Journal of Communicable Diseases
Volume 56, Issue 2 - 2024, Pg. No. 121-125
Peer Reviewed & Open Access Journal

Case Report

A Case of Tuberculous Meningitis in a Pregnant Woman with Miliary Pulmonary Tuberculosis: Challenges in Diagnosis and Management

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DOI: https://doi.org/10.24321/0019.5138.202438

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How to cite this article:
Turdumambetova G, Usubalieva E, Toktorgazieva K, Akhmetova R, Duishekeeva A, Myrzaliev B, Ahmatov M, Garg R, Zhumabekova A. A Case of Tuberculous Meningitis in a Pregnant Woman with Miliary Pulmonary Tuberculosis: Challenges in Diagnosis and Management. J Commun Dis. 2024;56(2):121-125.

Date of Submission: 2024-03-17
Date of Acceptance: 2024-06-26

A B S T R A C T

The case report describes a 34-year-old female patient who was diagnosed with tuberculous meningitis and miliary pulmonary tuberculosis (TB) during her 16th week of pregnancy. The patient presented with symptoms such as vomiting, severe debilitation, lethargy, and loss of appetite. Chest radiography revealed pulmonary TB with a disseminated pattern of small nodules throughout the lungs. Brain magnetic resonance imaging showed meningoencephalitis with lacunar infarctions in the right hypothalamic area and left internal capsule. The patient was diagnosed with tuberculous meningitis causing alternating Weber syndrome and brain coma. The patient received standard anti-TB treatment with rifampicin, isoniazid, pyrazinamide, and ethambutol for two months, followed by four months of rifampicin and isoniazid. An emergency caesarean section was performed, but the premature male and female infants did not survive. The patient was stable and showed no signs of deterioration.

Keywords: Tuberculous Meningitis, Pregnancy, Amniotic Fluid Leakage, Miliary Pulmonary Tuberculosis, Magnetic Resonance Imaging

Introduction

Tuberculosis (TB) is caused by Mycobacterium TB (MTB) and is a prevalent illness that claims the lives of 1.5 million individuals annually, despite being curable.[1] It is estimated that 9.1 million people are affected by this disease annually.[1] The vast majority of TB infections are dormant; however, if left untreated, they can lead to severe complications.[2]

Pregnant women with TB have a significantly increased risk

of perinatal and maternal mortality. This presents several challenges to medical professionals.[3] While the clinical presentation of TB infection is well documented in the medical literature, diagnosing TB in pregnant women can be difficult because of the possibility of attributing early clinical signs to the pregnancy itself.[4] Both extrapulmonary and pulmonary TB in pregnant women can lead to various obstetric complications such as a higher incidence of spontaneous abortion and increased infant mortality.[3,4]

Tuberculous meningitis (TBM) is a rare and severe form of TB that accounts for only 1% of all TB infections. The mortality rate of TBM ranges from 15% to 40%. The risk factors for TBM include head trauma, alcohol consumption, pregnancy, and reduced cellular immunity.[5,6]

In this clinical case, a patient who became pregnant through in vitro fertilisation was later diagnosed with widespread TB.

Case Presentation

A 34-year-old female was admitted to the outpatient diagnostic department of the National Centre for Phthisiology on June 24, 2023, with a diagnosis of TBM. The patient had miliary pulmonary TB and was 16 weeks pregnant. According to the patient's medical history, her family reported that she had become unwell one week prior. The onset of the disease was characterised by symptoms such as vomiting, severe debilitation, lethargy, and loss of appetite. On June 21, 2023, the patient was examined by an infectious disease specialist and referred to a urologist, who prescribed medications but the patient didn't start the course. As a result, the patient's health deteriorated with the intensification of the headache and a state of stupor.

Based on the recommendations of a neurologist, a computed tomography scan of the brain was performed. Chest radiography was recommended and the patient was subsequently hospitalised for a preliminary diagnosis of TBM. Radiography revealed pulmonary TB with a disseminated pattern of small nodules throughout the lungs (Figure 1). On June 24, 2023, a brain magnetic resonance imaging scan showed meningoencephalitis with lacunar infarctions in the right hippocampal area and left internal capsule (acute stage), along with mixed replacement hydrocephalus (Figure 2). However, thoracic computed tomography was not performed because of the potential risk of ionizing radiation exposure during pregnancy.

The patient was diagnosed with TBM causing alternating Weber syndrome and brain coma. The diagnosis remained the same on July 25, 2023. The patient was deeply stuporous and sluggish to external stimuli. On August 10, 2023, an oculist diagnosed the patient with retinal vascular angiopathy. A joint examination by a phthisiogynaecologist and gynaecologist-reproductologist on June 26, 2023, revealed that the patient was 16–17 weeks pregnant with twins. The patient had a history of secondary infertility for 10 years and had undergone a laparoscopy in June 2022 to treat tubal infertility.

