



Case Report

Generalized Pustular Psoriasis and Plaque Psoriasis Successfully Treated with Ixekizumab

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Citation: Gargiulo L, Pavia G, Ibba L, Fiorillo G, Bressan A, et al. (2022) Generalized Pustular Psoriasis and Plaque Psoriasis is Successfully Treated Ixekizumab. Clin Exp Dermatol Ther 7: 183. DOI: 10.29011/2575-8268.100183.

Received Date: 12 July 2022; **Accepted Date:** 18 July 2022; **Published Date:** 22 July 2022

Abstract

No standardized guidelines are available regarding the treatment of generalized pustular psoriasis with biological drugs. We report the case of a patient affected by concomitant plaque psoriasis and pustular psoriasis who was successfully treated with ixekizumab. Our findings showed that ixekizumab could represent a valid option also for the treatment of generalized pustular psoriasis.

Introduction

Generalized Pustular Psoriasis (GPP) is a subtype of pustular psoriasis, a group of inflammatory skin conditions characterized by infiltration of neutrophil granulocytes in the epidermis, that can present as an acute, subacute, or chronic pustular eruption on erythematous non-acral skin. According to the European Rare and Severe Psoriasis Expert Network (ERASPEN), GPP can occur with or without systemic inflammation, with or without psoriasis vulgaris and can either be a relapsing (>1 episode) or persistent (>3 months) condition [1]. The exact pathogenesis of this condition has not been fully understood. However, the evidence of sustained activation of IL-1 and IL-36 in GPP suggests that the IL-1/IL-36 inflammatory axis plays a key role [2]. In addition, in several patients with GPP has been detected the mutations in the IL36RN gene that encodes the interleukin-36 receptor antagonist (IL-36Ra), an anti-inflammatory cytokine in the IL-1 family [3].

The resulting upregulation of IL-36 activity promotes CD4+ T-cells proliferation with increased production of IL-17A, which represents a key mediator in GPP, such as in plaque psoriasis [4]. Given the rarity of this disease, there are no standardized guidelines for the treatment of GPP with biologics, in patients with contraindications or inadequate response to conventional immunosuppressive therapies.

Case Report

We report the case of a 56-year-old patient, who came to our attention reporting a 10-year history of psoriasis vulgaris. In the past, he had been treated with topical corticosteroids and UVB narrow band phototherapy, with only partial and temporary improvement. He had also a history of hypertension and type 2 diabetes mellitus. In 2013 he had a myocardial infarction, treated with angioplasty, and in 2019 he received antiviral therapy after the detection of hepatitis C infection, with subsequent viral

eradication. The patient came to our attention with erythematous plaques covered with severe scales on all four limbs. On the back, the patient exhibited several erythematous patches, surrounded by barely perceptible papules and pustules, all covered with excoriating crusts (Figure 1a-b).



Figure 1: a, b) Erythematous patches with mild scaling and some pustule on the back of a 56-year-old patient with a close-up of some cutaneous lesion on the upper back.

Erythematous patches, along with some pustules and scales, were also observed on the forehead (Figure 1c).



Figure 1: c) Erythema and pustule on the forehead of the patient.

The patient reported the appearance of these cutaneous lesions a month before and he recalled similar episodes during the past years. In the clinical suspicion of a GPP flare superimposed on plaque psoriasis, we performed a skin biopsy and prescribed the screening panel in the prevision of treatment with biologic drugs. The histopathology report described the presence of moderate acanthosis of the epidermis with ortho-parakeratosis, neutrophils, micro-pustules and superficial erosions; in the dermis, superficial mixed inflammatory infiltrates with the prevalent load on the papillary dermis (Figure 2, b).

