



Case Report

Pseudoxanthoma elasticum as a diagnostic challenge for pathologists: A rare case report

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1. Introduction

Pseudoxanthoma elasticum (PXE) is a rare hereditary disease characterized by calcification of the elastic fibers of the connective tissue. The prevalence of disease is about 1:50,000 in the world [1]. Females have a high predominance as compared to males, which is estimated to be 2:1 [2]. The earliest description of PXE was given by dermatologist Rigal in 1881 [3]. After a few years, Balzer described the association between elastic degeneration of the skin and cardiac alterations [2].

Darier coined the term "pseudo-xanthome elastique" due to its characteristic yellowish papular cutaneous lesions that give a "plucked chicken" appearance and resemble xanthomas seen in high lipid state [4]. Gronblad and Strandberg described the ocular alterations in PXE. Hence, PXE is also known as Gronblad-Strandberg syndrome to honor and recognize their contribution in the medical field [5]. Herein, we report a case of PXE in a girl child without systemic involvement. The SCARE criteria were utilized for this case report [6]. The parents of the patient have given the consent for the study to be published.

2. Case report

A 14-year-old girl presented in Dermatology outpatient department, with a few skin lesions over face and anterior aspect of her neck for one month (Fig. 1). The lesions measured approximately 2–5 mm in size. A history of pruritis was present. Clinically, differential diagnosis of Milia over erythematous base was suggested. A history of skin laxity or joint hypermobility was absent. The general physical examination and

systemic examination were within the normal limit. Family history was not significant. The clinician kept Milia en plaque and Pseudoxanthoma elasticum as differential diagnosis. A punch biopsy of the lesions was performed, and the tissue was sent for histopathological analysis to confirm the clinical diagnosis.

Hematoxylin and eosin (H&E) stained microsections examined from the skin biopsy submitted showed, a prominent granular layer with mild spongiosis and basal layer vacuolization. The papillary dermis was mildly edematous with evidence of mild lymphoplasmacytic infiltrate along with few histiocytes. The mid and lower dermis revealed a prominent zone of chronic inflammatory infiltrate comprising of lymphocytes, histiocytes, and occasional plasma cells. Giant cells were also evident in the mid-dermis. In the middle reticular dermis, deposition of basophilic mucoid material along with haphazardly arranged clumped fragmented elastic fibres were seen. This basophilic mucoid material stained positive for alcian blue, colloidal iron, and Von-Kossa (Fig. 2). The adnexal structures and subcutaneous adipose tissues were essentially unremarkable. Staining for acid-fast bacilli was non-contributory. Based on characteristic histopathology features, a diagnosis of PXE was offered.

3. Discussion

PXE is a rare autosomal recessive hereditary disease that involves multiple systems, e.g., the skin, eyes, and cardiovascular system. This disease is characterized by the mineralization of connective tissue, causing fragmentation of elastic fibers [1]. The genetic defect in the

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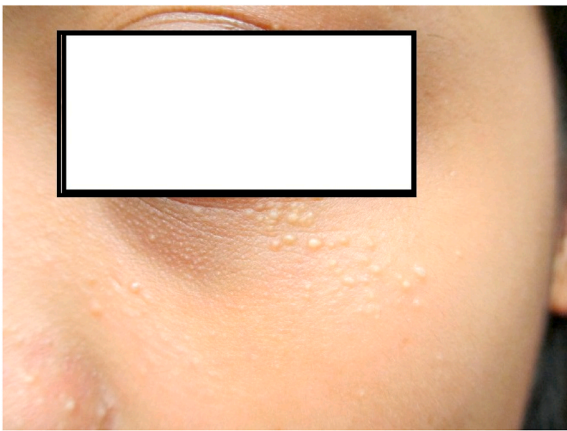


Fig. 1. 2–5 mm lesions (milia) over face.

ATP-binding cassette subfamily C member 6 (ABCC6) protein, also known as multidrug resistance-associated protein 6 (MRP6), is located on chromosome 16p13.1 and is predominantly expressed in the liver and kidney. More than 350 mutations have been identified in different diseases involving the ABCC6 gene, which encodes a cellular transport protein [7].

Studies show patients suffering with PXE have a defective assembly of elastic fibers. Other studies support that PXE is a systemic metabolic disorder with secondary mineralization of connective tissue [8]. The prevalence is higher in the South African population [9]. The major diagnostic difficulty is the accurate diagnosis of PXE due to its resemblance with other diseases such as cutis laxa, elastosis perforans serpiginosum, Ehlers-Danlos syndrome, Marfan syndrome, etc. Clinical symptoms of these entities overlap with PXE. Hence, to overcome this diagnostic challenge, histopathological examination is an important analytical tool to confirm the clinical suspicion of PXE [10].

