

IL-36 Receptor Antagonist Spesolimab for Generalized Pustular Psoriasis Combined with Palmoplantar Pustulosis: A Case Report

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Objective: We have entered the era of using biologics and small-molecule targeted drugs to treat diseases. Although there have been many reports on the use of the anti-interleukin-36 (IL-36) receptor antagonist spesolimab for the treatment of generalized pustular psoriasis (GPP) recently, the clinical application of spesolimab for the treatment of GPP combined with PPP (palmoplantar pustulosis) is rarely reported, and there is a lack of evidence on the safety and efficacy of the spesolimab. The clinical application of spesolimab for GPP combined with palmoplantar pustulosis (PPP) is rarely reported, and evidence on its safety and efficacy remains insufficient. We aimed to explore the use of spesolimab for GPP combined with PPP and observed significant efficacy without obvious side effects, thereby providing new ideas for the clinical treatment of GPP combined with PPP.

Methods: We reported a case of GPP combined with PPP treated with spesolimab, which achieved significant therapeutic effects without significant side effects.

Results: This case report shows that spesolimab has good clinical efficacy in treating GPP combined with PPP. In this case, the presence of PPP may have delayed the rapid and complete clearance of the skin lesions.

Conclusion: Spesolimab provides a new treatment option for patients with GPP combined with PPP.

Keywords: generalized pustular psoriasis, IL-36, spesolimab, palmoplantar pustulosis, secukinumab

Introduction

Generalized Pustular Psoriasis (GPP) is a rare, severe, immune-mediated inflammatory skin disease characterized by the sudden, widespread eruption of numerous sterile pustules on generalized painful erythematous and edematous skin.¹ Some of the pustules combine to form pustular lakes, and dry pustules form scales or scabs that gradually fall off, accompanied by obvious itching and burning sensation¹. Palmoplantar pustulosis (PPP) occurs only on the palms and/or soles of the feet.² The combination of GPP and PPP is rare and the treatment is challenging. Generalized pustular psoriasis usually occurs simultaneously with plaque psoriasis. Severe acute attacks of GPP may be life-threatening. There is currently no globally standardized guideline for GPP combined with PPP treatment. Traditional conventional drugs, biologics, JAK inhibitors, PDE-4 inhibitors, and other treatments for GPP or PPP have unsatisfactory therapeutic effects. The overactivation of the IL-36 pathway plays a crucial role in the pathogenesis of GPP. In addition to overactivity of the IL-36 pathway, activation of the IL-17 pathway can also be observed in PPP.³ Spesolimab is an IL-36 receptor antagonist that specifically binds to IL-36R, thereby blocking downstream inflammatory pathways mediated by IL-36R. This drug

has been approved in China, Europe, the United States, and other countries for the treatment of acute attacks of adult GPP. We reported a 55-year-old male patient diagnosed with GPP combined with PPP. After systemic treatment with oral cyclosporine, avilamycin, tofacitinib, and apremilast, the condition did not show significant improvement. After receiving treatment with the IL-36 receptor antagonist spesolimab, the patient's rash and systemic symptoms significantly improved. However, systemic scaling erythema was more pronounced, and long-term treatment with IL-17 receptor inhibitor secukinumab was necessary. This provides a new treatment option for GPP combined with PPP patients.

Case Presentation

The patient is a Chinese male surgeon who presented with a large number of sterile needle-tip-sized pustules on the basis of generalized scaly erythema. The number of pustules on the fingers increased significantly, leading to swelling, pain, obvious tenderness, and impaired flexion-extension movement. The patient visited our outpatient department and was diagnosed with GPP combined with PPP. Specialized examination: There were patchy erythema all over the body, with a large number of sterile needle-tip-sized pustules on top of the erythema, especially on the hands and feet, which merged into plaques. The GPPGA score was 9 points, and the body surface area (BSA) was $\geq 10\%$ (Figures 1–3). Laboratory examination showed no obvious abnormality (including routine blood test, biochemical test, and screening for tuberculosis, hepatitis B, HIV, syphilis, etc). Despite sequential therapy with cyclosporine, acitretin, tofacitinib, and apremilast, no significant clinical improvement was observed. Before using spesolimab, we conducted a thorough screening to rule out contraindications. After obtaining informed consent, the patient received a first single intravenous infusion of 900 mg spesolimab. Due to no significant clinical improvement observed after 24 hours (Figures 4–6), a second 900 mg intravenous infusion was administered one week later (Figures 7–9). After 24 hours, the patient's skin lesions improved significantly, pustules and swelling subsided almost completely, and skin pain, burning sensation, and itching were



