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Case Report

Miliary Tuberculosis with Tuberculous Meningoencephalitis in Children Under Two Years of Age with a Missed Opportunity of Immunization: A Case Report

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Abstract

Miliary TB is one of the manifestations of TB with incidence 3-7% among all TB cases and 13% can spread to brain as Tuberculous Meningitis (TBM). This case report discusses a case of miliary TB complicated with meningoencephalitis in children under two years of age without history of BCG vaccination. A 23-month-old girl with severe malnutrition, came to outpatient clinic with fever for 6 months, cough for 3 months, gland enlargement in the neck, no history of BCG and no history of TB contact. Because the chest x-ray showed miliary TB, we decided to hospitalized the patient. Suddenly she had loss of consciousness and seizures in the way to pediatric ward. After being managed and stabilized, we decided do head CT scan with contrast and found multiple rim enhancing lesions, with a smooth inner outer layer. Mycobacterium Tuberculosis was detected without rifampicin resistance by Polymerase Chain Reaction (PCR) TB from sputum speciment, but not detected in liquor cerebro spinal (LCS). Cerebrospinal fluid analysis showed mononuclear cell dominant (87%). The patient was given broad spectrum antibiotic, anti-seizures drug, and intensive phase anti-tuberculosis drugs with RHZE and steroid. The patient was discharged with clinical improvement after 3 weeks of treatment but had sequelae of cerebral palsy. Early detection and appropriate management are crucial in pediatric patients with miliary TB to reduce mortality rate and prevent TBM, which can lead to permanent neurological disabilities.

Keywords

Miliary TB, Tuberculous Meningitis, Children

1. Introduction

Tuberculosis (TB) is an infectious disease caused by Mycobacterium tuberculosis. In 2017, the World Health Organization (WHO) reported 10.4 million new cases of TB worldwide, with 1 million cases occurring in children. Nearly half a million children are affected by TB each year, and 20-30% of them have extrapulmonary TB [1]. Hematogenous spread of TB can lead to miliary TB with complications of extrapulmonary TB [2]. Miliary TB is considered a severe form of TB, accounting for 3-7% of all TB cases and having a high mortality rate (up to 25% in infants). In 2014, the Indonesian Ministry of Health reported 1,168 pediatric TB cases with positive acid-fast bacilli (AFB) results [3].

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According to a study in Vietnam, among all TB cases in children, Tuberculous Meningitis (TBM) occurs at a higher rate in children under 5 years old, accounting for 13% of cases. Furthermore, 17% of children without a history of BCG vaccination develop more severe forms of TB [4]. Epidemiological studies in China revealed that half of all TB cases occurring from 2002 to 2010 were extrapulmonary TB, with approximately 39% of those cases being TBM [5].

The mortality rate for miliary TB is usually around 25% but can reach 100% if left untreated [6]. TBM has a poor prognosis and often leads to neurological sequelae and significant disability [7]. In a study by Israni et al., the mortality rate for TBM was reported as 23.4% [8]. A meta-analysis by Chiang et al. showed that 19% of patients with TBM would experience mortality, and 53.9% of TBM survivors still had neurological sequelae [7, 10]. Mortality rates can reach 20-50% for TBM and up to 78% in cases with severe central nervous system involvement [9].

This case report discusses a case of miliary TB with TB meningoencephalitis in a child under two years old without a history of BCG vaccination. It highlights the progression of miliary TB to TBM and the management provided to address this severe form of TB infection.

2. Case Description

A 1 year and 11 months old female child weighing 8.5 kg presented to the pediatric outpatient clinic with complaints of recurrent fever, prolonged cough, and neck swelling. Chest X-ray revealed miliary tuberculosis (TB), leading to immediate hospital admission through the emergency department. Approximately one hour after admission, the patient experienced sudden loss of consciousness following a one-minute generalized seizure. The patient had a history of recurrent fever for the past six months, accompanied by a three-month cough, weight loss, and neck swelling. The patient had not received BCG immunization. On arrival, the patient had a Glasgow Coma Scale (GCS) score of E1V1M4, exhibited respiratory distress with subcostal retractions and fine moist and wheezing sounds in both lungs, positive neck stiffness, and clinical signs of malnutrition. The TB scoring system yielded a score of 6, including malnutrition (2), unexplained fever for ≥2 weeks (1), chronic cough for ≥2 weeks (1), bilateral non-tender cervical lymphadenopathy with a diameter of 1 cm (1), and chest X-ray showing diffuse infiltrates consistent with miliary TB (1). The chest X-ray confirmed the presence of miliary TB in both lung fields (Figure 1).

