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Ustekinumab Treatment in Patients with Moderate-to-Severe Psoriasis and Latent Tuberculosis Infection: A Study of 3 Case Reports

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Abstract

Background: Ustekinumab is a human monoclonal antibody that binds to the shared P40 subunit of interleukin (IL)-12 and IL-23 and is approved for the treatment of moderate-to-severe psoriasis. Latent tuberculosis (LTBI) was diagnosed based on a positive tuberculin skin test (TST) or QuantiFERON-TB test without evidence of active tuberculosis (TB). **Aim:** To evaluate the risk of active tuberculosis reinfection in patients with a history of psoriasis and LTBI after INH prophylaxis treated with Ustekinumab. **Case Report:** We are describing 3 patients with a history of moderate-to-severe plaque psoriasis and newly identified LTBI who have been treated with INH monotherapy before starting Ustekinumab therapy followed-up over 2 years for any sign of tuberculosis reinfection. **Conclusion:** Ustekinumab is an option for treating psoriasis and LTBI with minimal risk of reactivation after INH prophylaxis.

Keywords

Psoriasis, Ustekinumab, Latent Tuberculosis, QuantiFERON-TB Test

1. Introduction

Psoriasis is a chronic inflammatory skin disorder that affects approximately 2% to 3% of the population and can significantly impair a patient's quality of life [1] [2].

Biologics have become the main treatment modality for psoriasis in recent dec-

ades [3]. Ustekinumab a monoclonal antibody against human interleukin (IL)-12 and IL-23, exhibits high efficacy with relatively low adverse events among various biologics for psoriasis [4].

The incidence of tuberculosis varies worldwide, of those infected with *Mycobacterium tuberculosis*, only about 5% - 10% develop active tuberculosis during their lifetime [5] [6]. Most other patients carry latent tuberculosis infection remaining asymptomatic and noninfectious while their host immune response contains the infection. The immune system may then eradicate the LTBI, or the infection may remain and become activated at a later point in time, sometimes several years later [7]. However, patients with LTBI and an impaired immune system, such as those co-infected with human immunodeficiency virus or those receiving immunosuppressive treatment, have a much higher likelihood of developing active tuberculosis [8] [9].

The immune response produced by the interleukin (IL)-12 and IL-23 pathways is important for host protection against bacterial and parasitic infections and intracellular pathogens [10] [11] [12] [13].

In the present case reports, we are describing 3 patients with a history of moderate-to-severe psoriasis and newly identified LTBI who were treated with INH before starting Ustekinumab treatment without increasing the risk of TB reactivation over a 2 years followed-up period. The written consent form was taken from patients about the publication of their conditions.

2. Case Report 1

A 32-year-old male patient presented to our clinic with a 15 years history of moderate-to-severe plaque psoriasis without joint involvement. His previous treatments consisted of topical calcipotriol, narrow band UVB phototherapy, and methotrexate (MTX) with limited clinical response. Physical examination revealed multiple erythematous, scaly, and indurated plaques involving approximately 40% of body surface area (BSA) including the scalp, trunk, upper and lower extremities, with psoriasis area and severity index score (PASI) 13.5. Thus biological therapy was recommended and during screening, the patient had a positive Quantiferon test (QuantiFERON-TB test (Cellestis, Carnegie, Vic., Australia)), positive TST, and a negative chest x-ray, consistent with LTBI. Referred patient to pulmonology clinic and due to the concern for potential LTBI reactivation, they recommend INH 300 mg daily monotherapy prophylaxis for 9 months. The patient completed a 2-month course of INH therapy before starting the biological injection. Ustekinumab 45 mg was administered by subcutaneous injection at weeks 0 and 4, and then every 12 weeks thereafter. The patient experienced dramatic clinical improvement over the next 28 weeks with 1% BSA affected and a PASI score of 1.2.

Every 6 months the chest x-ray, and QuantiFERON-TB test was obtained and did not show any evidence related to reactivation of LTBI over 2 years of followed-up.

