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DERMATOLOGIC THERAPY WILEY

LETTER

Eczematous eruption after brodalumab successfully treated with guselkumab and dupilumab

Dear Editor,

Biological drugs have completely revolutionized the management of chronic inflammatory skin diseases, such as psoriasis. However, their use has also raised new possible adverse events.[1] Particularly, the so-called paradoxical reactions to biologics are emerging.[2] In this context, eczematous eruptions (EE), which have already been observed with anti-TNF-α, are increasingly being reported with anti-interleukin(IL)-17A (ixekizumab and secukinumab)[2–4]; conversely, to date no EE case linked to brodalumab (anti-IL17 receptor) has been described.

We report the first case of EE in a patient under brodalumab treatment. A 62-year-old man with a 15-year history of psoriasis presented with a diffuse pruritic rash. His medical history was negative for childhood atopic dermatitis (AD), although positive for allergic rhinitis, hypertension, latent tuberculosis infection (LTBI) and mild renal failure. He had been treated with methotrexate and apremilast with inconsistent improvements. After LTBI prophylaxis brodalumab was started with complete disease control (Psoriasis Area Severity Index decreased from 38 to 1.8 after 12 weeks). This result was maintained up to 8 months when the patient developed mild psoriasis recurrence and a diffuse pruritic eczematous rash. On physical examination he presented with palmoplantar psoriasis and eczematous patches on trunk and limbs with multiple excoriation and scratch marks (Figure 1A, Figure 2A,B). Indeed, an intense itch negatively influenced sleep quality. Blood tests were normal except for CRP and ESR. Histological examination revealed spongiosis, edema and perivascular lymphocytic infiltrate. Therefore, a diagnosis of suspected brodalumab induced EE eruption was made. Treatment with topical (mometasone) and systemic (betametasone and then triamcinolone) corticosteroids gave only transitory improvement: the rash reappeared after any decalage. Itch was very severe and not controlled by antihistamines (desloratadine up to three times/day). Cyclosporine treatment was excluded due to arterial hypertension. Hence, brodalumab discontinuation and switch to guselkumab was performed. After 8 weeks of treatment, itch was still severe and skin lesions only very little improved. For this reasons, we decided to add dupilumab treatment, obtaining an almost complete clearance and itch control at week 8 (Figures 1B and 2C,D). The patient is still on guselkumab and dupilumab combination treatment with stable results up to week 16.

The pathogenesis of biologic induced EE has not yet been clarified. Both psoriasis and eczema are caused by a dysregulation of Th1/Th2 immune responses, with prominence of the Th1 arm in psoriasis and Th2 in eczema.[2] EE during anti-IL-17A therapy may be explained by the block of Th1 pathway, thus increasing the activity of Th2 arm.[2,4,5] According to a recent study, EE develops in 2.2% of patients treated with anti-IL17A drugs, requiring discontinuation in 75%.[2] To date, no case of EE has been reported in literature during brodalumab. Indeed, according to Galluzzo et al,[6] brodalumab would be the biological of choice in paradoxical reactions to other anti-IL17s. Indeed, a case of ixekizumab induced EE successfully treated by brodalumab,[7] and a case of concomitant psoriasis and atopic eczema managed with brodalumab have been reported.[8] Brodalumab, acting on IL-17RA, unlike ixekizumab and secukinumab, would be able to inhibit a wider spectrum of inflammatory skin conditions, since it is at the cross of many cytokines signaling ways including IL-17C which has been postulated to be linked to EE eruption.[6] The immunological pathway of atopic eczema is complex and heterogeneous.[2,3] It is possible that interference with several members of the IL-17 family induced an imbalance towards the Th2 arm, although this is a rare event given the important role of IL-17 in atopic eczema. However, the pathogenesis of biologic induced EE is yet to be clarified as demonstrated by their possible occurrence also during anti-IL-23.[9] We decided to prescribe guselkumab as it has been recently shown to be the most widely used drug in patients with concomitant psoriasis and atopic eczema, sometimes in combination with dupilumab.[10] The pathogenesis of EE during biological therapy is still unknown. Even if brodalumab has been reported to be useful in this paradoxical condition, EE induced by its use may be possible even if very unfrequently.

AUTHOR CONTRIBUTIONS

Matteo Megna: conceptualization, validation, visualization, writing-original draft preparation, writing - review & editing. **Lucia Genco:** data curation, investigation, methodology, visualization, writing-original draft preparation. **Matteo Noto:** data curation, investigation, methodology, visualization, writing-original draft preparation. **Cataldo Patruno:** conceptualization, validation, visualization, writing-review & editing, supervision. **Gabriella Fabbrocini**: conceptualization, validation, visualization, writing-review & editing, supervision. **Maddalena Napolitano:** conceptualization, validation, visualization, writing-original draft preparation, writing - review & editing.

