

Development of alopecia areata after biological therapy with TNF- α blockers: description of a case and review of the literature

Sirs,
TNF- α blockers have demonstrated their efficacy and are widely used for the treatment of several inflammatory diseases. However, related adverse events, especially infections, have been described. We report a patient who developed alopecia areata (AA) following infliximab treatment that evolved favourably after discontinuation of biological therapy, with total recovery of hair loss. We performed a literature review of cases of this uncommon effect. A 20-year-old woman with HLA-B27 positive ankylosing spondylitis of 21 months duration, treated with different NSAIDs and sulfasalazine that resulted in only partial improvement, was seen by our department in July 2006. Due to the persistence of bilateral sacroiliac pain, biological therapy with infliximab was started at an intravenous dose of 5 mg/kg, with improvement of symptoms (daytime and night-time sacroiliac pain) after the first infusion. Treatment was continued at the same dose according to the standard

schedule: 2, 6, and every 8 weeks thereafter, and the patient remained symptom-free during therapy. However, she suffered hair loss 24-48 h after each infusion in different locations (occipital, temporal regions), which recovered totally in 1-2 weeks, but progressively increased in size. After the fourth infusion, the patient suffered extensive hair loss affecting nearly half the scalp, without any other symptom or sign. The analysis performed did not show any abnormality in the hemogram (white cell count, platelets) or biochemistry. Antinuclear and anti-DNA antibodies were negative previous and after infliximab therapy. Therapy with infliximab was discontinued and the patient evolved favourably, with total recovery of scalp hair in 2 weeks and no further alopecia. Seven months later, the patient again presented joint symptoms and NSAID therapy was initiated with partial improvement. Due to the intensity of the sacroiliac pain, treatment with etanercept was started at a weekly dose of 50 mg/sc, 9 months after the withdrawal of infliximab. A clinical improvement was observed after the second injection, with no adverse events. Currently, after 16 months of etanercept treatment, the patient is symptom-free with no further alopecia or other adverse event.

AA is considered an autoimmune disease mediated by T-lymphocytes, although some authors have suggested a possible role of TNF- α in its pathogenesis. Recently, a few cases of patients developing AA after biological therapy have been reported (1-7), whose clinical characteristics and outcomes are summarized in Table I. Although the underlying mechanism of AA is not known, it has been suggested that the blockage produced by TNF- α agents could promote dysregulation of cytokines such as α -interferon and the activation of self-reactive T cells leading to the development of AA (6). Reports of other TNF-blocker-related adverse events affecting the skin such as granuloma annulare (8) and vasculitis (9) suggest the skin may be an important organ target in these agents.

In our case, the appearance of AA 24-48h after the initiation of infliximab and the total recovery observed after drug discontinuation established a clear relationship between the drug and the adverse event. The patient does not developed any disease or condition known to be associated with AA, and did not show any abnormalities in analysis. These features, together with the absence of autoimmunity changes, ruled out the development of a SLE-like disorder,

Table I. Clinical characteristics and outcomes of patients developing alopecia areata after biological therapy.

Patient	Sex /Age	Disease	Anti-TNF- α	Time from beginning of anti-TNF- α	Type of AA	Withdrawal of anti-TNF- α due to AA	Treatment for AA and results	Personal or family history of AA	Author/Year
1	F / 51	RA+ SS	Infliximab	11 months	pAA (75%) + eyebrows and eyelashes	Yes	AAt despite discontinuation of infliximab	No personal history of AA	Ettefagh (2004) ¹
2	M / 49	RA	Etanercept	>24 months	Recurrence of pAA	–	Clobetasol foam + Minoxidil 5% + Intralesional triamcinolone injections Slight improvement	AA diagnosed at 33 years which resolved with corticosteroids	Posten (2005) ²
3	M / 43	PsP	Infliximab	3 months	pAA (40%)	Yes	Clobetasol 0.05% Complete regrowth	No personal or family history of AA	Tosti (2006) ³
4	M / 57	PsA	Efalizumab	2 months	Severe relapse of pAA (70%)	No	Clobetasol 0.05% Progression to AAt	Episodes of pAA since childhood	Tosti (2006) ³
5	F / 23	RA	Adalimumab	2 months	Recurrence of pAA that evolved to extensive hair loss	–	Topical dexamethasone. Evolution to AAu 4 months later	pAA diagnosed at 21 years, which resolved with topical corticosteroids	Garcia Bartels (2006) ⁴
6	M / 37	AS	Infliximab	6 weeks	AAt + eyelashes + eyebrows + trachyonychia + multiple halo nevi	No	–	Moderate pAA since childhood	Fabre (2008) ⁵
7	M / 43	PsA	Adalimumab	6 months	pAA (75%)	Yes	Potent topical corticosteroids Progression to AAt, and 2 months later to AAu	No personal or family history of AA	Pelivani (2008) ⁶
8	F / 38	RA	Adalimumab	24 months	AAt, and 3 months later evolved to AAu	Yes	–	No personal or family history of AA	Chaves (2008) ⁷
9	F / 20	AS	Infliximab	1-2 days	pAA	Yes	No treatment. Total recovery	No personal or family history of AA	Hernández 2008

M: Male; F: Female; RA: rheumatoid arthritis; SS: Sjögren's syndrome; PsP: psoriasis pustulosa; PsA: psoriatic arthritis; AS: ankylosing spondylitis; pAA: patchy-type AA; AAt: AA totalis; AAu: AA universalis.

described after therapy with these agents (10). The fact that AA did not develop after etanercept therapy and that most reported cases of AA related to TNF-blockers are secondary to a monoclonal antibody, may suggest a close association between AA and TNF- α antibody agents.

In conclusion, we report the case of a patient who developed AA following infliximab therapy, with total recovery after its withdrawal. This reflects the variety of adverse events associated with TNF- α blocker therapy.

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