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Pseudoxanthoma Elasticum a Rare Genetic Disorder : A Case Report

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Abstract

Pseudoxanthoma elasticum (PXE) is a rare hereditary condition marked by the accumulation of fragmented and calcified elastic fibers in the body's tissues, leading to skin, vascular, and ocular involvement. In clinical practice, the most prevalent and typically earliest indication of PXE is observed through skin manifestations, which include laxity and the presence of yellowish papules and plaques. Here we report a case of a 40-year-old woman from Nepal presenting with yellowish multiple papules and plaque around the neck and axilla for 20 years, slowly increasing in size and number. A skin biopsy revealed fragmented eosinophilic elastic fibers in the dermis, consistent with PXE. Echocardiography, slit lamp, and indirect ophthalmoscopic examination were done.

Keywords: Angioid Streaks, Elastic Fibers, Pseudoxanthoma Elasticum.

Introduction

Pseudoxanthoma elasticum (PXE), also known as Groenblad-Strandberg syndrome, is a hereditary disorder, with an estimated prevalence of 1 in 50,000. More women than men are affected; the clinical signs typically appear in the second or third decade of life, rarely at birth.[1] Usually, yellowish papules on the neck and other flexor surfaces are the initial sign of PXE. These 1-3 mm skin lesions can coalesce to form larger plaques. During the progression, the axillae, groin, antecubital fossa, and popliteal fossa, are mainly affected, with marked wrinkling and loosening of the skin.[2]

Disease is characterized by the mineralization of connective tissue. PXE is primarily caused by mutations in the *ABCC6* gene. The transmembrane protein ABCC6, which is mostly produced in the liver and kidneys and may function as a transporter, is encoded by this gene. The ABCC6 gene has been found to have more than 300 mutations.[3]

We present a case of a 40-year-old woman with non-pruritic, non-painful, yellowish papules and plaques on her neck for 20 years.

Case Report

A 40-year-old woman presented to the dermatology clinic with yellowish papules and plaques on the neck for 20 years (Figure 1). The lesions increased in size and number throughout her years and were non-pruritic, non-painful. She also developed similar lesions around her axillae bilaterally around 8 years ago (Figure 2). The general physical examination and systemic examination were within the normal limit. Mild laxity of skin around the medial aspect of the bilateral arms was noticed. Family history revealed similar yellowish papules over the neck of her older sister, which had been present since childhood (Figure 3). Routine blood tests were done. A punch biopsy of the lesions was performed, and the tissue was sent for histopathological analysis to confirm the clinical diagnosis.

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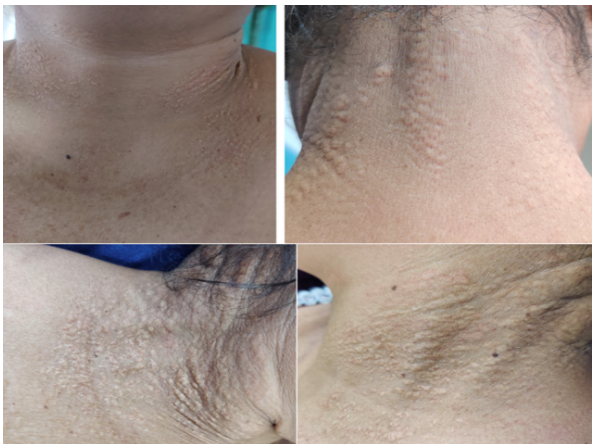

Figure 1: Yellowish papules coalescing to form plaque scattered on the neck

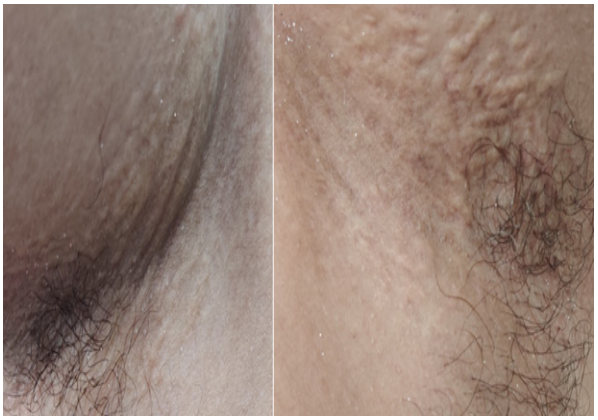

Figure 2: Yellowish papules scattered around bilateral axillae.

