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Case Report

Pseudoxanthoma elasticum: a rare case report

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ABSTRACT

Pseudoxanthoma elasticum (PXE) is a hereditary systemic connective tissue disease affecting mainly the skin, retina and cardiovascular system. Pathologically, it is characterized by mineralization and fragmentation of elastic fibers (so-called "elastorhexia"). PXE is associated with mutations in the ABCC6 (ATP binding cassette subtype C number 6) gene. Women are affected more than men. A 22-year-old woman came to our department with complaints of small, yellowish raised lesions in rows or lacy pattern on her neck since 2 years, some of which coalesced to form larger lesions. She also complains that the skin has been soft, flabby, and wrinkled since 2 years in the armpits, trunk, groin, and knees. On examination, the lesions were slightly pebbly in appearance; such papular lesions tend to coalesce gradually to form plaques with a cobblestone appearance. On histopathological examination, elastic fibers appear basophilic due to calcium deposition. The fibers were fragmented, swollen, and clustered in the middle and deep reticular dermis. The collagen fibers were split. Based on the above findings, a diagnosis of PXE was made. Due to the rarity of the disease, we are reporting this case. The course and prognosis were explained to the patient. Most of the pathological changes associated with PXE are irreversible, but prophylactic measures can be taken to minimize the course of the disease.

Keywords: Pseudoxanthoma elasticum, Connective tissue disease, ABCC6 gene

INTRODUCTION

Pseudoxanthoma elasticum (PXE) also known as Grönblad-Strandberg syndrome is an inherited systemic connective tissue disease affecting mainly the skin, retina and cardiovascular system. Pathologically, it is characterized by mineralization and fragmentation of elastic fibers (so-called "elastorhexia"). PXE is caused by mutations in the ABCC6 (ATP-binding cassette subfamily C member 6) gene, located on the short arm of chromosome 16, encoding an ATP-binding transmembrane anion transporter normally expressed in the liver and kidney. However, the pathophysiology remains largely unknown.[1,2] Women are affected more than men. The clinical prevalence of PXE is estimated to be 1 in 100,000 to 1 in 25,000. No definitive therapy is available to treat the disease. Some benefit may be achieved by limiting calcium and phosphorus intake in the diet.

CASE REPORT

A 22-year-old woman came to our department outpatient department (OPD) of R.D. Gardi Medical College with complaints of small, yellowish raised lesions in rows above the neck, some of which coalesced to form large lesions since 2 years. She also complained of soft, flabby, and wrinkled skin in the armpits, trunk, groin, and knees since 2 years. On examination, the lesions were slightly pebbly in appearance; in some places the papules coalesced to form plaques that gave a cobblestone appearance. Fundus examination showed angioid streaks on the retina. Apart from intermittent claudication, no significant cardiovascular abnormalities were observed.

On histopathological examination, the elastic fibers were fragmented, swollen, and clustered in the middle and deep reticular dermis and appeared basophilic due to calcium deposition. The collagen fibers were split.

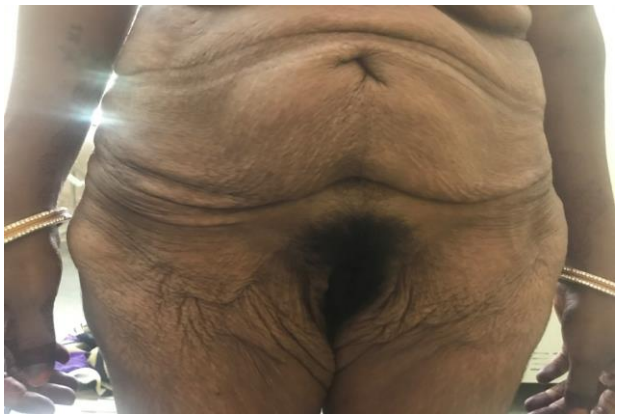

Figure 1: Characteristic advanced cutaneous feature of PXE – wrinkling of skin of trunk and groin.

Figure 2: Characteristic cutaneous feature of PXE: yellow papules on the nape of the neck.

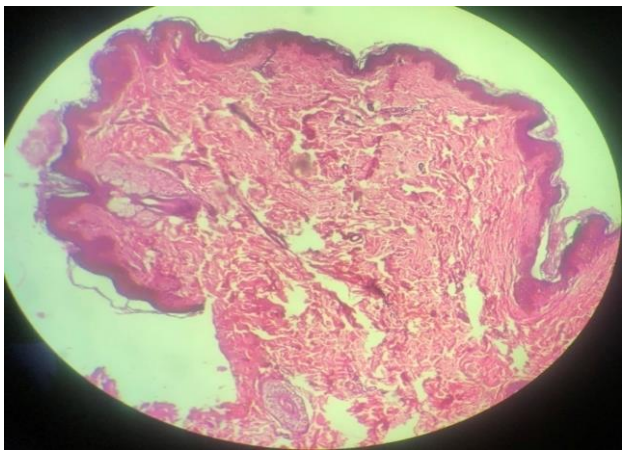

Figure 2: Histological characteristics of PXE skin biopsy of the neck with fragmentation and calcification of mid dermal elastic fibers on hematoxylin and eosin staining.

