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Severe Disseminated Tuberculosis in Late Pregnancy During Infliximab Therapy for Crohn's Disease Complicated by a Paradoxical Inflammatory Reaction

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Abstract

We report the case of a 30-year-old woman with Crohn's disease treated with infliximab and previously treated for latent tuberculosis (TB) who presented at 36 weeks of gestation with cough, dyspnea, and preterm prelabor rupture of membranes. Her condition rapidly deteriorated with acute pulmonary edema, new-onset atrial fibrillation, and respiratory failure, requiring urgent cesarean delivery. Bronchoalveolar lavage confirmed infection with drug-susceptible *Mycobacterium tuberculosis* complex, and standard four-drug anti-TB treatment was initiated. Following infliximab discontinuation, she developed hypoxemic respiratory failure. Imaging showed miliary TB with pleural, hepatic, and splenic involvement. After exclusion and treatment of concomitant bacterial infection, a paradoxical TB-associated immune reconstitution inflammatory syndrome was suspected. She improved with high-dose methylprednisolone and high-flow nasal oxygen. Her course was complicated by tuberculous pleural effusion, pneumothorax, and catheter-related *Candida albicans* candidemia, but she ultimately recovered with continued TB therapy. This case highlights the risk of severe disseminated TB in pregnant patients receiving tumor necrosis factor (TNF)-alpha inhibitors, despite previous treatment for latent TB, and the challenge of recognizing paradoxical inflammatory deterioration after anti-TNF withdrawal.

Categories: Obstetrics/Gynecology, Pulmonology, Infectious Disease
Keywords: crohn's disease, immune reconstitution inflammatory syndrome, infliximab, miliary tuberculosis, paradoxical reaction, pregnancy, tuberculosis, tumor necrosis factor-alpha inhibitor

Introduction

Tuberculosis (TB) remains a major global cause of morbidity and mortality. The risk of progression from latent TB infection to active disease is increased by impairment of tumor necrosis factor-alpha (TNF-α)-mediated immunity. TNF-α is important for granuloma formation and maintenance; consequently, TNF-α inhibitors, including infliximab, are associated with reactivation of latent TB and with severe, disseminated, and extrapulmonary disease presentations [1-3].

Pregnancy can obscure the recognition of TB because cough, fatigue, dyspnea, anemia, and constitutional symptoms may be attributed to pregnancy or to common obstetric conditions. However, active TB diagnosed in late pregnancy may have immediate implications for maternal respiratory stability, timing and mode of delivery, neonatal evaluation, and infection-control measures [4-6].

Paradoxical clinical worsening after initiation of effective anti-TB therapy is well recognized in people living with HIV after antiretroviral therapy initiation. However, similar inflammatory phenomena have also been reported in non-HIV-associated TB, especially after reduction or discontinuation of immunosuppressive therapy, including TNF-α inhibitors [7-9]. These reactions must be differentiated from inadequate drug exposure, drug resistance, nonadherence, uncontrolled infection, and superimposed bacterial or fungal infection.

We describe a case of severe disseminated, smear-positive pulmonary TB diagnosed around urgent cesarean delivery in a patient receiving infliximab for Crohn's disease. The course was complicated by acute respiratory failure, tuberculous pleural involvement, and a presumed paradoxical inflammatory reaction after infliximab withdrawal, requiring high-dose corticosteroids.

Case Presentation

A 30-year-old primigravida with a history of Crohn's disease, treated with infliximab since April 2017 and currently receiving subcutaneous injections every two weeks, was admitted in August 2024 at 36 weeks and three days of gestation because of preterm prelabor rupture of membranes. Her medical history further included perianal fistula surgery, glucose-6-phosphate dehydrogenase deficiency, and latent TB, diagnosed

in June 2023 following tuberculin skin test conversion after exposure to her father, who had active TB. A six-month course of isoniazid (300 mg once daily), with pyridoxine supplementation and monthly monitoring of liver function tests, was initiated in June 2023 and completed in December 2023, while infliximab therapy was maintained; the preventive regimen was completed without documented adverse effects or intolerance. She conceived in late December 2023, around the time the isoniazid course was completed, so that the current admission for active TB occurred approximately 14 months after the tuberculin skin test conversion and around eight months after completion of latent TB treatment. During several weeks before admission, she had experienced persistent cough, exertional dyspnea, palpitations, and intermittent chest discomfort, without documented fever or constitutional symptoms.