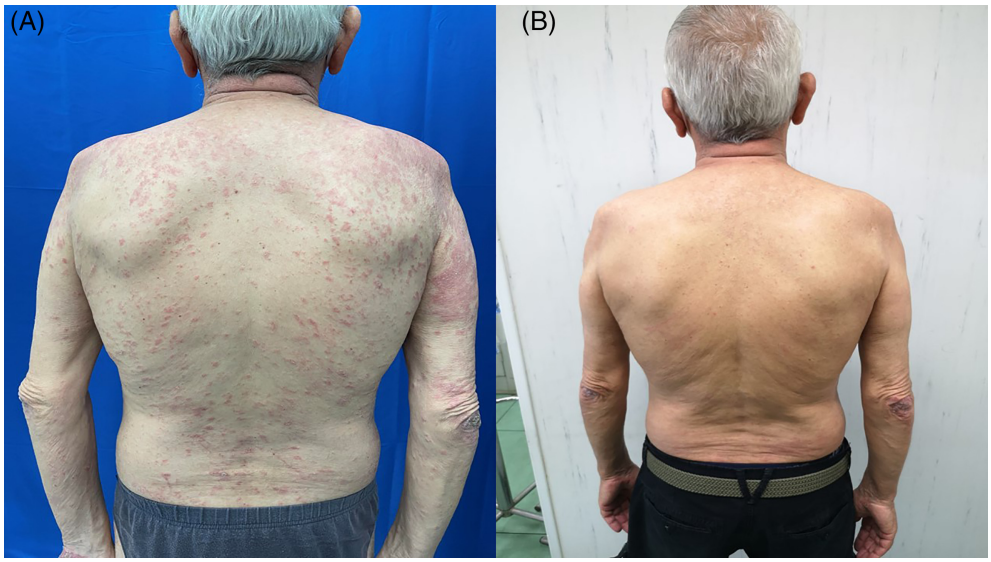

FIGURE 1 Back of the patient: A: after 8 months of brodalumab therapy; B: after 8 weeks of guselkumab and dupilumab therapy

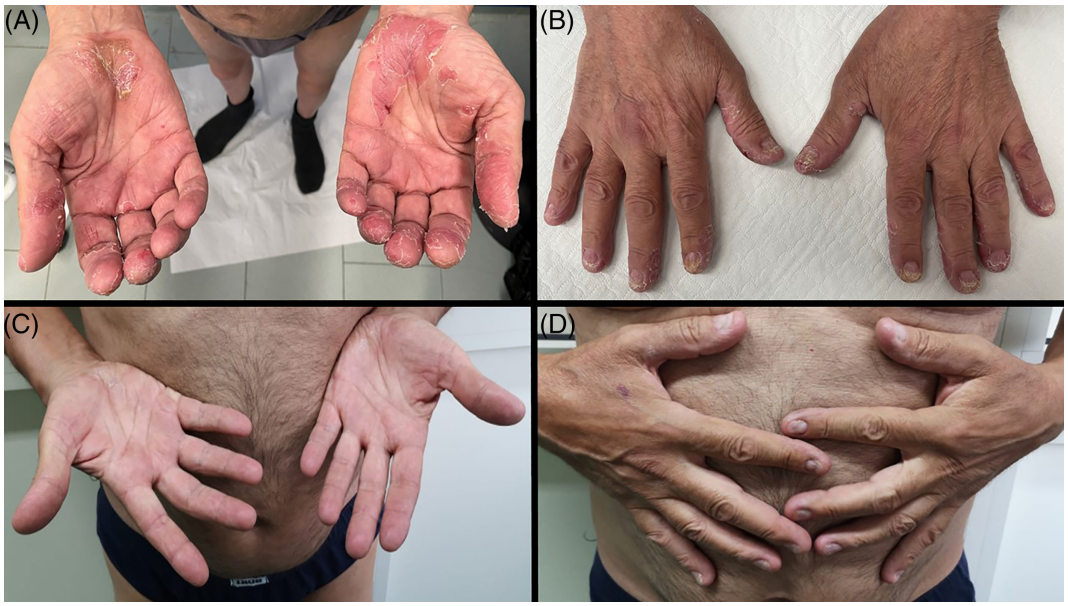

FIGURE 2 Hands of the patient: (A, B): after 8 months of brodalumab therapy; (C, D): after 8 weeks of guselkumab and dupilumab therapy

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CONFLICT OF INTEREST

Matteo Megna acted as a speaker or consultant for Abbvie, Novartis, Eli Lilly, Janssen, UCB, Amgen, Leo Pharma; Cataldo Patruno acted as investigator, speaker, consultant, and/or advisory board member for AbbVie, Amgen, Eli Lilly, Leo Pharma, Novartis, Pfizer, Pierre Fabre, and Sanofi; Gabriella Fabbrocini acted as a speaker or consultant for Abbvie, Novartis, Eli Lilly, Janssen, UCB, Amgen, Leo Pharma, Almirall. The remaining authors report no conflicts of interest; Maddalena Napolitano acted as a speaker or consultant for Abbvie, Eli Lilly, Sanofi and Leo-Pharma. Genco L, Matteo N have nothing to disclose.

DATA AVAILABILITY STATEMENT

Data sharing not applicable to this article as no datasets were generated or analyzed during the current study.

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