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CASE REPORT

Vunakizumab and Acitretin for Elderly Refractory Generalized Pustular Psoriasis: A Case Report and Comprehensive Literature Review

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Abstract: Generalized pustular psoriasis (GPP) is a severe and potentially life-threatening form of psoriasis. Although spesolimab, an inhibitor of the interleukin (IL)-36 pathway, has been approved for the treatment of GPP, access to this agent remains limited. Vunakizumab, a humanized IgG1/κ monoclonal antibody that selectively neutralizes interleukin (IL)-17A inhibitors, is not yet approved for GPP. We herein report a 72-year-old male with a 40-year history of plaque psoriasis who developed GPP refractory to methotrexate combined with guselkumab and acitretin (20 mg/day). Following switching to vunakizumab (240 mg intravenously every 2 weeks) in combination with acitretin (40 mg/day), the patient achieved a GPPASI 75 response within 2 weeks and near-complete clearance (GPPASI ≈ 100) by week 12. Six induction doses of vunakizumab were administered, and acitretin was tapered to 20 mg/day for long-term maintenance. Throughout 36 weeks of follow-up, no disease relapse or drug-related adverse events were observed. This case, together with a review of the literature, provides support for IL-17A blockade combined with acitretin as a feasible and fast-acting regimen for refractory GPP in elderly patients.

Keywords: generalized pustular psoriasis, GPP, vunakizumab, acitretin, IL-17 inhibitors

Introduction

Generalized pustular psoriasis (GPP), also known as von Zumbusch psoriasis, is characterized by widespread pustules, systemic immune dysregulation and inflammation, and significant morbidity.[1,2] As a rare subtype of psoriasis (accounting for 0.6–2.4%), it is marked by a high relapse rate and notable ethnic and geographical differences.[3,4] A proportion of GPP cases harbors various genetic mutations, with IL36RN, CARD14, AP1S3, MPO, SERPINA3, BTN3A3, and MEFV identified as GPP-associated genes.[5] Beyond these genetic predispositions, immunological dysregulation plays a pivotal role. For example, non-drug-induced GPP is characterized by upregulated expression of T helper 17 (TH17) cell-related genes.[6]

Treatment options for GPP can be classified into conventional therapies and biologic agents. Systemic treatment, particularly in severe cases, commonly employs acitretin as first-line monotherapy. For severe GPP, systemic therapy commonly utilizes acitretin as first-line monotherapy, given its proven efficacy in controlling pustular eruptions and systemic inflammation.[7] Currently, interleukin-36 (IL-36) inhibitors (eg, spesolimab) are the only biologic agents approved globally for the management and prevention of GPP flares, offering targeted efficacy for acute exacerbations. Notably, Japan has approved a broad range of biological agents for the management of GPP, including interleukin-17 (IL-17) inhibitors (eg, secukinumab, brodalumab, ixekizumab, and bimekizumab),[8] which thus provides more therapeutic options for local clinicians and patients. Additionally, with the continuous advancement of biological agents, vunakizumab, a novel-generation anti-IL-17A agent, has demonstrated consistent efficacy and favorable safety profiles in the treatment of moderate-to-severe chronic plaque psoriasis across various regions of China,[9,10] which also serves as a potential key basis for its use in GPP treatment. However, high-quality evidence from

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randomized controlled trials (RCTs) to guide optimal treatment strategies remains scarce, particularly for refractory or complex cases. Thus, the management of GPP continues to pose a significant clinical challenge. In selected cases, combining biologic agents with a conventional systemic therapy (eg, acitretin) may represent a rational therapeutic strategy to enhance efficacy and reduce the risk of relapse.

In the present study, we report the successful resolution of GPP with the combination of vunakizumab and acitretin in an elderly male patient refractory to multiple conventional therapies. Additionally, we summarize the current literature to evaluate this combination strategy for the treatment of GPP in elderly patients.

Case Report

A 72-year-old male was admitted to the Department of Dermatology, our hospital, due to extensive pustular eruptions on an erythematous base that had persisted for six months. He had a 40-year history of plaque psoriasis, with no family history of psoriasis or other autoimmune diseases. Laboratory tests for systemic inflammation showed leukocytosis (5.38×10^9cells/L) with an elevated neutrophil percentage (NEUT%) of 76.20%, an accelerated erythrocyte sedimentation rate (ESR) of 55 mm/h, and an increased C-reactive protein (CRP) level of 30.39 mg/dL; these findings were accompanied by persistent fever (body temperature > 38 °C). The patient was diagnosed with GPP based on clinical manifestations and histopathological examination (Figure 1A and B).[11]

