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Fabry's Disease: A Case Report and Review of Literature

Dr. A. V. Pitchi Reddy M. S[1], Dr. V. Raja Sekhar M. S[2]

[1]Assistant Professor of Ophthalmology, Guntur Medical College, Guntur-522001, Andhra Pradesh, India

[2]Assistant Professor of Ophthalmology, Guntur Medical College, Guntur-522001, Andhra Pradesh, India

Abstract: ***A 27 yr old male patient, pursuing his post graduation was referred from dermatology, with a chief complaint of small red raised lesions on flanks, abdomen and scrotum since the age of 12yrs. H/o present illness. Skin lesions 1st appeared - flanks 15 years back. Lesions gradually progressive - involved scrotum, thighs and medial aspects of upper arms over 6 years period. h/o lethargy and tiredness present. No h/o alterations in sweating. No h/o episodes of abdominal pain and diarrhea. No h/o intolerance to cold and heat . No h/o any growth abnormalities or developmental delay. No h/o defective vision.***

Keywords: Conjunctival vascular aneurysms, cornea verticillata, angiokeratoma, Orthohyperkeratosis, acanthosis, alpha galactosidase A, Fabry's outcome survey, Fabrazyme, Replagal.

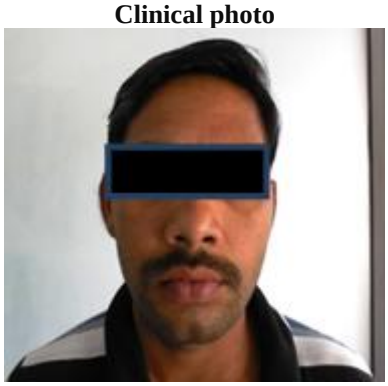
1. Introduction

a) **Past History:** burning and pricking sensation on hands and feet especially after physical stress, since the age of 5 yrs. No history of hypertension, diabetes mellitus, Coronary artery disease, cerebro vascular accidents.

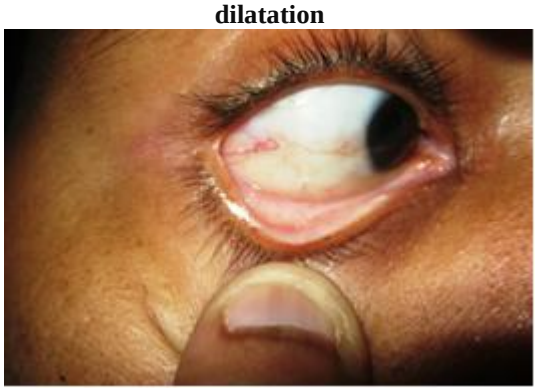
b) **Personal History:** nil

c) **Family History:** nil particular

Clinical photo



Slit lamp showing conjunctival vessel with Aneurysmal dilatation

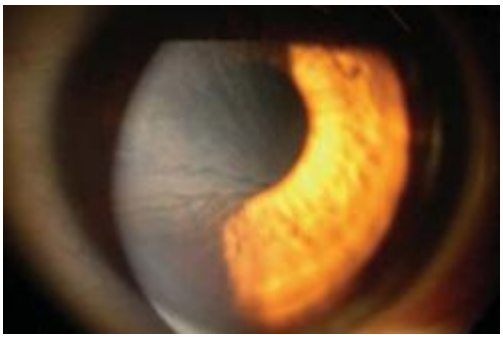


Ophthalmic examination
- Visual acuity – OD 6/6, OS – 6/6.
- Head posture, facial symmetry- normal

Extraocular movements normal
- On slit lamp examination : OU
- Conjunctiva - Aneurysmal dilatations of the conjunctival vessels present.
- Cornea – linear pigmented deposits within corneal epithelium that assume a characteristic whorl like pattern (i.e., corneal verticillata) are seen.
- A.C – normal in depth and nil contents.
- Pupils – NSRL
- Lens – transparent

Cornea verticillata -Diffuse beam

Slit view



- On fundoscopy – Normal

2. Cutaneous Examination

- Cutaneous examination revealed multiple, cherry red coloured, non- blanchable, angiomatous, raised,

hyperkeratotic lesions (1- 5 mm in size) with few cherry hemangiomas.
- They were present mostly over scrotum, upper and lateral aspects of thighs, flanks, back of trunk and upper arms.

Angiokeratomas over genital region

Angiokeratomas over skin.

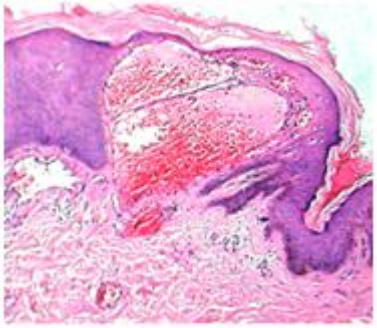
Work up
- All his blood investigations were normal.
- He had no proteinuria.
- His chest radiograph showed normal heart shadow and clear lung fields.
- Electrocardiogram was normal
- 2 D ECHO findings were normal with no increase in the size of chambers or any valvular vegetations.
- USG abdomen – normal study
- CT brain – Normal study
- No hearing impairment

HPE – H & E staining on light microscopy

a) Epidermis:
- Orthohyperkeratosis
- Irregular epidermal acanthosis
- elongated rete ridges enclosing the vascular channels.

b) Dermis: dilated thin walled congested capillaries in papillary dermis.

