Renal involvement in an Anderson-Fabry heterozygote

A 34 year old Algerian woman with no history of consanguinity was referred to the nephrology service in 1998 with oedema, proteinuria (3.5 g/24 hours), and hypoalbuminaemia (28 g/l). These abnormalities were identified immediately before pre-eclampsia precipitated the delivery of a healthy boy by caesarean section. Previously, a healthy girl had been delivered by caesarean section because of failure to progress in the second stage of labour in 1993. The patient’s past medical history included four earlier miscarriages, a deep venous thrombosis, homozgyosity for the factor V Leiden mutation, antinuclear antibodies, and a patent foramen ovale. After delivery the proteinuria was managed expectantly. However, four months after delivery proteinuria still remained in excess of 1 g/24 hours. Although renal function, as judged by serum creatinine, remained normal (73 µmol/l) a decision was made to undertake a kidney biopsy in the setting of persistent postpartum proteinuria, antinuclear antibodies, a documented prothrombotic risk factor, and pregnancy associated hypertension.

Light microscopy of the renal biopsy revealed non-specific findings. Segmental increases in mesangial cellularity and mesangial matrix were seen in 3/24 glomeruli sampled (see figs 1 and 2). However, electron microscopy demonstrated scattered epithelial cells within the glomeruli containing numerous laminated bodies very highly characteristic of Anderson-Fabry disease (fig 3).

Anderson-Fabry disease is a rare X-linked lysosomal deficiency of α-galactosidase A characterised by the cellular accumulation of glycosphingolipids. In addition to cutaneous angiokeratoma and a painful peripheral neuropathy affected individuals have microvascular disease of the kidneys, heart, and brain. In our case reduced levels of leukocyte and plasma α-galactosidase and the demonstration of corneal verticillata at ophthalmological examination confirmed the diagnosis of Anderson-Fabry disease. Although heterozygote female carriers of mutations in α-galactosidase A may be asymptomatic, clinical manifestations of the disease, including renal, neurological, and cardiac involvement are well recognised.

The serendipitous diagnosis of this X-linked trait has great significance in a woman with a young son. Non-invasive diagnosis of Fabry’s may be established by mutation analysis of the α-galactosidase gene, and techniques for prenatal diagnosis are available. These techniques may allow diagnosis before development of typical clinical features of Fabry’s in the patient’s son and will need to be considered in the event of a future pregnancy. Historically, early diagnosis of this condition had limited prognostic significance. However, the recent controlled trials of α-galactosidase replacement therapy in Anderson-Fabry disease are highly encouraging.

Trials have demonstrated improvements in neuropathic pain, creatinine clearance, glomerular histology, electrocardiographic abnormalities, and normalisation of cerebrovascular flow. The authors suggest that renal biopsy for unexplained proteinuria may yield unexpected findings that greatly alter the management of patients and their families.

Reference


