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# Case Report

# Miliary brain tuberculosis in an infant $^{\diamond, \diamond \diamond}$

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## ABSTRACT

Tuberculosis remains prevalent in developing countries. Central nervous system tuberculosis often occurs secondary to pulmonary tuberculosis, transmitted through the bloodstream, and has a high mortality rate. Meningitis is the most common presentation of central nervous system tuberculosis, followed by tuberculoma, tuberculous brain abscess, and miliary tuberculosis. In this report, we present a case of miliary tuberculosis in a 3 month-old boy. The patient had a fever and was breathless for 1 month. The patient appeared cyanotic, experienced a seizure, and became comatose. Chest computed tomography scan suggested a pulmonary miliary tuberculosis abscess in the right lung and mediastinal lymph node tuberculosis. Brain magnetic resonance imaging showed the lesions were homogeneously enhancing tiny 2-3 mm nodules characteristic of miliary TB. Polymerase chain reaction of the cerebrospinal fluid and sputum samples confirmed tuberculosis. The patient died 1 month after diagnosis.

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#### Introduction

Miliary tuberculosis (MTB) is uncommon, accounting for approximately 1% of all tuberculosis (TB) [1]. Lungs, liver, bone marrow, eyes, kidneys, and adrenals are the most commonly affected organs in MTB due to their high blood supplies [1]. Central nervous system (CNS) TB occurs in 1% of all TB cases; however, the incidence is markedly higher among MTB patients [2]. MTB is a life-threatening disease with a high mortality rate that can cause neurological deficits, even after MTB recovery [3]. Few published series have described MTB in chil-



Fig. 1 – Chest X-ray revealed consolidation in the right lung and diffuse, bilateral nodules, sized 1–3 mm in diameter, in both lungs. dren. In this article, we present a case of MTB with extensive involvement in the central nervous, respiratory, and lymphatic systems in a 3 month-old infant.

#### **Case report**

A 3 month-old boy was admitted to the hospital with seizure. One month before, the patient had a fever and appeared breathless, and the symptoms gradually increased. On admission, his initial vital signs were as follows: (1) cyanosis; (2) coma; (3) heart rate of 130 beats/min; (4) respiratory rate of 30 breaths/min; (5) body temperature of 39°C; and (6) oxygen saturation at 82% in room air. Physical examination showed decreased breath sounds upon auscultation. The patient received endotracheal intubation. Laboratory results showed lymphopenia (3.5 G/L) and C-reactive protein elevation (80 mg/L). Chest X-ray showed consolidation in the right lung and diffuse, bilateral nodules, sized 1-3 mm in diameter, which was uniformly distributed (Fig. 1). Chest computed tomography (CT) scan showed consolidation of the right upper lobe with central necrosis and diffuse, bilateral nodules, 1-3-mm in size and with a random distribution (Fig. 2 B). Necrotic mediastinal lymphadenopathies were also observed (Fig. 2).

The patient underwent brain magnetic resonance imaging (MRI) and lumbar puncture. The MRI showed diffuse mil-



Fig. 2 – Chest CT scan with contrast (A, C and D) and in lung window (B). Chest computed tomography scan showed consolidation of the right upper lobe with central necrosis (A, arrow). Diffuse bilateral nodules were observed with random distribution, smaller than 3 mm in size (B). Multiple necrotic mediastinal lymphadenopathies were observed (C and D, arrows).



Fig. 3 – Axial T1 MRI pre-contrast (A and B) and post-contrast (C and D). Diffuse, homogeneous enhancing nodules were observed in both supratentorial and infratentorial regions. These nodules were less than 2 mm in size.

iary lesions <2 mm, with homogeneous enhancement in the cerebral parenchyma (Fig. 3). Cerebrospinal fluid was yellowish in color, presented with an increased protein concentration (300 mg/dL) and a low glucose concentration (10 mg/dL) with elevated lymphocytes (40 cells/ $\mu$ L). Polymerase chain reaction (PCR) evaluations confirmed the presence of *Mycobacterium tuberculosis* in the cerebrospinal fluid (CSF) and sputum. Based on the imaging and PCR analyses of the CSF and sputum, a diagnosis of disseminated MTB was made. The patient was treated with daily isoniazid, rifampin, pyrazinamide, and ethambutol, and adjunctive corticosteroids (dexamethasone 0.4 mg/kg/day). However, the patient died after 1 month of treatment because of respiratory failure.

## Discussion

Disseminated TB is defined when two or more non-adjacent organs are involved [4]. The proposed mechanism of dissemination is that bacilli spread from the lungs to the blood allowing entry to extrapulmonary organs [5]. In this case, the patient had MTB of the pulmonary system and mediastinal lymph nodes, and the brain lesions were confirmed as caused by TB. CNS TB is a rare presentation, accounting for 1% of all TB cases, and tuberculous meningitis is the most common of CNS TB [2]. Some risk factors include young age, recent measles infection in children, immunodeficiency, malnutrition, and malignancies [6]. Children and immunocompromised patients have a higher risk of miliary TB [1,6]. We did not identify any of these contributing factors in this child, except for young age; however, this patient had not received the bacillus Calmette-Guérin (BCG) vaccination which is usually given at birth. Some studies showed that BCG protects against CNS TB around 75%-85% [6].

