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CASE REPORT

INTERMEDIATE

CLINICAL CASE

Pseudoxanthoma Elasticum With Detailed Analyses of Coronary Artery Disease

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ABSTRACT

A 60-year-old woman with pseudoxanthoma elasticum (PXE) underwent thorough coronary artery disease assessments. Intravascular imaging tests suggested fragmented and calcified elastic fibers in the internal elastic lamina, suggesting a possible pathophysiology of coronary artery disease in PXE. Our case report would allow clinicians to acknowledge the clinical picture of PXE. (**Level of Difficulty: Intermediate.**) (J Am Coll Cardiol Case Rep 2023;16:101894) © 2023 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

HISTORY OF PRESENTATION

A 60-year-old woman experienced her third lacuna stroke at age 58, 2 years prior to this presentation, and she was treated with conservative treatments. Furthermore, at age 59, she experienced left-sided visual impairment. She did not have any other neurologic symptoms or cardiovascular symptoms. She visited a local ophthalmology clinic, and fundoscopy demonstrated angioid streaks and choroidal neovascularization. She was given intravitreal injections of vascular endothelial growth factor antagonists. Her dermatologists for her skin lesions on flexor surfaces suspected a systematic disease involving her eyes and skin, and she was referred to our university hospital for further assessment.

LEARNING OBJECTIVES

- To recognize PXE as a possible diagnosis in an individual with dermatologic, ophthalmologic, and cardiovascular complications.
- To understand cardiovascular manifestations of PXE.

On presentation, her blood pressure was 100/70 mm Hg, heart rate was 76 beats/min, respiratory rate was 16 breaths/min, oxygen saturation was 98% in room air, and body temperature was 36.5 °C. The physical exam was notable for impaired left-eye vision (0.02), but other neurologic exams were grossly intact without aftereffects of her lacunar strokes. Yellowish papules were on the neck, axillae, and groins (Figure 1A). Angioid streaks in both eyes and retinal

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ABBREVIATIONS AND ACRONYMS

CAD = coronary artery disease

IVUS = intravascular ultrasound

OCT = optical coherence tomography

PXE = pseudoxanthoma elasticum

degeneration in the left eye were confirmed (Figure 1B). Auscultation revealed a regular rate rhythm and normal heart sounds without a murmur. There were no jugular venous distension, pedal edema, or coarse crackles. No bruits were heard on her neck. Pulses were normal and symmetric in radial, posterior tibial, and dorsalis pedis arteries.

PAST MEDICAL HISTORY

The patient had a past medical history of dyslipidemia, lacunar strokes at ages 54, 56, and 58, and systematic yellowish papules since adolescence. Her home medications were aspirin and rosuvastatin. She reported occasional drinking but denied cigarette or illicit drug use. Her family and social history were unremarkable.

