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Excellent response to tofacitinib treatment in a patient with alopecia universalis

Funda Erduran[1]✉, Esra Adışen[2], Ahmet Burhan Aksakal[2]

Abstract

Alopecia universalis (AU) is generally considered a variant of alopecia areata (AA), in which the treatment options seldom provide satisfactory results. However, successful treatment of several cases of AA and its variants with oral Janus kinase (JAK) inhibitors have been reported recently. Here we report a 23-year-old female patient with AU successfully treated with tofacitinib, a selective JAK-3 inhibitor. The initial tofacitinib dose was 5 mg twice daily. After 2 months of treatment, partial hair regrowth was seen on the scalp and eyebrows. Thereafter, the dose was increased to 10 mg in the morning and 5 mg at night. By 6 months of the treatment, there was complete hair regrowth throughout the entire body. Our patient tolerated tofacitinib well, without any significant side effects. Tofacitinib emerges as a promising novel therapy in alopecia universalis. We believe further study is required to establish the safety and confirm the efficacy of tofacitinib treatment for alopecia universalis.

Keywords: tofacitinib, alopecia universalis, Janus kinase inhibitor

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Introduction

Alopecia areata (AA) is an autoimmune disease that presents as well-demarcated patches of nonscarring alopecia on the skin. Alopecia universalis (AU) is generally considered a variant of AA in which there is a complete loss of scalp and body hair. Approximately 5% of cases progress to AU later on (1). Concerning all treatments that have been used in the treatment of AA—including topical/intralesional corticosteroids, systemic corticosteroids, contact immunotherapy, photochemotherapy, minoxidil, and oral cyclosporine—apart from contact immunotherapy, which achieved improvement in some of patients, treatment of AU is not satisfactory (2). Recently, several reports have shown that treatment of AA and its variants with oral Janus kinase (JAK) inhibitors (tofacitinib, ruxolinib, and baricitinib) results in a good clinical response (3–10). Tofacitinib is the first JAK-3 inhibitor investigated in human trials that is approved by the US Food and Drug Administration for the treatment of rheumatoid arthritis (4). Here we report a case of AU treated successfully with tofacitinib.

Case report

A 23-year-old female patient presented with AU; her hair loss started as characteristic AA of the scalp at age 14, and at age 19 progressed to AU. Her past medical history was otherwise unremarkable. Previous treatments included topical steroids, intralesional steroid injections, topical minoxidil, and systemic steroids, each of which were received several times, and oral cyclosporine, which lasted for 2 years. On dermatological examination no hair was observed on her scalp, extremities, torso, axilla, and groin. She had no eyebrows, but she had eyelashes (Figs. 1a–b).

Because our patient had failed to response to all previous treatments, we decided to use tofacitinib for treatment. The baseline laboratory investigation included a complete blood count, liver and

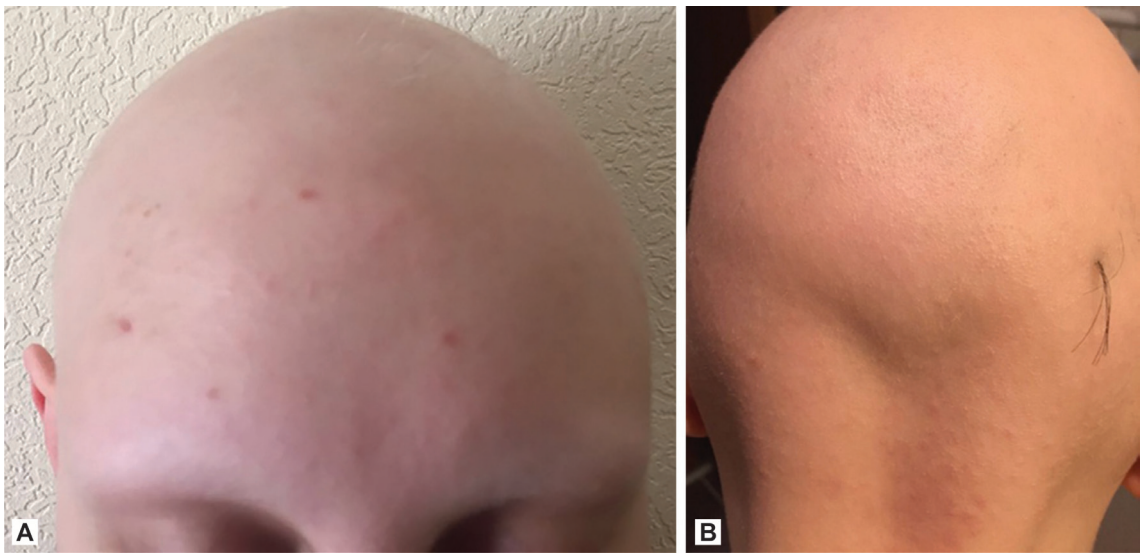

Figure 1 | a) and b) baseline photographs of the patient (SALT score = 100).

