disease is a caused by a deficiency of the enzyme beta glucocerebrosidase, which leads to an accumulation of glucocerebroside in cells and certain organs. This disease is the most common form of the lysosomal storage disease. Glucocerebroside particularly accumulates in macrophages leading to the formation of Gaucher’s cells, which are macrophages that look like crumpled tissue paper and organs including the liver, spleen, and bone marrow. Involvement of the liver and spleen causes hepatosplenomegaly, which is often painless. However, splenomegaly may decrease one’s appetite due to pressure on the stomach and also increase the risk of splenic rupture. The enlarged spleen can also lead to premature destruction of blood cells causing anemia, leukopenia, and thrombocytopenia. Involvement of the bone can cause severe pain in the joints and bones called bone crisis, often seen in the hips and knees. The accumulated glucocerebroside can also cause aseptic necrosis of the femur joint which causes a deformity of the distal femur that resembles the shape of an Erlenmeyer flask.



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Pathophysiology

Autosomal Recessive

Recessive-chocolate

Gauchers disease is inherited in an autosomal recessive modality. This means two copies of the abnormal gene must be present in order for the disease to develop.

Beta Glucocerebrosidase Deficiency

Beta-fish from Broken Glue-cerebro-guy-on-side

The enzyme beta glucocerebrosidase (also known as, beta-glucosidase) is deficient in Gaucher's disease. This enzyme has glucosylceramidase activity and cleaves the beta glucosidic linkage of the chemical glucocerebroside, which is an intermediate in glycolipid metabolism. A deficiency in this enzyme causes accumulation of glucocerebroside in macrophages and various organs.

Diagnosis

Lipid-laden Macrophages

Lips Mac-man

Due to a beta glucocerebrosidase deficiency, macrophages are unable to eliminate glucosylceramide. This leads to glycolipid-laden macrophages, which on microscopy, are called "Gaucher cells." These cells resemble crinkled tissue paper.

Crumpled Tissue Paper

Crumpled Tissue Paper

Glucocerebroside particularly accumulates in macrophages leading to the formation of Gaucher's cells, which are macrophages that look like crumpled tissue paper.

Signs and Symptoms

Osteoporosis

Ostrich-with-porous-bones

Osteoporosis occurs for multiple reasons in Gauchers disease. There are fatty deposits, which are unable to be broken down within bone, and there is an inflammatory state caused by macrophage damage. Increased IL-6 is secreted, which leads to increased bone resorption, and thinning of the bone.

Bone Crises

Skeleton Crying

Involvement of the bone can cause severe pain in the joints and bones called bone crisis, often seen in the hips and knees.

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Aseptic Necrosis of Femur

Necrosis-crow with femur

The accumulated glucocerebroside can also cause aseptic necrosis of the femur. This causes a deformity of the distal femur that resembles the shape of an Erlenmeyer flask.

Erlenmeyer Flask Deformity

Erlenmeyer Flask femur

The accumulated glucocerebroside can cause aseptic necrosis of the femur. This causes a deformity of the distal femur that resembles the shape of an Erlenmeyer flask.

Hepatosplenomegaly

Liver-and-spleen-balloons

Glucocerebroside often accumulates in the liver and spleen causing hepatosplenomegaly. Although painless, the enlargement of the spleen can decrease one's appetite due to pressure on the stomach and also increases the risk of splenic rupture. The enlarged spleen can also lead to premature destruction of blood cells causing anemia, leukopenia, and thrombocytopenia.

Pancytopenia

Pan-side-toe-peanut

Pancytopenia occurs for several reasons in Gauchers disease. Due to macrophage damage, inflammatory cytokines are released, influencing rapid red blood cell destruction. Furthermore, fatty cells infiltrate the bone marrow, impairing cell production. Finally, hypersplenism in this disease, due to Gaucher cells, increases the size of the spleen, causing pooling of blood cells outside of normal circulation.

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