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Diagnosis and Treatment for Gaucher and Fabry Disease

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Lysosomal storage disorders is caused by a deficiency of enzyme activity, resulting in the accumulation of the substrate. Therefore the clinical manifestation is dependent on where and what substrate accumulates and the treatment is based on the supply of enzyme protein with enzyme replacement (ERT), bone marrow transplantation (BMT) and gene therapy.

Gaucher disease (GD) is an autosomal recessive disorder, caused by glucocerebrosidase (GCR) deficiency. This deficiency results in glucocerebroside accumulation in cells of the reticuloendothelial system. Three clinical variants are recognized: type 1 (non-neuropathic), type 2 (acute neuropathic) and type 3 (subacute neuropathic).

Hepatosplenomegaly is a common clinical manifestation in all variants. The clinical feature of GD is a broad phenotypic expression. GD can be treated with ERT and BMT.

Fabry disease is an X-linked recessive disorder in which affected males are deficient in the α-galactosidase A (GalA). This deficiency leads to accumulation mainly in capillary endothelial cells. Three clinical variants are reported : classical type, cardiac variant and renal variant. In patients with classical type angiokeratoma, acroparesthesias, thromboembolism and progressive renal failure are the major clinical manifestations. Cardiac and renal variant are characterized by cardiomyopathy and renal failure without the clinical manifestations observed in the classical type, respectively. ERT is available in European countries. In other countries clinical trial is going on or finished.

In this lecture I will present the current status of the molecular genetics and treatment as well as therapeutic problems in these diseases.