History and Cause

The signs of Fabry disease were first identified in 1898 by two dermatologists working independently, Dr William Anderson in England and Dr Johannes Fabry in Germany. The disease (disorder) has a number of names, including angiokeratoma corporis diffusum, alpha-galactosidase A deficiency, and was for many years known as Anderson-Fabry disease, but is now usually referred to simply as Fabry disease. Further research established that Fabry disease results from abnormal deposits of a fatty substance, known as globotriaosylceramide.

Symptoms

• Burning sensations in the hands that get worse with exercise and hot weather
• Small, raised reddish purple blemishes on the skin
• Decreased sweating
• Fever
• Gastrointestinal difficulties, particularly after eating
• Some boys will also have eye manifestations, especially cloudiness of the cornea

GAMMA-LINOLENIC ACID (GLA) DEFICIENCY

*Mutations in the GLA gene cause Fabry Disease

In normal cell function Gb3 is broken down and removed from the cells or recycled. However, without the enzyme, Gb3 gradually builds up in the cells and affects their normal function. It's a bit like in a household when the trash bags containing the trash produced by the family are filled up and taken outside to the bin. If the bin is not put out for collection the trash will gradually build-up over time. Eventually they will take up all the space, leaving no room to do anything and causing lots of problems.

Treatment

Experts recommend that enzyme replacement therapy (ERT) be initiated as early as possible in all males with Fabry disease, including children and those with ESRD undergoing dialysis and renal transplantation, and in females with significant disease, because all are at high risk for cardiac, cerebrovascular, and neurologic complications.

Test and Diagnosis

In males, the most efficient and reliable method of diagnosing Fabry disease is the demonstration of deficient α-galactosidase A (α-Gal A) enzyme activity in plasma, isolated leukocytes, and/or cultured cells. In females, measurement of α-Gal A enzyme activity is unreliable; although demonstration of decreased α-Gal A enzyme activity is diagnostic of the carrier state, many carrier females have normal α-Gal A enzyme activity.

Miscellaneous

The GLA gene provides instructions for making an enzyme called alpha-galactosidase A. This enzyme is active in lysosomes, which are structures that serve as recycling centers within cells. Alpha-galactosidase A normally breaks down a fatty substance called globotriaosylceramide. Mutations in the GLA gene alter the structure and function of the enzyme, preventing it from breaking down this substance effectively.

References