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ALOPECIA AREATA DURING ANTI-TNF ALPHA TREATMENT FOR PSORIASIS: A CASE SERIES.

Dermatology

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ABSTRACT

Biologic drugs represent a substantial progress in the treatment of psoriasis vulgaris and psoriatic arthritis. However, its crescent use has revealed seldom reported or unknown adverse reactions, mainly associated with anti-tumor necrosis factor alpha (anti-TNF-α). Alopecia in patients exposed to these drugs was described in clinical trials before marketing. We present two cases of alopecia areata (AA) developed in patients with psoriatic arthritis while using Adalimumab. The role of anti-TNF-alpha therapy in the pathogenesis of AA is poorly understood. Activation of self-reactive T cells by anti-TNF-alpha could lead to the development of AA. The recognition of these effects by specialists is essential for the proper management and guidance of these patients.

KEYWORDS

Psoriasis, Alopecia Areata, Anti-TNF

Introduction:

The increased use of biologic drugs has been revealing new adverse effects. The most common adverse drug reactions (ADRs) to these agents are acute infusion reactions, infections and gastrointestinal symptoms. The development of alopecia related to anti-tumor necrosis factor alpha (anti-TNF-α), in particular alopecia areata (AA), is a possible although seldom reported collateral effect. [1]

AA is one of the most common causes of non-scarring hair loss, that may refer to any hairy skin area of the body, in particular the scalp, which is associated with the premature induction of hair follicle regression. The precise pathogenesis is unknown, but it is believed that CD4+ and CD8+ T cells attack a still unknown autoantigen of the hair follicle, thereby initiating an inflammatory process with the involvment of proinflammatory cytokines such as IFN-γ, TNF-α, IL-1 and IL-2 [2].

We present two cases of severe AA of the scalp developed in patients with psoriasis while using adalimumab, suggesting a causal relationship between them.

Case Reports

Case 1

Male patient, 51 years old, affected by psoriasis vulgaris and treated with adalimumab for 8 years, presented alopecia plaques on the parietal, occipital, and bilateral frontal region of the scalp and beard. The lesions showed clinical and dermoscopic aspects of AA: black spots and exclamation-mark hairs. Direct mycological examination was negative. Daily treatment was started with clobetasol foam, and minoxodil 5% lotion. Adalimumab therapy was maintained and after 6 months we observed the complete hair regrowth and remission of cutaneous lesions.

Case 2

Male patient, 48 years old, developed AA for the first time while being treated with adalimumab for 3 years due to psoriatic arthritis. Two years after starting adalimumab, the patient reported the appearance of bald patches on his scalp (Figure 1A). No scarring or redness was found. Laboratory values, including thyroid parameters (TSH, fT3, fT4,), and autoantibodies (ANA, dsDNA) were all unremarkable. Dermoscopy of the scalp demonstrated presence of dystrophic hair and black dots, with some yellowish spots compatible with AA. Based on the clinical dermoscopical evidences, we diagnosed AA caused by adalimumab. Given that the patient did not find his condition severe, we continued adalimumab and topical therapy with clobetasol foam with minoxidil 5% lotion was performed. After 18 months the patient progressed to an intense regrowth of scalp hair, but still with some alopecia areas (Figure 1B).

Discussion

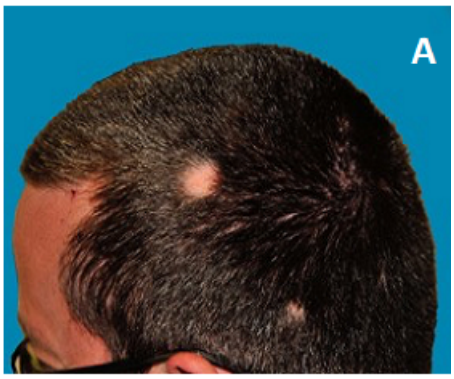
The pathogenesis of AA remains uncertain, but it is believed that a complex autoimmune mechanism involving T lymphocytes and proinflammatory cytokines, TNF-α, would be responsible for hair growth inhibition due to its inflammatory action on the hair bulb [2].Treatment of AA is often difficult and frustrating because of the lack of effective treatments. First-line therapy includes topical and intralesional glucocorticoids and topical immunotherapy; various second-line treatment options include systemic glucocorticoids, minoxidil, anthralin, phototherapy, prostaglandin analogues, cyclosporine, sulfasalazine, methotrexate, and azathioprine [3-4].

Among the immunobiologicals, adalimumab has as its action mechanism the selective inhibition of TNF-α and would be drug with possible applicability for treating AA, underlining the complexity of the immune pathogenesis of this disease. However, there are an increasing number of reports on anti-TNF-α agents, including adalimumab, promoting paradoxically AA. The pathomechanism for this effect remains unclear, but it probably involves plasmacytoid dendritic cells (PDCs) and INF-α [5]. Due to the lack of the inhibitory effect of TNF-α, PDCs produce an increased amount of IFN-α, IL-1, IL-12, and IL-15. The signal transmitted by IFN-α and IL-15 may promote the maturation of myeloid dendritic cells, prolonging their survival, which may increase the expression of Th1 cells. Additionally, anti-TNF-α agents may influence the distribution of Th1 lymphocytes, leading to their systemic activation and sequestration, what may lead to the formation of AA. The activated PDC in skin themselves may be responsible for the development of peribulbar lymphocytic infiltrate and hair loss in AA patients [6]. Alopecia in patients exposed to these drugs was described in clinical trials before marketing [7]. Remission of AA is shown after stopping treatment as well as with continued treatment with TNF-alpha inhibitors [7].

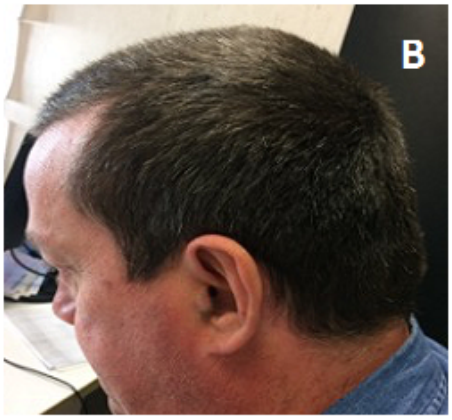
Of the 23 cases published until now on AA occurring in patients taking TNF-alpha inhibitors, 9 were patients taking adalimumab; in patients with psoriasis or psoriatic arthritis, the rate was even higher (4 patients out of 8). This may be due to the fact that adalimumab is an often-used treatment; or it could indicate that AA may be a specific side effect of adalimumab.

In summary, the pathogenesis of AA occurring in patients taking TNF-alpha inhibitors remains unclear. Due to the increasing number of patients under treatment with drugs that have anti-TNF properties, the knowledge and reporting of proportionally growing adverse effects turns out to be important. Furthermore, the recurrence or development of AA in patients under anti-TNF-α drugs makes it necessary to review the real importance of this cytokine and of T lymphocytes as important factors in the pathogenesis of AA, as well as the indication of biologicals for its therapy.

Figure 1. A Bald patches of the scalp.



B. Clinical resolution of alpecia areata.



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