Disseminated superficial actinic porokeratosis treated with tretinoin and calcipotriene

Kevin J. Severson, MD, Colleen M. Morken, MD, Steven A. Nelson, MD, Aaron R. Mangold, MD, Mark R. Pittelkow, MD, and David L. Swanson, MD

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INTRODUCTION

Disseminated superficial actinic porokeratosis (DSAP) is a chronic, benign condition characterized by red-brown colored macules to minimally elevated papules with classic peripheral, circumferential scale of cornoid lamellae photodistributed about the upper and lower extremities. Its often recalcitrant nature to treatment may be frustrating to both patient and provider. Commonly, first- and second-line treatments with cryotherapy, 5-fluorouracil 5% cream, imiquimod, retinoids, vitamin D3 analogs, topical diclofenac, or photodynamic therapy alone may be unsuccessful.[1] Topical retinoids, including topical tretinoin, and vitamin D analogs, such as calcipotriol twice daily, have demonstrated efficacy as alternative monotherapy lines for treatment of porokeratoses in the literature. Retinoids and vitamin D3 analogs (calcipotriene as a synthetic form of vitamin D3), play important roles in regulating genomic expression important to keratinocyte maturation and differentiation while modulating keratinocyte proliferation that may offer biological therapeutic advantage in treating porokeratoses.[2,3] However, when either is used as monotherapy alone, duration of therapy of up to 4 months may be needed before achieving significant improvement.[4-6]

Recent studies have identified defective mevalonate pathways in DSAP lesions that ultimately lead to dysregulated keratinocyte differentiation due to reduction of end pathway products, such as cholesterol, and toxic accumulation of mevalonate metabolites.[7,8] Although newer topical therapies such as lovastatin 2% alone or in combination with cholesterol 2% have shown therapeutic promise,[7,8] treatment failure occurs. Here, we report near complete response of extensive, refractory DSAP of the upper and lower extremities with combination therapy of tretinoin (0.025%-0.05%) cream with calcipotriene 0.005% cream.

Abbreviation used:

DSAP: disseminated superficial actinic porokeratosis

CASE REPORT

A 74-year-old man with a medical history of chronic lymphocytic leukemia and thrombotic thrombocytopenic purpura presented with an 8-year history of an established, clinical diagnosis of DSAP. He had previously failed cryotherapy, 5-fluorouracil 5% cream, and topical lovastatin 2%-cholesterol 2% lotion (once daily application for 1 year with minimal improvement). Examination revealed pink-red colored circular to ovoid minimally elevated papules with thin circumferential scale consistent with porokeratoses extensively involving the bilateral lower portion of the legs and forearms (Figs 1, *A*; 2, *A*; and 3, *A*). As a prior case report demonstrated significant improvement with combination 0.005% calcipotriol daily in morning

From the Department of Dermatology, Mayo Clinic Arizona, Scottsdale, Arizona.

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Correspondence to: Kevin J. Severson, MD, Department of Dermatology, Mayo Clinic Arizona, 13400 E Shea Blvd, Scottsdale, AZ 85259. E-mail: severson.kevin@mayo.edu.

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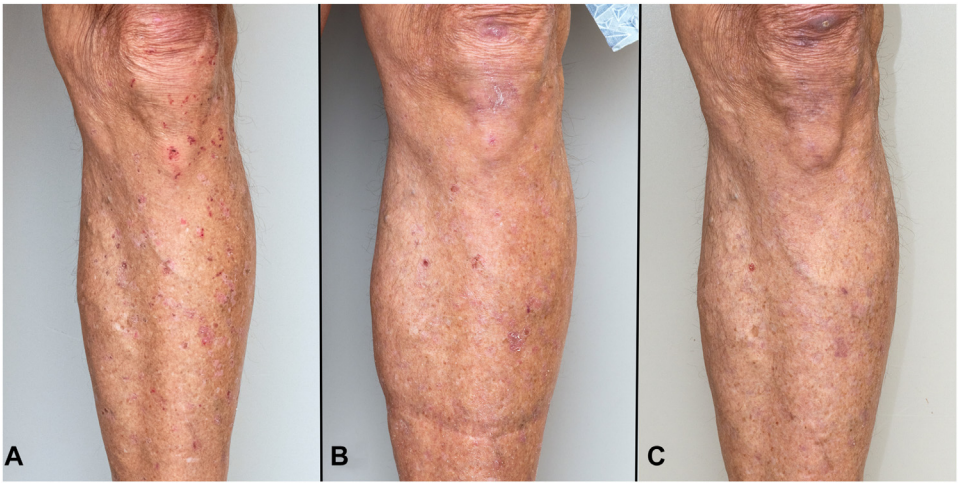

