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https://ojs.transpublika.com/index.php/COMORBID
Online ISSN 2809-9745

https://doi.org/10.55047/comorbid.v5i2.2093

Case Report

Unexpected Encephalitis in Active Miliary TB Undergoing Treatment in an Elderly Person: A Rare Case Report

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Received : 10 December - 2025
Accepted : 27 April - 2026
Published online : 30 April - 2026

Abstract

Miliary tuberculosis (TB) with central nervous system (CNS) involvement manifesting as unexpected encephalitis in the elderly is a rare and serious condition. This study aims to describe and analyze the clinical manifestations of unexpected encephalitis in elderly patients with active miliary TB undergoing treatment. A descriptive case study with a qualitative approach was used. The population was elderly patients diagnosed with active miliary TB complicated by CNS involvement, with a purposive sample of one 68-year-old female patient who presented with atypical neurological symptoms after approximately five weeks of multidrug therapy (MDT). Data were obtained from medical records, neurological physical examinations, laboratory results, and head CT scans. A narrative descriptive analysis integrated clinical and radiological findings to interpret the relationship between encephalitis manifestations and TB therapy progression. The results showed atypical encephalitis symptoms with CT evidence of hypodense lesions and central calcifications, highlighting the diagnostic challenge. Appropriate MDT therapy with adjuvant corticosteroids resulted in a good clinical response. The conclusions emphasize the importance of early detection and use of neuroimaging in elderly patients with miliary TB to reduce neurological complications. Further research with larger samples is recommended to strengthen the findings.

Keywords: Central Nervous System, Elderly, Encephalitis, Miliary Tuberculosis, Neuroimaging.

1. Introduction

Miliary tuberculosis (TB) is a form of massive lymphohematogenic dissemination of *Mycobacterium tuberculosis* that is often fatal and can affect various organs, including the central nervous system (CNS) (Sharma et al., 2016; Wang et al., 2022). Although pulmonary TB is the primary manifestation of tuberculosis, CNS involvement in miliary TB is rare and can potentially lead to serious complications with high mortality and neurological sequelae (Leonard, 2017; Tetsuka et al., 2020). Risk factors such as advanced age, HIV co-infection, and immunosuppression contribute to a worsening prognosis and increase the complexity of treatment (Teweldemedhin et al., 2018; Wang et al., 2022).

CNS involvement in miliary tuberculosis occurs in approximately 10-30% of cases, though this figure is likely underestimated prior to modern neuroimaging, with sensitive diagnostic evaluation suggesting considerably higher proportions (Wang et al., 2022; Sharma et al., 2016). Hematogenous dissemination of *Mycobacterium tuberculosis* can form rich foci in the brain that rupture, giving rise to meningitis, parenchymal lesions, and rarely

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encephalitis, particularly in elderly patients with miliary TB (Christie et al., 2008; Stahl, 2019). Clinical presentation is typically atypical, ranging from headache to hemiparesis and focal seizures, frequently causing diagnostic delays (He et al., 2023; Staal et al., 2024). In elderly patients, immunosenescence further obscures symptoms, which are often misattributed to age-related comorbidities, while neuroimaging remains essential for diagnosis, complication assessment, and disease monitoring (Stahl, 2019; Tetsuka et al., 2020; Khatri et al., 2018; Taheri et al., 2015).

Management of miliary TB with CNS involvement carries a poor prognosis, with significant risks of permanent neurological complications and mortality (Christie et al., 2008; Goulenok et al., 2017). Elderly, immunosenescent patients are particularly vulnerable to rapid disease progression and CNS dissemination, and the presence of drug resistance (such as rifampin resistance) may further compromise treatment outcomes (He et al., 2023; Staal et al., 2024; Mohammadian & Butt, 2019; Thwaites et al., 2005).

Appropriate therapy with a multidrug tuberculosis (MDT) regimen and adequate dosing of drugs such as isoniazid and rifampin are crucial to prevent disease progression and neurological complications (Heemskerk et al., 2016). However, evidence regarding the atypical presentation of miliary TB encephalitis in the elderly remains limited, particularly in cases that arise during treatment (Tetsuka et al., 2020). Furthermore, the use of corticosteroids as adjuvant therapy and indications for surgical intervention require further study in the context of TB encephalitis management in this population.

