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Generalized Pustular Psoriasis Including Nail Psoriasis Successfully Treated with Gulsekumab: Case Report

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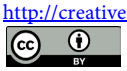


Abstract

We present a rare and potential life-threathning case of a 58-year-old man who came in with pruritic skin lesions that were intensively painful, small erythematous pustules that were sterile and scaly, located on both upper and lower extremities and lower back that gradually increased and spread to the limbs, trunk, face and scalp, alongside he was with nail thickening, yellow and white nail discoloration and onycholysis. These symptoms had persisted for over 20 years with multiple recurrences at different times. Despite past treatments with conventional treatments, the patient's symptoms worsened over time in several episodes. Initial lab results and clinical presentations were consistent with generalized pustular psoriasis (GPP) with nail psoriasis. The patient was initiated on Guselkumab (Tremfya), a subcutaneous IL-23 monoclonal antibody inhibitor, along with other medications for symptomatic relief. During a total of 10 visits within 18 months, the patient's symptoms dramatically improved, with the nail psoriasis largely resolved with no rebound of symptoms, and the therapy was effectively tolerated with no negative side effects reported. This rare case demonstrates the efficacy of Guselkumab subcutaneous injection in the treatment of GPP and nail psoriasis, indicating that it could be an effective therapeutic choice in other cases like this.

Subject Areas

Dermatology

Keywords

Guselkumab, Generalized Pustular Psoriasis, Nail Psoriasis, Interleukin-23, Recurrent Pustule

1. Introduction

The Generalized Pustular Psoriasis (GPP) we present in this case is a rare sub type of psoriasis, world widely GPP occurs with a prevalence ranging from 1 to 10 per million persons and is considerably greater in females and people with Asians ancestry [1] [2], In clinic the patients present with sterile macroscopically apparent pustular eruption mostly on non acral skin, which can be recurrent or chronic, with disfiguring fatal acute flare episodes. It can occur with or without psoriasis vulgaris, systemic inflammations including fevers, hepatic, gastrointestinal, musculoskeletal, renal, or pulmonary involvement. The GPP Flares can arise without a clear reason or be triggered by specific triggers or precipitating factors such as abrupt cessation of systemic corticosteroids, infections, pregnancy, menstruation, or stress. Hypocalcemia and immunization are two other presumed triggers that have been reported to be the cause of this condition, primarily through a small case series. Some medications have also been described as a precipitating factor, like dopamine, anti-seizures, anticholinergics, and some antibiotics [3]. The IL-1/IL-36 inflammatory pathway is an important aspect of GPP pathophysiology.

The Challenges and Innovations in the Treatment of Generalized Pustular Psoriasis (GPP)

GPP poses multiple treatment challenges due to its complex and heterogeneous nature as a rare, chronic, systemic neutrophilic inflammatory illness characterized by unpredictable flares and ongoing symptoms between episodes, complicating both diagnosis and management. In addition to its life-threatening complications, GPP can result in severe systemic inflammation, multisystem organ failure, and sepsis, exhibiting mortality rates ranging from 2% - 16%, necessitating prompt and effective treatment to avert fatal consequences, along with the absence of specific, actionable treatment objectives [4]. In the past, treatment objectives were unclear; current agreement underscores the importance of measurable results like pustule resolution in 7 days and decreased symptoms, stressing the necessity for swift, quantifiable reactions. The persistent nature of this disease weighs heavily on patients, as they endure persistent symptoms, fatigue, and a decline in quality of life (QoL) even in periods without flare-ups, requiring ongoing management approaches beyond just acute flare treatment. In approximately fifty percent of GPP patients, comorbid psoriatic diseases also include plaque psoriasis, necessitating the prioritization of GPP treatment to prevent complications, thereby complicating therapeutic decision-making. Approved therapies for GPP flares or maintenance are limited, resulting in off-label use of systemic immunosuppressants with inconsistent efficacy and safety issues.

Despite various challenges in managing GPP, numerous innovations in its treatment have surfaced: IL-36 Receptor Blockade (e.g., Spesolimab) was the first and only FDA-approved therapy specifically for GPP flares, with intravenous Spesolimab being an anti-IL-36 receptor monoclonal antibody. Subcutaneous Spesolimab is approved for ongoing management to avert flares and regulate disease

activity during intervals [5]. Additionally, the Delphi Consensus on Treatment Goals, a worldwide panel of patients and dermatologists, outlined specific short-term objectives (e.g., pustule resolution within 7 days, fever alleviation within 3 days) and long-term aims (flare prevention, enduring disease control, QoL enhancement), encouraging tailored, multidisciplinary care.

Another recommended method is a Multidisciplinary and Patient-Centered Approach that focuses on collaboratively creating customized treatment plans with patients, including ongoing evaluations and adjustments, while considering both physical and psychosocial components of GPP.

New international guidelines and clinical trials, including EFFISAYIL®, are integrating patient perspectives and showing the effectiveness of Spesolimab for managing chronic diseases, leading to standardized care. Innovations aimed at Long-Term Disease Control now focus on not just suppressing acute flares but also preventing recurrences and managing comorbidities, with the goal of lowering morbidity and enhancing functional status and quality of life [6] [7].

