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Paradoxical reversed plantar involvement during ixekizumab therapy for psoriasis

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Abstract

Palmoplantar psoriasis is a particularly challenging variant of psoriasis. Psoriasis at this location has a significant impact on health-related quality of life and is often recalcitrant. However, difficult cases may respond to biologic therapies. Paradoxical reactions during treatment with biological agents have been described, mostly during anti-tumor necrosis factor therapy. These typically present as a change in morphology or distribution of lesions. We present a patient with palmoplantar psoriasis treated with ixekizumab who achieved a favorable response that was coupled with a rare paradoxical reaction, reversed plantar involvement. The reason for this phenomenon and its clinical course are uncertain, but these new lesions are proving recalcitrant to complementary therapies. Provided the increasingly widespread use of biologic therapies, the incidence and diversity of paradoxical reactions are expected to increase.

Keywords: psoriasis, palmoplantar psoriasis, paradoxical reactions, biological therapy, ixekizumab, monoclonal antibodies

Introduction

Palmoplantar psoriasis, pustular and non-pustular, is a particularly challenging variant of psoriasis. These forms have a greater impact on health-related quality of life and impairment of mobility, self-care, and everyday activities [1]. Lesions are often recalcitrant to phototherapy and topical and

systemic treatments; in difficult cases they may respond to biologic therapies [2]. Ixekizumab is a monoclonal antibody against interleukin (IL)-17A that has been useful in treating plaque psoriasis and palmoplantar non-pustular psoriasis (PPP), [2]. Paradoxical reactions have been described following treatment with different biologic agents, mainly tumor necrosis factor (TNF) inhibitors [3]. We present a patient with a unique paradoxical reaction following treatment with ixekizumab for PPP.

Case Synopsis

A 53-year-old man with a 6-year-history of PPP was referred to our clinic for progressive worsening (**Figure 1A**). Topical therapy, systemic retinoids (acitretin), and ustekinumab did not achieve adequate response. The patient was unable to adhere to phototherapy regimens. Lesions were painful and invalidating, with significant impairment of quality of life and work performance. Ixekizumab was started with a 160mg starting dose, 80mg Q2W for 12 weeks and Q4W thereafter. He achieved rapid and favorable response of palmar psoriasis. Improvement of plantar involvement was slower and was accompanied by development of new lesions on the plantar vaults. No precipitating or perpetuating factors were identified to explain the latter. Furthermore, one year after initiating treatment he still exhibits complete clearance of initial lesions, but paradoxical plantar vault involvement persists despite added topical corticosteroids and emollients (**Figure 1B**).

Case Discussion

Psoriasis and psoriasiform eruptions may present as paradoxical reactions following treatment with biologic therapy. Although most cases have been associated with TNF inhibitors, there are also reports with agents directed against different targets, such as ustekinumab [3, 4]. However, paradoxical reactions to new biologic therapies have not been widely studied, so their therapeutic or prognostic implications and the precise etio-pathogenic and immunologic mechanisms behind them are not fully understood. A recent case of paradoxical



Figure 1. Palmoplantar psoriasis. **A)** Before therapy with ixekizumab: plantar lesions with marked hyperkeratosis and fissures, distributed over the plantar arch with sparing of the vault. **B)** After one year of therapy with ixekizumab: clearance of previous plantar lesions and development of new psoriasiform lesions on the plantar vault.

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eczematous reaction following ixekizumab therapy has been described, in which a switch to eczematous inflammatory phenotype secondary to decreased IL17 levels was hypothesized as a possible mechanism [5].

In patients with psoriasis, paradoxical reactions to biologic agents usually consist of a modification in morphology and/or distribution of preexisting phenotypes, with palmoplantar involvement being one of the most common presentations [3]. However, when re-evaluating these cases, distinguishing a paradoxical reaction from insufficient response to treatment might prove challenging. Our patient exhibited significant improvement of preexisting plantar plaques, which had persisted despite multiple topical and systemic therapies. He simultaneously developed identical lesions on the plantar vaults, which had always been spared. This points to a unique paradoxical reaction to ixekizumab. The reason for this phenomenon and its clinical course are uncertain. These new lesions are proving recalcitrant to complementary therapies.

Conclusion

Along with the increasingly widespread use of biologic therapies, the incidence and diversity of paradoxical reactions are expected to increase. Further study is warranted to improve our understanding of their etio-pathogenesis, adequate treatment, prevention, and implications of the management of biologics in these patients.

Potential conflicts of interest

The authors declare no conflicts of interests.