Ultrasound examination on July 10, 2023 revealed a twin pregnancy at 23 weeks, and on July 25, 2023, ultrasound showed a twin pregnancy at 25 weeks and 5 days, with holoprosencephaly II diagnosis, low placentation, and normal foetal Doppler findings.

On July 21, 2023, an obstetrician-gynaecologist diagnosed the patient with TB and left-sided hemiparesis. The patient had smear-negative miliary pulmonary TB. On July 31, 2023, the patient had anaemia with a haemoglobin level of 1 tbsp and a congenital malformation of central nervous system II in the foetus. The patient was recommended to be transferred to a maternity hospital for dynamic observation, further pregnancy management strategies, and delivery strategies if necessary. Owing to the leakage of the amniotic fluid. Additional diagnostic tests revealed a 6.5 cm area with infiltration along the blood vessels in the lungs dated August 14, 2023, thickening of the pleura, enlarged lymph nodes, and an enlarged heart shadow with smoothed contours.

The laboratory test results, including blood tests, biochemical tests, and comprehensive blood tests, are summarised in Table 1. Table 2 shows the results of various tests conducted on a patient.

The diagnosis was TB with impaired consciousness and function of the pelvic organs, left-sided hemiplegia, and miliary pulmonary TB. The patient received standard anti-TB treatment with rifampicin, isoniazid, pyrazinamide, and ethambutol for two months, followed by four months of rifampicin and isoniazid.

The patient was transferred to the Obstetrics and Gynaecology Department for observation and delivery. The patient continued to take anti-TB medications without interruption. An emergency caesarean section was performed due to regular labour under anaesthesia; however, premature male and female infants did not survive. The patient had lost 400 ml of blood. After 10 days, she was transferred to the intensive care unit with ongoing anti-tuberculosis treatment. The patient complained of headaches and general weakness, and her skin was pale and clean with smooth breathing and a normal oxygen saturation of 95%. Her heart rate was 74 bpm, and her respiratory rate was 140 bpm. Her liver was not enlarged and she underwent diuresis through a catheter. The patient had a moderate sanguineous-mucous discharge from the vagina.

The patient was stable and showed no signs of deterioration. They are conscious and oriented but report weakness, vaginal burning, and discharge. A gynaecologist found no

ISSN: 0019-5138
DOI: https://doi.org/10.24321/0019.5138.202438

meningeal symptoms. The patient's skin was pale, breathing was normal, and blood pressure was 112/68 mmHg. The heart sounds were muffled but the rhythm was correct. The abdomen was soft, retracted, and sensitive to touch.

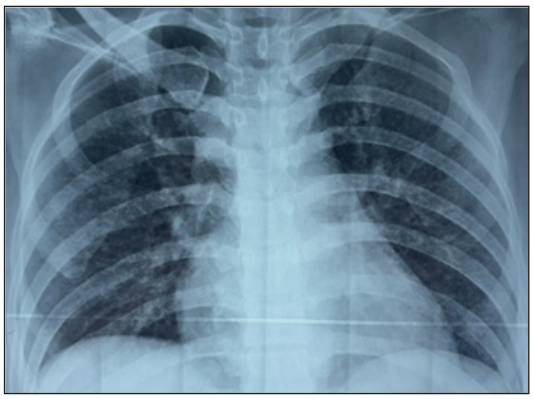

Figure 1.Chest Radiograph of Miliary Tuberculosis Showing Numerous Small Nodular Opacities Disseminated Throughout Both Lungs

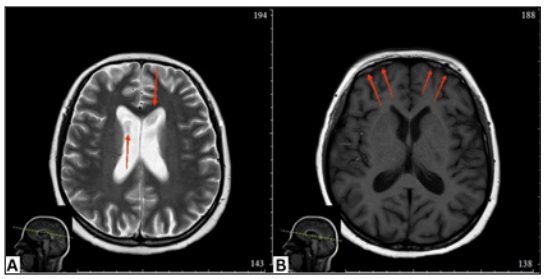

Figure 2.Magnetic Resonance Imaging of the Brain Without Contrast. (A) Axial T2-Weighted Image Demonstrating Meningoencephalitis with Lacunar Infarctions of the Hippocampal Region on the Right and the Internal Capsule on the Left (B) Axial T1-Weighted Image demonstrating Single Small Foci of Gliosis Bilaterally in The Frontoparietal Lobes

Table 1.Summary of Laboratory Test Results

1.	A blood test result from October 10, 2023 was used to assess clotting. The test duration was 13.4 seconds, with a PTI of 83.8% and an aPTT of 29.1 seconds. The fibrinogen level was 4 mg/L, and the thrombotest grade was 5. The ethanol test yielded negative results.
2.	Biochemical tests revealed total protein at 63 g/L, direct bilirubin at 4.5 µmol/L, and thymol test at 1.1 units. Glucose and blood amylase were 5.3 mmol/L and 66 mmol/L, respectively. Cholesterol, magnesium, and calcium levels were 4.05 mmol/L, 0.92 mmol/L, and 3.0 mmol/L, respectively. ALT, AST, and iron levels were 11, 18, and 16.9 µmol/L, respectively.
3.	Comprehensive blood tests revealed that leukocytes were 4.0x109/L, with eosinophils constituting 1% and neutrophils comprising 50% of the nucleated cells. Lymphocytes accounted for 40% of monocytes.

