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Pseudoxanthoma elasticum: Case series of three siblings

Psödoksantoma elastikum: Üç kardeşten oluşan bir olgu serisi

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Abstract

Pseudoxanthoma elasticum (PXE) is a rare multisystemic genetic disease with dermatologic, cardiovascular and ocular involvement. PXE primarily affects the skin, and the ocular involvement is noted in almost 85% of patients. Cardiovascular complications caused by PXE often develop in adults. Since the prognosis of PXE is primarily dependent on extracutaneous organ involvement, early diagnosis of PXE is of prime importance for taking preventive measures. In this report, we present three siblings diagnosed with PXE.

Keywords: Pseudoxanthoma elasticum, retinal pigmentation, angioid streaks

Öz

Psödoksantoma elastikum deri, kardiyovasküler sistem ve göz tutulumu olan, nadir görülen multisistemik ve genetik bir hastalıktır. Etkilenen esas organ deridir. Hastaların yaklaşık %85'inde göz tutulumu vardır. Kardiyovasküler komplikasyonlar, genellikle erişkinlerde ortaya çıkar. Prognozu genellikle ekstrakutanöz organ tutulumuna bağlı olduğu için hastalığın erken tanınması, koruyucu önlemler alınması açısından önem kazanmaktadır. Burada psödoksantoma elastikum tanısı konulan üç kardeşten oluşan bir olgu serisi sunulmaktadır.

Anahtar kelimeler: Psödoksantoma elastikum, retinal pigmentasyon, anjioid çizgiler

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Introduction

Pseudoxanthoma elasticum (PXE), also known as Grönblad–Strandberg syndrome, is a multi-systemic genetic disease with dermatologic, cardiovascular and ocular involvements, characterized by fragmentation and mineralization of elastic fibers [1, 2].

In this report, we present three siblings who presented to our clinic with yellowish papular lesions on the neck and were diagnosed with PXE.

Case Series

Case 1

A-14-year-old male sibling presented to our clinic with a 2-year history of yellowish papules on the neck. Family history indicated that his two siblings also had similar lesions on the neck. Skin examination revealed multiple yellowish papules measuring 1 to 2 mm in size on the neck (Figure 1a). Histopathological examination of the cutaneous lesions showed degeneration and fragmentation of elastic fibers in the dermis (Figures 1b,1c). A dilated fundus examination showed focal retinal pigment epithelium and angioid streaks in both eyes (Figure 1d). No additional pathology was found on cranial computed tomography (CT), transthoracic echocardiography (ECG), and upper gastrointestinal endoscopy. Depending on these findings, the patient was diagnosed with PXE.

The written consent was taken from the parents of the patient.

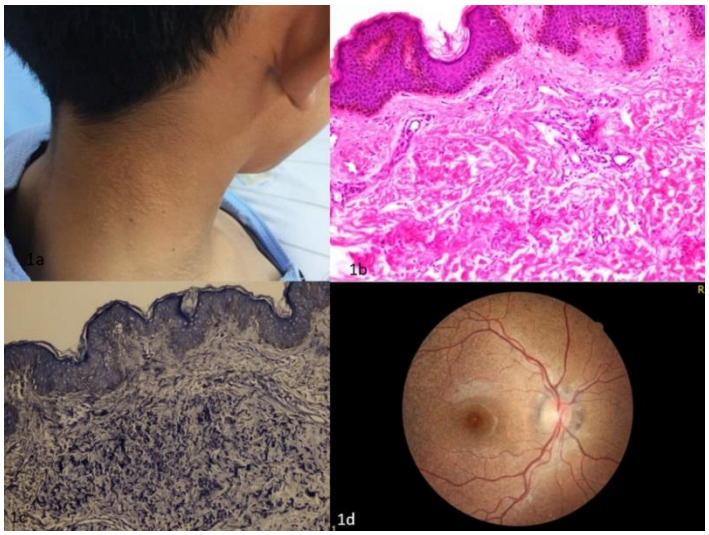

Figure 1: a) Multiple yellowish papules, measuring 1-2 mm in diameter, are observed on the neck, b) Destruction and globular configuration of dermal elastic fibers are noted (HE; X200), c) Degeneration and fragmentation are seen in elastic fibers (Verhoeff-van Gieson stain, x200), d) In color images of fundus, punctuate retinal pigmentation is noted in the right eye.