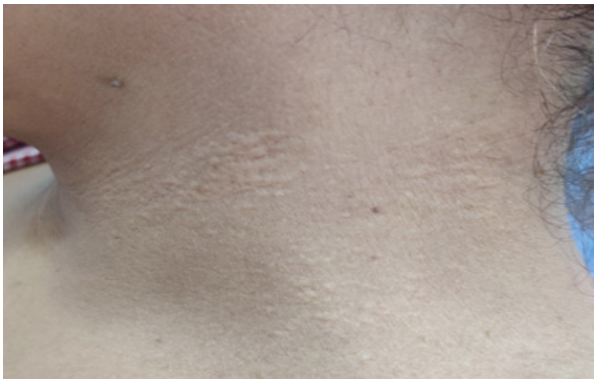

Figure 3: Few yellowish papules scattered over lateral surface of neck of patient's elder sister.

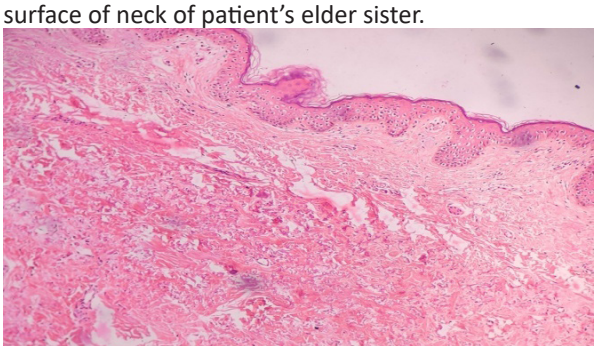

Figure 4: Section showing epidermis and dermis (H&E ×10). Epidermis shows normal orthokeratosis. Papillary dermis is spared. Mid to reticular dermis show fragmented eosinophilic elastic fibers.

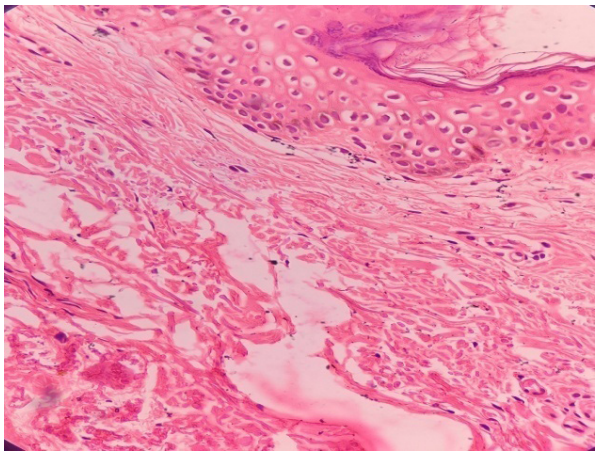

Figure 5: Section showing epidermis and dermis (H&E ×40). Mid dermis show fragmented eosinophilic elastic fibers.

Hematoxylin and eosin(H&E) stained microsections were examined from the skin biopsy specimen. Epidermis shows normal orthokeratosis. The papillary dermis is spared. Mid to reticular dermis show fragmented eosinophilic elastic fibers. Von Kossa stain was not done. Based on characteristic histopathology features on the H&E stain, a diagnosis of PXE was offered (Figures 4 and 5).

A cardiology consultation was done. Regular blood pressure monitoring for a week was advised. Echocardiography (ECHO) revealed Grade 1 left ventricular diastolic dysfunction.

