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Pseudoxanthoma elasticum and calcinosis cutis

Psödoksantoma elastikum ve kalsinozis kutis

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Summary

Pseudoxanthoma elasticum (PXE) is an inherited multisystem disorder with ectopic mineralization of connective tissues and characteristic clinical manifestations in the skin, eyes and cardiovascular system.

A 46-year-old woman was admitted to dermatology clinic with whitish/yellow papules that coalesce into cobblestone patterned plaques at the lateral, posterior aspect of the neck 6 previously. Two of the lesions were excised by plastic surgery. Histologically fragmented calcified elastic fibers were seen in the affected elastic tissue of the dermis accompanied by dystrophic calcinosis cutis in the superficial dermis. Fundoscopic examination revealed bilateral angioid streaks and peau d'orange lesions. Because of the typical skin findings proved by biopsy and ocular involvement, our diagnosis was PXE.

We should be aware of this entity since PXE is associated with considerable morbidity and mortality. The second important point is when we note calcinosis cutis, we should look for elastic tissue damage since calcium prefers depositing in those areas.

Key Words: Pseudoxanthoma elasticum, calcinosis.

Özet

Psödoksantoma elastikum (PXE), bağ dokuların ektopik mineralizasyonuna bağlı cilt, göz ve kardiyovasküler sistem bulgularıyla karakterize kalıtsal multisistemik bir hastalıktır. 46 yaşında kadın hasta, ilk kez 6 ay önce fark ettiği boyun yan, arka kısmında birleşerek kaldırım taşı paterni oluşturan sarı-beyaz papüler lezyonlar nedeniyle dermatoloji kliniğine başvurdu. Lezyonlardan ikisi plastik cerrahi tarafından eksize edildi. Lezyonların histolojik incelemesinde dermiste fragmante, kalsifiye, elastik lifler görüldü. Ayrıca yüzeyel dermada distrofik kalsinozis kutis izlendi. Fundus bakısında her iki gözde optik disk çevresinde radial yerleşim gösteren damarsı çizgilenmeler (anjioid streaks) ve makula temporalinde portakal kabuğu görüntüsü (peau d'orange) dikkati çekti. Ek olarak koroid neovaskülarizasyonu sekel dönemi ile uyumlu olabilecek bilateral subfoveal fibröz skar görüldü. Cilt biyopsisinde izlenen histopatolojik bulgular ve tipik göz bulgularıyla tanımız PXE ve buna eşlik eden kalsinozis kutis oldu. Ciddi morbidite, mortaliteyle ilişkili bu antiteyi akılda tutmalı ve kalsinozis kutis gördüğümüz biyopsileri elastik doku hasarı açısından da incelemeliyiz.

Anahtar Sözcükler: *Psödoksantoma elastikum, kalsinozis.*

Introduction

Pseudoxanthoma elasticum (PXE) is an autosomal recessive inherited disorder displaying ectopic mineralization of connective tissues, with clinical manifestations in the skin, the eyes, and the cardiovascular system.

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The prevelance of PXE is around one in 50,000 with a carrier frequency of ~ 1:150-300 (1). The mutations in the *ABCC6* gene which encodes a putative efflux transporter is responsible in most of the PXE cases (1). *ABCC6* protein transport anti-mineralization factors from hepatocytes to the circulation. In PXE, the absence of *ABCC6* activity causes a low concentration of anti-mineralization factors in circulation allowing abnormally calcified elastic tissue fibers in the retina, blood vessels, kidney and the skin (1).

PXE-like cutaneous changes, sometimes associated with angioid streaks can be found in patients with β-thalassemia and sickle cell anemia but it has been demonstrated that these individuals do not harbor mutations in the *ABCC6* gene. By targeted ablation of the *ABCC6* gene, transgenic knockout mice developed features of human PXE including autosomal recessive inheritance and deposition of mineral complexes in the skin, the retina and the vessels. Fibroblast cultures of PXE patients demonstrate low levels of *ABBC6*, altered growth, migration. The skin findings in PXE usually present at the second or third decade. The elastic tissue fibers differ from elastin isolated from normal tissue. The cobblestone appearance of the skin resembles that of a chicken, with marked laxity and redundancy (2).

Accurate diagnosis may not made until serious vascular or ocular complications develop. Symptoms of arterial disease occur in 14-18% of patients with PXE (3). Calcification of elastic tissue in the media of the arterial wall may lead to vascular occlusion or fragility (3). Cardiovascular hypertension, ischaemic heart disease and arrhythmias have been attributed to PXE. Coronary artery lesions have been found in teenagers with PXE, with a case of bypass grafting being required in an 18-year-old (3). Eye manifestations occur as a result of tears in a calcified Bruch's membrane, an elastin containing membrane that separates the vascular choroid from the retina. The resulting angioid streaks are seen in 80% of patients with PXE, with associated risks of retinal/vitreous haemorrhage and central blindness (2). Gastrointestinal (GI) hemorrhage is a rare complication of PXE. A case of PXE with Mallory-Weiss syndrome, who had repetitive and massive upper GI bleeding was reported in the literature (4).