Initially, the patient received a combination therapy consisting of oral methotrexate (MTX) 10 mg/week, subcutaneous guselkumab 100 mg/month, and oral acitretin 20 mg/day. However, half a month after the second guselkumab infusion, he experienced a severe exacerbation of GPP. Dermatological examination revealed widespread pustular papules, plaques, and confluent erythema involving the trunk and upper limbs. These lesions were studded with numerous yellowish, sterile pustules; on the trunk, some pustules fused to form pustular lakes. Additionally, eroded areas were observed on the back due to pustule rupture (Figure 1C and D). The patient's generalized pustular psoriasis area and severity index (GPPASI) score was 39 (range: 0–72), generalized pustular psoriasis physician global assessment (GPPGA) score was 4 (indicating severe disease), and dermatology life quality index (DLQI) score was 23 (indicating an extremely large impact on quality of life).[12,13]

Considering the severe disease status and refractory nature of the condition, the treatment regimen was adjusted to combination therapy with vunakizumab (240 mg intravenously every two weeks) and oral acitretin (40 mg/day). Significant clinical improvement was observed immediately after the first vunakizumab infusion. By week 2 (Figure 1E and F), the patient achieved a GPPASI 75 response (ie, a 75% reduction in GPPASI score from baseline). Subsequently, after complete clearance of pustules, the dose of acitretin was reduced to 20 mg/day. By week 12 (Figure 1G and H), the patient nearly achieved a GPPASI 100 response (near-complete clearance of lesions). A total of six doses of vunakizumab were administered, and maintenance therapy with oral acitretin (20 mg/day) was continued until week 36. No disease relapse or treatment-related adverse events were reported. This case report was approved by the Ethics Committee of Guangzhou Dermatology Hospital, and written informed consent was obtained from the patient for publication, including the publication of images (gzsp202508).

Discussion

GPP is an inflammatory skin disease mainly involving keratinocyte, neutrophils, and monocytes. Its core pathological process is driven by the IL-36, IL-1, or TNF-α/IL-17A pathways which are characterized by periodic cutaneous neutrophil infiltration and pustule formation.[14] Notably, IL-17 and IL-36 cytokines can induce each other in GPP, triggering systemic dissemination of inflammatory mediators that may lead to multisystem damage or psychological disorders.[15–17] Acitretin, a first-line agent for psoriasis, has been shown to significantly attenuate inflammatory responses in both GPP and psoriasis vulgaris (PV) patients, particularly by reducing IL-17 levels.[18,19] In a psoriasis-like mouse model, acitretin markedly downregulated IL-17A-induced IL-36β and IL-36γ expression at both the gene and protein levels in keratinocyte.[20] Previous studies have supported robust, safe, and durable therapeutic responses to monotherapy with IL-17 inhibitors or acitretin in psoriasis.[9,10,21,22] Furthermore, a meta-analysis of GPP treatments confirmed that IL-36 and IL-17 inhibitors yielded higher responder rates compared to TNF-α and IL-23 inhibitors; IL-36 inhibitors achieved the highest response rates within 4 to 8 weeks, whereas IL-17, TNF-α, and IL-23 inhibitors showed progressively increasing response rates up to 12 weeks.[23]

To contextualize our treatment approach, we conducted a systematic search of three major medical databases (PubMed, Scopus, and Web of Science) using the following terms: TNF-α inhibitors (adalimumab, infliximab, etanercept,