Ophthalmological slit lamp examination and indirect ophthalmoscopy revealed small, mottled spots diffusely present in the fundus of bilateral eyes. Patient was advised to follow up with Optical Coherence Tomography (OCT) macula and Fundus Photograph, but she lost to follow up.

A complete blood count, liver function test, lipid profile, thyroid function test and biochemical analysis are presented in Table 1**.**

Table 1: Laboratory investigations and findings

S. N.	Investigations	Results or Findings
1	Complete blood count	WBC: 6590 /cumm RBC: 4.57mill/mm3 Hemoglobin: 14.6 gm/dl PCV: 41.9 % MCV: 91.7 fl, MCH: 31.9 pg, MCHC: 34.8 g/L
2.	Liver function test	Total Bilirubin: 0.83 mg/dl Direct Bilirubin: 0.38mg/dl Alkaline Phosphatase: 62 U/L Alanine aminotransferase (ALT): 4262 U/L Aspartate aminotransferase (AST): 3662 U/L
3.	Lipid profile	Total Cholesterol: 198mg/dl HDL Cholesterol: 53mg/dl LDL Cholesterol: 107mg/dl Triglyceride: 116mg/dl
4.	Thyroid function test	Free T3: 2.28 pg/ml Free T4: 1.24 ng/dl TSH: 2.98µIU/ml
5.	Biochemistry	Fasting Blood Sugar: 117mg/dl Urea: 22mg/dl Creatinine: 0.57mg/dl

No specific treatment is available. We suggested to the patient a fractional CO_2 laser and suggested her for regular follow up at the ophthalmology and Cardiology Department.

Discussion

Pseudoxanthoma elasticum (PXE) is a genetic metabolic disease with autosomal recessive inheritance caused by mutations in the ABCC6 gene. The lack of functional ABCC6 protein leads to ectopic mineralization, which is most obvious in the elastic tissues of the skin, eyes, and blood vessels. Almost always, tiny yellow papules on the nape, sides of the neck, and flexural areas are the initial clinical signs of PXE. The skin becomes loose and wrinkled as the papules gather together.[4]

The earliest ocular finding is a diffuse mottling of the fundus known as peau d'orange. The characteristic eye finding is the angioid streaks. After peau d'orange, Bruch's membrane mineralization almost always results in the development of angioid streaks.[5]

One of the main causes of morbidity in these patients is cardiovascular symptoms, such as intermittent claudication, angina pectoris, and hypertension. Due to the mineralization of the blood vessel's internal elastic lamina, lipid changes, including hypertriglyceridemia and a decrease in high density lipoprotein (HDL) cholesterol in blood plasma, patients with PXE may also experience early atherosclerosis. This raises the risk of acute myocardial infarction and cerebrovascular accidents.[6]

The first feature of histology is that the middle dermal elastic fibers become mineralized and fragmented, creating an elastorrhexis pattern. Von Kossa and the Verhoeff-Van Gieson stain for elastic fibers demonstrate the calcification and fragmentation of the fibers, respectively.[7]

In our patient, histopathological examination of the skin lesion biopsy showed fragmented eosinophilic elastic fibers in the mid and lower dermis; there was no visual impairment, withsmall, mottled spots diffusely present in the fundus of bilateral eyes. Changes in ECHO were suggestive of Grade 1 LV diastolic dysfunction. Currently, effective and specific treatment is not available to prevent mineralization and fragmentation of elastic fibers in the skin, eyes, and blood vessels. Prognosis depends on the systemic involvement of the disease. Treatment options for retinal manifestations are described, ranging from photodynamic therapy and thermal laser coagulation to intravitreal injections of medicines that inhibit vascular endothelial growth factor.[8] Carbon dioxide lasers have better outcomes for corrections of texture and irregularity in cutaneous alterations.[9]

Conclusion

PXE is a rare disease; the early recognition may be necessary to decrease the serious complications. The diagnosis is based on a histopathology report. Mutation analysis of the ABCC6 gene can be done further.

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