Elastosis perforans serpiginosa in a case of pseudoxanthoma elasticum: A rare association

Konakanchi Venkatachalam, Kavya Chennamsetty

Department of Dermatology, Venereology and Leprosy, Andhra Medical College, Visakhapatnam, Andhra Pradesh, India

ABSTRACT

Elastosis perforans serpiginosa (EPS), characterized by transepidermal elimination of fragmented elastic fibers, clinically presents as hyperkeratotic papules. EPS is classified into three types: (1) Idiopathic; (2) reactive, with associated connective tissue diseases such as pseudoxanthoma elasticum (PXE), Ehlers–Danlos syndrome, cutis laxa, Marfan syndrome, osteogenesis imperfecta, Down's syndrome; (3) the one that is induced by D-penicillamine. A rare association of EPS with PXE, which is primarily a defect of transmembrane transporter protein with accumulation of certain metabolic compounds and secondary calcification of elastic fibers has been documented in the literature. We report a case of PXE with associated lesions that were histopathologically compatible with EPS.

Key words: Angioid streaks, elastosis perforans serpiginosa, prominent mental crease, pseudoxanthoma elasticum, transepidermal elimination

INTRODUCTION

Elastosis perforans serpiginosa (EPS), characterized by transepidermal elimination of fragmented elastic fibres, clinically presents as hyperkeratotic papules. It's rare association with pseudoxanthoma elasticum (PXE) has been documented in the literature. We report a case of PXE with associated lesions that were histopathologically compatible with EPS. 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, primary defect of which results in the accumulation of certain metabolic compounds with secondary calcification of elastic fibers. We also highlight the importance of the clinical finding of an exaggerated mental crease, which has been shown to be a sensitive and highly specific finding in patients under the age of 30 years with PXE.

CASE REPORT

A 22-year-old female, third of four siblings born of first-degree consanguinity presented with a three-year history of excess folds of the skin on the sides of the neck and a six months history of asymptomatic eruption on the neck. She did not have any visual disturbances. There was no history of intermittent claudication, chest pain, seizures, or melena. Physical examination revealed numerous small yellow brown non follicular papules about 1–2 mm in size arranged in a linear fashion on the sides of the neck. Skin of the neck was soft, lax and was hanging in folds on the sides of neck and in both the axillae [Figures 1 and 2]. A few brown to black distinctive hyperkeratotic nonfollicular papules about 5 mm in diameter arranged in a serpiginous fashion with a central plug, revealing a crateriform pit on dislodgment were seen on the sides of the neck [Figure 3]. There were atrophic scars in a serpiginous pattern on the sides of the neck. There was a single prominent mental crease [Figure 4]. There was no history of similar lesions in the family. The results of routine laboratory tests were within the normal

Access this article online
Website: www.idoj.in
DOI: 10.4103/2229-5178.178078
Quick Response Code:

Address for correspondence:
Dr. Kavya Chennamsetty, Plot No. 46, Pandurangapuram, Visakhapatnam, Andhra Pradesh, India.
E-mail: drkavyaderma@gmail.com

Cite this article as: Venkatachalam K, Chennamsetty K. Elastosis perforans serpiginosa in a case of pseudoxanthoma elasticum: A rare association. Indian Dermatol Online J 2016;7:103-6.

