SAGE Open Medical Case Reports

SAGE Open Medical Case Reports
JCMS Case Reports
Volume 8: 1–4

DOI: 10.1177/2050313X20901967
journals.sagepub.com/home/sco
SAGE

Lichen planopilaris induced by infliximab: A case report

Meghan L McPhie[1], Ami Wang[2], Sonja Molin[3] and Thomas Herzinger[3]

Abstract

Infliximab is a tumor necrosis factor-alpha inhibitor used to treat a range of inflammatory diseases. Most reports of cutaneous eruptions from tumor necrosis factor-alpha inhibitors have described the paradoxical development of psoriasis or psoriasiform drug reaction. In our report, we present a 31-year-old female with inflammatory bowel disease who developed an unusual lichenoid drug reaction to infliximab involving the hair follicles, resulting in progressive global alopecia. Clinical features and histopathological findings were consistent with drug-induced lichen planopilaris with eosinophils and lichenoid dermatitis.

Keywords

Infliximab, TNF-alpha inhibitors, lichenoid dermatitis, lichen planopilaris, drug eruption

Infliximab is a chimeric (human/mouse) monoclonal IgG1 anti-tumor necrosis factor-alpha (TNF-α) antibody.[1] It works by inhibiting the activity of TNF-α, a key pro-inflammatory cytokine involved in chronic inflammatory diseases. Infliximab is indicated for the treatment of various inflammatory disorders, such as rheumatoid arthritis, psoriatic arthritis, inflammatory bowel disease (IBD), ankylosing spondylitis, and psoriasis.

A variety of cutaneous adverse reactions have been reported in patients taking TNF-α inhibitors, including lichen planus–like eruptions,[2] psoriasis,[3] eczematous dermatitis,[4] alopecia areata,[5] and cutaneous manifestations of systemic lupus erythematosus.[6] A cohort study examining the long-term safety of infliximab for the treatment of IBD reported that 20% of patients experienced various skin eruptions while receiving therapy, most commonly psoriasiform dermatitis and eczema.[7] Lichenoid eruptions are a less common adverse effect of infliximab therapy, with only a few reports describing a paradoxical reaction with alopecia. Here, we describe a case of a patient with ulcerative colitis who developed drug-induced lichenoid dermatitis and lichen planopilaris (LPP) when treated with infliximab.

Case report

A 31-year-old Caucasian female presented to the dermatology outpatient clinic for evaluation and management of a widespread itchy rash and progressive hair loss. Prior to presenting to dermatology, the patient was started on intravenous infliximab for her IBD (ulcerative colitis) in January 2018. She first became symptomatic a couple of days after her initial infliximab infusion, with the development of widespread pruritus. The patient received a second loading dose and developed severe pruritus and a rash, which was more pronounced over her abdomen. It took until September 2018 for the rash to completely clear. In January 2019, the patient had a flare of her ulcerative colitis, which prompted the re-initiation of infliximab. Two weeks after her infliximab infusion, the patient developed a pruritic rash, which involved almost all of her integument, as well as marked alopecia involving 60% of her scalp and eyebrows. Her rash and severe pruritus failed to improve with conventional therapy, including 35 mg of oral prednisone daily and topical betamethasone valerate 0.1% ointment twice daily.

Upon presentation to dermatology in March 2019, the patient had a rash of grouped and confluent, flat-topped, erythemato-violaceous papules disseminated in a symmetric fashion over her trunk and extremities. Her palms and soles

[1]School of Medicine, Queen's University, Kingston, ON, Canada
[2]Department of Pathology and Molecular Medicine, Queen's University, Kingston, ON, Canada
[3]Division of Dermatology, Department of Medicine, Queen's University and Hotel Dieu Hospital, Kingston, ON, Canada

Corresponding Author:
Thomas Herzinger, Division of Dermatology, Department of Medicine, Queen's University and Hotel Dieu Hospital, Centenary 3-027, 166 Brock Street, Kingston, ON K7L 5G2, Canada.
Email: t.herzinger@queensu.ca

showed macular erythema (Figure 1). Her oral cavity did not show signs of a lichenoid rash, but some white film suggestive of oral thrush. On the scalp, the patient had mottled alopecia with intact hair follicles and perifollicular erythema (Figure 2). Dermoscopy of the scalp showed yellow dots.

Two skin punch biopsies were taken, one from the scalp and one from the dorsum of the right foot. The biopsy from the scalp showed mild perivascular and heavy lichenoid lymphocytic infiltrate of the hair follicles that focally obscured the junction between follicular epithelium and dermis, and extended into the basal follicular epithelium (Figure 3). Scattered eosinophils were also identified, in keeping with the drug-induced LPP. The biopsy from the right foot also displayed moderately intense lichenoid lymphocytic infiltrate at the dermoepidermal junction, with mild perivascular lymphocytic inflammation. Also apparent were patches of spongiosis associated with prominent lymphocytic exocytosis. Parakeratosis and individual apoptotic keratinocytes were identified.