On admission, she was tachycardic (116-120 beats/min) and hypoxemic, with an oxygen saturation of 91% on room air, improving to 95% with 2 L/min oxygen via nasal cannula. She rapidly developed acute pulmonary edema, ascites, and new-onset atrial fibrillation with rapid ventricular response. Chest radiography showed bilateral pleural effusions and bilateral infiltrates. Because of maternal cardiopulmonary deterioration and arrest of labor, urgent cesarean delivery was performed at 36 weeks and four days of gestation. Postoperatively, she was admitted to the ICU because of persistent hypotension requiring vasopressors. Echocardiography demonstrated preserved left ventricular systolic function without structural heart disease. CT pulmonary angiography excluded pulmonary embolism but showed bilateral patchy pulmonary infiltrates and pleural effusions (Figure *1*). Pleural fluid analysis showed a lymphocyte-predominant exudate (978 nucleated cells/μL, 83% lymphocytes). TB testing on pleural fluid was negative, including auramine staining for acid-fast bacilli, PCR for *Mycobacterium tuberculosis* complex, and mycobacterial culture. Given the persistent cough, previous treatment for latent TB, and abnormal thoracic imaging, bronchoalveolar lavage (BAL) was performed. Auramine staining and PCR were positive for *M. tuberculosis* complex, without a rifampicin-resistance mutation. Culture-based testing later confirmed susceptibility to rifampicin, isoniazid, ethambutol, and pyrazinamide. Standard four-drug anti-TB treatment with rifampicin, isoniazid, pyrazinamide, and ethambutol (RIPE) was initiated two days after delivery, and infliximab was withheld.

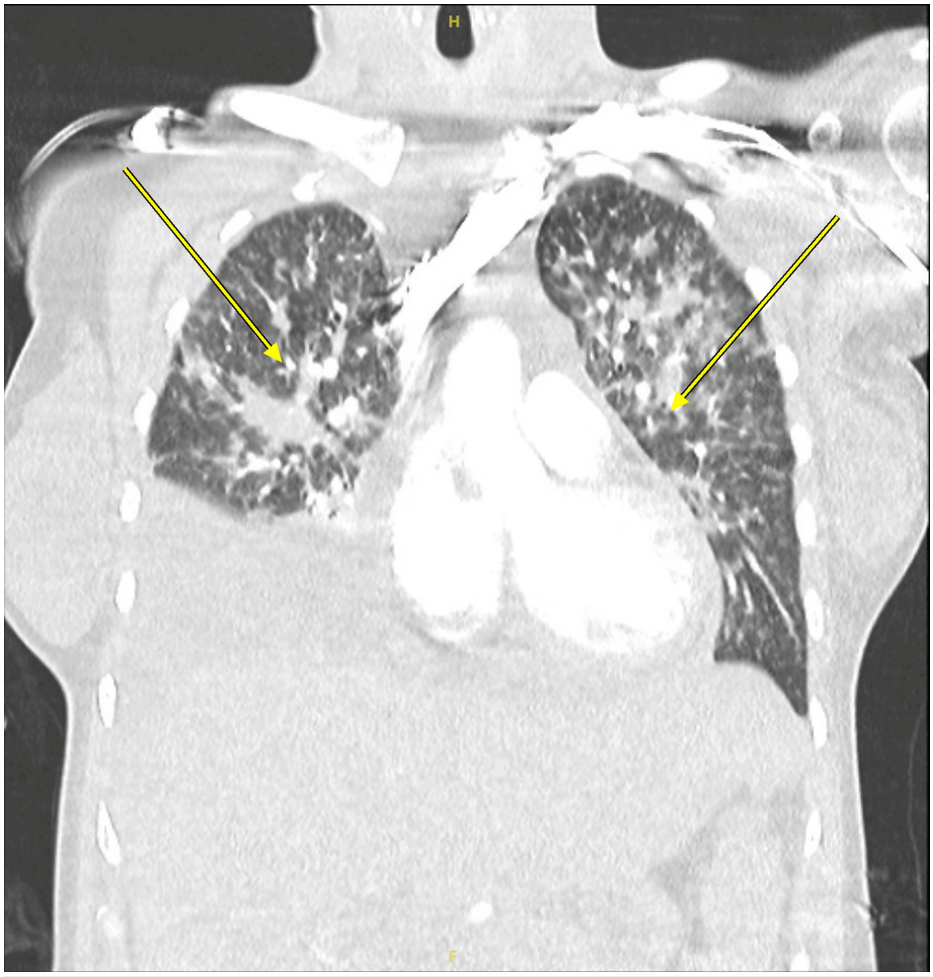


FIGURE 1: Initial CT pulmonary angiogram (coronal reconstruction).

