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CASE REPORT

Challenging diagnosis of central nervous system tuberculosis with joint involvement

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ABSTRACT

Challenging diagnosis of central nervous system tuberculosis with joint involvement

Central nervous system tuberculosis (CNS-TB) is a rare but severe form of extrapulmonary tuberculosis that can mimic various neurological conditions, making diagnosis challenging. We aimed to present a 70-year-old male patient who initially had non-specific symptoms, including dyspnea, malaise, and dizziness. His condition progressed to confusion and seizure, raising suspicion of central nervous system involvement. Initial imaging findings were inconclusive, and multiple diagnostic tests, including pleural fluid and joint biopsy, were negative for *Mycobacterium tuberculosis*. However, cerebrospinal fluid analysis confirmed CNS-TB through Xpert MTB/RIF polymerase chain reaction. Despite prompt initiation of anti-tuberculous treatment and intensive care support, the patient's condition worsened, and he succumbed to the disease. This case highlights the diagnostic difficulties associated with CNS-TB and underscores the importance of maintaining a high clinical suspicion in endemic regions, even when initial diagnostic tests are negative.

Key words: Tuberculosis; extrapulmonary; central nervous system; osteoarticular; diagnosis

ÖZ

Eklem tutulumlu merkezi sinir sistemi tüberkülozunda zorlu tanı

Santral sinir sistemi tüberkülozu (SSS-TB), çeşitli nörolojik hastalıkları taklit edebilen, nadir ancak ciddi bir ekstrapulmoner tüberküloz formudur. Bu olguda, başlangıçta dispne, halsizlik ve baş dönmesi gibi non-spesifik semptomlarla başvuran yetmiş yaşındaki erkek hasta sunulmaktadır. Hastada zamanla konfüzyon ve sonrasında nöbet gelişmesi, santral sinir sistemi tutulumu şüphesini artırdı. Plevral sıvı ile eklem biyopsisinde *Mycobacterium tuberculosis* tespit edilemedi. Ancak beyin omurilik sıvısında yapılan Xpert MTB/RIF polimeraz zincir reaksiyon testi ile SSS-TB tanısı doğrulandı. Hızlı başlanan anti-tüberküloz tedaviye ve yoğun bakım desteğine rağmen hastanın durumu kötüleşti ve hasta kaybedildi. Bu olgu, SSS-TB'nin tanınal zorluklarını vurgulamakta ve endemik bölgelerde, başlangıç testleri negatif olsa bile, hastalığın akılda tutulmasının önemini göstermektedir.

Anahtar kelimeler: Tüberküloz; ekstrapulmoner; santral sinir sistemi; osteoartiküler; tanı

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Data Sharing Statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

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INTRODUCTION

Tuberculosis (TB) continues to be a significant public health challenge in developing countries (1). In Türkiye, recent data from 2021 show a decreasing trend in TB incidence, reflecting ongoing efforts in disease control and prevention. However, the World Health Organization (WHO) has highlighted concerns that disruptions caused by the coronavirus disease-2019 pandemic may have led to undiagnosed and untreated cases, potentially masking the true burden of TB in some regions (2).

Central nervous system tuberculosis (CNS-TB) is a rare but severe manifestation of TB, accounting for only 1–5% of all cases. Its clinical presentations include meningitis, granulomas (tuberculomas), cerebritis, arachnoiditis, and spinal involvement. Cerebellar involvement is particularly uncommon and is often accompanied by other organ involvement. Early diagnosis is a crucial predictor of outcomes in CNS-TB, as delayed recognition significantly worsens prognosis (3). This case underscores the importance of always considering TB in the differential diagnosis, particularly in endemic regions or in patients with unexplained neurological symptoms.

CASE HISTORY

A man in his 70s presented to our department in June 2021 with complaints of dyspnea, malaise, and dizziness. His relatives added that he had recently been singing non-sensical songs.

Six months prior to his admission, the patient underwent thoracic computed tomography (CT) at another facility due to cough and chest pain. The scan revealed mediastinal lymphadenopathies. He was treated with antibiotics under suspicion of infection. Subsequently, he was admitted to the cardiology department for recurrent chest pain, where coronary angiography was performed, and two stents were placed.

One month before his admission to our institution, a follow-up thoracic CT revealed mediastinal and conglomerated paraesophageal lymphadenopathies, along with a more pronounced right-sided pleural effusion. No parenchymal pathological findings were observed. Therapeutic and diagnostic thoracentesis revealed an exudative effusion with benign cytology. Additionally, a paraesophageal lymphadenopathy

(LAP) sample obtained through endoscopic ultrasonography raised suspicion of malignancy. However, the findings were consistent with *Candida* esophagitis and non-caseating granulomatous lymphadenitis.