DIFFERENTIAL DIAGNOSIS

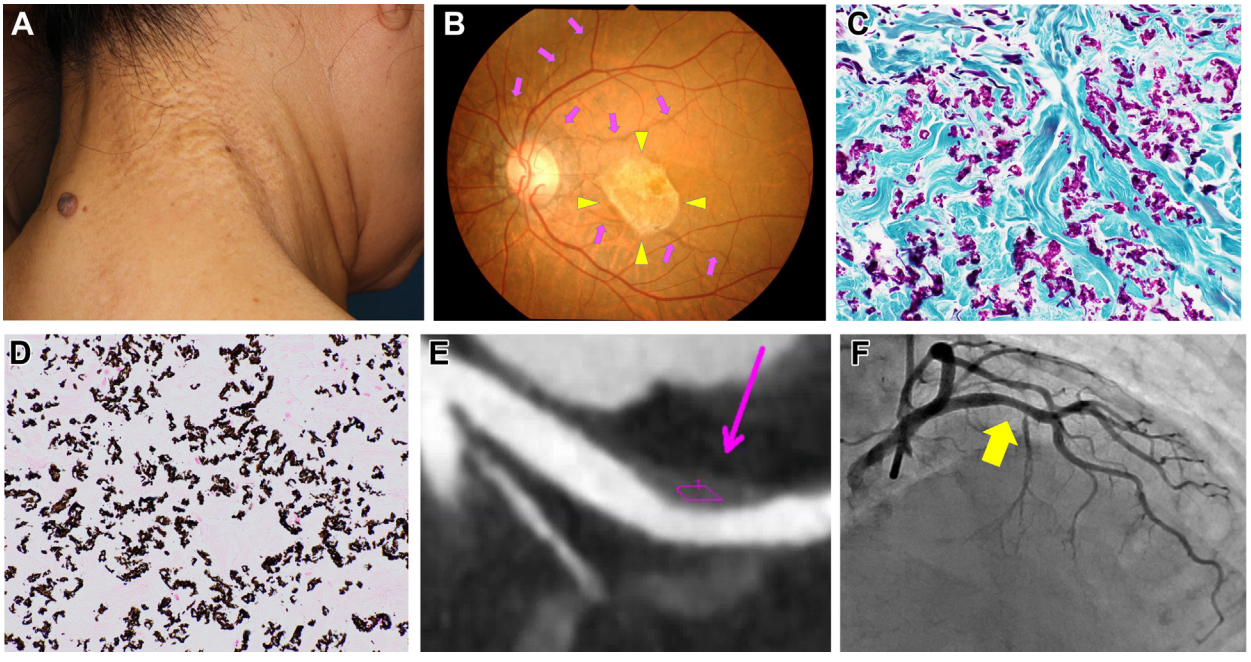
Given the patient's history of dermatologic (xanthoma-like papules on flexor surfaces), ophthalmologic (angioid streaks, choroidal neovascularization), and cardiovascular complications (strokes), pseudoxanthoma elasticum (PXE) was high on the differential. Diseases with similar presentations, such as PXE-like papillary dermal elastolysis, D-penicillamine intake, Paget disease of bone, sickle cell disease, Ehlers-Danlos syndrome, and age-related macular degeneration, were low on the differential. Coronary artery disease (CAD) was suspected because PXE is known to accelerate CAD.

INVESTIGATIONS

A biopsy of the right neck skin revealed lint-like fragmented elastic fibers and microcalcifications in the reticular layer of the dermis (Figures 1C and 1D), and the patient was given the definitive diagnosis of PXE.