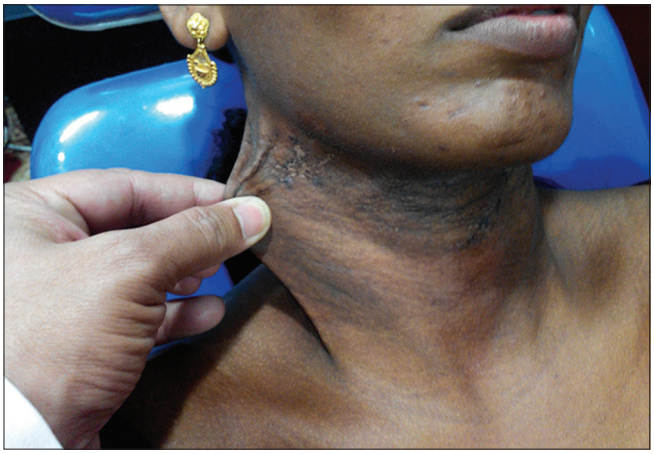

Figure 1: Lax skin demonstrated on the sides of neck

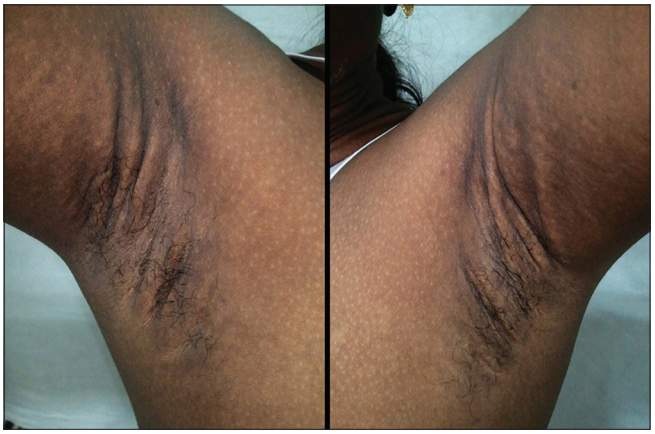

Figure 2: Lax skin hanging in folds in both the axillae

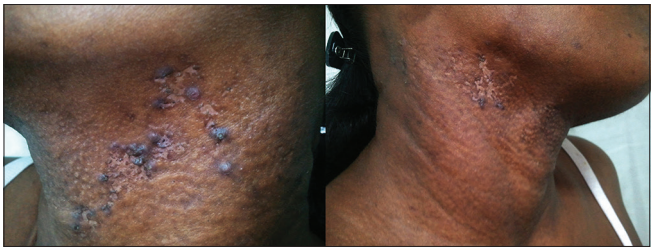

Figure 3: Hyperkeratotic nonfollicular papules and atrophic scars arranged in a serpiginous seen on the sides of the neck

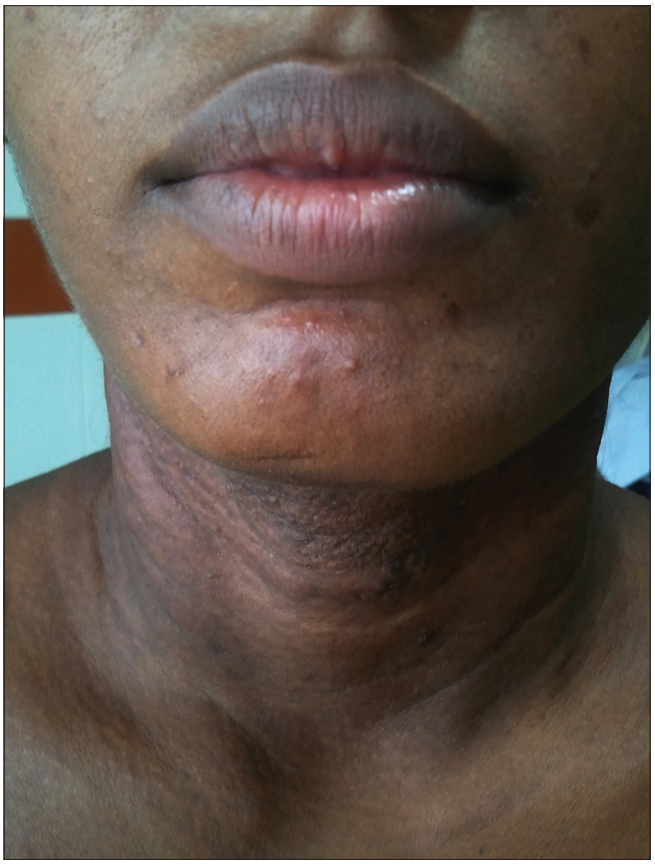

Figure 4: A single prominent mental crease

limits. Electrocardiogram (ECG), 2D ECHO, and radiography of the chest were normal. The ophthalmologic examination revealed the presence of angioid streaks in the fundus, which were clinically asymptomatic [Figure 5].Ophthalmological examination of the siblings revealed no abnormalities in the fundus.

