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CASE REPORT

Intralesional Spesolimab: A Novel and Effective Approach for Palmoplantar Pustulosis Treatment – A Case Report

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Abstract: Palmoplantar pustulosis (PPP) is a chronic condition characterized by the presence of sterile pustules on the palms and soles of the feet. As we all know, there is currently no gold standard for the treatment of this intractable disease. Currently, interleukin-36 receptor (IL-36R)-targeted biologics are emerging as promising treatments for PPP. Here, we were the first to report a Chinese male with PPP who received an intralesional injection of spesolimab. We found that only a small intralesional injection volume of spesolimab could effectively suppress PPP in this case.

Keywords: Palmoplantar pustulosis, spesolimab, intralesional injection, case report

Introduction

Palmoplantar pustulosis (PPP) is a chronic, relapsing inflammatory disease characterized by symmetric, sterile pustules and erythematous scales on the palms and soles. It is regarded as a distinct form of localized pustular psoriasis. Given the complex pathogenesis of PPP, there are currently no standardized and gold standard therapeutic options.

Spesolimab is a monoclonal antibody directed against interleukin 36 receptor (IL-36R) activation, a pathway within the immune system that has been shown to be involved in the pathogenesis of generalized pustular pustulosis (GPP).[1] It is the only antibody approved by the US Food and Drug Administration (FDA) to treat patients with GPP. In addition, spesolimab has also undergone some clinical trials in PPP, which have shown that targeting the IL-36 pathway has therapeutic potential in PPP.[2,3] In a phase IIb study, more non-Asian patients experienced disease improvement with intravenous spesolimab compared to their counterparts in the placebo group.[3] However, it should be noted that all these previous studies used intravenous and subcutaneous injections to deliver spesolimab, which places a heavy burden on patients. Therefore, it is more appropriate to look for the topical application.

In view of the efficacy of systemic spesolimab in the treatment of PPP and the good efficacy of local application of an anti-IL-17A antibody reported in the past,[4] we used the intralesional injection of spesolimab to treat a Chinese PPP patient and achieved good results. To our knowledge, there is currently no published literature documenting the intralesional injection of spesolimab for PPP.

Case Report

A 27-year-old Chinese man presented to our dermatology department with a 9-month history of bilateral plantar pustules accompanied by scaling. In September 2023, the pustules first appeared on both toes without any identifiable triggers, accompanied by itching and pain. He initially self-administered topical antifungal ointments such as Dermonistat. However, there was no improvement in his condition. Instead, the number of pustules gradually increased, along with

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exudation, worsening pain and itching. On 26 March 2024, he presented to our department. A physical examination at that time revealed hyperkeratosis, pustules and desquamation on both soles without involvement of the palms. In addition, he had no extra-cutaneous lesions such as joint symptoms, nail changes or focal infections. The patient reported a 7-year history of smoking, consuming 10 to 15 cigarettes per day, and denied any food or drug allergies, as well as a personal or family history of psoriasis. In addition, fluorescence microscopy showed a negative fungal culture. Based on the above evidence, he was diagnosed with PPP. Halometasone and Crisaborole Ointment were prescribed for external use. After treatment, the pustules showed a slight reduction. However, they recurred shortly after discontinuing the medication.

On 19 April 2024, the patient returned to our department for a follow-up visit. Physical examination revealed pustules and eczematous hyperkeratotic scaly plaques on both soles with no involvement of the palms (Figure 1A and B). Palmoplantar Pustular Psoriasis Area and Severity Index (PPP ASI) scores and Palmoplantar Pustulosis Physician Global Assessment (PPP PGA) scores were recorded as 9 and 2, respectively. Following informed consent for off-label treatment, the patient received a regimen consisting of an intralesional injection of 1 mg/mL spesolimab into the lesions, for a total dose of 2.5 mL. On 20 May 2024, the lesions showed dramatic improvement (Figure 1C and D), as evidenced by PPP ASI and PPP PGA scores of 1.2 and 1, respectively, indicating that the patient achieved PPP ASI75 (defined as ≥ 75% reduction from baseline PPP ASI). On 9 July 2024, the patient's PPP ASI and PPP PGA scores were 0.6 and 0, respectively, reflecting the achievement of PPP ASI90 (Figure 1E and F). No adverse events were reported during the intralesional injection treatment or in the two months following treatment.

Discussion

PPP is a chronic pustular dermatitis that primarily affects the palms and soles, characterized by the presence of pustules, erythema, and abnormal desquamation. It is rarely observed in children and predominantly affects adult females. The prevalence of PPP is estimated to be between 0.01% and 0.05% and its severity has been found to be associated with smoking status.[5,6] PPP typically presents as a chronic and recurrent condition that often does not respond effectively to conventional treatment approaches. Currently, biological therapies focusing on blocking IL-36 or IL-1 pathways have been extensively investigated as potential treatments for PPP.