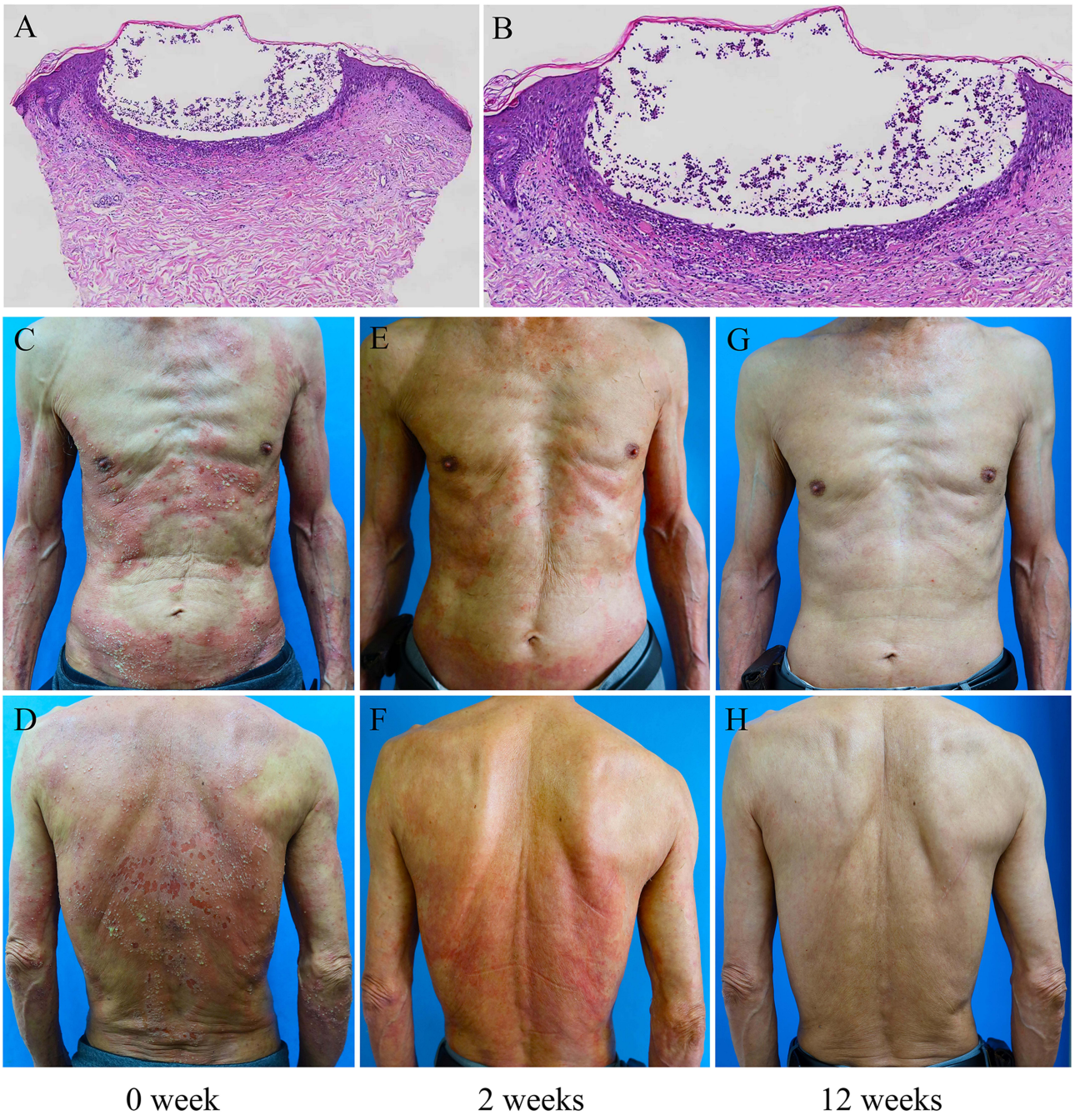

Figure 1 A biopsy of a pustular lesion revealed psoriasiform epidermal hyperplasia and intra-epidermal neutrophilic aggregates that formed pustules (H&E staining; (**A**) ×50; (**B**) ×100). A 72-year-old man presented with widespread erythematous plaques and coalescing pustules on the trunk, upper limbs, and back (**C** and **D**). Significant clinical improvement was observed at week 2 following the first vunakizumab infusion combined with Acitretin (**E** and **F**). Almost complete skin clearance was achieved at week 12 of treatment with vunakizumab combined with acitretin (**G** and **H**).

certolizumab pegol), IL-17 inhibitors (secukinumab, brodalumab, ixekizumab, bimekizumab, vunakizumab), IL-23 inhibitors (risankizumab, guselkumab), and "generalized pustular psoriasis". The search was limited to English-language studies and included records up to October 30, 2025. A total of 1706 published studies matching our predefined search strategy were identified. After removing duplicates and screening titles and abstracts, 97 potentially relevant full-text articles remained. These studies were subsequently assessed against the following inclusion criteria: (1) original research providing a detailed treatment course for patients diagnosed with GPP; (2) participants aged 65 years or older; and (3) concurrent administration of biologic therapy and oral acitretin. Ultimately, 5 eligible studies were selected for data extraction[24–28](Table 1). Most reported cases adopted an initial treatment strategy combining conventional agents

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Table 1 Summary of Our Case and Reported Cases of Elderly Patients (≥ 65 years Old) Whose Treatment of Biological Agents and Acitretin

