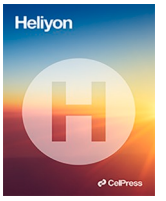
Heliyon 10 (2024) e28530

Contents lists available at ScienceDirect

Heliyon

journal homepage: www.cell.com/heliyon



Case report

# A pregnant woman with pre-XDR PTB giving birth to a healthy newborn: A case report

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ARTICLE INFO

*Keywords:*
Pre-extensively drug-resistant tuberculosis
Multidrug-resistant tuberculosis
Pregnancy
Treatment
Case report

ABSTRACT

We reported a late-pregnancy woman with pre-XDR PTB who had not received regular anti-tuberculosis treatment prior to delivery. Despite this, she successfully delivered a premature baby who exhibited normal growth and development, and subsequently completed her anti-tuberculosis treatment. This report suggests that delayed treatment for pre-XDR TB during late pregnancy does not necessarily increase the risk of treatment failure for the mother or the risk of neonatal tuberculosis.

## 1. Introduction

Multidrug-resistant (MDR-TB) and extensively-drug resistant tuberculosis (XDR-TB) remain a huge threat to global public health and tuberculosis (TB) control [1]. Management of MDR/XDR-TB in pregnancy is challenging, and the evidence to guide clinicians is very limited. Some studies have suggested that MDR-TB is associated with a higher risk of adverse maternal and perinatal outcomes [2,3]. Congenital infection via vertical transmission is rare but is associated with high neonatal mortality (up to 60%) and morbidity [4]. And there are many difficulties in the diagnosis of neonatal TB, especially the low sensitivity of immunological and microbiological tests. Clinical diagnosis of neonatal TB depends on symptoms, imaging results, possible exposure history and response to treatment [5,6]. Although there is evidence that early detection and treatment of maternal drug-sensitive TB could protect fetuses and newborns from congenital TB and preterm birth, clinicians could be confused by drug-resistant TB because of the high side effects of drugs and the lack of evidence-based medical evidence for the use of pregnant women [7,8]. In this report, we describe a woman in the third trimester who was diagnosed with pre-extensively-drug resistant pulmonary tuberculosis (pre-XDR PTB). Without formal anti-TB treatment before delivery, she successfully delivered a baby girl vaginally with normal growth and development until 17 months of follow-up, and subsequently completed 18 months of regular anti-TB treatment.

## 2. Case description

A 31-year-old woman, whose younger brother suffered from TB, was diagnosed as threatened preterm labor at a local obstetrics clinic due to paroxysmal abdominal pain for 6 days. However, she had been coughing and producing sputum repeatedly for 7 months and had fever for 10 days (maximum body temperature was 39 °C). Accompanied by sore throat, hoarseness and chest pain. Chest computed tomography (CT) scan suggested the possibility of cavitary TB in the left lung. Sputum acid-fast bacilli tested positive (4+).

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https://doi.org/10.1016/j.heliyon.2024.e28530
Received 25 November 2023; Received in revised form 10 March 2024; Accepted 20 March 2024
Available online 24 March 2024

Pulmonary tuberculosis (PTB) was diagnosed, and she started anti-TB treatment with isoniazid (300mg IV once daily), rifampin (450mg IV once daily) and ethambutol (750mg orally once daily) on the same day. After 3 days of anti-TB, sputum *Bacillus* (BAC) culture and drug sensitivity test results showed *Mycobacterium* tuberculosis (MTB) culture positive, and resistance to rifampin. Due to the limited drugs in the local hospital, she was transferred to the Department of Infectious Diseases of our hospital. Physical examination revealed bilateral cervical lymph node enlargement, approximately 3*4cm in size. Blood tests showed elevated WBC ($7.25*10^9$/L), decreased lymphocytes ($0.78*10^9$/L), elevated neutrophil rate (84.5%), moderate anemia (85g/L), thrombocytosis ($495*10^9$/L). Sputum acid-fast bacilli was positive (1+). The anti-TB regimen was adjusted to isoniazid (300mg IV once daily), pyrazinamide (1500mg orally once daily), ethambutol (750mg orally once daily) and linezolid (600mg orally once daily). During the inpatient anti-TB treatment in our hospital, the sputum acid-fast bacilli was repeated several times, and the results were 2+ and 3+, respectively. After only 4 days of use of the second anti-TB regimen, the patient stopped taking all drugs due to nausea and discomfort, and was discharged voluntarily. On Feb 6, 2022, a baby girl was delivered vaginally in the local hospital.

