CASE REPORT

Intisari Sains Medis 2024, Volume 15, Number 1: 433-436
P-ISSN: 2503-3638, E-ISSN: 2089-9084

Intisari Sains Medis

Published by Intisari Sains Medis

# A simultaneous case miliary tuberculosis presenting with tuberculous meningitis: a case report

I Gusti Ngurah Agung Jayadhi Widyakusuma[1*], Ni Putu Siadi Purniti[2], Ida Bagus Subanada[2], I Gusti Ngurah Made Suwarba[2], Dewi Sutriani Mahalini[2]

[1]Resident of Child Health Department, Faculty of Medicine, Universitas Udayana, Denpasar, Bali, Indonesia;
[2]Department Of Child Health, Faculty of Medicine, Universitas Udayana, Denpasar, Bali, Indonesia.

*Corresponding author:
I Gusti Ngurah Agung Jayadhi Widyakusuma;
Resident of Child Health Department, Faculty of Medicine, Universitas Udayana, Denpasar, Bali, Indonesia;
jayadhiwidyakusuma@gmail.com

Received: 2024-02-10
Accepted: 2024-03-22
Published: 2024-04-16

## ABSTRACT

**Background:** Miliary tuberculosis in children could occur 20-40% simultaneously with tuberculous meningitis (TBM). Dissemination of the tuberculous bacilli from the lungs to the meninges leads to the formation of small tuberculomas, leading to TBM. Despite the availability of effective therapy, diagnosis is usually late, and mortality remains high.

**Case Presentation:** A 15-year-old boy came to our emergency ward with the chief complaint of loss of consciousness two days before admission. The patient had a fever in the past month. Fever occurred in several episodes along with cough. The patient had a headache five days before admission. Projectile vomiting was denied. The patient had lost about five kilograms in the last month. Vital signs are stable and within normal limits. Physical examination showed lethargy, neck stiffness, and an enlarged lymph node on the neck. Neurologic examination was normal. Chest X-ray showed miliary opacities scattered over both lung fields. Cerebrospinal fluid (CSF) examination showed clear with low glucose and high cell count suggested to TBM. No bacteria were found in the CSF culture sample. A contrast head computed tomography (CT) scan revealed a leptomeningeal contrast enhancement. Active communicating hydrocephalus was also seen on a head CT scan. Eventually, Mycobacterium was detected *in* the gastric fluid. The patient was diagnosed with tuberculous meningitis. This patient was treated in an intensive phase of anti-tuberculous therapy and continued with an advanced phase.

**Conclusion:** We reported cases of miliary tuberculosis simultaneously with tuberculous meningitis in a 15-year-old patient. The timely diagnosis and management will reduce morbidity and mortality.

**Keywords:** *children, milliary tuberculosis, tuberculous meningitis*.
**Cite This Article:** Widyakusuma, I.G.N.A.J., Purniti, N.P.S., Subanada, I.B., Suwarba, I.G.N.M., Mahalini, D.S. 2024. A simultaneous case miliary tuberculosis presenting with tuberculous meningitis: a case report. *Intisari Sains Medis* 15(1): 433-436. DOI: 10.15562/ism.v15i1.1663

## INTRODUCTION

Tuberculosis is one of the top 10 causes of death worldwide, according to the World Health Organization (WHO).[1] Globally, in 2015, tuberculosis in the pediatric population was 1 million cases per year. WHO published pediatric-specific disease estimates of approximately 500,000 cases of TB among children younger than 15 years of age. In 2019, most of the estimated tuberculosis incidence occurred in the Southeast Asia Region (45%), and Indonesia was one of them.[2,3] While tuberculosis occurs in every part of the world, eight countries comprise two-thirds of global tuberculosis incidence, and Indonesia (202,000 cases) ranks second for the incidence of tuberculosis in the world after India (279,000 cases). The prevalence of tuberculosis was higher in males than females.[4-6]

