Use of JAK inhibitors in treatment of Alopecia areata

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Madam, Alopecia areata is due to autoimmune destruction of hair follicles resulting in round patches of hair loss surrounded by characteristic "exclamation mark" hairs. It is the second most frequent cause of hair loss after androgenetic alopecia and affects all ages and both genders.[1] This condition can significantly alter an individual's physical appearance and can potentially lead to great psychological distress. The patients may be treated with intralesional injectional corticosteroids. However, this treatment modality has limited efficacy and can lead to numerous side effects.

It is believed that under normal physiological conditions, the hair follicle is an "immune privileged" site and as such there is inhibition of surface molecules needed to present autoantigens to natural killer cells.[2] Studies show that in Alopecia areata, failure of this immune privilege results in type 1 cellular immunity mediated by cytotoxic T lymphocytes which attack hair follicles and prevent them from entering the growing phase of the hair cycle.[3] These cytotoxic T lymphocytes depend on the Interleukin-15 pathway which utilizes Janus Kinase (JAK) proteins for downstream signaling. The implicated role of JAK proteins in this disease process has led to two recent clinical trials which tested the ability of JAK inhibitors to suppress this inflammatory signaling.

The first study was conducted at Columbia University Medical Center and involved a total of 12 patients who were treated with ruxolitinib, a JAK inhibitor commonly used to treat myeloproliferative disorders.[4] Ruxolitinib was given, 20 mg twice daily, for a duration of 3-6 months. At the end of the prescribed treatment, 75% of patients showed remarkable improvement with hair regrowth estimated to be 92% on average. In addition, scalp biopsies taken at the end of the treatment showed suppressed cytoxic T cell inflammation as compared to pretreatment biopsies. No serious side effects were noted.

A second study conducted by Yale University and Stanford University tested a different JAK inhibitor called tofacitinib, a drug used in treatment of rheumatoid arthritis.[5] A total of 66 patients were given tofacitinib, 5 mg twice a day, for 3 months. At the end of the regimen, 64% of patients showed improvement and 32% showed 50% or greater hair regrowth. The drug was well tolerated with only grade 1 and 2 adverse effects being observed. It was noted that after discontinuation of tofacitinib, the disease did relapse in 8.5 weeks on average.

The results of these studies do offer new hope for Alopecia areata patients and promise a new evidence-based therapy for this frustrating disease process.

The results of these studies offer a new hope for alopecia areata, especially for the more severe forms of alopecia areata such as alopecia totalis and alopecia universalis where other treatment modalities are largely considered to be ineffective. As with treatment by other biologics, prior investigations are necessary, and a close follow-up to exclude any chance of developing malignancy.

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