Fig 1. Disseminated superficial actinic porokeratosis of the anterior aspect of the lower portion of the left leg. Anterior aspect of the lower portion of the left leg (**A**) at presentation, (**B**) at 3 month follow-up, and (**C**) at 6 month follow-up with application of topical tretinoin 0.025% cream with calcipotriene 0.005% cream every other night.

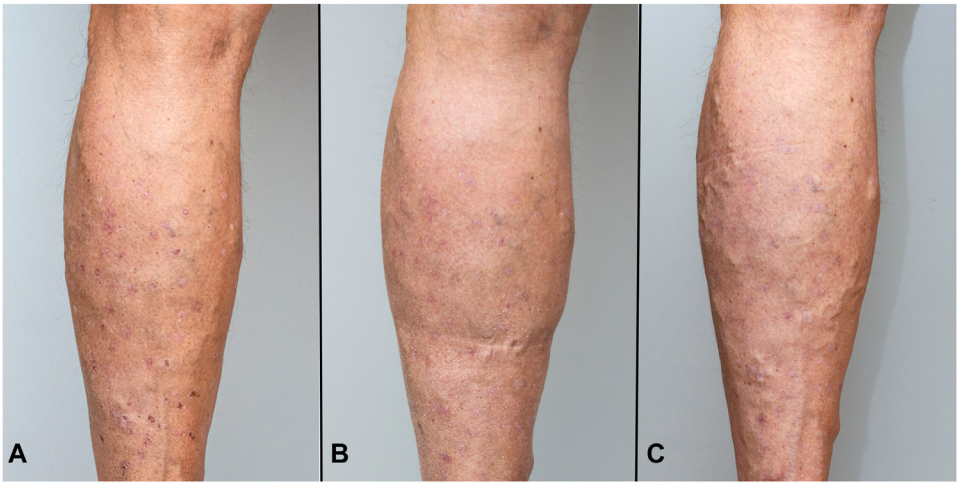

Fig 2. Disseminated superficial actinic porokeratosis of the posterior aspect of the lower portion of the left leg. Posterior aspect of the lower portion of the left leg (**A**) at presentation, (**B**) at 3 month follow-up, and (**C**) at 6 month follow-up with application of topical tretinoin 0.025% cream with calcipotriene 0.005% cream every other night.

with adapalene 0.1% gel nightly,[9] our patient was initiated on regimen with tretinoin 0.05% cream with calcipotriene 0.005% cream nightly as tolerated with encouragement to moisturize at least daily to avoid cutaneous irritation. Dual combined therapy was elected over monotherapy because the patient was highly motivated, and dual complimentary therapy was hypothesized to offer improved clinical response over either monotherapy alone. Tretinoin 0.05% strength was selected as 0.1% strength would be too irritating in the tretinoin-naïve patient but likely tolerable with moisturization.

