

# Recurrence of Alopecia Areata in a Patient Receiving Etanercept Injections

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**Background:** Alopecia areata is a common condition of patchy hair loss that has been postulated to have an autoimmune pathogenesis involving inflammatory cytokines, including tumor necrosis factor (TNF)  $\alpha$ . Etanercept is a novel medication that blocks TNF- $\alpha$ -mediated processes. We report a case involving the recurrence of alopecia areata in a patient receiving etanercept.

**Observations:** We describe a 49-year-old man with a history of rheumatoid arthritis and alopecia areata who

developed a recurrence of his alopecia areata while being treated with etanercept for more than 2 years.

**Conclusions:** The anti-TNF- $\alpha$  effect of etanercept therapy may not be sufficient to prevent the recurrence of alopecia areata. The possible role of TNF- $\alpha$  in the pathogenesis of alopecia areata may be called into question if our observation is repeated.

*Arch Dermatol.* 2005;141:759-760

**A**LOPECIA AREATA IS A COMMON type of hair loss, affecting approximately 1.7% of the population.<sup>1</sup> Clinically, patients present with patchy hair loss that can affect any part of the body. The pathogenesis of alopecia areata remains elusive, although the association of alopecia areata with autoimmune disease, the finding of an inflammatory infiltrate on histopathologic examination, and the hereditary nature of the disease suggest an autoimmune pathogenesis.

Much attention has been focused recently on the new use of biologic therapies in the treatment of autoimmune diseases. Etanercept is a novel medication that blocks tumor necrosis factor (TNF)-mediated processes and has shown promise in the treatment of other various autoimmune disorders. A phase 3 trial of etanercept in the treatment of psoriatic arthritis demonstrated statistically significant improvement of arthritis, skin disease, and extent of disability compared with placebo and paved the way for Food and Drug Administration approval of etanercept in the treatment of psoriatic arthritis.<sup>2</sup> In the early rheumatoid arthritis trial of therapies for rheumatoid arthritis, patients who received etanercept showed a more rapid rate and a greater amount of improvement in 6 months than those who received methotrexate.<sup>2</sup>

The pathogenesis of alopecia areata appears to involve inflammatory cytokines, in-

cluding TNF- $\alpha$ .<sup>3</sup> Etanercept is an all-human soluble TNF- $\alpha$  receptor that is fused to the Fc portion of IgG1. Therefore, one might expect etanercept therapy to have a beneficial effect on alopecia areata.

We describe a patient who developed a recurrence of alopecia areata while being treated with etanercept for rheumatoid arthritis. A review of the literature failed to identify similar cases.

## REPORT OF A CASE

A 49-year-old man presented with a 6-month history of patchy hair loss. Sixteen years earlier, he had been treated for similar signs and was diagnosed as having alopecia areata. He was treated with intralesional triamcinolone acetonide (3 mL of 10 mg/mL) on 3 occasions, with improvement and resolution of the alopecia. He also had a 6-year history of rheumatoid arthritis and had been treated with numerous therapies, including oral methotrexate sodium for approximately 3½ years, oral prednisone sporadically for approximately 3½ years, oral oxaprozin for approximately 3¼ years, and oral misoprostol sodium for approximately 3¾ years. Three years earlier, he had begun a twice-weekly subcutaneous course of 25-mg etanercept injections, which he said led to marked improvement of his arthritis and allowed him to discontinue the use of all other medications.

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**Financial Disclosure:** None.



**Figure 1.** Parietal region of scalp demonstrating focal patchy hair loss of 6 months' duration.



**Figure 2.** Posterior region of scalp showing focal patchy hair loss of 6 months' duration.

After more than 2 years of etanercept therapy, the alopecia areata recurred, with extensive, confluent 4- to 6-cm patches on the occipital and parietal regions of the scalp (**Figure 1** and **Figure 2**). Six months before the patient presented to our clinic, he had been treated with 0.05% clobetasol propionate foam twice daily, without noticeable improvement. Four months later, he underwent a trial of topical 5% minoxidil, once daily, also without improvement. Currently, his alopecia areata is being treated with clobetasol foam twice daily on weekends and topical 5% minoxidil twice daily, along with intralesional triamcinolone injections (10 mg/mL, up to 4 mL, total) to a few affected areas. Only slight improvement has been noted.

#### COMMENT

We report a case of recurrent alopecia areata that developed during etanercept therapy. In light of the reported relationship of alopecia areata and TNF- $\alpha$ , we found it surprising that the disease occurred during treatment with a drug that blocks this cytokine. Also, the disease has been somewhat treatment resistant.

Several findings have suggested an autoimmune pathogenesis for alopecia areata. An increased incidence of autoimmune diseases is also found in association with alopecia areata, including thyroid disease.<sup>4</sup> A family history is present in 24% of cases.<sup>5</sup> Human leukocyte antigen class II *DQ3*, *DR4*, and *DR11* genes appear to demonstrate increased susceptibility to alopecia areata, while *DRW52A* demonstrates resistance to development of alopecia areata.<sup>6</sup> On histopathologic examination, involved scalp areas reveal a peribulbar, perivascular, and outer root sheath mononuclear cell infiltrate of T cells and macrophages.<sup>7</sup>

Some recent research has attempted to further elucidate the autoimmune nature of alopecia areata. A study by Thein et al<sup>8</sup> examined cytokine profiles of infiltrating activated T cells in involved alopecia areata lesions. It was found that T-cell clones from involved lesions inhibited the proliferation of neonatal keratinocytes. In examining the cytokine profiles and relating them to growth regulatory capacity, the authors found that T-cell clones that released high amounts of interferon gamma and/or TNF- $\alpha$  inhibited keratinocyte growth.<sup>7</sup> Another study by Philpott et al<sup>3</sup> directly examined the effect of various interleukins on hair follicle growth in vitro and found that interleukin 1- $\alpha$ , interleukin 1- $\beta$ , and TNF also were potent inhibitors of hair follicle growth and resulted in the formation of dystrophic anagen hair follicles, similar to changes found in alopecia areata. These studies suggest that perhaps by altering the expression of various cytokines, a therapeutic response to alopecia areata may be effected.

We report the present case to highlight that a recurrence of alopecia areata developed during therapy with etanercept injections in the hopes of adding to the body of knowledge concerning alopecia areata. While it is only a single case, these findings, if confirmed by similar observations, would suggest that TNF- $\alpha$  may not be essential in the mechanism of this disease. Considerable effort is being made to elucidate the pathogenesis of alopecia areata.

Accepted for Publication: November 3, 2004.

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