

Fixed Drug Eruption to Biologics and Role of Lesional Patch Testing



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A 40-year-old cashier with ankylosing spondylitis (AS) on anti-TNF- α therapy presented to the Immunology Clinic with an intermittent rash over her shin. She had been on regular subcutaneous adalimumab (AbbVie, North Chicago, IL) for the past 5 years and her AS was in remission.

For the past 3 months, there was consistent recurrence of a solitary rash over her left anterior shin around 4 hours after every

and recurred after each dose. There was no interruption of her injections and no recent change in the “citrate-free” autoinjector formulation (confirmed with supplier). There were no new medications and she had no history of dermatological conditions. There was no history of trauma.

The lesions got progressively worse with subsequent injections, and there was a localized vesicular eruption on her

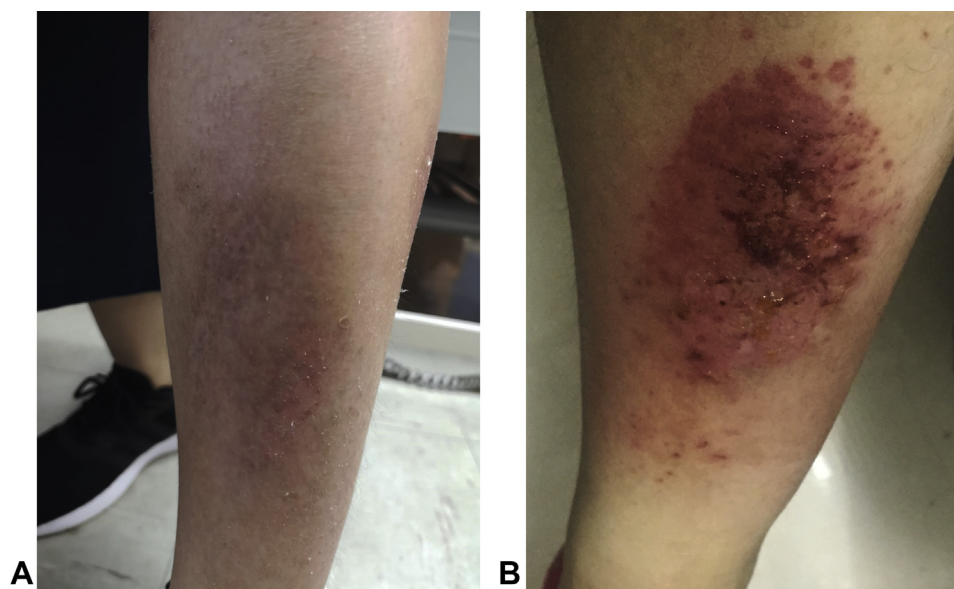


FIGURE 1. Residual hyperpigmentation (A) and subsequent reactivation of FDE (B) after adalimumab.

dose of adalimumab. Adalimumab was administered every 2 weeks to alternating thighs without history of local injection-site reactions. The lesions were well demarcated, beginning with an intense itch and burning sensation followed by a fixed erythematous oval plaque about 10 cm in diameter. The lesion would last for days with residual hyperpigmentation (Figure 1, A)

most recent episode (Figure 1, B). She declined a skin biopsy. Adalimumab was stopped and there was no recurrence of the rash.

A fixed drug eruption (FDE) was suspected and drug patch testing was performed 2 months later after complete healing of the rash. Patch testing was performed using IQ Ultra chambers

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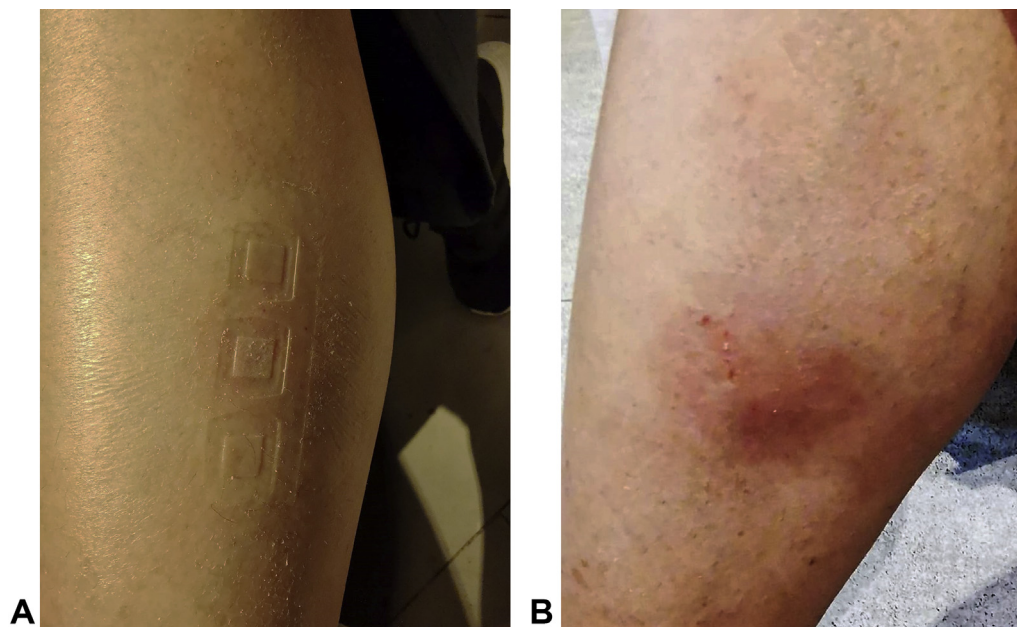


FIGURE 2. (A) Negative lesional patch testing at D2 and (B) strongly positive (++) with reactivation of residual FDE lesion at D4. Patch chambers from top to bottom: Empty chamber, adalimumab 1:10 aqueous, water for injection.

and adalimumab (directly extracted from the autoinjector and diluted 1:10 aqueous) with both control (uninvolved upper back skin) and lesional (residual pigmented lesion) patch test application. The patch tests were read on day 2 (D2) and day 4 (D4), in accordance with International Contact Dermatitis Research Group criteria.

Patch testing result was negative at the control site at D2 and D4. Patch testing result was negative at the lesional site at D2 (Figure 2, A), but strongly positive (++) at D4 (Figure 2, B) with reactivation of the residual FDE lesion with a crescendo effect. Given the positive lesional patch test result and the suggestive clinical features, she was diagnosed with an FDE due to adalimumab. In view of her favorable response to TNF- α blockade, she consented to provocation testing with subcutaneous golimumab (another anti-TNF- α antagonist), which was well tolerated. Her AS continues to be in remission with golimumab.

We previously reported on immediate-type hypersensitivity to adalimumab, and hypersensitivity reactions to biologics have

been increasingly identified.^{1,2} In this case, we report the first case of biologics-related FDE. An FDE is a delayed-type cutaneous hypersensitivity reaction to medication that recurs at the same site on further exposure and cross-reactivity is uncertain. In this case, tolerance to golimumab was demonstrated, suggesting a lack of cross-reactivity with an alternative anti-TNF- α antagonist. Adalimumab and golimumab are humanized IgG₁ anti-TNF- α antibodies but likely structurally dissimilar, because both are complex macromolecules derived from different biological cell lines. We highlight the utility of lesional patch testing in biologics-related FDE and suggest that tolerance to other anti-TNF- α antagonists is possible, but more studies are required to determine the true rate of cross-reactivity.

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