Treatment of pseudoxanthoma elasticum with probenecid

Case letter

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Pseudoxanthoma elasticum (PXE) is a rare connective tissue disorder characterised by calcification of elastic fibres within the skin, retina and vasculature. The estimated prevalence is between 1 in 25,000 to 100,000, with females more commonly affected than males.\(^1\)

The cutaneous features include yellowish papules which may progress to form plaques. The flexures are most commonly affected. In severe cases there is loss of skin laxity resulting in excess skin or skin folds.\(^1\)

PXE is an autosomal recessive disease, resulting from mutations on the ATP-binding cassette sub-family C member 6 transporter (ABCC6) gene.\(^2\) Abnormal ABCC6 function results in disruption of ATP transportation leading to increased extracellular ATP which is converted to pyrophosphate, a known inhibitor of mineralisation. In PXE, abnormal mineralisation produces calcified and fragmented elastic fibres.\(^2\)

Currently, there is no way to prevent or treat mineralisation in PXE. Several treatments have been suggested including; a high magnesium diet, phosphate binders and vascular endothelial growth factor inhibitors for ocular and cardiovascular disease.\(^13\)

Probenecid is an organic anion which interferes with the transport activity of ABCC6. Probenecid been demonstrated, in vitro, to help restore extracellular pyrophosphate which acts to inhibit calcification.\(^4\) Probenecid has been used for other diseases of ectopic calcinosis such as dermatomyositis and familial tumoral calcinosis, and been suggested as a treatment option for PXE based of this mechanism of action.\(^5\) It is commonly used for gout, with the most frequent side effects of nausea, vomiting and headache. Its use has also been associated with kidney stones, proteinuria and reduced urinary excretion of some medications.
We describe a case to highlight significant clinical improvement following treatment of PXE with probenecid. To our knowledge there are no previous case reports outlining the use of probenecid in PXE.

We present a 39-year-old female with PXE diagnosed age ten following presentation with skin changes of the neck. She had severe multisystem disease with cutaneous involvement of the neck, axillae, elbow and knee flexures, abdomen and groin. Additionally, she had optic and vascular complications with bilateral angioid streaks and aortic valve thickening and stenosis.

Previous treatment for her cutaneous disease included topical steroids, intralesional steroids and topical retinoids to minimal effect. She had also undergone surgical intervention for removal of excess skin in both axillae.

On review, she had progressing areas of biopsy proven PXE on her abdomen and thighs (Figure 1), with associated tenderness. She was commenced on a trial of probenecid 250mg twice daily. On review three months later, she reported an excellent response to treatment. Examination revealed significant improvement and her skin changes were less visible and no longer tender. Additionally, she had no new areas of cutaneous PXE. After six months of therapy, the probenecid was reduced to 250mg once daily and after 12 months she reported stable disease with no flares. The effect of probenecid on her ocular and cardiovascular PXE has not been assessed.

This case demonstrates that probenecid may be a useful treatment for the cutaneous manifestations of pseudoxanthoma elasticum. Further research is needed to understand the mechanism of action and efficacy of probenecid in the treatment of PXE.

Figure 1: Images of both medial thighs before and after treatment with probenecid. 1. Left thigh prior to treatment, 2. Left thigh 3 months after treatment, 3. Right thigh prior to treatment, 4. Right thigh 3 months after treatment


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