doi:10.36849/JDD.6098

Successful Treatment of Palmoplantar Pustulosis With Apremilast

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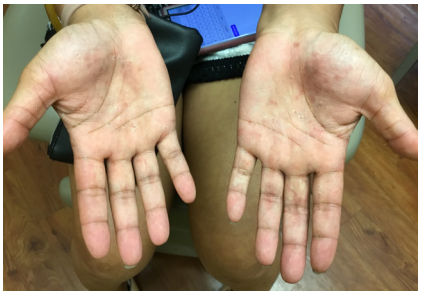
INTRODUCTION

Palmoplantar pustulosis (PPP) is a chronic, debilitating autoimmune skin disease characterized by the presence of recurrent neutrophilic pustules on acral surfaces. Although similarities exist, PPP is currently regarded as a distinct pathologic entity from palmoplantar psoriasis.[1] PPP is often refractory to topical treatments and therefore may benefit from the introduction of systemic or biologic therapy, although options are limited at this time. Few, yet promising, case reports exist highlighting the efficacy of oral apremilast, a phosphodiesterase-4 (PDE-4) inhibitor. Herein, we present a case of biopsy-proven PPP successfully treated with apremilast, along with a brief review of relevant literature supporting the use of apremilast.

CASE REPORT

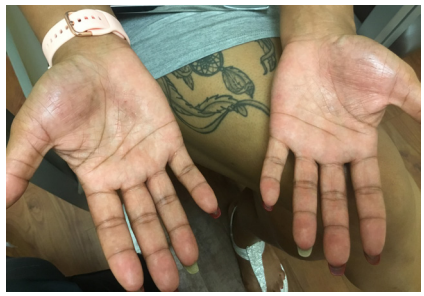
A 39-year-old African American female with a 10 pack-year smoking history presented to the dermatology clinic with a 6-month history of pruritic skin lesions on her hands. Physical examination demonstrated crops of pustules with associated erythema and desquamation located on the palmar surface bilaterally (Figure 1); punch biopsy revealed subcorneal pustules with neutrophils and parakeratosis, consistent with a diagnosis of palmoplantar pustulosis.

FIGURE 1. Crops of pustules with surrounding erythema and desquamation observed prior to initiation of apremilast.



She was initially treated with topical corticosteroids in the form of triamcinolone acetonide ointment, followed by halobetasol ointment, with little to no relief. The decision was ultimately made to initiate systemic therapy with apremilast. Near-complete resolution of the lesions was observed following 8 weeks of treatment (Figure 1), with significant improvement in associated pruritis and overall quality of life according to the patient. Disease remission was maintained after 6 months, and the medication was well-tolerated by the patient without any reported side effects.

FIGURE 2. Remarkable improvement of lesions illustrated at 8 weeks of treatment with apremilast.



DISCUSSION

Apremilast works via PDE-4 inhibition, resulting in an upregulation of intracellular cyclic adenosine monophosphate (cAMP) and subsequent suppression of interleukin-2 (IL-2), interleukin-8 (IL-8), interferon gamma (IFN-γ), and tumor necrosis factor-alpha (TNF-α).[2,3] Furthermore, increased levels of IL-8 have been demonstrated in lesions of PPP. Given its neutrophil chemoattractant properties, IL-8 is implicated in the underlying development of PPP.[1] The efficacy of apremilast in PPP is therefore presumed to be an effect of IL-8 inhibition, thus preventing formation of the characteristic pustules.

PPP refractory to topical treatments may benefit from the introduction of systemic and/or biologic agents. Anecdotal reports of success with etanercept (TNF-α inhibition), ustekinumab (IL-12/23 inhibitions), and secukinumab (IL-17 inhibition) exist, however, evidence is lacking and inconclusive.[4-6] Guselkumab, an IL-23 inhibitor, has demonstrated efficacy in a randomized controlled trial (RCT) and is currently approved for PPP in Japan.[7]

Systemic agents including methotrexate, acitretin, and cyclosporine have all shown efficacy, however, the adverse side effects associated with the aforementioned agents makes their use disfavorable.[8] Side effects of apremilast, on the other hand, primarily consist of diarrhea and depression, which are typically

TABLE 1.

Case Studies Investigating The Use of Apremilast In Refractory Palmoplantar Pustulosis Have Been Promising Thus Far

Citation	Age, Gender	Apremilast Dose	Response	Adverse Events
Haebich, et al.[9]	75 years, female	30mg twice daily	Symptom resolution	None
Haller, et al.[10]	57 years, female	30mg twice daily	Significant improvement	None
Adamo, et al.[11]	24 years, female	30mg twice daily	Disease control	Headaches, diarrhea, nausea, vomiting, with spontaneous resolution
Mikhailitchenko, et al.[12]	53 years, male	30mg twice daily	Almost clear	Three patients experienced loose stools that did not warrant a change in dosing. One patient reported more severe symptoms, and the dose was halved to 30mg once daily.
Mikhailitchenko, et al.[12]	65 years, female	30mg twice daily	Clear	
Mikhailitchenko, et al.[12]	54 years, female	30mg once daily	Mild	
Mikhailitchenko, et al.[12]	66 years, female	30mg twice daily	Clear	
Mikhailitchenko, et al.[12]	63 years, female	30mg twice daily	Almost clear	
Mikhailitchenko, et al.[12]	43 years, male	30mg twice daily	Almost clear	
Mikhailitchenko, et al.[12]	39 years, female	30mg twice daily	Moderate	
Mikhailitchenko, et al.[12]	64 years, female	30mg twice daily	Almost clear	
Carrascosa de Lome, et al.[13]	77 years, female	30mg once daily	Near-complete resolution	Mild diarrhea with 30mg twice daily, reduced to 30mg once daily

mild and resolve upon discontinuation.[9] The low risk of internal toxicity and favorable side effect profile makes apremilast a safer and more viable option for systemic treatment of PPP compared to alternative systemic agents.

Previous reports have demonstrated similar efficacy of apremilast in the treatment of PPP (Table 1). In a single case study, a 75-year-old woman with an 8-year history of PPP reported symptomatic resolution within 4 weeks of therapy.[10] A similar study showing successful treatment with apremilast was also reported in a patient with rheumatoid arthritis who developed PPP after rituximab therapy.[11] Additionally, apremilast also proved efficacious in PPP associated with SAPHO syndrome.[7] Mikhailitcheneko et al. reported efficacy of apremilast in the treatment of PPP in a case series of 8 patients.[12] An additional case study recently provided further support for the use of apremilast in PPP.[13] Our case, along with previous reports, provides further evidence supporting the need for clinical trials in order to implement apremilast as an option for systemic therapy in patients with refractory PPP.

DISCLOSURES

The authors have reported no conflicts.

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