Nevertheless, scientific evidence regarding the occurrence of encephalitis emerging during antituberculosis therapy in patients with miliary tuberculosis remains very limited, and the majority of available reports consist of individual case reports. Studies by Udani & Dastur (1970) and Pinzon et al. (2021) indicate that brain parenchymal involvement in miliary tuberculosis, including encephalitis, is a rare manifestation that has not been widely documented in the clinical literature. Further, research by Caraux-Paz et al. (2021) on tuberculosis in the elderly population demonstrates that clinical manifestations, including central nervous system involvement, are frequently atypical and remain poorly characterized, particularly in the context of disease progression during therapy. This condition indicates the existence of a significant knowledge gap regarding the clinical characteristics and disease dynamics in elderly patients with miliary tuberculosis who develop neurological complications.

This study aims to describe and analyze the manifestations of unexpected encephalitis in elderly patients with active miliary TB undergoing treatment. The urgency of this study lies in the need to document the rare and challenging clinical characteristics in the diagnosis and management of miliary TB encephalitis in the elderly, while emphasizing the importance of early and appropriate antituberculosis treatment. The novelty of this study is its focus on a rare case of miliary TB encephalitis that emerged during antituberculosis therapy in elderly patients, which has not been widely reported in the recent literature.

2. Methods

This type of research is a descriptive case study aimed at documenting and analyzing in depth the phenomenon of unexpected encephalitis in an elderly patient with active miliary tuberculosis undergoing treatment. A qualitative approach was used to gain a comprehensive understanding of the patient's clinical characteristics, supporting examination results, and therapeutic response (Creswell & Creswell, 2017; Sugiyono, 2021). This case study was chosen because the focus on a single, unique case allows for exploration of clinical and radiological

details that are difficult to obtain in large quantitative studies (Leonard, 2017; Sudaryono, 2021).

The primary instruments in this study were patient clinical data collected through medical records, neuromedical physical examinations, laboratory results, and radiological examinations such as head CT scans and other supporting data (Emzir, 2021; Stahl, 2019). Data analysis was performed using descriptive narrative techniques, integrating clinical examination results and radiological assessments to interpret the relationship between encephalitis manifestations and the course of miliary tuberculosis therapy (Staal et al., 2024; Tetsuka et al., 2020). Data validity was supported by repeated medical documentation and discussions with the medical team regarding this case (Creswell & Creswell, 2017).

The study population consisted of elderly patients diagnosed with active miliary tuberculosis and experiencing complications involving the central nervous system, particularly encephalitis, during antituberculosis treatment (Teweldemedhin et al., 2018; Wang et al., 2022). The sample selected was a 68-year-old female patient referred to the neurology clinic with atypical neurological symptoms that appeared after nearly 5 weeks of multidrug therapy (MDT). Purposive sampling was used to select cases that met specific criteria with relevant clinical and radiological features (Sudaryono, 2021; Sugiyono, 2021).

The research procedure included retrospective data collection from patient medical records and clinical observations during treatment at Bethesda Hospital Yogyakarta. Data were obtained from the initial medical history, miliary TB diagnosis, nursing care during therapy, and signs of encephalitis detected clinically and radiologically (Leonard, 2017; Stahl, 2019). All data were thoroughly analyzed to evaluate the relationship between immunosenescence and neurological complications and the effectiveness of antituberculosis treatment in this case context (He et al., 2023; Tetsuka et al., 2020). This study has strictly complied with the ethical principles of research. Ethical approval was obtained from the Health Research Ethics Committee of Bethesda Hospital Yogyakarta. Written informed consent was obtained from the patient or the patient's legally authorized representative prior to the use of data in this study. All patient identifying information was anonymized to protect patient confidentiality and privacy. This study was conducted in accordance with the principles of the Declaration of Helsinki (Creswell & Poth, 2018).

What distinguishes the data collection and analysis approach in this study is its integrative, multi-source triangulation strategy. Rather than relying on a single diagnostic modality, clinical interpretation was derived from the convergence of neurological examination findings, serial laboratory markers, and radiological imaging — particularly head CT scans performed at multiple time points — allowing for a dynamic, longitudinal assessment of disease progression. This approach enabled the identification of subtle radiological changes that may otherwise be overlooked in cross-sectional evaluation. Furthermore, the analysis placed particular emphasis on the temporal relationship between antituberculosis therapy initiation and the emergence of encephalitis symptoms, which is a clinically critical yet underreported phenomenon in the existing literature. By systematically mapping this timeline alongside immunological and therapeutic variables, this study offers a more nuanced clinical narrative than conventional case documentation, thereby contributing methodologically to the growing body of evidence on CNS complications in elderly miliary TB patients (Creswell & Creswell, 2017; He et al., 2023; Stahl, 2019).