Significant clinical manifestations are encountered primarily in the cutaneous, ocular, cardiovascular, and gastrointestinal systems [2]. Cutaneous alterations of PXE are characteristic. They begin in childhood or adolescence, progress slowly and manifest in late adulthood [11]. Early lesions appear on the lateral and posterior aspects of the neck. Cutaneous lesions are usually symmetrical and 2–5 mm in size, with yellowish papules. They may merge together to form a shape like a plaque and may give the appearance of plucked chicken, cobblestone, or Moroccan leather [12]. During the progression of disease, flexural areas, e.g., axillae and groin, are mainly affected, with marked wrinkling and loosening of skin [11]. In our patient, lesions were developed on the anterior aspect of the neck without laxity of the skin. The cutaneous lesions predict the risk of cardiovascular and ocular involvement [13].

Ocular manifestations of PXE include peau d'orange, comet lesions,

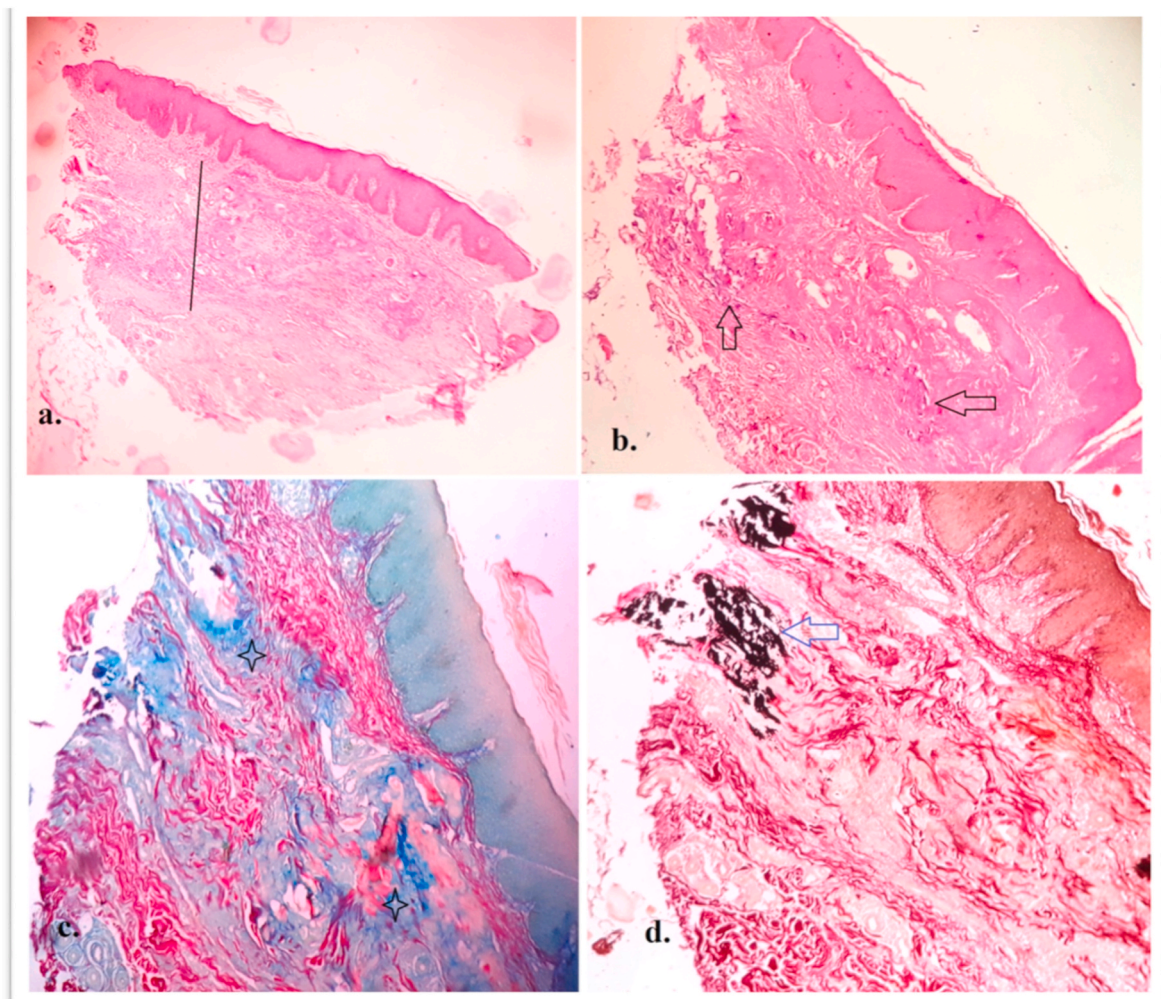


Fig. 2. Hematoxylin and Eosin stained section of skin biopsy showed (a) upper and mid dermis (demarcated by black line) involved with a prominent chronic inflammatory infiltrate, (b) Deep basophilic mucoid material in dermis (demarcated by arrow mark & star mark) stained positive for alcian blue and, (c) colloidal iron and, (d) Fragmentation and calcification of dermal elastic fibers is evident on Von Koss stain. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

angioid streaks, choroidal neovascularization, hemorrhage, and scar formation. The earliest ocular manifestation is "peau d'orange," which appears as small dark mottled spots in the periphery of the temporal zone of the retina. Although the exact pathogenesis is not known, it is assumed that they are formed due to progressive calcification of the bruch's membrane, which mainly consists of elastic fibers [14]. Peau d'orange precedes the angioid streaks. Angioid streaks are the most evident and consistent sign of PXE. They show cracks and fissures in the calcified, thickened Bruch's membrane on histopathology [15]. The only pathognomic features of PXE are the comet and the comet tail. They are chorioretinal atropic spots and show a tail pointing toward the optic nerve head known as the comet tail [5]. In PXE patients, choroidal neovascularization is the most common ocular complication. Other complications are hemorrhage, exudation, and fibrovascular scarring. If these complications are not managed early enough with treatment, they may lead to vision loss as the end result [16].

The cardiovascular system manifests itself in a variety of ways. They may appear with minor symptoms such as low pulse or life-threatening conditions like acute myocardial infarction. Gastrointestinal symptoms that appear due to hemorrhage are common and manifest as melena or hematemesis [17,18]. These manifestations are the result of mineralization and fragmentation of elastic fibres of medium-sized arteries, aorta, and arterioles, deposited in the internal elastic lamina, medial and adventitial layers [19].