Although the patient's IBD responded well to infliximab, the medication was discontinued due to poor tolerance. The patient continued with her regime of 35 mg of prednisone daily supplemented by topical betamethasone 0.1% valerate cream twice daily to cutaneous lesions, which resulted in partial improvement.

Discussion

Lichenoid drug eruptions are much less common than morbilliform drug exanthema or urticaria. They are often caused by certain drugs or drug classes, such as gold, antimalarial drugs, and beta-blockers.[8] Most reports of cutaneous eruptions from TNF-α inhibitors have described the paradoxical development of psoriasis and psoriasiform drug reaction; however, lichenoid reactions represent an emerging adverse effect of novel drugs such as anti-TNF-α therapy. We describe a case of patient who

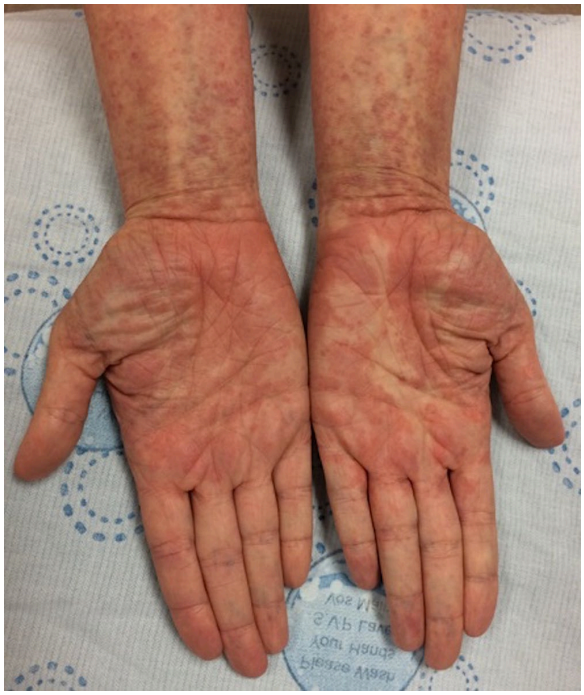

Figure 1. Macular erythema of the palmar aspect of the hand and flat-topped, erythemato-violaceous papules on the distal aspect of the volar forearm.

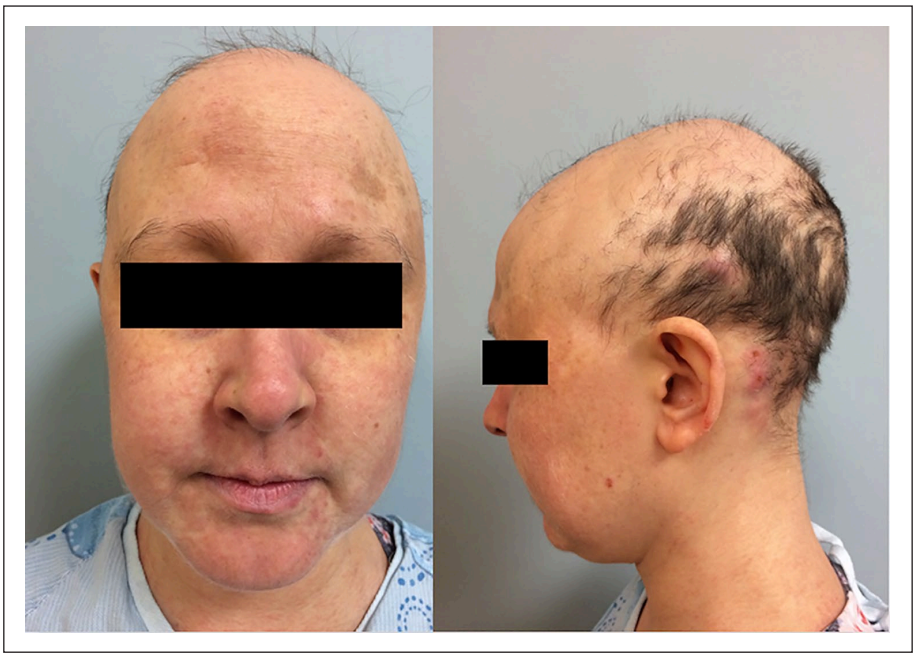

Figure 2. Mottled alopecia of the scalp and eyebrows.