Histopathology of the biopsy specimen from a hyperkeratotic papule revealed hyperplastic epidermis. There were numerous fragmented, stringy, and curled elastic fibers giving the appearance of revealed wool in the upper- and mid-reticular dermis [Figure 6]. There was a dilated disrupted follicle surrounded by foreign body–type granulomatous inflammation with several foreign body giant cells [Figure 7]. The infundibular wall showed collections of neutrophils with small fragments of elastic fibers. Special staining with Von Kossa stain revealed calcification of the elastic fibers in the reticular dermis and in the disrupted follicular infundibular wall. With the above clinical and histopathological evidence, we diagnosed the case as PXE with associated EPS.

DISCUSSION

PXE (MIM 264800), also known as systematized elastorrhexis or Gronblad–Strandberg syndrome is an autosomal recessive disease of the connective tissue, which primarily affects the dermis, retina, and the cardiovascular system.[1-4] The prevalence is currently estimated to be 1 in 25,000-70,000 live births.[1,3] The diagnosis of PXE is most often made late in the second or third decade of life.[1-4] Genetic studies have identified mutations in the MRP6/ABCC6 gene[5-7] on chromosome 16p13.1, which is a member of the ABC family and acts as a transmembrane transporter primarily in the liver and the kidney, primary defect of which results in the accumulation of certain metabolic compounds with secondary calcification of elastic fibers.[6-9] Characteristic skin lesions include yellow papules in a linear or reticulate pattern

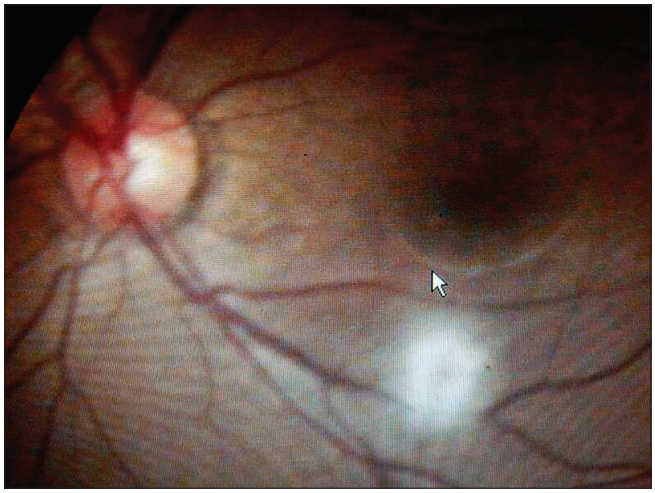

Figure 5: Angioid streaks in the fundus demonstrated on ophthalmoscopy

with soft, lax, wrinkled skin hanging in folds by the sides of the neck, below the clavicles, the axillae, abdomen, groins, perineum, and thighs described as "cobble stone," "Moroccan leather," or "chicken skin" appearance. Eye involvement results from breaks in Bruch's membrane at the posterior aspect of the retina (angioid streaks), which is symptomless but may be complicated by retinal neovessels, recurrent hemorrhage, disciform scarring, and eventual loss of central vision. Most of the cardiovascular manifestations are related to early arteriosclerosis as a consequence of degenerated elastic laminae, which manifest as disappearance of peripheral pulses, intermittent claudication, angina pectoris, rarely myocardial infarction, cerebral stroke, and visceral hemorrhage. Early diagnosis is important if the ocular and cardiovascular complications are to be prevented.

To facilitate and unify the clinical diagnosis for PXE, three major diagnostic criteria (characteristic yellow skin lesions in flexural sites, elastic fiber calcification in lesional skin, and ocular disease) and two minor criteria (histopathologic features in nonlesional skin and family history of PXE in a first-degree relative) have been adopted.[10] The presence of exaggerated mental crease has been shown to be asensitive and highly specific finding in patients under the age of 30 years with PXE. It may be the result of deterioration of elastic tissue in the lip and chin, or blood vessels supplying the jaw. The clinical finding of a horizontal chin crease in the presence of central loss of vision, arterial occlusive disease, or acute gastrointestinal hemorrhage should prompt the physicians to examine their patients for other features of PXE. We identified a similar prominent chin crease in our patient.