Case 2

A 20-year-old male sibling presented with a 3-year history of yellowish papules in the neck, similar to his siblings. Skin examination also revealed multiple yellowish papules measuring 1 to 3 mm in size in the neck (Figure 2a), histopathological examination also indicated degeneration and fragmentation of elastic fibers in the dermis (Figure 2b,2c), and a fundus examination also showed focal retinal pigment epithelium and angioid streaks in both eyes (Figure 2d). Depending on these findings, this sibling was also diagnosed with PXE.

The written consent was taken from the patient.

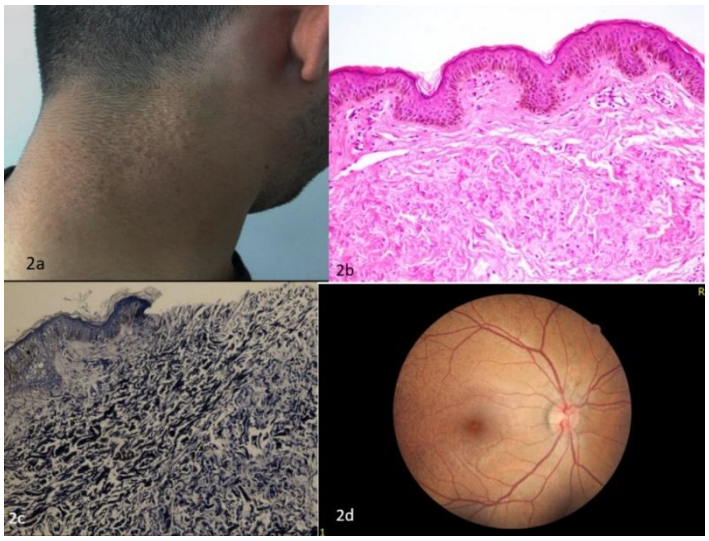

Figure 2: a) Multiple yellowish papules, measuring 1-3 mm in diameter, are observed on the neck, b) Destruction and globular configuration of dermal elastic fibers are noted (HE; X200), c) Degeneration and fragmentation are seen in elastic fibers (Verhoeff-van Gieson stain, x200), d) In color images of fundus, punctuate retinal pigmentation and angioid streaks are noted in the right eye.

Case 3

A-16-year-old male sibling presented with a 2-year history of yellowish papules in the neck, similar to his siblings. In a similar fashion, skin examination revealed multiple yellowish papules measuring 1 to 2 mm in size on the neck (Figure 3a), histopathological examination showed degeneration and fragmentation of elastic fibers in the dermis (Figure 3b,3c), and a fundus examination showed focal retinal pigment epithelium and angioid streaks in both eyes (Figure 3d). This sibling was also diagnosed with PXE.

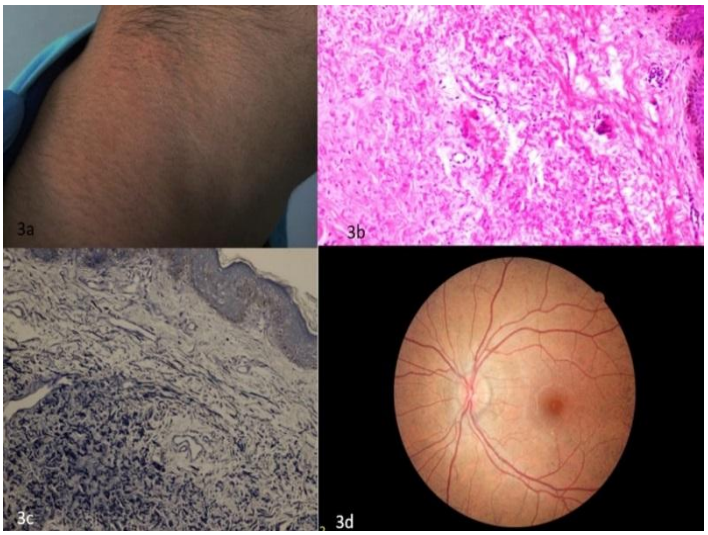

Figure 3: a) Multiple yellowish papules, measuring 1-2 mm in diameter, are observed on the neck, b) Destruction and globular configuration of dermal elastic fibers are noted (HE; X200), c) Degeneration and fragmentaton are seen in elastic fibers (Verhoeff-van Gieson stain, x200), d) In color images of fundus, punctuate retinal pigmentation and angioid streaks are noted in the left eye.

