A 23-year-old female patient presented with a 5-year history of 1–2 mm skin-colored to yellowish, linearly arranged non-scaled papules and plaques over the axillae and lateral aspects of the neck [Figures 1 a-c]. The lesions were gradually progressive and associated with increased skin laxity. Mucosae appeared normal. She had no systemic complaints. None of the family members had a similar lesion.

Routine laboratory investigations, radiography of the chest, echocardiography and ultrasonography of the abdomen were normal. Ophthalmological examination revealed “peau d’orange” like mottling in the macular area with multiple spot-like “comet tail lesions” in chorioretinal region. Skin biopsy taken from the axilla revealed features as shown in Figure 2. Special stain for elastic tissue was positive [Figure 3a and b].

**Question**

**What is your diagnosis?**

Figure 1: (a-c) Skin-colored to yellowish, discrete, and confluent papules and plaques over the axillae and neck

Figure 2: Hematoxylin and eosin stain showing clumped and degenerate elastic fibres in the dermis (×10)

Figure 3: (a and b) Swollen and irregularly clumped elastic fibres stained black with VVG stain (×40 and ×100)
Answer

Diagnosis: Pseudoxanthoma elasticum.

The histopathology showed innumerable broken fragments of elastic fibres with basophilic stippling in upper and mid reticular dermis [Figure 2]. On Verhoeff’s Van Gieson stain, elastic fibres appeared swollen, irregularly clumped, and black stained [Figure 3a and b].

Discussion

Pseudoxanthoma elasticum (PXE) or Grönblad–Strandberg syndrome is an inherited multisystem disorder primarily affecting the skin, eyes, and cardiovascular system. It is characterized by progressive calcification and degeneration of the elastic fibers throughout the body. The inheritance is autosomal recessive with high phenotypic variability and a female preponderance. Mutations in the ATP-binding cassette transporter C6 (ABCC6) gene on chromosome 16p13.1, which encodes a cellular transport protein, multidrug resistance-associated protein 6 (MRP6), have been found to be responsible.[2]

The skin manifestations, described by Rigal in 1881, are the most characteristic and often the first sign of PXE.[3] They are noted in the second or third decade and comprise flat-topped, discrete-to-confluent yellowish papules in a linear or reticular pattern over flexures and periumbilical skin giving a “cobbledstone,” “plucked chicken skin,” or “Moroccan leather” appearance.[4] The extracutaneous manifestations of PXE are responsible for the morbidity and mortality in this genetic disorder. Ocular changes include angioid streaks, retinal epithelial mottling (peau d’ orange), leopard spotting of the fundus, and healing subretinal haemorrhage (“salmon patches”). These changes are asymptomatic initially, but may lead to loss of central vision as the disease progresses. Calcification of vessels predominantly the larger arteries, the mesenteric and visceral arteries, or those of the extremities leads to vascular occlusion resulting in intermittent claudication, diminished peripheral pulses, hypertension, angina, myocardial infarction, cerebrovascular accidents, or recurrent mucosal haemorrhage. Gastrointestinal hemorrhage secondary to fragility of calcified sub-mucosal vessels is another common complication and may occur in the second decade of life.[5]

The clinical differential diagnosis of the skin lesions of PXE include conditions such as acquired pseudo-PXE related to hemoglobinopathy, skin aging (chronological and/or actinic), elastoma, Buschke Ollendorff syndrome, pseudo-PXE related to d-penicillamine, papular elastorrhexis, elastosis perforans serpiginosa, cutis laxa, etc. Histological examination of the skin lesions is characteristic and shows fragmented, swollen, degenerate, and clumped elastic fibers in the middle and deep reticular dermis with "ravelled wool" appearance. Collagen fibers are also abnormally split into small fibers. Diagnosis can be confirmed using special stains for elastic fibers (e.g., Verhoeff van Gieson, Orcein) and calcium deposits (e.g., von Kossa).[6]

Three major diagnostic criteria (characteristic skin involvement, characteristic histopathological features of lesional skin, and characteristic ocular disease) and two minor criteria (characteristic dermatopathological features in nonlesional skin and family history of PXE in first degree relatives) have been defined to facilitate and unify the diagnosis of PXE.[7]

PXE is an incurable disease requiring a multidisciplinary approach to address its varied manifestations. Although recent evidence suggests that dietary supplementation with oral phosphate binders and magnesium may alter the disease course, treatment is still aimed at the prevention and early detection of adverse ocular and cardiovascular complications.[1] If the skin lesions are cosmetically unacceptable, plastic surgery/collagen injections may improve the skin appearance. Laser photocoagulation can prevent retinal hemorrhages and neovascularization. The patient should be counseled on reduction of cardiovascular risk factors, avoidance of platelet inhibitors, and activities that may increase the risk for bleeding.

Regular follow-up with a retina specialist, cardiovascular surgeon, and gastrointestinal surgeon is needed for early detection of complications.

Learning points

- Early recognition of PXE is critical to prevent various systemic complications associated with the disease.
- Histology should always be obtained and shows fragmented, clumped elastic tissue fibres staining positively with Verhoeff’s Van Gieson stain.
- Skin lesions of PXE are characteristic with a “plucked chicken” appearance and predilection for flexures.
- Patients should have frequent evaluations by a cardiologist and an ophthalmologist.

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Conflicts of interest

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