



Generalized Pseudoxanthoma Elasticum with Perforating lesions-An Extremely rare entity with unusual presentation

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ABSTRACT

Pseudoxanthoma elasticum (PXE) is a genetically inherited disorder of elastic fibers. Occurrence of perforating lesions is quite uncommon and further rarer is cutis laxa like generalized skin involvement in PXE. It is characterized by elastorrhexia of cutaneous, ocular and cardiovascular elastic tissue. Skin is affected in flexures like neck, axilla and periumbilical region. Classical cutaneous lesions are yellow papulo-plaques over lax skin giving a characteristic plucked chicken appearance to affected area. Reports of cutis laxa like generalized PXE are very sparse, further associated perforating lesions have not been described in generalized PXE till now. Here we report a 53 year old female with generalized lax skin along with erythematous and atrophic plaques surmounted with keratotic papules over the trunk. Clinical possibility of generalized PXE with perforating lesions was further confirmed on histopathology. Haematoxyline and eosin staining revealed fragmented and swollen elastic fibers in mid dermis while dystrophic calcification was demonstrated with vonkossa stain. The highlight of our case is cutis laxa like generalized skin involvement coexisting with perforating lesions in a patient of PXE.

INTRODUCTION

The term pseudoxanthoma elasticum (PXE) was coined by Darier in 1896 in view of yellow cutaneous papules that result from elastorrhexia unlike of true xanthoma.^[1] It is a rare inherited disorder of elastic tissue with estimated prevalence ranging from 1: 25,000 to 1: 100,000.^[2] Generalized PXE was firstly mentioned in Pope's classification in 1975.^[3] He described two autosomal dominant (type1 and 2) and two autosomal recessive (type 1 and 2) variants of PXE. As per Pope's classification generalized PXE is the least common variant belonging to

autosomal recessive type 2 form. Its peculiar feature is that ocular and cardiovascular manifestations are not seen.^[3] Pope detected this variant in three British families. Later on three more cases of generalized PXE were reported from Italy and Korea. Rongioletti et al described generalized PXE with deficiency of vitamin K dependent factors.^[4] Lee et al and Kang et al reported the similar cases without any other co-morbidities.^[5, 6] This is the first case of generalized PXE coexisting with perforating lesions reported from India.

CASE REPORT

A 53 year old unmarried female presented with asymptomatic loose, pendulous and prematurely aged skin over entire body. She stated that these changes started in childhood from neck and axilla then gradually progressed to involve entire skin until the age of 30 years. Subsequently she noticed multiple red raised plaques over abdomen and back by the age of 50 years. They used to heal after topical steroid with atrophic scars. It was the development of pruritic, painful and keratotic lesions over these plaques which forced the patient for specialist consultation. She was a healthy product of non-consanguineous marriage moreover other family members had not such type of complaints. Cutaneous inspection revealed generalized lax skin with abundance of skin folds in axilla, groin and neck. (Figure1&2) Over the front and lateral aspect of trunk, there were multiple well demarcated atrophic and erythematous plaques surmounted with yellowish keratotic papules with overlying crusts. (Figure 3)



Figure 1



Figure 2



Figure 3

Figure 1&2: Generalized lax and folded skin.
Figure 3: Erythematous & atrophic plaques with keratotic papules at margins.

Oral mucosa revealed grayish white papulo-plaques over posterior half of hard palate. Heart, eyes and other systems were within normal limits on clinical examination. The routine laboratory tests, blood sugar, serum calcium and phosphate levels were within normal range. Fundus examination and echocardiography were also unremarkable. Histological examination of skin biopsy from affected skin revealed irregular, enlarged and fragmented elastic fibers in the mid and lower dermis on hematoxylin-eosin staining. (Figure 4) Von Kossa stain demonstrated calcific degeneration of elastic fibers. (Figure 5) On the basis of clinical and histopathology findings diagnosis of generalized PXE coexisting with perforating variant was made. Patient was counseled and advised to avoid strenuous physical work.

