

BRIEF ARTICLES

New-Onset Vitiligo Following Etanercept for Ankylosing SpondylitisCarly Dunn, BA¹, Stacy L. McMurray, MD¹, Allison Jones, MD¹, Debendra Pattanaik, MD²¹Department of Dermatology, University of Tennessee, Memphis, TN²Division of Rheumatology, University of Tennessee, Memphis, TN

ABSTRACT

Tumor Necrosis Factor-alpha (TNF- α) inhibitors, are used widely to treat a variety of chronic inflammatory conditions such as ankylosing spondylitis, Crohn's disease, rheumatoid arthritis, and psoriasis. Recently, there has been an increase in the number of reports of immune-mediated skin diseases, such as lichen planus, psoriasis, or granuloma annulare, following the initiation of TNF- α inhibitors. Although the exact mechanism is unknown, the proposed hypothesis is that TNF- α blockade results in a cytokine shift which activates autoreactive T cells and ultimately leads to an immunologic imbalance. We present a patient with ankylosing spondylitis previously treated with adalimumab who developed vitiligo shortly after switching to etanercept to achieve better control of his joint disease. There is no currently treatment algorithm for new-onset vitiligo following TNF- α inhibitor use. In many cases the drug is continued with a favorable outcome; however, withdrawal of the TNF- α inhibitor with initiation of an alternative TNF- α agent or biologic agent in a different class may be considered.

INTRODUCTION

Tumor Necrosis Factor-alpha (TNF- α) inhibitors are used widely to treat a variety of chronic inflammatory conditions such as ankylosing spondylitis (AS), Crohn's disease, rheumatoid arthritis, and psoriasis. Although TNF- α inhibitors have been proven to be effective and safe for use in many conditions, reports of paradoxical immunological skin conditions, such as psoriasis, granuloma annulare, lichen planus, and vitiligo, are associated with their use.^{1,2,3} We report a case of AS who initiated therapy with a TNF- α inhibitor and developed vitiligo shortly thereafter.

CASE REPORT

A 19-year-old male with diagnosis of AS was referred by rheumatology for evaluation of suspected vitiligo. The patient was initially treated for AS with adalimumab which failed to control the disease. He was subsequently switched to etanercept with marked improvement in his AS symptoms. However, within a month of starting etanercept, he developed depigmented macules and patches on his upper vermilion lip (figure 1), anterior base of the neck, dorsal hands (figure 2), volar wrists, and thighs. The patient had no personal or family history of vitiligo. Despite the marked improvement in AS symptoms, the decision was made per

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patient and physicians to switch from etanercept to secukinumab due to the vitiligo. At his 3-month follow up the patient's skin lesions were stable with no progression of disease.

Figure 1. Depigmented patch on patient's upper vermillion lip.



Figure 2. Well-circumscribed depigmented macules and patches on patient's dorsal hands.



DISCUSSION

TNF- α has been linked to the pathogenesis of vitiligo. This cytokine has been shown to inhibit melanocyte differentiation and function and can cause apoptosis of melanocytes.⁴ Simon et al showed that TNF- α blockade can improve existing vitiligo.⁵ However, there have been an increasing

number of reports of new-onset vitiligo following initiation of TNF- α inhibitors. Since the first case report of de novo vitiligo under infliximab in 2005,⁶ there have been at least 17 other case reports as well as a retrospective study and a population-based study detailing cases from use of various biological agents.^{1,3,7,8,9} One study estimates one per 5437 patients on a biologic agent will develop de novo vitiligo.⁹ Although the exact mechanism is unknown, it is postulated that TNF- α inhibition modifies the cytokine balance and affects downstream pathways, resulting in activation of autoreactive T cells and immunologic imbalance.^{4,7}

A retrospective study by Exarchou et al showed that 10 out of 183 (5.5%) patients with AS who had been treated with TNF- α inhibitors had immune-mediated skin lesions (with one case of vitiligo).¹ A 10-year population-based study demonstrated an increased risk of vitiligo in patients receiving TNF- α inhibitors, with an incidence rate of 5.9 vs 2.5 per 10,000 person-years in those on TNF- α inhibitors versus control, respectively. This translates to an overall increased risk of 1.99 in the treatment group. In subgroup analysis, they found that the risk of vitiligo was highest in female patients, those on etanercept, and patients with AS.⁷ Our patient adds to the growing number of reports of etanercept-induced vitiligo in AS after prior treatment failure with adalimumab.

As de novo vitiligo following TNF- α inhibitor use is rare, there is currently no treatment algorithm for this phenomenon. In a nationwide retrospective study by Mery-Bossard et al, 18 patients with de novo vitiligo were reported from July 2013 to January 2015.⁸ In most cases (66.6%) the drug was continued without any worsening of the vitiligo. However, in six of these cases

patients underwent treatment with topical steroids, which may be a confounding factor. In three cases, the TNF- α inhibitor was changed, due to the underlying inflammatory condition, without progression of the patients' vitiligo. The authors conclude that continuing anti-TNF- α therapy is appropriate if the underlying inflammatory condition is well-controlled. Other therapy options include an alternative TNF- α inhibitor or another biological agent in patients whose underlying inflammatory condition had not improved or whose skin lesions progress.⁸

With growing literature describing immune-mediated skin diseases following TNF- α inhibitors, dermatologists, rheumatologists, and gastroenterologists need to be aware of these potential side-effects. An interdisciplinary approach to a patient presenting with vitiligo following initiation of a TNF- α inhibitor can help determine whether the patient should continue the TNF- α inhibitor, switch to a different TNF- α inhibitor, or start an alternative biologic medication.

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