Minute yellowish papules on the lateral aspects of the neck and cubital fossa

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CLINICAL FINDINGS

A 65-year-old Kuwaiti female patient presented with a 5-year history of an asymptomatic eruption on the neck. The patient gave a history of gradual loss of vision since 2 years. Physical examination revealed numerous firm, round to oval, white-ivory to yellowish, non-follicular papules of a few millimeters in diameter, the lesions were distributed in the cubital fossa and the lateral aspects of the neck with a skin laxity in these areas (Fig. 1) and (Fig. 2). Blood pressure was 110/70 mmHg. Fundus examination showed angioid streak bilaterally. There were no other significant positive signs. Laboratory tests revealed: Hemoglobin 10 g/dl, Hematocrite 31.4%, white blood cell count. 9×109, platelets 319×109. Urinalysis was within normal limit. 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, PCO2:32.4 mmHg, PO2:98 mmHg. The electrocardiogram, echocardiography and abdominal ultrasonography were normal. Moreover, no family history of similar eruptions in first-degree relatives.

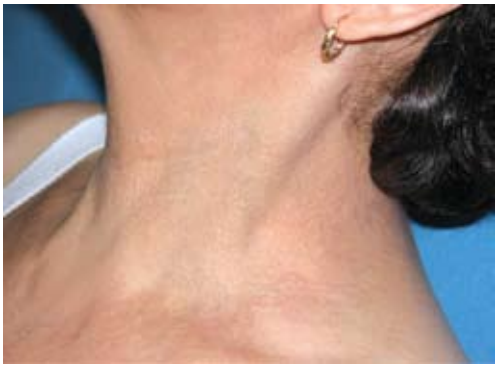

Fig. 1 Yellowish papules on the lateral aspect of the neck with a skin laxity.

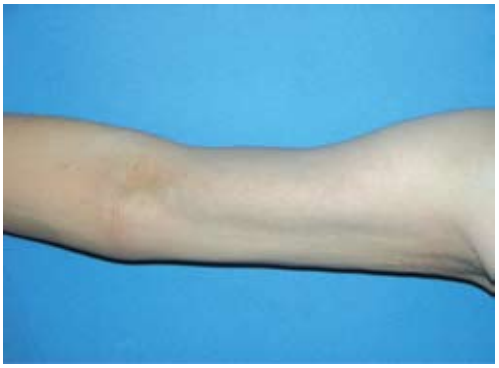

Fig. 2 Yellowish papules in the cubital fossa with a skin laxity.

What is your clinical differential diagnosis?

Pseudoxanthoma elasticum, cutis laxa, elastosis performance serpiginosa, solar elastosis and eruptive xanthomas

Pathological findings

Examination of a neck skin biopsy specimen, stained with hematoxylin-eosin (Fig. 3) and von Kossa stains (Fig. 4) showed fragmented and calcified elastic fibers in the mid-dermis.

DIAGNOSIS

Pseudoxanthoma Elasticum

COMMENTS

Pseudoxanthoma elasticum (PXE) is the name given to a group of connective tissue disorders that affects the elastic tissue of the skin, blood ves-

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Clinicopathological challenges of pseudoxanthoma elasticum.

