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Multiple fixed drug eruption to minocycline at sites of healed burn and zoster: An interesting case of locus minoris resistentiae

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Key words: burn; fixed drug eruption; isotopic response; locus minoris resistentiae; minocycline.

INTRODUCTION

Fixed drug eruptions (FDEs) are a subset of cutaneous drug reactions characterized by the development of well-demarcated nummular dusky erythematous plaques when exposed to an offending agent, which recur at the same site on re-exposure. With removal of the trigger, lesions disappear, often leaving residual hyperpigmentation.

The gold standard for FDE diagnosis is reproducible provocation of the lesions with the same offending agent.¹ Of the various agents associated with FDE, antimicrobial agents (sulfonamides, trimethoprim, and tetracyclines), analgesics (nonsteroidal anti-inflammatory drugs), sedatives (barbiturates), and anticonvulsants are among the most commonly reported.²

FDEs induced by minocycline have been identified since the 1970s.³ Although the exact incidence of tetracycline-associated FDEs is difficult to assess, multiple studies list the tetracyclines among the most common triggers,⁴ and some identify them as the most common in the case of genital FDEs.⁵ However, the pathophysiology of plaque recurrence at the same location is not fully understood. In some cases, these recurrences have been seen at former sites of trauma. We report a case of minocycline-induced FDE localized to sites of a previous burn and zoster.

CASE

A 34-year-old woman was prescribed minocycline, 100 mg twice a day, for acneiform lesions.

Abbreviations used:

FDE: fixed drug eruption
 LMR: locus minoris resistentiae

Within 4 days of starting the medication, a well-demarcated, tender, nummular dusky erythematous plaque developed on the right upper chest (Fig 1), the site of a healed curling iron burn that she sustained 2 months prior. The patient denied any other medication use or trauma to the affected site and noted that the lesion regressed on discontinuation of minocycline. Before this incident, she had taken minocycline with no side effects. The patient is a physician and suspected that she had an FDE to minocycline. Thus, 2 months later, after the site had fully healed, she rechallenged herself with this medication. Within 2 days of minocycline use, the plaque on the right upper chest recurred (Fig 2) along with an additional plaque of similar appearance on the right lateral chest situated under her brassiere strap. The minocycline was discontinued, and the lesions healed, leaving a hyperpigmented patch at the site of the right lateral chest (Fig 3). Upon further inquiry, the patient reported that she had an episode of shingles 15 years ago at the location of the second plaque. She declined biopsy because of concerns for scarring. Instead, she chose to rechallenge herself a final time with minocycline to confirm that the medication was the cause of these lesions.

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Fig 1. Dusky erythematous plaque after 4 days of minocycline use.

One month after her previous challenge, she took 1 dose of minocycline and noted that both lesions reappeared within 24 hours.

DISCUSSION

The term *fixed drug eruption* denotes one of the diagnostic characteristics of this condition: the recurrence of lesions at the same site. Much remains to be understood regarding why these plaques recur at the same locations, although in some cases, it is thought to be related to prior insult at the affected site.

As in the mythologic tale of the Greek hero Achilles, who was killed by an arrow striking his heel, which was the only vulnerable site on his body, the concept of *locus minoris resistentiae* (LMR) describes an area of the body more vulnerable than others, possibly as a result of a prior insult.⁶

In our case, this FDE caused by minocycline occurred at 2 sites of prior injury: a site of thermal injury and a site of prior herpes zoster infection that had also been subject to recurrent friction. These injured sites have a lower threshold for FDE lesion development, illustrating the concept of LMR. Cases of LMR similar to that of the first site of thermal injury have been documented in other patients, although these cases were caused by other forms of electromagnetic radiation, such as sun exposure.⁷

The eruption at the patient's second site of injury showed a phenomenon similar to LMR but more specific to dermatology: Wolf's isotopic response. This term describes the occurrence of a new



Fig 2. Well-demarcated dusky erythematous plaque after minocycline rechallenge.



Fig 3. Residual hyperpigmentation on the right lateral chest.

dermatosis at the exact site of another previously unrelated and healed skin lesion (classically herpes zoster).⁸ This case shows the simultaneous occurrence of LMR and Wolf's isotopic response in the same FDE as a result of 2 different types of prior insult.

Although much remains to be learned regarding the pathophysiology of these phenomena, it was theorized that resident T cells recruited from the bloodstream after an insult (eg, infection or trauma) may remain in the affected area for long periods after resolution of the initial insult. In FDEs, these cells may cross-react with a triggering antigen and become reactivated upon re-exposure to the agent.⁹

Although FDEs at sites of prior trauma have been reported,¹⁰ this is the first case, to our knowledge, of minocycline triggering the

phenomenon of LMR in the form of an FDE at a burn site, and then on re-exposure to the drug, simultaneous development of a Wolf's isotopic response at a second site of chronic friction and resolved varicella-zoster virus infection.

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