Efficacy of systemic minoxidil and tofacitinib combination in treatment-resistant alopecia universalis

Running Head: *minoxidil in alopecia universalis*

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Abstract

Alopecia areata (AA) is an autoimmune nonscarring alopecic disorder, which presents with varying amounts of hair loss, ranging from focal patchy loss to entire scalp and body hair loss. Treatment of AA is a challenging issue within dermatology practice. Although many treatment options are present, response to medications remains unsatisfactory, especially in severe and recalcitrant cases. In this study we present a case of treatment-resistant AU which was successfully treated by the combination of tofacitinib and oral minoxidil.

Key words: alopecia areata, alopecia universalis, tofacitinib, oral minoxidil

Introduction

Alopecia areata (AA) is a chronic immune-mediated disorder characterized by nonscarring patchy hair loss with an estimated prevalance of 1/1000 [1]. Alopecia universalis (AU) is a severe form of AA, which presents with the complete loss of hair on the scalp and the body and it is generally resistant to treatment [1].

Topical and intralesional corticosteroids and immune contact therapy are often sufficient in mild to modarate cases, whereas severe cases may require systemic steroids, cyclosporine, methotrexate, diphenylcyclopropenone, azathioprine as well as Janus kinase inhibitors [2].

Tofacitinib, which is a Janus kinase inhibitor, has been reported to be a beneficial alternative for the treatment of AA in current studies [3-5]. Topical minoxidil is another alternative treatment for AA. This may be used in combination with other therapies [6]. However, knowledge is still limited on the efficacy of oral minoxidil in the management of AA [7].

Herein, we present a case of AU which was successfully treated by the combination of tofacitinib and oral minoxidil.

Case Report

A 31-year-old male patient was admitted to our outpatient clinic for AU. Systemic corticosteroid treatment was used for 6 months but there was no complete response to treatment. The patient's the Severity of Alopecia Tool Score (SALT) score was 100 (Figure 1). Routine laboratory tests were in normal limits.

Cyclosporine treatment was started at a dose of 3 mg/kg/day. Since there was no improvement in clinical findings within 3 months, tofacitinib was administered with non-indication approval with a dose of 10 mg/kg daily for 6 months. However, there was no response to the tofacitinib and this course of medication was ended. Thereafter, the patient used a powder (used orally) with unknown content, which was imported from South Korea for 6 months. Hair growth started within a month. The patient was readmitted to our clinic after 5 months of treatment with promising outcomes. The SALT score had dropped to 35% (Figure 2). A sample from the aforementioned powder was sent to XXX Faculty of Pharmacy (Ministry of Health) for analysis. Pharmacological examination revealed large amounts of minoxidil in its content. Thermo Scientific TSQ Quantum Access MAX Triple Quadrupole Mass Spectrometer and mass selective detector were used in this analysis. Using these methods, the sample was found to contain undeclared minoxidil (Figure 3). The patient was referred to the cardiology department for control and no pathology was detected.

Discussion

Although the pathophysiology of AA has not been completely understood, T cell-mediated immune attacks on cells within the hair bulb seems to be responsible for this disease [1]. Spontaneous hair regrowth is common; approximately 50% of patients recover within a year. However, AA may persist for years and approximately 10% of patients with patchy disease progress over time to alopecia totalis or AU [8]. The prognosis is generally poor in relation to AU, since the disease is resistant to treatment in most cases. Treatment options include various systemic and topical medications [2]. However, there are conflicting results in the literature and the ideal treatment modality has not been determined [1,2].

The effect of systemic tofacitinib has been investigated in various studies [3-5]. In a retrospective study including 90 patients with severe AA, improvement in SALT scores were observed, particularly in the majority of patients whose duration of the current disease episode lasted 10 years or less [3]. A 2-center, open-label, single-arm trial conducted on 66 patients reported ≥50% of improvement in SALT scores in 32% of the patients [4]. Furthermore, in a small retrospective cohort of 13 patients, a regrowth rate of at least 50% was achieved in 7 (53.8%) patients [5]. However, response to treatment was transient and less effective in some patients according to the findings of these studies [3-5].

Studies in the literature had some limitations, such as the small number of cases, lack of comprehensive study design and poor interpretation of the results [6]. For this reason, topical minoxidil is generally being used as a combination therapy with other treatment modalities. A meta-analysis consisted of 6 selected randomised controlled studies and 3 meta-analysis reported favorable outcomes with topical minoxidil in patchy cases of AA [6].

In the literature only one case series on the use of systemic minoxidil to treat AA has been reported. In this retrospective study evaluating the efficacy of the combination of tofacitinib and oral minoxidil, from amongst 12 severe AA patients there was a reported ≥75% scalp hair regrowth in 8 (67%) patients. The authors concluded that the combination tofacitinib and oral minoxidil therapy might be more efficacious than tofacitinib monotherapy [7]. Dramatic improvements were observed in our treatment-resistant AU case with no adverse drug effects. This finding is consistent with the current literature [7].

In conclusion, the combination of tofacinib and oral minoxidil may be an effective alternative treatment approach in severe AA cases. Further studies are necessary in order to confirm this result.

Acknowledgement

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Disclosure

The authors state that they have no conflict of interest in this study. Informed consent was taken from the patient. No funding was used for this study.

Figure Legends

Figure 1: Dermatological examination showing the loss of all scalp and body hairs , on non-scatrical ground. The patient's the Severity of Alopecia Tool Score (SALT) score was 100.

Figure 2: Promising results after the treatment with minoxidil and tofacitinib combination, The patient's the Severity of Alopecia Tool Score (SALT) score was 35.

Figure 3: Detection of minoxidil GC–MS showing a total ion chromatogram (TIC) and mass spectrum of minoxidil

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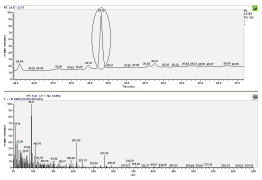

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