Diagnosis	Clinical	Histopathological
Solar elastosis	• Papular or plaque like areas with a distinctly yellowish hue, often separated by exaggerated skin folds and furrows • Patulous follicular orifice around the lateral forehead and cheeks • Open and closed comedones are frequently present • Prominent and deeply fissured skin folds on the posterior and lateral neck.	• Abnormal elastic tissue located in the upper dermis beneath a small zone of spared papillary dermis • Elastic fibers with an eosinophilic to amphophilic to gray blue appearance with H&E • Elastic tissue stains reveal thick, tangled elastic fibers within amorphous ground substances • Calcium deposition does not occur.
Elastosis perforance serpiginosa	• Rare, none inherited • Around the nape of the neck, face and arms • Numerous small keratotic papules ,many with peripheral erythema, develop in unusual annular or circinate configurations	• Increased elastic fibers in papillary dermis • Epidermal or follicular hyperplasia forming transepidermal channels. • Perforation from channels into papillary dermis • Altered elastic fibers within perforations and channels
Cutis laxa	• Congenital or acquired • Autosomal dominant or recessive, or X-linked • Loose, pendulous skin giving prematurely aged appearance • May preceded by inflammatory eruption • Systemic involvement(lung, bladder, GIT, hiatal hernia)	• Elastic fibers diminished throughout dermis or the decrease of the elastic fibers confined to upper or lower dermis • Remaining elastic fibers are short and fragmented • Inflammatory infiltrates' of lymphocytes, histiocytes, or neutrophils may be present.
Eruptive Xanthomas	• Small,yellowish papules with an erythematous base • Appear on the buttock, shoulders, and extensor surfaces of extremities • Usually seen in patients with hypertriglyceridemia, secondary hyperlipidemia, high concentration of chylomicron and VLDL,	• Perivascular and interstitial pattern of foamy macrophages with greater number of lymphocytes, neutrophils and macrophages • One hallmark of eruptive xanthoma is the Presence of both interacellar and extracellar lipid that can be stained with fat stains as scarled red or sudan red

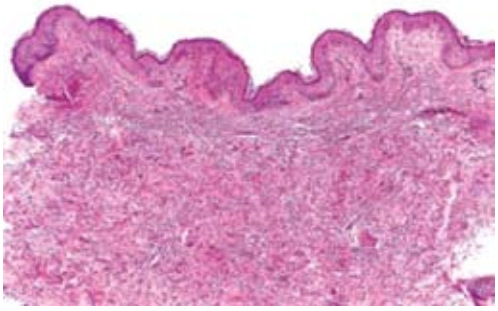

Fig. 3 H&E revealed fragmentation of elastic fibers in mid dermis.

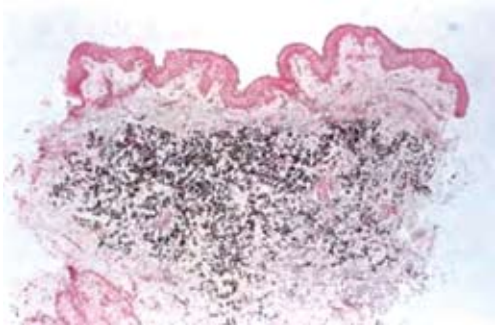

Fig. 4 Von Kossa stain revealed calcification of elastic fibers in mid dermis.

sels, and the eyes. It is also known as Gronblad-Strandberg syndrome.It affects about 1 in every 160,000 people.[1]

The basic fault in PXE appears to relate to genetic abnormalities on chromosome 16p13.1. The disease involves the transporter genes MRP6 or ABCC6 in at least some affected families.PXE may be inherited as autosomal or recessive. There is good evidence that, in affected individuals, collagen and ground substance are abnormal. Calcium then accumulates in abnormal elastic fibres in the skin, blood vessels, eyes and heart.[2]

Individuals with PXE have distinctive skin lesions, eye abnormalities, and changes of blood vessels but these may vary in distribution and severity. The skin lesions of PXE are character-

istic. They consist of small, yellowish bumps in rows or a lacy pattern, which may join to make large patches. The skin is soft, lax and slightly wrinkled. The patches may be slightly pebbly in appearance, which has been described as cobblestone. The common sites affected are the sides of the neck, below the collar bones, the armpits, abdomen, groins, perineum and thighs. Similar changes may occur in the soft palate, inside the lips, and lining of the stomach, rectum and vagina. These skin changes may develop in childhood but usually develop in early adulthood (before the age of 30). They may, in some cases, first appear in old age. Once they appear, they usually persist unchanged indefinitely.[3,4]

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.[5]

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.[6]

Gastrointestinal hemorrhage, apparently due to fragile submucosal vessels, may occur early. Bleeding may occur in the urinary tract. For unknown reasons cerebrovascular disease appears. There may be an increased risk of miscarriage in the first trimester in women.[7]

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, elastosis performance serpiginosa. 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]

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

The most important aspect of management of patients with pseudoxanthoma elasticum is evaluation for cardiovascular and ophthalmologic sequelae. Genetic counseling is indicated for the patient's relatives.[9]

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