3. Case Report 2

A 37-year-old male patient presented to our clinic with an 8 years history of severe plaque psoriasis without joint involvement.

Previous treatment consists of multiple topical steroids, narrow band UVB phototherapy, and oral acitretin with limited clinical response.

Physical examination revealed multiple erythematous, scaly, and indurated plaques involving approximately 55% of BSA including the scalp, trunk, upper and lower extremities, with a PASI score of 21. Thus biological therapy was recommended and during screening, the patient had a positive QuantiFERON-TB test, positive TST, and a negative chest x-ray consistent with LTBI. Referred patient to pulmonology clinic who decide to start INH prophylaxis 300 mg daily over 9 months. The patient completed a 2 months course of INH prophylaxis before starting the biological injection. Ustekinumab 90 mg was administered by subcutaneous injection at weeks 0 and 4, and then every 12 weeks thereafter. The patient experienced dramatically clinical improvement over the next 28 weeks with less than 1% BSA affected and a PASI score of 1.3.

Every 6 months chest X-ray and QuantiFERON-TB test were obtained and did not show any evidence related to reactivation of LTBI over 2 years followed-up.

4. Case Report 3

A 45-year-old male patient presented to our clinic with a 2 years history of moderate-to-severe plaque psoriasis without joint involvement.

Previous treatment consists of topical vitamin D derivatives, narrow band UVB phototherapy, and oral MTX with limited clinical response.

Physical examination revealed multiple erythematous, thick scaly plaques involving both palms and lower legs with BSA was 14% and PASI scores of 12.8. Thus biological therapy was recommended and during screening, the patient had a positive QuantiFERON-TB test, positive TST, and a negative chest x-ray consistent with LTBI. Referred to pulmonology clinic who decide to start prophylaxis INH monotherapy dose 300 mg daily for 6 months. The patient completed 2 months of treatment with INH before starting the biological injection. Ustekinumab 45 mg was administered by subcutaneous injection at weeks 0 and 4, and then every 12 weeks thereafter with a continuous course of INH therapy. Then increased dose of Ustekinumab to 90 mg subcutaneous injection due to partial response. The patient experienced dramatically clinical improvement over the next 28 weeks with 1% BSA affected and a PASI score of 1.2.

Every 6 months the chest X-ray and QuantiFERON-TB test were obtained and did not show any evidence related to reactivation of LTBI over 2 years of followed-up.

5. Discussion

The National Psoriasis Foundation recommends that patients with psoriasis who are candidates for biologic treatment should be screened for LTBI and, where ap-

propriate, receive anti-tuberculosis prophylaxis before initiating biologic therapy [9].

INH is commonly employed as first-line tuberculosis chemoprophylaxis in most countries [14] [15].

While studies indicate that patients with inborn errors of IL-12/23–IFN-α mediated immunity are at high risk for developing *Mycobacterium tuberculosis* infections, the impact of Ustekinumab blockade of IL-12 and IL-23 on pathogen immunity in genetically normal humans is unknown [4]. However Risks of TB and LTBI reactivation are generally considered lower for Ustekinumab compared to TNF-blockers [16].

In our cases, we reported 3 patients with psoriasis and newly identified LTBI who have been treated with INH monotherapy before starting Ustekinumab treatment. One patient body weight was 106 kg and on a 90 mg dose of Ustekinumab. INH therapy was well tolerated during the treatment course. The screening for the patients with chest X-ray and QuantiFERON-TB test was repeated every 6 months without any signs of TB reactivation. Regarding the response to therapy with Ustekinumab, the improvement was dramatically observed with sustained efficacy during the treatment.

In conclusion, Ustekinumab is an option for treating psoriasis and LTBI with minimal risk of TB reactivation after INH prophylaxis. However, further studies are recommended on a larger population to determine the safety of using Ustekinumab and assess TB QuantiFERON screening during treatment.

Disclosure

This study is an independent study and not funded by any of the drug companies.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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