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CASE REPORT

# Peripheral Vascular Disease as a Mode of Presentation of Pseudoxanthoma Elasticum

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**Summary: Peripheral vascular disease as a mode of presentation of pseudoxanthoma elasticum.** M. L. Wahlqvist, R. M. Fox, A. M. Beech and I. Favilla, *Aust. N.Z. J. Med.*, 1977, **7,** pp. 523–525.

*Two men presenting with premature peripheral vascular disease and minimal risk for atherosclerosis were found to have pseudoxanthoma elasticum (PXE). Fluorescein angiography was found to be of potential value in the early recognition of angioid streaks and pseudoxanthoma elasticum. There was evidence of disruption of arterial elastic tissue which may contribute to atherogenesis in PXE. Management is presently limited largely to minimizing risk factors for atherosclerotic vascular disease.*

The occurrence of peripheral vascular disease in early life with minimal identifiable risk for atherosclerotic disease is unusual.[1, 2] One condition which may account for this presentation is pseudoxanthoma elasticum (PXE).[3, 4, 5] PXE is a genetically determined, probably autosomal recessive, disorder of elastic tissue with cutaneous, ocular, vascular and gastro-intestinal manifestations. Its prevalence is of the order of 1 in 70,000 to 1 in 160,000.[5] In this report two cases of PXE presenting as peripheral vascular disease are described.

## Case Reports

*Case* 1

A 28-year-old man presented with a story of increasing intermittent claudication since the age of 13 years. Otherwise in good health, he could only walk 200 metres before the onset of foot and calf pains. There was no family history of premature vascular disease. He had smoked only two or three cigarettes a day since the age of 21 years. He was not overweight. His peripheral pulses were absent below the femorals. He had a right femoral bruit. His blood pressure in the left arm was 110/80 and in the right arm 130/80. He had a grade $\frac{3}{6}$ aortic ejection systolic murmur, but no clinical evidence of aortic stenosis. There were no stigmata of hyperlipoproteinaemia. The skin of his neck and axillae showed changes consistent with early PXE (Fig. 1). Early angioid streaking was visible in each ocular fundus (Fig. 2).

Plain X-ray of his thighs revealed extensive calcification of the femoral arteries (Fig. 3). There was no evidence of calcification in upper limb, coronary or abdominal vessels. Angiography showed almost total occlusion of both femoral arteries. His plasma cholesterol was modestly elevated at 6·6 mmol/*l* (upper limit of normal 6·2) and his fasting serum triglycerides were at the upper limit of normal at 1·7 mmol/*l*. An oral glucose tolerance test was normal. Thyroid function tests were normal. An exercise test on a cycle ergometer was concluded when claudication occurred; neither angina pectoris nor electrocardiographic evidence of myocardial ischemia were provoked. Echocardiography provided no evidence of valvular heart disease. Fluorescein angiography demonstrated several angioid streaks in each ocular fundus which were not seen during routine ophthalmoscopy (Fig. 2).

*Case* 2

A 46-year-old man was admitted to hospital with incipient bilateral gangrene. He had a six year history of intermittent claudication. Six months earlier he had a haematemesis of unknown etiology. He had been well otherwise. There was no family history of vascular disease. He smoked 10 to 15 cigarettes a day. Pedal and popliteal pulses were impalpable.

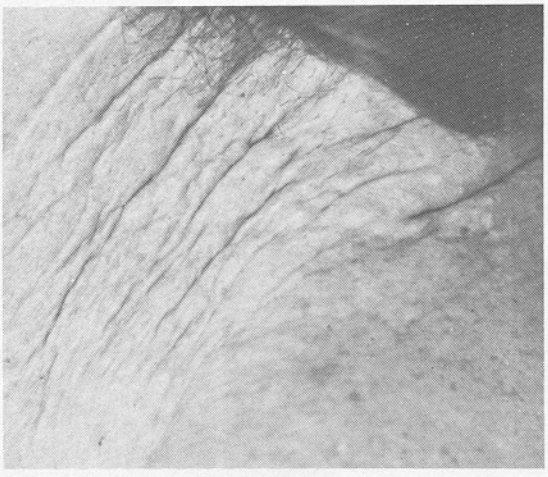

FIGURE 1. Early changes of pseudoxanthoma elasticum in skin of neck in Case 1, a 28-year-old man with intermittent claudication and pseudoxanthoma elasticum.