3. Results and Discussion

3.1. Results Analysis

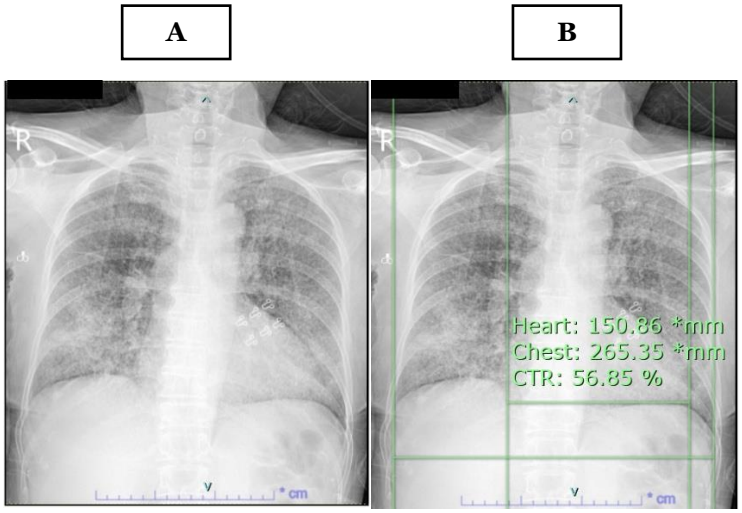

Figure 1. Chest X-ray findings: (A) peribronchial nodular consolidation with air bronchogram sign and increased bronchovascular markings bilaterally; (B) mild cardiomegaly (CTR > 0.5)

The chest radiograph in Figure 1 demonstrates the presence of peribronchial nodular consolidation with a distinct air bronchogram appearance and increased coarse bronchovascular markings in both lung fields. These findings are suggestive of a diffuse pulmonary inflammatory or infectious process, such as miliary tuberculosis or bronchogenic pneumonia, in which the distribution of lesions follows the bronchial pathway. Furthermore, in image (B), an increase in cardiac size is observed with a cardiothoracic ratio (CTR) value of >0.5, indicating mild cardiomegaly, possibly related to a comorbid condition or a systemic response to chronic infection.

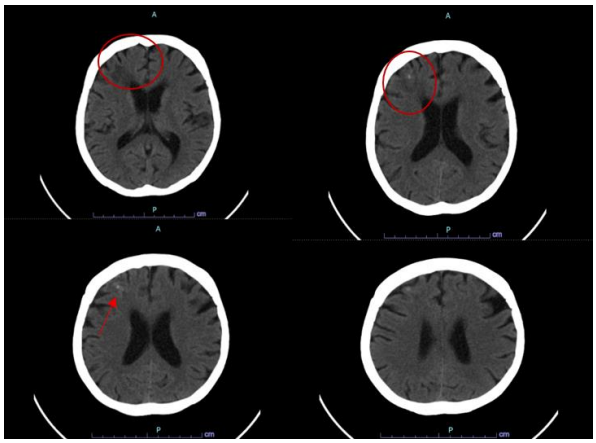

Figure 2. Axial CT scan showing a faint hypodense lesion with central calcification in the right fronto-parietal region (red circle and arrow)

Meanwhile, in Figure 2, which consists of axial head CT scan images, a faint hypodense lesion is visible in the right fronto-parietal region marked by a red circle, accompanied by a central calcification point indicated by a red arrow. This appearance may suggest a chronic granulomatous process such as a tuberculoma, particularly in the context of systemic

tuberculosis infection. The hypodense lesion represents an area of edema or necrosis, whereas central calcification is frequently associated with a longstanding process or partial healing. Overall, the combination of these thoracic and cerebral radiological findings supports the possibility of disseminated tuberculosis with neurological manifestations, which requires correlation with the clinical presentation and other supporting investigations.

3.2. Discussion

Based on comparisons between international studies, the diagnosis of encephalitis is generally established through a combination of major and minor criteria encompassing clinical, laboratory, and neuroimaging findings (Staal et al., 2024). Encephalitis itself can exhibit atypical symptoms, ranging from mild symptoms such as mild headache, hemiparesis, numbness, to focal seizures, especially in cases of neurotuberculosis, which can complicate early diagnosis. In advanced stages of the disease, encephalitis may be accompanied by symptoms such as altered mental status, confusion, or severe headache. Brain parenchymal involvement can manifest as tuberculomas or abscesses. This inflammation can lead to vasculitis, resulting in vascular occlusion and symptoms similar to stroke. The majority, approximately 75%, of infarcts occur in the region of the caudate nucleus, ventral thalamus, and anterior limb of the internal capsule, which are supplied by branches of the middle cerebral artery. In our patient, atypical symptoms of headache, malaise, tremor, and left-sided hemiparesis with 4/5 extremity muscle strength were observed. These atypical neurological manifestations warrant further investigation in all pulmonary tuberculosis patients, particularly those with miliary TB and lymphohematogenous spread.