A contrast-enhanced head CT scan revealed multiple rim-enhancing lesions with smooth inner and outer layers suggestive of TB meningitis. Molecular Rapid Testing (MRT) of sputum showed low detection of Mycobacterium tuberculosis and no detectable resistance to rifampicin. MRT of cerebrospinal fluid was negative, but cerebrospinal fluid analysis revealed negative nonne, positive pandys, protein level of 50, glucose level of 57, leukocyte count of 15, erythrocyte count of 50/mm3, polymorphonuclear cells (PMN) at 13%, and mononuclear cells (MN) at 87%, consistent with TB meningitis.

Based on the history, clinical examination, and supporting diagnostic tests, the patient was diagnosed with TB meningoencephalitis and miliary TB. The patient received intensive anti-tuberculosis therapy for 2 months, followed by a continuation phase of 10 months. During the intensive phase, the patient received a combination of four drugs: Isoniazid (H) (10 mg/kg body weight), rifampicin (R) (15 mg/kg body weight), pyrazinamide (Z) (35 mg/kg body weight), and ethambutol (E) (20 mg/kg body weight) (2HRZE). Isoniazid, rifampicin, and pyrazinamide were given as fixed-dose combination tablets once daily, while ethambutol was given once daily. During the continuation phase, the patient received isoniazid (10 mg/kg body weight) and rifampicin (15 mg/kg body weight) (10HR) in the form of fixed-dose combination tablets once daily. The treatment regimen during the intensive and continuation phases followed the guidelines for the management of TB in children (2016).

Additional therapies included broad-spectrum antibiotics (ceftriaxone), corticosteroid (methylprednisolone), and antiepileptic medication (diazepam). After three weeks of hospitalization, the patient's condition improved, with a GCS score of E4V2M4, reduced respiratory distress, and weight gain to 9 kg, indicating improved nutrition and a favorable response to the provided therapy and management. Chest X-rays from the anteroposterior and lateral views showed a reduction in infiltrates in both lung fields after three weeks of TB treatment (Figure 2). The patient was discharged with clinical symptoms indicating neurological sequelae, specifically cerebral palsy.

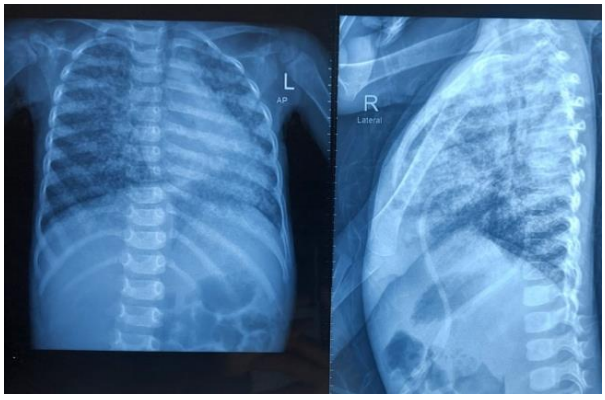

Figure 1. *Anteroposterior (AP) and lateral chest X-ray images showing infiltrates consistent with the appearance of miliary tuberculosis (TB) in both lung fields.*

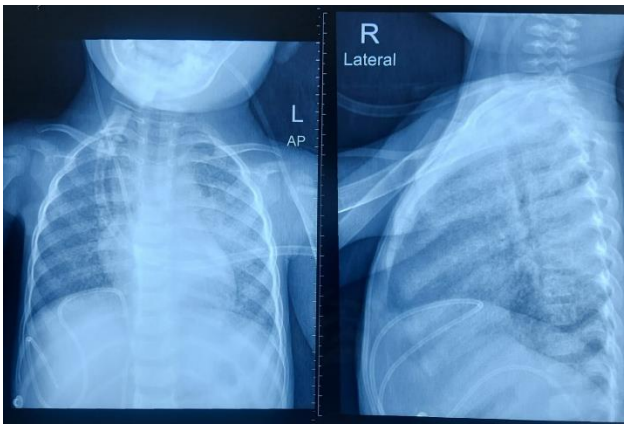

Figure 2. *Evaluation of anteroposterior (AP) and lateral chest X-ray images after three weeks of therapy.*

