



# Novel posterior auricular cutaneous reaction after anti-TNF- $\alpha$ infusion in young women with Crohn's disease

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## INTRODUCTION

Tumor necrosis factor (TNF)- $\alpha$  is a cytokine critical for effective immune surveillance. Abnormally elevated TNF has been implicated in the pathogenesis of many inflammatory conditions. Anti-TNF medications are an effective targeted therapy for these conditions.

Cutaneous reactions after treatment with anti-TNF medications have been well documented in the literature. Complications include hypersensitivity reactions, psoriasiform eruptions, lupuslike syndrome, and cutaneous vasculitis.<sup>1,2</sup> The mechanism for these paradoxical immune reactions is unclear. One hypothesis is that blocking TNF- $\alpha$  leads to unopposed production of interferon- $\alpha$ , a cytokine frequently implicated in the induction of autoimmunity.<sup>3</sup>

We present 7 patients with inflammatory bowel disease (IBD) who had cutaneous reactions characterized by painful, fissured, erosive plaques in the postauricular region after treatment with anti-TNF therapy. After this rash, several of these patients subsequently had a similar eruption in the scalp associated with prominent alopecia.

## CASES

### Patient 1

A 32-year-old woman with Crohn's disease (CD) who was receiving infliximab for 6 years presented with months of a painful eruption in the postauricular region. She received multiple courses of antibiotics for presumed infection without improvement. Examination found painful erythematous

### Abbreviations used:

CD: Crohn's disease  
IBD: inflammatory bowel disease  
TNF: tumor necrosis factor

plaques with fissuring and yellow crust in the postauricular region (Fig 1). She did not respond to treatment with topical and intralesional corticosteroids, and subsequently infliximab was transitioned to adalimumab with no improvement. We then switched to ustekinumab at IBD dosing (90 mg subcutaneous injection every 2 months), which resulted in clearance of her cutaneous eruption within 3 months.

### Patient 2

A 28-year-old woman with CD who was receiving infliximab for 2 years was recently transitioned to adalimumab because of treatment failure. While on infliximab, a painful eruption developed in the posterior auricular region. Examination found erythematous, superficially eroded plaques with linear fissuring and yellow crusting in the postauricular regions (Fig 2). The patient was successfully treated with 3 months of topical and intralesional corticosteroids and was able to remain on adalimumab.

### Patient 3

A 31-year-old woman with CD who was receiving infliximab for 5 years, presented with a painful

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**Fig 1.** Drug eruption. The right posterior auricle of patient 1, notable for erythematous plaques with fissuring and yellow crusts.



**Fig 2.** Drug eruption. The left posterior auricle of patient 2, notable for erythema with superficially eroded plaques. This area was exquisitely tender to light touch.

eruption in the posterior auricular region for 1 year, which later involved the scalp, causing alopecia (Fig 3). Examination found erythematous fissured plaques with associated yellow crusting in the posterior auricular region and in the scalp. The patient's lesions resolved approximately 3 months after transition from infliximab to adalimumab.

#### **Patient 4**

A 21-year-old-woman with CD who was receiving infliximab for 3 years, presented with a weeping eruption in the postauricular area. Two months later, a similar rash developed on the scalp, which was associated with hair loss. It had been treated as psoriasis, folliculitis, and fungal infection without resolution. Examination found eroded erythematous plaques in the bilateral posterior auricular regions and a large plaque of alopecia with underlying



**Fig 3.** Drug eruption. The scalp of patient 3, which exhibited a weeping, scaly, erythematous eruption with associated alopecia.

erythematous plaques and yellow crusting. The patient's lesions resolved over several months with topical corticosteroids and after switching therapy from infliximab to adalimumab.

#### **Patient 5**

A 29-year-old-woman with CD who was receiving infliximab for 4 years, presented with a painful eruption in the postauricular area. Examination found erosive, erythematous plaques with fissuring in the posterior auricular area and on the scalp vertex. The patient was successfully treated with intralesional corticosteroids and transition from infliximab to adalimumab. Five years later, she experienced a similar eruption on adalimumab and has since been successfully treated with ustekinumab at IBD dosing (90 mg subcutaneous every 2 months).

#### **Patient 6**

A 36-year-old woman with ulcerative colitis who was receiving infliximab for 7 years, presented with a painful posterior auricular and scalp eruption associated with hair loss. Examination found erythematous fissured plaques in the posterior auricular region and scalp with associated yellow crusting and alopecia. The patient's eruption resolved within 3 months of transitioning from infliximab to vedolizumab.

#### **Patient 7**

A 26-year-old woman with CD who was receiving infliximab for 5 months presented for a painful eruption in the bilateral posterior auricular regions, which started 3 months after her first dose of infliximab. Examination found erythematous plaques with deep linear fissures and impetiginized

crust. The lesions resolved over 6 months of intralesional corticosteroids.

## DISCUSSION

Skin is one of the most frequently involved organs in anti-TNF- $\alpha$  adverse reactions, with cutaneous lesions reported in 20% to 30% of IBD patients.<sup>1,4</sup> To our knowledge, painful, fissuring, impetiginized plaques in the posterior auricular region have not been reported.

New-onset or worsening psoriasis with the use of anti-TNF therapy has been well described in the literature.<sup>5</sup> Although the scalp is a known site for anti-TNF psoriasiform lesions, there are only 15 reported cases of severe alopecia resulting from these eruptions, and the lesions are described as nontender, scaly, and hyperkeratotic, which differs still from the painful, erosive lesions seen in our patients.<sup>6-9</sup> Notably, all of our patients initially presented with posterior auricular involvement, which may be a unique clinical entity seen in anti-TNF-induced psoriasis and also a cutaneous clue for a potential future severe scalp eruption with alopecia.

Recent literature suggests that TNF inhibition may be associated with persistent *Staphylococcus aureus* carriage,<sup>10</sup> which may account for the fissuring and crusting morphology of the patient rashes. However, only 3 lesions were cultured, and of those, only one grew out *S aureus*. Culturing these lesions may be a useful tactic in future cases, as infection may exacerbate cutaneous inflammation. Furthermore, it may be valuable to check vitamin D levels in these patients, whose IBD makes them susceptible to nutritional deficiencies that may contribute to increased inflammation of the skin.<sup>11</sup>

Of note, the unique cutaneous side effects described here affected only young women (<40 years) with IBD, most of whom had CD, and who were all treated with infliximab before the eruption. This observation is perhaps more noteworthy when considering a recent retrospective study that identified CD (vs ulcerative colitis), young age at initiation of medication (age <28 years), and female gender as risk factors for adverse dermatologic reactions after anti-TNF therapy.<sup>12</sup>

All conditions improved within 3 to 6 months of treatment with topical or intralesional corticosteroids or cessation of infliximab. In some but not all cases, switching to another anti-TNF agent was effective. Successful treatment with transition to an alternate biologic class such as anti-IL12/23 and anti-integrin was more predictable. This finding further supports that the anti-TNF therapy may be the cause of this

cutaneous eruption. This presentation should be recognized by dermatologists, as it may be more common than in these limited observations. In addition, these lesions caused significant psychosocial stress in affected patients, most of whom prioritized cessation of hair loss and control of skin rash over control of their IBD. Early recognition and treatment of this adverse effect is crucial to holistic patient care, and further investigation is merited to uncover its pathophysiological mechanism and risk factors.

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