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PSEUDOXANTHOMA ELASTICUM - A RARE CASE REPORT

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Abstract : Pseudoxanthoma elasticum is an autosomally inherited disorder with incidence ranging from 1 in 70,000 to 1 in 100,000 live births. It is characterized by progressive calcification and fragmentation of elastic fibers in the skin, the retina, and the cardiovascular system. The diagnostic criteria are the typical histopathological appearance in the skin biopsy and the presence of angioid streaks in the retina. We report a case of 25 year old female with history of asymptomatic skin lesions over both sides of the neck since 13 years. Punch biopsy of skin sent for histopathological examination and special stain which revealed the diagnosis of pseudoxanthoma elasticum. Fundus examination of eye showed evidence of Angioid streaks.

Keyword : Pseudoxanthoma elasticum, elastic fibers, angioid streaks.

Introduction:

Pseudoxanthoma elasticum (Gronblad-Strandberg syndrome) is a rare genetic disorder characterized by progressive calcification and fragmentation of elastic fibers. It is caused by mutations in the adenosine triphosphate binding cassette transporter C6 , also known as multidrug resistance-associated protein 6 gene. The genetic defect of this disorder is located on chromosome 16p 13.1. It affects predominantly the dermis of skin, blood vessels and Bruch´s membrane of the eye.1,2,3

Case Report

A twenty five year old female presented with history of asymptomatic skin lesions over both sides of the neck since 13 years. Clinical examination revealed multiple, well defined skin coloured linear papules and plaques around the neck except for the area on the posterior aspect and nape of the neck. Punch biopsy of skin was taken from the neck and sent for histopathological examination. We received a well fixed, piece of skin with attached subcutaneous tissue measuring 0.4 cm x 0.2 cm. Histopathological examination revealed short, curled, frayed, basophilic elastic fibers in the upper and mid dermis. Special stain with Verhoeff - Van Gieson method revealed marked degeneration of elastic fibers with short and curled appaearance. Direct ophthalmoscopy examination of both eyes revealed **-** Angioid streaks in the retina.

FIGURE 1 : Multiple, well defined skin coloured linear papules and plaques

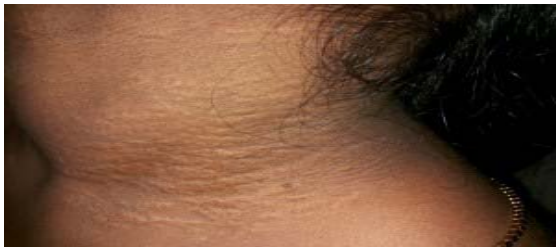

FIGURE 2: Papules and plaques on the lateral aspect of the neck

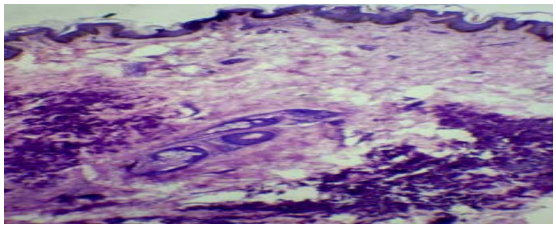

FIGURE 3: Low power view shows degenerated elastic fibers in the dermis(H&E)

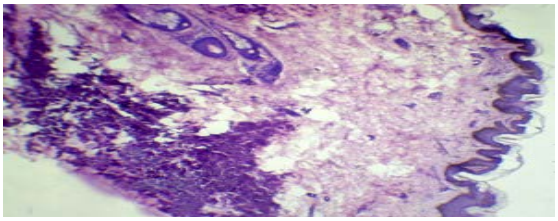

FIGURE 4: Low power view shows degenerated elastic fibers in dermis(H&E)

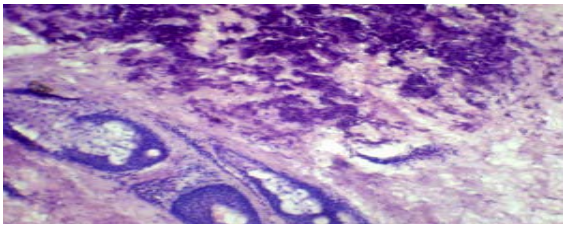

FIGURE 5: High power view shows degenerated elastic fibers in dermis (H&E)

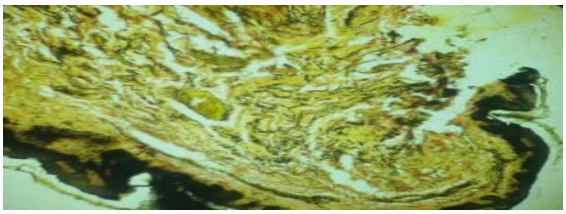

FIGURE 6: Vehoeff-Van Gieson showing degenerated elastic fibres

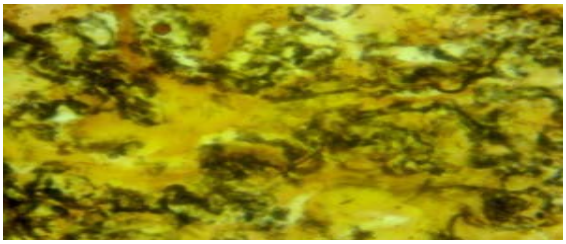

FIGURE 7: Verhoeff- Van Gieson showing degenerated elastic fibers (high power view)

