Drug-induced pityriasis lichenoides from infliximab in a patient with juvenile idiopathic arthritis

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INTRODUCTION

Pityriasis lichenoides, which includes 2 subtypes, pityriasis lichenoides et varioliformis acuta (PLEVA) and pityriasis lichenoides chronica (PLC), is a rare disease that can range from an acute, inflammatory eruption to a mild, chronic form. PLEVA, the acute, severe subtype, can result in erythematous patches that progress to papules that can become hemorrhagic or crusted.[1] The chronic form of pityriasis lichenoides, PLC, usually presents as papules that gradually progress to flat patches and are typically not associated with pain and itching, compared with the lesions seen in PLEVA. Despite these 2 distinct subtypes, an overlap can sometimes occur, with lesions resembling both PLEVA and PLC.[1] We present a pediatric case of pityriasis lichenoides with overlapping features of PLEVA and PLC, which was incited by the infliximab therapy used for the treatment of juvenile idiopathic arthritis.

Abbreviations used:

PLC:	pityriasis lichenoides chronica
PLEVA:	pityriasis lichenoides et varioliformis acuta
TNF:	tumor necrosis factor

CASE REPORT

A 15-year−old girl with a past medical history of juvenile idiopathic arthritis presented with a painful, pruritic, generalized rash that had been present for 3 weeks. To help control her symptoms of juvenile idiopathic arthritis, she had undergone multiple treatments, including etanercept, adalimumab, and nonsteroidal anti-inflammatory drugs. She had taken etanercept for 13 years, before switching to adalimumab. Methotrexate was added 1 month before switching biologics because of poor control of her arthritic symptoms. She took adalimumab for 3 months and switched medications from adalimumab to infliximab. When the infliximab infusions were initiated, she received treatment every 4 weeks for approximately 3 months; the treatment was subsequently increased to every 3 weeks. Her mother noticed the rash shortly after the first infusion of infliximab with increased frequency.

Physical examination revealed red, scaly papules and plaques located mostly on her extremities (Figs 1 and 2). Pertinent medical history included the presence of a recent respiratory illness, which had resolved by the time she was seen at the clinic. The results of skin scraping and KOH preparation were negative. A punch biopsy specimen was obtained from the back of her right upper arm, which revealed a section of skin showing hyperkeratosis with areas of confluent parakeratosis, mild irregular hyperplasia, and mild intraepidermal intercellular edema (spongiosis). Within the dermis, there was a moderately dense and lichenoid inflammatory infiltrate of lymphocytes and mononuclear cells, which obscured the dermoepidermal junction, and scattered dyskeratotic keratinocytes were noted (Fig 3). In addition, there was extension of lymphocytes around vessels of the superficial plexus. The deep vascular plexus was uninvolved. Periodic acid−Schiff stain for fungi was negative. Treatment

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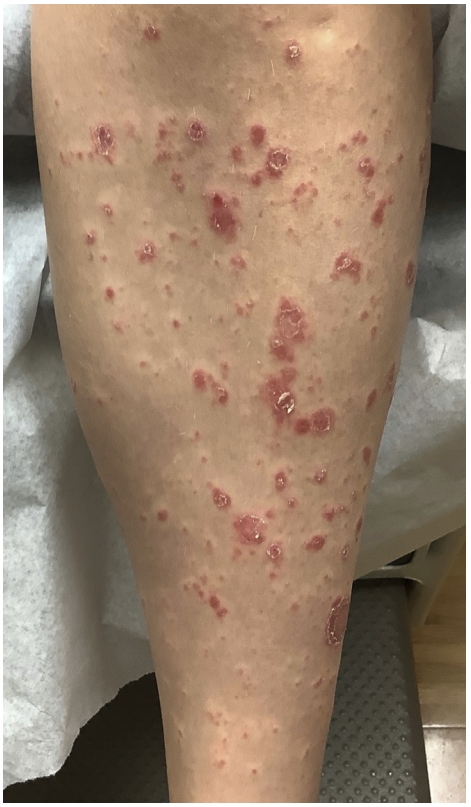

Fig 1. Pityriasis lichenoides lesions with trailing scale on the lower portion of the left leg.

