Active pulmonary tuberculosis in a patient with secukinumab treatment✩✩✩

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Introduction

Spondyloarthritis is a chronic inflammatory arthritis condition that affects the joints and extra-articular organs, causing spinal stiffness, peripheral joint destruction, and organ damage, including to the eyes and intestines, reducing quality of life. Biological therapeutic agents are highly effective in controlling the symptoms of spondyloarthritis and slowing disease progression. Secukinumab, a fully human monoclonal antibody directed against interleukin (IL)-17A, was approved by the Food and Drug Administration for the treatment of ankylosing spondylitis in 2015 [1]. Secukinumab has also been

Abstract

Numerous investigations have documented active tuberculosis (TB) infection following biologic treatment. One of the most secure biologic medications for infections is secukinumab. Additionally, no cases of active TB while receiving secukinumab therapy were recorded. Secukinumab 150 mg per month has been administered for a 19-year-old man with spondyloarthritis since May 2020. A diagnosis of pulmonary TB was made when the patient complained of a moderate fever, a productive cough, and weight loss after 2 years. His fever and respiratory symptoms were relieved after 6 weeks of treatment by stopping secukinumab and utilizing 4 antibiotics: isoniazid, rifampicin, pyrazinamide, and ethambutol, while non-steroidal anti-inflammatory drugs reduced his joint and back discomfort. During biological therapy, even with secukinumab, annual screening for latent and active TB is crucial. We require additional study on secukinumab-treated patients with active TB in nations with high TB burdens, including Vietnam.

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shown to be effective in patients with radiographic and non-radiographic axial spondyloarthritis [2–5].

However, the use of biological therapeutic agents can increase the risk of infections, such as TB caused by Mycobacterium tuberculosis, which is the leading cause of infection agent-related death. More than 1.5 million deaths are estimated to be caused by TB [6]. Vietnam is considered to have a high burden of TB, and new TB infections in 2018 were identified in approximately 174,000 people, with deaths reported in 12,000 cases [7]. Most cases were diagnosed as pulmonary TB, increasing the risk of transmission and the burden of disease. Many studies have shown that anti-tumor necrosis factor (TNF) therapy is associated with TB outbreaks, including cases of patients with spondyloarthritis who were diagnosed with TB while undergoing TNF treatment [8–11]. Secukinumab has a good long-term safety profile, with no cases of active TB reported during therapy to date [12–15]. We report the first case of active pulmonary TB in a patient being treated with secukinumab.

Case report

A 19-year-old man presented with peripheral spondyloarthritis characterized by typical magnetic resonance imaging (Fig. 1). The patient was prescribed 150 mg secukinumab monthly starting in May 2020 after a poor response to sulfasalazine and non-steroidal anti-inflammatory drugs. Before receiving biologic therapy, the patient was screened for latent TB and was found to have a negative QuantiFERON-TB test and a normal chest X-ray. The patient had a good response to secukinumab, and musculoskeletal symptoms improved significantly after several months of treatment.

In April 2022, the patient complained of fatigue, mild fever, productive cough, and weight loss lasting for 2 weeks. Physical examination revealed crackle rales in the left lung and no abnormalities in any other organs. Laboratory results demonstrated an elevated C-reactive protein level of 44 mg/dL and an erythrocyte sedimentation rate of 75 mm. Other hematological and biochemical tests, such as complete blood count, liver enzymes, renal function, glycemia, and thyroid function, were normal. The patient tested negative for human immune-deficiency virus, hepatitis B virus, and hepatitis C virus. Chest X-ray showed left upper lobe consolidation (Fig. 2), and a bronchoalveolar lavage test indicated a negative acid-fast Bacilli smear and detected M tuberculosis, which was found to be sensitive to rifampicin and isoniazid by a line probe assay. Bronchoscopic biopsy demonstrated caseating granulomatous inflammation (Fig. 3).