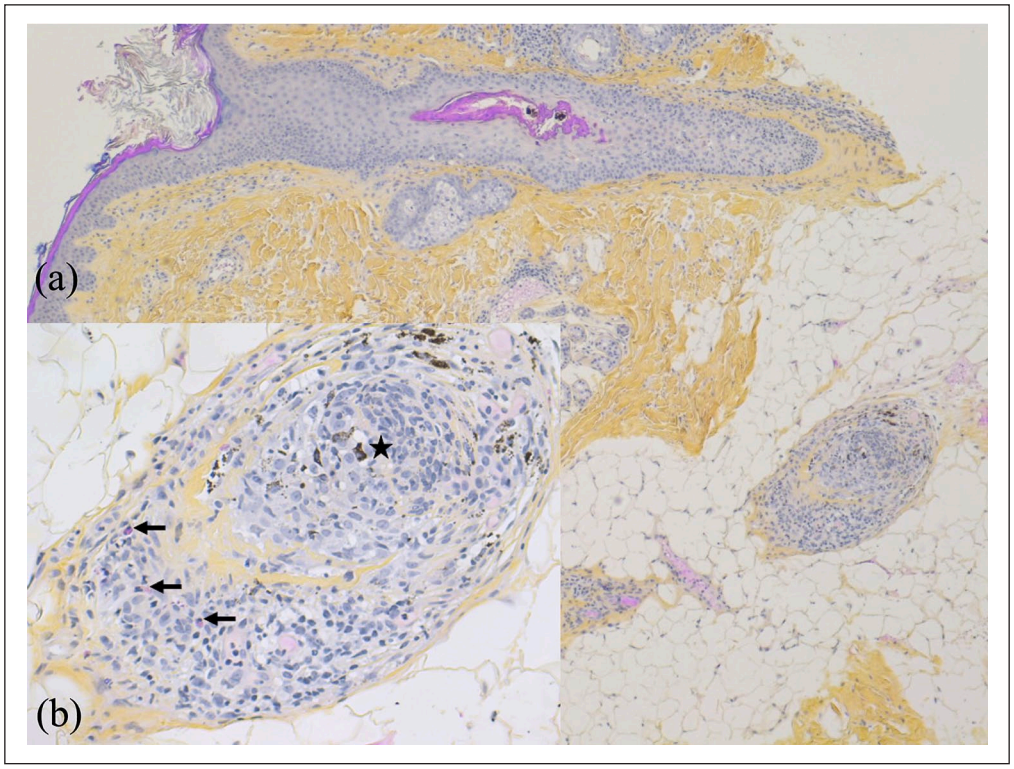

Figure 3. (a) Lichenoid interface dermatitis involving the hair follicles with hematoxylin phloxine saffron (HPS) stain and 50× magnification; (b) lichenoid inflammatory infiltrate around the hair bulb (star) composed of predominantly lymphocytes with scattered eosinophils (arrows) with HPS stain and 100× magnification.

developed lichenoid dermatitis and LPP while on the TNF-α inhibitor, infliximab, for the treatment of her IBD.

Four patterns of lichenoid reactions have been described in the literature based on their unique clinical features and common lichenoid histology: lichen planus, maculopapular lichenoid reaction, psoriasis-like with lichen planus histology, and LPP.[9] A recent review of the literature revealed 21 reported cases of lichenoid reactions to various TNF-α inhibitors.[10] These cases have been reviewed and summarized elsewhere.[2,9,10]

LPP is the most recent cutaneous lichenoid adverse reaction to anti-TNF-α therapy, with the first case reported by Garcovich et al.[11] in 2008 from etanercept. LPP is a lymphocytic inflammatory disorder that selectively involves the hair follicles, leading to a scarring alopecia that presents with perifollicular erythema, hyperkeratosis, and patchy hair loss. To our knowledge, there are only five other reported cases of anti-TNF-α-induced LPP, with only one resulting from infliximab.[9–13]

The pathophysiology of anti-TNF-α-induced lichenoid eruption is yet to be elucidated;[2] however, a number of mechanisms have been proposed using models of psoriasis, lupus-like eruptions, and dermatomyositis. Some authors have suggested that the inhibition of TNF-α leads to upregulation of opposing cytokines, such as interferon-alpha (IFN-α), which may activate T cells and dendritic cells, resulting in an inflammatory reaction.[14] Similarly, it has also been proposed that in select genotypes the effect of TNF-α inhibition might disrupt the delicate immune milieu, thereby accelerating IFN-α production and triggering pathological activation of T cells and dendritic cells.[3,15] Plasmacytoid dendritic cells are the primary source of IFN-α and have been found in great abundance in cutaneous and oral lichen planus lesions.[16,17] Furthermore, there is evidence that type 1 IFNs (IFN-α and IFN-β) play an important role in the pathogenesis of lichen planus through activation of cytotoxic $CD8^+$ T cells, which have the ability to autoactivate against keratinocytes.[18]