Histopathological features of cutaneous tissue are PXE characteristics, including swollen, fragmented, clumped basophilic elastic fibres in the middle and deep reticular dermis. The basophilic appearance of elastic fibres is a result of calcium deposition, which is confirmed by the special stain von Kossa. A special stain for elastic fibre includes Verhoeff van Gieson. These special stains are crucial for the diagnosis of PXE [20]. In our case, mucoid material was the additional finding along with classical features which stained positive for colloidal iron and alcian blue special stain. Similar histopathological changes are seen in the ocular, myocardium, aorta, and coronary vessels [18,21].

Prognosis depends on the involvement of other organs. Acute myocardial infarction, cerebral hemorrhage, and ocular complications may be fatal. Therefore, early detection, medical care, a low calcium diet, weight loss exercise, and regular monitoring of the ocular and cardiovascular systems may help to avoid serious complications. Currently, effective and specific treatment is not available to prevent mineralization and fragmentation of elastic fibres in skin, eyes, and blood vessels. A few treatment options are available to prevent ophthalmologic complication includes, laser photocoagulation, photodynamic therapy and anti-vascular endothelial growth factor [22]. Cutaneous sagging can be corrected by surgery for cosmetic improvements [23]. Carbon dioxide laser has better outcomes for corrections of texture and irregularity of cutaneous alterations [24].

4. Conclusion

PXE is an extremely rare autosomal recessive disease. It involves major systems in the body like the cutaneous, ocular, cardiovascular, and gastrointestinal. Histopathological examination reveals similar patterns in all the affected systems. The characteristic histopathological features are calcification and fragmentation of the elastic fibres. Currently, specific or effective treatment is not available. Hence, the patient is managed on a symptomatic basis. Modified diet, exercise, and regular follow-up may improve the quality of life and prevent life-threatening complications.

Ethical approval

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Authors contribution

1. Dr. Namita Bhutani: assisted in framing manuscript 2. Dr. Kamlesh: data collection 3. Dr. Akhil Nadesan: written the manuscript.

Research registration

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Patient consent statement

Parents of patient have given consent to publish the case report.

Declaration of competing interest

We don't have any conflict of interest.

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