FABRY'S DISEASE (A Case Report)

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Introduction

Fabry's disease is a rare, inherited, X-linked, metabolic storage disease where, due to alpha-galactosidase A deficiency, ceramide hexoside is stored in various body tissues. Patients with classical Fabry's disease have a combination of skin lesions and involvement of certain internal organs particularly the heart, central nervous system, blood vessels, and kidneys. However, a patient with typical Fabry's disease with oligosymptomatic phenotype presents with symptoms restricted to cardiocytes or the kidney and might be diagnosed by chance during a routine endomyocardial or renal biopsy examination. We describe a young male patient presenting with mild proteinuria where diagnosis could be made only by electron microscopic study of renal biopsy specimen.

Case Report

A 26-year-old male presented with a history of facial puffiness of 10 months duration. The facial puffiness was more in the mornings and was increasing progressively. He had no other systemic symptoms such as acral pain, paraesthesia, febrile episodes, arthralgia, myalgia or gastrointestinal symptoms. The 30-year-old brother of the index case had undergone renal transplant for chronic renal failure 2 years earlier. The transplant was rejected in the immediate post-operative period and the patient died subsequently.

Physical examination revealed a well built man who appeared to be in good health. On examination there was edema over the face and feet. Pulse was 78/min and blood pressure 130/80 mmHg with no postural drop. Examination of the other systems showed no abnormality. Investigations showed haemoglobin to be 11.2 g/dL. The WBC count was 4500/mm³, blood urea 40 mg/dL, serum creatinine 1.6 mg/dL. Urine examination showed mild proteinuria and urine sediment contained 5-10 RBC and 3-5 WBC per high power field. Twenty four hour

urinary protein was 290 mg. A chest radiograph showed no abnormality. The patient underwent a renal biopsy and histopathologic examination of the biopsied tissue showed the epithelial cells in the glomeruli and tubules to be enlarged and containing multiple uniform vacuoles. These vacuoles gave the cells a foamy appearance suggestive of a storage disorder (Fig 1). Electron microscopic study was conducted for definitive diagnosis. This showed characteristic lamellated, whorled, osmiophilic inclusions commonly called myelin or zebra bodies. These inclusions were seen in renal epithelial, endothelial, and mesangial cells (Fig 2). Based upon the characteristic ultrastructural features a diagnosis of Fabry's disease was made.

Slit lamp examination of the eyes, done subsequently, revealed dilated and tortuous retinal and conjunctival vessels and corneal sub-epithelial opacities. Dermatologic examination showed no skin lesions.

Discussion

The disorder designated as Fabry's disease, Anderson - Fabry disease, or alpha-galactosidase A deficiency was described almost simultaneously by Anderson in England and Fabry in Germany in

Fig. 1 : Renal biopsy showing foamy appearance of epithelial cells in the glomeruli (HE, 40x).

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Fig. 2 : Electron microscopic photograph of glomerular visceral epithelial cell with lamellated deposits (original magnification 5000x).

1898 [1,2]. It is an X-linked disorder that is highly penetrant in the hemizygote. The biochemical defect is defective activity of the lysosomal enzyme α -galactosidase A leading to intracellular accumulation of ceramide trihexoside, a glycosphingolipid, which is deposited primarily in cells of blood vessels, renal epithelium, corneal epithelium, myocardium and ganglion cells of the autonomic nervous system. Less affected sites include cells of the monocyte macrophage system of the liver, spleen, bone marrow and lymph nodes [3]. The involved viscera show vacuolation of the cytoplasm of certain cells due to the stored lipid.

Patients present with renal dysfunction beginning with mild proteinuria (0.5-2.0 g/24h) usually in the 3rd decade of life. Uremia and hypertension develop in the 4th and 5th decades [4]. Our patient also presented with only mild proteinuria.

The cutaneous abnormalities, i.e. angiokeratoma appear between the ages of 10 and 20 years. The skin lesions take the form of purple or dark-red spots or slightly elevated papules. They tend to occur in clusters. They are seen in the distribution of the belt line, abdomen, buttocks, hips, genitalia and upper thighs. However, similar skin abnormalities may occur in other enzyme deficiencies and may even be absent in Fabry's disease [5,9] as happened in our patient. Other manifestations in-

clude acral paraesthesia, hypohidrosis, ischemic cerebrovascular disease and cardiac manifestations.

Corneal opacities, known as corneal verticillata, are seen in virtually all hemizygotes. Other ocular findings include dilated and tortuous retinal and conjunctival vessels, lid and retinal edema, and posterior capsule cataracts [6].

Untreated cases die of uraemia, many by the age of 42 years. Several therapeutic modalities, including renal transplantation, have been tried without much success. Although transplanted kidneys may not improve the systemic manifestations of Fabry's disease but long-term function and amelioration of end-stage renal disease has been reported [7].

The patient now reported differed from those with classic hemizygous Fabry's disease in several aspects. The most conspicuous difference was the absence of the full spectrum of clinical signs and symptoms. Several atypical variants of Fabry's disease have been reported in hemizygous males. In these atypical patients lipid storage is restricted solely to cardiocytes or the kidney [8,9]. Diagnosis of these oligosymptomatic or monosymptomatic disease variants is often made incidentally during routine endomyocardial or renal biopsy examination [10]. In the present case, Fabry's disease was never suspected before pathologic examination of the renal biopsy was performed. This case exemplifies oligosymptomatic Fabry's disease.

In conclusion, Fabry's disease rarely presents with a typical oligosymptomatic phenotype and should be considered as one of the causes of mild proteinuria in young men.

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