A rare association of PXE with EPS such as lesions characterized by spontaneous perforating lesions with transepidermal elimination of fragmented elastic fibers, clinically presenting as hyperkeratotic papules has been reported.[11] EPS is classified into three types: (1) Idiopathic; (2) reactive,

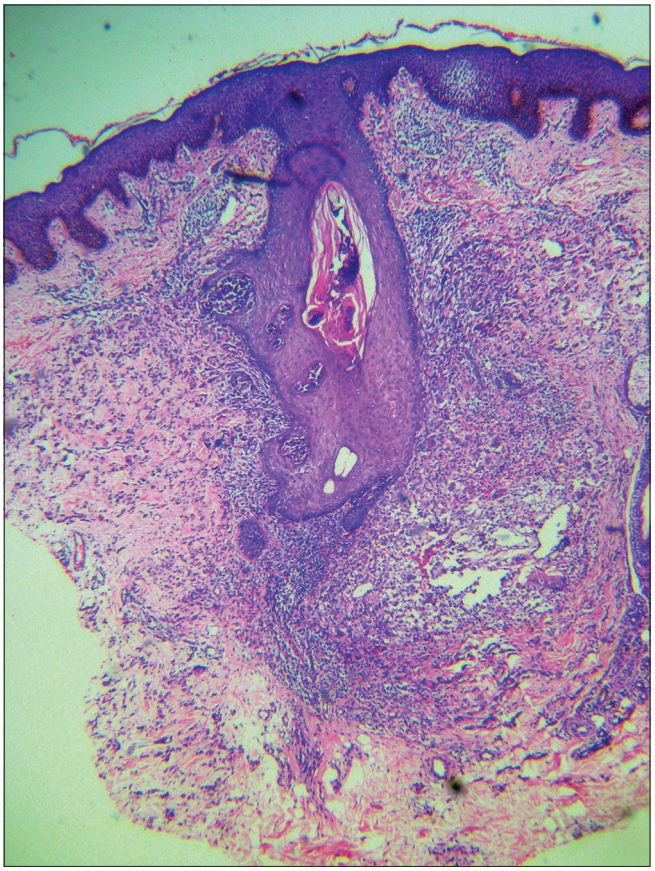

Figure 6: Histopathology revealing numerous fragmented, stringy, and curled elastic fibers giving the appearance of raveled wool in the upper- and mid-reticular dermis [H and E, ×10]

associated in 25% of cases with connective tissue diseases; (3) induced by D-penicillamine.[11]

Confusion exists whether these perforating lesions should be considered as EPS associated with PXE[12-14] or simply as perforating PXE.[15-17] The first group includes patients previously diagnosed with generalized hereditary PXE, who in the course of their disease progression develop clinical lesions that are histopathologically indistinguishable from EPS.[12,13] The second group is characterized by transepidermal elimination of altered elastic fibers occurring in a localized, acquired form of PXE usually in the periumbilical region, who do not develop other ocular, vascular, and visceral manifestations of hereditary PXE.[15,16] The two entities were described as distinct entities by Lund and Gilbert. The term periumbilical perforating PXE was first proposed by Hicks *et al.*, in 1979, for the second entity.[16] Later, Neldner and Martinez-Hernandez proposed the term "localized acquired cutaneous pseudoxanthoma elasticum," as they believed that the process was "acquired" and was lacking "systemic involvement."[18]

Differentiating the above conditions is important as the prognosis differs and a close follow up is needed in the hereditary form of PXE to rule out the systemic involvement.

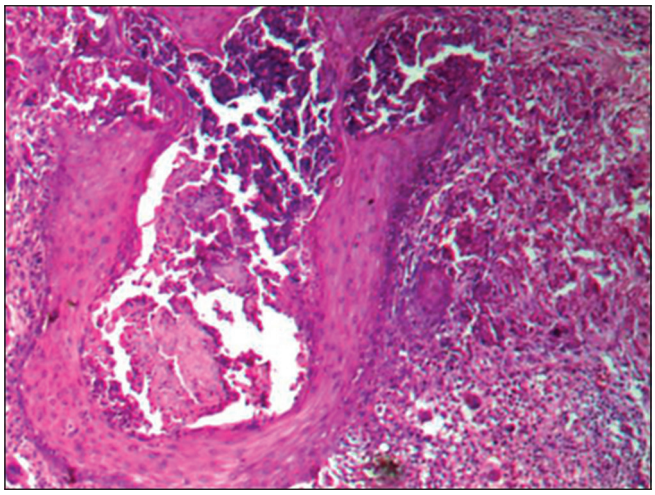

Figure 7: Higher magnification revealing disrupted follicle surrounded by foreign body–type granulomatous inflammation with several foreign body giant cells and neutrophils with small fragments of elastic fibers in the infundibular wall [H and E, ×40]