In addition, nail psoriasis is notably important in cases of generalized pustular psoriasis (GPP) since it commonly appears and greatly affects patients' quality of life (QoL). Approximately 80% of individuals with psoriasis experience issues with their nails, causing both physical and emotional distress, leading to greater disease severity and reduced quality of life scores compared to those without nail complications. In generalized pustular psoriasis, quality of life is significantly compromised both generally and in dermatological terms, with patients indicating poorer quality of life than those who only have plaque psoriasis. Nail psoriasis in GPP increases this burden by leading to pain, aesthetic issues, and functional restrictions, which amplify the physical discomfort and psychological distress faced by patients; therefore, treating nail psoriasis can enhance QoL, emphasizing the necessity of addressing nail issues swiftly in GPP management to alleviate physical symptoms and enhance emotional health. In summary, nail psoriasis in GPP cases significantly impacts QoL, highlighting the necessity for thorough care approaches that address both skin and nail symptoms [8] [9].

The treatment guidelines for GPP are not well established. Currently, only one biological GPP-specific therapy, the interleukin-36 receptor antagonist (IL-36Ra) Spesolimab, that is administered via intravenous infusion, has been approved only in the United States. Additional therapies include biologics like anti-IL-36, IL-17, IL-23, and TNF-α inhibitors, non-biological treatments like retinoids, cyclosporine, and methotrexate [10] [11]. Treatment options vary around the world, with most countries using retinoids, cyclosporine, and methotrexate as first-line non-biological treatments.

However, no GPP-specific biological treatments have been approved for use in China or the United Kingdom [12] [13], although Japan has approved many. In this present case, the patient had clinical remission with subcutaneous Guselkumab treatment, a fully human monoclonal interleukin-23p19-subunit inhibitor that is usually used for the treatment of plaque psoriasis, psoriatic arthritis, pus-

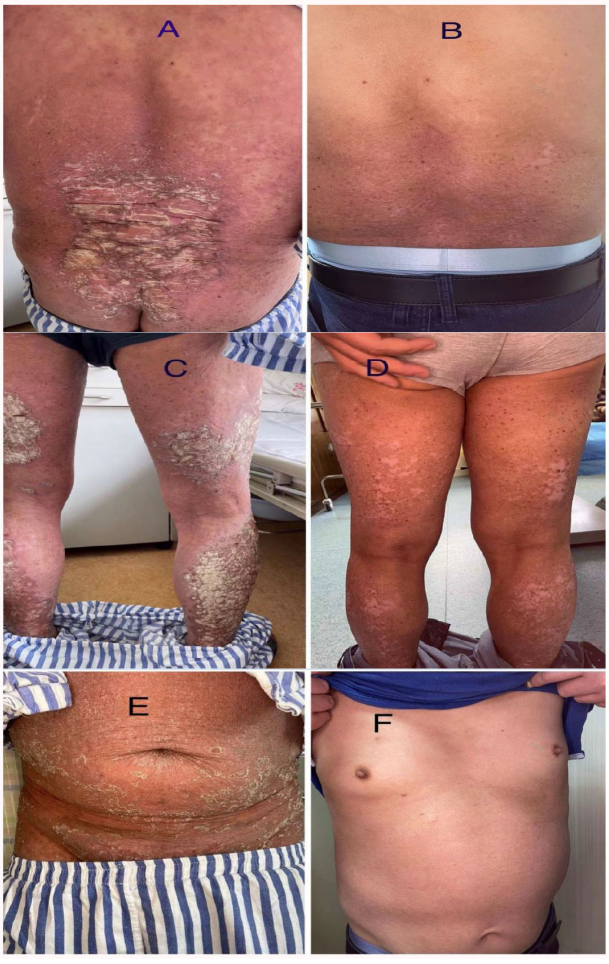
tulosis palmaris et plantaris (PPP), and ulcerative colitis [14]. Guselkumab, subcutaneously administered, has been proven to alleviate the signs and symptoms of GPP and nail psoriasis significantly from 4 weeks of initiation of the treatment, which further increased gradually throughout these 18 months of follow-up with no rebound of symptoms, and the therapy was effectively tolerated with no negative side effects.