Performed at admission for maternal cardiopulmonary deterioration. Pulmonary embolism was excluded. Bilateral patchy pulmonary infiltrates (arrows) and a unilateral pleural effusion are shown.

During her initial ICU stay of approximately five days, she required vasopressor support and temporary high-flow nasal oxygen. Her hemodynamic and respiratory status gradually improved, allowing vasopressor discontinuation and transfer to the pulmonary ward on 2 L/min oxygen via nasal cannula, with mild residual dyspnea.

Nineteen days after starting antituberculous therapy, she was readmitted to the ICU with high fever, marked tachycardia, worsening bilateral pulmonary infiltrates, and severe hypoxemic respiratory failure requiring high-flow nasal oxygen (HFNO). CT imaging demonstrated diffuse miliary pulmonary nodules, hepatosplenomegaly, and suspected hepatic and splenic lesions (Figure *2*); both the hepatosplenomegaly and the suspected lesions were new compared with the initial CT pulmonary angiogram. A concurrent *Pseudomonas aeruginosa* respiratory infection and erysipelas at the cesarean wound were treated with piperacillin-tazobactam. Nevertheless, persistent fever, elevated inflammatory markers, and respiratory impairment despite drug-susceptible TB, adequate drug exposure, and treatment of bacterial co-infection raised suspicion of paradoxical TB-associated immune reconstitution inflammatory syndrome following infliximab withdrawal.

