CASE REPORTS

FABRY'S DISEASE

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A case of Fabry's disease (angiokeratoma corporis diffusum universale) is reported. Presence of uncommon physical features like large thick lips, large ears and abnormal skeletal proportion are high-lighted.

Key words : Angiokeratoma, Acroparaesthesia, Corneal verticillata, α-galactosidase A.

Angiokeratoma corporis diffusum universale (Fabry's disease) is a rare, sex-linked recessive disorder,[1] characterised by deficiency of the enzyme α galactosidase A. There is accumulation and subsequent deposition of the glycolipid ceramide trihexoside in the endothelium and pericytes of blood vessels, kidneys, myocardium, lungs, intestines, brain, skin and other tissues. The disorder presents with burning sensation in the hands and feet (acroparaesthesia), multiple angiomas over the genitals, lower back, upper thighs and around the umbilicus. Gradual but progressive renal failure is the common cause of death. Because of multisystem pathology and clinical symptomatology, Fabry's patient may present in the departments of neurology, cardiology, nephrology or dermatology. A case of this rare disorder is reported.

Case Report

A 19-year male student complained of generalised anhidrosis for ten years and pin-point reddish lesions over the body for six years. An extreme degree of distress and burning felt in the hands and feet was exacerbated by hot weather and exertion. Angiomas were first noted over the lower back and later on thegenitals, upper thighs and arms. The lesions subsequently became numerous and prominent. He then developed polyuria, polydypsia, anorexia and puffiness of the lower eyelids. History of unconsciousness, seizures, paresis, vomiting, malabsorption, bleeding diathesis, palpitation, headache, chest pain or edema feet was absent. There was no history of consanguinity, or similar complaints in the other family members. Examination revealed a moderately built young boy with a stooping posture and disproportionately longer upper extremities. He was afebrile, the pulse rate was 90 per minute, regular; and blood pressure in the right arm was 110/70 mm of Hg, lying down. His height, span and weight were 164 cm, 175 cm and 40 kg respectively. Face gave a dull vacant look; the anterior hair-line was low, eyebrows were bushy and confluent in the midline; lips were large and thick; and the ears were also large (Fig. 1). Front teeth were widely spaced and projected forward. There was a diffuse swelling of the gums. Skin was pale and

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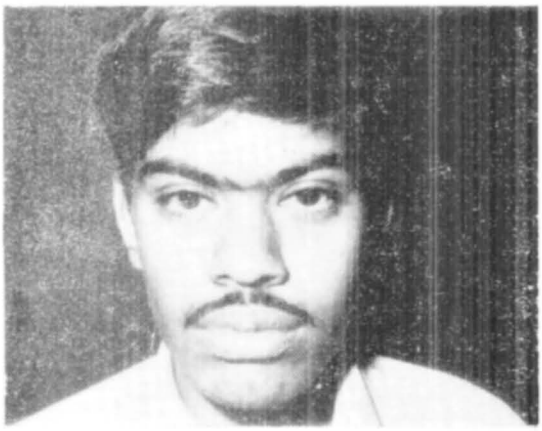

Fig. 1. Large thick lips, large ears and confluent bushy eyebrows.

dry, studded with multiple 0.3-3.0 mm, bright pink to red macules and papules present maximally on the lower back (Fig. 2), genitals, upper

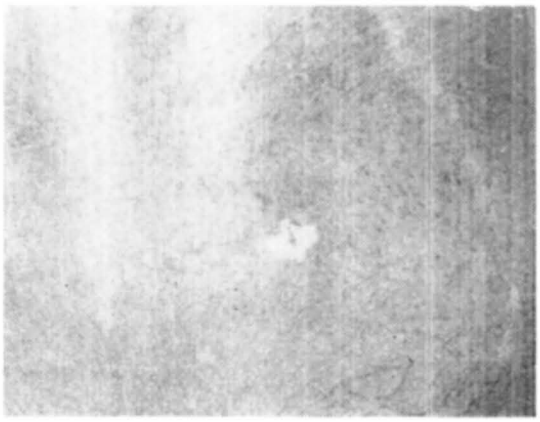

Fig. 2. Angiokeratomas on the lower back.

medial thighs, and scattered over the chest, abdomen, upper back and arms. Axillae were spared; there was no aggregation of lesions around the umbilicus. The lesions on the upper thighs were dark brown and hyper keratotic. Oral and ocular mucosae were congested but there were no definite ectasias. Genital mucosa was normal. Scalp hair were coarse, but beard, axillary and pubic hair had normal texture and pattern. Testicular volume was normal. Nails were white and convex longitudinally (turtle back convexity). Examination of the cardio-vascular, respiratory and nervous systems did not reveal any abnormality. Average IQ was 129. Ophthalmological examination showed corneal verticillata. Lens, fundus and fluorescein angiography were normal. Sun exposure and exercise failed to produce sweating, but not acroparaesthesias. Bromophenol blue test showed absence of sweating compared to the normal controls. Autonomic function tests e.g. Valsalva manoeuvere, orthostatic adaptation of blood pressure, tachycardia response to standing, hand immersion in ice water; bradycardia response to carotid massage, apnoea, and face immersion in water did not reveal any abnormality.