On Feb 9, 2022, the puerpera was admitted to hospital for the second time. Sputum BAC culture and drug susceptibility test results showed *mycobacterial* culture positive, and resistance to isoniazid, rifampin, streptomycin, fluoroquinolones, levofloxacin, moxifloxacin and rifabutin. The results of sputum molecular testing (Gensizer targeted sequencing technology) showed that the human *Mycobacterium* tuberculosis complex was detected and resistant to isoniazid, rifampin, streptomycin, ethambutol and fluoroquinolones. Bilateral cervical lymph node aspiration showed lymphocytes and necrosis. CT scan showed secondary PTB in both lungs with dissemination and cavitary lesion formation, caseous pneumonia in the left lung, partial lung consolidation and atelectasis in the upper and lower lobes of the left lung, and bilateral pleural thickening (Fig. 1A). Pre-XDR PTB was diagnosed. On Feb 11, 2022, she started anti-TB treatment with bedaquiline (400mg orally once daily for the first two weeks, then adjusted to 200mg orally three times weekly), prothionamide (300mg orally every 12 hours), cycloserine (250mg orally every 12 hours), ethambutol (750mg orally once daily), pyrazinamide (1500mg orally once daily) and amikacin (600mg IV once daily), and the total course of treatment was 18 months. At the end of the 4th, 10th, and 13th month of anti-TB treatment, the symptoms continued to decrease. CT scan showed that a continuous reduction in lesions in the upper and lower lobes of both lungs. From the end of the 5th and 6th months, sputum acid-fast bacilli and sputum BAC culture were negative. At the end of the 18th month, compared with the initial image, CT scan showed that the lesions in both lungs were significantly reduced, the cavities were shrunk, and part of the lung tissue had expanded (Fig. 1B).

### 2.1. Newborn condition

A 2400g female infant was delivered vaginally after spontaneous premature labor at 35 weeks of gestation with Apgar score of 1-5-10 minutes (10-10-10). Blood tests showed leukocytosis ($10.32*10^9$/L) and elevated procalcitonin (0.176ng/ml). MTB IgG antibody test result showed positive. Anteroposterior chest X-ray showed slightly increased markings in both lungs. Sputum acid-fast stained smear, sputum culture and blood culture tests were all negative. The diagnosis of neonatal amniotic fluid aspiration pneumonia, premature infant and low birth weight infant were made. She was discharged after a brief empiric antibiotic treatment. At 12 months of follow-up, MTB IgM antibody was tested negative and IgG antibody was tested positive. Purified protein derivative (PPD) intradermal skin test result showed negative. Anteroposterior chest X-ray at 14 months showed increased and disordered markings in both lungs. At 17 months, chest CT showed some inflammation or poor aeration in the posterior segment of the upper lobe of the left lung, and the rest was normal. PPD intradermal skin test result showed negative. During the follow-up, the baby did not show any obvious symptoms of tuberculosis infection such as cough, sputum, night sweats, or fever. She received regular physical examinations at the childcare clinic, and her growth and development were not significantly different from those of ordinary children.