Miliary tuberculosis accounts for 1-2% of all tuberculosis and 8% of extrapulmonary tuberculosis (EPTB) cases, while tuberculous meningitis is a serious illness that affects 2-9% of all tuberculosis cases and 20% of EPTB cases. Even with proper and approved treatment, 63% of patients with tuberculous meningitis will die. Tuberculous meningitis can occur in 20-40% of children simultaneously with miliary tuberculosis. Delays in diagnosing tuberculous meningitis and miliary TB can result in serious complications, including hydrocephalus, cranial nerve involvement, convulsions, and death.[6] The purpose of this case report is to expand our knowledge on clinical manifestation, diagnostic approach, or therapeutic alternative of tuberculous meningitis and, ultimately, to improve the quality of care provided to our patients.

## CASE PRESENTATION

A 15-year-old boy came to our emergency ward with the chief complaint of loss of consciousness 2 days before admission. The patient looked confused but could follow a simple command. The patient's body looked thin as the patient had lost his weight about 5 kilograms in the last month. The patient had a fever in the past month. Fever occurred in several episodes along with cough. Cough was said with clear phlegm. The patient had headaches 5 days before admission. The headache was accompanied by nausea and vomiting. Projectile vomiting was denied.

The patient lived in an Islamic boarding school for 2 years. The patient's family and

