CASE REPORT

ATYPICAL FABRY’S DISEASE
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ABSTRACT: Fabry’s disease (angiokeratoma corporis diffusa) is an X linked recessive lysosomal storage disorder caused by the deficiency of alpha galactosidase A (alpha gal A) which causes progressive accumulation of glycosphingolipids in the visceral tissue & vascular endothelium. Patients with typical Fabry’s disease usually present with characteristic cutaneous angiokeratoma, corneal dystrophy, painful acroparesthesia, cardiovascular disease & heavy proteinuria. We are reporting a 24 year old male who presented with painful acroparesthesia, occasional polyarthralgia & low grade intermittent fever since 12 years. He was found to have very low serum alpha galactosidase A levels. The nerve biopsy revealed chronic axonopathy which showed typical “zebra bodies” under electron microscope which is characteristic of Fabry’s disease. Our patient did not have angiokeratomas, corneal opacities, renal or cardiac involvement. The case is being reported for its rarity & characteristic ‘zebra bodies’ on electron microscopic study in the absence of typical clinical presentation like angiokeratoma & systemic involvement.

KEYWORDS: Fabry’s disease, angiokeratomas, alpha galactosidase, painful acroparesthesia, zebra bodies.

INTRODUCTION: Fabry’s disease is an under-recognised, X linked lysosomal storage disease. The incidence is around 1 in 50,000 males. It results from deficient activity of the enzyme A-galactosidase (a-Gal A) & progressive lysosomal deposition of globotriasoylceramide (GL-3) in cells throughout the body. The various synonyms used for this disorder are A-galactosidase A deficiency, ceramic trihexosidase deficiency, GLA deficiency, Anderson-Fabry’s disease, angiokeratoma corporis diffusum & hereditary dystopic lipidosis.

It has its onset in childhood with periodic crisis of severe pain in the extremities (acroparesthesias). The other features include vascular cutaneous lesions (angiokeratomas), hypohidrosis, characteristic corneal, lenticular opacities & proteinuria. Untreated, the disease causes gradual deterioration of renal function to end-stage renal disease, which usually occurs in the third to fifth decade of life. Cardiovascular & cerebrovascular diseases are other major causes of morbidity & mortality.

We are reporting a 24 year old male who presented with painful acroparesthesia, occasional polyarthralgia & low grade fever since 12 years. He was found to have very low serum alpha galactosidase levels. Nerve biopsy revealed chronic axonopathy with typical “zebra bodies” on electron microscopic study which is characteristic of Fabry’s disease. Patient did not have angiokeratomas, corneal opacities, renal involvement or cardiac involvement.

CASE REPORT: A 24 year old male, presented to us with a history of low grade fever, burning sensation in hands & feet since 12yrs and polyarthralgia since 6 months. Fever was low grade, evening rise of temperature, not associated with chills and rigors. It is associated with bilateral
frontal head ache. The patient also had burning sensation over soles & feet during sun exposure, temperature variations and working for some time.

**On examination:** He was febrile. No pallor. Cardiovascular, respiratory, abdomen. CNS & PNS examinations were normal.

Investigations for all infective causes of fever & all known inflammatory causes of pain were inconclusive.

Patient was investigated to rule out any connective tissue disorder. CT, MRI brain, 2D Echo were normal. ANA profile (12 screen) was also negative for ANA, p-ANCA, ds DNA. Bronchoalveolar lavage was also normal. Bone marrow biopsy revealed normal marrow. EMG & nerve conduction study was normal.

Fundus showed papilledema with conjunctival microaneurysm. With continued symptoms of fever & acroparaesthesia we decided to get an Alpha galactosidase estimation done. It revealed 5.80nmol/hr. (normal >60.00); which being low was suggestive of Fabry’s disease. Further nerve biopsy done showed chronic axonopathy with ultra-structural demonstration of ZEBRA bodies (figure 1 & 2) which confirmed the diagnosis of Fabry’s disease.

![Fig. 1: Nerve Biopsy - High Magnification of Vascular smooth muscle cell showing “ZEBRA BODIES”](image1)

![Fig. 2: Nerve Biopsy – High magnification of perineurium showing “ZEBRA BODIES”](image2)
DISCUSSION: The diagnosis of Fabry’s disease among children and adult is difficult in the absence of a family history. The average age at diagnosis is 23 years. Non-specific symptoms and a lack of physical findings often lead to a delay in the diagnosis of Fabry’s disease. Because of typical skin lesions (angiokeratomas) dermatologists are often the first to make a diagnosis. Average duration of onset of symptoms & diagnosis is around 10.8 years in adult males. Many patients do not have classical angiokeratomas, like in our patient. Isolated renal, cardiac or cerebrovascular symptoms manifest in some patients. Sensory neurons in spinal ganglia & small myelinated & unmyelinated fibres are affected preferentially. Ocular examinations may show tortuosity & dilatation of conjunctival vessels. Its non-specific symptoms often lead to delay in diagnosis. Limited awareness of the disease and lack of easy availability of enzyme assay also contributes to delay in the diagnosis.

Our patient did not have any classical features like angiokeratomas, visceral involvement, corneal opacity etc. which are classic of Fabry’s disease. Patient had low grade fever, painful extremities, small fibre axonal neuropathy and conjunctival aneurysms. Alphagalactosidase a Enzyme levels & electron microscopic studies confirmed the diagnosis.

So in the presence of low grade fever, acroparaesthesia of long standing duration, one should suspect Fabry’s disease as Enzyme Replacement Therapy is available now. Average life span in untreated case is about 40 yrs.

REFERENCES:
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