The IL-36 cytokine family, a subfamily of the IL-1 superfamily, acts through the IL-36R, including three agonists (IL-36α, IL-36β, and IL-36γ) and one antagonist (IL-36Ra).[7] IL-36α, IL-36β, and IL-36γ trigger immune cell infiltration and inflammatory pathways by activating IL-36R, whereas IL-36Ra, encoded by IL36RN, acts as an anti-inflammatory factor by inhibiting IL-36R signaling.[7] Mutations in IL-36RN result in the inactivation of IL-36Ra, which leads to continued abnormal activation of IL-36R, resulting in failure to inhibit IL-36 signaling and induction of inflammatory responses. Previous studies have defined IL36RN mutations as a major predisposing factor for GPP.[8] In addition, Twelves et al showed that the association between IL36RN mutations and PPP was statistically significant.[1]

Spesolimab, a humanized IL-G1 monoclonal antibody, selectively binds to IL-36R and prevents the activation of the IL-36 signaling pathway. It is currently approved in 51 countries for the treatment of GPP flares, including the FDA, European Medicines Agency (EMA) and China National Medical Products Administration (NMPA). Several studies currently underway to evaluate the efficacy of subcutaneous spesolimab in PPP.[2,3] In a Phase IIa pilot study, 79 patients with PPP were randomized to receive either 900 mg or 300 mg of spesolimab or placebo intravenously every 4 weeks until week 12 in patients with PPP.[2] Although the primary efficacy endpoint (PPP ASI50) was not met at week 16, there was a faster reduction in the severity of PPP over time in the spesolimab group compared with the placebo group.[2] However, limitations of the current study include the small sample size and patient demographics at enrollment, which are not typically representative of the wider PPP population.[2] In addition, the natural resolution of disease between screening and baseline may have masked any treatment effect of spesolimab in patients with PPP.[2] In a Phase IIb study, 152 patients were randomized into five groups, with the patients in four groups receiving different intravenous doses of the drug and the patients in one group receiving placebo.[3] The primary efficacy endpoint was the percentage change from baseline in the PPP ASI at 16 weeks.[3] At week 16, there was no significant change from baseline in this efficacy endpoint between the spesolimab and placebo groups.[3] In addition, compared to the Asian patient population, more people in the