2. Case Presentation

A 58-year-old man presented with painful and intensely pruritic skin lesions that were covered in erythematous pustules with scales on his extremities and lower back. These symptoms had persisted for over 20 years and had recurred multiple times. Although the patient had previously sought medical help and was hospitalized several times, he had been diagnosed with "psoriasis vulgaris." Despite treatment with conventional therapy for GPP, the patient continued to experience short-lived relief, with symptoms worsening upon recurrence. In our clinic physical exam, the patient was found to have a fever of 38.4˚C, thinning nail cuticles with local blood capillary telangectasia while nail bed was pitting thickening with subugual hyperkeratosis, yellow and white opaque nail discoloration and leukolysis with salmon patch, longitudinal ridges and subungual splinter hemorrhages (**Figure 1(G)**, **Figure 1(H)**, **Figure 1(I)**, **Figure 1(J)**). The small visible pustules were with sterile exudates, scaly on an erythematous background, scattered throughout his trunk, limbs, and lower back. The patient's skin lesions were small, greasy, yellow, and lacked punctate hemorrhage. Additionally, his hair appeared sparse and thin, and was not bundled as seen in images (**Figure 1(A)**, **Figure 1(C)**, **Figure 1(E)**, **Figure 1(K)**, **Figure 1(M)**, **Figure 1(O)**). The patient in our case had Generalized Pustular Psoriasis Physician Global Assessment (GPPGA) that was 3.5, Generalized Pustular Psoriasis Area and Severity Index (GPPASI) was 32.6, and Dermatology Life and Quality Index (DLQI) was 30.0 (**Figure 1(A)**, **Figure 1(C)**, **Figure 1(E)**, **Figure 1(K)**, **Figure 1(M)**, **Figure 1(O)**), **Table 1**. From the reported severe skin pain, with a Numerical Rating Scale for Pain (pain NRS) of 9/10 and a typical psoriasis area surface index (PASI) was estimated to be 50.

Initial laboratory findings showed leukocytosis of 14.6×10^9/L with 81.0% neutrophil predominance, elevated C-reactive protein (57.8 mg/L), and increased erythrocyte sedimentation rate (33 mm/h), elevated creatinine (135 μmol/L), and uric acid 717 μmol/ L, confirming the diagnosis of GPP based on history and clinical findings. The patient was initiated on subcutaneous injection of Guselkumab at a dosage of 100 mg one shot at week 0. After six days of initiation of Guselkumab treatment he patient the patient's systemic desquamation increased on most of the skin areas, skin flushing improved, he had visible normal new skin arising, a normal body temperature and improved lab results with: white blood cell 9.8, neutrophil% 62.2%, lymphocyte% 18.0%, hemoglobin 117 g/L, red blood cell 3.60×10^{12}/L, platelets 595×10^9/L, C-reactive protein27.3 mg/L. Other biochemical tests: Albumin: 33.6 g/L, creatinine 129 μmol/L, uric acid 646 μmol/L, LDH 356

U/L; he was discharged from the hospital on supportive symptomatic treatment and a monthly follow-up. During the initial follow-up appointment four weeks after the initial dose, the patient reported noticeable improvements in symptoms, with a reduced pruritus and a significant decrease in skin lesions. The blood standard coagulation test, liver, and kidney function tests were within normal range. The patient continued with a one-month follow-up. Four weeks after the initial dose (**Figure 1(D)**, **Figure 1(F)**, **Figure 1(I)**). The symptoms continued to improve gradually, the blood test results remained within normal ranges for the other follow-up visits, At six months visit (24 weeks after the first dose), the lesions were almost invisible and nail psoriasis had improved significantly (**Figure 1(H)**, **Figure 1(J)**, **Figure 1(L)**) with no recurrence of symptoms. Later on, monthly follow-up was changed to a 3-month follow-up that went on until 18 months (72 weeks after the initial dose). (GPPGA = 0.5; GPPASI = 2.3, with pustulation sub-score = 0; DLQI = 1; pain NRS = 0/10 (**Figure 1(B)**, **Figure 1(D)**, **Figure 1(F)**, **Figure 1(L)**, **Figure 1(N)**, **Figure 1(P)**), nail psoriasis Severity Index (NAPSI) (24) (**Figure 1(H)** and **Figure 1(J)** which took a little longer course that the other parts of the body. Later on monthly follow-up was changed to a 3-month follow-up that went on until 18 months (72 weeks after the initial dose), as seen in **Table 1**.



