Clinical Experience with Oral Tofacitinib in a Patient with Alopecia Areata Universalis and Rheumatoid Arthritis

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ABSTRACT

Alopecia areata (AA) is a chronic and autoimmune disease frequently characterized by a challenge management between dermatologists. At present, JAK-inhibitors have demonstrated encouraging results in AA treatment. Therefore, this study reports a case of alopecia universalis in a patient with rheumatoid arthritis (RA), whose methotrexate therapy shown unsatisfactory response in RA control. After the introduction of 10 mg (oral route) per day of tofacitinib, a JAK-inhibitor, an improvement of almost 50% in severity alopecia tool score occurred with maintained response even after 3 months of medication suspension. From this time, we corroborate the effectiveness of JAK-inhibitors presented in the scientific literature. In addition, we inquiry the real impact of methotrexate on JAK-start signaling inhibition in AA pathophysiology.

Key words: Alopecia areata, JAK-inhibitors, methotrexate, rheumatoid arthritis, tofacitinib

INTRODUCTION

Alopecia areata (AA) is an autoimmune disease with an estimated prevalence of 1 in 1000 people. Men and women appear to be equally affected, and there is no known ethnicity predisposition. The disease is responsible for the majority part of nonscaring hair loss during adulthood and mainly, in childhood. AA can manifest itself as an acute and self-limiting disorder or as a chronic and remitting disease over the years, resistant to treatment in some cases. Clinical manifestations of hair loss in AA can vary from a patchy to total (AT) and universal (AU) alopecia. Its variants can promote significant disfigurement exerting a detrimental impact on patient well-being, which may be independent of the disease objective severity.

The pathogenesis of AA includes an inflammatory microenvironment, which involves an activation, by cytotoxic T lymphocytes, of cytokine receptors coupled with Jak-Stat signaling. Jak kinases are also implicated in atopic dermatitis, psoriasis, and vitiligo pathogenesis. This inflammatory cascade is activated in hair follicles mainly by gamma interferon, generating an amplification response through a positive feedback mediated by several interleukins.

Therapeutic alternatives for the treatment of AA are ample and include both topical and systemic drugs. Among the systemic treatments available, methotrexate, a drug widely used as a first-line treatment for autoimmune inflammatory diseases, such as rheumatoid arthritis (RA), psoriasis, and Crohn’s disease, has been exerted in the treatment of severe cases of AA. Besides the anti-inflammatory and immunosuppressant effect of methotrexate, its role as an...
inhibitor of Jak-Stat pathway has recently being recognized, which reinforces its use in AA.\(^6\)

Once the Jak-Stat pathway participates in an important role of pathogenesis of AA, studies regarding the use of JAK-inhibitors have been developed. These drugs have an anti-inflammatory property and have been approved in many countries for the treatment of RA (tofacitinib and baricitinib), and myelofibrosis and polycythemia vera (ruxolitinib).\(^6,8\)

Accordingly, this study aims to relate a case of alopecia universalis in a patient with RA, whose methotrexate therapy shown unsatisfactory response in RA control. However, as a result of the tofacitinib introduction, the patient manifested an important repilation.

**CASE REPORT**

A 57-year-old white male, started at the age of 30 with significant hair loss. At his first medical appointment, we observed a noncicatricial alopecia in plaques, thinning of eyebrows, and hair from other body regions, clinically accordant to AA (initial severity alopecia tool [SALT] score 94.1%) \(^5\) [Figure 1a-d]. During the follow-up period, the patient was treated with minoxidil 5%, triamcinolone infiltration, and systemic corticosteroids, and no response to all of them was reported. In 2012, the patient was diagnosed with RA and began the follow-up at rheumatology service. At this time, no improvement in the joint symptoms occurred after the administration of methotrexate and mild scalp repilation was observed. In July 2019, due to joint symptoms and activation of RA, tofacitinib 10 mg daily (selective inhibitor drug for JAK receptors) was introduced by rheumatologist. Since then, a significant improvement in the capillary condition was noted (SALT score 53.8%) \(^4\) [Figure 2a-d]. Unfortunately, due to the difficulty of obtaining the medication, the treatment was suspended after 2 months of use. Even so, 3 months after the suspension, the patient maintained stable repilation.

**DISCUSSION**

Tofacitinib is a competitive and reversible JAK inhibitor, specific for JAK1 and JAK3. Since 2014, its use has been approved in Brazil for the treatment of patients with active RA who have experienced therapeutic failure.\(^7\) Attributable to its action on the Jak-Stat signaling pathway, several studies have assembled its use in the treatment of AA.

Serdaroğlu et al., in a cohort study conducted with 63 patients, demonstrated the effectiveness of oral tofacitinib in the management of AA. Based on the SALT score, 39.7% of this sample showed complete repilation (improvement of more than 90% in SALT score) after using the medication for an average of 12 months at a dose of 10 mg daily.\(^8\)

![Figure 1: (a-d) Before treatment with tofacitinib](image1)

![Figure 2: (a-d) After treatment with tofacitinib](image2)
Phan and Sebaratnam in a systematic review and meta-analysis, in which 289 patients were included, indicated that 72.4% of patients had a response in any stage, and 45.7% of them were considered to have a good response. The oral route of administration of tofacitinib showed a significantly greater response compared to topical. Also, the average time to start repilation was 2.2 months.[4]

Complications and side effects related to JAK inhibitors are infrequent. The most common side effects are upper respiratory tract and urinary tract infections. Laboratory abnormalities are usually mild, such as transaminases elevation and low-density lipoprotein elevation.[9]

Methotrexate, on the other hand, is an antimetabolic agent that is known to inhibit folate metabolism. Nevertheless, recent studies have shown that a significant part of its anti-inflammatory activity is also related to inhibiting the Jak-Stat signaling pathway.[6]

In the treatment of AA, methotrexate is usually started at a dose of 5–10 mg per week, with a gradual increase according to the patient’s tolerance, until reaching 20–30 mg per week. In general, its use in monotherapy is not enough. About half percent of patients need concomitant use of systemic or infiltration routes for corticosteroids to maintain the disease in remission.[1]

This study describes a longtime case of AA with unsatisfactory response to methotrexate therapy. Consequently, following the introduction of tofacitinib, the patient presented important repilation with maintenance of the results after 3 months of medication suspension.

Although recent studies have shown the activity related to inhibiting the Jak-Stat signaling pathway by methotrexate, this report demonstrates that possibly the inhibition mechanisms differ from JAK-inhibitors, since the responses to these two drugs were not similar in the same patient.

In conclusion, the literature still requires studies including larger samples to better outline treatment protocols and prognostic factors regarding the use of tofacitinib in the treatment of AA.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot bechrological order guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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