

BRIEF ARTICLES

**Extensive Tinea Associated with Tofacitinib Therapy
Masquerading as New-Onset SCLE**Connor R. Buechler BS¹, Elena Kurland MD², Jesse Veenstra MD, PhD²¹Wayne State University School of Medicine, Detroit, MI²Department of Dermatology, Henry Ford Health System, Detroit, MI**ABSTRACT**

Rheumatoid arthritis is a chronic autoimmune disorder that often requires treatment with immunomodulatory agents. However, such interventions are not without risk of opportunistic infection. Monitoring for such conditions is critical, though recognition and treatment can prove challenging, as they may manifest atypically or masquerade as another condition entirely. We present a case of extensive tinea corporis with concomitant tinea capitis masquerading as new-onset SCLE in a patient being treated for rheumatoid arthritis with the Janus kinase inhibitor tofacitinib.

INTRODUCTION

Fungi of the genera *Microsporum*, *Trichophyton*, and *Epidermophyton* are frequent colonizers of the epidermis. Each is normally readily controlled by the immune system, and therapies that dampen immune surveillance can predispose to fungal colonization. These infections, commonly referred to as tinea or dermatophytosis, can mimic a number of other cutaneous conditions, such as psoriasis, parapsoriasis, atopic dermatitis, mycosis fungoides, lupus and other connective tissue disorders complicating diagnosis in the absence of elevated clinical suspicion.¹ Tofacitinib is a small-molecule Janus kinase inhibitor that is approved for treatment of adults with rheumatoid arthritis, psoriatic arthritis, or ulcerative colitis who have had inadequate response to or were intolerant of methotrexate.² While infrequent cases of tinea pedis were observed in some clinical

trials,^{3,4} there have as yet been no reports of more generalized dermatophytosis as a result of tofacitinib therapy. Here, we report an interesting case of extensive tinea corporis and capitis developing in a woman shortly after starting tofacitinib treatment for rheumatoid arthritis.

CASE PRESENTATION

A 71-year-old African American woman presented with an intermittently pruritic rash on the upper body, beginning three months prior. She stated that this rash had spread from her stomach to her chest, back, shoulders, and scalp during this time. She denied recent fevers, chills, illnesses, unintentional weight loss, changing or bleeding lesions, or oral lesions. She did admit to recent weakness and hair loss, and EMR review revealed a recent visit with chief complaint of unexplained weight loss. Her past medical history was significant for a

September 2020 Volume 4 Issue 5

three-year history of inadequately controlled rheumatoid arthritis, for which tofacitinib 5mg BID was recently added to her prior regimen of prednisone 10mg daily after she was unable to tolerate methotrexate. She started tofacitinib approximately 1-month prior to onset of the rash.

Autoimmune workup in the past had been significant for ANA 1:640 (homogenous pattern) and negative DsDNA, RNP antibody, Smith antibody, SSA, SSB and complement C3 and C4 within normal limits. On exam there was diffuse poorly adherent white scale throughout the scalp (Figure 1), scattered erythematous papules on the infraorbital medial cheeks and upper cutaneous lip (Figure 2), large geometric to annular, well-demarcated, erythematous to hyperpigmented patches and thin plaques with erythematous raised plaques along the borders and diffuse fine scale on the upper chest (Figure 3), back, shoulders, neck, conchal bowls, axillae, and abdomen. KOH prep of scrapings from the chest showed fungal hyphae. Biopsy of the right upper back was consistent with dermatophytosis, and fungal culture from her scalp grew *Trichophyton* species.

A six-week course of oral terbinafine 250 mg daily resulted in significant reduction in pruritis and normalization of the cutaneous physical findings, with the exception of a mild residual scaling on the scalp which again grew *Trichophyton* on repeat fungal culture at three-month follow-up. A second course of oral terbinafine is in progress.

DISCUSSION

The risk of fungal infection is thought to be increased in those on long-term tofacitinib therapy, largely due to inhibition of signaling via cytokine and chemokine cascades that are necessary for the destruction of fungi.⁵

Clinical trial and long-term follow-up data of patients treated with tofacitinib show an increase in opportunistic infections (OIs) with the median occurrence of non-TB OIs at 40 weeks after treatment onset.⁶ While studies have shown increased incidence of dermatophytosis in those on anti-TNF- α therapy,⁷ there have been no reports of tofacitinib-associated dermatophytosis with the exception of infrequent tinea pedis.^{3,4}

Figure 1. Hair loss and diffuse scaling on the scalp



The present case highlights the need for frequent monitoring for OIs in those receiving immunosuppressant therapy. Our patient exhibited an extensive JAK-inhibitor associated dermatophytosis that developed early in the treatment course, roughly four weeks from the first dose of tofacitinib and well before the median occurrence at 40

weeks. Although it's difficult to determine if the primary tinea infection pre-dated or occurred after initiation of tofacitinib treatment, she had no similar issues while on prednisone or previously with methotrexate. Despite this, there have been reports of exuberant tinea corporis in the context of chronic oral steroid use.⁸ Monitoring for OIs is particularly important as the indications for tofacitinib continue to expand. Additional treatment indications for other conditions, including plaque psoriasis, alopecia areata, vitiligo, and atopic dermatitis, are still under active investigation.⁹

