Received: 3 March 2024 | Revised: 16 August 2024 | Accepted: 16 September 2024

DOI: 10.1111/ajd.14367

CLINICAL LETTER

Australasian Journal of Dermatology

Pyoderma gangrenosum during infliximab in severe hidradenitis suppurativa: A paradoxical event

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Pyoderma gangrenosum (PG) is a rare neutrophilic dermatosis which may be associated with systemic diseases like inflammatory bowel diseases, inflammatory arthritis or hematologic disorders. Several drugs have been shown to be related with PG, leading to the hypothesis of a so called 'drug-induced' PG entity.[1]

We present the case of a 60-year-old man with a long history of hidradenitis suppurativa (HS) previously treated with multiple antibiotic therapies, acitretin and then with the monoclonal antibody anti-tumour necrosis factor (TNF)-alpha adalimumab, interrupted due to inefficacy after 1 year.

At the clinical evaluation, the patient presented with several fistulas, nodules and abscesses involving the armpits, the inguinal region and the buttocks (severe HS: Hurley stage 3).

In light of the high disease burden and the previously failed lines of therapy, treatment with another anti TNF-alpha antibody, infliximab, was started at dosage of 7.5 mg/kg iv., according to the recent literature evidence.[2]

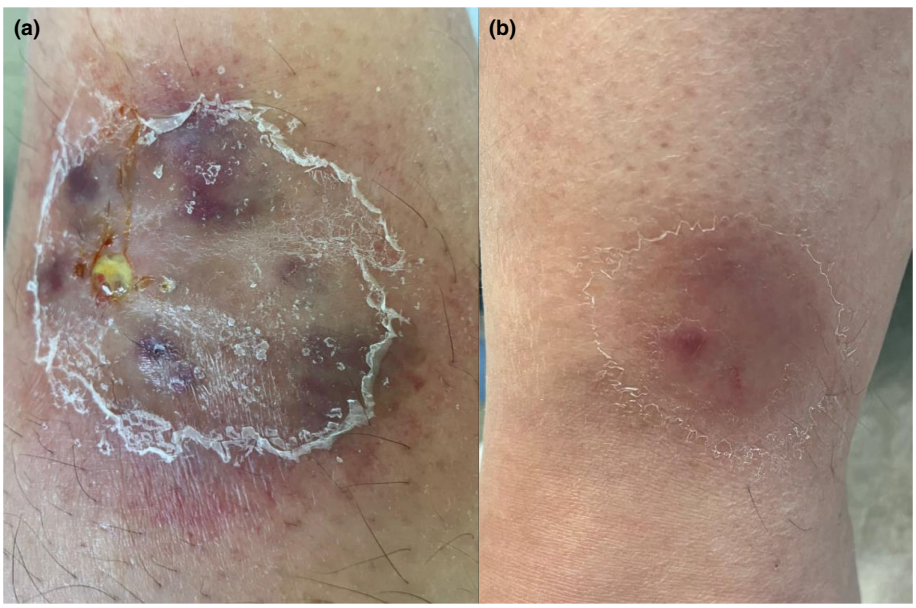

FIGURE 1 (a) PG on the left leg after 1 month of therapy with infliximab. (b) Remission of PG after 4 weeks from the interruption of infliximab and steroid therapy.

