



Case Letter

Penicillamine-induced elastosis perforans serpiginosa and pseudo-pseudoxanthoma elasticum



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Dear Editors,

We report on a case of a 55-year-old woman who presented with two 2-cm, painful nodules at the apices of an excision scar from a squamous cell carcinoma of the neck 2 years prior. The patient's medical history was significant for recurrent cystinuria nephrolithiasis, for which she took penicillamine for 43 years until 1 year before presentation, when she was switched to tiopronin. Additionally, she had been taking captopril for 10 years. Shave biopsy of the lesions demonstrated serrated elastic fibers with transepidermal elimination, consistent with elastosis perforans serpiginosa (EPS; Fig. 1).

The patient was lost to follow-up for 1 year. After 1 year, the lesions on her neck had progressed, demonstrating serpiginous borders that were intermittently painful, bleeding, and crusting, with redundant, wrinkled skin (Fig. 2A). These same changes were noted on the right upper arm and axilla. Intralesional triamcinolone (5 mg/mL) was initiated at a 6- to 8-week interval, and daily application of 0.05% tretinoin cream alternating with desonide was prescribed. Modest improvement was noted after 21 months. To expedite improvement, red light photodynamic therapy (PDT; 635 nm) was initiated on the neck (Wang et al., 2015). The treatment protocol was 5-aminolevulinic acid with a 2-hour incubation and exposure dose of 99 J/cm².

After three weekly PDT treatments, the lesions on the neck (Fig. 2B) and right arm and axilla were thinner, less painful, and

less pruritic. Over 3 years, the patient received an average of six yearly PDT treatments, coupled with triamcinolone, tretinoin, and desonide. The neck lesions showed significant improvement, demonstrating normal skin between scattered keratotic papules. One year later, the neck lesions were stable (Fig. 2C), but new serpiginous, red plaques with numerous central firm cores were seen in the bilateral axillae (Fig. 2D).

EPS is a rare primary perforating dermatosis that presents as a serpiginous or annular pattern of papules on the face, arms, or neck (Polańska et al., 2016). EPS may be idiopathic, induced by medications such as penicillamine or captopril, or associated with connective tissue diseases, including Marfan and Ehlers-Danlos syndrome, cutis laxa, and pseudoxanthoma elasticum (PXE; Polańska et al., 2016).

PXE is a metabolic and connective tissue disorder caused by autosomal dominant mutations in *ABCC6* that manifests with dystrophic calcification distorting elastic fibers within the skin, blood vessels, and eye (Germain, 2017). Characteristic skin findings include coalescing yellow papules and excess wrinkling of the skin on the neck and intertriginous regions (Germain, 2017). Pseudo-PXE, in which clinical and dermatopathological findings of PXE are present without causative mutations, has been associated with penicillamine and captopril treatment (Bécuwe et al., 2005).

Penicillamine induces widespread damage to elastic fibers, possibly by decreasing the cross-linking activity of copper-dependent lysyl oxidase or impairing elastic fiber maturation (Light et al., 1986). Long-term exposure to penicillamine and related thiol drugs (tiopronin, captopril) likely promoted the development of EPS and pseudo-PXE in this patient. This case is unique because

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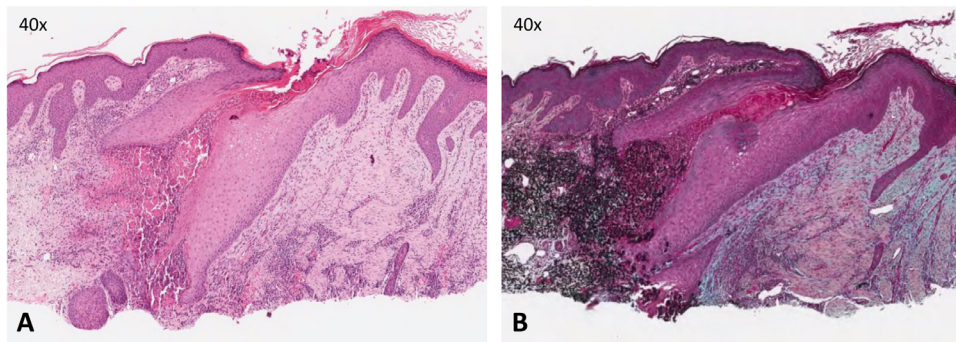


Fig. 1. Histopathology of elastosis perforans serpiginosa. (A) Hematoxylin and eosin stain demonstrating abnormal elastic fibers with transepidermal elimination. (B) Movat's pentachrome stain demonstrating serrated elastic fibers.



Fig. 2. Elastosis perforans serpiginosa and pseudo-pseudoxanthoma elasticum in a 55-year-old woman with a history of penicillamine and captopril treatment. (A) Lesions on the neck demonstrated serpiginous borders and redundant, wrinkled skin. (B) The neck lesions improved after three weekly photodynamic therapy (PDT) treatments. (C) One year after completing 3 years of PDT, the neck lesion remained stable. (D) New serpiginous, red plaques were noted in the bilateral axillae 1 year after completing PDT.

Conflict of Interest

None.

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Study Approval

The author(s) confirm that any aspect of the work covered in this manuscript that has involved human patients has been conducted with the ethical approval of all relevant bodies.

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the ongoing use of captopril after penicillamine discontinuation continued to drive these clinical changes. Despite this, the patient had a good response to PDT.