Predisposing factors for CNS TB are generally related to failure to maintain immune control against focal TB infection, whether active or dormant, in the brain or other body tissues. This is seen in children under 3 years of age, malnourished individuals, the elderly, and other adults undergoing immunosuppressive treatment or infected with human immunodeficiency virus (HIV). In this case, a notably relevant predisposing factor is immunosenescence, given the patient's advanced age of 68 years. Furthermore, CNS TB commonly occurs as a complication of clinically apparent, progressive miliary TB. However, encephalitis is one of the least frequently reported CNS involvements in miliary tuberculosis due to the paucity of literature and case reports linking the two events. A possible predisposing factor based on the patient’s history is immunosenescence, particularly in elderly patients. HIV serology testing using the enzyme-linked immunosorbent assay (ELISA) method was negative in the patient, so it is assumed there are no other predisposing factors possibly associated with miliary tuberculosis metastasis to the brain parenchyma. CD4 cell measurements were also not considered because the innate immunity of patients in prime condition does not take into account the non-modifiable factor of age.

Essentially, the best radiological examination for diagnosing encephalitis is MRI, but CT scanning can also be used if MRI accommodation is not possible. In most cases, there are no typical features of tuberculous encephalitis, except in cases of cerebral abscess or granulomatous lesions. Necrosis may occur in the central portion, leading to a caseous abscess, which may undergo calcification or liquefaction. Based on existing research, CNS TB is divided into meningeal TB and parenchymal TB. Parenchymal tuberculoma is the dominant variant of intracranial parenchymal tuberculosis. This tuberculoma develops due to the confluence of tuberculous microgranulomas, which are usually located at the gray and white matter interface, due to the interruption of hematogenous spread of infection due to narrowing of the blood vessel diameter in that region. Lesions can sometimes form in the brain parenchyma due to the spread of infection from the cerebrospinal fluid through the perivascular spaces (Virchow-Robin). This condition can manifest in almost any region of the

brain, including the ventricular system, basal cisterns, brainstem, cerebellar hemispheres, and sulcal spaces. On non-contrast CT scans, tuberculomas may appear isodense, hyperdense, or exhibit mixed densities. On contrast-enhanced CT scans, images may show ring-like enhancement, or may appear as irregular, inhomogeneous areas of nodular enhancement. These tuberculomas are most commonly found in children and are primarily located infratentorially. In adults, tuberculomas are usually located supratentorially.

Miliary tuberculosis, which often occurs in immunocompromised patients with small non-caseating granulomas measuring <2 mm. On CT scan, these lesions sometimes appear as small hypodense lesions. Detection with MRI will show homogeneous post-contrast enhancement on T1W sequences and hypointense on T2W sequences, indicating a caseating process. Tuberculous abscesses are generally rare and are thought to result from liquefaction of tuberculomas, which appear as well-circumscribed hypodense lesions >3 cm with peripheral edema and a characteristic mass effect on CT scan. Other manifestations of parenchymal tuberculosis, such as tuberculous cerebritis, tuberculous rhombencephalitis, and tuberculous encephalopathy, are also present. In our patient, a head CT scan showed a faint hypodense lesion in the right frontoparietal region with calcified spots in the center of the lesion. This suggests that tuberculous encephalitis is less typical and is often referred to as "multifaceted."

Delays in initiating anti-tuberculosis therapy in individuals with tuberculous encephalitis are correlated with increased mortality and the risk of neurologic manifestations. The regimen administered to this patient is consistent with the recommendations for the management of tuberculous meningitis, which advocate the use of a four-drug combination during the intensive phase followed by continuation therapy with two primary drugs (Marx & Chan, 2011). Isoniazid serves as the principal component due to its excellent penetration into the cerebrospinal fluid, whereas rifampin remains an essential drug despite its lower penetration owing to its important role in reducing mortality (Imron et al., 2025; Wasserman et al., 2019). Furthermore, the use of corticosteroids as adjuvant therapy has been demonstrated to help reduce inflammation and improve neurological outcomes in tuberculous meningitis (Kaojarern et al., 1991).

