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ENDGAMES

CASE REVIEW

Subtle skin changes that suggest severe disease

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A 53 year old woman presented to the dermatology department with insect bites to the dorsum of the hands. On examination, yellow skin lesions were found on both sides of her neck (fig 1). The lesions, which were confluent papules 2-4 mm in diameter, had appeared several years before. The woman had no other symptoms.

She was taking duloxetine and clonazepam for depression, and dexketoprofen, calcium, and vitamin D supplements for chronic cervical spine pain.

The patient did not recall any other similar cases of skin lesions in her family.

Questions

1. What condition has caused the coalescent yellow papules?
2. What regions of the body are predominantly affected by this disease?
3. How should this patient be managed?

Answers

1.
What condition has caused the coalescent yellow papules?

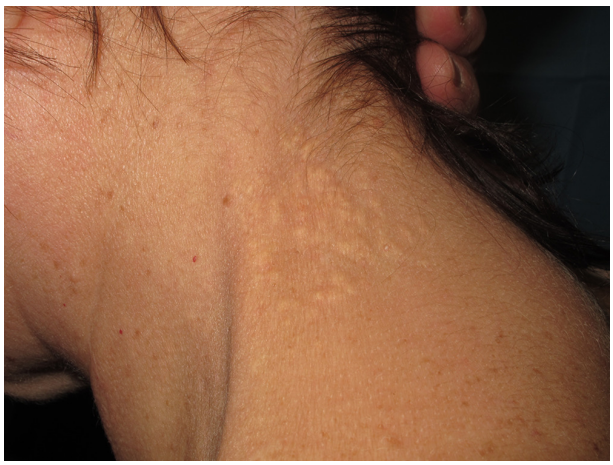
Short answer

Pseudoxanthoma elasticum (PXE), a genetic disease causing yellowish papular lesions and redundant folds in flexural areas.

Discussion

PXE is an autosomal recessive disease caused by a mutation in gene *ABCC6* on chromosome 16, which affects the connective tissue, causing ectopic mineralisation and fragmentation of elastic fibres.[1] The term "pseudoxanthoma elasticum" was coined to indicate that the yellowish papules of PXE differed from authentic xanthomas (skin lesions caused by the accumulation of fat in macrophage cells) and to indicate that PXE papules are related to elastic tissue fragmentation.

Primary PXE skin lesions are yellowish papules 1 to 5 mm in diameter. They tend gradually to coalesce to form plaques, which have a cobblestone appearance. Skin lesions of PXE are typically found on the lateral sides of the neck and in flexural areas (fig 1).



Coalescent yellow papules on the left side of the neck

At the point of maximum papular coalescence, skin loses its elasticity and typical redundant skin folds develop.

2.
What regions of the body are predominantly affected by this disease?

Short answer

PXE mainly affects the cutaneous, ocular, and cardiovascular systems. PXE has an estimated prevalence of 1:25 000-100 000.

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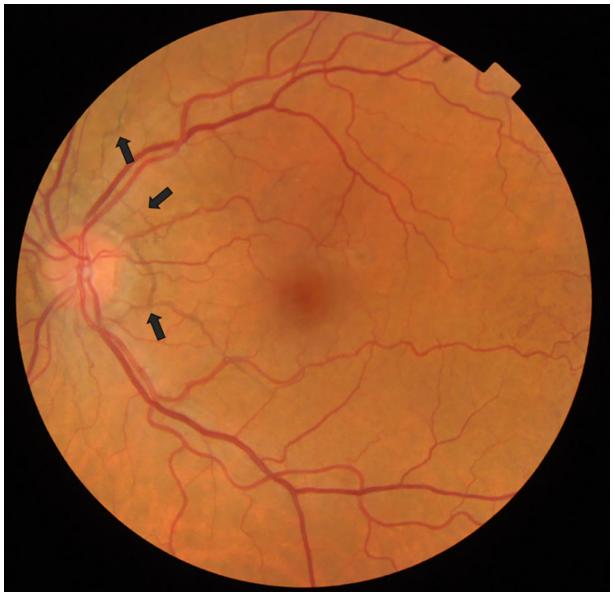
Discussion

PXE skin changes usually appear during childhood, but the diagnosis is frequently not made until more serious complications develop in the third or fourth decade of life.