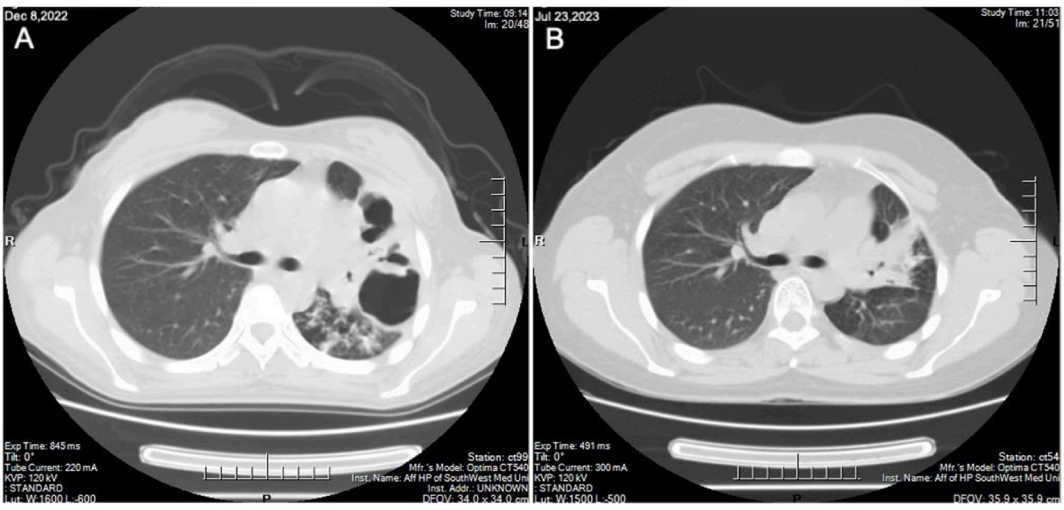


**Fig. 1.** Changes in CT scan A and B showed that the lesions in both lungs were significantly reduced, the cavities were shrunk, and part of the lung tissue had expanded after treatment.

## 3. Discussion

We described a woman diagnosed with pre-XDR PTB in the third trimester who received anti-TB therapy for only 7 days before delivery. At 6 months of anti-TB treatment after delivery, the sputum smear and sputum BAC culture turned negative. After 18 months, the patient's symptoms disappeared, and the imaging lesions were significantly reduced. This case suggests that delay in treatment for pre-XDR-TB in the third trimester does not necessarily increase the risk of maternal treatment failure. However, some studies have shown that pregnant women with XDR-TB can receive bedaquiline and linezolid treatment in the last 3 weeks of pregnancy without serious side effects [9]. Therefore, the timing of anti-TB treatment in pregnant women with XDR-TB, especially in the third trimester, is questionable.

The newborn in this report was a preterm infant with low birth weight. However, despite not receiving preventive anti-TB treatment and living with her mother after birth, the baby was in good health at 17 months of follow-up. In a cohort study in South Africa, although 48% of pregnant women had adverse pregnancy outcomes, including 28% of preterm births and 35% of low birth weight infants, but more than 80% of the infants were healthy and growing normally at 12 months of follow-up [10]. Because multiple second-line anti-TB drugs are potentially teratogenic to the fetus [11], the potential risks to the fetus must be weighed against the risks of delayed treatment. This suggests that natural exposure to pre-XDR TB and delayed treatment by the mother do not necessarily increase the risk of neonatal congenital TB infection in the third trimester, and that prophylactic anti-TB therapy after birth also needs to be comprehensively evaluated.

Due to the rarity of pre-XDR PTB pregnant patients currently admitted in clinical work, the clinical data we can collect in this area is extremely limited, resulting in limitations in our research. In future research, we will strive to expand the sample size of such patients and continue to explore relevant high-quality evidence to provide more detailed theoretical guidance for the treatment of XDR-TB in pregnancy.

## Funding

This work was supported by the Sichuan Provincial Science and Technology Department Research Project (2020YFS0514); National 'Prevention and Control of Major Infectious Diseases such as AIDS and Viral Hepatitis' Science and Technology Major Project of the 13th Five-Year Plan - Research on New Traditional Chinese Medicine Treatment Regimen for Drug-Resistant Pulmonary Tuberculosis (Project Number: 2018ZX10725509-001-011).

## Ethical approval

Informed consent was obtained from the patient's relative for the publication of all images, clinical data and other data included in the manuscript. The institution operates in accordance with the 1964 Helsinki declaration and its later amendments.

## Data availability

Data included in article/supp. material/referenced in article.

## CRediT authorship contribution statement

**Lei Wang:** Writing – original draft, Software, Project administration, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Xin Zhang:** Software, Investigation, Data curation. **Weiyang Wang:** Software, Investigation, Data curation. **Fuli Huang:** Writing – review & editing, Validation, Supervision, Methodology, Funding acquisition, Conceptualization.

## Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

## Acknowledgements

We thank all study subjects and collaborating clinicians for participating and contributing to the study.

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