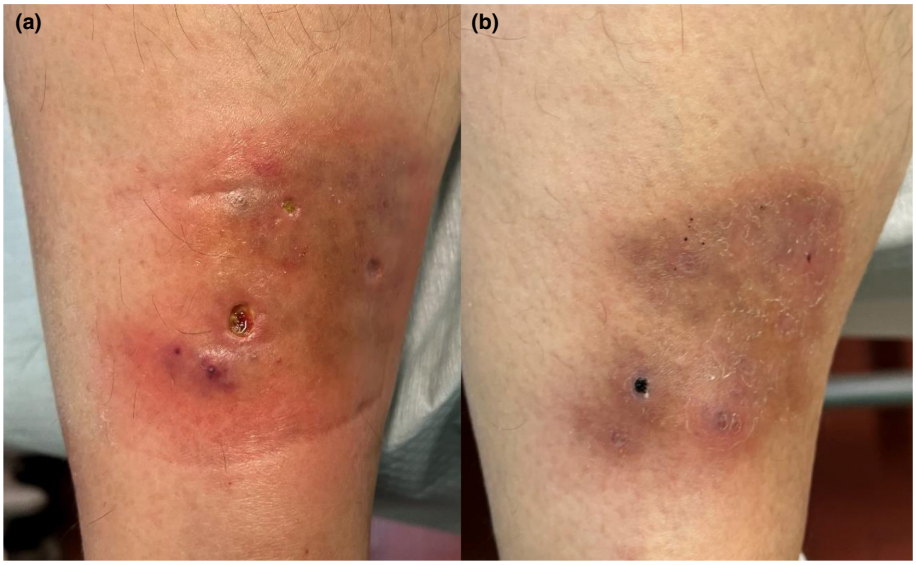

FIGURE 2 (a) PG on the left leg after the reintroduction of infliximab. (b) Partial remission of PG after the interruption of Infliximab.

After just 1 month of therapy, a remarkable clinical improvement was observed, with swift reduction in inflammation and pain.

Unfortunately, 4 weeks later the patient started developing a highly painful erythematous plaque later evolving into an ulcer involving the distal third of the left leg (Figure 1). No history of infection nor trauma at the site were reported. A PG was suspected and an incisional biopsy was performed. Histological examination revealed a granulomatous inflammation with giants cells in an oedematous dermis with neutrophils and diffuse lymphoplasmacytic infiltrates. These findings ruled out other autoimmune/vasculitis-like conditions and supported the hypothesis of PG-like drug-induced reaction.[1] Consequently, infliximab was discontinued, and oral prednisone was initiated at a dosage of 0.5 mg/kg. After only 2 weeks of steroid therapy the lesion had shrunk dramatically. A progressive tapering of the steroid therapy was performed, with a complete resolution of PG within a month. The histological features and clinical course confirmed the diagnosis of PG, according to the PARACELSUS criteria.[3] As the HS began to worsen, a new attempt to reintroduce Infliximab was undertaken, given its previously demonstrated efficacy. Unfortunately, after only 2 weeks the PG reappeared in the same previous area (Figure 2). The likelihood of a drug induced adverse event was confirmed (Naranjo algorithm score of 9/13).[4]

To date, few cases of PG after TNF-alpha inhibitors have been described, posing diagnostic and therapeutic challenges, as these agents show potential benefits in PG treatment.[2] It can be difficult to distinguish between the natural disease course and a paradoxical drug-induced event. In all reported cases, anti-TNF was prescribed for diseases involved in the spectrum of syndromic PG, such as psoriatic arthritis, ulcerative colitis, and HS.[1]

As TNF-alpha antagonists are known to inhibit CD4+ T-cell proliferation, lower IFN-gamma and reduce the Th1 and Th17 response, a possible explanation for this paradoxical event could be a cytokine imbalance.[5] Specifically, the TNF-alpha inhibition may lead to IFN-alpha overproduction by unopposed regulation of plasmacytoid dendritic cells in predisposed patients.[5] Additionally, CD4+ lymphocytosis due to decreased apoptotic mechanisms can be induced by TNF-alpha antagonists. As these mechanisms may play a role in the pathogenesis of PG-like drug-induced reaction, dermatologists should be aware of this rare but potentially challenging clinical scenario.

FUNDING INFORMATION

None.

CONFLICT OF INTEREST STATEMENT

None declared.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

CONSENT STATEMENT

Patient's written consent was obtained for the publication of the manuscript.

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How to cite this article: Giordano S, Repetto F, Boskovic S, Roccuzzo G, Ortoncelli M, Dapavo P, et al. Pyoderma gangrenosum during infliximab in severe hidradenitis suppurativa: A paradoxical event. Australas J Dermatol. 2024;00:1–3. https://doi.org/10.1111/ajd.14367