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CASE REPORT

Multiple cranial tuberculomas with meningitis and miliary tuberculosis in an immunocompetent adult

Ahmet Doğan[1], **Hasan Tahsin Gözdaş**[1], **Tayibe Bal**[1], **Sultan Beste Şahin**[1]

[1]Department of Infectious Diseases and Clinical Microbiology, Faculty of Medicine, Bolu Abant İzzet Baysal University, Bolu, Türkiye

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ABSTRACT

Miliary brain tuberculosis (TB) is a rare and highly lethal clinical form resulting from the extensive lymphohematogenous spread of Mycobacterium tuberculosis. Widespread brain involvement often suggests immunosuppression. However, cases have been reported in immunocompetent adults. Prognosis depends largely on prompt diagnosis and initiation of treatment. This case report presents an immunocompetent adult with miliary pulmonary TB diagnosed by bronchoalveolar lavage (BAL) fluid analysis and diffuse brain tuberculomas on brain magnetic resonance imaging (MRI).

Keywords: adult, immunocompetent, miliary tuberculosis, tuberculoma

INTRODUCTION

Miliary brain tuberculosis (TB) is still endemic in developing countries (1). It can affect any organ. Disseminated TB is a rare entity that often constitutes a diagnostic trap due to its misleading aspects and the frequent negativity of bacteriological samples. Subacute or chronic constitutional symptoms such as fever, weight loss, or night sweats are often observed and should prompt this diagnosis, particularly in endemic areas (2). It is mainly encountered in immunocompromised patients, but rare cases have been reported in immunocompetent patients (3).

CASE

A 19-year-old male from Afghanistan, with no history of chronic illness, presented to the emergency department with confusion and fever. Physical examination revealed a fever of >38°C. Neurological examination showed neck stiffness, with negative Kernig and Brudzinski signs. Extensive crackles were heard on lung auscultation. Other systemic examinations were unremarkable. Brain magnetic resonance imaging (MRI) showed lesions consistent with widespread supra and infratentorial tuberculomas (Figure 1). Chest computed tomography (CT) revealed

Corresponding author: Ahmet Doğan **E-mail:** uzdrahmetdogan@gmail.com
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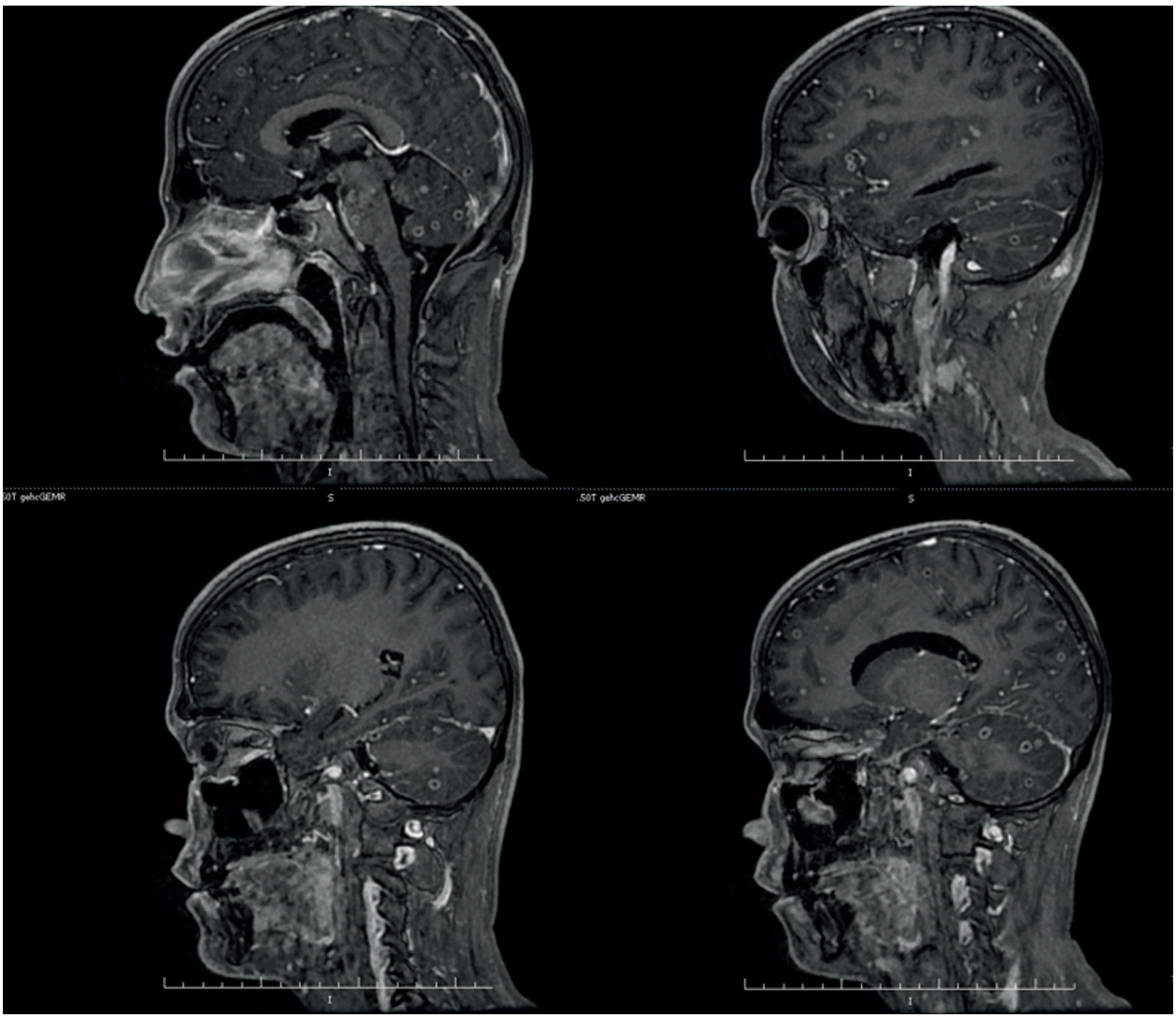