Cases/ Reference	Age (Years) /Gender	Duration of Disease	Type of Psoriasis	Comorbidities	Previous Treatments/ Reason for Discontinuation	Current Treatment Combination	Outcome	Side Effects
1/Our case	74/Male	Six months	PsO, GPP	None	Acitretin combined with MTX and guselkumab/Loss of efficacy	Vunakizumab (240 mg every two weeks) combined with acitretin (40 mg/day, maintained with 20 mg/day)	Almost complete clearance at week 12, no disease relapse During the 36-week follow-up period	None
2/Ekinci et al[24]	76/Male	2 years	PsO, PP, GPP	DM, HT, AF, COPD, obesity, hepatic steatosis	Acitretin alone and combined with ustekinumab,/Side effects, inefficacy	Secukinumab combined with acitretin (25 mg/day)	Complete clearance at week 24, remained lesion-free at a-year visit	None
3/Routhouska et al[25]	72/ Female	10 years	GPP	NA	Etretinate, isotretinoin, dapsone, CsA, infliximab combined with MTX and acitretin/Insurance issues of infliximab	Etanercept (25 mg twice weekly) combined with acitretin (25 mg/day) and MTX.	Achieved sustained disease control; successfully tapered off MTX; relapse following acitretin discontinuation and resolution after reinitiation	NA
4/Tang et al[26]	72/Male	1 month	GPP	DM, HT, CRI, hyperlipidemia	NA/NA	Infliximab (5 mg/kg) combined with acitretin (35 mg/day, maintained with 10 mg/day)	Complete remission sustained for over 24 months	No worsening of CRI
5/Samotij et al[27]	72/ Female	NA	GPP evolution from ACH	ACH	Acitretin combined with hydrocortisone/Inefficacy	Infliximab (5 mg/kg) combined with acitretin (50 mg/day, maintained with 35 mg/day)	Complete clearance after first injection	NA
6/ Kołt-Kamińska et al[28]	73/ Female	Several months	GPP	NA	Acitretin, MTX, CsA, methylprednisolone/Side effects, loss of efficacy	Infliximab (5 mg/kg) combined with acitretin (50 mg/day, maintained with 20 mg/day)	Almost complete clearance after the third injection; but relapse following acitretin discontinuation and resolution after reinitiation	Herpes zoster at week 6

Abbreviations: PsO, plaque psoriasis; GPP, generalized pustular psoriasis; MTX, methotrexate; PP, pustular psoriasis; DM, diabetes mellitus; HT, hypertension; AF, atrial fibrillation; COPD, chronic obstructive pulmonary disease; NA, not available; CsA, cyclosporine A; CRI, chronic renal insufficiency; ACH, acrodermatitis continua of hallopeau.

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with biologics;[24,25,27,28] however, acitretin was often the preferred long-term maintenance therapy. Clinical improvement with acitretin monotherapy was gradual, typically requiring 3 to 6 months to reach peak efficacy.[29] Specifically, among these cases, one patient was switched to an IL-17 inhibitor due to inadequate response to an IL-23 inhibitor,[24] and another transitioned from biologics to conventional therapy (oral MTX) due to financial constraints.[25] Two additional patients experienced acitretin-related adverse events, leading to drug discontinuation and subsequent disease flare.[24,28] In one case, acitretin (50 mg daily) was added to a TNF-α inhibitor regimen.[27] Tang et al[26] reported a severe GPP case where complete lesion resolution was achieved with initial combination therapy of infliximab and acitretin.

Consistent with these findings, our elderly patient achieved favorable therapeutic outcomes with the combination of the IL-17A inhibitor vunakizumab and acitretin (40 mg/day). Although the current evidence base for GPP treatment is predominantly composed of case reports, it consistently demonstrates that this combination approach offers high efficacy and rapid clinical responses. However, several limitations of this study should be acknowledged. First, the absence of genetic testing limits our understanding of potential GPP-associated mutations. Second, the lack of long-term follow-up precludes assessment of the durability of treatment response and the potential for late-onset adverse effects. Most importantly, as a case report, this study is subject to the inherent limitations of anecdotal evidence, and its findings may not be generalizable to the broader GPP population.

Conclusion

Owing to impaired immune function and the presence of comorbidities, the management of GPP in elderly patients poses substantial challenges. Findings from this review indicate that acitretin is an effective and safe component of combination therapy, particularly when combined with IL-17 inhibitors. This study highlights the potential of acitretin-biologic combination therapy as an alternative strategy for GPP management. Further exploration of such combination regimens in RCTs is warranted. Ultimately, the overarching goal is to ensure that all GPP patients—regardless of age, geographical location, or comorbidities—have access to rapidly acting, safe, and durable therapeutic options.

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Disclosure

All authors declare no competing interests in this work.

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