Familial pseudoxanthoma elasticum: Report of three case series in a single family

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Abstract
Pseudoxanthoma elasticum is a rare autosomal recessive skin disease with a slight female preponderance and often presents a therapeutic challenge due to additional risk to eyes and cardiovascular system. Clumping and distortion of elastic fibres in target organ leads to deposition of calcium and impair the function of elastic fibres of mid and deep dermis, media and intima of midsized arteries, Bruch’s membrane in eye. Here we present three cases in the same family who presented with yellowish flat plaques, papules in the front and lateral side of the neck.

Key words
Pseudoxanthoma elasticum, ABC6 gene.

Introduction
Pseudoxanthoma elasticum (PXE) is a systemic disease and a heritable disorder of the connective tissue in which the primary defect appears to be the production of abnormal elastic fibres with secondary calcification.1 PXE is due to the mutations in the MRP6/ABCC6 gene, which is a member of the ATP-binding cassette (ABC) family and acts as a transmembrane transporter primarily in the liver and the kidney.2 Manifestations of the disease are seen in the skin, cardiovascular system and eyes. We are reporting three cases of PXE from the same family with partial response to treatment with isotretinoin in one patient.

Case Report

Case 1
A 25-year-old black woman, second of 4 siblings, came to our outdoor. She presented with chief complaint of developing asymptomatic yellowish papules and plaques over her neck. Her medical history was normal. Cutaneous examination revealed confluent papules that gave the skin a “plucked chicken” appearance on the lateral and anterior aspect of neck (Figure 1, 2). The patient stated that the changes in her skin had started in the lateral aspect of neck at about 8 years ago and had since been slowly progressive. Her visual acuity was 6/6 in both eyes. Slit-lamp examination showed no abnormalities. Findings from fundal examination revealed temporal disc pallor on right eye. Routine laboratory tests and ECG were within normal limits. Echocardiography showed mild mitral valve prolapse. Skin biopsy (skin tissue from the neck) was taken and diagnosis of PXE was confirmed. Histopathologic findings revealed fragmented and calcified elastic fibre in dermis visible under haematoxylin-eosin stains and which is more evident in specific elastic fibre, von Kossa stains (Figure 3, 4 and 5). She informed us that her mother and her brother had similar type of skin lesions (presented in case 2 and 3). She was treated with isotretinoin 20 mg daily for one month followed by tapering doses of isotretinoin for another one month. She was reviewed after two months. Skin
lesions diminished in size and thickness (Figure 6).

Case 2 The 26-year-old elder brother was examined and found to have yellowish papules and plaques over neck, axilla for last 8 years (Figure 7). His medical history was normal. His visual acuity was 6/6 in both eyes. External and anterior segment examinations (of his eyes) were unremarkable. Intraocular pressure was normal. Fundoscopy revealed granular pigmented changes in subretinal plexus.

Case 3 The 45-year-old mother of the previous patient was examined. At examination, she
was found to have PXE. Her medical history was significant for systemic hypertension since last 5 years and blindness of right eye with whitish opacity (Figure 8). On physical examination, raised (yellow) papillary lesions, of pseudoxanthoma were found on the neck (Figure 8). She underwent ocular examination 6 month back and was found to have diminution of vision to the extent of perception of light positive. Fundoscopy revealed subretinal blood vessels in right eye.

Diagnosis of both the case 2&3 were confirmed by histopathological examination.

**Discussion**

PXE (synonym Grönblad–Strandberg syndrome) is a rare, inherited multisystem disorder primarily affecting the skin, eyes, and cardiovascular system. It is characterized by progressive calcification and degeneration of elastic fibres. PXE is caused by mutations in the ABCC6 gene located on chromosome 16p13.1. This gene encodes MRP6, an adenosine-5”-triphosphate-binding cassette transmembrane transporter protein primarily expressed in the liver and the kidneys. The prevalence of PXE is estimated at 1 in 25,000 to 100,000 with an almost 2:1 female preponderance. Autosomal dominant and autosomal recessive patterns of inheritance, also sporadic cases, have been described. Recent molecular genetic studies show evidence for a recessive inheritance pattern only. PXE has no particular racial patient predilection. No specific geographic region has been identified. Most cases of PXE are diagnosed in the age group from 10 to 15 years, but cutaneous lesions have been reported in infancy. Multiple organs are affected, including the skin, eyes, and cardiovascular system, and the pathogenic changes include lax and inelastic skin, angioid streaks in the retina, and mineralization of the internal elastic lamina of midsized arteries, including the cerebral, coronary, gastrointestinal and peripheral vasculature. PXE can be associated with considerable morbidity and significant mortality, with a highly variable phenotypic spectrum with both inter- and intrafamilial heterogeneity. The histology of PXE is characteristic. In skin lesions, swollen, clumped, and fragmented elastic fibres and calcium deposits are found in the middle and deep reticular dermis with normal morphology in the papillary dermal layers. Similar changes occur in elastic fibres of the blood vessels, Bruch’s membrane of the eye, endocardium and other organs. Currently, diagnosis of PXE relies on clinical examination for characteristic skin lesions and angioid streaks or von Kossa staining of a biopsy of skin lesions looking for calcification of dystrophic dermal elastic fibres.

Our cases, confirmed these findings. Two among three patients described in this study were women and presented with skin lesions of PXE. In one patient, skin changes and asymptomatic mitral valve prolapse were found. One patient had systemic hypertension, ocular complications, which could be related to PXE.

These cases demonstrated that PXE affects all races and can have myriad manifestations.

**References**