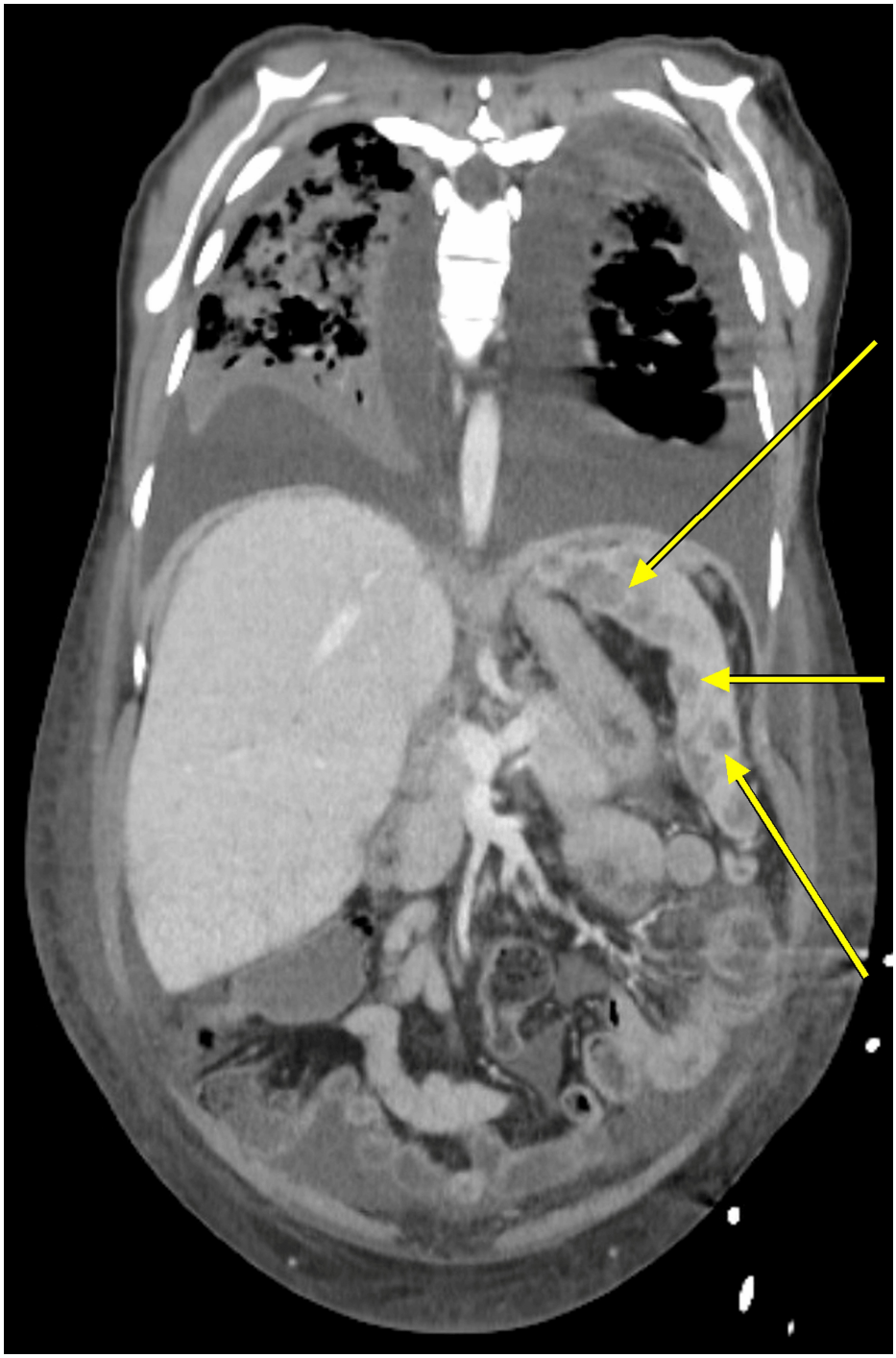


FIGURE 2: Follow-up contrast-enhanced CT (coronal reconstruction).

Performed 19 days after initiation of antituberculous treatment, demonstrating diffuse miliary pulmonary nodules, hepatosplenomegaly, and multiple hypodense splenic lesions (arrows).

Methylprednisolone at 1.5 mg/kg/day was initiated for presumed paradoxical inflammatory deterioration. Bilateral pleural effusions, already present at admission and subsequently confirmed to be tuberculous, required repeated thoracenteses and bilateral chest drain placement. The course was further complicated by a left apical pneumothorax and catheter-associated *Candida albicans* candidemia. The infected catheter was removed, and treatment with caspofungin was followed by oral fluconazole according to antifungal susceptibility testing.

At discharge from the pulmonary ward, 65 days after delivery, she no longer required supplemental oxygen and had regained a regular cardiac rhythm. After completion of the intensive phase, treatment was continued with rifampicin and isoniazid for a total treatment duration of 12 months given the severe

disseminated presentation. During outpatient follow-up, she reported gradual improvement, with persistent fatigue but minimal respiratory symptoms and favorable radiographic evolution. Infliximab was not restarted. At gastroenterology follow-up in May 2026, her Crohn's disease remained in deep remission without disease-specific therapy, and future anti-TNF treatment was considered best avoided.

Discussion

This case illustrates severe disseminated TB arising during late pregnancy in a patient receiving infliximab for Crohn's disease, despite previous treatment for latent TB. TNF-α is essential for granuloma maintenance and containment of *M. tuberculosis*; therefore, TNF-α inhibitors increase the risk of TB reactivation and are associated with extrapulmonary and disseminated presentations [1-3,10]. Although screening and preventive treatment reduce this risk, they do not completely eliminate it, and both false-negative interferon-γ release assays during infliximab therapy and, as illustrated by the present case, insufficient preventive treatment duration in high-risk patients can contribute to breakthrough disease. In this patient, it was not possible to distinguish definitively between reactivation and reinfection.

The possibility that the six-month isoniazid regimen provided incomplete protection deserves particular attention. While six to nine months of isoniazid is typically recommended for latent TB infection, Comstock's re-analysis of the United States Public Health Service and Bethel, Alaska, prevention trials showed that six months does not provide optimal protection and that nine to 10 months appears to be the optimal duration, particularly in high-risk groups [11]. Our patient's uninterrupted infliximab therapy placed her in a high-risk category for reactivation, for which the nine-month duration would have been the more optimal choice; no specific rationale for the six-month duration or for the choice of isoniazid over rifampicin was documented, and no intolerance or hepatotoxicity prompted shortening. In retrospect, the six-month duration may have been inadequate in this high-risk setting and cannot be excluded as a contributor to treatment failure, particularly since pregnancy and the postpartum period themselves increase the risk of progression from latent to active TB [6,12]. When latent TB infection is treated in patients receiving TNF-α inhibitors, the nine-month isoniazid regimen should therefore be strongly preferred.

