Ustekinumab-induced fixed drug eruption

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INTRODUCTION

Fixed drug eruption is a cutaneous drug reaction that characteristically recurs in the same location on reexposure to the offending drug. It usually presents with dusky red or violaceous plaques that resolve, leaving postinflammatory hyperpigmentation. Rare severe atypical variants of fixed drug eruption include multiple, nonpigmenting, and generalized bullous variants. Intraepidermal $CD8^+$ T cells are thought to have a key role in mediating the localized epidermal lesions that characterize fixed drug eruption. Inflammatory mediators, such as granzyme B, interferon γ, and perforin, along with neutrophils, destroy keratinocytes and melanocytes.[1]

CASE REPORT

A 36-year-old healthy man with no known drug allergies presented to the dermatology clinic with a 2-year history of a generalized body rash. In accordance with clinical and histopathologic features (parakeratosis, acanthosis, psoriasiform hyperplasia, and absent granular layer), he received a diagnosis of moderate chronic plaque psoriasis without psoriatic arthritis, and ustekinumab was prescribed. He received a 90-mg subcutaneous initial dose, another similar dose 4 weeks later, and another 90 mg after 12 weeks.

Two days after the second injection of ustekinumab, the patient developed a single, itchy, and painful lesion on his right calf. The lesion recurred in the same site 2 days after the third injection. There was no history of any associated systematic symptoms nor the use of any concomitant medications. On skin examination, a solitary, well-demarcated, rounded, erythematous plaque with a dusky purple center surrounded by an erythematous rim was noticed over the right calf (Fig 1). Nail and mucous membrane examination results were normal.

Abbreviation used:

IL: interleukin

Histologic examination showed vacuolar degeneration at the dermoepidermal junction, necrotic keratinocytes scattered in the epidermis, papillary dermal edema, dermal melanophages, and a dermal perivascular inflammatory infiltrate composed of lymphocytes and eosinophils (Fig 2).

In accordance with the findings, the patient received a diagnosis of fixed drug eruption. He was treated with clobetasol propionate 0.05% ointment twice a day, with improvement after 10 days of treatment. Ustekinumab therapy was discontinued to allow consideration of switching to another biologic.

DISCUSSION

Ustekinumab is a fully humanized IgG1k monoclonal antibody with high specificity and affinity to the p40 subunit shared by interleukin (IL) 12 and IL-23. This binding prevents subsequent interaction with the IL-12Rβ1 receptor expressed on immune cells and suppressing IL-12e— and IL-23e—mediated inflammation associated with psoriasis. It is Food and Drug Administration approved for the treatment of moderate to severe plaque psoriasis in adults and patients aged 12 to 17 years, psoriatic arthritis, and Crohn's disease.[2] Most common adverse reactions in psoriatic patients receiving ustekinumab are nasopharyngitis, upper respiratory tract infection, headache, and fatigue, reported in greater than or equal to 1%. Although ustekinumab is an immunomodulatory drug, safety data have showed no evidence of increased risk of malignancy or severe infections. Uncommon adverse effects include reversible

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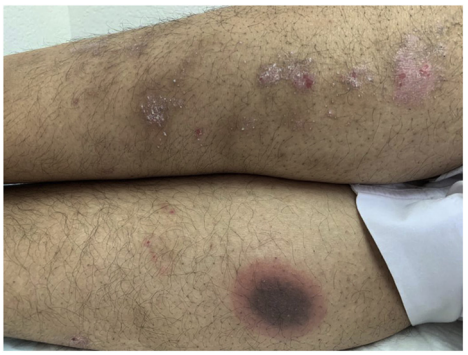

Fig 1. Multiple erythematous scaly plaques on left calf, representing psoriatic lesions. Well-demarcated rounded erythematous plaque with a dusky purple center on the right calf.

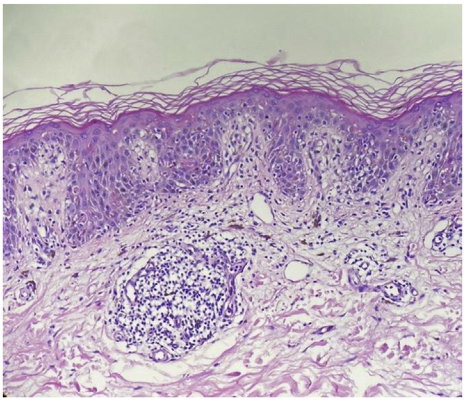

Fig 2. Histopathologic features: vacuolar degeneration at the dermoepidermal junction, necrotic keratinocytes scattered in the epidermis, and papillary dermal edema with dermal melanophages. Dermal perivascular lymphocytic infiltrate with eosinophils. (Hematoxylin-eosin stain; original magnification: ×10.)

posterior leukoencephalopathy syndrome, noninfectious pneumonia, and adverse cardiovascular events. Cutaneous adverse reactions associated with ustekinumab are rare and occur at rates less than 1%. Such reactions include cellulitis, herpes zoster, lymphomatoid drug eruption, urticaria, injection site reactions, recurrent erythema annulare centrifugum, bullous pemphigoid, erythema multiforme, and eczematous drug eruptions.[3-8]

Drugs frequently associated with fixed drug eruption include antibacterial agents (trimethoprim-sulfamethoxazole, tetracyclines, penicillins, quinolones, and dapsone), nonsteroidal anti-inflammatory drugs (acetylsalicylic acid, ibuprofen, naproxen, and mefenamic acid), acetaminophen (paracetamol), barbiturates, antimalarials (quinine), and anticonvulsants (carbamazepine).[1]

Our patient presented with fixed drug eruption induced by ustekinumab. This may be the first case reported with such a reaction. Other biological agents reported to cause fixed drug eruption include adalimumab and abatacept.[9,10]

Although advanced genetic engineering technology is improving the efficacy of monoclonal antibodies in terms of increased selectivity and improved pharmacokinetics, rare adverse reactions are still observed.

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