FABRY DISEASE

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This condition was first described by Fabry and Anderson in 1898. Fabry disease is a rare X-linked disorder estimated to have an occurrence of 1:40,000. This means that it is a genetic condition passed from one generation to the next on the "X" chromosome. In other words it is passed from the mother to her offspring. It is also known as *angiokeratoma corporis diffusum* as well as *alpha-galactosidase-A deficiency*. The condition is due to the lack of or ineffective enzyme known as alpha-glycosidase-A. This enzyme is needed in order for the body to effectively metabolize lipids or fats. In this condition it results in the buildup of a particular type of fat known as globotriaosylceramide. When these fats are not adequately metabolized, as in Fabry disease, they will build up in the body resulting in the signs and symptoms associated with the disease. There are multiple areas of the body that are affected.

In the skin the patient will develop skin lesions called **angiokeratomas**. These lesions develop slowly as red punctate telangiectatic changes in the superficial skin. They may be flat or slightly raised. The lower part of the body and groin areas are commonly involved as are the conjunctiva of the eyes and the oral mucosa. Roughly about 2/3s of male patients and 1/3 of female patients develop angiokeratomas. In addition patients may also develop hypohidrosis or the inability to produce adequate sweat. About one quarter of male patients develop anhidrosis, the complete inability to produce sweat. This results in heat intolerance and can be quite debilitating.

The single most debilitating symptom associated with Fabry disease is pain. The patient develops significant burning pain in the extremities especially affecting the palms and soles. But there may also be pain in the abdominal area which can be misdiagnosed as appendicitis's or kidney stones. The pain is generally episodic but can last for hours with some patients complaining of chronic persistent pain in the hands and feet. The complaint of pain is often the symptom that leads to the initial diagnosis.

Other areas of involvement include organs supplied by the vasculature system including the kidneys, heart, abdominal viscera and central nervous system (CNS). The buildup of lipids in the kidneys results in proteinuria and eventually azotemia. Examination of the urine with polarized light will show characteristic 'Maltese Cross' lipid globules. Renal failure generally occurs in the 4th decade of life unless patients use hemodialysis or get renal transplantation.

Cerebrovascular involvement results in cerebrovascular accidents (stroke) with lipid deposition in the vasculature of the CNS. Because of these changes patients may develop seizures, clots, cerebral hemorrhage as well as personality changes or psychotic behavior. Heart disease develops including hypertension, chest pain due to decrease blood flow (ischemia), heart attack (myocardial infarction), congestive heart failure and even cardiac arrhythmias may develop secondary to occlusion of coronary arteries. Patients develop opacities of the cornea that typically appear whorl-like. In addition about half of these individuals may also develop spoke like cataracts.

Treatment of Fabry disease is based on enzyme replacement therapy can reverse the deposition of lipids and reverse some of the other problems associated with the condition. This may result in stabilization of kidney function, reduction of pain in the extremities and relief of gastrointestinal symptoms. However there does not seem to be any reversal of coronary vascular disease. Treatment of the pain related to Fabry disease does not typically respond well to conventional analgesic agents. There has been some success using carbamazepine and diphenylhydantoin prophylactically for pain relief.

All families who are found to have Fabry disease should be offered genetic counseling. Since it is transmitted by the "X" chromosome, women with this defective gene will have 50% of sons with the disease and 50% of daughters being carriers. If a male patient with Fabry disease has children then all of his sons will be free of the genetic defect but all of his daughters will be carriers of the condition.

This information has been provided to you compliments of the American Osteopathic College of Dermatology and your physician.