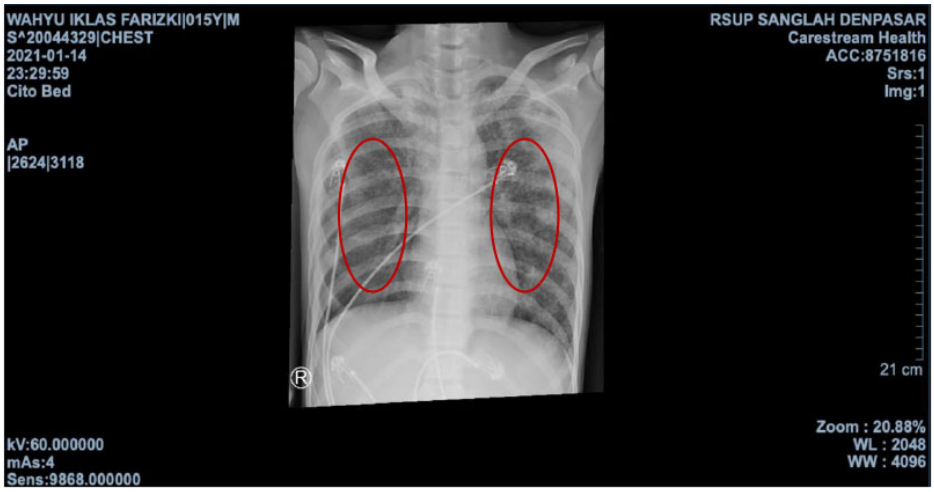


**Figure 1.** Chest X-ray with military pattern and pneumonia.

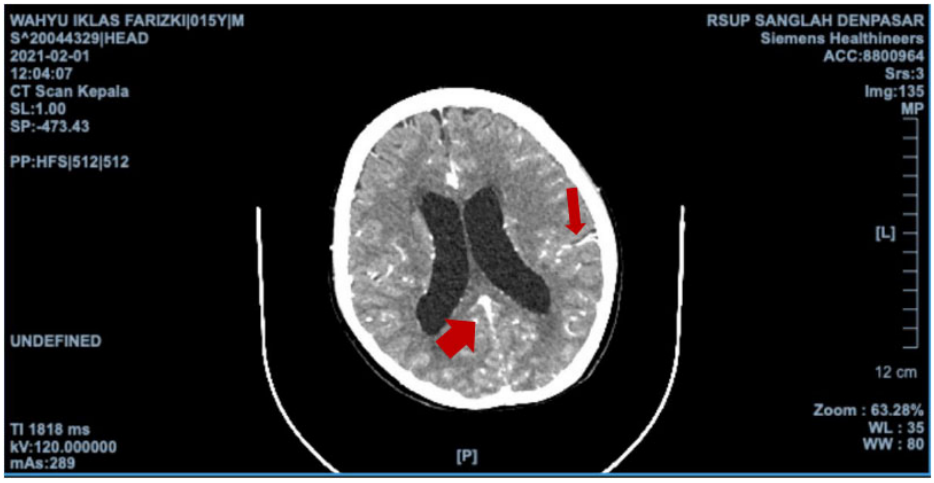


**Figure 2.** MRI brain with leptomeningeal contrast enhancement and hydrocephalus.

his peers in Islamic boarding schools didn't have a history of tuberculosis. History of contact with the tuberculosis patient was denied. Status present was heart rate 110 times per minute, respiration rate 20 times per minute, body temperature 36.7°C, and oxygen saturation 96% with room air.

Physical examination showed lethargy, neck stiffness, and an enlarged lymph node on the neck. The Bacillus Calmette Guerin (BCG) vaccine was not given at birth, and no BCG scar on the arm. The patient weighed 58.3 kilograms and was 165 centimeters tall. His weight lost about 5 kilograms in the last one month. Overall, the patient still had a good nutrition status. Neurologic examination showed normal reflexes, negative meningeal sign, and no lateralization.

Chest X-ray showed miliary opacities scattered over both lung fields, confirmed miliary tuberculosis on both lungs and pneumonia. Cerebrospinal fluid examination suggested meningitis tuberculosis that showed xanthochrome color with positive (4+) none and positive (4+) pandy, the cell count was 111 with mononuclear predominance (90%), total protein was 1766.4, and CSF glucose level was 46 mg/dL. However, no bacteria were found in the CSF culture sample. A head computed tomography (CT) scan with contrast also showed imaging of tuberculous meningitis that revealed a leptomeningeal contrast enhancement in the right and left parietal region, ganglia basalis, and periventricular lateralis. Active communicating hydrocephalus was also seen on a head CT scan. Eventually, Mycobacterium was detected on *GeneXpert* examination from the gastric fluid specimen.

Diagnosis of tuberculous meningitis was made according to anamnesis, physical examination, laboratory, and radiology examination.

This patient was treated with anti-tuberculous therapy intensive phase for 2 months with a fixed drug combination 4 tablets a day, each containing isoniazid (75 mg), rifampicin (150 mg), pyrazinamide (400 mg), ethambutol (275 mg) and continued with advanced phase 4 tablets a day each contained with isoniazid (150 mg), rifampicin (150 mg). The patient was also treated with corticosteroid (prednisone) 2 mg/kg/day given every 6 hours, which was planned for 4 weeks, along with anti-tubercular treatment. The patient was consulted by the child surgery division for hydrocephalus management. The patient was planned to get a ventriculoperitoneal shunt placement but was still denied by the family.

## DISCUSSION

This case reports a 15-year-old boy with a diagnosis of miliary tuberculosis followed by tuberculous meningitis. WHO published pediatric-specific disease estimates of approximately 500,000 cases of TB among children younger than 15 years of age. The mechanism of tuberculosis infection is initiated by inhaling M. tuberculosis and then ingested by alveolar macrophages, which form caseating granulomas to contain the bacilli. Macrophages transport some bacilli to the regional lymph nodes. Before an adequate immune response is mounted, the bacilli can transit from the regional lymph nodes via the lymphatic duct or directly into the systemic circulation. This occult lymphohematogenous spread disseminates bacilli to various organs, where they may survive for decades. Disseminated TB disease results if the dissemination is not controlled by the developing acquired immune response. This spread will cause serious conditions such as miliary tuberculosis and tuberculous meningitis. Disseminated TB and TB meningitis tend to be early manifestations, often presenting 2–6 months after the initial infection has occurred. The primary complex and its complications become apparent most often 3–6 months after infection.[6,8]

