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A Silent Threat: Development of Pulmonary Tuberculosis After JAK Inhibitor Therapy in Severe Atopic Dermatitis

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Abstract

Janus kinase (JAK) inhibitors have emerged as an important therapeutic option for severe atopic dermatitis refractory to standard therapy. However, their immunosuppressive mechanism poses an increased risk of opportunistic infections, including tuberculosis (TB). We describe an 18-year-old male with severe atopic dermatitis who developed pulmonary TB several months after initiation of tofacitinib, despite having a negative baseline Interferon-Gamma Release Assay (IGRA). The patient presented with persistent cough, low-grade fever, fatigue, and weight loss. Radiological evaluation suggested pulmonary involvement, and microbiological confirmation established the diagnosis of active TB. Discontinuation of tofacitinib and initiation of standard anti-tubercular therapy led to gradual clinical improvement. This case highlights the need for vigilant monitoring, periodic re-evaluation, and heightened awareness of infectious complications in patients receiving JAK inhibitors, even when initial screening for latent TB infection is negative.

Keywords: NIL

Introduction

Atopic dermatitis (AD) is a chronic inflammatory skin disorder characterized by pruritus, xerosis, and recurrent eczematous lesions. Severe cases may require systemic immunomodulatory therapy when conventional topical and systemic treatments fail. JAK inhibitors, such as tofacitinib, have shown promising results in reducing disease severity by targeting intracellular signaling pathways involved in cytokine-mediated inflammation.

Despite their therapeutic potential, JAK inhibitors are associated with immunosuppression, leading to an elevated susceptibility to infections, including herpes zoster, opportunistic fungal infections, and mycobacterial infections. Tuberculosis reactivation is a recognized complication of immunosuppressive therapy. Therefore, screening for latent TB infection (LTBI) using IGRA or tuberculin skin testing (TST) is routinely recommended prior to initiation of JAK inhibitors.

However, even after negative screening, the risk of new TB infection or false-negative results—particularly in patients with chronic inflammation or immune dysregulation—remains. This case report presents an instance of pulmonary TB developing after tofacitinib therapy in an immunocompromised patient with severe AD, highlighting the limitations of baseline testing and the importance of continuous clinical monitoring.

Case Report

An 18-year-old male with a 5–7-year history of severe atopic dermatitis presented with gradually worsening respiratory symptoms while undergoing systemic therapy. His dermatitis had been refractory to potent topical steroids, topical calcineurin inhibitors, antibiotics, and phototherapy. Due to persistent disease activity and poor quality of life, systemic immunomodulation was considered.

Before initiation of therapy, routine baseline investigations including complete blood count, liver and renal function tests, and infectious disease screening were performed. An IGRA test was negative, ruling out latent tuberculosis infection at the time. Consequently, the patient was started on tofacitinib in May 2025.

For the first few months, the patient experienced significant improvement in pruritus, erythema, and skin lesions. However, approximately three months into therapy, he developed a persistent dry cough, intermittent low-grade fever, decreased appetite, and progressive fatigue. Over an 8-week period, he reported unintentional weight loss of approximately 4 kg.

Due to the persistent nature of his symptoms, he sought evaluation. On examination, the patient appeared tired but hemodynamically stable. Respiratory examination showed mild crepitations in the right upper lung field. No lymphadenopathy was noted. Skin examination showed partial improvement of AD but with ongoing xerosis and excoriations.

Diagnosis

Given the chronicity of respiratory symptoms in an immunosuppressed patient, a high index of suspicion for infectious etiology was maintained. A chest radiograph revealed patchy infiltrates in the right upper lobe, prompting further imaging. High-resolution computed tomography (HRCT) demonstrated tree-in-bud nodules, parenchymal infiltrates, and early cavitary changes suggestive of pulmonary tuberculosis.

Subsequently, sputum samples were obtained. Ziehl-Neelsen staining showed acid-fast bacilli, and cartridge-based nucleic acid amplification testing (CBNAAT) confirmed Mycobacterium tuberculosis, without rifampicin resistance. Mycobacterial culture further supported the diagnosis.

In view of the temporal association between initiation of tofacitinib and the onset of symptoms, as well as the known risk of immunosuppression-induced TB reactivation, a diagnosis of tofacitinib-associated pulmonary tuberculosis was established.

Management

Upon diagnosis, tofacitinib was immediately discontinued. The patient was started on standard first-line anti-tubercular therapy under national guidelines, consisting of isoniazid, rifampicin, pyrazinamide, and ethambutol for the intensive phase, followed by isoniazid and rifampicin for the continuation phase.

