

Late reaction to ustekinumab infusion

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Abstract

Psoriasis is a chronic inflammatory disease that directly affects the quality of life. Biologics are prescribed for patients unresponsive to conventional treatments and with severe forms of the disease. Ustekinumab is a fully human monoclonal antibody against the p40 subunit of interleukins 12/23 that is being used with satisfactory responses, achieving an improvement in the baseline Psoriasis Area and Severity Index of approximately 75% after 12 weeks of treatment. It has few side effects, including greater susceptibility to infections and development of reactions to the drug. Our report discusses a case of a cutaneous reaction to the use of ustekinumab in a 27 year-old male patient after the third dose of the medication. No similar case has been reported in the literature.

Introduction

Psoriasis is a chronic inflammatory skin disease with courses of remission and worsening, which can have great impact on quality of life. Patients with moderate-to-severe psoriasis usually require continuous treatment with higher chances of toxicity. The biologics are used in patients whose condition could not be controlled with conventional treatments, or had to discontinue it due to side effects or toxicity.^{1,2} Ustekinumab is a human monoclonal antibody indicated for the treatment of moderate-to-severe psoriasis. Its mechanism of action is based on the inactivation of interleukins 12 and 23 p40 subunit. Patients treated with this medication are being monitored for a better definition of long-term effectiveness and side effects.^{2,3}

This paper describes a case of late onset reactions to ustekinumab infusion.

Case Report

A 27-year-old man, diagnosed with psoriasis since he was 15, had been treated with acitretin, methotrexate, cyclosporine and pho-

totherapy. However, since his symptoms became refractory to treatment, ustekinumab has been indicated. Baseline Psoriasis Area and Severity Index (PASI) was 11.2, BSA>10%, and a DLQI>10. He was administered one subcutaneous injection of 45 mg of ustekinumab on week 0 and a subsequent injection of 45 mg after 4 weeks, which led to the complete resolution of the lesions. As public supply of the medication was restrained, the patient only received the first maintenance dose 11 months after the last infusion. A week after reintroduction of ustekinumab, pruritic and erythematous annular eruptions occurred on the patient's trunk and limbs (Figures 1 and 2). Blood test shows eosinophilia. Dexchlorpheniramine was prescribed. The patient returned after two weeks showing complete improvement of lesions.

Discussion and Conclusions

Psoriasis is the most common immune-mediated chronic inflammatory disease affecting approximately 2% to 3% of the world's population.¹⁻⁶ Around 80% of patients present localized plaque psoriasis, while the generalized forms comprise less than 20%. The disease has a major impact on the quality of life and can be compared to diabetes mellitus, rheumatoid arthritis, depression and cancer. Typically, psoriasis patients will usually cycle through therapies and sometimes will require indefinite treatment.¹

In the psoriasis pathophysiology, IL-12 activates CD4 T cells and natural killer cells that induce the production of type 1 cytokines (TNF interferon alpha), while IL-23 stimulates the proliferation and increases the half-life of T cells, which produce IL-17. The IL-2 and IL-23 are secreted after the activation of antigen-presenting cells and both present p40 sub-unit in their molecules.⁵

Ustekinumab is a fully human monoclonal antibody that binds to the p40 subunit of the interleukins 12 and 23. Three randomized controlled trials have demonstrated that both 45 mg and 90 mg doses showed a high efficacy in the treatment of psoriasis with 67% to 72% of patients achieving a PASI response of 75 at week 12. Ustekinumab presents few side-effects.⁷⁻⁹

In the PHOENIX 1 study, the most common adverse reactions were upper respiratory tract infection, nasopharyngitis, headache and arthralgia, affecting 0.8% of patients who were taking 45 mg, and 1.6% of those who used 90 mg.⁸ In PHOENIX 2, rates of serious infections were low in all treatment groups. The occurrence of injection site reactions was 1% of 5632 injections of ustekinumab and 0.4% of 14,919 placebo injections, which could in part

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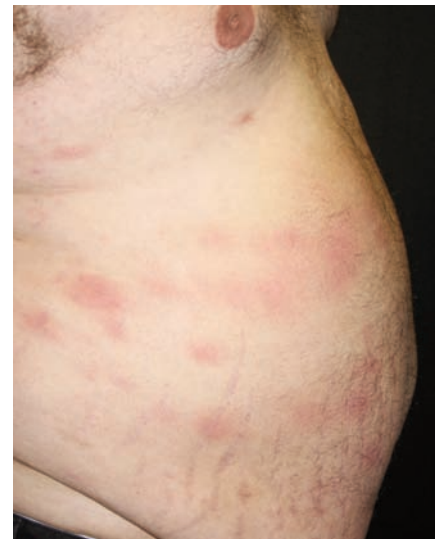


Figure 1. Macular eruption after the treatment.



Figure 2. Exanthematous eruptions after the treatment.

be related to the infrequent dosing interval.⁹ The acute reactions occur during the infusion or in the first 24 hours. The majority can be classified as mild or moderate reactions and only few are severe. Late reactions occur between 24 hours and 14 days after an infusion, in most cases symptoms include arthralgia, myalgia, influenza-like symptoms, headache and rash or urticaria.¹⁰ In patients with Crohn's disease treated with infliximab 61% patients had detectable antibodies against infliximab after the fifth infusion. They found a strong relation between the concentration of antibodies against the infliximab and the occurrence of an infusion reaction. The study showed a cumulative incidence of infusion reactions of 27%, no one occurred during the first infusion and the incidence increased during the subsequent infusions.¹¹

In PHOENIX 1 and 2 the immunogenicity rates were low, with approximately 5% patients developing anti-ustekinumab antibodies and these were not associated with injection site reactions.^{8,9} Our patient have presented late reaction to ustekinumab when the treatment was discontinued and antibodies were probably produced. No report on this type of reaction during the use of ustekinumab was found in the literature. More studies are necessary to understand the relation between antibodies against ustekinumab and infusion reactions.

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