Figure 1. Appearance of tuberculomas from different slices on brain magnetic resonance imaging of the case.

bilateral miliary involvement and cavitation areas (Figure 2). Suspecting tuberculous meningitis, a lumbar puncture was performed. Cerebrospinal fluid (CSF) analysis showed white blood cells (WBC): 20/mm^3, red blood cells (RBC): 170/mm^3, protein: 1851 mg/L (150-400), glucose: 24 mg/dL (40-70) (simultaneous blood glucose: 91), chloride: 118 mmol/L (118-132). The purified protein derivative (PPD) test was anergic. Laboratory values are detailed in Table 1.

The patient was admitted to the intensive care unit (ICU) due to poor general condition. CSF, blood, and urine cultures showed no growth. Polymerase chain reaction (PCR) testing of the throat swab for respiratory viruses was negative. CSF acid-fast bacilli (AFB) staining was also negative. The CSF sample was sent to the laboratory for *M. tuberculosis* culture and PCR analysis. HBs Ag, Anti HCV, and Anti-HIV were all negative. Complement C3, C4, and immunoglobulin levels were normal. On the third day of ICU stay, the patient regained consciousness, and vital signs stabilized. He was transferred to the general ward. In coordination with the tuberculosis control program, a treatment regimen was initiated consisting of Isoniazid 1x300 mg/day, Rifampicin 1x600 mg/day, Ethambutol 1x15 mg/kg/day, and Pyrazinamide 1x25 mg/kg/day.