During his follow-up at another hospital, the patient developed neurological symptoms, including dizziness, headache, and nonsensical singing. Cranial CT and magnetic resonance imaging (MRI) were performed, which reported chronic atrophic changes without any specific findings.

METHODS/INVESTIGATIONS

The patient, who had not received any prior treatment for his reported conditions, presented to our department in July 2021 in a poor general condition. On examination, his vital signs were as follows: A fever of 37.1 °C, a pulse rate of 82 beats per minute, and an oxygen saturation of 93% in ambient air. Chest X-ray revealed a bulky hilum and right costophrenic blunting.

Contrast-enhanced thoracic CT showed periarticular soft tissue thickening in both sternoclavicular joints, suggestive of severe synovitis with a compressive effect on the thyroid gland (Figure 1). Mediastinal LAP and pleural effusion, previously observed in earlier imaging, were still present.

Laboratory investigations included serological tests, which returned negative for *Brucella* agglutination, VDRL-RPR, and anti-HIV. However, the Quantiferon test was positive. Biochemical analysis of pleural effusion obtained via thoracentesis showed an exudative fluid with low adenosine deaminase levels.

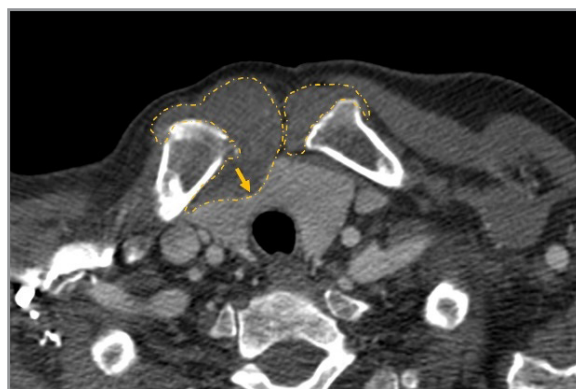


Figure 1. In both sternoclavicular joints, periarticular soft tissue thickenings (regions within dashed lines) surrounding the clavicle heads and compressing the right lobe of the thyroid gland on the right are observed.

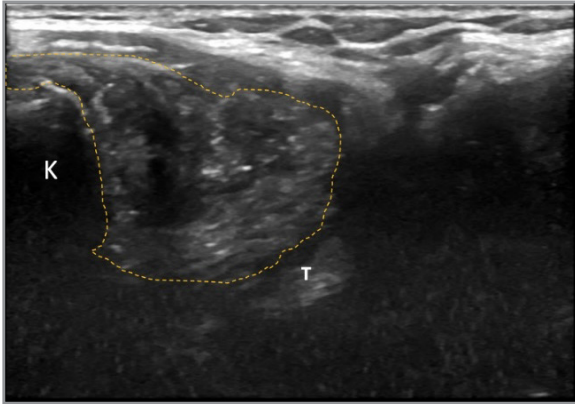


Figure 2. Ultrasonography image of soft tissue (dashed lines) surrounding the right clavicle head (K) and compressing the thyroid gland (T).

TB polymerase chain reaction (PCR) testing, performed with Xpert MTB/RIF (Cepheid, USA), and acid-fast bacilli (AFB) examination were negative, but lymphocytic inflammation was noted.

In addition, a sample from the soft tissue surrounding the right sternoclavicular joint was obtained under ultrasonography guidance (Figure 2). Histopathological analysis revealed proliferated fibrohistiocytic cells consistent with granulation tissue. AFB staining, PCR test and later *Mycobacterium tuberculosis* (MTB) culture of this sample were negative.

The patient's neurological condition rapidly deteriorated, culminating in an epileptic seizure. Cranial CT, MRI, and electroencephalogram evaluations were

performed. MRI findings revealed multiple millimeter-sized lesions with faint hyperintensity, diffusion restriction, and nodular/ring-like contrast enhancement on T2-weighted images. These lesions were identified in the left temporal lobe, right half of the corpus callosum splenium, right external capsule, and the right frontal and bilateral parietal lobes. Additional lesions were observed in both hemispheres of the cerebellum (Figure 3). Prompt cerebrospinal fluid (CSF) analysis was conducted.

RESULTS

Following the lumbar puncture, which was promptly performed, the meningitis panel returned negative results, as did the CSF routine culture. However, CSF biochemistry revealed low chloride and glucose levels along with elevated protein levels. The PCR test via Xpert MTB/RIF for TB was positive in the CSF and there was no drug resistance.

Based on these findings, treatment for MTB was initiated, including isoniazid, rifampicin, pyrazinamide, and ethambutol (HRZE) in combination with adjunctive dexamethasone therapy. On the 10th day of treatment, the CSF MTB culture yielded positive results, supporting and confirming the diagnosis of CNS-TB.