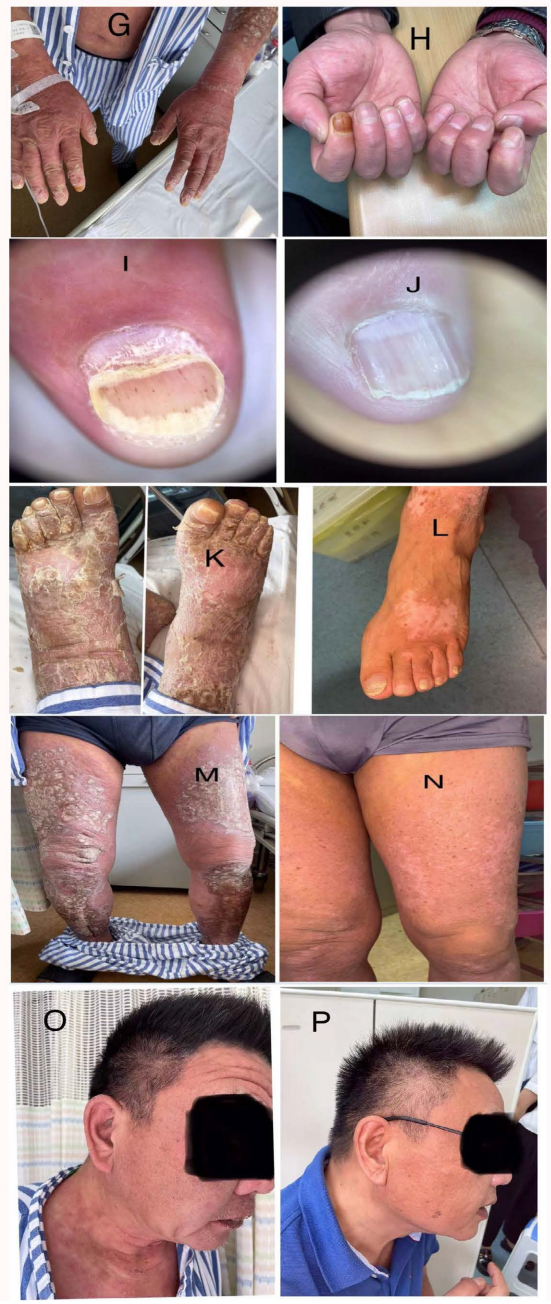


Figure 1. Patient with GPP (A) at initiation of Guselkumab week 0. The same Patient with GPP at week 4 (B) of Guselkumab treatment; patient with GPP (C) at initiation of Guselkumab week 0. The same Patient with GPP at week 4 (D) of Guselkumab treatment; patient with GPP (E) at initiation of Guselkumab week 0. The same Patient with GPP at week 4 (F) of Guselkumab treatment; patient with GPP, including nail psoriasis (G) at initiation of Guselkumab week 0. Then at the third review (week 28 after Guselkumab treatment initiation) with almost resolved nail psoriasis (H); patient with GPP including nail psoriasis at initiation of Guselkumab treatment week 0 (I). Then at the third review week 28 after Guselkumab treatment initiation) with almost resolved nail psoriasis (J) (I and J Images taken with Dermlite DL5 dermoscopy); patient with GPP (K) at initiation of Guselkumab week 0. The same Patient with GPP at week 4 (L) of Guselkumab treatment; patient with GPP (E) at initiation of Guselkumab week 0. The same Patient with GPP at week 4 (F) of Guselkumab treatment; patient with GPP (O) at initiation of Guselkumab week 0. The same Patient with GPP at week 4 (P) of Guselkumab treatment.

Table 1. Comparative table throughout the visits.

	NAPSI	GPPASI	DLQI	GPPGA
WEEK 0	120	32.6	30.0	3.5
WEEK 4	120	30.0	28.0	3.0
WEEK 8	100	28.0	25.0	3.0
WEEK 12	96	23.5	20.0	2.5
WEEK 16	88	20.0	15.0	2.0
WEEK 20	80	17.5	10.0	2.0
WEEK 24	72	14.0	5.0	1.5
WEEK 36	56	8.0	5.0	1.5
WEEK 42	40	5.7	3.0	1
WEEK 60	32	2.3	3.0	1
WEEK 72	24	2.3	1.0	1

NAPSI: Nail Psoriasis Severity Index; GPPASI: Generalized Pustular Psoriasis Area and Severity Index; DLQI: Dermatology Life and Quality Index; GPPGA: Generalized Pustular Psoriasis Physician Global Assessment.

3. Discussion

Generalized pustular psoriasis (GPP), a rare form of psoriasis, is a severe immune-mediated inflammatory skin condition that often leads to systemic symptoms and extracutaneous manifestations, with an incidence of 1 to 10 cases per million individuals. These flares may occur spontaneously or due to infection, pregnancy, discontinuing systemic corticosteroids, and also stress, and hypoparathyroidism, which leads to hypocalcemia.

3.1. The Diagnosis Criteria

The criteria for diagnosing GPP differ globally, with each country having its own set of diagnostic guidelines. In some instances, the diagnosis can be made solely based on the examination of clinical symptoms, eliminating the need for skin biopsy. This is because the histological characteristics of GPP can be nonspecific, potentially delaying treatment of life-threatening conditions. The latest diagnostic standards for GPP in various regions where the condition is more common, the European Rare and Severe Psoriasis Expert Network (ERASPEN) defines GPP as a primary, sterile, and macroscopically visible type of epidermal pustule on the skin that is not located on the palms or soles. According to their guidelines, GPP can present with or without systemic inflammation, with or without the presence of plaque psoriasis, and can either recur more than once or persist for more than three months.

The China Psoriasis Guideline for 2023 categorizes GPP based on four key factors: 1) systemic symptoms, such as fever or fatigue; 2) systemic or widespread flushing accompanied by the appearance of multiple sterile pustules; 3) the pres-

ence of neutrophilic subcorneal pustules, which are characterized by Kogoj spongiform pustules under a microscope; and 4) the recurrence of these clinical and histological features. While in Japan, a definitive diagnosis of GPP is made when all four criteria are met, and the condition is suspected in those who meet criteria 2 and 3. Besides the previous criteria, laboratory results and other clinical observations that suggest a GPP flare include elevated levels of C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), hypocalcemia, hypoalbuminemia, neutrophilia, and abnormal liver function tests. During a GPP flare, high fever has been reported in approximately 24% - 96% of patients with neutrophilia-dominated leukocytosis, with a range of 30% - 70% of patients experiencing this condition. Iron deficiency anemia is also common. The range and severity of both skin and systemic symptoms can vary greatly between and within individuals, making GPP difficult to predict.