The patient was diagnosed with active pulmonary TB. The initial treatment for TB was 4 antibiotics: isoniazid, rifampicin, pyrazinamide, and ethambutol. Secukinumab was discontinued due to concerns regarding the reactivation of latent TB. Joint pain and back pain were eased by high doses of non-steroidal anti-inflammatory drugs. After 8 weeks of anti-TB treatment, the patient’s fever and respiratory symptoms resolved, and the lesion on the chest X-ray improved. Joint pain and back pain were mostly controlled.

Discussion

The cell-mediated immune pathway is fundamental in generating the body’s defenses against infection, with interferon production playing a crucial role in controlling bacterial proliferation, including M tuberculosis, the causative agent for TB [16]. Although the mechanism involved in the increased risk of TB infection when undergoing biological anti-TNF therapy is understood [17], the role of IL-17 in TB pathogenesis remains controversial. Several studies have shown that IL-17 plays a protective role against TB infection, acting as a modulator of the inflammatory response [18].

In an IL-123 p19-deficient mouse model, the number of IFN-producing, antigen-specific CD4 T cells did not decrease, even after most IL-17-producing CD4 T cells were lost [19]. These data support the hypothesis that the depletion of IL-17-producing CD4 T cells is unrelated to the progression of M tuberculosis. In a meta-analysis of 28 clinical trials, including 12,319 patients with spondyloarthropathy who received an average of 5 years of secukinumab treatment, only 7 patients were diagnosed with latent TB infections, and no cases of active TB were reported. Notably, most trials included in this meta-analysis were conducted in developing countries where the prevalence of TB is low [20].
Fig. 2. – Chest X-ray. (A) Normal chest X-ray before secukinumab treatment. (B) Chest X-ray performed after 2 years of secukinumab therapy showed consolidation in the left upper lobe (long white arrows). (C) Chest X-ray after 4 months of anti-TB therapy showed that consolidation was reduced significantly.

Fig. 3. – Histologic examination of a bronchoscopic biopsy sample (hematoxylin and eosin), showing granulomatous inflammation (black arrows: giant cells; blue arrows: histiocytes; red arrows: lymphocytes).

Biologic-naive patients with spondyloarthritis do not have a significantly increased TB risk compared with the general population [20]. In this case, aside from the use of biologic drugs, the patient had no additional risk factors for TB, such as the long-term use of corticosteroids, frailty, immunodeficiency diseases (eg, human immune-deficiency virus), or latent TB. Screening for latent TB is intended to detect and treat endogenous M tuberculosis infections to prevent the progression to active TB. However, patients are at a high risk of exogenous M tuberculosis infections for the duration of biologic treatments, especially in high TB burden countries, such as Vietnam. Unfortunately, this patient was not screened for latent TB annually during the 2 years of biologic therapy.

Whether the risk of new TB infections increases when using secukinumab remains inconclusive, as this is the only case reported of a patient developing TB while receiving secukinumab. However, this is the first report of an active TB diagnosis during secukinumab treatment in a patient that was previously free of either latent or active pulmonary TB.

This case report demonstrates that both before and during biologic therapy, even with secukinumab, patients should be screened for latent M tuberculosis infections annually, even if previous tests were negative, to facilitate the early detection of such infections and allow for prompt treatment before progression to active TB [21]. TB prophylaxis with isoniazid alone or isoniazid combined with rifampin is recommended for patients who have positive tests for latent infections. Increased attention to clinical symptoms, such as fatigue, fever, prolonged cough, and weight loss, can also be used to monitor for active pulmonary TB. Chest X-rays should be performed yearly to screen for the early stages of active pulmonary TB, even before symptom onset.

Conclusion

In countries with a high TB burden, patients receiving biologic treatments should be screened for TB annually. Both latent and active TB should be monitored to provide appropriate treatment to resolve TB sequelae, reducing morbidity and mortality from the disease. Additional research regarding active TB in patients treated with secukinumab remains necessary, particularly in high-burden TB countries such as Vietnam, to clarify the risk of TB in these patients.

Availability of data and materials

Data sharing is not applicable to this article as no datasets were generated or analyzed during the current study.

Authors’ contributions

Cao TN and Nguyen MD contributed equally to this article as co-first authors. All authors read and approved final version of this manuscript.
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