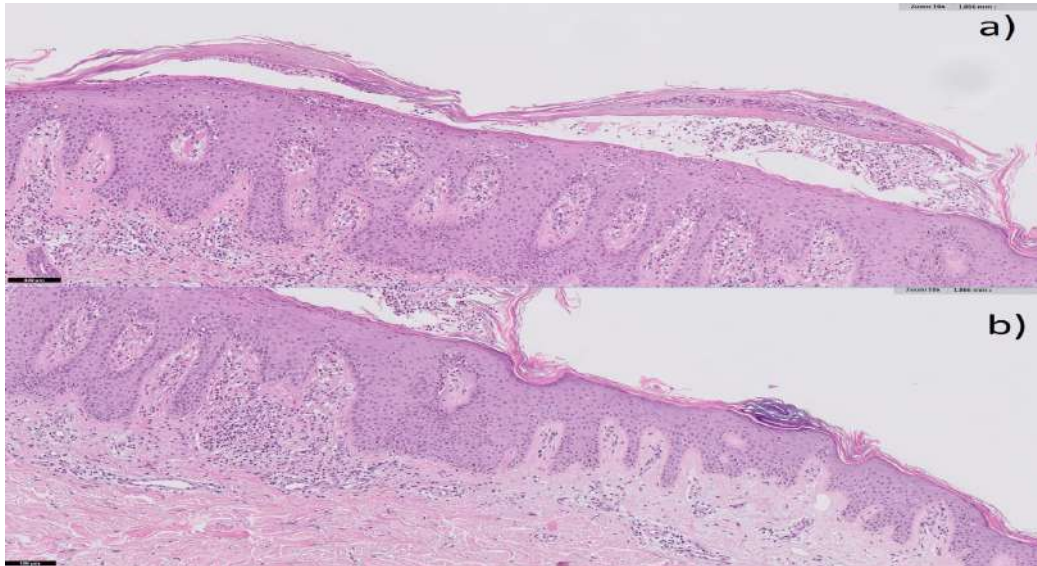


Figure 2: a) Histological image showing neutrophilic pustule and in the epidermal layers; 10X magnification, Hematoxylin and eosin stain; **b)** Acanthosis and ortho-parakeratosis of the epidermis; 10X magnification, Hematoxylin and eosin stain.

A diagnosis of pustular psoriasis was made. As blood exams were all in the normal ranges and the hepatologist gave the approval to start the biologic therapy, we prescribed therapy with ixekizumab, an anti-IL-17A drug: 160mg given subcutaneously at week 0, followed by 80mg at weeks 2, 4, 6, 8, 10, and 12. The patient came back at week 12, showing complete skin clearance (Figure 3).



Figure 3: a, b, c) Complete skin clearance observed after 12 weeks of treatment with ixekizumab.

Subsequently, he started the maintenance phase of the treatment, with 80mg every four weeks. At weeks 24 and 52, the patient came to our attention without any sign of psoriasis. No adverse reactions were reported. The patient also underwent periodical hepatologic visits and no signs of viral reactivation were observed.

No standardized guidelines for the specific treatment of GPP with biologics are available. Spesolimab, an anti-IL-36 receptor, is currently under investigation for the prevention of GPP flares in Phase 3 clinical trials. Despite the promising results, spesolimab has not yet been approved [5]. Given the key role of IL-17A in the pathogenesis of GPP, anti-IL-17 drugs have been used in isolated case series of patients with both GPP and palmoplantar pustular psoriasis. Ixekizumab is an anti-IL-17A monoclonal antibody approved for the treatment of moderate-to-severe plaque psoriasis in Europe and the United States. In Japan, ixekizumab has been successfully used also in patients affected by GPP, in both clinical trials [6] and real-life case series [7]. This level of response was sustained with continued treatment over three years [8]. However, data on this population are limited to very small groups of patients. We decided to prescribe ixekizumab for various reasons: first, the presence of some data regarding the management of GPP with ixekizumab [7]; second, our favorable experience with this drug, also in patients with multiple comorbidities, such as previous malignancies [9] and serological evidence of viral hepatitis [10]; third, the rapid onset of action of ixekizumab, as the patient's quality of life was greatly affected by the disease.

Conclusion

Based on our experience, ixekizumab was successful in treating a severe case of GPP and psoriasis vulgaris, without adverse effects until week 52. Longitudinal studies with numerous cohorts of patients are needed to assess the role of ixekizumab in the treatment of GPP.

Ethics/Patient Consent Statement: The patient gave his written informed consent to the publication of the details of his case, including the clinical pictures.

Conflicts of Interest: Antonio Costanzo has been a consultant and/or speaker for Abb-Vie, Almirall, Amgen, Janssen, Leo Pharma, Eli Lilly, Galderma, Boehringer, Novartis, Pfizer, Sandoz, and UCB. Alessandra Narcisi has been a consultant and/or speaker for Abb-Vie, Almirall, Amgen, Janssen, Leo Pharma, Eli Lilly, Boehringer, Novartis, Pfizer and UCB.

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