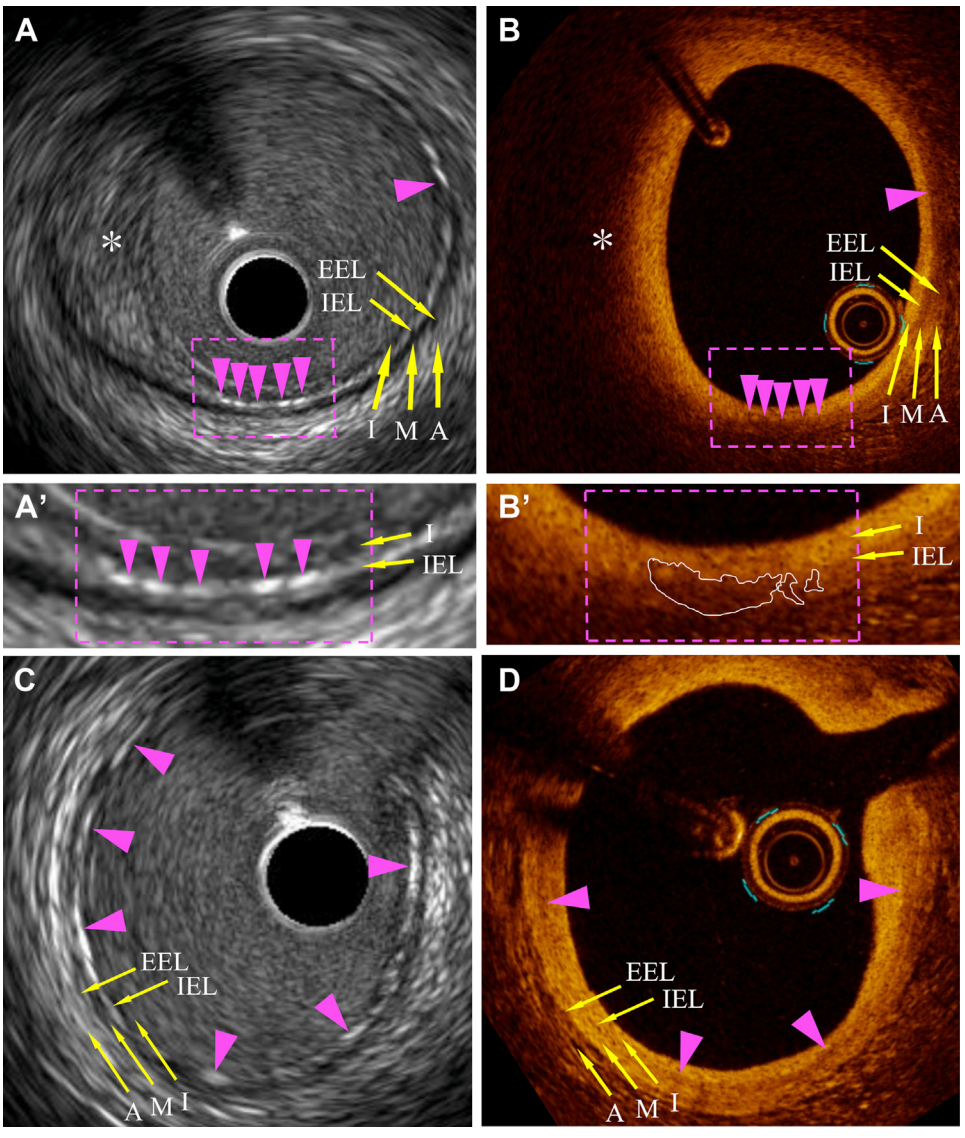
Patients with PXE are known to have an increased risk of ischemic heart disease. Therefore, the patient underwent cardiac work-ups. The electrocardiogram showed normal findings except for negative T-wave inversion in leads V_2 and V_3. Myocardial scintigraphy with ergometry stress test showed inconclusive upsloping ST-segment depression in leads II, III, aVF, V_4, V_5, and V_6 in the electrocardiogram, and there was a sign of mild ischemia in the septum and

FIGURE 1 Dermatologic, Ophthalmologic, and Cardiovascular Manifestation in a 60-Year-old Woman With PXE



Yellowish papules with 2-5 mm diameter on the right neck **(A).** Angioid streaks **(pink arrows)** and retinal degeneration **(yellow arrowheads)** in the left eye **(B).** Lint-like fragmented elastic fibers in the reticular layer of the dermis stained **purple** by the Elastica Masson Goldner stain **(C).** Calcification in fragmented elastic fibers in the reticular layer of the dermis stained **black** by the von Kossa stain **(D).** An intermediate stenotic lesion in the proximal left anterior descending artery shown by coronary computed tomography angiography **(pink arrow) (E)** and invasive coronary angiogram **(yellow arrow) (F)**. PXE = pseudoxanthoma elasticum.