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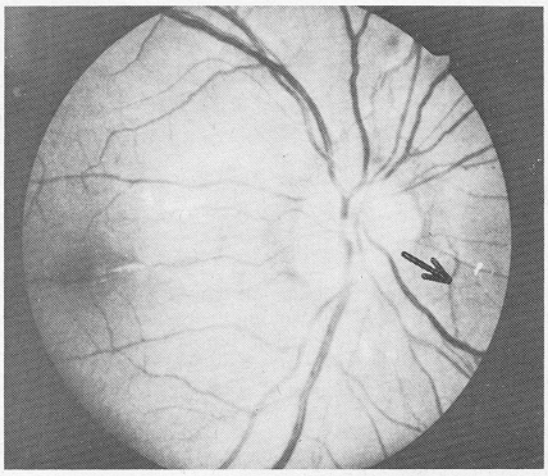

FIGURE 2A. Fundal appearance of right eye in Case 1 prior to fluorescein angiography. Drusen are evident on the nasal side of the optic disc. An angioid streak can be seen on the nasal side of the optic disc and directed inferiorly.

Both radial arteries felt rigid. His blood pressure was 135/65. There were no xanthelasmata, xanthomata, or corneal arcus. Typical skin changes of pseudoxanthoma (PXE) were evident in the neck, axillae and groins. Drusen (colloid bodies), but not angioid streaks, were evident on ophthalmoscopy.

Skin biopsy confirmed the diagnosis of PXE. Plain X-rays demonstrated calcification of the radial arteries (Fig. 4), femoral and popliteal arteries. His plasma cholesterol was 3·6 mmol/*l*. An oral glucose tolerance test was marginally abnormal with a peak blood glucose of 11·6 mmol/*l* and a two hour value of 7·2 mmol/*l*. Left ventricular hypertrophy was evident on the electrocardiogram.

The patient ultimately required a left mid-thigh amputation and this provided vascular material for histo-pathological examination. There was extensive atherosclerotic vascular disease with medial calcification. Patchy calcification of the internal elastic lamina was especially notable (Fig. 5). In some sections fragmentation and disorganization of medial elastic tissue was evident (Fig. 5).

**Discussion**

These two case histories show that patients with previously unrecognized PXE may present with intermittent claudication. Physical examination alone allowed the diagnosis of PXE to be made in each case. The search for PXE would appear particularly worthwhile where the patient is young and where there is minimal risk for atherosclerotic vascular disease as in Case 1.

When a young patient with intermittent claudication has no physical signs of PXE, fluorescein angiography may be of value in demonstrating otherwise undetectable angioid streaks.[6]

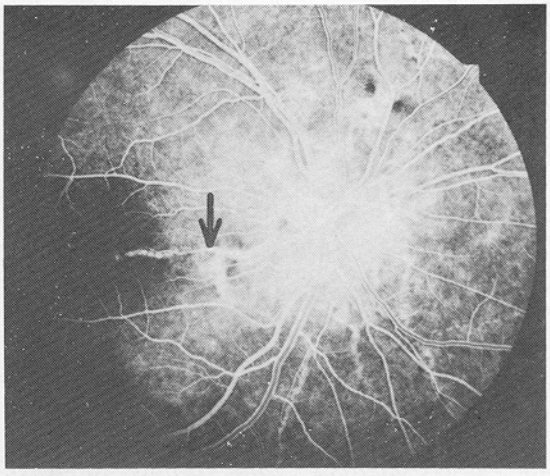

FIGURE 2B. With fluorescein angiography, the inferior nasal angioid streak is more evident and other streaks have become evident. An arrow marks an angioid streak directed from the disc temporally to the macula.