Additional clinical signs of illness may also manifest as discomfort, fever, irritation, general feeling of sickness, flaking, tiredness, inflammation, a sensation of heat, edema, aching in joints, dryness, uveitis, and development of pus-filled blisters on an erythematous background, among other symptoms.

3.2. Pathogenesis

Multiple studies have emphasized the vital importance of the interleukin-36 (IL-36) pathway in the pathology of GPP. The development of the condition is primarily driven by abnormal activation of the interleukin (IL)-36 pathway in the innate immune system, along with further involvement from the adaptive immune system. A significant number of patients possess null mutations in the gene encoding the IL-36 receptor antagonist.

The IL-36 Cytokine Axis involves the overproduction and modified processing of IL-36 cytokines (IL-36α, IL-36β, IL-36γ) along with their receptor, resulting in a positive feedback mechanism that causes heightened inflammatory signaling in keratinocytes. Neutrophil proteases enhance IL-36 cytokines by as much as 500-fold, increasing inflammation. Additionally, Neutrophil Dominance represents another pathophysiological aspect in GPP, marked by significant neutrophil infiltration into the epidermis, fueled by chemokines triggered by IL-36 signaling. Neutrophils secrete enzymes that further stimulate IL-36 cytokines, perpetuating the inflammatory cycle.

The pathogenesis in GPP and psoriasis models shows evidence of a reciprocal relationship between the IL-23/Th17 axis and IL-36 activation. IL-36 acts upstream to produce IL-23, while IL-23/Th17 cytokines promote IL-36 production, creating a harmful inflammatory loop. According to research conducted in mouse models, IL-36R signaling stimulates the production of IL-23, IL-17, and IL-22 at the earliest stages of psoriasis-like inflammation. Initially, keratinocytes' IL-36 signaling is essential for the early production of IL-23. The inflammatory cycle is reinforced when IL-23/Th17 cytokines (IL-17, IL-22) cause keratinocytes to produce IL-36, while IL-36 causes macrophages to secrete IL-23, particularly when

primed with IFNγ, increasing inflammation. In IL-23-induced psoriasis mice, blocking IL-36 reduces disease severity, underscoring the interconnectedness of these pathways. By breaking this loop, therapeutic inhibition of IL-23, which targets the Th17 pathway, indirectly decreases inflammation produced by IL-36. Inhibition of IL-23 dampens the pathogenic effects of IL-36 by lowering downstream Th17 cytokines that stimulate IL-36 production.

Consequently, in GPP, uncontrolled IL-36R activation results in the synthesis of IL-23 and Th17 cytokines, which promote inflammation and neutrophil recruitment. Clinically effective IL-36 pathway inhibitors, such as Spesolimab, highlight the critical function of IL-36 and its relationship to the IL-23/Th17 axis. Thus, by interfering with the IL-36/IL-23/Th17 inflammatory feedback loop that propels GPP and psoriasis development, IL-23 blockage indirectly reduces IL-36 [15].

Mutations in genes associated with the IL-36 receptor antagonist (IL36RN) and additional regulators of NF-κB signaling (such as CARD14) contribute to the risk of disease by disrupting the regulation of IL-36-driven inflammation. In contrast to plaque psoriasis, GPP features a primary autoinflammatory response led by IL-36, rather than adaptive immune responses. As a result, skin inflammation will produce systemic symptoms owing to cytokine spillover. This insight has resulted in targeted treatments like Spesolimab, an IL-36 receptor blocker, which has been approved in certain countries for managing GPP flares.

Conversely, IL-23 is crucial in the development of generalized pustular psoriasis (GPP) by engaging with both innate and adaptive immune mechanisms. Here's an in-depth analysis of its participation: initially, IL-23 and Th17/IL-17 Pathway: IL-23 promotes the activation and sustainment of Th17 cells, which generate pro-inflammatory cytokines such as IL-17, IL-21, and IL-22. Then IL-17 attracts and stimulates neutrophils, a characteristic of pustular lesions in GPP. This pathway coincides with mechanisms seen in plaque psoriasis, though it plays a lesser role in GPP when compared to the IL-36-driven innate immune response.

Engagement with the IL-36 Pathway: IL-23/IL-17 signaling enhances the IL-36 pathway, which plays a key role in the autoinflammation of GPP. IL-17 stimulates keratinocytes to generate IL-36 cytokines (such as IL-36α, IL-36γ), forming a feedback loop that worsens neutrophil infiltration and systemic inflammation. Genetic mutations (e.g., IL36RN, CARD14) have been shown to interfere with IL-36 regulation, further enhancing the inflammation mediated by IL-23/IL-17 [16] [17].

Thus, a new treatment has recently emerged, featuring IL-12/IL-23 inhibitors: Ustekinumab (anti-IL-12/IL-23 p40) has demonstrated effectiveness in GPP by diminishing IL-23-mediated inflammation [17]. IL-23-specific inhibitors: Guselkumab and Risankizumab (anti-IL-23 p19) are authorized in Japan for GPP, with clinical studies showing symptom improvement in approximately 78% of patients [18] [19].

