SKIN

BRIEF ARTICLE

A Case of Lichenoid Drug Eruption Following Risankizumab Therapy

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ABSTRACT

Psoriasis (PsO) is a chronic inflammatory disorder that significantly impairs quality of life and is associated with numerous comorbidities. Risankizumab, a biologic therapy targeting the p19 subunit of interleukin (IL)-23, has emerged as a potent treatment option due to its ability to disrupt the IL-23/IL-17 inflammatory cascade responsible for psoriatic pathogenesis. Despite its demonstrated efficacy and safety, risankizumab's potential for rare adverse reactions necessitates vigilant post-marketing surveillance. This case reports the first documented instance of a lichenoid drug eruption in a 79-year-old female with psoriasis following treatment with risankizumab. The reaction manifested as erythematous patches across her chest, face, neck, and calf, which improved upon cessation of risankizumab and resumption of methotrexate supplemented by narrow-band UVB therapy. This case highlights the need for ongoing surveillance of adverse side effects associated with newer biologic therapies to enhance patient management and safety.

INTRODUCTION

Psoriasis (PsO) is a chronic, systemic inflammatory disorder associated with a wide array of comorbidities such as psoriatic arthritis, cardiovascular disease, kidney disease, gastrointestinal disease, and mood disorders. Characterized by erythematous, scaly plaques varying in severity, PsO negatively impacts patients' quality of life and psychological well-being. Insights on the immunopathogenesis underpinning psoriasis manifestation have revolutionized treatment options and significantly improved prognostic outlook, enabling a shift from chronic management to potential long-term remission and total skin clearance.[1]

Risankizumab, a recent addition to the array of biologic therapies for inflammatory conditions, is a humanized IgG1 monoclonal antibody that targets the p19 subunit of interleukin (IL)-23.[2] Binding to this subunit inhibits the ligation of IL-23 to its receptor, a key step moderating the IL-17/23 inflammatory pathway. IL-23 supports the differentiation, maintenance, and proliferation of T-helper-17 cells, which are major producers of pro-inflammatory cytokine IL-17. This cytokine is crucial in perpetuating a self-amplifying, positive feedback loop, thereby sustaining both systemic and cutaneous psoriatic inflammation. By disrupting the IL-23-receptor interaction, risankizumab effectively reduces the downstream effects of this inflammatory

cascade, addressing an underlying cause of inflammatory disease.[3]

Clinically, risankizumab is a valuable treatment option for PsO patients with common inflammatory comorbidities, including moderate-to-severe Crohn's disease and active psoriatic arthritis.[4] Risankizumab also demonstrated superior efficacy in treating PsO compared to ustekizumab, adalimumab, and secukinumab.[5] An integrated analysis of safety outcomes across clinical trials has indicated a favorable short and long-term safety profile, with upper respiratory tract infections being the most frequently reported adverse event.[6] However, due to its relatively recent market introduction, continuous monitoring and reporting of adverse events associated with risankizumab are essential. In this report, we present a novel case of lichenoid drug eruption following treatment with risankizumab.

CASE REPORT

A 79-year-old female with a 5-year history of psoriasis without psoriatic arthritis presented with burning, erythematous, confluent, non-scaly patches on her upper chest, face, and neck (**Figure 1A**). The patient also had 1-4 cm erythematous, scaling, hyperkeratotic patches on her back and extremities (**Figure 1B).** The patient received two loading doses of Risankizumab at weeks 0 and 4 and presented at the practice one month after receiving the second dose. Prior to switching to risankizumab, she had been treated with oral methotrexate for the last four years and achieved skin clearance with prolonged methotrexate use (cumulative dose: 2,000 mg). A week following her initial visit to the practice, the patient presented with a new onset erythematous, scaling patch with central desquamation and erosion on her right pretibial calf. Two punch biopsies of her left clavicular neck and right pretibial calf demonstrated lichenoid drug reaction with neutrophils and eosinophils, consistent with a cutaneous drug eruption to a systemically administered medication (**Figure 2**).

Upon histopathological review, risankizumab was discontinued, and she was restarted on methotrexate via weekly 15mg intramuscular injections. Additionally, the patient also began receiving narrow-band UVB treatments with excimer laser three times per week in attempt to clear her psoriasis, treat the drug eruption, and eventually taper and discontinue methotrexate. While the patient's psoriasis cleared with methotrexate and narrow-band UVB treatments, the lichenoid eruptions took six months to significantly improve, which aligns well with the half-life of Risankizumab being 27 to 34 days, leaving approximately 3% of the drug in the system at 170 days.

