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Tumor necrosis factor-α inhibitor-induced follicular psoriasiform eruption

Tal Goldberger MD[1] | Stephanie Benshushan MD[2] | Zev Davidovics MD[3] | Michael Wilschanski MD[3] | Vered Molho-Pessach MD[1]

[1]Department of Dermatology, The Faculty of Medicine, Hebrew University of Jerusalem, Hadassah Medical Center, Jerusalem, Israel

[2]Department of Pathology, The Faculty of Medicine, Hebrew University of Jerusalem, Hadassah Medical Center, Jerusalem, Israel

[3]Department of Pediatric Gastroenterology, The Faculty of Medicine, Hebrew University of Jerusalem, Hadassah Medical Center, Jerusalem, Israel

Correspondence
Vered Molho-Pessach, Pediatric Dermatology Service, Department of Dermatology, Hadassah-Hebrew University Medical Center, Kiryat Hadassah, POB 12000, Jerusalem 9112001, Israel.
Email: rverem@hadassah.org.il

Abstract

Tumor necrosis factor-α inhibitor-associated adverse cutaneous reactions are common in patients with inflammatory bowel disease. Infection-related dermatoses and psoriasiform eruptions are seen most frequently. We describe a follicular psoriasiform eruption that appeared during treatment with infliximab in two adolescents with Crohn's disease.

KEYWORDS
drug reaction, inflammatory disorders, psoriasis

1 | INTRODUCTION

Psoriasis and infectious folliculitis are both well-known tumor necrosis factor-α (TNF-α) inhibitor-associated adverse cutaneous reactions in patients with inflammatory bowel disease (IBD).[1–4] These cutaneous reactions are often difficult to treat and may impose physical and emotional distress. We observed a follicular psoriasiform eruption in two adolescents with Crohns disease during treatment with infliximab. This pattern of psoriasiform eruption with follicular accentuation in association with TNF-α inhibitor treatment is underrecognized.

2 | PATIENT 1

A 13-year-old boy presented to our clinic with a widespread rash which appeared 13 months following the initiation of infliximab therapy at a maximal dosage of 7 mg/kg every 4 weeks for Crohn's disease. Concurrent treatment with budesonide 3 mg daily was used during the first 3 weeks of infliximab. The patient had a familial, but

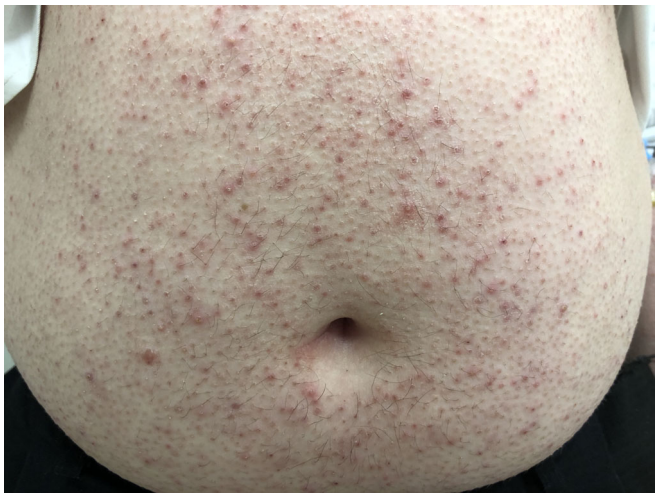

FIGURE 1 Abdominal eruption consisting of tiny follicular papules covered with fine white scale, erythematous follicular papules and pustules in patient 1

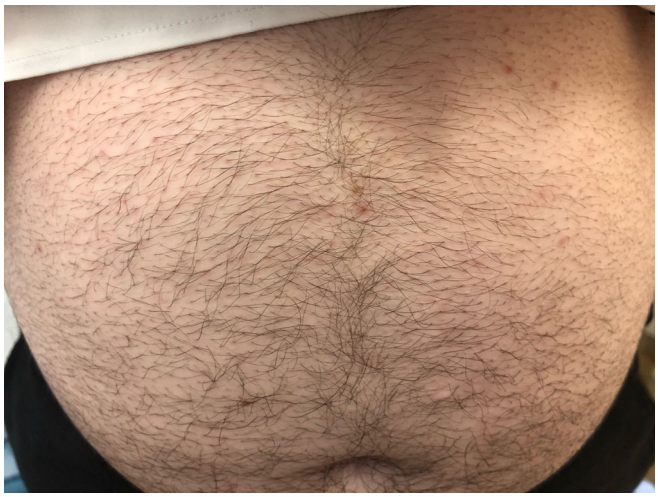

FIGURE 2 Clinical findings in patient 1 following the discontinuation of infliximab and the initiation of treatment with ustekinumab

no personal history of psoriasis and his Crohn's disease was responding well to infliximab.

