Net Case

Pseudoxanthoma elasticum: Description of a late onset case

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ABSTRACT

Pseudoxanthoma elasticum (PXE) is a genetic multisystem disorder characterized by ectopic mineralization of connective tissues with primary manifestations in the skin, retina and cardiovascular system, and a phenotypic spectrum highly variable.This article presents the case of a 46-year-old male patient with sporadic late-onset PXE, without severe systemic complications.

Key words: Pseudoxanthoma elasticum, adenosine triphosphate binding cassette-C6, elastic tissue disorder

INTRODUCTION

Pseudoxanthoma elasticum (PXE) is an inherited connective tissue disorder characterized by an abnormal calcification of the elastic tissue network of the skin, retina and cardiovascular system.[1] The prevalence is currently estimated at 1 in 25,000–70,000.[2] The disorder results from mutations in a gene located at chromosome 16p13.1, which encodes for the transmembrane transporter protein adenosine triphosphate binding cassette-C6 (ABC-C6).[1] Autosomal dominant and autosomal recessive patterns of inheritance, such as sporadic cases, have been described.[3] Recent molecular genetic studies show evidence for a recessive inheritance pattern only.[4] Skin lesions consist of yellowish papules or plaques with an associated increase in skin laxity. Commonly affected sites are the flexures and periumbilical skin. Mucous membrane involvement is not rare. Ocular involvement is characterized by angioid streaks, breaks in the Bruch's membrane, with secondary changes of the retinal pigmented epithelium (peau d'orange) and choriocapillaris. These ocular defects are asymptomatic at first, but may be complicated by retinal neovessels, recurrent hemorrhage, disciform scarring and eventual loss of central vision. Cardiovascular manifestations usually develop last and result from slowly progressive calcification of elastic arterial walls with an increased risk of accelerated peripheral vascular disease, ischemic heart disease, hypertension and cerebrovascular disease.[1,5] Histology of skin lesions shows calcification, alteration and fragmentation of elastic structures in the mid-dermis.[1] The diagnosis is most often made late in the second or third decade of life.[6] We describe the case of a male patient who developed lesions referable to PXE after the age of 40 years, in the absence of severe systemic complications.

CASE REPORT

A 46-year-old male patient, a Caucasian in good health, presented with a 5-year history of an asymptomatic eruption on the neck. He did not have any significant history of sun exposure. Physical examination revealed numerous firm, round to oval, white-ivory to yellowish, non-follicular papules of a few millimeters in diameter, coalescing into plaques with a symmetric disposition around the neck and skin laxity in this area [Figures 1 and 2]. The results from routine laboratory tests were within normal limits. Electrocardiography (ECG) and radiography of the chest were normal. The ophthalmologic examination revealed the presence of "peau d'orange" changes, clinically asymptomatic. Moreover, no family history of similar eruptions in

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first-degree relatives was recorded. Examination of a neck skin biopsy specimen, stained with hematoxylin-eosin [Figure 3] and von Kossa stains [Figure 4] showed fragmented and calcified elastic fibers in the mid-dermis. On the basis of clinical, histopathologic and other findings, diagnosis of "sporadic" PXE was made. Therefore, a prophylactic lifestyle, medical-instrumental monitoring and genetic counseling were recommended.

DISCUSSION

Although PXE can be associated with considerable morbidity and significant mortality, the phenotypic spectrum is highly variable with both inter- and intrafamilial heterogeneity.[7]

The clinical variability is evident by observations that the involvement of all three major organ systems, i.e., skin, eyes and the cardiovascular system, is encountered in some patients, whereas others, even within the same family, have a limited involvement of one of these organs. This may indicate that disease expression is possibly influenced by environmental factors.[1]

The assessment of inheritance is complicated by the clinical heterogeneity and highly variable age of onset of the disease. Specifically, in rare cases, the manifestations are noted during infancy, whereas in most cases the clinical signs are not evident until the second or third decade of life, sometimes more lately like the case described here. It has been estimated that the average time between the onset of skin lesions and the diagnosis is about 20-25 years. This prolonged time lapse can be explained by the