The severity of the symptoms is modulated by the genetic background, epigenetic factors, lifestyle variables. There is no specific or effective treatment for PXE (5).

Cutaneous calcification occurs as a result of calcium disregulation by local or systemic events. Calcinosis cutis can be divided into four subgroups: metastatic, dystrophic, idiopathic and iatrogenic (6). When systemic calcium or phosphate metabolism is abnormal, metastatic calcification occurs in normal tissue. Dystrophic calcification occurs with normal calcium and phosphate metabolism in association with connective tissue disease or at sites of damaged tissue.

PXE is rarely associated with cutaneous calcification (7). Here we present a case with clinical and histologic manifestations of both calcinosis cutis and PXE.

Case Report

A 46-year-old woman with multiple medical problems including non-insulin dependent diabetes mellitus, hyperlipidemia, hypertension was admitted to dermatology clinic for further evaluation of skin lesions. Physical examination revealed small whitish-yellow papular lesions merging into plaques and cobblestone appearance on the posterior and lateral aspect of the neck. The patient stated that the changes in her skin had begun on the neck about 6 months ago. She had also been experiencing deteriorating vision in both eyes. She delivered 2 healthy children by ceserean (C/S) at 2002 and 2004. The antenatal course was unremarkable. But loss of vision acuity progressed after the second C/S in 2004. It was associated with anaesthetic medications. Findings from fundus examination revealed angioid streaks, peau d'orange and bilateral subfoveolar fibrous scar (Figure-1A).

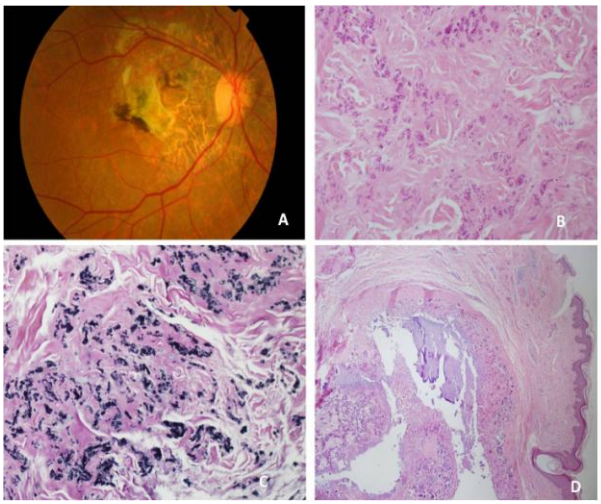

Figure 1-A. Angioid streaks and Peau d'orange lesions under fundoscopic examination
B. Irregular clumped and fragmented elastic tissue (HE, x200)
C. The elastic tissue is highlighted with elastic tissue stain (Verhoeff-van Gieson stain, x400)
D. Well circumscribed dermal agregate of cystic cavity containing calcified material with a surrounding granulomatous infiltrate (HE, x40).

Her family history was unremarkable. Her relatives exhibited none of the dermatological or ophthalmic signs of the disease. Skin biopsy was taken from lesional area of the neck by plastic surgery. Histopathologic findings revealed fragmented, calcified elastic tissue in reticular dermis (Figure-1B,C). Also we noted calcified well circumscribed nodule in the papillary dermis (Figure-1D). There was no elastic change in the papillary dermis, no melanophages and dermal fibrosis.

Discussion

Elastic fibers are components of dermal connective tissue that can be affected in several acquired disorders. We should differentiate PXE from PXE-like elastic tissue

disorders including PXE-like papillary dermal elastolysis (PDE), white fibrous papulosis (WFP) and perforating PXE (PPXE).

PDE is a rare acquired elastic tissue disorder occuring in postmenopausal and elderly women characterized by soft yellow papules with a tendency to coalesce into cobblestone plaques on the neck, axillae, forearm, inframammary folds (8). This entity simulates inherited PXE but no systemic involvement has been reported. Histopathological clues are, bandlike loss of elastic fibers in the papillary dermis and the presence of sparse melanophages in the papillary dermis within the zone of elastic loss (8).

WFP of the neck also mimic PXE. The clinical presentation is characterized by nonconfluent whitish, firm papules on back of the neck (9). Histopathologic examination shows loss of elastic fibers in papillary dermis and dermal fibrosis (9).

PPXE is a disorder of coalescing keratotic papules with altered elastic fibers and transepidermal elimination (10). PPXE is considered as a localized cutaneous form of hereditary PXE (10). It usually presents as a hyperpigmented plaque over the periumblical region and affects middle-aged, obese women. Histopathology reveals altered short elastic fibers with calcification in the reticular dermis extruding through the epidermis.

In our case, typical skin findings and additional systemic symptoms were consistent with PXE.

Several features of PXE are of relevance to anaesthesia so any patient with a multi-system disease should be included in guidelines to maximise the detection of potential anaesthetic problems.

In conclusion, PXE cases should receive counselling from a clinical geneticist regarding the risk of transmission to their offspring.

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