Figure 1 Clinical manifestations of the hands at baseline (pre-treatment); the Generalized Pustular Psoriasis Area and Severity Index (GPPGA) score was 9.



Figure 2 Clinical manifestations of the feet at baseline (pre-treatment); the GPPGA score was 9.



Figure 3 Clinical manifestations of the trunk at baseline (pre-treatment); the GPPGA score was 9.



Figure 4 Clinical manifestations of the hands 24 hours after the first spesolimab administration; no significant resolution of the rash was observed.



Figure 5 Clinical manifestations of the feet 24 hours after the first spesolimab administration; no significant resolution of the rash was observed.



Figure 6 Clinical manifestations of the trunk 24 hours after the first spesolimab administration; no significant resolution of the rash was observed.



Figure 7 Clinical manifestations of the hands prior to the second spesolimab administration; the rash was slightly alleviated compared with that at 24 hours after the first treatment.



Figure 8 Clinical manifestations of the feet prior to the second spesolimab administration; the rash was slightly alleviated compared with that at 24 hours after the first treatment.



Figure 9 Clinical manifestations of the trunk prior to the second spesolimab administration; the rash was slightly alleviated compared with that at 24 hours after the first treatment.



Figure 10 Clinical manifestations of the hands 24 hours after the second spesolimab administration; significant improvement was achieved, with pustules and swelling essentially completely resolved; the corresponding GPPGA score was 4.



Figure 11 Clinical manifestations of the feet 24 hours after the second spesolimab administration; significant improvement was achieved, with pustules and swelling essentially completely resolved; the corresponding GPPGA score was 4.



Figure 12 Clinical manifestations of the trunk 24 hours after the second spesolimab administration; significant improvement was achieved, with pustules and swelling essentially completely resolved; the corresponding GPPGA score was 4.

reduced significantly. His GPPGA score was 4 points (Figures 10–12). However, it was observed that the erythema on his skin gradually became more apparent, and maintenance treatment was initiated with the IL-17 receptor inhibitor secukinumab. Although the patient did not undergo genetic testing, previous studies have shown that spesolimab is effective in treating GPP regardless of IL36RN mutation status.⁴

Discussion

Generalized pustular psoriasis (GPP) is a rare but severe inflammatory skin disease,⁵ and traditional drug treatment has poor clinical efficacy. Spesolimab is a selective and humanized antibody targeting IL-36R, and its application in GPP combined with PPP is rarely reported. Before the use of spesolimab, we screened the patient for hepatitis B, tuberculosis, and other conditions, and found no obvious abnormalities. After treatment, we achieved significant efficacy, and there were no side effects such as upper respiratory tract infection, urinary tract infection, or nausea, etc. Our study suggests that the presence of PPP in this case may have delayed the complete clearance of skin lesions by spesolimab compared to GPP alone. Our case had a limitation: we did not conduct genetic testing on the patient. Our report has shortcomings, as the follow-up time is short and insufficient to evaluate long-term efficacy and safety. A recent study has confirmed that subcutaneous administration of spesolimab (a loading dose of 600 milligrams followed by 300 milligrams every 4 weeks) can effectively prevent GPP attacks.⁶

Conclusion

Therefore, the IL-36 receptor antagonist spesolimab is a promising option for treating GPP combined with PPP. In future, larger sample sizes and clinical studies are required to provide more evidence.

Ethics Statement

Signed consent was obtained from the patient for the publication of case details and accompanying images. Institutional approval was not required to publish the case details.

Consent Statement

Written informed consent was provided by the patient for publication of images and information.

Disclosure

Hongyan Tan and Yu Zhang are co-first authors for this study. The authors declare that they have no conflicts of interest in this work.

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