Although dermatological signs are common, the main burden of PXE results from complications in the visual and cardiovascular systems.[2] Progressive calcification of elastic fibres in the mid and deep dermis, the media and intima of mid-sized arteries, and Bruch's membrane of the eye produce the characteristic clinical and histopathological changes of PXE.

The characteristic ocular defects of PXE are angioid streaks of the retina, characterised by reddish brown curvilinear bands that radiate from the optic disk (fig 2, arrows). The most common retinal feature associated with angioid streaks is the presence of "peau d'orange," a mottled fundus appearance that usually precedes the appearance of the streaks. Choroidal neovascularisation secondary to angioid streaks leads to severe vision loss.[3]



Funduscopy in another patient with PXE reveals angioid streaks in both eyes (black arrows). These are brownish lines representing ruptures in Bruch's membrane that radiate from the optic nerve in an irregular pattern

Cardiovascular manifestations of PXE can cause morbidity and might even result in early death. The arteries throughout the body are affected. Calcification of the elastic media with subsequent intimal proliferation leads to the formation of atheromatous plaques.[2]

There might be intermittent claudication with diminished or absent peripheral pulses.[4] Ischaemic heart disease is thought to be more frequent (although this fact is not clearly established) and in PXE patients ischaemic heart disease typically occurs at a much younger age than in the general population. Hypertension is caused by renal artery involvement.[5]

Cardiomyopathy[6] and mitral valve prolapse[7] have also been reported.

Calcified blood vessels of the gastric and intestinal mucosa have an increased tendency to haemorrhage.[8] Upper gastrointestinal tract haemorrhage occurs in 13% of patients with PXE and is often resistant to conventional methods of treatment.[9]

Death can result from cerebral haemorrhage, coronary occlusion, or massive gastrointestinal haemorrhage.

Involvement of other systems, including the central nervous system, the urinary tract, and the respiratory system, has also been reported.[10]

3.

How should this patient be managed?

Short answer

There is no specific treatment for PXE. Management involves prevention and monitoring of complications and involves the multidisciplinary team. Early recognition and lifestyle adjustments are important to reduce morbidity. Genetic counselling might be helpful and PXE support groups can be valuable.

Discussion

Patients with PXE have an increased risk of cardiovascular diseases, and extra monitoring of modifiable risk factors is warranted. General practitioners should recommend lifestyle changes such as smoking cessation, maintaining an adequate weight, and moderate physical exercise. If necessary, drug treatment for correction of hyperlipidemia and hypertension can be added.

Patients should be monitored on a regular basis with clinical examinations, exploration of the vascular system, and fundus examination of the posterior pole of both eyes.

Non-steroidal anti-inflammatory drugs (especially aspirin) and anticoagulant drugs should be restricted in PXE patients, to prevent haemorrhage.[11]

Regular fecal occult blood testing and urinalysis should be performed to evaluate gastrointestinal or urinary tract bleeding.

Trauma to the head and eye should be avoided, because even slight impact can cause retinal haemorrhage.[12] Patients should be advised to avoid contact sports and other activities that might result in normally minor eye or head trauma, for example boxing, rugby, American football, soccer. Even heavy weight lifting could lead to retinal haemorrhage in patients with PXE. Also, patients should be advised to wear protective eyeglasses when engaging in potentially dangerous activities such as racket sports. Non-contact sports like swimming and cycling, however, should be encouraged.[11]

Intravitreal vascular endothelial growth factor inhibitors (such as bevacizumab and ranibizumab) are currently the treatment of choice in the management of choroidal neovascularisation.[13]

Recent studies suggest that antimineralisation approaches might be useful, since PXE is characterised by aberrant mineralisation of connective tissues.[14-16] The results of a small case series also suggests that oral phosphate binders might lead to improvement clinically and histopathologically.[17]

First degree family members should be carefully screened for any cutaneous or ophthalmological features of PXE. Patients and their families should also receive genetic counselling.

PXE support groups (www.pxe.org, www.pxe.org.uk) can be a valuable tool for patients with PXE.

Patient outcome

After six years of follow-up, the cutaneous lesions have remained unchanged. The patient is being monitored by her general practitioner and has regular appointments with a dermatologist, ophthalmologist, and cardiologist. To date, she has not presented with any complications. The patient has been advised on the prevention of cardiovascular risk factors and encouraged to follow a healthy lifestyle.

We have read and understood The BMJ policy on declaration of interests and declare that we have no competing interests.

Patient consent obtained.

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