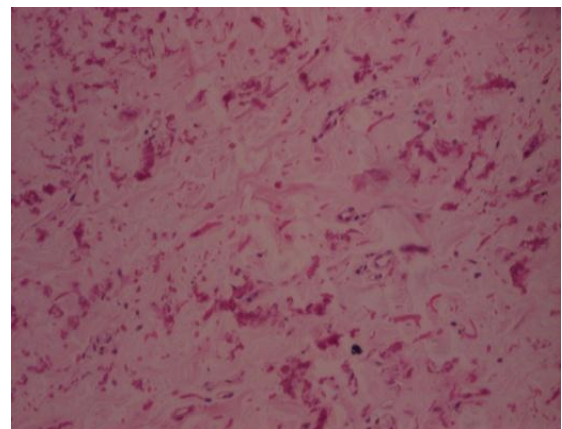


Figure 3: H&E stain showing large & fragmented elastic fibers in lower dermis

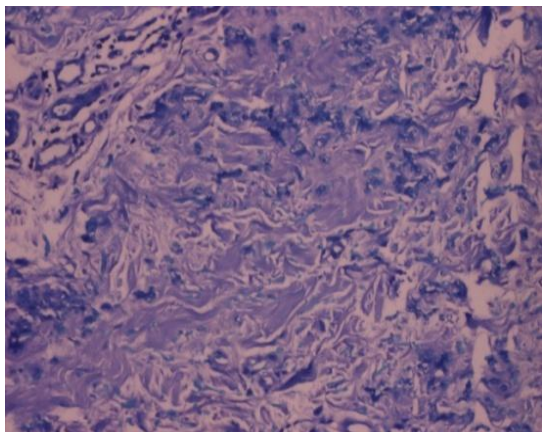


Figure 4: Vonkossa stain showing calcific degeneration of elastic fibers.

DISCUSSION

PXE is a genetic metabolic disorder resulting from mutations in the *ABCC6* gene. This gene is predominantly expressed in liver and kidney, but phenotype is expressed primarily in skin, eyes and heart. Pathologically there is dystrophic calcification of elastic fibers, especially in the dermis, Bruch's membrane of retina and the internal elastic lamina of medium arteries.^[1] The skin is the first organ to be affected in childhood in about 70% of cases.^[7] Commonly affected sites are the flexures, periumbilical region and oral mucosa. Plucked chicken or cobblestone appearance of skin is characteristic of PXE. But cutis laxa like generalized skin laxity, as observed in our case is a very rare presentation. In advanced stage of classic PXE, calcium deposits may extrude out from skin and this unusual variant is described as "perforating PXE".^[8] In some cases, it occurs as a localized form without systemic involvement. Other cases are reported to have angioid streaks and flexural lesions of hereditary systemic PXE.^[8] Mechanical factors like obesity, multiparity, abdominal trauma and surgeries are supposed to induce perforating lesions. Further, diabetes and hypertension are commonly associated with perforating PXE. Our case had generalized PXE with perforating lesions in the absence of any of these risk factors.

Ocular findings are seen in up to 86% cases and angioid streaks are most characteristic but not pathognomic of PXE.^[8] Cardiovascular

manifestations appear usually in third to fourth decade of life. Vascular calcification leads to intermittent claudication, renovascular hypertension, coronary/cerebrovascular disease and even hemorrhagic complications. The mean age at onset is approximately 13 years but diagnosis is delayed to until the fourth or fifth decade of life due to asymptomatic and heterogeneous clinical manifestations.^[9] Although, generalized PXE is very well described by Pope but his classification was refuted by other authors due to certain reasons.^[3] To facilitate the clinical diagnosis for PXE, three major diagnostic criteria (characteristic skin lesions in flexural sites, elastic fiber calcification in lesional skin on histology and ocular disease) and two minor criteria (histopathology features in nonlesional skin and family history of PXE in a first-degree relative) have been formulated.^[2] In spite of these diagnostic criteria, diagnosis is sometimes challenging due to considerable inter and intrafamilial heterogeneity. In some family members skin manifestations are predominant with minimal to absent ocular or cardiovascular lesions while other families can have vice versa presentation. A possible influence by environmental factors has been implicated but exact reason for this phenotypic heterogeneity is unclear.^[10] Presently, there is no treatment for this disorder but ingestion of calcium has been recommended but dose should not exceed the recommended daily allowance. Avoidance of head trauma and heavy straining is needed to prevent hemorrhage. Plastic surgery may be helpful in improving the cosmetic appearance but it has no role in generalized PXE.

CONCLUSION

Cutis laxa like generalized PXE is an extremely rare condition. Occurrence of perforating lesions has been described in classic PXE and in periumbilical perforating PXE (PPPXE). But coexistence of PPPXE with generalized skin involvement or generalized PXE with perforating lesions has not been described in literature.

Considerable morbidity and significant mortality occur due to cardiac and ocular events. Cosmetic disfigurement is the only cutaneous problem of generalized PXE but overall prognosis is good with normal life expectancy.

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