Although terbinafine and griseofulvin are both seen as first-line treatments for tinea capitis, terbinafine has been shown to be more effective for *Trichophyton*-associated

Figure 2. Erythematous papules on the face



cases and requires shorter treatment durations to achieve similar effect.¹⁰ However, as our experience demonstrates, tofacitinib-associated dermatophytosis may require longer or repeated courses of treatment. Close follow-up is warranted to ensure complete resolution, and a prolonged initial course of therapy may be helpful in these immunocompromised patients. If a prolonged or repeated course of therapy is indicated, CBC and liver function tests should be acquired at baseline and periodically during treatment.²

Figure 3. Well-demarcated erythematous thin plaques with fine overlying scale on the chest and neck



In our patient with new-onset face and torso rash, several months of increasing fatigue, recent complaint of weight loss, a strongly positive ANA and uncontrolled autoimmune disease, and known propensity of biologic therapies that alter immune function to paradoxically unmask autoimmune and connective tissue disease,¹¹ it would have been easy to fixate on a diagnosis of new-onset SCLÉ with a differential diagnosis also including dermatomyositis, photodermatitis,

or a nonspecific eczematous process. Dermatophyte infections are infamous for being difficult to diagnose based on appearance alone, further emphasizing the importance of maintaining a high index of suspicion in patients on therapies that may make such infections manifest in ways they might not otherwise—such as extending across the torso, face, and scalp within mere weeks. By avoiding the temptation to anchor on the most straightforward explanation, we were able to perform the appropriate workup to arrive at the true diagnosis. Misdiagnosis of another disease on the differential might have led to treatment with powerful topical steroids that would have exacerbated rather than treated our patient's already extensive infection.

CONCLUSION

Frequent and early skin examinations along with rapid follow-up on cutaneous complaints is a necessary part of care for those undergoing immunosuppressive treatments. Although not previously known to predispose to extensive dermatophytosis, initiation of tofacitinib should be considered a risk factor for such infections, which can be diagnosed with KOH prep and treated with antifungals without the cessation of immunosuppressive therapy.

Conflict of Interest Disclosures: None

Funding: None

Corresponding Author:

Dr. Elena Kurland, MD
3031 W. Grand Blvd
Ste. 800
Detroit, MI 48202
Phone: 313-916-2151
Fax: 313-916-5334
Email: ekurlan1@hfhs.org

References:

1. Atzori L, Pau M, Aste N, Aste N. Dermatophyte infections mimicking other skin diseases: a 154-person case survey of tinea atypica in the district of Cagliari (Italy). *Int J Dermatol*. 2012;51(4):410-415.
2. Xeljanz medication guide. United States Food and Drug Administration. Updated May, 2018. https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/203214s018lbl.pdf. Accessed April 18, 2020. In.
3. Hall S, Nash P, Rischmueller M, et al. Tofacitinib, an Oral Janus Kinase Inhibitor: Pooled Efficacy and Safety Analyses in an Australian Rheumatoid Arthritis Population. *Rheumatol Ther*. 2018;5(2):383-401.
4. Asahina A, Etoh T, Igarashi A, et al. Oral tofacitinib efficacy, safety and tolerability in Japanese patients with moderate to severe plaque psoriasis and psoriatic arthritis: A randomized, double-blind, phase 3 study. *The Journal of Dermatology*. 2016;43(8):869-880.
5. Chen Y, Gong FY, Li ZJ, et al. A study on the risk of fungal infection with tofacitinib (CP-690550), a novel oral agent for rheumatoid arthritis. *Sci Rep*. 2017;7(1):6779.
6. Winthrop KL, Park SH, Gul A, et al. Tuberculosis and other opportunistic infections in tofacitinib-treated patients with rheumatoid arthritis. *Ann Rheum Dis*. 2016;75(6):1133-1138.
7. Bardazzi F, Balestri R, Rech G, Antonucci A, Patrizi A. Dermatophytosis during anti-TNF-alpha monoclonal antibody therapy. *Mycoses*. 2011;54(5):e619-620.
8. Sena LB, Oliveira DC, Paula CD, Costa MC, Franceschi LE, Costa IM. Trichophyton rubrum dermatophytosis in a patient under chronic use of systemic corticoids: an exuberant presentation. *An Bras Dermatol*. 2015;90(4):598-599.
9. Montilla AM, Gómez-García F, Gómez-Arias PJ, et al. Scoping Review on the Use of Drugs Targeting JAK/STAT Pathway in Atopic Dermatitis, Vitiligo, and Alopecia Areata. *Dermatol Ther (Heidelb)*. 2019;9(4):655-683.
10. Newland JG, Abdel-Rahman SM. Update on terbinafine with a focus on dermatophytoses. *Clin Cosmet Investig Dermatol*. 2009;2:49-63.
11. Her M, Kavanaugh A. Alterations in immune function with biologic therapies for autoimmune disease. *J Allergy Clin Immunol*. 2016;137(1):19-27.