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CASE REPORT

Case Report: Rare Dupilumab-Associated Pulmonary and Extrapulmonary Tuberculosis

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Abstract: Dupilumab, a fully human monoclonal antibody targeting the interleukin-4 receptor alpha (IL-4Rα), has revolutionized the management of moderate-to-severe atopic dermatitis (AD) by inhibiting signaling of interleukin-4 (IL-4) and interleukin-13 (IL-13). Our case report is about a 71-year-old man with a history of AD who developed pulmonary tuberculosis (PTB) and extrapulmonary tuberculosis (EPTB) after treatment with dupilumab. The mechanism is unclear, but it may be related to the fact that dupilumab inhibits the expression of pro-inflammatory response-related genes and the innate immunity of macrophages, thereby aggravating TB infection. This is the first report of PTB and EPTB associated with dupilumab treatment, and it may be useful for clinicians to enhance TB vigilance in patients receiving dupilumab therapy, particularly in endemic regions.

Keywords: dupilumab, tuberculosis, atopic dermatitis

Introduction

Globally, TB persists as a major public health threat, with an estimated 10.8 million new cases and 1.25 million deaths in 2023 alone.[1] Latent tuberculosis infection (LTBI) affects approximately one-quarter of the world's population, posing a significant risk for reactivation under immunosuppressive therapies.[1] Dupilumab is a biologic that inhibits the signaling of IL-4 and IL-13 for treating moderate-to-severe AD.[2] Since its approval in 2017, dupilumab has demonstrated favorable safety in clinical trials, with common adverse events limited to conjunctivitis, headaches, and oral herpes.[3] However, its potential association with TB reactivation is scarcely documented. This case report suggests the possibility that dupilumab use may lead to TB reactivation, highlighting a critical pharmacovigilance gap.

Case Summary

The patient was a 71-year-old male with a 9-year history of AD and frequent rashes on extremities and itching throughout his body. Treatment response to oral antihistamines, tripterygium glycosides, and topical corticosteroids was poor. In April 2023, he developed symptoms of a cough with sputum production. Chest CT imaging demonstrated bilateral patchy infiltrates suggestive of pneumonia, for which antibiotic treatment was initiated. Initial workup showed a positive T-SPOT.TB result (Oxford Immunotec, Abingdon, UK), while sputum smear for acid-fast bacilli (AFB) and molecular testing (Xpert MTB/RIF assay) were both negative. Given the LTBI diagnosis, TB preventive treatment (TPT) was administered from April to July 2023 (isoniazid 0.3 g once daily and rifampicin 0.6 g once daily). On 18 May 2023, dupilumab was started to treat AD (600 mg initially, then 300 mg subcutaneously every 2 weeks). Following 5 months of therapy, there was a noticeable improvement in AD. However, the patient had a cough without fever and night sweats. Additionally, a 2 cm × 1.5 cm (diameter × height), tender, dome-shaped mass with an erythematous surface was observed on the left anterior chest wall in the subclavicular region. The lesion remained intact without signs of rupture (Figure 1). A chest CT scan revealed widespread lesions, and calcified, enlarged hilar and mediastinal lymph nodes (Figure 2). During tracheoscopy, neoplasms were found close to the basal portion of the left and right main bronchus (Figure 3). Granulomatous lesions were confirmed by pathology.

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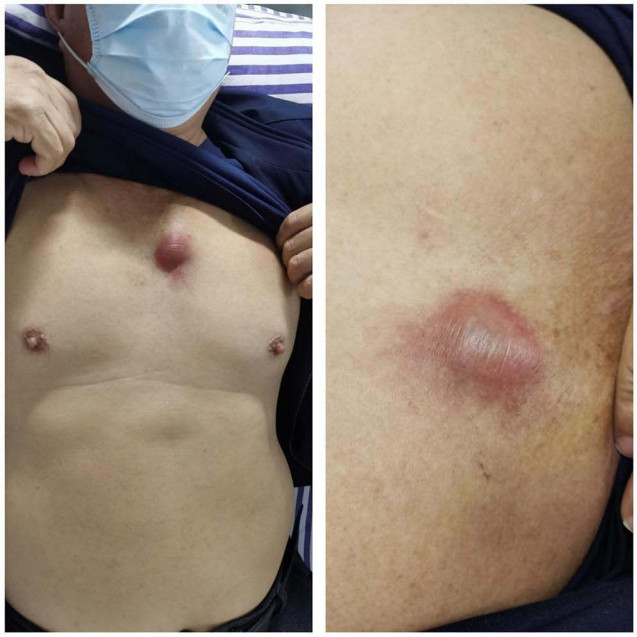

Figure 1 Chest wall mass.

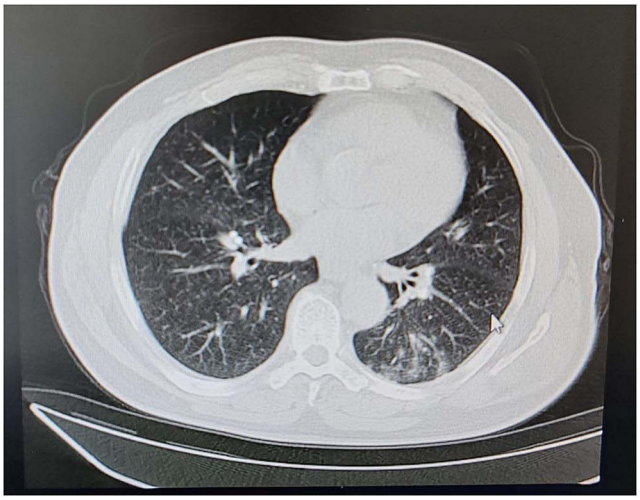

Figure 2 Widespread lesions in both lungs on chest CT.
Abbreviation: CT, computed tomography.

