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CLINICAL VIGNETTE

Efficacy of Janus Kinase Inhibitors in Difficult-to-Treat Alopecia Universalis

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Alopecia areata (AA) is a common autoimmune skin disease causing hair loss. The most severe form of AA, called alopecia universalis (AU), is characterized by the complete loss of hair on the scalp, face, and body, and is associated with significant psychological distress. Tofacitinib citrate (Xeljanz) is a small molecule selective Janus kinase 1/3 (JAK 1/3) inhibitor that is FDA-approved for the treatment of moderate-to-severe rheumatoid arthritis, psoriatic arthritis, and moderate-to-severe ulcerative colitis. We report a case highlighting the effectiveness of the JAK inhibitor, tofacitinib, in the treatment of refractory AU.

Case Report

The patient is a 41-year-old woman who presented for management of hair loss, which had begun 1 month after a thyroidectomy for thyroid carcinoma. She reported sudden and profound hair loss on the scalp, eyebrows, eyelashes, and face. She had a history of bipolar disorder, on lithium therapy. There was no family history of alopecia. On examination, she had no eyebrows, eyelashes, or facial hair.

She was initially treated with topical steroids in combination with topical minoxidil, with no improvement. Intralesional steroids were not attempted given the extent of her disease. Topical immunotherapy with squaric acid dibutyl ester was given for 6 months with no benefit. Despite adding topical anthralin, her condition remained refractory. Because of the lack of response to multiple topical therapies, the patient was started on off-label tofacitinib at a dose of 11 mg orally daily. The patient declined systemic glucocorticoids and other anti-immune agents such as methotrexate due to fear of toxicities.

After 10 months of treatment with tofacitinib, the patient experienced complete hair regrowth on all the affected body parts. Importantly, no adverse effects were reported in terms of clinical symptoms and abnormal laboratory tests.

Discussion

The recent introduction of JAK inhibitors into the management of several autoimmune diseases has been a landmark progress since the advancement of biologic agents. The JAKs family of kinases comprise four members, JAK1, JAK2, JAK3, and tyrosine kinase 2 (TYK2). JAKs are located intracellularly transmitting extracellular cytokine signals into the cell. Tofacitinib is the first orally administered pan-JAK inhibitor preferentially inhibiting JAK1 and JAK3 and, to a lesser extent,

JAK2 with minimum effect on TYK2.¹ It acts to suppress inflammation by inhibiting multiple cytokine pathways.

The pathogenesis of AA and AU involves marked interferon response, which activates CD8⁺ T cells and contributes to immune privilege collapse of hair follicles.² The JAK signaling pathway serves as a pathway for interferon signaling, and therefore, plays a crucial role in mediating the CD8⁺ T cells reaction. Inhibition of the JAK pathway is an appealing option for the treatment of AA and AU.

Efficacy of tofacitinib in AU was first reported by Craiglow and King in 2014.³ Since then, several retrospective studies have been published. The largest study to date evaluated tofacitinib in 90 patients with AA and its variants.⁴ Sixty-five patients (72%) were classified as potential responders. Of the potential responders, 13 patients (20%) were complete responders.⁴ Ruxolitinib, another JAK inhibitor FDA-approved for the treatment of myelofibrosis with myeloid metaplasia, has also shown favorable response in small case series.⁵

Tofacitinib has a wide range of potential adverse effects including severe bacterial, fungal, mycobacterial, and viral infections (mainly herpes zoster). Other adverse effects include Pancytopenia, and elevated transaminase, cholesterol, and creatinine.^{6,7} The risk of malignancy is still unknown. In addition, tofacitinib is prohibitively expensive. Therefore, a fully informed and responsible treatment decision demands a sober risk–cost–benefit calculation, given that AA is not a life-threatening disease.

JAK inhibitors can change the life of affected AA and AU patients; however, we remain challenged to carefully balance clinical benefits against possible risks and adverse effects. Clearly, trials addressing the long-term efficacy and safety of JAK inhibitors in AA and AU are warranted.

REFERENCES

1. O'Shea JJ, Kontzias A, Yamaoka K, Tanaka Y, Laurence A. Janus kinase inhibitors in autoimmune diseases. *Ann Rheum Dis*. 2013 Apr;72 Suppl 2:ii111-5. doi: 10.1136/annrheumdis-2012-202576. Review. PubMed PMID: 23532440; PubMed Central PMCID: PMC3616338.
2. Petukhova L, Duvic M, Hordinsky M, Norris D, Price V, Shimomura Y, Kim H, Singh P, Lee A, Chen WV, Meyer KC, Paus R, Jahoda CA, Amos CI, Gregersen

PK, Christiano AM. Genome-wide association study in alopecia areata implicates both innate and adaptive immunity. *Nature*. 2010 Jul 1;466(7302):113-7. doi:10.1038/nature09114. PubMed PMID: 20596022; PubMed Central PMCID: PMC2921172.

3. **Craiglow BG, King BA.** Killing two birds with one stone: oral tofacitinib reverses alopecia universalis in a patient with plaque psoriasis. *J Invest Dermatol*. 2014 Dec; 134(12):2988-2990. doi: 10.1038/jid.2014.260. Epub 2014 Jun 18. PubMed PMID: 24940651.
4. **Liu LY, Craiglow BG, Dai F, King BA.** Tofacitinib for the treatment of severe alopecia areata and variants: A study of 90 patients. *J Am Acad Dermatol*. 2017 Jan;76(1): 22-28. doi: 10.1016/j.jaad.2016.09.007. Epub 2016 Nov 2. PubMed PMID:27816293.
5. **Mackay-Wiggan J, Jabbari A, Nguyen N, Cerise JE, Clark C, Ulerio G, Furniss M, Vaughan R, Christiano AM, Clynes R.** Oral ruxolitinib induces hair regrowth in patients with moderate-to-severe alopecia areata. *JCI Insight*. 2016 Sep 22;1(15):e89790. doi: 10.1172/jci.insight.89790. PubMed PMID: 27699253; PubMed Central PMCID: PMC5033756.
6. **Winthrop KL.** The emerging safety profile of JAK inhibitors in rheumatic disease. *Nat Rev Rheumatol*. 2017 Apr;13(4):234-243. doi: 10.1038/nrrheum.2017.23. Epub 2017 Mar 2. Review. Erratum in: *Nat Rev Rheumatol*. 2017 May;13(5):320. PubMed PMID: 28250461.
7. **Chen Y, Gong FY, Li ZJ, Gong Z, Zhou Z, Ma SY, Gao XM.** A study on the risk of fungal infection with tofacitinib (CP-690550), a novel oral agent for rheumatoid arthritis. *Sci Rep*. 2017 Jul 28;7(1):6779. doi: 10.1038/s41598-017-07261-1. PubMed PMID: 28754958; PubMed Central PMCID: PMC5533717.

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