Diagnosis was challenging because the patient's cough and exertional dyspnea developed without fever or clear constitutional symptoms and could initially be attributed to physiological changes of pregnancy. Pregnancy-related immune modulation may mask or make TB symptoms nonspecific; fatigue and dyspnea in particular overlap with common pregnancy symptoms [5,6,12]. Concurrent infliximab therapy, through TNF-alpha blockade, further increased the risk of active TB and may have contributed to an atypical or less inflammatory clinical presentation [1,10]. Her acute presentation with pulmonary edema, atrial fibrillation, pleural effusions, and respiratory failure led to urgent cesarean delivery. BAL confirmed drug-susceptible pulmonary TB, while subsequent CT imaging demonstrated miliary disease with pleural and probable hepatosplenic involvement. Given the disseminated presentation, TB treatment was continued beyond the standard six-month regimen [13,14].

A major challenge was clinical deterioration approximately three weeks after initiation of RIPE therapy and withholding infliximab. Although *P. aeruginosa* respiratory infection, cesarean-wound erysipelas, and later catheter-related candidemia were identified and treated, they did not fully explain the diffuse infiltrates with severe hypoxemia. In the absence of drug resistance or inadequate drug exposure, the temporal association with infliximab cessation and improvement after corticosteroids supported a presumed paradoxical TB-associated immune reconstitution inflammatory syndrome. Such inflammatory reactions can occur after withdrawal of immunosuppressive therapy, including TNF-α inhibitors [8,9].

High-dose methylprednisolone, high-flow nasal oxygen, targeted antimicrobial therapy, pleural drainage, and multidisciplinary management led to gradual recovery without the need for invasive mechanical ventilation. This case highlights the importance of maintaining suspicion for active TB in pregnant patients receiving immunosuppression and the challenge of distinguishing paradoxical inflammatory deterioration from treatment failure or superinfection.

A further discussion point is why infliximab was not restarted once a diagnosis of paradoxical TB-associated immune reconstitution inflammatory syndrome was made. Restarting TNF-α inhibition could theoretically dampen the paradoxical inflammation, and infliximab has paradoxically been reported as a treatment for mycobacterial IRIS in selected cases, including tuberculous meningitis [15,16]. In this patient, the decision was not to restart infliximab during active disseminated TB.

Conclusions

Active TB should be considered promptly in pregnant or postpartum patients receiving TNF-α inhibitors who develop persistent cough, dyspnea, unexplained pulmonary infiltrates, pleural effusions, or systemic inflammation, even when latent TB has previously been treated. Furthermore, in patients receiving TNF-α inhibitors, latent TB infection should be treated with the nine-month isoniazid regimen or a short-course rifamycin-based regimen, as six months of isoniazid may not provide optimal protection in this high-risk group. The clinical course may be atypical, with rapidly progressive or disseminated disease, unusual

pulmonary manifestations, and features mimicking obstetric or cardiac emergencies, potentially delaying diagnosis.

Clinical deterioration after initiation of antituberculous treatment and withdrawal of TNF-α inhibition requires systematic exclusion of drug resistance, inadequate drug exposure, nonadherence, and concomitant infection. Once these alternative explanations have been excluded, a paradoxical TB-associated inflammatory reaction should be considered as a cause of progressive inflammatory lung disease despite appropriate treatment. In life-threatening cases, carefully monitored corticosteroid therapy may be considered within a multidisciplinary approach.

Additional Information

Author Contributions

All authors have reviewed the final version to be published and agreed to be accountable for all aspects of the work.

Concept and design: Maarten Claes, Abraham Van Poppel, Eric Florence, Symen Ligthart

Acquisition, analysis, or interpretation of data: Maarten Claes, Abraham Van Poppel, Eric Florence, Symen Ligthart

Drafting of the manuscript: Maarten Claes

Critical review of the manuscript for important intellectual content: Maarten Claes, Abraham Van Poppel, Eric Florence, Symen Ligthart

Supervision: Abraham Van Poppel

Disclosures

Human subjects: Informed consent for treatment and open access publication was obtained or waived by all participants in this study. **AI use statement:** The authors used Perplexity as follows: translation, language polishing in Introduction, Case Presentation. AI was used solely for language polishing and translation, not to generate factual content, statistics, or references. Verification of these elements was therefore not applicable. The authors confirm that they have reviewed and verified all AI-assisted content and take full responsibility for the work. **Conflicts of interest:** In compliance with the ICMJE uniform disclosure form, all authors declare the following: **Payment/services info:** All authors have declared that no financial support was received from any organization for the submitted work. **Financial relationships:** All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. **Other relationships:** All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