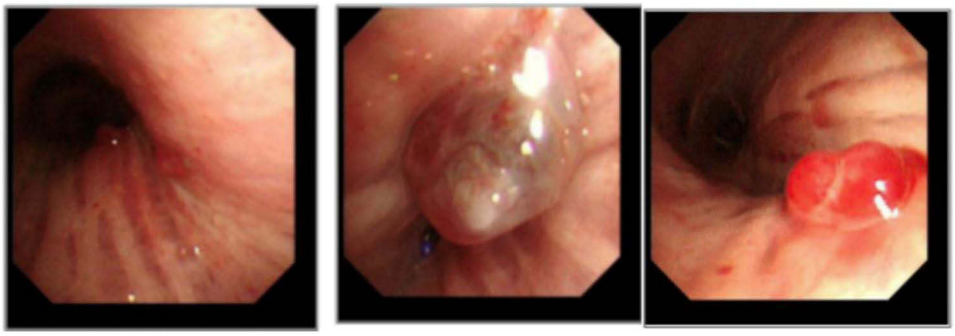

Figure 3 Endobronchial neoplasms.

Mycobacterium tuberculosis complex was detected by metagenomic next-generation sequencing (mNGS: KingMed Diagnostics, Guangzhou, Guangdong, China) in the pierced tissue of the chest wall mass. Before starting treatment, drug susceptibility testing was performed and the results were negative. The treatment regimen included 0.3 g of isoniazid once daily, 0.6 g of rifampicin once daily, 1 g of ethambutol once daily, and 0.5 g of pyrazinamide three times a day. The bulk of the mass in the chest wall significantly decreased during the 2-month follow-up. Following tracheoscopy, endobronchial neoplasms were reduced in size by January 2024. The results of the sputum culture and sputum smear were negative. Following 6 months of anti-TB therapy, the infection was cured, and symptoms were resolved.

Discussion

The development of *Mycobacterium tuberculosis* within the lungs is termed PTB,[4] while EPTB refers to the infection involving organs outside the pulmonary system (such as the lymph nodes, bones, skin, urogenital system, neurological system, etc).[5] Among the clinical signs are weight loss, exhaustion, and fever. Dupilumab inhibits intracellular inflammatory signal transmission by blocking IL-4Ra, the co-receptor of IL-4 and IL-13, thus contributing to the regulation of T-helper 2 (Th2) mediated inflammatory responses.[2] A PubMed search from March 2017 to March 2025 using the keywords "dupilumab" AND "tuberculosis" revealed a reported case, which is TB lymphadenitis (right neck and groin area) in a young female with severe AD following 3 months of dupilumab treatment. The lymphadenopathy completely disappeared after 7 months of anti-TB treatment.[6] Notably, our patient manifested concurrent endobronchial and chest wall TB following 5 months of dupilumab treatment. Partial clinical overlap can be observed between these two cases.

Neutrophil recruitment to TB foci and subsequent granuloma maturation constitute indispensable components of the early host defense against TB.[7] Dupilumab potently suppresses IL-17-related genes (CXCL1/2, S100),[8,9] particularly impairing the CXCL1/2-dependent neutrophil recruitment,[10] potentially facilitating TB infection via Th17-CXCL1/2 axis inhibition. In the in vitro experiments conducted by Lundahl et al,[11] Th2 cytokines, IL-4 and IL-13, can activate M2 macrophages, increase oxidative phosphorylation, boost pro-inflammatory cytokine response, and thwart TB assault. Dupilumab, by inhibiting IL-4/IL-13 signaling, may impair macrophage bactericidal function.[12]

According to a thorough pooled analysis of seven clinical trials using dupilumab, there was no increase in TB infection.[13] Nevertheless, in this patient, dupilumab therapy was associated with the development of PTB and EPTB, which may be linked to predisposition from chronic immunosuppressant exposure or inadequate initial TPT duration. Although the risk of TB reactivation associated with dupilumab is lower than that with TNF-α inhibitors,[14] it nevertheless warrants clinical vigilance. Before initiating dupilumab, TB screening is essential, particularly for the elderly, immunocompromised individuals, and those from TB-endemic regions.[15] Standardized management, including a complete course of treatment for LTBI, is mandatory. When conventional diagnostics yield inconclusive results, mNGS enables rapid identification of fastidious pathogens in atypical presentations, preventing significant morbidity associated with diagnostic delays.[16] Although other Th2-targeting biologics (eg, lebrikizumab, tralokinumab[17,18]) show no TB signals in the current study, we recommend uniform vigilance for these agents until population-level surveillance confirms differential risk profiles.

Conclusion

To the best of our knowledge, this is the first instance of an association between dupilumab use and PTB and EPTB. However, as this is an isolated occurrence, the causality remains presumptive and warrants validation through larger pharmacovigilance studies. We caution clinicians that when using dupilumab, it is essential to emphasize baseline TB screening, maintain vigilance for TB symptoms during treatment, and extend prophylaxis in high-risk cases.

Patient Consent

Informed consent was obtained from the patient for publication of the case details and accompanying images. Institutional approval for publication was obtained from the Ethics Committee of Huzhou Central Hospital.

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Disclosure

No conflict of interest.

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