

Two cases of pseudoxanthoma elasticum with renal involvement

Esmat Ghanei¹, MD, Seyyed Mohammad Homayouni², MD, Alireza Nasrollahi³, MD

Dept. of Internal Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran.

Abstract

Pseudoxanthoma elasticum is a rare, hereditary, multisystemic disease affecting the skin, eye, and cardiovascular system. Renal involvement is uncommon.

We describe two cases of pseudoxanthoma elasticum (PXE) in two women with distinctive skin lesions and nephrocalcinosis that renal ultrasonography showed a characteristic pattern of dotted increased echogenicity in the corticomedullary junction. One of them had IgA nephropathy that was proven by kidney biopsy. Skin biopsy and fundus examination confirmed the diagnosis. Early diagnosis of PXE is important for minimizing systematic complications and informing the other family members through genetic counseling. Our case with PXE and IgA nephropathy is the first case report.

Keywords: Pseudoxanthoma Elasticum - nephrotic syndrome - IgA nephropathy

Introduction

Pseudoxanthoma Elasticum is an inherited disorder of connective tissue characterized by skin, eye and cardiovascular system involvement. Renal involvement includes renovascular hypertension and calcification of the interlobar and arcuate arteries [1].

Patients with PXE are presented to physicians with skin lesions, advanced loss of vision, significant bleeding in gastrointestinal system and intermittent claudication due to presence of abnormal elastic fibers.

While generally, autosomal recessive inheritance is determined (80%), autosomal dominant and sporadic cases have been reported, as well. A mutation in the gene which codes ABCC6 (MRP6) transmembrane transporter protein was reported to be a possible cause of PXE [2].

Case 1

A 36 years old woman was admitted at our hospital in December 2006 for evaluation of hematuria.

She had visual loss since adolescence. Physical examination revealed body mass index (BMI), 22 kg /m² and blood pressure of 110/70 mmHg. Fundus examination showed angioid streaks radiating out wards from the peripapillary area bilaterally. Thickened yellowish skin was noticed in neck, axillar and abdominal wall, (Figs. 1-5). She was visited by ophthalmologist and dermatologist, who both of them were in agreement with PXE, and the skin biopsy had documented this diagnosis. There were no other significant positive signs. In family history, her brother had PXE with skin lesions. Laboratory tests revealed: hemoglobin 13.6 g/dl, hematocrit 41%, white blood cell count 10100, platelets 256×10⁹, Erythrocyte sedi-

1. **Corresponding author**, Department of Internal Medicine of Shohada Hospital . Assistant professor of Shahid Beheshti University of Medical Sciences, Tehran , Iran. Email: dr-e-ghanei@yahoo.com, Tel : +9821 22733252.

2. Assistant Professor, Department of Internal Medicine of Shohada Hospital. Shahid Beheshti University of Medical Sciences, Tehran, Iran.

3. Assistant Professor, Department of Internal Medicine of Shohada Hospital. Shahid Beheshti University of Medical Sciences, Tehran, Iran.



Fig. 1. Thickened yellowish skin lesion in neck (antero-lateral).



Fig. 2. Thickened yellowish skin lesion in neck (posterior).

mentation rate 8, C-Reactive Protein <2 mg/l, Anti streptomycin-O(ASO)< 160 Iu/ml.

Urinalysis was revealed many red blood cells and six to eight white blood cells, protein 3+ with dipstick test, one granular cast in high power field and specific gravity 1012. Serum electrolytes, liver enzymes, and thyroid function tests were within normal limits. Blood urea nitrogen was 24 mg/dl, serum creatinine was 0.8 mg/dl, and creatinine clearance was 117 ml/minute. 24 hours protein and calcium excretion were 3900 mg and 168 mg, respectively. In order to assess the cause of nephrotic syndrome, the following tests were performed: Anti nuclear antibody, Antibody neutrophilic cytoplasmic antibody, Anti ds - DNA Antibody, Hepatitis B Surface antigen and antibody, Hepatitis C Virus antibody, Human Immunodeficiency virus antibody, were negative (C3 122 mg/dl (Normal range 90-180), C4 21 mg/dl (Normal range 10-40), CH 50 94% (Normal range 90-98%)). VDRL and RPR were negative. In serum protein electrophoresis there was slightly hypoalbuminemia and somewhat increased beta globulins, the remaining was within normal range. Abdominal ultrasound showed normal liver, spleen, but there were some fine hyperechogenic spots suggesting small calcifications at the corticomedullary junction, howev-

er, normal waveforms were obtained at the level of intraparenchymal renal vessels. The size of both kidneys was normal. Intravenous pyelography was normal, too. We performed kidney biopsy for evaluation of nephrotic syndrome. Kidney biopsy studies including Immunofluorescence microscopy and light microscopy were compatible with IgA nephropathy.

Case 2

A 30 year-old woman was hospitalized in June 2006 for an episode of flank pain. She has had history of intermittent flank pain, skin lesions and visual loss since 15 years ago. The skin biopsy which was performed 3 years ago, documented Pseudoxanthoma Elasticum.

Physical examination revealed blood pressure of 110/70 mmHg. She was afebrile. Fundus examination showed angioid streak bilaterally. Thickened yellowish skin was noticed in the axillar, neck, antecubital, inguinal regions and on the abdominal wall. There were no other significant positive signs. Laboratory tests revealed:

Hemoglobin 10 g/dl, Hematocrit 31.4%, white blood cell count 5.9×10^9 , platelets 319×10^9 , erythrocyte sedimentation rate 9 Urinalysis was within, normal limits on several occasions.