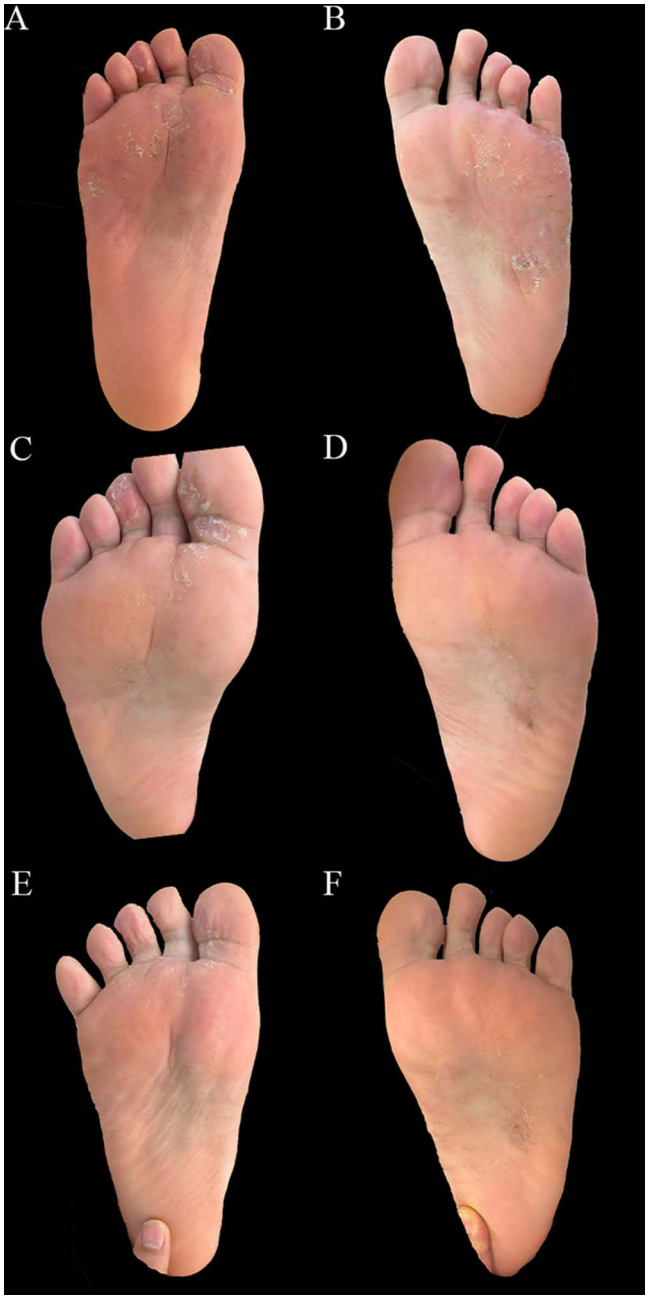

Figure 1 Lesions of palmoplantar pustulosis on both feet prior to treatment (**A** and **B**), one month following a single intralesional treatment with spesolimab (**C** and **D**), and two months after treatment (**E** and **F**).

non-Asian patient population experienced disease improvement with spesolimab treatment than their counterparts in the placebo group.[3]

Based on this evidence, we attempted to treat PPP with an intralesional injection of spesolimab. Then, we were surprised to find that direct injection of spesolimab into PPP lesions in the skin yielded promising results, with no observed side effects or complications following the intralesional injection. However, several limitations of the present study must be acknowledged. Firstly, our study was based on a single patient, and replication based on a larger patient sample is necessary to wider applicability of the results in the future. Secondly, intralesional spesolimab was not compared with other treatments, leaving unanswered questions about how intralesional spesolimab compares with existing treatments. Thirdly, follow-up was relatively short, which

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limits our assessment of durability of response, risk of relapse and long-term safety. Finally, the intralesional injection method is associated with significant pain, and another patient with PPP discontinued treatment due to pain intolerance.

Conclusion

Despite the numerous treatment strategies proposed, effective management of PPP remains a major challenge. Given the pivotal role of the IL-36 pathway in the pathogenesis of PPP, we administered an intralesional injection of spesolimab to our patient and observed a rapid regression of skin lesions. To our knowledge, this is the first documented case of PPP responding to a single intralesional injection of spesolimab with an excellent safety profile. Our observations strongly support the rapid and safe clinical response to this method. Further studies are warranted to investigate the efficacy and safety of intralesional spesolimab injection in PPP in the future.

Ethics Statement

This report does not contain any personal information that could identify the patient and is therefore exempt from ethical approval.

Patient Consent

The patient consented the off-label treatment and permitted the clinical case to be written up and for the photographs to be published. Data are available upon request to the corresponding author.

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Disclosure

The authors declare no conflicts of interest for this article.

References

1. Twelves S, Mostafa A, Dand N, et al. Clinical and genetic differences between pustular psoriasis subtypes. *J Allergy Clin Immunol*. 2019;143(3):1021–1026. doi:10.1016/j.jaci.2018.06.038
2. Mrowietz U, Burden AD, Pinter A, et al. Spesolimab, an Anti-Interleukin-36 Receptor Antibody, in Patients with Palmoplantar Pustulosis: results of a Phase IIa, Multicenter, Double-Blind, Randomized, Placebo-Controlled Pilot Study. *Dermatol Ther*. 2021;11(2):571–585. doi:10.1007/s13555-021-00504-0
3. Burden AD, Bissonnette R, Navarini AA, et al. Spesolimab Efficacy and Safety in Patients with Moderate-to-Severe Palmoplantar Pustulosis: a Multicentre, Double-Blind, Randomised, Placebo-Controlled, Phase IIb, Dose-Finding Study. *Dermatol Ther*. 2023;13(10):2279–2297. doi:10.1007/s13555-023-01002-1
4. Xia R, Liu J, Gao Y, et al. Local injection of micro-dose anti-interleukin-17A antibody for palmoplantar pustulosis: a real-world study. *Clin Immunol*. 2023;253:109694. doi:10.1016/j.clim.2023.109694
5. Mrowietz U, Van De Kerkhof PCM. Management of palmoplantar pustulosis: do we need to change? *Br J Dermatol*. 2011;164(5):942–946. doi:10.1111/j.1365-2133.2011.10233.x
6. Benzian-Olsson N, Dand N, Chaloner C, et al. Association of Clinical and Demographic Factors With the Severity of Palmoplantar Pustulosis. *JAMA*. 2020;156:1216–1222. doi:10.1001/jamadermatol.2020.3275
7. Yuan ZC, Xu WD, Liu XY, Liu XY, Huang AF, Su LC. Biology of IL-36 Signaling and Its Role in Systemic Inflammatory Diseases. *Front Immunol*. 2019;10:2532. doi:10.3389/fimmu.2019.02532
8. Marrakchi S, Guigue P, Renshaw BR, et al. Interleukin-36-receptor antagonist deficiency and generalized pustular psoriasis. *N Engl J Med*. 2011;365(7):620–628. doi:10.1056/NEJMoa1013068