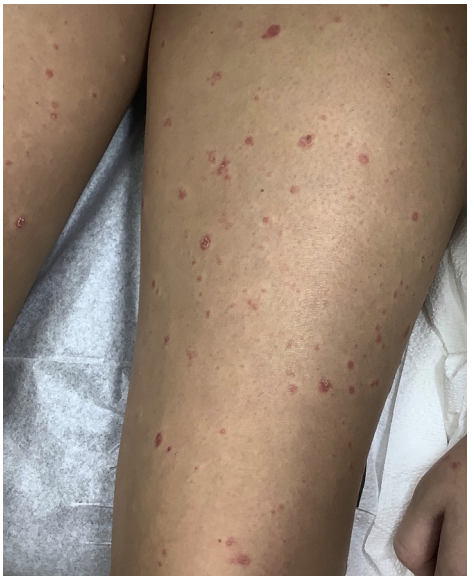

Fig 2. Pityriasis lichenoides lesions with trailing scale on the upper portion of the left leg.

included application of triamcinolone (0.1%) topical cream on the lesions, exposure to light, and cessation of infliximab. Owing to the resolution of her lesions with the cessation of the infliximab therapy, her clinical presentation, and the histopathologic findings, drug-induced pityriasis lichenoides with overlapping PLEVA and PLC from infliximab therapy was diagnosed.

DISCUSSION

Pityriasis lichenoides, including the subtypes PLEVA and PLC, is not very well understood, with multiple theories of the etiology, including infection, immune-complex hypersensitivity vasculitis, and lymphoproliferative disorder.[1] The acute subtype, PLEVA, presents as erythematous patches that progress to painful, pruritic papules that may have a hemorrhagic crust, whereas the chronic subtype, PLC, typically presents as symptomless papules that gradually flatten into plaques.[1] Comparison of the histologic findings of PLEVA and PLC indicates that PLEVA commonly has both a superficial and a deep dermal lymphocytic infiltrate that is typically wedge-shaped, whereas PLC commonly has a superficial dermal infiltrate. The histologic findings of PLEVA can also include a necrotic, hemorrhagic crust, with thinning of the granular layer, whereas PLC has no crust or preservation of the granular layer.[2] A vacuolar interface dermatitis is also seen in PLEVA, unlike PLC, which has an obscured dermoepidermal junction. Because PLEVA and PLC are on a disease spectrum, their clinical and histologic features can overlap.

In addition to drug-induced PLEVA and PLC, the differential diagnosis included lichenoid drug eruption caused by treatment with infliximab, a tumor necrosis factor α (TNF-α) inhibitor. It is known that TNF-α inhibitors can cause a wide array of cutaneous reactions, including lichenoid drug eruption and other lichenoid reactions.[3,4] Although lichenoid drug eruptions can sometimes mimic pityriasis lichenoides, with overlapping histopathologic findings, lichenoid drug eruptions usually occur after several months of the offending drug therapy and are known to worsen after subsequent exposure to the same class of the offending drug. Our patient did not have a rash before the infliximab treatment, despite having previously taken the other TNF-α inhibitors, etanercept and adalimumab. Lichenoid drug eruptions often have histopathologic features resembling lichen planus, including irregular epidermal hyperplasia with elongation of the rete pegs and a prominent bandlike lymphocytic infiltrate.[5] Eosinophils may also be present. These features were not identified in this case.

Although the etiology of pityriasis lichenoides is poorly understood, we believe that this case may point more toward immune dysregulation as a cause. TNF blockade is known to upregulate type 1

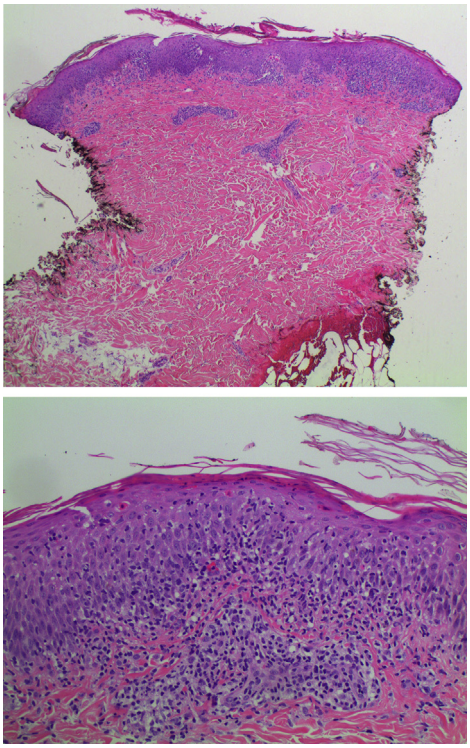

Fig 3. Punch biopsy of the back of the upper portion of the right arm.

interferons via plasmacytoid dendritic cells.[6] This imbalance of TNF-α and type 1 interferons is thought to be the cause of the paradoxical psoriasis sometimes seen with TNF-α inhibitors.[7] PLEVA, specifically, has been shown to increase the level of plasmacytoid dendritic cells, along with TNF-α.[8] We propose a similar mechanism as the cause of TNF-α—induced pityriasis lichenoides, with overlap between PLEVA and PLC with decreased TNF-α from blockade with subsequently increased type 1 interferon, leading to the clinical and histologic presentation of pityriasis lichenoides.

Conflicts of interest

None disclosed.

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