Miliary tuberculosis is a rare form of disease caused by deficient T-cell containment of M. Tuberculosis as a consequence of bacilli hematogenous

spread. The following criteria have been suggested for the diagnosis of miliary tuberculosis such as the presence of miliary pattern on chest radiograph with or without evidence of multi-organ involvement, along with one or more of the following features: clinical features compatible with tuberculosis, including cough for 3 weeks or more, fever, weight loss, night sweats, loss of appetite or hemoptysis, and responding to antituberculosis treatment, positive smear or culture for tuberculosis and histopathological evidence of tuberculosis.[9,10]

In our case, A 15-year-old boy patient had a fever in the past one month. Fever occurred in several episodes along with cough. Cough was said with clear phlegm. The patient had headaches 5 days before admission.

Physical examination showed an enlarged lymph node on the neck and no BCG scar on the arm. The patient's body looked thin as the patient had lost his weight about 5 kilograms in the last one month. Chest X-ray showed miliary opacities scattered over both lung fields, confirmed miliary tuberculosis on both lungs and pneumonia. Eventually, Mycobacterium was detected on *GeneXpert* examination from the gastric fluid specimen. Miliary tuberculosis who had one or more of the following features was diagnosed as having CNS involvement: neuroimaging abnormal presentations (hydrocephalus, basal meningeal enhancement, infarcts, tuberculoma, and pre-contrast basal hyperdensity), bacteriological evidence of tuberculosis with CSF examination by conventional and/or molecular tests, had likely neural symptoms (one or more of the following: headache, irritability, vomiting, fever, neck stiffness, convulsions, focal neurological deficits, or altered consciousness) with supportive CSF biochemistry examination outcomes (a lymphocytic pleocytosis with cells 10–500/mm$^3$ (>50% lymphocytes), moderately to severely elevated protein content (0.5–3.0 g/l) and glucose levels lower than 45 mg/dl or below 40–50% of serum glucose).[11]

In our case, the patient had a loss of consciousness 2 days before admission. The patient looked confused but could follow a simple command. The patient had headaches 5 days before admission. The headache was accompanied by nausea and vomiting. Projectile vomiting was denied.

Physical examination showed lethargy, neck stiffness, and an enlarged lymph node on the neck. Neurologic examination showed normal reflexes, negative meningeal sign, and no lateralization.

Cerebrospinal fluid examination suggested meningitis tuberculosis that showed xanthochrome color with positive (4+) none and positive (4+) pandy, the cell count was 111 with mononuclear predominance (90%), total protein was 1766.4, and CSF glucose level was 46 mg/dL. However, no bacteria were found in the CSF culture sample. A head computed tomography (CT) scan with contrast also showed imaging of tuberculous meningitis that revealed a leptomeningeal contrast enhancement in the right and left parietal region, ganglia basalis, and periventricular lateralis. Active communicating hydrocephalus was also seen on a head CT scan.

Neurological involvement occurs in the form of headache secondary to TBM with or without tuberculoma formation and motor or sensory abnormality because of thoracic transverse myelopathy. Tuberculous meningitis has been described in 20-40% of children with miliary tuberculosis.[9]

On average, TBM occurs 6 to 12 months after the primary infection. *Mycobacterium tuberculosis* can invade and traverse the blood-brain barrier, which is dependent on the presence of certain virulence factors, exocytosis, and longer intracellular survival.[11-13]

In our case, tuberculous meningitis was diagnosed according to anamnesis, physical examination, laboratory, and radiology examination.

