Anderson-Fabry's disease with marfanoid features

Sir,

Anderson-Fabry's disease also known as angiokeratoma corporis diffusum universale, is a disorder caused by the deficiency of the lysosomal enzyme, alpha-galactosidase A. It results in progressive deposition of uncleaved neutral glycosphingolipids, predominantly, alpha-galactosyl-lactosyl ceramide (trihexosyl ceramide), within the lysosomes of endothelial, perithelial, and smooth muscle cells, autonomic nervous system, kidneys, eyes and heart.[1] This disease is rare and was first independently described by Anderson and Fabry in 1898.[2] We present here a case with marfanoid features.

A 12 year-old male patient presented with a tingling and burning sensation along the extremities with reddish-brown eruptions on his abdomen, back, buttocks, genitals and

thighs, since last two years. The skin lesions started around the umbilicus and subsequently spread to the other sites. There was no history of consanguinity or of any similar disease in his family. There was no history of chest pain, breathlessness, oliguria, or any eye complaints.

On general examination, his blood pressure was found to be 180/90 mm of Hg. He had arachnodactyly, a high arch palate, pes cavus, pectus excavatum with an arm span that was greater than his height, and positive thumb and wrist signs, which were suggestive of marfanoid features. Multiple angiokeratomas were present on his back, around the umbilicus, genitals and thighs in a "swimming suit" pattern [Figure 1]. Ophthalmic examination showed corneal opacities, tortuous retinal vessels and limbal hypermalanosis [Figure 2]. Hemogram, liver and renal function tests, and X-ray of the chest were normal. Electrocardiogram showed left ventricular hypertrophy and his echocardiography and lipid profile were normal. Routine urine examination and 24 hour urine showed proteinuria. Examination of the urinary sediment by polarizing microscopy showed birefringent, lipid-containing cells with the "Maltese cross" pattern [Figure 3]. Histopathology of the skin lesions showed features of angiokeratoma. Due to the lack of facilities however, specific tests to detect alpha-galactosidase-A deficiency and urinary ceramide trihexoside could not be performed.

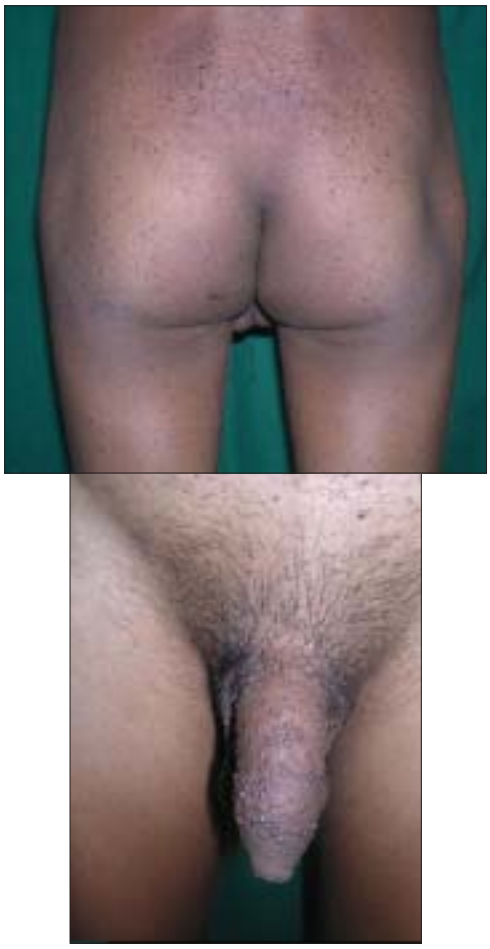

Figure 1: Multiple angiokeratomas present over shaft of penis, pubic region, thighs, back and buttocks

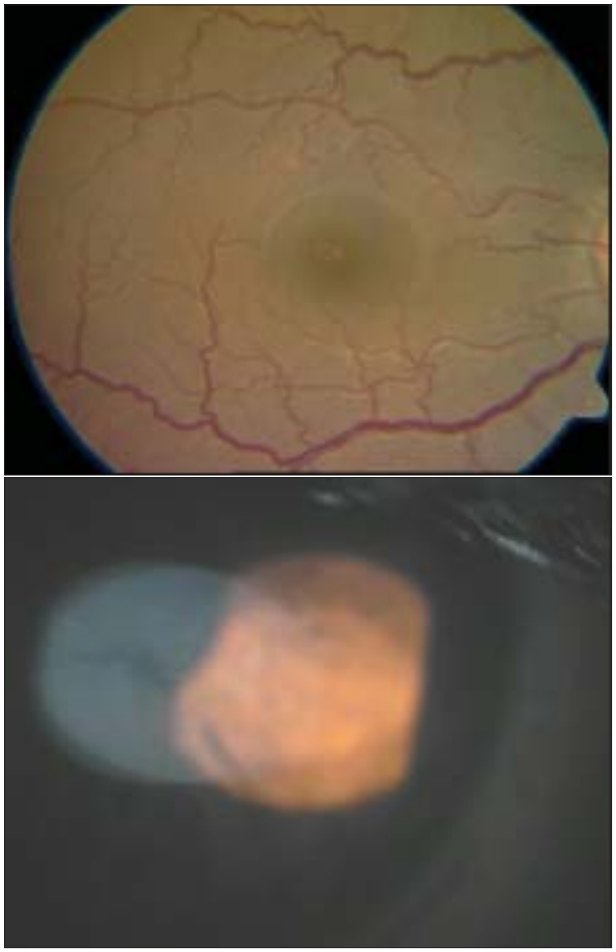

Figure 2: Ocular examination showing corneal opacities on slit lamp (bottom) and tortuous retinal blood vessels on fundoscopy (top)

Figure 3: Polarized light microscopy of urine showing "Maltese cross" pattern

The patient and parent were counseled and the patient was started on antihypertensive medications (oral atenolol and enalapril), low-dose aspirin, and oral carbamazepine, and was advised regular follow-up for cardiac and renal monitoring.

Anderson-Fabry disease is a rare, X-linked, inborn error of glycosphingolipid catabolism, resulting from mutations in the alpha-galactosidase A gene at Xq22.1.[3] The disease usually starts in early childhood and manifests with acral paresthesia. Renal pathology is one of its hallmarks and progressive glycosphingolipids deposition in the kidney results in proteinuria. During the initial stages, protein, casts, red cells, and desquamated kidney and urinary tract cells may appear in the urine. Polarization microscopy of the urinary sediment demonstrates birefringent lipid globules with the characteristic Maltese cross configuration, which was also seen in our case. Gradual deterioration of renal function and the development of azotemia usually occur in the 3rd to 4th decades of life.

The earliest ocular lesion is a diffused haziness in the subepithelial layer and later, whorl-like corneal opacities appear. Anterior capsular deposits in the lens or granular, spoke-like deposits on the posterior lens termed "Fabry cataract"; tortuosity of retinal vessels and conjunctival vein aneuysmal dilation are also found.[4] Our patient had corneal opacities and tortuous retinal vessels.

Prognosis is bad and patients usually die in their third or fourth decade of life from stroke or uremia. Treatment is symptomatic and enzyme replacement therapy can reverse substrate storage in the lysozyme.[5] To the best of our knowledge, this is the first report of association of Fabry's disease with Marfanoid features.

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