FABRY DISEASE

More than a hundred years ago, in 1898, two dermatologists, William Anderson in England and Johannes Fabry in Germany, independently reported on patients with multiple angiokeratomas as well as some other symptoms. Today, the disease is called Anderson-Fabry or only Fabry disease, or angiokeratoma corporis diffusum, the latter being more often found in dermatologic literature. Fabry disease is a rare X-linked disorder caused by deficient activity of the lysosomal enzyme α-galactosidase A, characterized by angiokeratomas in the skin, along with severe multiorgan dysfunction and premature death. The estimated incidence of this panethnic disease is 1:40,000 in male or 1:117,000 in the general population. The defective gene is located on chromosome Xq21-22 and encodes for α-galactosidae. The lack of this enzyme activity results in progressive accumulation of neutral glycosphingolipids, primarily globotriaosylceramide (Gb3), within lysosomes of cells in various organ systems, leading to a wide variety of progressive clinical manifestations in affected individuals. The accumulation of Gb3 leads to various symptoms, which appear in different periods of life. The earliest symptoms are usually pain and angiokeratomas that appear in childhood or adolescence, the progression of disease being associated with cardiac, cerebral and vascular involvement. The symptoms that can raise suspicion of Fabry disease are early stroke, left ventricular hypertrophy, hypohidrosis, renal insufficiency, acroparesthesias and angiokeratomas.

Angiokeratomas are a classic finding in Fabry disease; these are small, dark red papules, usually less than 5 mm in size, which blanch poorly on diascopy. They usually appear in adolescence and are localized in the umbilical, genital and gluteal region, on buttocks, and may also be located periorally. The lesions are called angiokeratomas, however, it is specific for angiokeratomas in Fabry disease that they lack keratosis, which differs them from other angiokeratomas.

Making the diagnosis usually takes some time, and patients visit nine different specialists on an average before the diagnosis is established. The diagnosis and treatment of Fabry disease require team work of a general practitioner, dermatologist, cardiologist, genetician, ophthalmologist, gastroenterologist, pediatrician, neurologist and nephrologist. The diagnosis can be confirmed with laboratory tests confirming α-galactosidase deficiency in plasma, leukocytes or tears.

Unfortunately, in most cases the diagnosis of Fabry disease is made in late stages of the disease. What is the advantage of early diagnosis of the disease? Discovering one patient usually leads to other family members possibly suffering from Fabry disease. Early diagnosis allows for early introduction of appropriate therapy in order to stop the accumulation of GL3 before they cause organ damage. Until recently, Fabry disease was treated with supportive measures only, but today enzyme replacement therapy is available. Infusions of agalsidase alfa or agalsidase beta result in clearance of Gb3.

To date, only one case of Fabry disease has been diagnosed in Croatia, however, the estimated number of these patients is higher. Although the symptoms from other organs pose a higher risk for the patients life, angiokeratomas on the skin are a very good marker of the disease. This fact could lead dermatologist in search for these patients because early diagnosis implies a much better prognosis *quoad vitam*.

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