At 3-month follow-up, patient reported he had maintained therapy compliance for approximately 3 weeks after his last appointment. He then held therapy as he had significant response to the bilateral lower extremity lesions (and to lesser degree bilateral forearm lesions), although had experienced cutaneous irritation with the regimen despite moisturizing daily. Compared with baseline lesion count, the patient was pleased with the 80% noted lesion reduction of lower portion of the legs, although he perceived minimal to no improvement of the forearms yet (Figs 1, *B*; 2, *B*; and 3, *B*). Clinical lesion

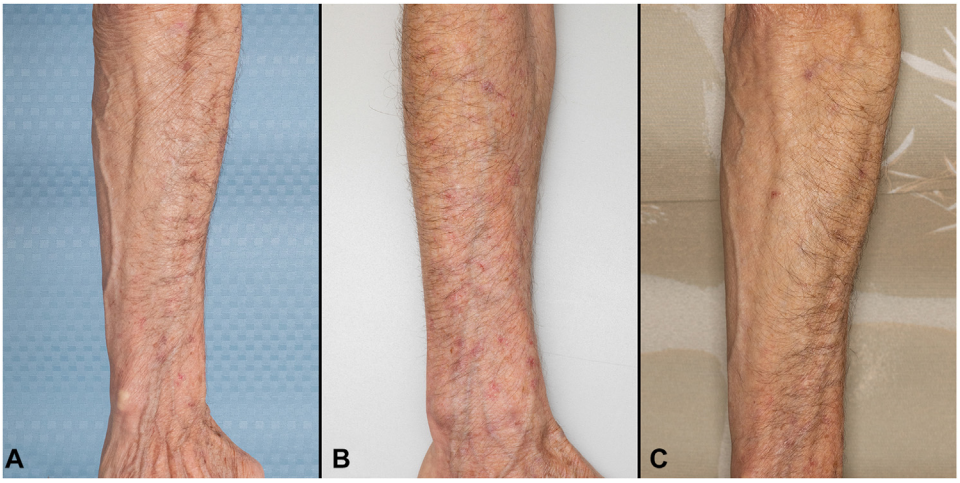

Fig 3. Disseminated superficial actinic porokeratosis of the posterior aspect of the right forearm. Posterior aspect of the right side of the forearm (**A**) at presentation, (**B**) at 3 month follow-up, and (**C**) at 6 month follow-up with application of topical tretinoin 0.025% cream with calcipotriene 0.005% cream every other night.

count was assessed by the treating physician (K.J.S.) at each visit with individual count of each present porokeratosis. Overall improvement at 3-month follow-up was 75% reduction in total lesion count despite holding therapy 9 weeks prior. Because of reported irritation, his regimen was amended to topical tretinoin 0.025% cream with calcipotriene 0.005% cream every other night as tolerated.

At follow-up 3 months later (6 months after initial therapy with tretinoin and calcipotriene), he reported 100% therapy compliance, continued improvement and near complete response with 94% reduced lesion count of the lower portion of the legs, 79% reduced lesion count of bilateral forearms, and overall 91% reduced lesion count compared with baseline (Figs 1, *C*; 2, *C*; and 3, *C*). Surrounding postinflammatory pigment changes were evident in prior areas of involvement. With moisturizing daily, patient denied any adverse effects of topical tretinoin 0.025% cream with calcipotriene 0.005% cream every other night, although did report return of cutaneous irritation when he attempted to increase frequency of dual therapy to nightly as tolerated for a short period.

CONCLUSION

Significant improvement was realized as soon as 3 weeks by the patient with combination tretinoin and calcipotriene creams in this case of refractory DSAP, whereas typically longer course durations are needed when treating with monotherapy of either alone.[4-6] Porokeratoses represent lesions characterized by abnormal keratinocytes maturation with dyskeratotic keratinocytes often found at the base of their cornoid lamellae. Thus, combination therapy of topical tretinoin with calcipotriene working in tandem to promote normal keratinocyte maturation and differentiation may offer synergistic therapeutic response compared with either monotherapy alone. Maintenance of disease clearance has been successfully described with intermittent application of topical retinoids or calcipotriol every other day to twice weekly.[9,10] Further case series and prospective controlled trials are needed to assess the efficacy, safety, and tolerability of topical tretinoin combined with calcipotriene in the treatment of DSAP. Furthermore, given variability in patient tolerance and response to therapy, the preferred topical retinoid with vitamin D analog regimen to clear and maintain disease clearance remains to be characterized.

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Conflicts of interest

None disclosed.

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