

# Verrucous Psoriasis Treated With Methotrexate and Acitretin Combination Therapy

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## PRACTICE POINTS

- Verrucous psoriasis is an uncommon but recalcitrant-to-treatment variant of psoriasis that is characterized by hypertrophic plaques.
- The diagnosis of verrucous psoriasis is challenging, as it can mimic other entities such as verruca vulgaris and squamous cell carcinoma.
- Although the etiology of this entity is unknown, an association with diabetes mellitus, pulmonary disease, lymphatic circulation disorders, and immunosuppression has been described.
- The combination of methotrexate and acitretin is a safe and effective option for these patients in the absence of comorbid conditions.

To the Editor:

A 76-year-old woman with venous insufficiency presented with numerous thick, hyperkeratotic, confluent papules and plaques involving both legs and thighs as well as the lower back. She initially developed lesions on the distal legs, which progressed to involve the thighs and lower back, slowly enlarging over 7 years (Figure 1). The eruption was associated with pruritus and was profoundly malodorous. The patient had been unsuccessfully treated with triamcinolone ointment, bleach baths, and several courses of oral antibiotics. Her history was remarkable for marked venous insufficiency and mild anemia, with a hemoglobin level of 11.9 g/dL (reference range, 14.0–17.5 g/dL). She had no other abnormalities on a comprehensive blood test, basic metabolic panel, or liver function test.

A punch biopsy specimen from the left lower back was obtained and demonstrated papillomatous psoriasiform epidermal hyperplasia with broad parakeratosis, few intracorneal neutrophils, hypogranulosis, and suprapapillary thinning (Figure 2). She was initially treated with oral methotrexate (20 mg weekly), resulting in partial improvement of plaques and complete resolution of pruritus and

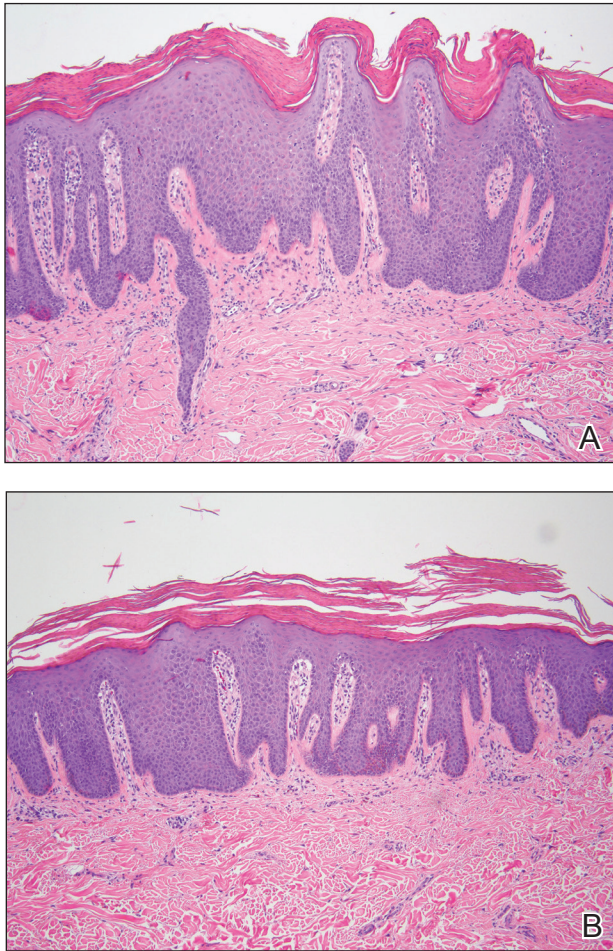


**FIGURE 1.** Verrucous psoriasis. Hyperkeratotic papules and plaques on the left anterior leg prior to initiation of treatment.

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**FIGURE 2.** A and B, Punch biopsy specimen from the left lower back showed papillomatous psoriasiform epidermal hyperplasia with broad parakeratosis, few intracorneal neutrophils, hypogranulosis, and suprapapillary thinning (both H&E, original magnification  $\times 10$ ).

malodor. After 15 months of treatment with methotrexate, low-dose methotrexate (10 mg weekly) in combination with acitretin 25 mg daily was started, resulting in further improvement of hyperkeratosis (Figure 3). The patient also was given a compounded corticosteroid ointment containing liquor carbonis detergens, salicylic acid, and fluocinonide ointment, achieving minor additional benefit. Comprehensive metabolic panel, lipid panel, and liver function tests were obtained quarterly. Hemoglobin levels remained low, similar to baseline (11.3–12.5 g/dL), while all other values were within reference range. The patient tolerated treatment well, reporting mild dryness of lips on review of systems, which was attributed to acitretin and was treated with emollients.