Skin examination demonstrated a widespread symmetric eruption with tiny erythematous follicular papules covered with white scale, follicular pustules (Figure 1), and erythematous plaques with mild scale over the scalp, behind the ears, in the axillae, gluteal, and inguinal folds, clinically consistent with inverse psoriasis. Bacterial culture from a follicular pustule was positive for methicillin-susceptible *Staphylococcus aureus* (MSSA). A 3-mm punch biopsy of a follicular papule demonstrated psoriasiform acanthosis overlying a predominantly lymphocytic folliculitis. The infiltrate was strongly CD3 positive, with sparse CD20 on immunohistochemistry. No bacteria or fungi were visualized.

The patient was treated with topical glucocorticoids (mometasone furoate, betamethasone valerate), mupirocin, and pimecrolimus cream, chlorhexidine gluconate rinse, and narrow-band UVB (27 treatments) without improvement. Methotrexate was commenced (15 mg/kg/week) with partial response. Doxycycline 100 mg twice daily for several months and cephalexin 1000 mg three times a day for 2 weeks did not yield significant improvement. Following a consultation with the Pediatric Gastroenterology Unit, infliximab treatment was halted and ustekinumab 90 mg every 8 weeks was initiated to treat his Crohn's disease, with gradual and continuous improvement of the eruption, which almost cleared 8 months later (Figure 2).

3 | PATIENT 2

A 13-year-old girl presented with a widespread rash which appeared 12 months following initiation of infliximab therapy for Crohn's disease. The patient had a favorable response to infliximab at a dosage of 5 mg/kg every 8 weeks. During the first 3 months of infliximab treatment, she was treated concomitantly with azathioprine 100 mg daily and mesalamine 1000 mg three times daily. She had a familial but no personal history of psoriasis.

Physical examination revealed a widespread symmetric eruption with tiny erythematous follicular papules with fine scale, as well as follicular pustules (Figure 3), along with intertriginous erythematous plaques with variable silvery-white scale. Bacterial culture from a follicular pustule grew MSSA. A 3-mm punch biopsy of a follicular papule demonstrated acanthosis with focal parakeratosis overlying folliculitis with a mixed lymphocytic and neutrophilic infiltrate. No bacteria or fungi were observed.

The patient was treated with topical corticosteroids (mometasone furoate, betamethasone valerate), tacrolimus ointment, topical erythromycin, chlorhexidine gluconate rinse, narrow-band UVB (30 sessions), oral doxycycline 100 mg twice daily for several months (without concomitant phototherapy), and cephalexin 1000 mg three times a day for 2 weeks. The eruption resolved, which enabled the continuation of infliximab treatment. She experienced a relapse of the eruption 7 months later; therefore, infliximab was discontinued and the patient started on ustekinumab 90 mg every 8 weeks, with gradual improvement 8 weeks later (Figure 3C).