We categorize our patient into the hereditary form with systemic involvement such as angioid streaks and having associated EPS lesions. We also highlight the importance of prominent mental crease, which when identified in an individual less than 30 years should prompt a search for PXE, which is often diagnosed as in our patient.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Chassaing N, Martin L, Calvas P, Le Bert M, Hovnanian A. Pseudoxanthoma elasticum: A clinical, pathophysiological and genetic update including 11 novelABCC6 mutations. J Med Genet 2005;42:881-92.
2. Neldner KH. Pseudoxanthoma elasticum. Clin Dermatol 1988;6:1-159.
3. Pfendner EG, Uitto J, Gerard GF, Terry SF. Pseudoxanthoma elasticum: Genetic diagnostic markers. Expert Opin Mol Diagn 2008;2:63-79.
4. Vanakker OM, Leroy BP, Coucke P, Bercovitch LG, Uitto J, Viljoen D, *et al*. Novel clinico-molecular insights in pseudoxanthoma elasticum provide an efficient molecular screening method and a comprehensive diagnostic flowchart. Hum Mutat 2008;29:205.
5. Le Saux O, Urban Z, Tschuch C, Csiszar K, Bacchelli B, Quaglino D, *et al*. Mutations in a gene encoding an ABC transporter cause pseudoxanthoma elasticum. Nat Genet 2000;25:223-7.
6. Bergen AA, Plomp AS, Schuurman EJ, Terry S, Breuning M, Dauwerse H, *et al*. Mutations in ABCC6 cause pseudoxanthoma elasticum. Nat Genet 2000;25:228-31.
7. Ringpfeil F, Lebwohl MG, Christiano AM, Uitto J. Pseudoxanthoma elasticum: Mutations in the MRP6 gene encoding a transmembrane ATP-binding cassette (ABC) transporter. Proc Natl Acad Sci USA 2000;97:6001-6.
8. Le Saux O, Bunda S, VanWart CM, Douet V, Got L, Martin L, *et al*. Serum factors from pseudoxanthoma elasticum patients alter elastic fiber formation *in vitro*. J Invest Dermatol 2006;126:1497-505.
9. Jiang Q, Uitto J. Pseudoxanthoma elasticum: A metabolic disease? J Invest Dermatol 2006;126:1440-1.
10. Lebwohl M, Neldner K, Pope FM, De Paepe A, Christiano AM, Boyd CD, *et al*. Classification of pseudoxanthoma elasticum: Report of a consensus conference. J Am Acad Dermatol 1994;30:103-7.
11. Mehta RK, Burrows NP, Payne CM, Mendelsohn SS, Pope FM, Rytina E. Elastosis perforans serpiginosa and associated disorders. Clin Exp Dermatol 2001;26:521-4.
12. Schutt D. Pseudoxanthoma elasticum and elastosis perforans serpiginosa. Arch Dermatol 1965;91:151-2.
13. Caro I, Sher MA, Rippey JJ. Pseudoxanthoma elasticum and elastosis perforans serpiginosa. Report of two cases. Dermatologica 1975;150:36-42.
14. Lund HZ, Gilbert CF. Perforating pseudoxanthoma elasticum. Its distinction from elastosis perforans serpiginosa. ArchPathol Lab Med 1976;100:544-6.
15. Schwartz RA, Richfield DF. Pseudoxanthoma elasticum with transepidermal elimination. Arch Dermatol 1978;114:279-80.
16. Hicks J, Carpenter CL Jr, Reed RJ. Periumbilical perforating pseudoxanthoma elasticum. Arch Dermatol 1979;115:300-3.
17. Smith EW, Malak JA, Goodman RM, McKusick VA. Reactive perforatingelastosis: A feature of certain genetic disorders. Bull Johns Hopkins Hosp 1962;111:235-51.
18. Neldner KH, Martinez-Hernandez A. Localized acquired cutaneous pseudoxanthoma elasticum. J Am Acad Dermatol 1992;1:523-30.