The clinical course in this patient was relatively favorable, with mild symptoms and a good short-term prognosis, and was managed on an outpatient basis through the neurology clinic with symptom-directed therapy. This outcome underscores the importance of early recognition and timely intervention when encephalitis emerges during antituberculosis treatment, particularly in elderly patients, where immunosenescence may predispose to central nervous system (CNS) dissemination while simultaneously attenuating clinical severity, thereby complicating timely diagnosis.

Standard therapy consists of a four-drug combination: isoniazid 5 mg/kg/day, rifampin 10 mg/kg/day, pyrazinamide 30 mg/kg/day (maximum 2 grams/day), and ethambutol 20 mg/kg/day for 2 months. This therapy is followed by a two-drug combination of rifampin and isoniazid for 7-12 months. Isoniazid is a fast-acting bactericidal drug, exhibiting good diffusion in the cerebrospinal fluid. After standard dosing (3-5 mg/kg/day), isoniazid concentrations in the cerebrospinal fluid are 10-15 times the minimum inhibitory concentration for M. tuberculosis. Some publications recommend increasing the isoniazid dose to more than 5 mg/kg/day, particularly to 10-20 mg/kg/day in pediatric patients. However, efficient cerebrospinal fluid diffusion will be inadequate in susceptible strains of *Mycobacterium tuberculosis*. Pyridoxine, at a dose of 25 or 50 mg per day, should be administered concurrently to avoid neurologic complications associated with isoniazid-induced pyridoxine deficiency.

Rifampin does not achieve good CSF levels because its concentration is <30% of serum concentration. Nevertheless, the mortality associated with rifampin-resistant central nervous system tuberculosis underscores the importance of this antibiotic as a key partner in treatment. Ethambutol is generally recommended as a fourth-line treatment due to its limited CNS diffusion, but its penetration may be enhanced when used in conjunction with a fluoroquinolone. Certain adjuvant therapies may be given to enhance recovery from non-infectious complications of TB encephalitis, such as brain edema and vasculitis. The approved adjuvant therapy for TB encephalitis without HIV coinfection is corticosteroids, with the recommended dose of dexamethasone or prednisolone set at approximately 0.4 mg/kg/day for adults and 0.6 mg/kg/day for children. Corticosteroid therapy is typically given for 4 weeks, followed by a gradual dose taper over the next 4 weeks. Urgent surgical indications are performed in cases of TB encephalitis, brain abscess, and hydrocephalus with the aim of reducing intracranial pressure and bacterial inoculum.

In this case, the patient was diagnosed with encephalitis after approximately 5 weeks of antituberculosis treatment. TB therapy, along with additional oral pyridoxine, was continued in accordance with established recommendations. As the patient presented with mild symptoms and a good prognosis, outpatient management from the neurology clinic focused primarily on symptomatic relief.

4. Conclusion

This study reveals an unexpected manifestation of encephalitis in an elderly patient with active miliary tuberculosis undergoing antituberculosis treatment. Key findings suggest that encephalitis, a complication of miliary TB in the elderly, can present with atypical symptoms and is often diagnosed late, potentially increasing the risk of permanent neurological complications. Imaging-based diagnostics, particularly head CT scans, play a crucial role in detecting subtle hypodense lesions and calcifications suggestive of inflammation and tuberculoma. Appropriate multidrug therapy for tuberculosis and adjuvant corticosteroids has been shown to provide a good clinical response, although this is a rare case. However, this study is limited to a single case, such that a causal relationship between the administration of therapy and clinical improvement cannot be established, and generalization of the findings requires confirmation through studies with larger samples and more extensive quantitative methods. Nevertheless, these results are consistent with reports in the previous literature.

These limitations provide opportunities for further research focusing on the mechanisms of immunosenescence and specific risk factors that worsen the prognosis of encephalitis in elderly patients with miliary TB. Longitudinal and interventional studies would be highly beneficial in formulating more precise clinical guidelines and evaluating the effectiveness of therapeutic regimens tailored to the needs of elderly patients. Practically, this study emphasizes the importance of high clinical vigilance in elderly patients with miliary TB for early detection of encephalitis and the need for optimal use of neurodiagnostic imaging. A multidisciplinary approach to treatment and follow-up is also strongly recommended to minimize the risk of death and long-term neurological impacts.

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