There has been controversy, largely because of inadequate data, about the pathophysiology of intermittent claudication in PXE.[3, 4, 5] Accelerated atherosclerosis, perhaps on the basis of medial elastic tissue change, is one possibility. In Case 2, medial smooth muscle cells were seen rounded up at the intimomedial junction. According to some workers[7, 8], these cells can generate intimal foam cells commonly

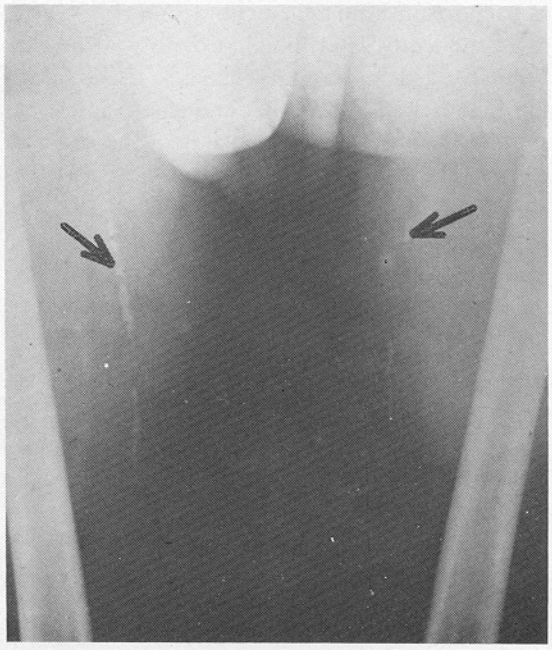

FIGURE 3. Plain X-rays of thighs in Case 1. Arrows indicate calcification in femoral arteries.

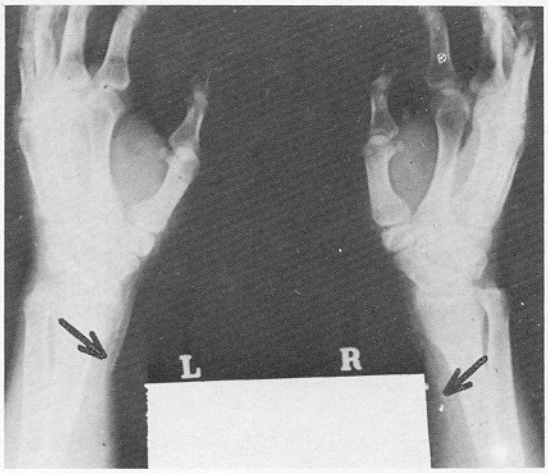


FIGURE 4. Plain X-ray of the forearm in Case 2, a 46-year-old man with peripheral vascular disease and pseudoxanthoma elasticum. Arrows indicate calcification in the radial arteries.

FIGURE 5. Photomicrograph of femoral artery in Case 2. Arrows indicate fragmented and disorganized elastic tissue in the media. The internal elastic lamina is well preserved, but calcium deposition is evident. The intima is thickened. Verhoeff-Van Gieson stain (× 800).

seen in atherosclerotic lesions. It is conceivable that both the disruption of elastic tissue and the deposition of calcium in elastic tissue may facilitate the development of foam cells from intimo-medial smooth muscle cells. Medial thickening is another possible mechanism for occlusive vascular disease in PXE.[4] Arterial smooth muscle cells form elastic fibres, collagen and glycosaminoglycan and these cells could also be responsible for the formation of an abnormal extracellular matrix in PXE.[8]

Although both patients presented with peripheral vascular disease, they may have had other manifestations of PXE. Case 2 had had an upper gastrointestinal haemorrhage which is a recognized complication of PXE. It has been suggested that affected arteries supplying the gut may be unable to contract.[5] The cause of the left ventricular hypertrophy in the absence of systemic hypertension in Case 2 is uncertain. Coronary artery disease is well recognized in PXE, but was not clinically evident in this patient. Endocardial and pericardial, but no specific myocardial changes have been described.[3] Valvular heart disease has also been attributed to PXE[3] and may account for the aortic ejection murmur in Case 1, although this did not seem haemodynamically significant. Thyroid arteries can be affected in PXE and it has been suggested that PXE patients with severe peripheral vascular disease are likely to be hypothyroid.[5] Both our patients were euthyroid. The 28 year old is at risk from macular haemorrhage and degeneration since an angioid streak runs to the macula.

There is no specific treatment for PXE. It would seem advisable to recognise the disease as early as possible in order to control as far as possible the known risk factors for atherosclerotic vascular disease. Thus we have maintained serum lipids well within the normal range, carefully monitored blood pressure, and recommended abstinence from smoking. The only other measure which has been suggested to be of value is the administration of Vitamin E. This is controversial.[3] Successful vascular reconstructive surgery has been reported.[3, 9]

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