Recent research on LPP has demonstrated decreased expression of peroxisome proliferator-activated receptor gamma (PPARγ), a transcription factor that regulates the expression of genes involved in inflammation and lipid homeostasis. PPARγ is important for healthy pilosebaceous units, and loss of function has been implicated in the pathogenesis of LPP.[19] INF and TNF can reduce PPARγ expression; therefore, it is thought that unopposed IFN may result in the downregulation of PPARγ, thereby leading to the development of LPP in patients on TNF-α inhibitors.[9,19]

Lichenoid eruptions represent a rare adverse effect of TNF-α inhibitors. We describe a case of a patient who presented with lichenoid dermatitis and LPP from infliximab. Clinicians managing patients with immune conditions should be aware of this adverse reaction to biologics. It is uncertain whether a

lichenoid eruption warrants discontinuation of TNF-α therapy; however, the decision should be made on an individual basis.[11]

Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Ethical approval

Ethical approval was granted through the Health Sciences and Affiliated Hospitals Research Ethics Board.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

Informed consent

Informed written consent was obtained for patient information and images to be published.

References

1. Klotz U, Teml A and Schwab M. Clinical pharmacokinetics and use of infliximab. *Clin Pharmacokinet* 2007; 46: 645–660.
2. Asarch A, Gottlieb AB, Lee J, et al. Lichen planus-like eruptions: an emerging side effect of tumor necrosis factor-α antagonists. *J Am Acad Dermatol* 2009; 61: 104–111.
3. de Gannes GC, Ghoreishi M, Pope J, et al. Psoriasis and pustular dermatitis triggered by TNF-alpha inhibitors in patients with rheumatologic conditions. *Arch Dermatol* 2007; 143(2): 223–231.
4. Lee HH, Song IH, Friedrich M, et al. Cutaneous side-effects in patients with rheumatic diseases during application of tumour necrosis factor-a antagonists. *Br J Dermatol* 2007; 156: 486–491.
5. Ormaechea-Pérez N, López-Pestaña A, Muñagorri-Santos AI, et al. Alopecia areata in a patient receiving infliximab. *Indian J Dermatol Venereol Leprol* 2013; 79: 529–531.
6. Costa MF, Said NR and Zimmermann B. Drug-induced lupus due to anti-tumor necrosis factor α agents. *Semin Arthritis Rheum* 2008; 37: 381–387.
7. Fidder H, Schnitzler F, Ferrante M, et al. Long-term safety of infliximab for the treatment of inflammatory bowel disease: a single-centre cohort study. *Gut* 2009; 58(4): 501–508.
8. Merk HF, Vanstreels L and Megahed M. Lichenoid drug reactions. *Hautarzt* 2018; 69: 116–120.
9. McCarty M, Basile A, Bair B, et al. Lichenoid reactions in association with tumor necrosis factor alpha inhibitors: a review of the literature and addition of a fourth lichenoid reaction. *J Clin Aesthet Dermatol* 2015; 8(6): 45–49.
10. Jayasekera PSA, Walsh ML, Hurrell D, et al. Case report of lichen planopilaris occurring in a pediatric patient receiving a tumor necrosis factor α inhibitor and a review of the literature. *Pediatr Dermatol* 2016; 33: e143–e146.
11. Garcovich S, Manco S, Zampetti A, et al. Onset of lichen planus during treatment with etanercept. *Br J Dermatol* 2008; 158: 1161–1163.
12. Fernandez-Torres R, Paradela S, Valbuena L, et al. Infliximab-induced lichen planopilaris. *Ann Pharmacother* 2010; 44(9): 1501–1503.
13. Abbasi NR and Orlow SJ. Lichen planopilaris noted during etanercept therapy in a child with severe psoriasis. *Pediatr Dermatol* 2009; 26(1): 118–118.
14. Seneschal J, Milpied B, Vergier B, et al. Cytokine imbalance with increased production of interferon-α in psoriasiform eruptions associated with antitumour necrosis factor-α treatments. *Br J Dermatol* 2009; 161: 1081–1088.
15. Fiorentino DF. The yin and yang of TNF-alpha inhibition. *Arch Dermatol* 2007; 143(2): 233–236.
16. De Vries HJ, van Marle J, Teunissen MB, et al. Lichen planus is associated with human herpesvirus type 7 replication and infiltration of plasmacytoid dendritic cells. *Br J Dermatol* 2006; 154(2): 361–364.
17. Santoro A, Majorana A, Roversi L, et al. Recruitment of dendritic cells in oral lichen planus. *J Pathol* 2005; 205(4): 426–434.
18. Wenzel J, Scheler M, Proelss J, et al. Type I interferon-associated cytotoxic inflammation in lichen planus. *J Cutan Pathol* 2006; 33(10): 672–678.
19. Karnik P, Tekeste Z, McCormick TS, et al. Hair follicle stem cell-specific PPARγ deletion causes scarring alopecia. *J Invest Dermatol* 2009; 129: 1243–1257.