DISCUSSION

Lichenoid drug eruptions, although rare and unexpected, have been documented with systemic biologic treatments for PsO, notably with TNF-α inhibitors such as adalimumab, infliximab, and etanercept.[7-9] Additionally, there has been at least one report of an oral lichenoid eruption associated with IL-17 inhibitor, secukinumab.[10] IL-23 p19 subunit inhibitors have been linked to eczematous eruptions, but this is the first reported case of a lichenoid drug eruption.[11]

Mechanistically, it is speculated that TNF-α inhibition permits the upregulation of interferon (IFN) – α, which then activates resident T-cells and myeloid dendritic cells, potentially leading to subsequent paradoxical lichenoid eruptions. Evidence supporting this model includes substantial increases in

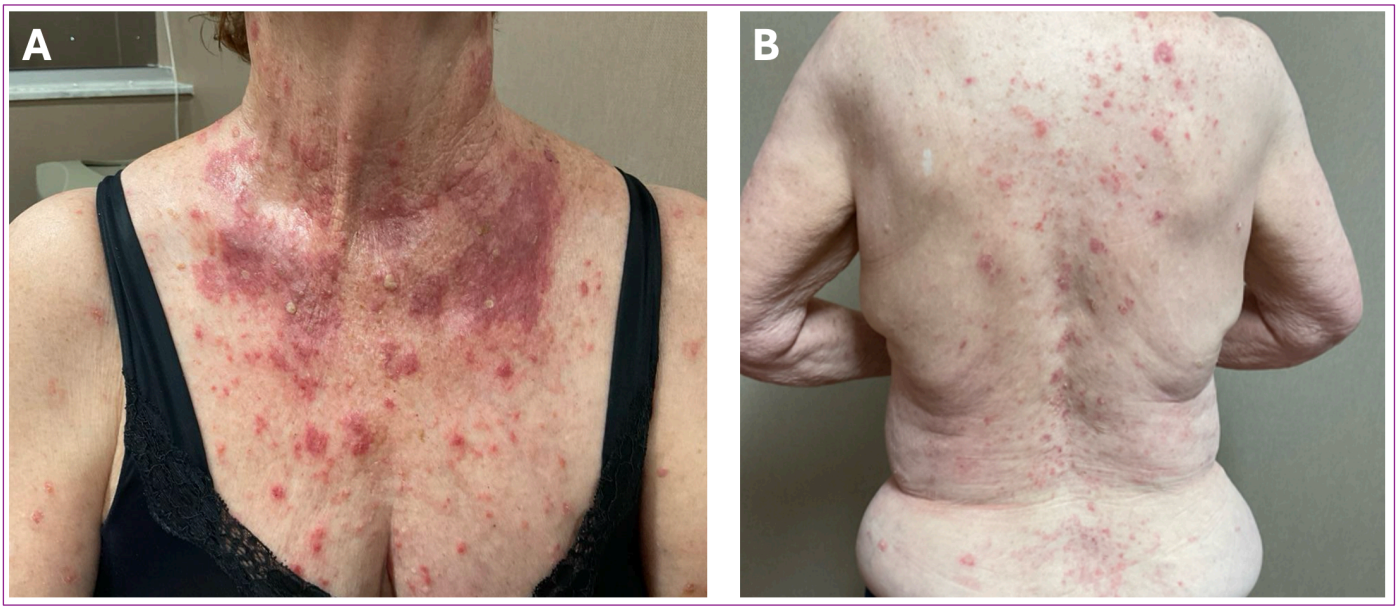

Figure 1 – Lichenoid eruption post-treatment with risankizumab (**A**) Chest and neck (**B**) Back.

