A clinical vignette

Anderson-Fabry disease (Angiokeratoma corporis diffusum universale)

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First described by the two eponymous dermatologists in 1898, Anderson-Fabry disease is due to an X-linked recessive inherited deficiency of the enzyme α -galactosidase A. Glycosphingolipid is deposited in the smaller blood vessels of skin and viscera, resulting in multisystem disease. The incidence is one in 40,000.

In affected hemizygous males the onset of clinical disease is often heralded in childhood by periodic attacks of severe pain and paraesthesiae in the extremities (Fabry crises). These may be precipitated by emotional or physical stress and sudden changes in temperature or humidity. The patient is often labelled as neurotic. The duration and severity of attacks usually decrease with age. The pains probably result from direct involvement of peripheral and central nerve cells. A selective loss of unmyelinated and small myelinated fibres in peripheral nerves has been observed. Lipid is also deposited in the vasa nervorum.¹

The characteristic angiokeratomas first appear shortly before puberty.² They are multiple, small (1–5 mm), dark red to blue-black, macular or papular lesions in a “swim-suit” distribution favouring the scrotum and peri-umbilical area but often involving the hips, back, thighs, penis and mucosal surfaces. They must be distinguished from the more common angiokeratomas of Fordyce which may appear on the scrotum in the second or third decade, the incidence increasing with age.³

Renal disease often presents during childhood or adolescence as proteinuria with or without red cells and casts in the urine. Renal function gradually declines with time and prior to haemodialysis and renal transplantation the mean age of death from uraemia was 42 years.⁴

Multifocal involvement of cerebral vessels may lead to focal neurological or personality changes and psychotic behaviour. Cardiac involvement is common consisting of ischaemic heart disease, cardiac failure, conduction disturbances and valvular disease. Echocardiography is indicated if a murmur is detected clinically.⁴

The diagnosis should be suspected on the basis of a typical history and skin lesions. It is supported by finding typical corneal and lenticular opacities on slit-lamp examination.⁵ Confirmation comes from skin or renal biopsy, detecting characteristic lipid-laden cells on polarised microscopy of urinary sediment, or by demonstrating reduced enzyme levels in plasma, leucocytes or cultured fibroblasts. In one series the mean age at diagnosis was 29 years.⁴

Heterozygous females often lead completely normal lives. In later life they may exhibit in attenuated form, some of the symptoms seen in affected males—infrequent pains in the extremities (10%) or scanty angiokeratomas (30%).¹ Slit-lamp examination reveals ocular abnormalities in almost all cases.⁵ Confirmation of their carrier state by histological or biochemical methods is the same as for hemizygotes.

Treatment is largely symptomatic. Pain is the most debilitating symptom. It responds poorly to analgesics but may be alleviated by phenytoin and/or carbamazepine. Renal failure necessitates chronic dialysis or renal transplantation. Patients surviving more than 10 years after transplantation often succumb to cardiac complications.

Attempts to remedy the underlying defect by enzyme replacement therapy or foetal liver transplantation have proved unrewarding. Gene replacement therapy is a theoretical hope for the future.⁴

Families of afflicted individuals should be offered screening for heterozygotes and genetic counselling. Pre-natal diagnosis by chronic villous sampling or amniocentesis is possible allowing the option of abortion of a male foetus.

Specialists in genitourinary medicine need to be

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aware of this serious multi-system disease which may present as a genital dermatosis. They must be vigilant lest cases are overlooked in their clinics.

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