The guidelines enacted by the American Thoracic Society, the Centers for Disease Control and Prevention of America, the Infectious Diseases Society of America, and the British Thoracic Society state that 6 months of treatment will be administered to miliary tuberculosis in the presence of associated TBM, treatment needs to be given for at least 12 months. The regimens recommended by WHO for pulmonary tuberculosis and TBM are drugs with better blood-brain barrier penetration efficiency, such as isoniazid, pyrazinamide, fluoroquinolones, and linezolid.[5] According to the WHO recommendations, in the case of tuberculous meningitis, treatment should be prolonged to 12 months, with (HRZE) for 2 months followed by HR for 10 months, The doses recommended for the treatment of tuberculous meningitis are the same as those described for pulmonary TB as the following dosages: isoniazid (H), 10 mg/kg (range 10–15 mg/kg) and a maximum dose 300 mg/day; rifampicin (R), 15 mg/kg (range 10–20 mg/kg) with a maximum dose of 600 mg/day, pyrazinamide (Z), 35 mg/kg (range 30–40 mg/kg) and ethambutol (E), 20 mg/kg (range 15-25 mg/kg). In patients with tuberculous meningitis, an initial adjuvant corticosteroid therapy with dexamethasone or prednisolone tapered over 6–8 weeks should be used.[10,14]

Our M. Tuberculosis patient was treated with ATT intensive phase for 2 months with a fixed drug combination of 4 tablets, each containing isoniazid (75 mg), rifampicin (150 mg), pyrazinamide (400 mg), ethambutol (275 mg) and continued with advanced phase 4 tablets each contained with isoniazid (150 mg), rifampicin (150 mg). The patient was also treated with corticosteroid (prednisone) 2 mg/kg/day given every 6 hours planned for 6 weeks along with anti-tubercular treatment. The patient was consulted by the child surgery division for hydrocephalus management. The patient was planned to get a ventriculoperitoneal shunt placement but was denied by the family.

The single most important complication of milliary tuberculosis in children is TBM, and a major cause of significant mortality and morbidity. Tuberculous meningitis can occur in 20-40% of children with miliary tuberculosis. A high level of CSF protein indicates disruption of the blood-brain barrier and the subarachnoid blockage of the CNS circulation in the central nervous system involvement of tuberculosis. A high level of CSF protein was identified as a significant risk factor for poor outcomes in children with TBM.[14,15] In a study among 84 children with miliary tuberculosis, TBM (28.5%) was the most frequent complication with mortality in 38% than without TBM.[16]

In our case, the patient was discharged from the hospital after the finished intensive phase of ATT. The patient never came to policlinic. We suggested that the patient continue taking ATT for the next 10 months. The patient was planned to get a ventriculoperitoneal shunt placement but was still denied by the family.

## CONCLUSION

We presented cases of tuberculous meningitis in a 15-year-old boy patient. In this case, the patient was found to have miliary tuberculosis that lately has central nervous system involvement because of the hematogenous spread of bacilli to the brain. The symptoms began with chronic fever, chronic cough, and decreased body bodyweight. The central nervous system involved was loss of consciousness and neck stiffness. Thorax X-ray revealed miliary tuberculosis. A Head CT scan revealed a leptomeningeal contrast enhancement and hydrocephalus. In the end, Mycobacterium was detected on *Xpert M. Tuberculosis* from the gastric fluid. We decided to treat the patient with an ATT intensive phase and planned to do a ventriculoperitoneal shunt procedure. In addition, we highlighted the importance of considering the diagnosis of tuberculous meningitis in children along with integrated management. The timely diagnosis and management will reduce tuberculous meningitis morbidity and mortality.

## ACKNOWLEDGMENT

We thank all of the patients who participated in this research and all of the research staff in our hospital for their invaluable support regarding the making of this manuscript.

## CONFLICT OF INTEREST

There is no competing interest regarding the manuscript.

## ETHICS CONSIDERATION

Ethics approval has been obtained from the Ethics Committee, Faculty of Medicine, Universitas Udayana, Prof. dr. I.G.N.G Ngoerah Hospital, Bali, Indonesia, before the study was conducted.

## FUNDING

None.

## AUTHOR CONTRIBUTIONS

All authors equally contribute to the study from the conceptual framework, data acquisition, and data analysis, until reporting the study results through publication.