The written consent was taken from the parents of the patient.

Discussion

With an estimated prevalence of 1:50,000, PXE is a rare connective tissue disease. PXE is twice more common in women than in men and there is no geographical or racial predisposition reported in the literature [2,3]. PXE rarely manifests itself in infants and is usually recognized in the second or third decades of life. Although most cases are sporadic and the majority of familial cases exhibit autosomal recessive inheritance (90%), autosomal dominant inheritance can also be seen [1,4]. In our patients, PXE developed in the second decade of life, which was consistent with the literature.

The primary cause of PXE is considered to be the mutations in the ABCC6 gene that encodes the trans-membrane protein ABCC6 which has been reported with more than 300 mutations [5]. Since the symptoms of PXE vary even between the members of the same family, PXE is considered to be a disease that does not only show genetic inheritance but also interacts with genetic and environmental factors, hormonal status, and nutrition [1, 5].

Skin is the primary organ affected by PXE. Mean age at onset for the skin lesions is 13.5 years. In PXE, the skin is often loose and wrinkly and the lesions are usually characterized by yellowish papules or coherent reticular plaques measuring 1 to 3 mm in diameter, mostly localized in the neck, antecubital fossa, inguinal region, and periumbilical areas. Moreover, the lesions may also be seen in the oral, nasal, vaginal, and rectal mucosa. However, the absence of skin lesions does not rule out PE [2, 4, 5]. In our patients, the lesions were localized in the neck but no lesions were detected in any mucosa.

Ocular involvement has been reported in almost 85% of the patients with PXE. Ocular involvement is usually bilateral and develops between the ages of 20-40 years. PXE manifests its principal signs in the fundus by influencing the Bruch's membrane. The primary ocular sign is focal retinal pigment epithelium, followed by angioid streaks, peau d'orange, optic disc drusen, comet sign, and choroid neovascularization. In PXE patients, the visual function can often be preserved by laser therapy; therefore, early diagnosis of ocular disorders is crucially important [1, 6]. In our patients, both focal retinal pigment epithelium and angioid streaks were present.

Cardiovascular complications arising from PXE often develop in adults. Intermittent claudication is the most common and the earliest cardiovascular symptom. Moreover, PXE has also been shown to cause angina pectoris, arterial hypertension, restrictive cardiomyopathy, mitral valve prolapse, mitral stenosis, and sudden cardiac death. On the other hand, the damage in the elastic fibers of the blood vessels may result in gastrointestinal hemorrhage which is often recurrent and has gastric origin and is mostly seen in pregnant patients [7,8]. In our patients, no cardiovascular complications and gastrointestinal hemorrhage were observed.

The histological examination of cutaneous lesions is essential for the definitive diagnosis of PXE. The primary histological feature of PXE is progressive mineralization and fragmentation of mid-dermal elastic fibers, resulting in a histological image pattern known as elastorrhexis [2, 9]. In line with the literature, the histological examination of the lesions in our patients showed degeneration and fragmentation of elastic fibers in the dermis.

The main dermatological diseases considered in the differential diagnosis of PXE include cutis laxa, fibroelastolytic papulosis, PXE-like papillary dermal elastolysis, late-onset focal dermal elastosis, and perforating calcific elastosis [2, 7]. In our patients, no such diseases were detected.

No specific or effective treatment is currently available for the systemic mineralization and fragmentation of elastic fibers in the skin, eyes and arterial blood vessels caused by PXE [10]. However, regular exercise, weight control, and treatment of hypertension and hyperlipidemia are mandatory for the treatment of cardiovascular symptoms. Moreover, drugs that may cause gastrointestinal bleeding and hormone replacement therapies should be avoided. Laser therapy is performed for choroidal neovascularization [4, 10]. In a similar fashion, it is logical to advise patients to perform regular exercise and weight control, to avoid drugs that may cause gastrointestinal bleeding, and to undergo regular eye examination for the early diagnosis of ocular disorders.

The prognosis of PXE is primarily dependent on extracutaneous organ involvement; therefore, early diagnosis of PXE is of prime importance for taking preventive measures and to decrease the morbidity rate. PXE should be considered in the family members presenting with the same xanthomatous lesions and systemic screening should be performed for all the family members.

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