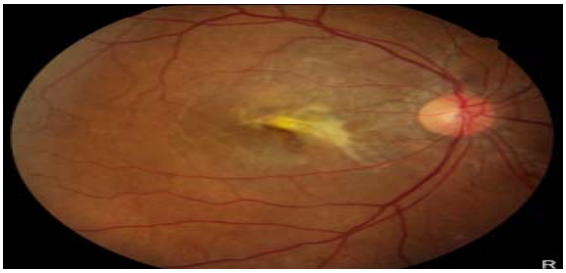

FIGURE 8: Direct ophthalmoscopic examination showing angioid streaks in the right eye

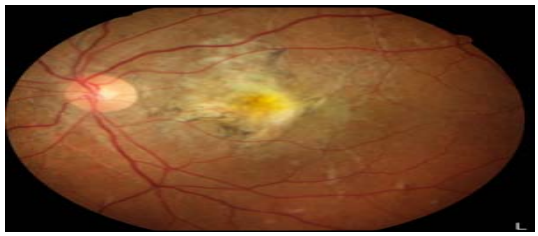

FIGURE 9: Direct ophthalmoscopic examination showing angioid streaks in the left eye

DISCUSSION

Pseudoxanthoma elasticum is a rare connective tissue disorder, predominantly affecting the dermis of skin, media, intima of blood vessels of gastric mucosa, coronary arteries and large peripheral arteries and Bruch's membrane of the eye. About 90% are inherited as autosomal ressesive.1 It is caused by mutations in the adenosine triphosphate binding cassette transporter C6, also known as multidrug resistance-associated protein 6 gene. The genetic defect of this disorder is located on chromosome 16p 13.122,3. Skin shows characteristic small yellowish papules, presenting classically along the sides of neck, giving rise to 'plucked chicken skin appearance'. The other sites affected are axillae, periumblical area, groin, perineum, thighs, soft palate, inner aspect of lips and vagina. The affected skin appears loose and wrinkled. The cutaneous lesions usually appears first in the second or third decade of life and are generally progressive in extent and severity.1 The commonest ocular change is the presence of Angioid streaks which result from calcification of the elastic fibres in Bruch's membrane of the retina, with cracking and fissuring. They are grey to reddish brown curvilinear bands radiating from the optic disc. This ocular disease is bilaterally symmetrical and occurs several years after the onset of cutaneous lesions, in patients aged 20-40 years. They are usually asymptomatic and occurs in almost all patients with pseudoxanthoma elasticum. Progressive visual diminution, retinal haemorrhage, and occasionally total blindness may occur. Unaffected family members may have abnormal visibility of choroidal vessels4. Involvement of the arteries of the gastric mucosa may lead to gastric haemorrhage. Involvement of coronary arteries may result in attacks of angina pectoris, although myocardial infarction is rare. Involvement of the large peripheral arteries may cause intermittent claudication. Risk of cardiovascular diseases may be correlated with presence of Angioid streaks. Patients typically have a normal life span, with the morbidity varying based on the extent of extracutaneous involvement1,5,6. Histopathology examination usually reveals short, curled, frayed, basophilic elastic fibers in the reticular dermis, particularly in the upper and mid parts. The papillary dermis is spared except at sites of transepidermal perforation. If perforation is present, there is a focal central erosion or tunnel with surrounding pseudoepitheliomatous hyperplasia. Basophilic elastic fibers are extruded through this defect. Sometimes foreign body type of giant cells with engulfed elastic fibers, histiocytes and chronic inflammatory cells are seen5,6,7. Vascular involvement consists of fragmentation of the internal and external elastic laminae, accompanied by intimal thickening, resulting in weakness of the vessel wall7. Ocular changes are calcifications and small breaks in of Bruch's membrane, which separates the choroid from the pigment epithelium of the retina4.

Special stains

In Verhoeff method the elastic fibers stain black, nuclei – grey black, collagen-red and other structures stain yellow. The elastic fibers in the affected skin are stained black with the Von kossa method7.

Electron microscopy:
Calcification occurs initially in the central zones of the elastic fibers. There is also some calcification of intercellular spaces and occasionally also of collagen fibers. The latter change may be reversible. There is continuing elastogenesis with some normal elastic fibers. Twisted collagen fibrils nd thread material which has been found to contain fibrinogen, collagenous protein and glycoprotein are also present7.

DIFFERENTIAL DIAGNOSIS:
The differential diagnoses are cutis laxa, solar elastosis, Buschke-Ollendorf syndrome and lateonset focal dermal elastosis.

Cutis laxa: In this condition there is loss of elastic tissue in papillary and reticular dermis and fibers are shortened, tapered and degenerated. Pseudoxanthoma elasticum like papillary dermal elastolysis may appear similar but occurs in elderly females and systemic lesions are absent. There is partial or complete elastolysis in the papillary dermis but calcification is typically absent with normal collagen fibers8.

Solar elatosis: In this condition wrinkled skin at sites of sun exposure are usually seen in the elderly or in persons with excess exposure to ultraviolet light. Microscopically amorphous, acellular basophilic material replaces the papillary and superficial reticular dermis7.

Buschke-Ollendorff syndrome: This disease is caused by loss-of-function mutations LEMD3 gene, encoding an inner nuclear membrane protein. It is an autosomal dominant disease, characterised by disseminated connective tissue nevi and osteopoikilosis. The presenting symptom may be disseminated lesions on the trunk, upper arms, and thighs. In this dermal elastic fibers may be increased in number and size with hypertrophy8.

Late-onset focal dermal elastosis: Normal elastic fibers in the mid and deep dermis, with no evidence of calcification7

CONCLUSION:
This case is reported here for its rarity. Diagnosis of early cutaneous manifestations prompts frequent ophthlmological follow up and thereby prevents vision loss. Microscopic examination, Verhoeff- Van Gieson staining and angioid streaks in the eye are gold standard for diagnosis.

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