References

1. Keane J, Gershon S, Wise RP, et al.: Tuberculosis associated with infliximab, a tumor necrosis factor α-neutralizing agent. N Engl J Med. 2001, 345:1098-104. 10.1056/NEJMoa011110
2. Dixon WG, Hyrich KL, Watson KD, Lunt M, Galloway J, Ustianowski A, Symmons DP: Drug-specific risk of tuberculosis in patients with rheumatoid arthritis treated with anti-TNF therapy: results from the British Society for Rheumatology Biologics Register (BSRBR). Ann Rheum Dis. 2010, 69:522-8. 10.1136/ard.2009.118935
3. Solovic I, Sester M, Gomez-Reino JJ, et al.: The risk of tuberculosis related to tumour necrosis factor antagonist therapies: a TBNET consensus statement. Eur Respir J. 2010, 36:1185-206. 10.1183/09031936.00028510
4. Sugarman J, Colvin C, Moran AC, Oxlade O: Tuberculosis in pregnancy: an estimate of the global burden of disease. Lancet Glob Health. 2014, 2:710-6. 10.1016/S2214-109X(14)70330-4
5. Mathad JS, Gupta A: Tuberculosis in pregnant and postpartum women: epidemiology, management, and research gaps. Clin Infect Dis. 2012, 55:1532-49. 10.1093/cid/cis732
6. Jonsson J, Kühlmann-Berenzon S, Berggren I, Bruchfeld J: Increased risk of active tuberculosis during pregnancy and postpartum: a register-based cohort study in Sweden. Eur Respir J. 2020, 55:10.1183/13993003.01886-2019
7. Meintjes G, Brust JC, Nuttall J, Maartens G: Management of active tuberculosis in adults with HIV . Lancet HIV. 2019, 6:e463-74. 10.1016/S2352-3018(19)30154-7
8. Church LW, Chopra A, Judson MA: Paradoxical reactions and the immune reconstitution inflammatory syndrome. Microbiol Spectr. 2017, 5:10.1128/microbiolspec.TNMI7-0033-2016
9. Rivoisy C, Tubach F, Roy C, et al.: Paradoxical anti-TNF-associated TB worsening: frequency and factors associated with IRIS. Joint Bone Spine. 2016, 83:173-8. 10.1016/j.jbspin.2015.04.022
10. Parita S, Vivek K, Stephan K, William P, Yizhak K: Infliximab therapy leading to pulmonary tuberculosis in a patient with negative interferon γ release assay (IGRA)-based QuantiFERON Gold test. J Investig Med High Impact Case Rep. 2017, 5:2324709617717540. 10.1177/2324709617717540

11. Comstock GW: How much isoniazid is needed for prevention of tuberculosis among immunocompetent adults?. Int J Tuberc Lung Dis. 1999, 3:847-50.
12. Wen J, He JQ: Clinical characteristics and pregnancy outcomes in pregnant women with TB: a retrospective cohort study. Ann Med. 2024, 56:2401108. 10.1080/07853890.2024.2401108
13. WHO Consolidated Guidelines on Tuberculosis: Module 4: Treatment: Drug-Dusceptible Tuberculosis Treatment. World Health Organization, Geneva, Switzerland; 2022.
14. Saukkonen JJ, Duarte R, Munsiff SS, et al.: Updates on the treatment of drug-susceptible and drug-resistant tuberculosis: an official ATS/CDC/ERS/IDSA clinical practice guideline. Am J Respir Crit Care Med. 2025, 211:15-33. 10.1164/rccm.202410-2096ST
15. Hsu DC, Faldetta KF, Pei L, et al.: A paradoxical treatment for a paradoxical condition: infliximab use in three cases of mycobacterial IRIS. Clin Infect Dis. 2016, 62:258-61. 10.1093/cid/civ841
16. Azeem A, Ahmad F, Velagapudi M: Infliximab for immune reconstitution inflammatory syndrome (IRIS) in tuberculous meningitis; a treatment paradox. Open Forum Infect Dis. 2021, 8:S785. 10.1093/ofid/ofab466.1593