Serum electrolytes, liver enzymes and kidney function test were within normal limits. Serum calcium was 8.6-10.3 mg/dl. Serum PTH and 24 hours urine calcium were normal. Arterial blood gas revealed pH:7.45, PCO_2 : 32.4 mmHg, PO_2 : 98 mmgh, and HCO_3 :23 mmo/L.

The electrocardiogram and echocardiography were normal. Renal ultrasonography showed both kidneys normal size with smooth outline, multiple medullary calcification, and medullary nephrocalcinosis.

Discussion

Pseudoxanthoma Elasticum (PXE) is an inherited disorder of connective tissue characterized by generalized elastorrhexis affecting the elastic tissue in the dermis, the blood vessels, and Bruch's membrane of the eye. Calcium accumulates in the abnormal fibers [1,3].

At least two forms of PXE exist, autosomal recessive (the more common form) and autosomal dominant. A gene for both forms maps to human chromosome 16 and has been identified as encoding one of the adenosine triphosphate (ATP)- binding cassette transporters. Because of the prominent histopathologic feature of calcification of elastic tissue, this gene may be important in calcium homeostasis [4].

The exact frequency of PXE is unknown, but it is probably underdiagnosed. Rough approximations suggest a prevalence of 1 in 100,000. Male and female are equally affected, although women are more likely to seek medical attention out of concern for the skin changes.

The hallmark of PXE, and an important diagnostic clue, is the histopathologic finding of hyperproliferated elastic fibers in the middermis, there fibers become fragmented, clumped, and calcified. An arteriolar - sclerosis develops in the media of muscular arteries and arterioles, the lumen may become progressively and concentrically narrowed. Alternatively, micro aneurysms can form.



Fig. 3. Thickened yellowish skin lesion in neck (posterolateral).



Fig. 4. Thickened yellowish skin lesion in abdominal wall.



Fig. 5. Thickened yellowish skin lesion in abdominal wall

Thickening of the endocardium, especially atrial endocardium develops in some patients.

In the eye, Bruch's membrane becomes calcified and fragmented [4].

Clinical manifestations

Skin: Yellowish papule giving a "plucked chicken" appearance in flexural skin occur at an average age of 13-13.5 years [5,6].

Commonly affected areas include antecubital, popliteal, inguinal, neck, axilla, and periumbilical areas, as well as oral, vaginal, and rectal mucosa. In time, the skin may become lax a hang in folds, particularly in the neck, axilla, and groin. Diagnosis can be made by biopsy of affected skin. The characteristic histology consists of fragmentation and calcification of elastic fibers in the middle and lower third of the dermis.

Although, normal elastic fibers don't stain with hematoxylin eosin, altered elastic fibers from patients with PXE stain blue because of their calcium content.

Ocular: Angioid streaks, the characteristic ocular lesion of PXE, are red to brown curvilinear bands radiating from the optic disk. Angioid streaks apparently result from breaks in bruch's membrane associated with faulty elastic fibers in its outer portion, the lamina Elasticum. Fibrovascular ingrowth may result in retinal hemorrhage, detachment, and severe visual loss [6].

Vascular Disease: Calcification of the elastic media of blood vessels with subsequent intimal proliferation leads to serious complications, in this disorder. Calcification is the most common problem; pulses in adult are often obliterated.

Angina pectoris or abdominal angina may become incapacitating. Hypertension is prevalent in adults and appears to be associated with renal artery, involvement. It may occur early, in the disease.

Gastrointestinal hemorrhage, apparently due to fragile submucosal vessels, may occur early. Bleeding may occur in the urinary tract. For unknown reasons cerebrovascular disease ap-

pears to be less common than expected [2,6].

Cardiovascular manifestations are due to abnormal arterial calcification. They most commonly affect the medium - sized arteries of the extremities, but any artery may be involved. Peripheral vascular disease leads to intermittent claudication, weak or absent pulses, and limb fatigue. Other potentially serious complications include hypertension and gastrointestinal hemorrhage. Angina pectoris may develop, but myocardial infarction and cerebrovascular accidents are rare [5-8]

Renal: Renovascular hypertension has been reported in 25% of patients with PXE, and commonly occurs in adults. Due to calcification of the interlobar and arcuate arteries, a characteristic pattern of dotted increased echogenicity is seen in the corticomedullary junction, by renal ultrasonography. This increased echogenicity can also be seen in the spleen and pancreas [9].

There are a few cases report of PXE with renal involvement. Fabre [10] reported a case of 42-year-old man with PXE and recurrent nephrolithiasis, in march 2005. Hodson EM, reported a 4.5 -year-old girl with PXE and renovascular hypertension, in November 1992 [11].

Crespi [12] reported sonographic findings observed in a young patient with PXE at the level of the kidneys, which included fine hyperechogenic spots, in 1992.

Suarez MJ, reported a case of PXE in a child with skin lesion and renal ultrasonography showed a characteristic pattern of dotted increased echogenicity in the corticomedullary junction, in 1991 [13].

In our patients there were visual loss and angioid streaks of the retina and skin lesions compatible with PXE. Both of them had nephrocalcinosis, one of them with nephrotic syndrome and IgA nephropathy. In the best of our knowledge this case is the first case report of IgA nephropathy with PXE. Although these two diseases may be separate of each other.

Because PXE can be an inherited disorder the family of the patient was evaluated. There was

no parental consanguinity, but her brother had skin lesion and visual loss similar to our patients without kidney disease.

Treatment of PXE consists of close ophthalmologic management, monitoring and treatment of any cardiovascular symptoms, and dietary consultation.

Patients should be educated to avoid contact sports, (because of the risk of ocular disease) and referred for genetic counseling.

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