Abstract Title: Difficulties in the diagnosis and challenges for Fabry disease

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Abstract: Fabry disease is a treatable X-linked lysosomal storage disorder with a wide phenotypic spectrum. It has a wide spectrum of clinical phenotypes ranging from the “classic” severe phenotype in males to totally asymptomatic females, with a group of patients in between with predominant cardiac or renal involvement or stroke presenting as “late onset” variants. In patients with the classical onset phenotype, symptoms can manifest by 3 to 10 years in boys and around 13 years in girls. While demonstration of α-galactosidase A deficiency is a definitive method of diagnosis in affected males, it fails to identify up to 60% of affected females and therefore, molecular studies of the GLA gene are the preferred diagnostic method in females. Diagnostic delays up to 15 years are described in Fabry disease due to late-onset presentations (cardiac and renal variants) and variable presentations within extended family members (stroke, renal failure, cardiomyopathy). Slit lamp examination for cornea verticillata is a cost-effective tool for early detection of Fabry disease among patients with idiopathic chronic kidney disease(CKD), hypertrophic cardiomyopathy (HCM), and cryptogenic stroke. Family screening is the most efficient way to identify asymptomatic relatives. On average, five family members are diagnosed for every proband with Fabry disease. It is ideal to include enzyme analysis for α-galactosidase A while evaluating male patients with idiopathic CKD, HCM, and cryptogenic stroke, as early identification is the key for preventing multisystem organ damage and enzyme replacement therapy or migalastat

(small-molecule pharmacological chaperone) can be started early to halt the progression of the disease and for improving the quality of life.

Area of expertise: Lysosomal storage disorders; Skeletal dysplasia