## REFERENCES

1. Chakaya J, Khan M, Ntoumi F, et al. Global Tuberculosis Report 2020 - Reflections on the Global TB burden, treatment and prevention efforts. Int J Infect Dis. 2021;113 Suppl 1(Suppl 1):S7-S12. https://doi.org/10.1016/j.ijid.2021.02.107.
2. Ministry of Health Republic of Indonesia. National Strategic Plan of Tuberculosis Control 2016-2020. 2016. p1-119.
3. Noviyani A, Nopsopon T, Pongpirul K. Variation of tuberculosis prevalence across diagnostic approaches and geographical areas of Indonesia. PLoS One. 2021;16(10):e0258809. https://doi.org/10.1371/journal.pone.0258809.
4. Haerana BT, Prihartono NA, Riono P, et al. Prevalence of tuberculosis infection and its relationship to stunting in children (under five years) household contact with new tuberculosis cases. Indian J Tuberc. 2021;68(3):350-355. https://doi.org/10.1016/j.ijtb.2020.10.011.
5. Thomas TA. Tuberculosis in Children. Thorac Surg Clin. 2019;29(1):109-121. https://doi.org/10.1016/j.thorsurg.2018.09.009.
6. Borah P, Deb PK, Venugopala KN, et al. Tuberculosis: An Update on Pathophysiology, Molecular Mechanisms of Drug Resistance, Newer Anti-TB Drugs, Treatment Regimens and Host- Directed Therapies. Curr Top Med Chem. 2021;21(6):547-570. https://doi.org/10.2174/1568026621999201211200447.
7. Sayyed GM, Abdol SP, Ehsan A, Alacsandra B, and Azadeh E. Tuberculous meningitis and miliary tuberculosis in Iran: A review. Asian Pacific Journal of Tropical Medicine. 2022;15(4). p143-152. https://doi.org/10.4103/1995-7645.343880.
8. Wilmott RW, Deterding R, Li A, Ratjen F, Sly P, Zar HJ, and Bush A. Kendig's Disorders of the Respiratory Tract in Children. Elsevier. 2019;9(29). p475-97.
9. Gurkan F, Bosnak M, Dikici B, et al. Miliary tuberculosis in children: a clinical review. Scand J Infect Dis. 1998;30(4):359-362. https://doi.org/10.1080/00365549850160648.
10. Galvis A, Beatrice B, Pecson I, and Nakamura C. A Domestic Case of Pediatric Miliary Tuberculosis. 2021. p1-7. https://doi.org/10.20944/preprints202103.0437.v1.
11. Wang G, Liang R, Sun Q, Liao X, Wang C, Huang H. Extremely high levels of central nervous system involvement in miliary tuberculosis. BMC Infect Dis. 2022;22(1):417. https://doi.org/10.1186/s12879-022-07390-7.
12. Daniel BD, Grace GA, Natrajan M. Tuberculous meningitis in children: Clinical management & outcome. Indian J Med Res. 2019;150(2):117-130. https://doi.org/10.4103/ijmr.IJMR_786_17.
13. Shah I and Pereira NMD. Tuberculous Meningitis in Children: a Review Article. Current Infectious Disease Reports. 2020:22(4). p1-6. https://doi.org/10.1007/s11908-020-0720-7.
14. Ganiem AR, Djung LW, Chaidir L, Gamayani U. Microbiological Testing of Gastric Aspirate Improves the Diagnosis of Pulmonary Tuberculosis in Unconscious Adults with TB Meningitis. Infect Dis Rep. 2020;12(3):134-140. https://doi.org/10.3390/idr12030025.
15. Wang MS, Zhao M, Liu XJ. Risk factors for poor outcome in childhood tuberculous meningitis. Sci Rep. 2021;11(1):8654. https://doi.org/10.1038/s41598-021-87082-5.
16. Daniel BD, Grace GA, Natrajan M. Tuberculous meningitis in children: Clinical management & outcome. Indian J Med Res. 2019;150(2):117-130. https://doi.org/10.4103/ijmr.IJMR_786_17.