Lichen striatus after interferon therapy

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INTRODUCTION

A variety of cutaneous reactions have been described in patients receiving tumor necrosis factor alfa (TNF-α) inhibitors.[1] Of particular interest in this scenario is the development of lichen planus and lichen planus–like eruptions. Because TNF-α is recognized as a significant factor in the induction of these dermatoses, their appearance after inhibition of TNF-α is perplexing.[2] The leading theory postulates that a disturbance in the balance between inflammatory cytokines occurs with TNF-α inhibition, leading to increased expression of other cytokines such as interferon.[1-3] Interferon then induces an endogenous inflammatory response that clinically manifests as a cutaneous lichenoid eruption.[1-3]

Lichen striatus is an acquired inflammatory dermatosis that follows the lines of Blaschko.[4] Blaschko lines are invisible in normal skin but may become apparent in various skin conditions.[5] It has been postulated that the cells along Blaschko lines contain distinct genotypes that may ultimately permit a unique response to stimuli such as interferon. This heightened sensitivity to interferon is likely the underlying explanation for the appearance of segmental lichenoid reactions after treatment with TNF-α inhibitors. However, reports of these eruptions after interferon are lacking, and the evidence to support this concept is primarily substantiated by reports of segmental lichenoid reactions after anti-TNF agents.

CASE REPORT

A 64-year-old man with a 5-year history of hepatitis C presented with a linear cutaneous eruption affecting the right lower extremity. The onset of this cutaneous eruption occurred after the 24th week of treatment with interferon. Before consultation with the dermatology department, the patient had been using triamcinolone 0.025% ointment twice a day to affected regions with no improvement. The patient denied history of previous treatment for hepatitis C, including interferon. Physical examination found grouped erythematous scaly papules arranged in a strikingly linear distribution extending from the dorsal penis to the distal right plantar foot (Figs 1 to 3). A punch biopsy of the thigh found a lichenoid lymphocytic infiltrate at the dermoepidermal junction along with dyskeratotic keratinocytes and periecrine lymphocytic infiltrate, findings consistent with lichen striatus (Figs 4 and 5). The patient received 28 weeks of treatment with interferon, after which it was discontinued and was never reinitiated. The rash completely resolved 6 months after discontinuation of interferon 7 months after its initial appearance. He has since had no recurrence of the eruption. Additionally, the patient's viral load was monitored throughout the 28 weeks of treatment with interferon. At the start of interferon therapy, viral load was 5,965,981 IU/mL. By week 8, viral load became undetectable and remained so for the additional 20 weeks of therapy.

DISCUSSION

A substantial portion of the medical literature is devoted to the proposed role of interferon in the development of lichenoid eruptions and Blaschkoid dermatoses and even in the development of autoimmunity itself.[6-8] With the increased use of TNF-α inhibitors, the frequency of these phenomena has increased.[1,2,9-11] Multiple studies have independently concluded that TNF-α inhibition leads to increased amounts of interferon, which then induces these eruptions. This conclusion is strengthened by

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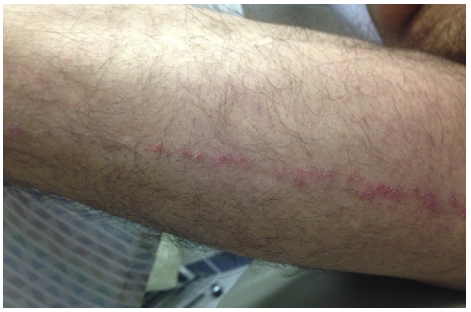

Fig 1. Located on the right lower leg in a linear distribution are violaceous and erythematous papules with overlying tightly adherent scale.

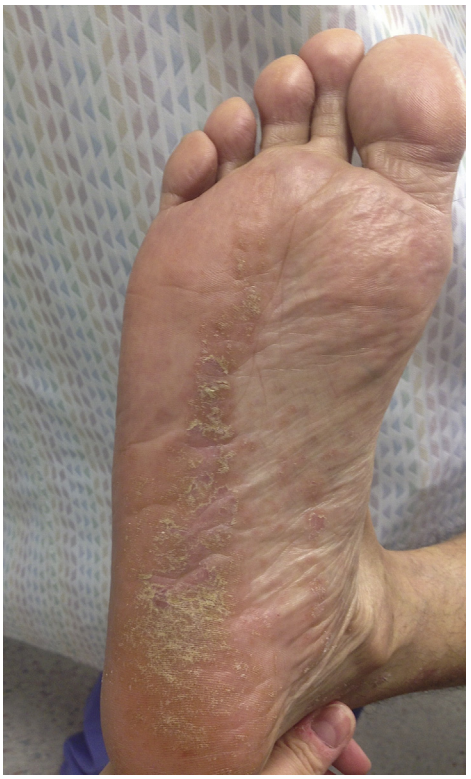

Fig 2. Faint pink and violaceous hyperkeratotic papules extending in a linear array from the plantar heel to the base of the third metatarsal.

our case, assuming that interferon was responsible for triggering our patient's lichenoid eruption.

