Successful Use of Apremilast in Psoriasiform Dermatitis Refractory to Biologics

Christopher S Yang, BA1, Victor Quan, MD1, Ahmad Amin, MD1

1Department of Dermatology, Northwestern University Feinberg School of Medicine, Chicago, IL

ABSTRACT
Psoriasis is a common immune-mediated disease that can affect the skin, nails, and joints. Management is usually comprised of topical therapy and/or systemic therapy, either biologic or nonbiologic. This case shows a psoriasiform dermatitis with primary response failure to several systemic biologic and nonbiologic therapies for atopic dermatitis (methotrexate, dupilumab) and psoriasis (cyclosporine, adalimumab, ustekinumab, guselkumab, ixekizumab). Ultimately, the patient was treated successfully with apremilast. This case suggests that certain cases of psoriasis may improve exclusively with PDE-4 inhibition. Conversely, this could also suggest existence of a separate entity of psoriasiform dermatitis that is primarily mediated by PDE-4. We encourage a trial of apremilast in patients presenting with disease mimicking psoriasis who fail multiple therapies.

INTRODUCTION
Psoriasis is a common immune-mediated disease that can affect the skin, nails, and joints, seen in approximately 2% of the population. The most common form of the disease is chronic plaque psoriasis (psoriasis vulgaris), which presents as sharply demarcated erythematous plaques with silvery scales. Histologic hallmarks include epidermal acanthosis, parakeratosis, and inflammatory infiltrate. Management is usually comprised of topical therapy and/or systemic therapy, either biologic or nonbiologic. Biologic therapies for psoriasis include TNF-alpha inhibitors, as well as interleukin (IL)-12/23, IL-23, and IL-17 inhibitors. Nonbiologic systemic therapies include methotrexate, cyclosporine, acitretin, and phosphodiesterase-4 inhibitors.

CASE REPORT
We present the case of a 34-year-old female with a history of exercise-induced asthma and a 16-year history of psoriasiform dermatitis without joint involvement. At age 18, she presented with erythematosus pruritic plaques with silvery scale symmetrically on the dorsal feet, and a clinical diagnosis of moderate to severe psoriasis was made. She noted worsening with psychological stress. The patient has a family history of mild psoriasis in her mother and grandfather, both well-controlled with topical therapy alone. She was initially treated with clobetasol, cyclosporine, and methotrexate with little improvement. She was then treated with efalizumab, which led to nearly complete resolution of her condition until the drug was taken off the market in 2009.4 After discontinuing efalizumab, she developed new psoriasiform plaques on the feet, hands.
and fingers, elbows, forearms, shins, and upper back, affecting approximately 10% of her total body surface area (BSA) (Figure 1). She was placed on Humira 40mg every other week without improvement.

Over the next 4 years, various biologic drugs typically used for psoriasis were trialed, including ustekinumab, guselkumab, and ixekizumab. She had intermittent periods of mild improvement but no meaningful response to any medications. Given her lack of response to multiple drugs normally effective in psoriasis and considering her history of asthma, an alternate diagnosis of atopic dermatitis was considered. She was placed on dupilumab for 2 months but still did not show any improvement.

A punch biopsy from the dorsal ankle was performed. Figure 2. A) (4X H&E) Regular acanthosis with thinning of the suprapapillary plates and confluent parakeratosis with a mild perivascular infiltrate and minimal spongiosis consistent with a psoriasiform dermatitis. B) (10X H&E) There is confluent parakeratosis with few foci of neutrophilic microabscesses in the stratum corneum with focal areas of hypogranulosis. Ectatic superficial vessels in the papillary dermis are seen. No eosinophils are noted.

Figure 1. A) On the bilateral dorsal feet there are large pink erythematous plaques with abundant silvery scale. After 8 weeks on apremilast, the patient has almost complete resolution with only faintly pink patches.
performed in November of 2020 showed confluent parakeratosis with focal neutrophils in the stratum corneum, regular acanthosis with focal loss of the granular layer, and a lymphohistiocytic perivascular infiltrate, most consistent with psoriasiform dermatitis (Figure 2). There was no T-cell clonality. In January of 2021, the patient started apremilast 60mg per day. Within 4 weeks, she noted significant improvement in the thickness and redness of her plaques. She also reported drastic improvement in pruritus and overall appearance, which she had never experienced with any previous medications. After 8 weeks she had near complete clearance (Figure 1).

Apremilast has been demonstrated to be an effective treatment for both psoriasis\(^5\) and atopic dermatitis.\(^6\) We report a case of a psoriasiform dermatitis refractory to several systemic therapies for atopic dermatitis (methotrexate and dupilumab) and several systemic and biologic therapies for psoriasis (cyclosporine, adalimumab, ustekinumab, guselkumab, and ixekizumab), which ultimately cleared with apremilast. Of note, the patient reported clearance on efalizumab but had to stop therapy when it was discontinued from the market.

While apremilast has shown to be effective in patients with moderate-to-severe psoriasis who have received prior systemic therapy (conventional and/or biologic),\(^7,8\) it is still highly unusual for psoriasis to show primary response failure to this extensive degree of topical and biologic therapies.

Given our patient’s rapid and profound response to apremilast, we believe that this case suggests that certain cases of psoriasis may improve exclusively with PDE-4 inhibition. Conversely, this could also suggest existence of a separate entity of psoriasiform dermatitis that is primarily mediated by PDE-4. We therefore encourage a trial of apremilast in patients presenting with disease mimicking psoriasis who fail multiple therapies.

Conflict of Interest Disclosures: None

Funding: None

Corresponding Author:
Christopher S. Yang, BA
Department of Dermatology
Northwestern University Feinberg School of Medicine
676 N. St Clair St., Suite 1600
Chicago, IL 60611
Phone: 312-695-8106
Fax: 312-695-0007
Email: christopher.yang@northwestern.edu

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