DISCUSSION

The term “pseudoxanthoma elasticum” was coined by the French dermatologist Ferdinand-Jean Darier in 1896[4] skin plaques in what was probably PXE were first described by Rigal in 1881.[5] The link between retinal angioid streaks and skin features in PXE was reported by Grönblad and by Strandberg in 1929, and PXE is occasionally referred to as Grönblad-Strandberg syndrome.[6,7] PXE is a genetic disease with autosomal recessive inheritance in which dystrophic calcification (i.e. the abnormal accumulation of calcium/phosphate complexes) leads to cutaneous, ocular, cardiovascular and other manifestations.[8,9] The effects of calcification are most apparent in the elastic tissues in the skin, eyes and blood vessels.[10] PXE involves the connective tissues of the skin, eye, and cardiovascular system. Skin changes are manifested by small, circumscribed, yellow papules on the side of the neck and folds that create a "plucked chicken skin" appearance. The skin becomes lax, sagging and wrinkled. The peau d'orange of the retina is visible. The characteristic retinal change is one or more angioid streaks (each at least as long as one disc diameter)—the result of breaks in Bruch's elastic membrane. One or more "wing signs" in the retina. Vascular damage leads to haemorrhages. Vascular events are caused by the degeneration of elastic fibers in the vascular medium. Differential diagnosis of PXE - Intense solar elastosis of the nape of the neck in the elderly, macroscopic PXE-like skin lesions are also seen after chronic D-penicillamine therapy and in “acquired PXE” (perforating calcific elastosis), rare skin diseases like late onset focal dermal elastosis, papillary dermal elastolysis, mid-dermal elastolysis, PXE-like skin manifestations with retinitis pigmentosa, thalassemic patients with PXE-like skin lesions also exhibit PXE-like vascular changes, body skin hyperlaxity due to vitamin K dependent coagulation factor deficiency, it must also be distinguished from the PXE-like syndrome, Cutis Laxa.[11-14] The main cause of morbidity in these patients is cardiovascular manifestations; hypertension, angina pectoris and intermittent claudication. These patients may also develop early atherosclerosis due to mineralization of the internal elastic lamina of blood vessels and a decrease in high-density lipoprotein (HDL) cholesterol levels in the blood plasma and hypertriglyceridemia. This contributes to a higher incidence of acute myocardial infarction and stroke.[3] There is no definitive treatment. Management of cutaneous manifestations - due to aesthetic concerns some patients seek treatment, surgery for such non-life-threatening symptoms should be avoided.[22] Possible role of oxidative stress has led to an attempt at antioxidant therapy with tocopherol acetate and ascorbic acid.[15] Management of ophthalmologic manifestations - Intravitreal treatment with vascular endothelial growth factor (VEGF) inhibitors (such as bevacizumab) is an effective treatment to choroidal neovascularization (most critical symptom of PXE).[16-18] Management of vascular and systemic manifestations - the current approach to delay cardiovascular manifestations is based on lifestyle changes

like smoking cessation, weight loss, and moderate physical exercise. Acetylsalicylic acid is contraindicated in PXE due to risk of bleeding from a diseased retinal neovasculature.[19] In case of arterial stenosis, standard surgical bypass or percutaneous angioplasty can be performed.[20,21] It has also been suggested that a high calcium intake in early life correlates with severity of PXE, limiting calcium and phosphorus in the diet can help. Gene therapy can also be used in some cases.

CONCLUSION

PXE is a rare, autosomal recessive, metabolic, genetic disease of ectopic mineralization that can cause cutaneous, cardiovascular and retinal manifestations. Although PXE is not life-threatening, it is associated with a risk of blindness, reduced quality of life, and peripheral vascular compromise. PXE cannot be cured and patients have to be monitored regularly. If the skin manifestations are significantly bothering, plastic surgery can be considered. Precautions must be taken before vascular surgery. Exact pathophysiological mechanisms underlying the disease have not been identified yet, the suggested role of PPI as the circulating anti-mineralization factor opens up opportunities for the clinical development and validation of disease-modifying treatments. Diagnosis is based on histopathology and patients may also be tested for ABCC6 gene mutation. Early diagnosis and careful monitoring will allow early preventive measures to be taken to control and prevent adverse events caused by the disease.

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