[1]Yozgat State Hospital, Department of Dermatology, Yozgat, Turkey. [2]Gazi University Hospital, Department of Dermatology, Ankara, Turkey. ✉ Corresponding author: fnderdrn@gmail.com

renal function tests, electrolytes, viral markers for hepatitis B, C, and HIV, a chest X-ray, and a tuberculin skin test. There were no notable laboratory findings except for tuberculin skin test positivity (12 mm). Therefore, isoniasid 300 mg daily was started to prevent a potential tuberculosis reactivation before the start of the tofacitinib treatment. Oral tofacitinib was prescribed 5 mg twice daily (the dose approved for rheumatoid arthritis). We evaluated hair regrowth using changes in SALT (Severity of Alopecia Tool) scores, which is a validated tool that quantities percent scalp hair loss (11). The initial SALT score of our patient was 100, which indicates complete absence of hair (11). At the end of the first month, very fine tiny hair could be observed. After 2 months of the treatment, partial hair regrowth was seen on the scalp and eyebrows, and the SALT score was 52. Thereafter, the dose was increased to 10 mg in the morning and 5 mg at night. By 6 months of the treatment, there was complete hair regrowth throughout the entire body, and the last SALT score was 0. Our patient tolerated tofacitinib well, without any significant side effects. Figure 2(a–g) presents a timetable that shows the excellent month-by-month improvement of our patient.

Discussion

Compliant with the cases in the literature, our patient responded well to oral tofacitinib in the absence of significant adverse side effects. Within only 6 months, 10 to 15 mg daily doses of tofacitinib achieved excellent hair regrowth in our patient.

Tofacitinib is a targeted kinase inhibitor that selectively inhibits JAK-3, thus blocking γ chain receptors. Interferon gamma (IFN-γ) receptors and γc family receptors signal through JAK1/2 and JAK 1/3, respectively. In mouse models, it has been shown that a cytotoxic subset of CD8+NKG2D+ T cells producing IFN-γ is necessary and sufficient for induction of AA. In addition, systemic tofacitinib treatment has been found to reduce the frequency of CD8+NKG2D+ T cells. Thus, it is believed that tofacitinib exerts its effects through these molecular events and contributes to histological and clinical reversal of AA/AU (5).

Very few AA cases treated with tofacitinib or other JAK inhibitors have been reported to date (3–7). Craiglow and King were the first to observe the effectiveness of oral tofacitinib in the treatment of AA based on the observation that oral tofacitinib maintained good clinical responses in both diseases of a patient that had AU and concomitant plaque psoriasis (3). Xing et al. reported successful treatment of three patients with AA with oral ruxolinitib, JAK1/2 inhibitor. In 5 months, substantial hair regrowth was observed in all of the patients (5). Gupta et al. recently reported two patients with AU that experienced full hair regrowth at 8 months of tofacitinib treatment (4). Anzengruber et al. reported a patient with AU and retinal vasculitis that received tofacitinib 5 mg twice daily and concurrent methotrexate 15 mg per week with weak and transient response to the treatment (7). Whether concomitant methotrexate use was the reason for this therapeutic failure or not remains a matter of debate. Only two studies have been reported to date on tofacitinib for the treatment of alopecia areata and variants (8–9). Promising results were attained in Crispin et al.'s study, which was an open-label clinical trial involving 66 patients treated for 3 months with tofacitinib 5 mg twice daily (8). In a recent retrospective study of 90 patients, a clinical response was achieved by 77% of patients achieving an intermediate or complete response over 4 to 18 months of treatment. In that study, after the first 2 to 3 months of tofacitinib twice daily therapy, a higher dose of tofacitinib up to 10 mg twice daily with or without an adjuvant therapy of prednisone 300 mg once monthly for three doses (pulsed prednisone) was applied if the patients did not demonstrate a robust response to the initial treatment. It was suggested that concomitant use of pulsed prednisone contributed to sustained hair regrowth in that study (9). In a series of eight adolescent patients with alopecia universalis, treatment with tofacitinib 5 mg twice daily for 5 to 18 months resulted in significant regrowth (> 50%) of scalp and body hair in all of the patients (10).