PTI: Plasma protein thiolation index, aPTT: Activated partial thromboplastin time, ALT: Alanine transaminase, AST - Aspartate transaminase

Table 2.Summary of Various Test Results

Date		Test	Result
1.	June 26, 2023	Rapid tests for screening HBV, HCV, and HIV	Negative
		AFB microscopy of throat smear for..... MBT	Negative
		GeneXpert MTB/ RIF	Negative
		GenoType MTBDRplus	Negative
		Mycobacteria Growth Indicator Tube	Negative

ISSN: 0019-5138
DOI: https://doi.org/10.24321/0019.5138.202438

		CSF analysis (lumbar puncture)	Colour: grayish; Transparency: slightly cloudy; Reaction of Pandy: positive; Nonne-Apelt reaction: positive; Cytosis: 120 cells in 1 mm^3; Protein: 0.97 g/L; Lymphocytes: 68%; Glucose: 0.2 mmol/L; Chloride: 84.2 mmol/L
2.	July 28, 2023	AFB microscopy of throat smear for MBT	Negative
		GeneXpert MTB/ RIF	Positive
		GenoType MTBDRplus	Positive
		Mycobacteria Growth Indicator Tube	Positive
		CSF analysis (lumbar puncture)	Colour: grayish; Transparency: full; Reaction of Pandy: positive; Nonne-Apelt reaction: negative; Cytosis: 30 cells in 1 mm3; Protein: 0.34 g/L; Lymphocytes: 66%; Glucose: 0.11 mmol/L; Chloride: 83.9 mmol/L

HBV: Hepatitis B Virus, HCV: Hepatitis C Virus, HIV: Human Immunodeficiency Virus, AFB: Acid-Fast Bacilli, MTB: Mycobacterium Tuberculosis, RIF: Rifampin, CSF: Cerebrospinal fluid

The patient was then transferred to the Pulmonary Therapy Department for further observation and treatment.

Discussion

Tuberculosis, primarily affecting the respiratory system or gastrointestinal tract, can lead to the formation of a primary complex in the liver.[7] Extrapulmonary cases of TB, such as gastrointestinal, congenital, and breast TB, are relatively rare and are unusual manifestations of the disease.[8–12]

Research suggests that a delayed diagnosis of a certain procedure during pregnancy increases the likelihood of obstetric morbidity by approximately fourfold and the risk of premature birth by nearly ninefold.[13] The combination of certain conditions in women often leads to the development of issues throughout all stages of pregnancy, including placental abnormalities, bleeding, severe symptoms of intoxication, prior complications, and pulmonary haemorrhage.[14,15]

Immunocompromised individuals are at a higher risk of developing extrapulmonary TB infections, which can lead to severe harm to the central nervous system and are considered to be one of the most perilous consequences. This condition has the potential to be lethal, even with appropriate medical treatment.[16,17]

TBM predominantly affects young children and individuals with compromised immune systems, such as those infected with HIV or those undergoing immunosuppressive therapy.[18] Additionally, the disease affects elderly people, particularly those aged ≥ 50 years.[19] Despite the availability of effective treatments, the mortality rate of TBM remains high, especially in underdeveloped countries where diagnostic equipment and treatments may be scarce.

A 16-week pregnant woman with symptoms of intoxication and nervous system damage but without cough was diagnosed with TB late. No family or household contact with a patient with TB was reported during anamnesis data collection. Regarding infertility, there have been four in vitro fertilisation-related facts. Gynaecological and hormonal studies on urogenital infections are limited. Despite weight loss, sweating, and weakness before pregnancy, TB screening was not performed. All the symptoms increased during pregnancy up to the 16th week.

Conclusions

This report emphasises the necessity of implementing consistent guidelines for screening, diagnosing, and treating pregnant women with TB to avert severe health consequences and minimise mortality rates during childbirth. Prompt detection of the disease through accurate diagnosis allows for the initiation of early treatment, thereby limiting the transmission of infection.

Timely diagnosis and treatment of active TB are essential to reduce maternal and neonatal mortality rates. Rapid molecular assays with drug susceptibility testing can help prevent late detection of generalised forms of TB, especially with the advanced screening methods currently available. Studies have also shown that first-line drugs are safe for TB treatment.[17]

It is recommended that all women planning to undergo an in vitro fertilisation procedure, regardless of whether they exhibit symptoms of TB infection, undergo the interferon-gamma release assay test available in this region. If test results are positive, additional testing methods for TB,

ISSN: 0019-5138
DOI: https://doi.org/10.24321/0019.5138.202438

such as genotypic studies and radiographic diagnostics, should be considered.

Source of Funding: None

Conflict of Interest: None

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