

Angiokeratoma Corporis Diffusum - A Case Report

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Abstract: Angiokeratoma corporis diffusum, a rare clinical type of angiokeratoma, reported in association with various diseases of which Fabry disease is most common. Fabry disease, an X-linked recessive inborn error of glycosphingolipid metabolism due to deficiency of lysosomal enzyme α -galactosidase A. Clinically the disease is characterized by acroparesthesias, multiple cherry red coloured raised angiomatous hyperkeratotic lesions over trunk, abdomen, sides of buttocks and genitalia. A 27-year-old male born to a consanguineous marriage presents with acroparaesthesias and multiple cherry red and hyperkeratotic lesions over trunk, abdomen, sides of buttocks and genitalia. Histopathological examination is consistent with angiokeratoma and our case was diagnosed as angiokeratoma corporis diffusum. This case is being reported because of its rarity.

Keywords: Angiokeratoma corporis diffusum, fabry disease, X-linked recessive disease, α -galactosidase A, acroparaesthesias

I. Introduction

Fabry disease is an X-linked inborn error of glycosphingolipid metabolism resulting from deficient or absent activity of lysosomal enzyme α -galactosidase A. The enzyme defect leads to accumulation of globotriaosyl ceramide (GL-3) and related glycosphingolipids in plasma and tissue lysosomes. Males are primarily affected, females are carriers.

In classically affected males symptoms begin in childhood with acroparesthesias, burning and tingling pain in upper and lower extremities, hypohidrosis, even anhidrosis. Angiokeratomas typically present on abdomen, buttocks, flanks, penis and scrotum. It may also present with corneal opacities, left ventricular hypertrophy, proteinuria. With advancing age patient may present with ischemic heart disease, cerebrovascular accidents and renal failure and premature death in fourth to fifth decades.

II. Case Report

A 27-year-old male born of a consanguineous marriage complaints of acroparaesthesias since 20 years and multiple (>200) red lesions over genitals, lower back, lateral aspect of buttocks since 15 years. The lesions first appeared in early childhood and had increased in number and size since then to present size. The lesions were asymptomatic. There were no features suggestive of gastrointestinal, cardiovascular, musculoskeletal, central and peripheral nervous system and renal involvement or hearing and speech impairment. The patient demonstrated normal physical and mental development.

His both parents were phenotypically normal except for mother is having cornea verticillata on ophthalmological examination. His brother is having similar red lesions over genitals, lower abdomen since 10 years.

Clinical examination revealed a young man of medium built with multiple angiokeratomas over body. His blood pressure was 110/70 mmHg and pulse was 84/minute. There was no visceromegaly, no growth retardation, no lymphadenopathy. Pseudo acromegalic face was noted.

His cutaneous examination revealed multiple, cherry red angiofibromas over genitals, lateral aspect of gluteal region, lower abdomen (Figure 1).

Ophthalmological examination revealed cornea verticillata and dilated tortuous conjunctival vessels (Figure 2).

Laboratory studies revealed normal hematocrit, hemoglobin, white blood cell count, differential count, platelet count, ESR, RFT, LFT, CT, BT. HIV was nonreactive. His ECG and 2D echo were normal. Chest X-ray was normal.

Skin biopsy revealed orthohyperkeratosis, irregular epidermal acanthosis, elongated rete ridges enclosing vascular channels. Dermis showed dilated thin walled ectatic congested capillaries in papillary dermis (Figure 3).

Based on clinical features and histopathology findings he was diagnosed as Angiokeratoma corporis diffusum (Fabry disease).

III. Discussion

Angiokeratomas are dark violaceous to black papules that is hard upon palpation and cannot be compressed by diascopy. Angiokeratomas can be classified into localized and generalized forms. Localized angiokeratomas further classified into Fordyce's angiokeratoma (distributed on genitals), Miebelle's angiokeratoma (dorsum of toes and fingers) and Angiokeratoma circumscriptum naeviforme (unilateral large keratotic plaques). Generalized form, Angiokeratoma corporis diffusum.