AA is a new indication for tofacitinib, and so it is not surprising that a standard treatment protocol is lacking. Our patient tolerated the treatment well and the blood tests checked monthly were normal in the first 2 months of the treatment. In order to stimulate

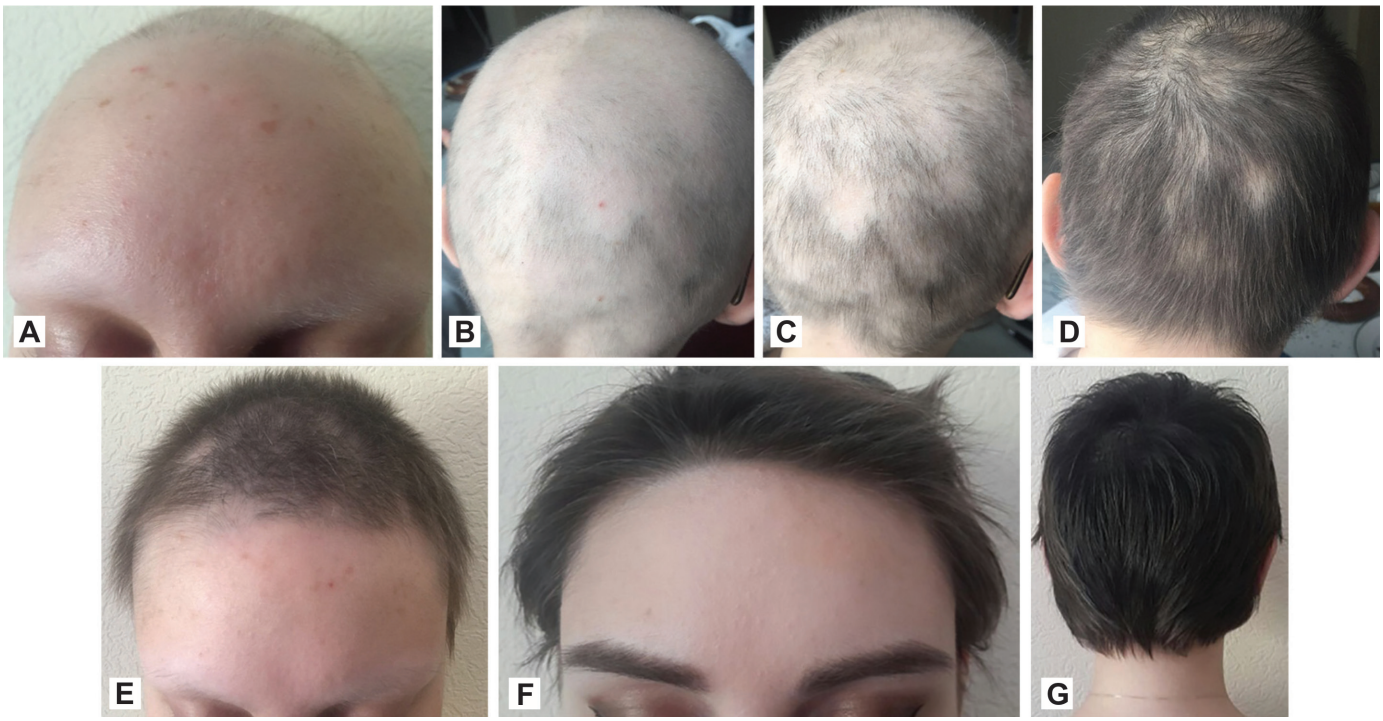

Figure 2 | Facial and scalp hair; a) and b) at the end of 2 months of therapy (SALT score = 52); c) at the end of 3 months of therapy (SALT score = 17); d) and e) at the end of 4.5 months of therapy (SALT score = 6); f) and g) at the end of 6 months of therapy (SALT score = 0).

more hair regrowth and increase treatment efficacy, we increased the dose from 10 mg to 15 mg daily. However, Gupta et al. preferred to use fixed 10 mg daily doses throughout their study (4). It seems that, even with different daily doses of the agents, JAK inhibitors have the potential to treat AA within a few months. The duration of the tofacitinib treatment is not currently known. The longest duration of treatment reported to date is 18 months in Liu et al.'s study (9). They suggest maintenance therapy for continued remission of the disease, and 12.3% of the patients had a relapse during treatment in that study. Our patient is in the 19th month of tofacitinib treatment and the current dose is 15 mg daily. At month 12, when the dose was tapered to 10 mg daily, we observed patchy hair loss in some areas and we increased the dose to 15 mg daily again. We are planning to continue tofacitinib treatment based on the current literature because relapse is expected after cessation of therapy.

Conclusion

Considering the good responses for this psychologically devastating disease, the promising efficacy of oral tofacitinib in AU requires further study to address questions such as length of treatment, duration of response, factors affecting the response, relapse rates, and side effects of JAK inhibitors in this population.

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