Histopathology of skin lesions: Showing above features



Based on history, dermatological and ophthalmological findings, examination of other family members and histopathological report of skin biopsy diagnosis of Fabry's disease was made, even though alpha galactosidase enzyme estimation was not available.

DD for cornea verticillata (1):
Aminoquinolones (chloroquine, hydroxychloroquine, amodiaquine), Amiodarone, Atovaquone, Biaxin (clarithromycin), Clofazimine, Phenothiazine (chlorpromazine), Gentamicin (subconjunctival), Gold, Ibuprofen, Indomethacin, Mepacrine, Monobenzone (topical skin ointment), Naproxen, Perhexiline maleate, Suramin, Tamoxifen, Thioxanthines (chlorprothixine, thiothixine), nlorone hydrochloride

3. Conclusion

- Ophthalmological manifestations are common in Fabry disease.
- The most specific ocular manifestations are conjunctiva vascular abnormalities, corneal opacities (cornea verticillata), lens opacities and retinal vascular abnormalities.
- These do not usually cause significant visual impairment or other ocular symptoms,
- But can nevertheless be important because they can act as markers of the disease, with diagnostic and prognostic implications.
- Being an external organ and easily investigated with minimally invasive technologies, the eye may be useful for monitoring the natural history of Fabry disease and the response to enzyme replacement therapy.
- Fabry Outcome Survey: (4)
- The Fabry Outcome Survey –provides comprehensive data on the ocular manifestations of Fabry disease.
- Cornea verticillata was the most frequently reported ophthalmic abnormality in both homozygous males and heterozygous females, and may represent a useful diagnostic marker.
- Tortuous vessels and Fabry cataracts were more frequent in males than in females.
- Vessel tortuosity was associated with a more rapid progression of the disease and may have some value in predicting systemic involvement and natural progression of disease.

4. Discussion

1) Fabry and Anderson first described angiokeratomacorporisdiffusum as a dermatological disorder in 1898.
2) Later on, Rutter and Pompen suggested it to be a possible familial systemic vascular disease.
3) In his first paper on this subject, Fabry (1898) called the skin lesions 'purpurapapulosahaemorrhagicaHebrae,'(5) suggesting that they had previously been described by Hebra, the famous Austrian dermatologist.
4) Cornea verticillata, the most typical ocular sign in Fabry disease, was first described by Fleischer in 1910. (5)
5) Franceschetti et al. (1969) reexamined a family with 'cornea verticillata' reported by Gruber (1946) and showed that Fabry disease was responsible for the corneal change.(5)

6) This deposition of glycosphingolipids - Globotriaocylceramide occurs in endothelium, fibroblasts, pericytes, heart, kidneys, autonomic nervous system and cornea giving rise to the symptoms and signs of Fabry's disease.
7) Ophthalmological manifestations are common in Fabrydisease .
8) The most specific ocular manifestations are conjunctival vascular abnormalities, corneal opacities (cornea verticillata), lens opacities and retinal vascular abnormalities.
9) These do not usually cause significant visual impairment or other ocular symptoms.
10) Rare ophthalmological manifestations:Lid oedema, angiokeratomas, A dry eye syndrome, altered pupillary motility, retinal artery and vein occlusions, anterior ischaemic optic neuropathy, choroidalischaemia, Optic atrophy or papilloedema, Myelinated nerve fibres, Abnormalities of the peripheral retinal pigment epithelium(4)

Pain: acroparesthesia

Kidney:
Renal insufficiency, Proteinuria is often the first sign of kidney involvement. End-stage renal failure results finally.

Cardiac manifestations:
A common heart symptom in Fabry patients is mitral valve prolapse, hypertension and cardiomyopathy are commonly observed.

Dermatological manifestations:
Angiokeratomas, anhidrosis, and less commonly hyperhidrosis, Raynaud's disease-like symptoms with neuropathy.

CNS manifestations: neuropathy ,increased risk of stroke The rate of stroke is reportedly 10-24%(3)

Other manifestations:
Fatigue, tinnitus , vertigo, nausea, inability to gain weight, and diarrhea are other common symptoms.

Treatment:
Enzyme replacement (6)
- αGalactosidase B (Fabrazyme)
- αGalactosidase A (Replagal)

Pain associated can be treated by medications such as Tegretol, Dilantin or Neurotin. Metoclopramide, Lipisorb, Pancrelipase are beneficial in treating Gastrointestinal hyperactivity.

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