Fabry’s Disease

A 30 year old man, born to non consanguineous parents presented with history of reddish skin lesions all over the body since childhood. He also complained of severe neuropathic pain over the extremities especially during summer which was associated with intermittent fever and pedal oedema. There was no history of abdominal or renal colic, angina or seizures. There was no family history of similar illnesses.

On examination his blood pressure was 100/80 mm of Hg. He had bilateral pitting pedal oedema. Cutaneous examination revealed telangiectasias over the face with multiple petechiae and purpuric papules seen over the trunk, thighs and the palms and soles (Figs. 1 and 2). Similar lesions were seen over the lips, tongue, cheek mucosae and anterior pillar of fauces. Multiple angiokeratomas were seen over the scrotum and penis. Examination of the eye showed dilated and prominent conjunctival vessels and vortex keratopathy (Fig. 3).

On investigation he was found to have significant proteinuria of 1.96 g/day. Urinary sediments under light microscopy showed ‘mulberry like’ cells (Fig. 4). Ultrasonogram revealed grade 2 renal parenchymal disease and renal biopsy showed focal and segmental glomerulosclerosis.

Light microscopy of the skin lesions showed angiokeratomas with cytoplasmic vacuolation in the endothelial cells (Fig. 5).

A presumptive diagnosis of Anderson Fabry disease was made on the basis of characteristic diffuse angiokeratomas (angiokeratoma corporis diffusum) with vacuolated endothelial cells on light microscopy, vortex keratopathy and typical ‘mulberry’ cells in urine microscopy. Measurement of alpha-galactosidase activity and electron microscopy could not be done in this patient.

Anderson Fabry disease, an inborn error of glycosphingolipid metabolism, results from the defective activity of the lysosomal enzyme, alpha-galactosidase A. This enzymatic defect is transmitted by an X- linked recessive gene and leads to the progressive deposition of neutral glycosphingolipids (predominantly globotriaosylceramide) with terminal alpha-galactosyl moieties, which accumulates within the vascular epithelium, heart, kidneys, cornea, and other tissues, causing angiokeratomas, painful acroparesthesias, hypohidrosis, renal failure, cardiac and cerebrovascular disease and ultimately leading to early death. Management is usually symptomatic. Painful crisis may respond to phenytoin, gabapentin or carbamazepine. Early use of antiplatelet agents may mitigate embolic or thrombotic cerebrovascular accidents. Renal or cardiac transplantation has been undertaken for end stage disease. Enzyme replacement therapy using human recombinant alpha-galactosidase A has resulted in symptomatic improvement as well as documented reduction in globotriaosylceramide deposits.

Angiokeratoma corporis diffusum have been described with other enzyme deficiencies including β-galactosidase, neuraminidase, β mannosidase, α-N-acetylgalactosaminidase and L-fucosidase.

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