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BRIEF REPORT

Paradoxical Flare of Psoriasis after Ustekinumab Therapy

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Dear Editor:

Psoriasis is a chronic, inflammatory, and immune-mediated disease with a high morbidity rate in affected patients. The advent of biologics that target specific molecules in the immune system has revolutionized the treatment of psoriasis. Ustekinumab, one of most recent biological agents approved for the treatment of patients with moderate to severe plaque psoriasis, is a human monoclonal antibody that binds to the p40 subunit of interleukin (IL)-12 and IL-23[1]. Excellent results of ustekinumab therapy for severe psoriasis have been reported in several cases, with remarkable improvement and no severe adverse effects[2]. However, we experienced a case of paradoxical flare of psoriasis after ustekinumab therapy.

A 24-year-old male patient had suffered from psoriasis vulgaris for 7 years. Although he had been treated with conventional treatment such as narrow band ultraviolet B (NBUVB) phototherapy, acitretin, methotrexate, and cyclosporine, his lesions had not improved sufficiently. He complained of side effects including dry mouth, nausea, and abdominal discomfort when he was treated with methotrexate or cyclosporine. The treatment was changed to subcutaneous injection of ustekinumab 45 mg according to the conventional dosing schedule. His lesions markedly improved after the first injection (Fig. 1), but slowly reappeared after the third injection. The day following the fourth injection, his skin lesions suddenly expanded to multiple, scaly erythematous plaques on face, trunk, and

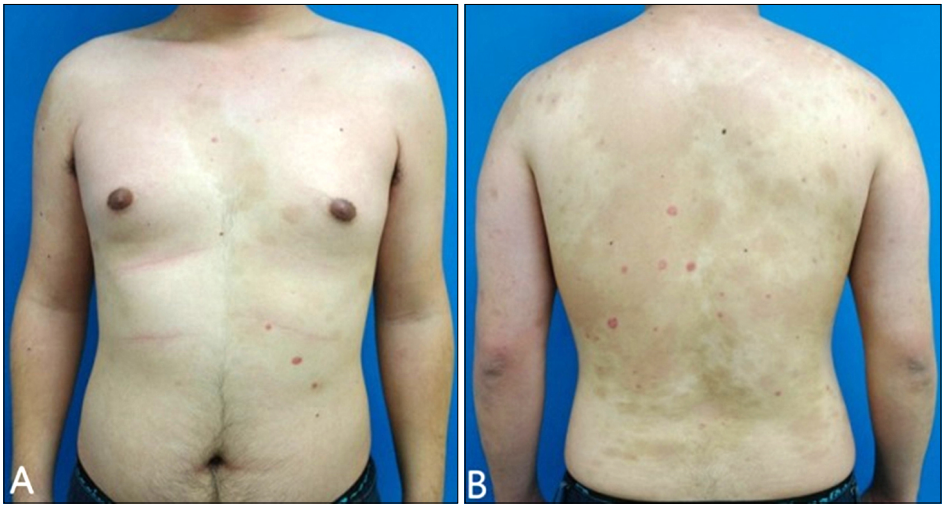

Fig. 1. Before the second ustekinumab injection. Skin lesion was dramatically improved.

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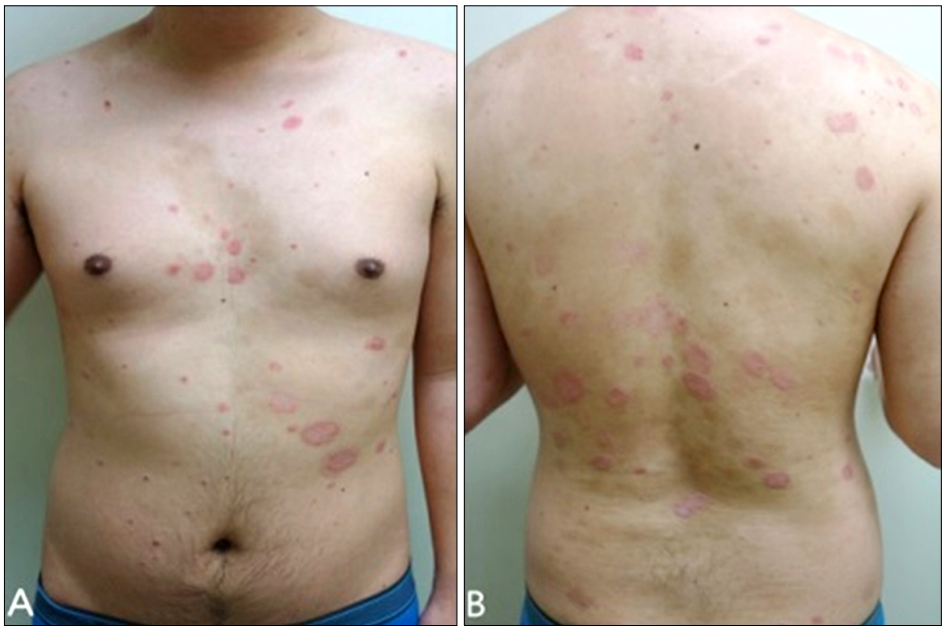

Fig. 2. (A, B) Paradoxical flare of plaque type psoriasis after the fourth injection.

extremities (Fig. 2). The treatment was changed to systemic steroid and NBUVB phototherapy and his lesions came under control. However, after 2 weeks of flare phenomenon, he discontinued treatments arbitrarily and did not visit our department again.

There have been only two previous case reports of paradoxical flare after ustekinumab therapy. Wenk et al.[3] first reported a case of paradoxical flare of psoriasis after ustekinumab injection, in which the patient experienced worsening of skin lesions whenever she was injected. Her flares were reportedly controlled with topical steroid and acitretin. Hay and Pan[4] reported a paradoxical flare of psoriasis triggered after the second injection of ustekinumab, with progressively worsening plaque type psoriatic lesions leading to pustulation. They injected a subcutaneous loading dose of adalimumab 80 mg and subsequent dose of 40 mg every 2 weeks. Unlike our case, these prior cases featured an altered morphology from plaque type psoriasis to pustular type psoriasis after ustakinumab injection. Furthermore, while our case showed good response after secondary injection, previously reported cases did not experience any effect of ustekinumab therapy.

The pathophysiology of paradoxical phenomenon remains unknown. However, it is hypothesized that tumor necrosis factor (TNF) inhibitor possibly induces psoriasis because of cytokine imbalance, such as increasing plasmacytoid dendritic cell interferon-alpha (IFN-α) production, which is normally suppressed by TNF-α[5]. Ustekinumab blocks IL-23 activity and may decrease IL-23 and T helper 17 cell-induced TNF-α. IFN-α worsens psoriasis by promoting increased T-cell activation and decreased TNF-α[3-5]. This theory is based on induction or worsening after treatment with IFN-α; however, it is insufficient to explain this phenomenon and the reason for a good response after secondary injection, in our case. Further study of additional cases is needed to clearly elucidate the mechanism involved in paradoxical flare after ustekinumab therapy.

CONFLICTS OF INTEREST

The authors have nothing to disclose.

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