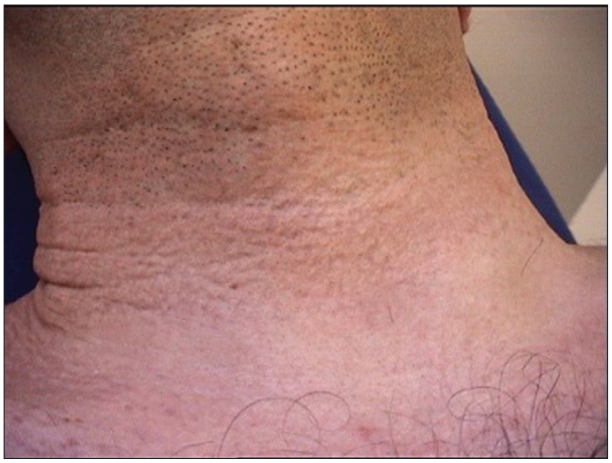

Figure 1: Yellowish papules and plaques on the neck, characteristic of PXE

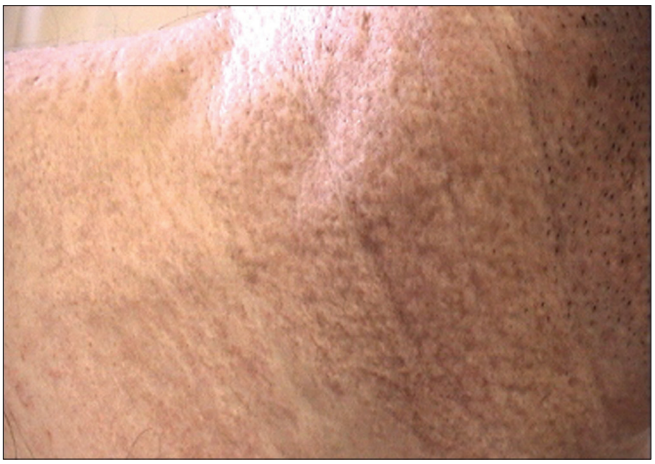

Figure 2: Close-up of Figure 1

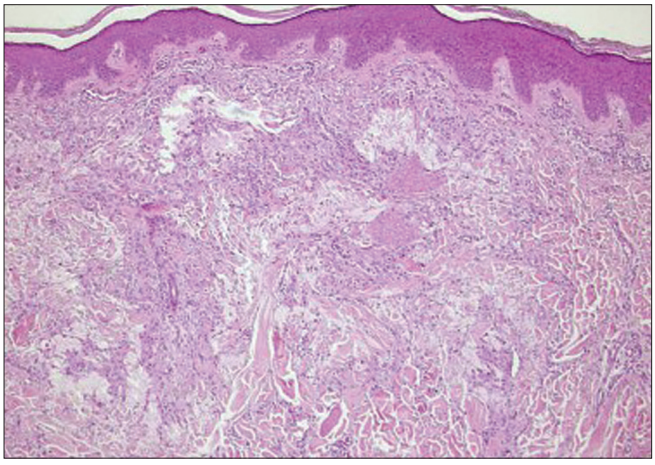

Figure 3: The elastic fibers in the mid-dermis are clumped, degenerated, fragmented and swollen (H and E, ×100)

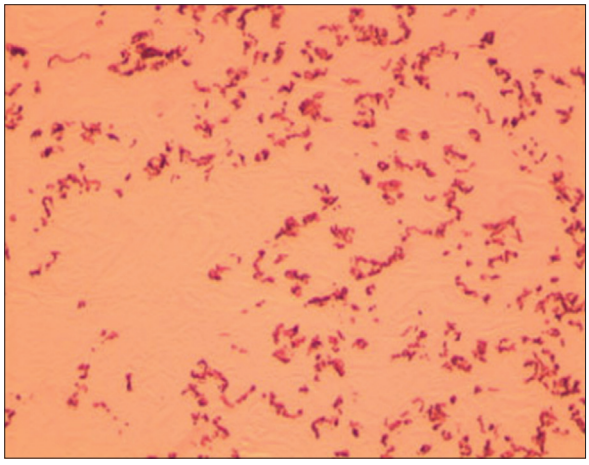

Figure 4: Von Kossa staining shows fragmented and calcified elastic fibers (original magnification ×200)

fact that majority of the patients were not concerned about their skin lesions and did not seek medical advice until signs of a generalized disorder, such as ophthalmic involvement, presented in middle age.[1,4] However, 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 developed.[8]

More than 120 different mutations in ABC-C6 have been identified, and PXE is now considered to be recessively inherited in most cases.[4] ABC-C6 is predominantly expressed in the liver and kidneys, suggesting that transporter dysfunction may lead to accumulation of an unknown substrate in the blood causing secondary dystrophic changes of elastic tissues. Therefore, PXE would not seem to be a primary disorder of elastic fibers, rather than a systemic metabolic disease.[1,9]

Diagnosis of the disease is important, although there is no treatment for the basic defect.

It is important to keep in mind that sporadic late onset cases of PXE must be distinguished from skin lesions that superficially resemble PXE, such as solar elastosis, cutis laxa, penicillamine therapy, lesions secondary to vitamin D toxicity or renal disease and with other conditions termed "age-related fibroelastolytic syndromes (ARFS)" such as pseudoxanthoma elasticum-like papillary dermal elastolysis (PDE), fibroelastolytic papulosis of the neck (FEPN), white fibrous papulosis of the neck (WFPN) and possible overlaps between the clinical and pathologic features of these conditions in some cases. Particularly, the real incidence of "fibroelastolytic conditions" of intrinsic aging is probably underestimated and its distinction from PXE is important to spare patients from useless investigations. Routine histopathology is not specific and a clinic-pathologic correlation with special microscopic stains is necessary to make the right diagnosis.[10]

However, the later age onset, the absence of retinal and vascular changes, and the lack of elastic fiber fragmentation and calcium deposition are all factors that must be considered for an ARFS.

In this case report, typical histologic findings and early retinal changes were decisive to consider the diagnosis of "sporadic late onset PXE".

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