Guselkumab, with brand name Tremfya used in our case report, is a human

monoclonal antibody that specifically targets interleukin-23 (IL-23), a cytokine that plays a role in inflammatory processes. It functions by antagonising the IL-23 pathway, leading to decreased inflammation and lower production of other inflammatory cytokines such as IL-17A, IL-17F, and IL-22, which are crucial in conditions like moderate to severe plaque psoriasis in adults, particularly when other systemic treatments are ineffective or not contraindicated.

Management of active psoriatic arthritis, whether alone or combined with methotrexate, in adults who have had an inadequate response or adverse reactions to prior disease-modifying antirheumatic drugs (DMARDs). Management of moderately to severely active ulcerative colitis in adults that was approved by FDA in 2024 [19].

Guselkumab is administered via subcutaneous injection, usually starting with an induction phase, followed by maintenance doses every 4 to 8 weeks based on the indication. Clinical trials demonstrated greater efficacy compared to placebo and other therapies such as adalimumab, with a high percentage of patients attaining marked skin clearance (PASI 90) and improvement in lesions in plaque psoriasis. Some reported negative effects include upper respiratory infections, headaches, reactions at the injection site, joint discomfort, diarrhea, fungal infections, and herpes simplex infections as a result of its immune modulation.

During clinical presentation, Flare is a distinctive clinical hallmark of GPP and is characterized by the sudden emergence of large, painful erythematous plaques covered by primary, sterile, macroscopically visible pustules, usually but not limited to non-acral cutaneous pustules that may appear with or without systemic inflammation. With or without systemic inflammation, either relapsing (>1 episode) or persistent for >3 months (but can also be a shorter period), with or without abnormal laboratory tests, such as elevated white blood cell count, increased erythrocyte sedimentation rate, and additional histopathological diagnosis, which is required only when the case is atypical and cannot be clinically diagnosed, which will appear with Kogoj spongy edema pustule and Munro micro abscess.

GPP manifests as recurring episodes of dispersed, sterile, monomorphic pustules against the backdrop of extensive erythema. Many patients are severely ill, with high temperatures, discomfort, and arthralgia. Laboratory tests frequently demonstrate leukocytosis, high C-reactive protein levels, hypoalbuminemia, and microcytic anemia.

Skin biopsy is not necessary for the diagnosis of GPP because histological findings may be nonspecific, thus delaying the treatment of this life-threatening illness.

Histology of GPP reveals subcorneal and intraepidermal pustules, but often does not provide any information beyond what is clinically visible.

Histology is frequently identical to clinical differential diagnosis, including acute generalized exanthematous pustulosis (AGEP) [19].

3.3. Efficacy and Safety Assessment for Choosing Guselkumab over Spesolimab

Spesolimab, a monoclonal antibody against the IL-36 receptor, was recently ap-

proved only in the USA for the treatment of GPP flares by the Food and Drug Administration and European Medicines Agency the fact which may make it not easily accessible in other parts of the world. The mortality rate during a GPP flare ranges from 2% to 16%, and treatment with available drugs is unsatisfactory and/or frequently recurrent.

Spesolimab (an IL-36 inhibitor) acts on the IL-36 receptor, directly obstructing a crucial pathway that drives GPP flare-ups. Clinical studies demonstrate quick and efficient removal of pustules, with 54% of patients clearing pustulation by week 1 and maintaining remission for up to 48 weeks. It is explicitly authorized for acute GPP flare-ups and the prevention of flares, featuring a favorable safety profile but with some risks of infections and infusion reactions [19] [20]. Guselkumab (IL-23 inhibitor) influences upstream inflammatory pathways related to psoriasis, including GPP, demonstrating effectiveness in alleviating skin symptoms and systemic inflammation. It is typically well accepted but might have a delayed onset relative to Spesolimab and lacks specific approval for acute GPP flare-ups.

The rationale for Not Testing Spesolimab: Treatment environment: Spesolimab is mainly used for quick management of acute GPP flare-ups, whereas Guselkumab might be better suited for ongoing disease management or for patients not experiencing active flare-ups. Factors specific to the patient, such as mutations in the IL-36 pathway (e.g., IL36RN), indicate a better response to Spesolimab; if these mutations are absent, inhibition of IL-23 may be preferred. Administration and logistic also play a part since Spesolimab is administered via intravenous infusion, potentially restricting its use relative to subcutaneous Guselkumab.

Safety aspects since Spesolimab demonstrates a favorable safety profile, certain patients might have contraindications or opt for treatments with alternative safety profiles, making Gulsekumab a potential choice [21].

3.4. The Increased Skin Desquamation around Day Six of Initiation, Elevated Creatinine and Uric Acid

Paradoxical flares, like early worsening with increased desquamation around 6 days after treatment, are known occurrences with certain biologics, yet they are not well documented specifically for Guselkumab in GPP. The majority of noted paradoxical reactions are associated with IL-17A inhibitors (such as secukinumab and ixekizumab), which may lead to the induction or exacerbation of pustular psoriasis, occasionally occurring weeks to months after the initiation of treatment. Conversely, Guselkumab, an IL-23 inhibitor, is typically linked to a reduced likelihood of paradoxical skin reactions when compared to IL-17 or TNF inhibitors [22]. Although paradoxical pustular flares have been observed with other biologics, such as ustekinumab and TNF inhibitors, there is scant evidence of such early paradoxical exacerbation specifically associated with Guselkumab in GPP. Consequently, although paradoxical flares are a recognized class effect for certain biologics, the early flare accompanied by heightened desquamation at 6 days after Guselkumab is not a well-known or frequently documented occurrence in GPP

therapy. Careful observation is recommended, yet this might indicate a rare or unique reaction instead of a standard paradoxical flare linked to Guselkumab [23].