Angiokeratoma corporis diffusum considered as hallmark of Fabry disease. Widespread angiokeratomas also occur in patients with several additional enzyme deficiencies which include α -fucosidase (fucosidosis), neuraminidase (sialidosis), aspartylglycosamine (aspartylglucosaminuria), β -mannosidase (β -mannosidosis), α -N-acetyl galactosaminidase (Kansaki disease) and β -galactosidase (adult onset GM1 gangliosidosis).

Fabry disease is a rare X-linked recessive inborn error of glycosphingolipid metabolism due to deficiency of α -glucosidase A. Incidence is 1:40,000 to 1:60,000. Males are affected, females are carriers. More than 200 mutations were identified on long arm of chromosome X (Xq22.1).

The deposition of globotriaosyl ceramide (GL-3) and related glycosphingolipids in lysosomes of endothelium, fibroblasts, pericytes, heart, kidney, autonomic nervous system giving rise to various symptoms of Fabry disease. It is characterized by episodic acroparesthesias, anhidrosis, angiokeratomas, cornea verticillata, ischemic heart disease, renal disease, cerebrovascular diseases.

Histologically there is acanthosis, hyperkeratosis in epidermis. Dermis shows dilated capillaries in papillary dermis. Polarized microscopy shows presence of refractile lipid inclusions (Maltese crosses) in endothelial cells. The gold standard for diagnosis is enzyme estimation. Unfortunately α -Galactosidase level was not measured due to lack of facility in our institution and patient's financial constraint. Treatment is usually symptomatic. Carbamazepine, gabapentin, phenytoin are used for acroparesthesias. Laser therapy for angiokeratomas, antiplatelets for cerebrovascular accidents, antihypertensives for renal disease. Enzyme replacement therapy with recombinant human α -galactosidase A is treatment of choice. All families that have member with Fabry disease should receive genetic counseling. Gene therapy is being developed.

IV. Conclusion

Fabry disease is a rare condition. A high index of suspicion needed when one encounters angiokeratoma. Patients with Fabry disease have premature death due to vascular complications. Treatment is usually symptomatic. Institution of enzyme replacement therapy might alter progression of disease.

References

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Figures



Figure 1: Multiple angiokeratomas on scrotum, penis

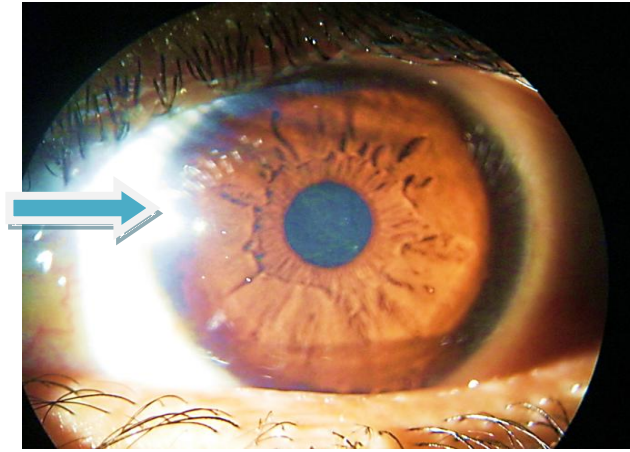


Figure2: Eye examination showing cornea verticillata

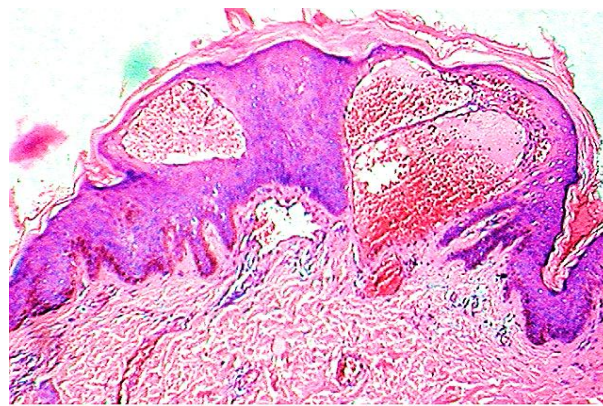


Figure3: Skin biopsy revealed orthohyperkeratosis, irregular epidermal acanthosis, elongated rete ridges enclosing vascular channels. Dermis showed dilated thin walled ectatic congested capillaries in papillary dermis