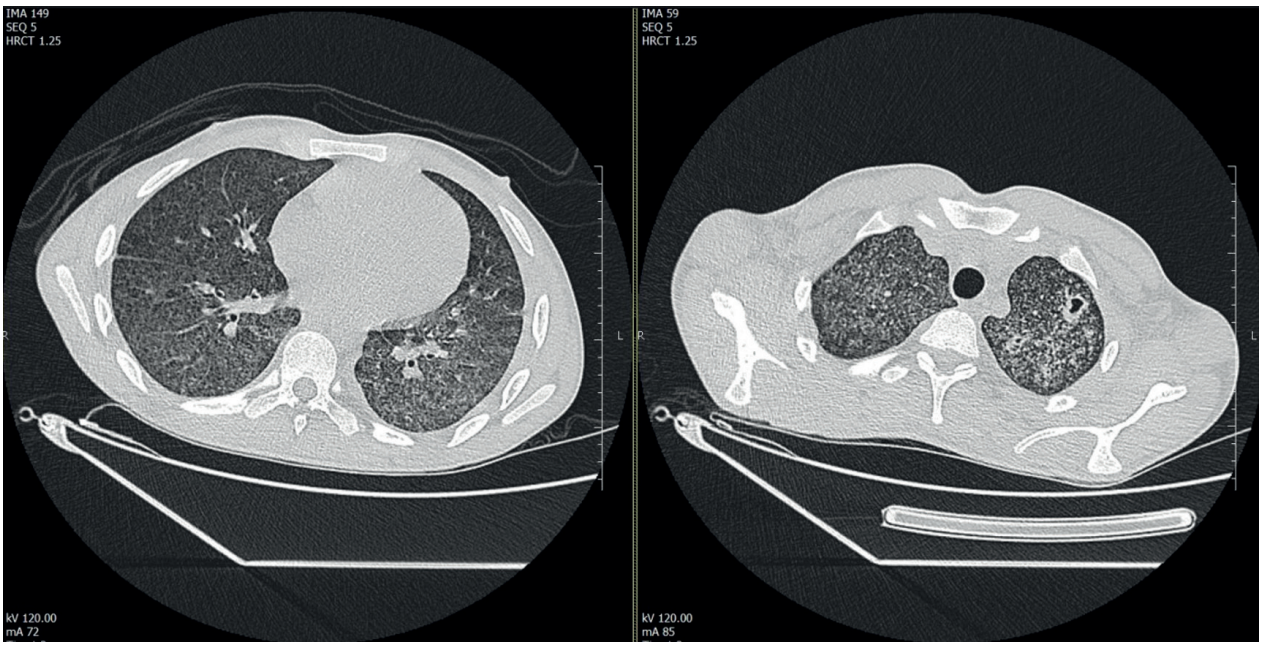

Figure 2. Diffuse miliary involvement and cavity areas on chest computer tomography of the case.

Table 1. Patient's Hemogram and Biochemistry Tests

Parameters	Results	Normal Range
Blood white blood cell (WBC)	6,61	4,5 - 11.0 K/uL
Hemoglobin (HGB)	11,8	11,5 - 17,5 g/dL
Platelet (PLT)	304	140 - 400 K/uL
Neutrophils (NEU%)	76,9	40 - 66 %
Lymphocytes (LYM%)	13,8	25 - 46 %
Fasting Blood Glucose	114	75 - 100 mg/dL
C-reactive protein (CRP)	14,9	0 - 5 mg/L
Urea	39	12 - 42 mg/dL
Creatinine	0,54	0,72 - 1,25 mg/dL
Alanine Aminotransferase (ALT)	27	0 - 55 U/L
Aspartat Aminotransferaz (AST)	39	5 - 34 U/L
Alkaline phosphatase (ALP)	90	40 - 150 U/L
Gamma Glutamyl Transferase (GGT)	47	12 - 64 U/L
Total bilirubin	0,36	0,2 - 1,2 mg/dL
Direct bilirubin	0,17	0 - 0,5 mg/dL
Lactate dehydrogenaz (LDH)	438	125 - 220 U/L

Dexamethasone was planned as 1x0.4 mg/kg/day for the first week, 1x0.3 mg/kg/day for the second week, 1x0.2 mg/kg/day for the third week, and 1x0.1 mg/kg/day for the fourth week, along with Pyridoxine 1x50 mg/day. Bronchoscopy was performed on the non-expectorating patient, and bronchoalveolar lavage (BAL) fluid was obtained. While AFB staining of BAL fluid was negative, *M. tuberculosis* PCR was positive. On the third day of antituberculosis treatment, AST and ALT values increased threefold, but the patient had no symptoms. Liver enzymes began to decrease by the end of the first week. On day 15, the patient was stable and symptom-free. The patient was discharged with detailed instructions for maintenance therapy and follow-up recommendations.