Moreover, increased creatinine and uric acid levels in GPP patients treated with Guselkumab may indicate existing kidney issues, a known comorbidity in psoriasis and GPP stemming from systemic inflammation and potential kidney conditions like IgA nephropathy. Guselkumab is effective in managing skin symptoms, but it may not improve kidney function, with reports indicating instances of worsening kidney function during treatment. Renal impairment might influence the metabolism and clearance of the drug, yet no specific studies have thoroughly outlined Guselkumab pharmacokinetics concerning renal impairment. Close observation is recommended as declining kidney function may affect prognosis and complicate treatment. Additionally, kidney impairment is linked to poorer overall outcomes in patients with psoriasis, highlighting the need for comprehensive care kidney along with dermatoses management [24] [25].

4. Limitations

Effective long-term treatments for GPP are lacking, and the disease course tends to be recurrent and life-threatening. Limited studies exist regarding the use of Gulsekumab for the treatment of GPP as well as nail psoriasis. Further studies and broader trials are needed to assess the long-term efficacy and safety of Gulsekumab in patients with GPP and nail psoriasis.

Declaration of Patient Consent

The authors affirm that they have secured all necessary patient consent forms. In these forms, the patient(s) have granted permission for their images and other clinical data to be published in the journal. The patients are aware that their names and initials will remain confidential, and reasonable measures will be taken to protect their identities.

Conflicts of Interest

The authors declare no conflicts of interest.

References

[1] Armstrong, A.W., Elston, C.A., Elewski, B.E., Ferris, L.K., Gottlieb, A.B., Lebwohl, M.G., *et al.* (2024) Generalized Pustular Psoriasis: A Consensus Statement from the National Psoriasis Foundation. *Journal of the American Academy of Dermatology*, **90**, 727-730. https://doi.org/10.1016/j.jaad.2023.09.080

[2] Burden, A.D., Choon, S.E., Gottlieb, A.B., Navarini, A.A. and Warren, R.B. (2022) Clinical Disease Measures in Generalized Pustular Psoriasis. *American Journal of Clinical Dermatology*, **23**, 39-50. https://doi.org/10.1007/s40257-021-00653-0

[3] Rivera-Díaz, R., Daudén, E., Carrascosa, J.M., Cueva, P.D.L. and Puig, L. (2023) Generalized Pustular Psoriasis: A Review on Clinical Characteristics, Diagnosis, and Treatment. *Dermatology and Therapy*, **13**, 673-688. https://doi.org/10.1007/s13555-022-00881-0

[4] Yiu, Z.Z.N., Becher, G., Kirby, B., Laws, P., Reynolds, N.J., Smith, C.H., *et al.* (2022) Drug Survival Associated with Effectiveness and Safety of Treatment with Guselkumab, Ixekizumab, Secukinumab, Ustekinumab, and Adalimumab in Patients with Psoriasis. *JAMA Dermatology*, **158**, 1131-1141. https://doi.org/10.1001/jamadermatol.2022.2909

[5] Antony, A.S., Allard, A., Rambojun, A., Lovell, C.R., Shaddick, G., Robinson, G., *et al.* (2019) Psoriatic Nail Dystrophy Is Associated with Erosive Disease in the Distal Interphalangeal Joints in Psoriatic Arthritis: A Retrospective Cohort Study. *The Journal of Rheumatology*, **46**, 1097-1102. https://doi.org/10.3899/jrheum.180796

[6] Committee on Psoriasis and Chinese Society of Dermatology (2023) Guideline for the Diagnosis and Treatment of Psoriasis in China (2023 Edition). *Chinese Journal of Dermatology*, **56**, 573-625.

[7] Part, M. (2024) Successful Treatment of Generalized Pustular Psoriasis with Guselkumab. *Journal of Dermatological Treatment*, **35**, Article 2331807.

[8] Brembilla, N.C. and Boehncke, W. (2023) Revisiting the Interleukin 17 Family of Cytokines in Psoriasis: Pathogenesis and Potential Targets for Innovative Therapies. *Frontiers in Immunology*, **14**, Article 1186455. https://doi.org/10.3389/fimmu.2023.1186455

[9] Sano, S., Kubo, H., Morishima, H., Goto, R., Zheng, R. and Nakagawa, H. (2018) Guselkumab, a Human Interleukin-23 Monoclonal Antibody in Japanese Patients with Generalized Pustular Psoriasis and Erythrodermic Psoriasis: Efficacy and Safety Analyses of a 52-Week, Phase 3, Multicenter, Open-Label Study. *The Journal of Dermatology*, **45**, 529-539. https://doi.org/10.1111/1346-8138.14294