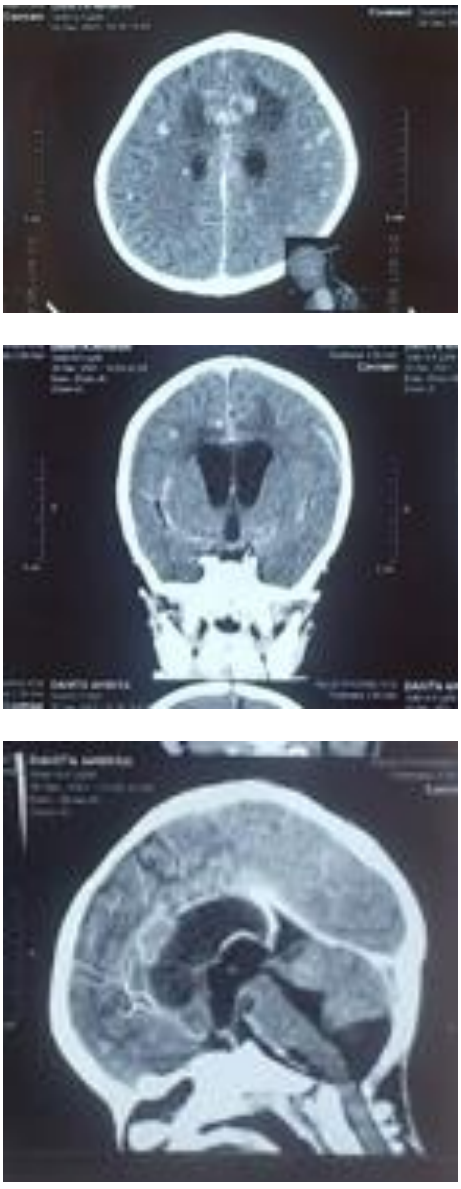

Figure 3. *Head CT scan showing multiple rim-enhancing lesions with smooth inner and outer layers suggestive of tuberculous meningitis.*

3. Discussion

Risk factors that increase the occurrence of Tuberculous Meningitis (TBM) include young age, measles infection, immunodeficiency conditions, malnutrition, and malignancy [18]. Children under the age of 5 who suffer from miliary TB have a higher risk of developing severe complications and life-threatening meningeal TB [11]. The incidence of TBM in children under the age of five usually presents with severe conditions [3, 11, 14]. In a study conducted by Cruz et al., it was reported that children under the age of 5 are more likely to experience progressive extrapulmonary TB and more severe clinical TB [19]. Another study by Awaluddin et al. in Malaysia showed that the highest number of TB cases occurred in children aged 10-14 years, followed by children aged 0-4 years, and the youngest age group had a 10-20% risk of developing TB meningitis or miliary TB [20]. Therefore, age can depict the distribution of pulmonary and extrapulmonary TB incidence in each country's pediatric TB cases [20]. The most common age for TBM occurrence is below 3 years, accounting for 60% of cases, while cases above 3 years occur in 16% of cases [21]. Globally, children under 5 years old are the most vulnerable population to develop extrapulmonary TB, especially TBM [8]. The incidence of TBM is rarely found in infants under 3 months, and the highest incidence occurs between the ages of 2 and 4 years [6]. In this patient, several factors increase the risk of developing miliary TB and TBM, including young age below 5 years, malnutrition, and a history of no BCG vaccination.

The relatively underdeveloped immune response in children under 5 years increases the risk of developing TBM in patients with miliary TB at a young age. Dissemination of bacteria through the hematogenous route and their spread to the brain and meninges mark the early development of TBM in children. In a study conducted by Bos et al., the mean age of patients with miliary TB and TBM was 17 months compared to a mean age of 30.5 months in patients with TBM alone [22]. The progression of primary infection to TBM usually takes 6 to 12 months [6]. Research by Cherian et al. mentions that progression and neurological symptoms typically appear 3 months after the onset of primary infection [23]. In children, the progression tends to occur faster than in adults [2]. Additionally, the duration from the onset of non-specific symptoms to the appearance of TB infection in the central nervous system is consistent with previous research, ranging from 6 to 12 months after primary infection [6]. In this case, the patient, a 1-year and 11-month-old child (below 5 years), initially presented conscious but experienced a decrease in consciousness accompanied by seizures with a history of fever for 6 months, cough for 3 months, and a neck lump. The long-standing symptoms and delay in examination resulted in the diagnosis of TB only after the infection had affected the central nervous system. The patient was diagnosed with miliary TB, which carries a high risk of developing TBM.

