

# Effective treatment of disseminated superficial actinic porokeratosis using a novel topical cholesterol/simvastatin combination cream

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### **Effective treatment of disseminated superficial actinic porokeratosis using a novel topical cholesterol/simvastatin combination cream**

Disseminated superficial actinic porokeratosis (DSAP) is the most common subtype of porokeratosis. It is characterised by pink-brown papules or plaques with a ridge-like border affecting areas of sun-exposed skin.<sup>1</sup> Sporadic and autosomal dominant inheritance patterns have been described and pathogenic germline mutations identified in the mevalonate pathway genes.<sup>2</sup> DSAP has been reported to undergo malignant transformation, most commonly to squamous cell carcinoma (SCC) but also basal cell carcinoma (BCC).<sup>3</sup> Current treatments include topical therapy such as imiquimod, 5-fluorouracil, retinoids, corticosteroids, vitamin-D analogues; systemic retinoids and physical therapies such as cryotherapy.<sup>4</sup> A recent small case series described the successful treatment of porokeratosis using a combination of topical 2% cholesterol and 2% lovastatin.<sup>1</sup> Lovastatin is not readily available in Australia nor the UK. Herein we present two patients with DSAP treated with an off-label combination of 2% cholesterol and 2% simvastatin cream.

Case 1: A 63-year-old female presented for a routine skin check. Her past medical history included two previously excised BCCs and frontal fibrosing alopecia. On examination, she had scattered pink-brown papules with a raised ridge-like border on the legs, consistent with DSAP. After an informed discussion, she was commenced on a compounded, twice-daily, topical 2% cholesterol/2% simvastatin cream. On three-month review, there was subjective and objective improvement in the lesions to which she had applied the cream. There were no adverse effects.

Case 2: A 52-year-old female presented with a 15-year history of DSAP affecting her arms and legs. She reported similar lesions in her mother and grandmother. Previous ineffective treatments included cryotherapy and 5-fluorouracil cream. On examination, there were scattered pink-brown papules with a ridge-like border on her legs and forearms consistent with DSAP (Figure 1). Given these characteristic clinical findings, no biopsy was performed. The patient commenced treatment with topical 2% cholesterol/ 2% simvastatin cream. On three-month review, there was an objective and subjective reduction in the number of lesions, with a markedly fainter appearance (Figure 1). She did not report any adverse effect from the cream and is continuing treatment.

Loss of function mutations in genes in the mevalonate pathway result in a reduction in its end products, including cholesterol, as well as accumulation of toxic intermediate metabolites.<sup>1</sup> Cholesterol is required to maintain skin integrity as it forms a key component of the extracellular lipid matrix in the stratum corneum. Cholesterol deficiency leads to increased keratinocyte sensitivity to apoptosis.<sup>5</sup> Premature apoptosis and dysregulated keratinocyte differentiation have been identified in prokeratosis.<sup>2</sup> Consequently, it has been hypothesised that a cream containing an HMG-CoA reductase inhibitor (statin), that would prevent toxic metabolite accumulation, together with cholesterol to replenish essential mevalonate pathway end-products might be effective in prokeratosis. This was recently demonstrated by Atzmony *et al.*, who showed clinical improvement in one patient with DSAP, two patients with prokeratosis palmaris et plantaris disseminata and two patients with linear prokeratosis treated with topical 2% cholesterol/2% lovastatin ointment.<sup>1</sup>

To the best of our knowledge, our two patients with DSAP are the first cases in Australia treated with topical 2% cholesterol/2% simvastatin cream, a pathogenesis-directed approach. We demonstrate simvastatin can be substituted for lovastatin in the compounded topical formulation. Our study is limited by the lack of placebo control and further controlled studies are required to verify the efficacy and safety of the medication as well as clarify the role of other toxic metabolites and depleted end-products that may play a role in prokeratosis pathogenesis.

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**Figure 1: Disseminated superficial actinic porokeratosis on the upper extremities of a 52-year-old female (a) left (b) right. Treatment response after twice daily application of topical cholesterol 2%/simvastatin 2% cream for three months (c) left (d) right**



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