

## Methotrexate Treatment for Alopecia Areata with Greater than 50% Involvement

Joseph C English\* and Silke Heinisch

Department of Dermatology, University of Pittsburgh, Presbyterian South Tower Suite 3880, Pittsburgh, PA 15213, USA

### Abstract

Alopecia areata is a non-scarring alopecia that can present as patches of hair loss (areata, AA), complete scalp hair loss (totalis, AT) or complete scalp and body hair loss (universalis, AU). It is an autoimmune disease mediated via CD8+ T-cell activation and NKG28 signaling targeting the hair bulb. Previous reports indicate that systemic treatment with methotrexate (MTX) benefits patients with AT or AU when used alone or with systemic corticosteroid administration. This study evaluates the utilization of MTX as a treatment modality in patients with alopecia areata who have greater than 50% hair loss.

**Keywords:** Alopecia areata; Hair loss; Dermatology; Methotrexate

### Introduction

Alopecia areata is a non-scarring alopecia that can present as patches of hair loss (areata, AA), complete scalp hair loss (totalis, AT) or complete scalp and body hair loss (universalis, AU). It is an autoimmune disease mediated via CD8+ T-cell activation and NKG28 signaling targeting the hair bulb [1]. Previous reports indicate that systemic treatment with methotrexate (MTX) benefits patients with AT or AU when used alone or with systemic corticosteroid administration [2-5]. This study evaluates the utilization of MTX as a treatment modality in patients with alopecia areata who have greater than 50% hair loss.

### Methods

An IRB-approved retrospective chart review of patients selected with the ICD-9 code for AA seen at the University of Pittsburgh Department of Dermatology from 2009-2011 was performed. Charts were individually reviewed for an established diagnosis of AA, AT, or AU. Patients were selected who had been evaluated to have >50% scalp alopecia and subsequently treated with MTX (15-20 mg per week) with or without an initial 1 mg/kg/day, 21 day, oral prednisone taper. The elements of the medical record that was extracted included: age, gender, alopecia type (AA/AT/AU), time to clinical hair regrowth, time to complete (cosmetically acceptable) hair regrowth, and time to relapse.

### Results

Thirty-one patients were identified during the three year period, with demographics consisting of age ( $40 \pm 13.7$  years), gender (27% male, 73% female), and alopecia type (58% AA (of which 27% was AA-ophiasis pattern), 29% AT, 13% AU). The majority, 71% (22/31), of treated patients showed at least a partial hair re-growth response to MTX treatment. In the 22 patients who responded, the average clinical response time occurred by 9 weeks ( $8.8 \pm 4.4$  weeks). Response time of hair re-growth did not differ between the MTX only ( $10.2 \pm 4.8$  weeks) and MTX pretreated with a 21-day prednisone taper treatment groups ( $6.8 \pm 3.0$ ) (t-test, 0.13). In patients who developed hair regrowth with MTX  $\pm$  prednisone treatment, 36% (8/22) were noted to have complete hair regrowth, which was seen at an average of  $12 \pm 6.8$  months. 7/8 complete responders relapsed when MTX was either discontinued (4/7 patients, average 2.3 months), the dose lowered to 7.5 mg or 5 mg of MTX (2/7 patients, average 4.5 weeks) or while on MTX treatment (1/7). Of note, one complete responder did not have a relapse since the patient was currently undergoing MTX treatment at the endpoint of this study. The majority of partial or complete responders had AA (19/22, 86%) [AA (12/22) or AA-ophiasis (7/22)] vs. AT (3/22, 14%).

Patients who failed treatment (9/31) had either AT or AU, and most of these patients also notably failed further treatment with DPCP and Cyclosporine. No patient with AU responded to MTX treatment.

### Comment

Methotrexate appears to be an effective short-term treatment option for patients with AA, including AA-ophiasis type, showing an overall 71% response rate, of which 36% of treated patients had complete re-growth (Figures 1 and 2). Hair regrowth occurred in 1-3 months with complete hair growth seen from 6-18 months, suggesting



Figure 1: Alopecia Areata >50% loss baseline.

**\*Corresponding author:** Joseph C. English, Department of Dermatology, University of Pittsburgh, Presbyterian South Tower Suite 3880, Pittsburgh, PA 15213, USA, Tel: 412-613-2867; Fax: 412-846-3737; E-mail: [englishjc@upmc.edu](mailto:englishjc@upmc.edu)

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**Figure 2:** Alopecia Areata with cosmetically acceptable regrowth with methotrexate.

treatment with MTX should continue until an 18 month endpoint unless complete response is observed beforehand. An initial 21-day prednisone taper with MTX did not enhance hair regrowth and may be unnecessary. Unfortunately, almost every complete responder relapsed when MTX was discontinued or when the dose was tapered.

MTX may restore hair in AT patients, although unfortunately the majority of AT as well as all of the AU patients in this study failed to respond. Likewise in children with severe AA, MTX has been shown to have variable effects [5]. Higher doses of MTX may be necessary to suppress the immune system response in these patients with widespread alopecia [2]. Although additional prospective studies are necessary regarding MTX treatment modalities for alopecia areata (long-term or pulse dosing), our study supports the use of MTX as an effective albeit temporary treatment option for AA and AA-ophiasis with >50% loss.

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