DISCUSSION

CSF findings are not always helpful in the diagnosis of tuberculous meningitis or cerebral tuberculoma without meningitis due to their variable nature. While lymphocytic pleocytosis is typically expected in CSF, neutrophilia may be present in early stages. Similarly, in our case, there was no significant leukocytosis in the CSF. Despite certain disadvantages, radiological imaging can contribute significantly to the diagnosis. Brain MRI is more advantageous than brain CT for the detection of tuberculomas, while chest CT is more advantageous than x-ray for the detection of miliary TB (4). However, CSF glucose and protein levels were indicative of bacterial meningitis. CSF AFB and CSF TB PCR negativity does not exclude TB meningitis. False negative results on the PPD test are another challenge in reaching a diagnosis. The contribution of CSF culture to diagnosis requires a long process, and its positivity rate remains around 30%. The positivity rate for AFB is approximately 10% (5). However, false negative results may lead to delays in treatment.

In smear-negative pulmonary tuberculosis cases, BAL fluid analysis is another useful diagnostic method. Studies have shown the diagnostic value of measuring interleukin 27 (IL-27), tumor necrosis factor alpha (TNF-alpha), IL-2, and interferon gamma (IFN-gamma) in BAL (6-8). In our case, the diagnosis was confirmed by the TB PCR result from BAL fluid. Despite extensive pulmonary TB with cavitations, meningitis, and widespread tuberculomas, other diagnostic tests were not helpful.

In tuberculosis-related brain involvement, clinical forms like meningitis followed by tuberculomas, brain abscesses, and miliary involvement, are common (9). However, cases of tuberculoma without meningitis have also been reported (10). Cases often present with mental status changes, meningeal signs, seizures, cranial nerve palsies, and focal neurological deficits (11). Even with effective antiTB treatment, about half of the cases may experience neurological sequelae (12). In a study, presenting TB culture-confirmed cases in Türkiye, the PCR positivity rate in TB cases was reported as 17.6%, while the PCR positivity rate in TB meningitis cases was reported as 12.5% (13). In a systematic review of 53 studies from 28 countries, the mortality rate of TB meningitis was found to be 42% (14). In our case, the patient regained consciousness with supportive care in the ICU before initiation of antiTB treatment, and vital signs returned to normal. On the third day of ICU admission, the patient was conscious and asymptomatic, and was transferred to the ward for the initiation of antiTB treatment plan. The patient's headache and fever lasted only two days and subsided without treatment. Despite the presence of tuberculoma foci spreading almost throughout the brain parenchyma and cerebellum, no seizures or neurological deficits were observed during follow-up. The young age of the patient and the absence of immunosuppression undoubtedly played a role in this outcome.

AntiTB-associated hepatotoxicity presents a significant challenge in patient management. Isoniazid, rifampicin, pyrazinamide, and their combinations are associated with hepatotoxicity (15). In our case, the ALT value tripled on the third day of treatment without symptoms. However, the treatment was continued without dose reduction or change. On the seventh day of treatment, the ALT value was observed to return to normal. It was concluded that in asymptomatic cases, continuation of the same treatment is necessary even with liver enzyme elevations up to three times the normal level.

CONCLUSION

Miliary TB is generally seen in infants or immunosuppressed patients, but it can rarely occur in young adults without immunodeficiency. Despite the availability of many tests for diagnosis, it is not always possible to diagnose with these tests. In such cases, BAL fluid may be helpful. In cases of brain involvement, tuberculomas may not always be accompanied by meningitis. Despite widespread tuberculomas in the brain, there may be no accompanying focal neurological deficit, cranial nerve involvement, or seizures. During antiTB treatment, especially in cases of ALT elevation up to three times without symptoms, it is not necessary to immediately stop the treatment, reduce the dose, or change the treatment regimen. Continuing the current treatment regimen with close monitoring may be sufficient.

Ethical approval

Written informed consent was obtained from the participants.

Author contribution

Surgical and Medical Practices: AD, HTG, TB, SBŞ; Concept: AD, HTG; Design: AD, HTG, TB; Data Collection or Processing: AD, HTG, SBŞ; Analysis or Interpretation: AD, HTG, TB; Literature Search: AD; Writing: AD, HTG. All authors reviewed the results and approved the final version of the article.

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Conflict of interest

The authors declare that there is no conflict of interest.

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