

Partial Reversal of Androgenetic Alopecia With Methotrexate Therapy for Psoriasis

Shannon Famenini, BS; Jashin J. Wu, MD

Practice Points

- Partial reversal of androgenetic alopecia may be observed after methotrexate therapy.
- Discontinuation of methotrexate may again result in hair loss.

We report the case of a 64-year-old man with androgenetic alopecia who was started on methotrexate therapy for treatment of psoriasis after traditional modalities failed. Following treatment with methotrexate, he noted hair regrowth on the scalp. We propose that methotrexate may inhibit gonadal steroidogenesis, therefore leading to lower testosterone levels, or may increase testosterone aromatization at the hair follicles. These mechanisms may account for the hair growth observed in our patient, which indicates that partial reversal of androgenetic alopecia may be a side effect of methotrexate therapy.

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Case Report

A 64-year-old man with a history of psoriasis that had been recalcitrant to traditional treatment modalities presented seeking more aggressive therapy. Prior treatments included topical steroids and triamcinolone acetonide intramuscular injections administered by his primary care physician for many years. Following initial presentation, the triamcinolone acetonide injections were discontinued

and narrowband UVB phototherapy was started. After 6 treatment sessions, the patient showed no improvement. Phototherapy then was discontinued and methotrexate therapy (7.5 mg once weekly) was initiated; 2 months later, the dose was increased to 10 mg once weekly. Three months following initiation of methotrexate therapy, the patient's total body surface area affected by psoriasis decreased from 8% to 2%.

The patient, who had been completely bald on the frontal scalp since 50 years of age due to androgenetic alopecia, experienced growth of terminal hairs on the mid frontal scalp in a horizontal pattern 3 months after starting methotrexate therapy (Figure), which he attributed to the methotrexate. Subsequently, methotrexate therapy was discontinued for 1 month, and the patient showed exacerbation of his psoriasis and a slowed regrowth of hair. Once-weekly treatment with methotrexate (7.5 mg) was reinitiated. Eleven months later, his psoriasis was well controlled with a total body surface area affected by psoriasis of 0.1% and stabilized partial hair growth on his frontal scalp.

Comment

Our patient's long-term hair loss was the result of androgenetic alopecia. Dihydrotestosterone, which is produced by the peripheral conversion of testosterone by 5α -reductase, binds to androgen receptors in hair follicles and activates the genes responsible for hair thinning.¹ Additionally, patients with androgenetic alopecia have lower levels of cytochrome P-450 aromatase, which is responsible for the conversion of testosterone to estradiol in hair follicles. The clinical manifestations of androgenetic alopecia depend on

Ms. Famenini is from the David Geffen School of Medicine, University of California, Los Angeles. Dr. Wu is from the Department of Dermatology, Kaiser Permanente Los Angeles Medical Center.

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Correspondence: Jashin J. Wu, MD, Department of Dermatology, Kaiser Permanente Los Angeles Medical Center, 1515 N Vermont Ave, 5th Floor, Los Angeles, CA 90027 (jashinwu@hotmail.com).



A patient with androgenetic alopecia who experienced hair regrowth after methotrexate therapy for psoriasis (A and B).

the activity levels of 5α -reductase and cytochrome P-450 aromatase in the different regions of the scalp.¹

Prior studies have suggested that methotrexate may interfere with testosterone synthesis or activity. Cases of gynecomastia have been reported in patients with rheumatoid arthritis who were being treated with methotrexate,^{2,3} suggesting that methotrexate may cause an imbalance in estrogen and testosterone levels, which might be attributed to the reduced production of testosterone or enhanced aromatization of androgens. Methotrexate therapy also has been associated with sexual impotence, which further validates the notion that methotrexate might decrease testosterone synthesis.^{4,5} Reports of oligospermia caused by methotrexate also have been documented.^{6,7}

Animal studies have illustrated that methotrexate inhibits gonadal steroidogenesis. When rats were treated with methotrexate, a marked reduction in serum testosterone levels was measured in correlation with therapy duration.⁸ Additionally, methotrexate treatment in rabbits led to a decrease

in serum testosterone levels and an increase in plasma androstenedione levels, indicating an inhibitory effect on gonadal steroid synthesis rather than adrenal androgenesis.⁹ We hypothesize that a similar mechanism in humans could help explain hair growth resulting from methotrexate therapy. One report described a patient who presented with methotrexate-related gynecomastia and was found to have reduced testosterone levels.¹⁰ If methotrexate inhibits gonadal steroidogenesis, less testosterone would be available for conversion to dihydrotestosterone, the main hormone responsible for hair loss in cases of androgenetic alopecia.

Conclusion

We propose that methotrexate could be causing hair growth in the patient via 2 mechanisms: the inhibition of gonadal steroidogenesis and reduced testosterone levels, or increased levels of testosterone aromatization at the hair follicles. Partial reversal of androgenetic alopecia can be a secondary effect observed in patients treated with methotrexate for psoriasis.

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