Research by Rock et al. demonstrates the protective effect of BCG vaccination in preventing TBM, with a rate of 75% to 85% [18]. In this patient, the risk factors for miliary TB and TBM include the absence of BCG vaccination that should have been given in the neonatal period.

Tuberculosis in children can generally be suspected if clinical symptoms include cough lasting more than 2 weeks, fever lasting more than 2 weeks, weight loss, and malaise lasting more than 2 weeks. The miliary pattern can be observed on chest X-rays within 2-3 weeks after hematogenous spread of bacteria [3, 12]. In a study conducted by Mert et al., common symptoms of miliary TB include fever, malaise, night sweats, cough, shortness of breath, loss of appetite, and weight loss that lasts for weeks (generally more than 3 weeks) [13]. Miliary TB can spread to various organs, including the brain, with TB meningitis being the most common manifestation. About 18% of miliary TB cases in children develop into TBM [13]. The clinical onset of TBM is usually characterized by nonspecific symptoms such as malaise, subfebrile temperature, cough, cold symptoms, or other symptoms of pulmonary TB [15]. Other symptoms that may appear in the early phase include headache, vomiting, and irritability. In the later phase, symptoms such as meningeal irritation, increased intracranial pressure, cranial nerve weakness, neurological deficits, sensory disturbances, and motor disorders may occur [16]. The progression of infection leads to basilar meningitis with compression of cranial nerves, manifested by meningeal irritation, increased intracranial pressure, decreased mental status, and coma. TBM is often diagnosed late in 50% of TBM cases and has a worse outcome and prognosis based on various studies [17]. In this case, the patient experienced a decrease in consciousness accompanied by seizures with a history of fever for 6 months, cough for 3 months, and a neck lump. Physical examination revealed subcostal retractions and coarse, fine, and wheezing rhonchi in both lungs, positive neck stiffness, and clinical signs of malnutrition.

Based on a case report conducted by Uwe et al. in Nigeria, treatment for miliary TB with TBM involved 2RHZE/10RH anti-tuberculosis therapy along with a combination of prednisolone and phenobarbital [24, 25]. The patient was hospitalized for 9 days and then continued with outpatient care for ongoing anti-tuberculosis therapy until the advanced phase, while the temporarily interrupted steroid therapy was continued for 4-6 weeks, with monitoring of the patient's nutritional status. During follow-up, the patient showed improvements in physical examination, weight gain, and chest X-ray evaluations. The patient received anti-tuberculosis therapy for 12 months. Therefore, it is concluded that early initiation of standard anti-tuberculosis treatment for miliary TB can save lives [11]. The patient was treated with fixed-dose combination (FDC) anti-tuberculosis therapy for the intensive phase for 2 months and the continuation phase for 10 months, following the Guidelines for Management and Treatment of Childhood TB 2016, along with other therapies such as broad-spectrum antibiotic ceftriaxone, methylprednisolone corticosteroid, and anticonvulsant diazepam.

In a study by Israni et al., the mortality rate of TBM reached 23.4% [8]. In a meta-analysis study by Chiang et al., 19% of patients with TBM experienced mortality, and 53.9% of TBM survivors still had neurological sequelae [7]. The mortality rate can reach 20-50% for TBM and up to 78% when there is severe central nervous system involvement [9]. The patient showed improvement but had neurological sequelae in the form of cerebral palsy.

4. Conclusion

Early detection and appropriate management should be implemented in pediatric patients with miliary tuberculosis (TB) to reduce mortality rates and prevent the occurrence of tuberculous meningitis (TBM), which can lead to permanent neurological disabilities in children. Furthermore, the importance of BCG vaccination is a crucial measure in preventing severe TB in children.

Abbreviations

TB	Tuberculosis
TBM	Tuberculous Meningitis
BCG vaccine	Bacille Calmette-Guérin Vaccine
GCS	Glasgow Coma Scale

Conflicts of Interest

The authors declare no conflicts of interest.

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