FIGURE 2 **Intravascular Images in a 60-Year-old Woman With PXE**



Comparison of intravascular ultrasound images and optical coherence tomography images of the stenotic lesion at the proximal left anterior descending artery **(A, A′, B, and B′)** or normal segment of the left anterior descending artery **(C, D).** The **pink arrowheads** signify high echoic lesions without acoustic shadowing detected by intravascular ultrasound or low signal lesions detected by optical coherence tomography. The magnified images **A′** and **B′** correspond to images **A** and **B**, respectively. The **solid white line (B′)** outlines the contour of low-signal lesions. The asterisk **(*) (A, B)** signifies fibroatheroma. A = adventitia; EEL = external elastic lamina; I = intima; IEL = internal elastic lamina; M = media; PXE = pseudoxanthoma elasticum.

inferolateral areas with summed difference score of 3. Coronary computed tomography angiography indicated a noncalcified plaque causing mild to moderate stenosis in the proximal segment of the left anterior descending artery (Figure 1E). Consistently, an invasive coronary angiogram confirmed intermediate coronary stenosis (Figure 1F). The physiological assessment by resting full-cycle ratio ruled out the functional significance of epicardial coronary stenosis. Microcirculation physiological indices (index of microvascular resistance and coronary flow reserve) also ruled out coronary microvascular dysfunction.

Two intravascular imaging modalities (intravascular ultrasound [IVUS] and optical coherence tomography [OCT]) revealed a fibroatheroma in the stenotic segment (Figures 2A and 2B). In both regular

and stenotic segments of the left anterior descending artery, high echoic lesions without acoustic shadowing in the internal elastic lamina were detected by IVUS, corresponding to the low signal lesions detected by OCT (**Figures 2A to 2D**).

MANAGEMENT

For her stable CAD, a percutaneous coronary intervention was deferred and conservative management was continued.

DISCUSSION

In patients with PXE, several inhibiting pathways for ectopic mineralization are impaired because of *ABCC6* sequence variants.[1] These sequence variants lead to disruption and calcification of elastic fibers and manifest as dermatologic (eg, xanthoma-like papules on flexor surfaces), ophthalmologic (eg, angioid streaks, choroidal neovascularization), and cardiovascular complications (eg, stroke, CAD, peripheral artery disease). In this case, the clinical manifestation and the histopathologic findings satisfied the definitive diagnostic criteria of PXE.[1]

Accelerated CAD is a major complication of PXE.[1,2] The present case adds to the published reports because thorough assessments for epicardial coronary arteries, coronary microcirculation, and intravascular imaging (IVUS and OCT) were performed for this rare disease.

With IVUS, we demonstrated unique high echoic components without acoustic shadowing in the internal elastic lamina. The IVUS findings could represent fragmented and calcified elastic fibers in the internal elastic lamina because previous articles reported similar IVUS findings and studies with arterial biopsy showed fragmentation of the elastic lamina in patients with PXE.[3,4]

OCT images revealed microcalcifications as tiny low-signal lesions in the internal elastic lamina corresponding to the IVUS findings. Calcified lesions were fragmented and small in this case, and it was not easy to identify without an IVUS guide. Hence, our study suggests that IVUS rather than OCT is helpful in identifying pathologic lesions in the coronary arteries in patients with PXE.

For the epicardial artery, it is unclear whether the lesions in the elastic lamina played a role in promoting the atherosclerotic lesion in addition to conventional risk factors in this case. Interestingly, we demonstrated abnormal findings even in the nonstenotic segment, suggesting a preclinical coronary artery involvement of PXE.

Microvascular dysfunction was ruled out for coronary microcirculation, which is an informative finding because microcirculation in patients with PXE has never been reported.

FOLLOW-UP

To assess CAD progression, the patient is monitored for ischemic symptoms. In addition, treatment with etidronate is being discussed because etidronate might effectively reduce arterial calcification.[5]

CONCLUSIONS

In summary, our patient with PXE underwent thorough cardiovascular assessments. Intravascular imaging tests suggested fragmented and calcified elastic fibers in the internal elastic lamina, proposing a possible pathophysiology of CAD in PXE. Awareness of the clinical picture of PXE would allow early recognition of CAD, and further studies are warranted to elucidate the pathophysiology of CAD in PXE.

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The authors have reported that they have no relationships relevant to the contents of this paper to disclose.

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KEY WORDS coronary artery disease, intravascular ultrasound, optical coherence tomography, pseudoxanthoma elasticum