Verrucous psoriasis is an uncommon variant of psoriasis that presents as localized annular, erythrodermic, or drug-induced disease, as reported in a patient with preexisting psoriasis after interferon treatment of hepatitis C.<sup>1,2</sup> It is characterized by symmetric hypertrophic verrucous plaques that may have an erythematous base and



**FIGURE 3.** A and B, Combination therapy with methotrexate and acitretin showed partial response after 8 months, with scattered hyperkeratotic papules. There was persistent venous insufficiency with edema.

involve the legs, arms, trunk, and dorsal aspect of the hands<sup>3</sup>; malodor is frequent.<sup>1</sup> Histopathologically, overlapping features of verruca vulgaris and psoriasis have been described. Specifically, lesions display typical psoriasiform changes, including parakeratosis, epidermal acanthosis with elongation of rete ridges, suprapapillary thinning, epidermal hypogranulosis, dilated or tortuous capillaries, and neutrophil collections in the stratum corneum (Munro microabscesses) or stratum spinosum (spongiform pustules of Kogoj).<sup>3</sup> Additional findings of papillomatosis and epithelial buttressing are highly suggestive of verrucous psoriasis,<sup>3</sup> though epithelial buttressing is not universally present.<sup>4-6</sup> Similarly, although eosinophils and plasma cells have been described in some patients with verrucous psoriasis, this finding has not been consistently reported.<sup>4-6</sup> Our biopsy specimen (Figure 2) lacks the epithelial buttressing but does exhibit subtle papillomatous hyperplasia consistent with the diagnosis of psoriasis.

The etiology of this entity is unknown. An association with diabetes mellitus, pulmonary disease, lymphatic circulation disorders, and immunosuppression has been proposed. Others have reported repeated trauma as contributing to the pathogenesis.<sup>1</sup> For our patient, trauma secondary to scratching, long-standing venous insufficiency, and neglect likely contributed to the development of verrucous plaques.

The diagnosis of verrucous psoriasis can be challenging because of its similarity to several other entities, including verruca vulgaris; epidermal nevus; and squamous cell carcinoma, particularly verrucous carcinoma.<sup>4,6,7</sup> The diagnosis has been less challenging in areas where prior typical psoriatic lesions evolved into a verrucous morphology. Our patient presented a diagnostic challenge and draws attention to this unique variant of psoriasis that could easily be misdiagnosed and lead to inappropriate treatment.

Verrucous psoriasis can be recalcitrant to therapy. Although studies addressing treatment modalities are lacking, several recommendations can be derived from case reports and our patient. The use of topical therapies, including topical corticosteroids (eg, fluocinonide, clobetasol, halobetasol), keratolytic agents (eg, urea, salicylic acid), and calcipotriene, provide only minimal improvement when used as monotherapy.<sup>1</sup> Better success has been reported with systemic therapies, mainly methotrexate and acitretin, with anecdotal reports favoring the use of oral retinoids.<sup>1,6</sup> Conversely, biologic medications such as etanercept, ustekinumab, adalimumab, and infliximab have only provided a partial response.<sup>1</sup> Combination therapies including intralesional triamcinolone plus methotrexate<sup>4</sup> or methotrexate plus acitretin, as in our patient, seem to provide additional benefit. Methotrexate and acitretin combination therapy has traditionally been avoided because of the risk for hepatotoxicity. However, a case series has demonstrated a moderate safety profile with concurrent use of these drugs in treatment-resistant

psoriasis.<sup>8</sup> In our case, clinical response was most pronounced with combination therapy of methotrexate 10 mg weekly and acitretin 25 mg daily. Thus, strong consideration should be given for combination methotrexate-acitretin therapy in patients with recalcitrant verrucous psoriasis who lack comorbid conditions.

We present a case of verrucous psoriasis, a variant of psoriasis characterized by hypertrophic plaques. We propose that venous insufficiency and long-standing untreated disease was instrumental to the development of these lesions. Furthermore, retinoids, particularly in combination with methotrexate, provided the most benefit for our patient.

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