The clinical presentations of MTB can vary, depending on the affected organs. CNS MTB in children is closely associated with disseminated TB [3]. Neurological symptoms in children often develop within 3 months of primary TB infection [3]. Children often present with fever, stiff neck, seizures, focal neurological deficits, and even coma [6]. In children, the symptoms often develop more rapidly than in adults [6]. Patients may present with symptoms due to TB in other organs, such as anorexia, fatigue, dyspnea, night sweats, abdominal pain, hemoptysis, lymphadenopathy, diarrhea, vomiting, hepatomegaly, splenomegaly, or jaundice [5].

MRI is the primary imaging test for the diagnosis of CNS TB due to its superiority compared to CT [2]. In adults, intraparenchymal tuberculomas TB often appears in the frontal and parietal lobes; however, the infratentorial region is more commonly affected in children [7]. The imaging findings of brain miliary tuberculomas on MRI include tuberculosis that are often smaller than 2.5 cm in diameter, hypointense lesions on T1-weighted image (T1W), hypo- or hyperintense lesions on T2-weighted image (T2W), with a central hypointensity on T2W and homogeneous enhancement in the initial stage and ring enhancement in the late stage [7]. In our case, MRI showed diffuse miliary lesions smaller than 2 mm in diameter, with homogeneous enhancement in the cerebral parenchyma. These lesions were difficult to observe on T1W and T2W due to their small size and lack of edema. The diagnosis of CNS TB is defined by the detection of the tubercle bacilli in the CSF. Multiple methods can be used, including PCR, antibody detection, antigen detection, staining, and culturing of CSF samples [3]. On imaging, the findings of the chest CT and brain MRI were typical of military TB.

Patients with MTB must be promptly treated with standard anti-TB therapy because of the severe neurological sequelae and high rate of mortality [8]. Corticoids can be used as adjunctive therapy for the treatment of CNS TB [6]. The mortality rate is 20%-50% in patients treated for MTB, reaching as high as 78% among patients with severe CNS damage [6]. This patient was diagnosed with disseminated TB and presented with coma and seizure, which was classified as severe CNS damage. This is also the severe complication of CNS TB. Although the patient received appropriate anti-TB therapy, the patient died 1 month after therapy initiation.

## Conclusion

In conclusion, we report a rare case of disseminated MTB involving the CNS. This disease is common in children and patients with multiple risk factors. Due to the very high mortality rate, early detection and prompt treatment are necessary.

#### **Patient Consent**

Informed consent for patient information to be published in this article was obtained.

# **Ethical Statement**

Appropriate written informed consent was obtained for the publication of this case report and accompanying images.

# Author contributions

Le AD, Tran H, and Nguyen MD contributed equally to this article as co-first authors. All authors have read the manuscript and agree to the contents.

#### REFERENCES

[1] Mert A, Arslan F, Kuyucu T, Koç EN, Yilmaz M, Turan D, et al. Miliary tuberculosis: Epidemiological and clinical analysis of large-case series from moderate to low tuberculosis endemic country. Medicine 2017;96(5):e5875. doi:10.1097/MD.000000000005875.

- [2] Vasconcelos G, Santos L, Couto C, Cruz M, Castro A. Miliary brain tuberculomas and meningitis: tuberculosis beyond the lungs. Eur J Case Rep Int Med. 2020 (LATEST ONLINE). doi:10.12890/2020\_001931.
- [3] Cherian A, Thomas SV. Central nervous system tuberculosis. Afr Health Sci 2011;11(1):116–27.
- [4] Goncalves R, Lopes P, Mendes P, Trêpa J, Rua J, Sá R, et al. Miliary tuberculosis with cerebral, liver, prostate and retroesophageal involvement. Idcases 2017;9:25–7. doi:10.1016/j.idcr.2017.03.011.
- [5] Khan FY. Review of literature on disseminated tuberculosis with emphasis on the focused diagnostic workup. J Family Community Med 2019;26(2):83–91. doi:10.4103/jfcm.JFCM\_106\_18.
- [6] Rock RB, Olin M, Baker CA, Molitor TW, Peterson PK. Central nervous system tuberculosis: pathogenesis and clinical aspects. Clin Microbiol Rev 2008;21(2):243–61 table of contents. doi:10.1128/CMR.00042-07.
- [7] Machida M, Toyoda K, Matsuda M, Sumida K, Yamamoto A, Sakurai K, et al. Extensive perivascular dissemination of cerebral miliary tuberculomas: a case report and review of the literature. Acta Radiol Open 2018;7(12):2058460118817918. doi:10.1177/2058460118817918.
- [8] Sharma SK, Mohan A, Sharma A. Challenges in the diagnosis & treatment of miliary tuberculosis. Indian J Med Res 2012;135(5):703–30.