Elastosis perforans serpiginosa associated with pseudo-pseudoxanthoma elasticum after treatment with D-penicillamine in a patient with cystinuria

Spyridon Kampantais, Theodora Stasinou, Joseph Ingoe, Graham Young
Department of Urology, University Hospital of South Manchester, Wythenshawe, Manchester, UK

Abstract
D-Penicillamine has been used for the prevention of stone formation in patients suffering from cystinuria and its use has been associated with numerous side-effects. We present an unusual case of elastosis perforans serpiginosa associated with pseudo-pseudoxanthoma elasticum after treatment with D-penicillamine. These cutaneous lesions persisted for years despite discontinuation of the treatment.

Introduction
Cystinuria is caused by an autosomally recessive inherited inborn error of metabolism that causes decreased proximal tubular reabsorption of the dibasic amino acids cystine, ornithine, lysine and arginine. Cystine is insoluble in acidic urine and homozygous state results in supersaturation and cystine crystal formation. D-Penicillamine (DPA) is a first-generation chelating agent that forms a disulfide complex with cystine which is up to 50 times more soluble thus preventing stone formation and possibly dissolving existing cystine stones [1]. Degenerative dermatoses such as elastosis perforans serpiginosa (EPS) and cutaneous changes resembling pseudoxanthoma elasticum (PXE) are described as late-onset side effects of treatment with DPA due the effect on elastin and collagen [2].

Case presentation
A 60-year-old lady with cystinuria was referred to our stone clinic. Her initial diagnosis with cystinuria was done about 15 years ago. Clinical examination revealed skin lesions in the nape, in the upper extremities and in her back just lateral to the right scapula. The dermatological diagnosis of the first two was consistent with pseudo - pseudox-

Key words
D-penicillamine; Elastosis perforans serpiginosa; Pseudoxanthoma elasticum; cystinuria

Citation

Corresponding author:
Kampantais Spyridon MD, FEBU, 130 Glendale Gardens, Southend-on-Sea, Essex, United Kingdom
E-mail: kabspir@hotmail.com
anthoma elasticum (pseudo - PXE) (Figures 1, 2) while the latter represented elastosis perforans serpiginosa (EPS) (Figure 3). Both of these skin disorders are associated with the use of D-penicillamine (DPA); DPA had indeed been prescribed in average daily doses of 1 gr for the management of her cystinuria in the past. The above lesions became apparent at least 5 years after drug administration and despite discontinuation of treatment they remained virtually stable in the years that followed.

**Discussion**

EPS is a rare skin disorder affecting connective tissue. Clinically, serpiginous or annular patterned lesions up to several centimetres are the common lesions. These consist of keratinized papules, 2-5 mm in diameter and are typically located on the neck, face or arm, as was the case in our patient. Sometimes, these lesions resolve spontaneously, however usually persist for several years [3]. EPS can present in three clinical entities; idiopathic, reactive and drug-induced form. Idiopathic EPS accounts for 65% of the total cases. Reactive EPS, accounting for approximately 25-30% of the total, is often associated with systemic diseases or other fibrous degeneration diseases, such as Ehlers-Danlos syndrome, Marfan's syndrome, osteogenesis imperfecta and Down’s syndrome [3]. The only drug that appears to be associated with this condition is DPA. It is likely that DPA impairs collagen deposition and interferes with the production of new elastic fibres. This could explain why the lesions usually occur after long term therapy [1]. EPS has been widely in patients suffering from Wilson’s disease and rheumatoid arthritis who received treatment with high dose of DPA (equal or higher of 1 gr) [4]. However similar reports in cystinuric patients are rare [5].

PXE is a rare genetic disease characterised by calcification and fragmentation of elastic fibers that primarily affects the skin and the retina. However, many other skin disorders mimic pseudoxanthoma elasticum and are referred to as PXE - like disease or pseudo - PXE [2]. One of these elastopathies has been related to morphologic changes in elastic fibers secondary to prolonged therapy with DPA [6]. None of the various treatments that have been employed in the past managed to completely eliminate these skin lesions.
Η D-πενικιλλαμίνη έχει χρησιμοποιηθεί για την πρόληψη της ουρολιθίασης σε ασθενείς που πάσχουν από κυστινουρία και η χρήση της έχει συσχετισθεί με πολλές παρενέργειες. Παρουσιάζουμε μια ασυνήθιστη περίπτωση έρποσας και διατιτραίνουσας ελάστωσης σε συνδυασμό με ψευδο-ελαστικό ψευδοξάνθωμα μετά από θεραπεία με D-πενικιλλαμίνη. Οι παραπάνω δερματικές βλάβες παρέμειναν σταθερές για χρόνια, παρά τη διακοπή της θεραπείας.

References