A 17-year-old brother was having a few angiomas 1-2 mm in size, confined to the chest and upper back. Genitals and mucosae were unaffected.

Complete haemogram, fasting and postprandial blood sugar, blood urea, serum creatinine, bilirubin, electrolytes, total and differential proteins, alkaline phosphatase, serum transaminases, calcium and inorganic phosphorus, and coagulogram were within normal limits. Urine showed albumin, granular casts, 8-10 RBC/PHF and no pus cells. 24-hours urine albumin was 600 mg. Examination of the urinary sediment under polarised light showed birefringent 'Maltese cross' crystals and PAS positive diastase resistant material which could also be stained with sudan black B. Skiagrams of the chest, abdomen, skull, hands and spine were normal.

Skin biopsies of the angiomatous papules from the patient and the other sib showed dilated channels lined by a single layer of endothelial cells, containing erythrocytes in the upper dermis (Fig. 3). Vaculoation of endothelial cells or significant cellular infiltrate were not present. Sweat glands were not encountered in

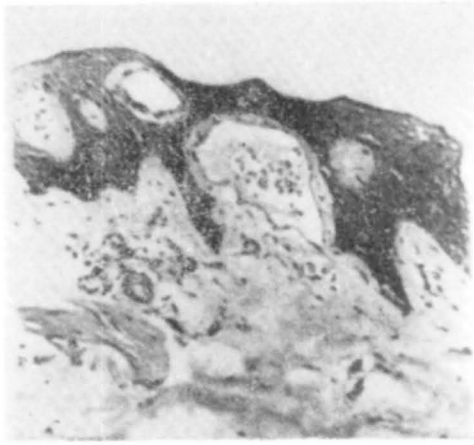

Fig. 3. Dilated vascular channels in theup per dermis, lined by a single layer of endothelial cells (Haematoxylin-eosin x 140).

any of the biopsies from the patient. Snap frozen sections of a skin lesion from both the sibs showed PAS positive diastase resistant material in the endothelial cells and pericytes of capillaries. This material also stained positively with sudan black B. Kidney biopsy from the patient showed several normal and sclerosed glomeruli. Vacuolation of the endothelial cells of glomeruli, resulting in soap-bubble appearance, was evident due to glycolipid getting dissolved during processing. This deposit stained positively with PAS (diastase resistant) and sudan black B. Granular casts were present in several tubules. Due to lack of facilities, α-galactosidase A deficiency and presence of ceramide trihexoside in urine could not be confirmed.

Comments

The present case of Fabry's disease had a peculiar stooping posture, skeletal disproportion and an abnormal facial appearance in addition to the classical features such as acroparaesthesias, angiokeratomas, corneal verticillata and renal involvement. Stooping posture and large lips were previously described by Flynn et al.[2] Skeletal disproportion and large lips and ears were reported by Gemmingen et al.[3] Anhidrosis which was the presenting feature of this case is also a well documented feature.[3-5] However, it is not clear whether anhidrosis is due to absence or the reduced number of eccrine sweat glands[19] or autonomic changes.[7] Gemmingen et al[3] reported normal eccrine sweat glands in the anhidrotic area, but found an abnormal reaction of skin to various chemical stimuli. In the present case, sweat glands were not found in any of the three biopsies studied, and clinical tests revealed no evidence of autonomic neuropathy. Thus, we tend to agree with Burkholder et al[6] that anhidrosis may be due to reduced/absent eccrine sweat glands. Premature loss of permanent teeth was reported by Fessas et al.[7] The patient under report had generalised gingivitis. However, the teeth may be lost later.

Fabry's disease is a sex-linked recessive disorder,[1] females act as carriers and males get the full-blown disease. In the family under report, mother was a carrier (corneal verticillata were present), and father was normal. Out of the three offsprings, the patient had classical features of Fabry's disease and the daughter was apparently unaffected. The second son had only a few angiomas with PAS positive diastase resistant material around capillaries in the skin biopsy, but there were no corneal verticillata or evidence of renal involvement. The findings in the family are consistent with sex-linked recessive inheritance.

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