

Palmoplantar Pustular Psoriasis Following Initiation of a Beta-blocker: Disease Control With Low-Dose Methotrexate

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Practice Points

- Beta-blockers, lithium, tetracyclines, nonsteroidal anti-inflammatory drugs, adalimumab, synthetic antimalarials, angiotensin-converting enzyme inhibitors, interferons, terbinafine, infliximab, and etanercept can aggravate preexisting psoriasis, provoke lesions in uninvolved skin in individuals with psoriasis, and induce psoriasis in patients without a personal or family history of psoriasis.
- Methotrexate can be effective and safe in treating palmoplantar pustular psoriasis when prescribed at a low dose.

Palmoplantar pustular psoriasis is a debilitating chronic disease that can have a serious impact on patients' quality of life. There currently is no therapeutics standard for controlling palmoplantar pustular psoriasis, but various treatments, many of which have serious toxic side effects, have been used to treat this disease, including methotrexate. We report a case of palmoplantar pustular psoriasis in a 76-year-old woman that was triggered by initiation of a beta-blocker. The patient's condition was controlled with a low-dose regimen of methotrexate. It is important for dermatologists to recognize that pustular psoriasis can be treated with low-dose methotrexate to avoid potentially toxic effects of higher doses of methotrexate, which is especially true in cases of drug-induced disease, as seen in our patient.

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Psoriasis affects 1% to 2% of individuals in the United States, typically within the third decade of life.^{1,2} Psoriasis lesions may be persistent or relapsing plaques or pustules. The epidermal thickening that often is noted in psoriasis is secondary to the elongation of rete ridges. Parakeratosis, which also is often noted in psoriasis, is the accumulation of cells with retained nuclei within the cornified layer. Localized pustular psoriasis is a variant of psoriasis that displays scaling erythematous plaques studded with pustules. The pustules are most frequently observed on the palms, soles, and nails of affected individuals.¹ Palmoplantar pustular psoriasis is most commonly seen in women in their fifth and sixth decades of life.³ One agent commonly used in the treatment of psoriasis is methotrexate, a prodrug that is converted to polyglutamyl derivatives and acts as a dihydrofolate reductase inhibitor.^{4,5} We report a case of palmoplantar pustular psoriasis that was triggered by initiation of a beta-blocker. The patient's condition was controlled with a low-dose methotrexate regimen.

Case Report

A 76-year-old woman with a history of hypertension, hyperlipidemia, and hypothyroidism presented with erythema and pustules on the bilateral palms and soles 6 weeks following initiation of a beta-blocker.

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On discontinuation of the beta-blocker, the lesions showed minimal improvement without resolution. The patient then was started on fluocinonide ointment 0.05% and acitretin 25 mg 3 times weekly. Improvement (25%) was noted over the course of 9 months; acitretin then was increased to 25 mg 4 times weekly, but no change was noted (Figure). Acitretin then was discontinued and she was started on methotrexate 2.5 mg weekly, followed by improvement of the lesions on the palms and soles. This regimen was continued and the patient was stable at 2-year follow-up with moderate hyperpigmentation of the palms and minimal hyperpigmentation of the soles, both without erythema or exudates.

Comment

Palmoplantar pustular psoriasis is a rare form of psoriasis; it may, however, be induced by a variety of medications.⁶ A causal relationship to psoriasis has been documented with beta-blockers, lithium, tetracyclines, nonsteroidal anti-inflammatory drugs, adalimumab, and synthetic antimalarials. Other drugs linked to psoriasis are angiotensin-converting enzyme inhibitors, interferons, and terbinafine.⁷ Anti-tumor necrosis factor α agents such as infliximab and etanercept also have been reported to induce pustular psoriasis.⁶ These drugs have been reported to aggravate preexisting psoriasis, provoke lesions in uninvolved skin in individuals with psoriasis, and induce psoriasis in patients without a personal or family history of psoriasis.⁸ The pathogenesis of psoriasis triggered by beta-blockers is thought to be due to decreased intraepidermal cyclic adenosine monophosphate, leading to an increase in epidermal cell turnover.⁷

Palmoplantar pustular psoriasis is a debilitating chronic illness that can span decades.⁹ Not only can it be socially stigmatizing, but it also interferes with patients' quality of life.¹⁰ Various therapies are used to treat this condition including coal tar, topical corticosteroids with or without polythene occlusion, photochemotherapy, tetracyclines, systemic retinoids, cyclosporine, biologics, and methotrexate.⁹ There currently is no therapeutic standard for controlling this disease, as treatment often is fraught with medication resistance and intolerance as well as frequent relapses. Many medications also are used without firm evidence proving they are beneficial.¹¹

Despite the advent of biologics, methotrexate remains commonly used in the treatment of psoriasis as monotherapy or in combination with other drugs. In comparison to biologics, methotrexate is less expensive, has established efficacy data, and can



Palmoplantar pustular psoriasis on the soles of both feet prior to treatment with methotrexate.

be administered orally.¹² Although it was previously believed that the antiproliferative action of methotrexate via antifolate metabolism led to improvement of psoriatic lesions, in vitro data point to the anti-inflammatory activity of methotrexate playing the more dominant role in disease improvement. Methotrexate also inhibits 5-aminoimidazole-4-carboxamide ribonucleotide transformylase, leading to the buildup of adenosine in tissue and consequently contributing to its anti-inflammatory properties.¹²

In psoriasis patients, methotrexate is commonly used in dosages up to 30 mg weekly.⁵ Our patient demonstrates a rare case of palmoplantar pustular psoriasis that was well controlled using low-dose methotrexate (2.5 mg weekly). Some cases report low doses of 15 to 20 mg for long-term control in psoriasis.¹³ However, the successful use of doses as low as 2.5 mg for control of any variant of psoriasis is rare.

Conclusion

Although it has been shown to be effective in the treatment of psoriasis, the use of methotrexate is not benign; it has been associated with hepatotoxicity and bone marrow toxicity.¹² It is important for dermatologists to recognize that pustular psoriasis can be treated with low-dose methotrexate to avoid potentially toxic effects of higher doses of methotrexate, which is especially true in cases of drug-induced disease, as seen in our patient.

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QUICK POLL QUESTION

Do you use low-dose methotrexate in your patients with drug-induced psoriasis?

- a. Yes
- b. No, I prefer other therapies
- c. No, but I will now

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