[10] Tillett, W., Egeberg, A., Sonkoly, E., Gorecki, P., Tjärnlund, A., Buyze, J., *et al.* (2023) Nail Psoriasis Dynamics during Biologic Treatment and Withdrawal in Patients with Psoriasis Who May Be at High Risk of Developing Psoriatic Arthritis: A Post Hoc Analysis of the VOYAGE 2 Randomized Trial. *Arthritis Research & Therapy*, **25**, Article No. 169. https://doi.org/10.1186/s13075-023-03138-z

[11] Peyrin-Biroulet, L., Allegretti, J.R., Rubin, D.T., Bressler, B., Germinaro, M., Huang, K.G., *et al.* (2023) Guselkumab in Patients with Moderately to Severely Active Ulcerative Colitis: QUASAR Phase 2b Induction Study. *Gastroenterology*, **165**, 1443-1457. https://doi.org/10.1053/j.gastro.2023.08.038

[12] Dai, C. and Huang, Y.H. (2024) Infliximab-Induced Psoriasis in an Ulcerative Colitis patient Successfully Treated with Guselkumab. *Revista espanola de enfermedades digestivas*, **116**, 176-177.

[13] Campa, M., Mansouri, B., Warren, R. and Menter, A. (2016) A Review of Biologic Therapies Targeting IL-23 and IL-17 for Use in Moderate-to-Severe Plaque Psoriasis. *Dermatology and Therapy*, **6**, 1-12. https://doi.org/10.1007/s13555-015-0092-3

[14] Germán, B., Wei, R.C., Hener, P., *et al.* (2019) Disrupting the IL-36 and IL-23/IL-17 Loop Underlies the Efficacy of Calcipotriol and Corticosteroid Therapy for Psoriasis. https://pmc.ncbi.nlm.nih.gov/articles/PMC6413797/

[15] Goldstein, J.D., Bassoy, E.Y., Caruso, A., *et al.* (2020) IL-36 Signaling in Keratinocytes Controls Early IL-23 Production in Psoriasis-Like Dermatitis. https://pmc.ncbi.nlm.nih.gov/articles/PMC7190273/

[16] Parigi, T.L., Iacucci, M. and Ghosh, S. (2022) Blockade of IL-23: What is in the Pipeline? *Journal of Crohn's and Colitis*, **16**, ii64-ii72. https://academic.oup.com/ecco-jcc/article/16/Supplement_2/ii64/6584458

[17] Ahmad, F., Alam, M.A., Ansari, A.W., *et al.* (2024) Emerging Role of the IL-36/IL-36R Axis in Multiple Inflammatory Skin Diseases. *Journal of Investigative Dermatol-*

ogy, **144**, 206-224.
https://www.sciencedirect.com/science/article/pii/S0022202X23031147

[18] Krueger, J.G., Eyerich, K., Kuchroo, V.K., *et al.* (2024) IL-23 Past, Present, and Future: A Roadmap to Advancing IL-23 Science and Therapy.
https://www.frontiersin.org/journals/immunology/articles/10.3389/fimmu.2024.1331217/full

[19] Sugiura, K. (2022) Role of Interleukin 36 in Generalised Pustular Psoriasis and Beyond. https://pmc.ncbi.nlm.nih.gov/articles/PMC8850521/

[20] Mizumaki, K., Horii, M., Kano, M., Komuro, A., *et al.* (2021) Suppression of IL-23-Mediated Psoriasis-Like Inflammation by Regulatory B Cells.
https://www.nature.com/articles/s41598-021-81588-8

[21] Bridgewood, C., Fearnley, G.W., Berekmeri, A., *et al.* (2018) IL-36γ Is a Strong Inducer of IL-23 in Psoriatic Cells and Activates Angiogenesis.
https://www.frontiersin.org/journals/immunology/articles/10.3389/fimmu.2018.00200/full

[22] Murakami, M. (2020) Guselkumab for the Treatment of Palmoplantar Pustulosis. *Expert Opinion on Biological Therapy*, **20**, 841-852.
https://doi.org/10.1080/14712598.2020.1760244

[23] Boehringer Ingelheim (2024) CDSCO Approves SPEVIGO® (Spesolimab)—The First Treatment Option for Generalized Pustular Psoriasis Flares in Adults.
https://www.boehringer-ingelheim.com/in/cdsco-approves-spevigo-Spesolimab-first-treatment-option-generalized-pustular-psoriasis-flares

[24] Anders, H.J., Chan, T.M., Sanchez-Guerrero, J., Wofsy, D., *et al.* (2025) Efficacy and Safety of Guselkumab in Patients with Active Lupus Nephritis: Results from a Phase 2, Randomized, Placebo-Controlled Study. *Rheumatology*, **64**, 2731-2740.
https://academic.oup.com/rheumatology/advance-article-pdf/doi/10.1093/rheumatology/keae647/60933585/keae647.pdf

[25] Camela, E., Potestio, L., Fabbrocini, G. and Megna, M. (2022) Paradoxical Reactions to Biologicals for Psoriasis. *Expert Opinion on Biological Therapy*, **22**, 1435-1437.
https://www.tandfonline.com/doi/full/10.1080/14712598.2022.2153593