His clinical symptoms gradually improved over the following weeks, with resolution of fever and reduction in cough. Appetite and energy levels returned, and weight stabilized. Periodic liver function tests were conducted due to the hepatotoxic potential of both anti-tubercular drugs and prior immunomodulatory therapy.

Dermatitis symptoms remained partially controlled with optimized topical therapy, regular emollients, and antihistamines. A multidisciplinary approach involving dermatology, pulmonology, and infectious disease specialists ensured safe and coordinated care.

Discussion

JAK inhibitors have revolutionized the management of several chronic inflammatory conditions, including atopic dermatitis. Tofacitinib modulates multiple cytokine pathways—such as IL-4, IL-13, IL-31, and interferons—that play crucial roles in the pathophysiology of AD. However, this broad immunosuppressive mechanism impairs cell-mediated immunity, particularly the interferon-gamma pathway, which is essential for the containment of Mycobacterium tuberculosis.

While guidelines mandate TB screening prior to initiating JAK inhibitor therapy, limitations exist. False-negative IGRA results may occur in patients with chronic inflammation, malnutrition, or underlying immune dysregulation. Additionally, a negative IGRA does not protect against new TB exposure, especially in high-prevalence regions such as India.

This case underscores several important considerations:

1. Baseline screening alone is insufficient. Patients on long-term immunosuppressive therapy should receive periodic re-evaluation, especially in endemic regions.
2. Clinicians must maintain vigilance for subtle symptoms such as persistent cough, fatigue, or low-grade fever.

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3. The temporal association with immunosuppression supports the possibility of reactivation or new infection.
4. Multidisciplinary collaboration is crucial for safe management of both AD and infectious complications.
5. This case adds to the limited literature on TB reactivation associated with tofacitinib in dermatology, emphasizing the need for robust monitoring protocols.

Conclusion

Pulmonary tuberculosis may develop in patients receiving JAK inhibitors, even after negative baseline TB screening. This case highlights the need for ongoing clinical vigilance, early recognition of respiratory symptoms, and timely diagnostic evaluation. Regular monitoring in high TB-burden settings is crucial. Discontinuation of immunosuppressive therapy and prompt initiation of appropriate anti-tubercular treatment can lead to full recovery. A multidisciplinary approach ensures optimal outcomes in managing both severe atopic dermatitis and associated infectious complications.

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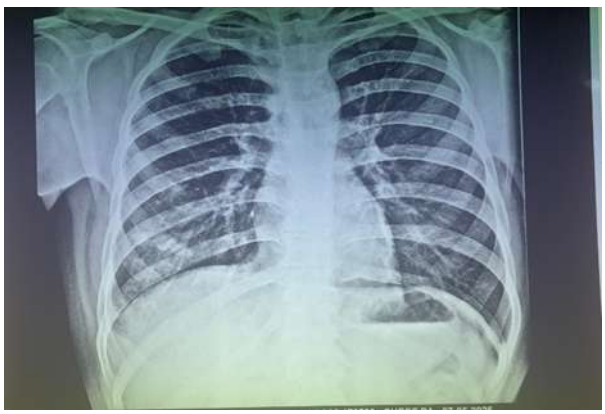

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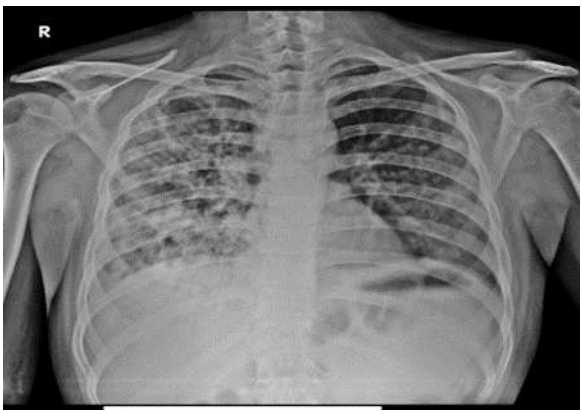

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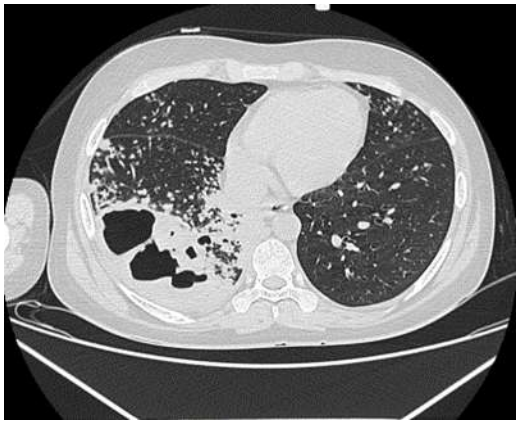

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