

## BRIEF ARTICLE

## A Case of Refractory Cutaneous Sarcoidosis Successfully Treated with Infliximab

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### ABSTRACT

Sarcoidosis is an inflammatory granulomatous disease affecting multiple organs with cutaneous sarcoidosis occurring in 25% of patients.<sup>1</sup> There are several treatment options available, but alternative therapies should be considered in patients with refractory disease to standard intervention. Although TNF-alpha inhibitors are not FDA-approved for sarcoidosis, they have demonstrated significant therapeutic benefit through targeting proinflammatory cytokines involved in the pathogenesis of sarcoidosis. Herein, we present a case of refractory cutaneous sarcoidosis successfully treated with infliximab therapy with significant hair regrowth on the scalp.

### INTRODUCTION

Sarcoidosis is a multisystem granulomatous disease with cutaneous sarcoidosis presenting as one manifestation in up to 25% of patients with systemic disease.<sup>1</sup> Some patients present with cutaneous lesions as the only feature of the disease, which include papules, plaques, annular, lichenoid, psoriasiform, lupus pernio and deep nodules.<sup>2</sup> Herein, we present a middle-aged female with cutaneous sarcoidosis that failed conventional treatment and was successfully treated with infliximab therapy with a noticeable hair regrowth on the frontal and vertex scalp.

### CASE REPORT

A 53-year-old African American female with a past medical history of diabetes mellitus, hypertension, and asthma presented to the

clinic for evaluation of asymptomatic indurated red-brown to violaceous papulonodules on her central forehead and multiple indurated erythematous papulonodules on the nose and right breast (**Figure 1A**). Additionally, indurated 2-3 cm pink plaques with associated hair loss were present on the vertex and frontal areas of the scalp (**Figure 2A**). On dermoscopy, yellow dots, black dots, exclamation marks and short vellus hairs were shown; all demonstrating characteristic features of non-scarring alopecia. A skin biopsy performed on her right breast demonstrated fibroadipose tissue with non-necrotizing granulomatous inflammation consistent with granulomatous sarcoidosis. Additionally, a skin biopsy on the forehead performed at an outside dermatologist was consistent with cutaneous sarcoidosis. Radiological investigation including chest X ray was unremarkable and not consistent with pulmonary sarcoidosis changes. Inflammatory and biochemical laboratory

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**Figure 1.** Indurated red-brown to violaceous papulonodules on central forehead and nose prior to treatment with infliximab (A). After 5 months of infliximab infusion with significant improvement (B).



**Figure 2.** Indurated erythematous plaques with noticeable hair loss on frontal and vertex the scalp before infliximab (A). After 5 months of infliximab infusions with improvement in indurated plaques and regrowth of hair on scalp (B).

markers including serum calcium, ACE level and C-reactive protein were normal. The patient was initiated on topical tacrolimus and 20 mg of prednisone with minimal change in cutaneous lesions. The patient began additional adalimumab therapy with no significant effect for four months, prompting discontinuation of previous treatments and initiation of infliximab infusions 10 mg/kg at week 0,2 and then every 4 weeks. Improvement in hair regrowth and cutaneous

lesions was noted over 5 months of treatment with infliximab (**Figure 1B & 2B**).

## DISCUSSION

We present a case of cutaneous sarcoidosis with multiple papulonodules on the breast and lupus pernio-like features on the face, as well as non-scarring alopecia on the frontal and vertex scalp. Cutaneous sarcoidosis is a Th1 mediated disease characterized by

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cytokines including interleukin (IL)-2, IL-12, IL-18 interferon (IFN)- $\gamma$ , and tumor necrosis (TNF)-alpha. A feature of sarcoidosis is granuloma maintenance by macrophage and CD4+ release of TNF-alpha which recruits T-cells at the site of granuloma formation.<sup>3</sup>

The patient's cutaneous lesions progressed despite prednisone treatment for four weeks. Adalimumab was added to monitor treatment response and for tapering the prednisone considering her history of diabetes mellitus. Nevertheless, the cutaneous lesions continued to progress and infliximab was initiated as an alternative option upon discontinuation of adalimumab. The patient's lupus pernio-like lesions on the forehead and nose began to improve and reached near complete resolution upon the third infusion which started to heal with post-inflammatory hyperpigmentation. Additionally, the patient reported a noticeable improvement with hair regrowth on the affected areas of the scalp and a decrease in progression of hair loss with subsequent infusions.

Infliximab is a chimeric monoclonal antibody targeting TNF-alpha. It is FDA-approved for the treatment of ankylosing spondylitis, Crohn's disease, ulcerative colitis, rheumatoid arthritis, psoriatic arthritis, and severe plaque psoriasis.<sup>4</sup> However, there have been clinical case studies reporting successful treatment of cutaneous sarcoidosis with infliximab through antagonism of TNF-alpha which controls the granulomatous inflammation.<sup>5</sup>

Despite several articles reporting TNF-alpha inhibitor-induced hair loss, our patient demonstrated hair regrowth in her frontal and vertex scalp after the initiation of infliximab infusion therapy.<sup>6,7</sup> The patient denied additional topical and systemic hair regrowth therapies following treatment. Although the mechanism of infliximab induced hair

regrowth remains unknown, a study by Philpott et al showed that levels of IL-1 $\beta$ , IL-1 $\alpha$  and TNF-alpha are potent inhibitors of hair follicle growth in vitro.<sup>8</sup> Also a high concentration of TNF-alpha causes changes in hair follicle morphology and transition from anagen to catagen phase.<sup>8</sup> It is likely that upon suppression of inflammatory cytokines and TNF-alpha blockade, there was stimulation of regrowth, thus preventing further autoimmune processes in the hair follicle.

Our study supports the use of infliximab in refractory cases of cutaneous sarcoidosis in which conventional treatment failed to improve the granulomatous lesions. It is shown to not only be effective for cutaneous lesions, but in scalp hair regrowth for those with non-scarring alopecia. Although the mechanism of action is unknown, our case study provides limited data and also shows the potential effect of infliximab on hair regrowth. Further studies are necessary to prove this phenomenon given its lack of current scientific evidence.

**Conflict of Interest Disclosures:** None

**Funding:** None

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