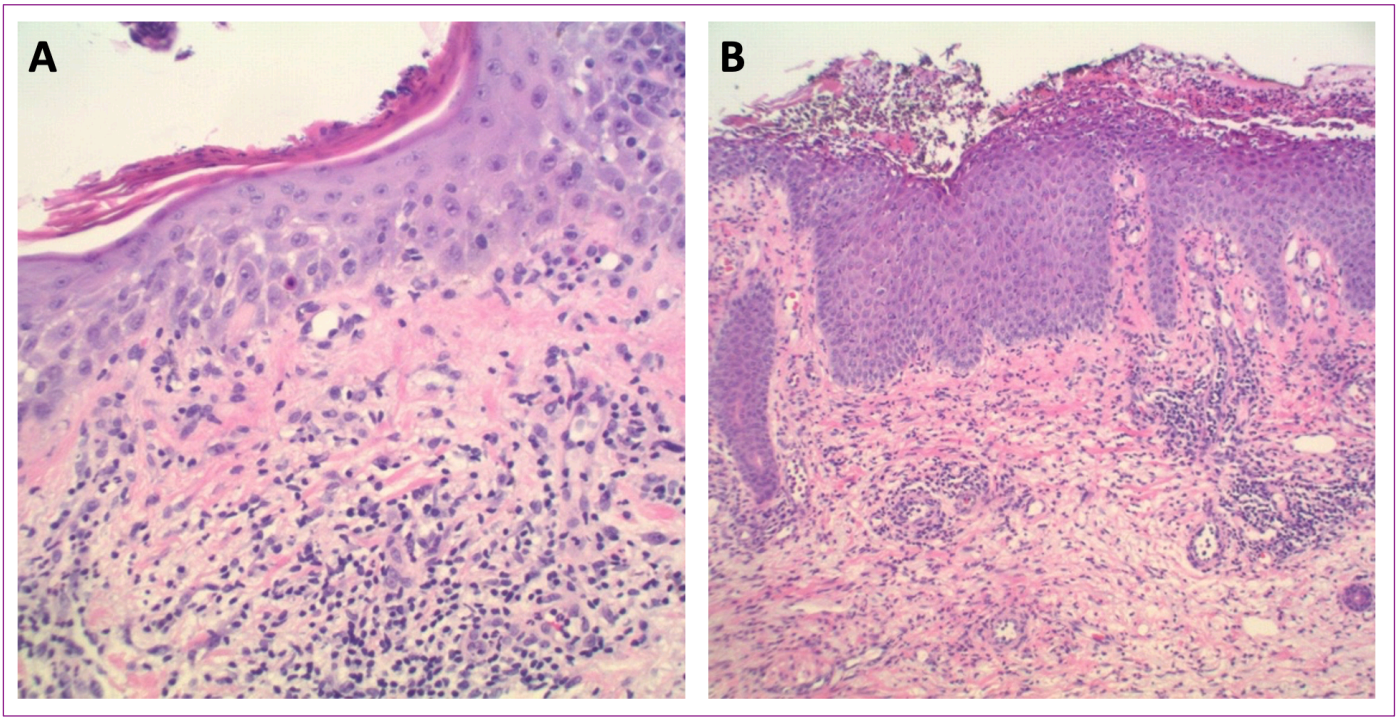

Figure 2 – Skin Biopsy of cutaneous eruption. Hematoxylin and Eosin (H&E). (**A**) Left clavicular neck. (**B**) Right pretibial calf.

plasmacytoid dendritic cells, important producers of IFN-α, observed in cutaneous and oral lichen planus lesions. Additionally, Type I interferons, notably IFN-α, have been linked to the activation of cytotoxic CD8+ T cells, which may induce lichen planus. Cases of lichen planus following IFN-α therapy for hepatitis C, cutaneous lymphoma, and malignant melanoma further reinforce this connection.[7]

The established link between TNF-α inhibitors and lichenoid eruptions leads to an exploration of similar effects with IL-23 inhibitors. In psoriasis, TNF-α is involved in a negative feedback loop that regulates IFN-α production by inducing dendritic cell maturation. Simultaneously, TNF-α and IL-23 activate T-cells to produce IL-17 and IL-22, driving a positive feedback loop that exacerbates inflammation and keratinocyte proliferation, characteristic of psoriatic lesions.[12]

However, TNF-α inhibition can disrupt these feedback mechanisms, leading to unregulated IFN-α production and paradoxical psoriasis. This occurs because anti-TNF therapy prevents the maturation of dendritic cells, sustaining an IFN-α driven inflammatory response independent of T-cells.[12]

CONCLUSION

We propose that IL-23 inhibition might mimic the paradoxical inflammatory pathways triggered by TNF-α inhibitors, potentially leading to a similar shift in the delicate immune balance resulting in increased IFN-α production implicated in lichenoid drug eruptions.

This case study highlights the complex nature of cytokine interactions in dermatologic treatments. It emphasizes the need for careful monitoring and a deep understanding of immune modulation by biologic therapies to prevent and manage adverse effects.

Conflict of Interest Disclosures: ZL, SR, GDB, SAS report no disclosures. ABG has received honoraria as an advisory board member and consultant for Amgen, Eli Lilly, Highlights Therapeutics, Janssen, Novartis, Sanofi, SunPharma, Takeda, Teva, UCB, and Xbiotech (stock options for RA); and research/educational grants from Avalo Therapeutics, Bristol-Myers Squibb, Janssen, Moonlake, and UCB Pharma, (all paid to Mount Sinai School of Medicine).

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