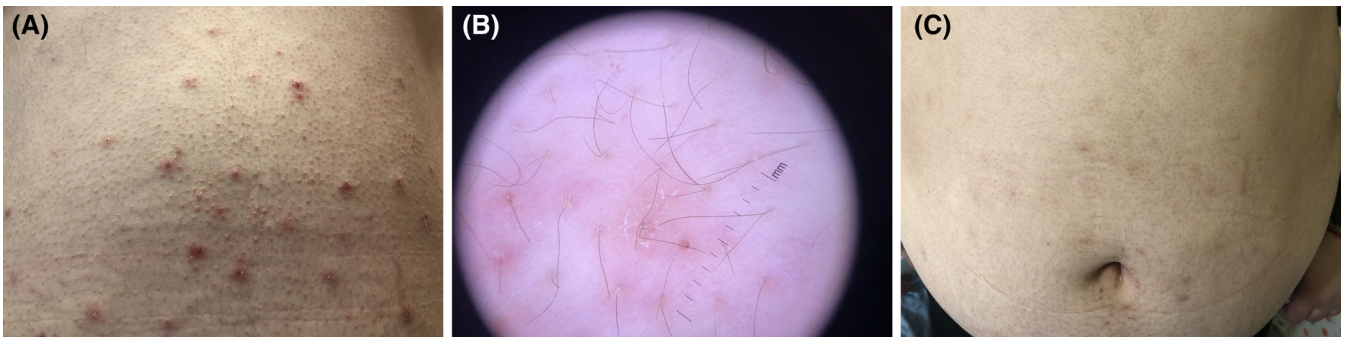

FIGURE 3 A, Abdominal eruption consisting of tiny erythematous follicular papules covered with white scale, and several pustules. B, Dermoscopy of the follicular rash. C, Clinical findings in patient 2 following the discontinuation of infliximab and the initiation of treatment with ustekinumab

4 | DISCUSSION

We present two adolescents with Crohn's disease who developed a follicular psoriasiform eruption associated with treatment with a TNF-α inhibitor, with simultaneous appearance of both follicular and the psoriasiform features approximately 1 year into infliximab treatment. TNF-α inhibitors have cutaneous side effects in approximately a quarter of rheumatologic and IBD patients.[5] In a large cohort of 732 adult IBD patients treated with the infliximab and adalimumab, the largest subgroup of cutaneous adverse events was infection-related dermatoses (13.5%) such as erysipelas, folliculitis, fungal, viral and parasitic eruptions, while psoriasiform eruptions (5.3%) were the next largest subgroup.[1] In contrast, in a cohort of 343 pediatric IBD patients treated with TNF-α inhibitors, psoriasiform eruptions were the most common skin manifestation (5.8%), located mostly in the folds and the scalp, while skin infections (2.9%) and eczematous eruptions (1.5%) were less common.[6] In this cohort, a bacterial superinfection was diagnosed in 25% of the patients with psoriasiform eruptions. In another large cohort of 409 pediatric patients treated with TNF-α inhibitors for IBD, psoriasiform eruptions were also the most common cutaneous side effect, and were more likely associated with infliximab than with adalimumab.[7] TNF-α inhibitor-induced psoriasiform eruptions are not confined to IBD patients and have been described in children with various inflammatory disorders.[8]

Unlike previously described TNF-α inhibitor-induced psoriasiform eruptions, a psoriasiform eruption with marked follicular accentuation, as seen in our patients, has not been clearly described in the literature. We identified a single report with similar histopathology but lacking clinical images and detailed description, and a second report, without clinical images, in which psoriasiform lesions appeared 3 years after the onset of the follicular lesions, unlike the concurrent polymorphic appearance presented in our cases.[3,9] The follicular nature of the eruption in our patients raised several differential diagnoses, including follicular psoriasis, pityriasis rubra pilaris and follicular mycosis fungoides. However, the association with TNF-α inhibitor treatment, the histopathological findings, and the marked improvement with cessation of infliximab support the diagnosis of a TNF-α inhibitor-induced psoriasiform follicular eruption. Despite isolation of MSSA in both of our patients, we believe the etiology of the follicular psoriasiform eruption described here is not infectious. This is supported by the lack of pathogens in histopathology, the polymorphic nature of the eruption, and by the lack of satisfactory response to multiple culture-guided antimicrobial treatments. The MSSA was likely a secondary superimposed pathogen. We believe this pattern of follicular psoriasiform eruption induced by TNF-α inhibitors is under recognized, and increased awareness of this novel morphology of TNFα inhibitors' cutaneous adverse reaction will enable better delineation of its risk factors, clinical behavior, and treatment.

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CONFLICT OF INTEREST

The authors have no conflicts of interest to disclose.

DATA AVAILABILITY STATEMENT

Data sharing not applicable to this article as no datasets were generated or analysed during the current study

ORCID

Tal Goldberger https://orcid.org/0000-0002-5232-4969

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