Our claim that interferon resulted in our patient's lichenoid eruption is supported by several elements of our case. It is well recognized that lichenoid drug eruptions are delayed drug reactions, showing delay in both timing of appearance after drug initiation and prolongation after drug discontinuation.[4,12] In our patient, Lichen striatus appeared 6 months into treatment with interferon and resolved 6 months after discontinuation; we believe these features are most consistent with a lichenoid

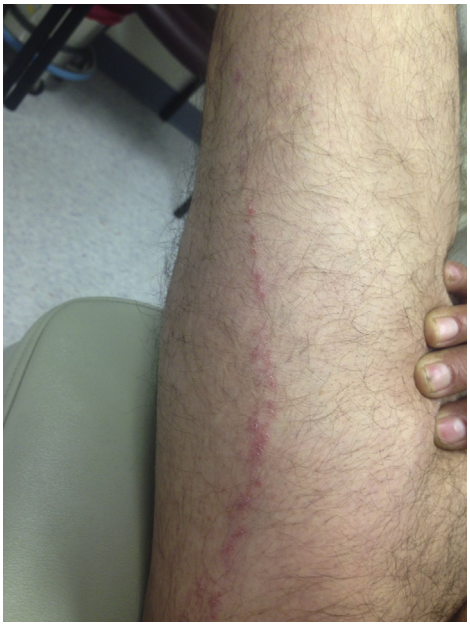

Fig 3. The linear lichenoid eruption extends to involve the superior leg.

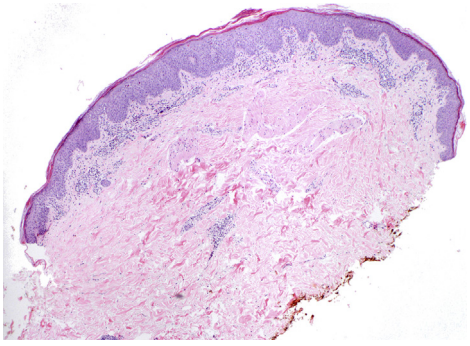

Fig 4. Punch biopsy shows a lichenoid lymphocytic infiltrate at the dermoepidermal junction with dyskeratotic keratinocytes. (Hematoxylin-eosin stain.)

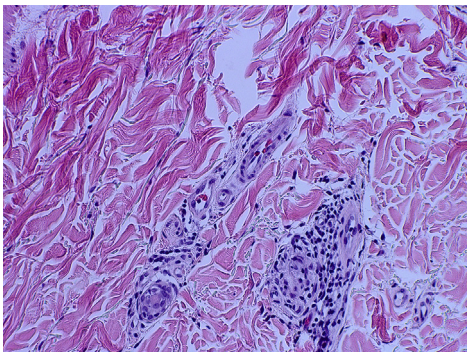

Fig 5. Perieccrine lymphocytic infiltrate. (Hematoxylin-eosin stain.)

drug eruption. Because idiopathic lichen striatus spontaneously resolves in most cases, the argument could be made that the disappearance of our

patient's lichenoid eruption is insufficiently supportive of a drug reaction.[4,12] However, the timing of resolution of our patient's reaction is more supportive of drug-induced lichen striatus, as idiopathic lichen striatus resolves after an average duration of 1 year.[4,12] It is also possible that the true inflammatory component of the rash may have lasted less than 6 months, and the latter end of this stated duration may have simply represented post-inflammatory hyperpigmentation. Because follow-up occurred after resolution of the rash, we cannot state with certainty how long the lichen striatus truly lasted. Rechallenge with interferon was discussed with our patient but was not a feasible option, as he experienced significant depression throughout the course of treatment and expressed resistance to rechallenge with the medication. Finally, the viral load recorded in our patient is supportive of a relation of lichen striatus to interferon rather than to underlying hepatitis C. At the start of interferon therapy, viral load was 5,965,981 IU/mL. By week 8 of therapy, viral load became undetectable and remained so for the remaining 20 weeks of therapy. The patient's lichenoid eruption appeared after he received 24 injections of interferon during this period of an undetectable viral load. Because the eruption appeared after introduction of interferon, and because a 16-week aviremic period was demonstrated, we believe the patient's lichenoid eruption is more likely to be related to the interferon rather than hepatitis C.

Mosaic dermatoses (such as lichen striatus) triggered by medications are notable examples of the interaction between environmental stimuli and genotype, which allows the upregulation of a self-reactive lymphocytic response.[11,12] In our patient, interferon triggered a self-inflammatory response in the cells residing along Blaschko lines, rendering mosaicism phenotypically apparent. Although it is well known that anti-TNF therapy can induce segmental lichenoid reactions, direct evidence of interferon in the induction of these cutaneous eruptions is lacking.[2] We believe our case lends direct support to the hypothesis of interferon playing a central role in autoimmune dermatoses in the setting of TNF-α inhibition.

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