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Adalimumab-induced systemic lupus erythematosus: A case report and review of the literature

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Abstract

Adalimumab is a tumor necrosis factor inhibitor that has been widely used since the early 2000s for the treatment of psoriasis and psoriatic arthritis. All tumor necrosis factor inhibitors have been identified as causative agents in drug induced lupus, particularly etanercept and infliximab. There have been few reported cases of systemic lupus erythematosus induced by adalimumab, many more are attributable to treatment with etanercept or infliximab. We present the case of a patient with long-standing psoriasis and psoriatic arthritis who was successfully treated with adalimumab, but developed anti-tumor necrosis factor-induced lupus.

Keywords

Adalimumab, psoriatic arthritis, drug induced systemic lupus erythematosus

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Introduction

Adalimumab is a tumor necrosis factor (TNF) inhibitor which has been widely used for over 20 years in the treatment of several immune-mediated conditions including psoriasis, psoriatic arthritis, rheumatoid arthritis, and Crohn's disease.[1–5] Adalimumab is a bivalent monoclonal antibody that binds directly to TNF and inhibits its interactions with TNF receptors 1 and 2 (TNFR1 and TNFR2), thereby blocking downstream signaling and any resulting inflammation.[6] Other available TNF inhibitors include etanercept, infliximab, certolizumab, and golimumab with etanercept, infliximab, and adalimumab being the most widely used. Adalimumab has been well studied and is considered to be generally safe with a black box warning outlining the increased susceptibility to tuberculosis and pneumocystis pneumonia as well as an increased risk for the development of lymphoma or other cancers.[7]

We present the case of a female patient with long-standing psoriasis and psoriatic arthritis who was successfully treated with adalimumab, but developed anti-TNF-induced lupus (ATIL).

Case report

This 48-year-old female with a 39-year history of psoriasis was treated with multiple agents throughout the years, including tar creams, ultraviolet therapy, and methotrexate, without control of her disease. In 2011, this patient had moderate to severe plaque psoriasis present on her scalp, trunk, upper and lower extremities, vulva, and perineum. She also subsequently began to develop joint pain and was diagnosed with psoriatic arthritis.

Treatment with standard dosing of adalimumab was initiated which quickly alleviated all of her joint and cutaneous signs and symptoms. This patient's psoriatic disease was well managed with this treatment until 2022 when she presented with increased inflammatory axial joint pain and dactylitis. Antibody screening was performed revealing positive serology for antinuclear antibodies (ANA), ribonucleoprotein (RNP) antibodies, and double stranded DNA (dsDNA) antibodies, which in previous years had been negative. Additionally, a magnetic resonance imaging was performed revealing a worsening of her psoriatic arthritis. There were no other signs or symptoms of evolving connective tissue disease. At this point a diagnosis of ATIL was made and a

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plan was formed to switch this patient from adalimumab to separate agent with a different mechanism of action.

Discussion

Infliximab, adalimumab, and etanercept are TNF inhibitors which have been widely used since the early 2000s for the treatment of psoriasis and psoriatic arthritis. With the increasing use of these drugs, ATIL has become more of a concern among clinicians. Post-marketing studies have suggested the incidence of ATIL to be 0.19–0.22% secondary to infliximab, 0.18% secondary to etanercept, and 0.10% secondary to adalimumab.[8] More recently, the BIOGEAS registry found that anti-TNF drugs were the main culprit in the development of drug-induced lupus (DIL). Within this registry, 140 cases of ATIL were investigated; among these, 37% were due to the use of infliximab, 33% from etanercept, and 25% from adalimumab.

Despite the increasing incidence of ATIL, there is no current standardized diagnostic criteria for ATIL, however one has been proposed. This requires at least one serologic and one non-serological criteria to be met as per the American College of Rheumatology criteria. Additionally, both the presenting symptom(s) and serology need to be related temporally to treatment with a TNF inhibitor.[9]

The onset of clinical symptoms from ATIL can vary from months to years after the initiation of a TNF inhibitor. ATIL presents with cutaneous and or systemic manifestations commonly associated with systemic lupus erythematosus (SLE), but these tend to be milder in severity than in idiopathic lupus. Cutaneous manifestations have been reported in up to 67% of those with ATIL; these include malar rash, photosensitivity, and purpura.[8] The pathology of these lesions is similar to those in idiopathic SLE and therefore diagnosis of ATIL is based solely on the temporal relationship of anti-TNF initiation and the observed clinical symptoms. The frequency of specific non-cutaneous symptoms vary, but those most commonly associated with ATIL include new onset polyarthritis and arthralgia, or a worsening of pre-existing joint symptoms. Constitutional symptoms are also common, particularly in association with positive serology for ANA and dsDNA antibodies.[8]

TNF inhibitors are reported to induce autoantibodies in up to 50% of patients.[10] The potential of auto-immunogenicity with TNF inhibitors means that many patients being treated with these agents may have positive serology for auto-antibodies, even in the absence of SLE systemic symptomatology.[9] A review by Ramos-Casals et al. reported positive ANA serology in 79% of patients investigated and positive anti-dsDNA serology in 72%. It is interesting to note that those with DIL predominantly have elevated titers of dsDNA antibodies of the immunoglobulin M (IgM) subtype without accompanying IgG antibodies. Conversely, in patients with idiopathic SLE it is rare to see elevated IgM without concomitant elevation of IgG.[8] Although positive serology may be helpful in making a diagnosis of ATIL, it is not recommended in patients who are not displaying systemic signs or symptoms of ATIL.[11]

Our patient had a worsening of axial arthritis, new onset dactylitis, and positive serology for ANA, RNP antibodies, and dsDNA antibodies. Although she had been maintained on adalimumab for 11 years with no adverse effects, the presence of two systemic symptoms in conjunction with positive serology fits within the proposed diagnostic criteria for ATIL. It could be argued that this patient had latent autoimmunity and was predisposed to the development of SLE. This is why, prior to initiating treatment with a TNF inhibitor, proper screening for lupus should be performed, as these drugs are contraindicated in patients with SLE. Once a diagnosis of ATIL is made, prompt cessation of the causative drug should occur. In most cases with only cutaneous involvement and positive serology this is sufficient. However, if there is significant systemic involvement, corticosteroids or immunosuppressive agents may be used to prevent further complications.[8,11] It should be noted that autoantibodies often persist even once the TNF inhibitor has been discontinued and any non-serologic symptoms have resolved. Serology should therefore not be used to track disease progression, instead the systemic manifestations should be monitored to help guide treatment.

Conclusion

Adalimumab, although a generally safe drug, does have the potential to cause DIL, albeit at a lower rate than other anti-TNF drugs. This case highlights the importance of follow-up with patients being treated with adalimumab, even many years after the initiation of treatment. This patient's psoriatic arthritis had been well under control with minimal side effects for 11 years. Additionally, we emphasize that there is no need for serological monitoring for autoantibodies without the presence of systemic symptoms of SLE due to the high proportion of people who develop inconsequential positive serology while taking TNF inhibitors.

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Patient consent

Written informed consent was obtained from the patient for publication of this case report. Ethical approval is not required for this study in accordance with the national guidelines.

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