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When the eye leads to the diagnosis of pseudoxanthoma elasticum: a case revealed by angioid streaks and choroidal neovascularisation

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Dear Editor,

Pseudoxanthoma elasticum (PXE) is a rare autosomal recessive disorder caused by pathogenic variants in the *ABCC6* gene, resulting in progressive calcification and fragmentation of elastic fibres involving the skin, retina, and cardiovascular system.[1-3] Cutaneous manifestations classically consist of yellowish papules and plaques affecting flexural areas, particularly the lateral neck and axillae, although cutaneous findings may occasionally be subtle.[3-5] Ocular involvement is characterised by angioid streaks, representing breaks in Bruch's membrane that may predispose to choroidal neovascularisation (CNV), retinal haemorrhage, and progressive visual impairment.[3,6,7] Cardiovascular involvement results from progressive mineralisation and degeneration of elastic fibres within the arterial wall and may manifest as accelerated peripheral arterial disease, intermittent claudication, reduced arterial compliance, and premature vascular calcification.[2,5,8,9] Although cutaneous manifestations frequently represent the earliest signs of PXE, they may remain unrecognized when subtle, leading to diagnosis only after the onset of ophthalmologic complications such as angioid streaks or CNV.[5-8] We report the case of a patient in whom subtle cervical cutaneous changes suggestive of PXE were recognized following ophthalmologic presentation with CNV and angioid streaks, leading to histopathologic and molecular confirmation of the diagnosis.

In May 2025, a 56-year-old man was hospitalised because of sudden, painless visual loss in his left eye over the previous few days. His medical history was unremarkable for cardiovascular disease, diabetes, or hypertension. At admission, best-corrected visual acuity (BCVA) was 0.32 decimal equivalent in the left eye and hand-motion vision in the right eye. Fundus examination, infrared reflectance, and optical coherence tomography (OCT) revealed widespread bilateral angioid streaks and active CNV with massive submacular haemorrhage in the left eye.[6,7] The right eye showed an advanced disciform macular scar secondary to a previous untreated ophthalmological event. Dermatological examination revealed subtle and atypical cutaneous findings characterised by bilateral cervical skin laxity and fine wrinkling, without the classic yellowish papules or *peau d'orange* plaques typically associated with PXE (Figure 1).[3-5] The clinical appearance initially raised the differential diagnosis of mid-dermal elastolysis, an acquired elastolytic disorder that may present with localised wrinkling and skin laxity. Histopathological examination of a punch biopsy from the lateral cervical region demonstrated focal calcification within the reticular dermis. Von Kossa staining highlighted calcium deposition along abnormal elastic fibres, consistent with PXE.[2-4] Targeted molecular analysis of the *ABCC6* gene identified the homozygous pathogenic frameshift variant c.3774_3775insC (p.Trp1259LeufsTer19), providing molecular confirmation of the diagnosis. The confirmed diagnosis prompted multidisciplinary assessment, revealing fibrocalcific

carotid plaques, moderate peripheral atherosclerosis, and reduced arterial compliance despite the absence of previous cardiovascular symptoms or conventional cardiovascular risk factors. These findings were compatible with vascular involvement in PXE, highlighting the importance of systemic evaluation.[8,9] The patient was referred for long-term cardiovascular follow-up. Intravitreal aflibercept therapy was initiated using a loading phase followed by a treat-and-extend regimen.[8,10] Serial OCT examinations demonstrated complete resolution of the submacular haemorrhage and subretinal fluid, with improvement of BCVA in the left eye from 0.32 to 0.98 decimal equivalent at the 8-month follow-up. Conversely, the right eye remained severely impaired because of irreversible macular scarring.

This case illustrates how subtle cutaneous manifestations of PXE may remain unrecognised until ophthalmological complications prompt multidisciplinary investigation. In particular, cervical skin laxity and wrinkling without characteristic yellowish papules may mimic mid-dermal elastolysis. However, unlike this acquired elastolytic disorder, PXE is a progressive multisystem disease with potentially severe ocular and cardiovascular complications.[2,3,8] Histopathological examination, including Von Kossa staining, and molecular analysis were crucial in establishing the diagnosis.[2-4] The identification of previously unsuspected vascular abnormalities further underscores the importance of early recognition and comprehensive systemic assessment. Clinicians should therefore consider PXE in the differential diagnosis of atypical cervical skin laxity, particularly in patients presenting with angioid streaks or CNV, to facilitate appropriate ophthalmological management, genetic counselling, family screening, and cardiovascular surveillance.[3,5,8,9]

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Figure 1. Clinical presentation of the cervical skin. Lateral, posterior, and anterior cervical views showing subtle cutaneous involvement characterised by redundant, finely wrinkled skin with lax, cerebriform folds, in the absence of the classic yellow papules typically associated with PXE.