Despite initiating appropriate anti-tuberculous therapy, the patient's condition deteriorated further. He developed abdominal respiration, worsening consciousness levels, and increased oxygen requirements, necessitating admission to the intensive care

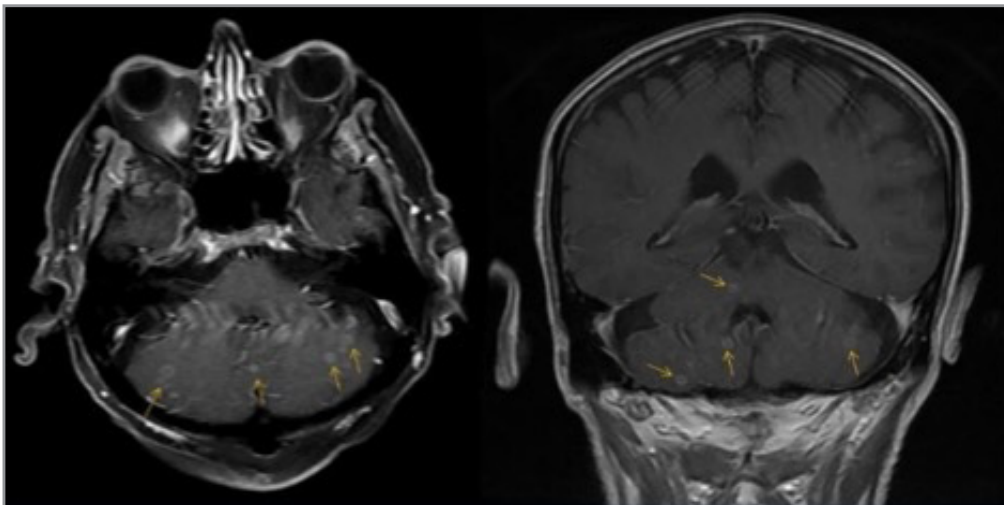


Figure 3. MRI images showing nodular/ring-like contrast enhancements on T2-weighted imaging (indicated by arrows).

unit (ICU). Upon ICU admission, the patient required intubation on the first day of MTB treatment. Unfortunately, despite intensive care management, the patient did not regain consciousness and succumbed during the second month of hospitalization.

DISCUSSION

TB can manifest as either pulmonary or extrapulmonary (EP-TB), potentially affecting any anatomical site in the body (4). The pathophysiology of CNS-TB involves the hematogenous spread of MTB to the CNS, where it can cause meningitis, tuberculomas, cerebritis, or arachnoiditis. In this case, the patient demonstrated multiple CNS lesions and was eventually diagnosed with TB meningitis, one of the most severe manifestations (5). Radiologic features of CNS-TB may appear individually or in combination and can often remain undetected on imaging until the disease progresses to an advanced stage (6).

This case highlights the complexity and varied presentation of EP-TB, and particularly CNS-TB. The patient initially presented with non-specific symptoms such as dyspnea, malaise, and dizziness, which are common in many systemic diseases. The non-specific initial findings and the patient's history of mediastinal LAP and pleural effusion further complicated the clinical picture, leading to a broad differential diagnosis that did not immediately point towards CNS-TB. The progression of neurological symptoms, including confusion, nonsensical singing, and eventually seizure activity, alongside the radiological findings of ring-enhancing lesions in the brain, raised the suspicion of CNS involvement. The WHO recommends GeneXpert as a critical diagnostic tool for individuals with suspected TB; however, its results should be interpreted cautiously. GeneXpert is best utilized as a "rule-in" test rather than a "rule-out" diagnostic tool (7). Despite negative initial tests of pleural effusion PCR or joint sample PCR for MTB, the diagnosis was confirmed by a positive CSF PCR analysis for MTB.

Despite appropriate anti-tuberculous therapy and supportive care in the ICU, the patient's condition deteriorated, leading to death. Although pulmonary TB is the most common manifestation, CNS-TB is more challenging to diagnose and is associated with a poorer prognosis, particularly when treatment is delayed (8). This case underscores that there may be

false negatives in the investigations and the importance of maintaining a high clinical suspicion for MTB, especially in CNS-TB. Clinicians should include TB in the differential diagnosis of unexplained neurological symptoms, particularly in patients from endemic regions or with a history of TB exposure, to avoid delays in treatment, even if initial diagnostic tests are negative.

In conclusion, CNS-TB remains a critical diagnostic consideration in patients with complex and unexplained neurological symptoms. Early recognition and prompt initiation of appropriate therapy are essential to improve outcomes (9). However, as demonstrated in this case, even with timely treatment, the prognosis can be poor, underscoring the need for continued research and improved diagnostic methods to enhance early detection and treatment strategies for CNS-TB.

PATIENT CONSENT

Patient consent was obtained.

Peer-review: Externally peer-reviewed.

CONFLICT of INTEREST

The authors have no conflict of interest to declare.

AUTHORSHIP CONTRIBUTIONS

Concept/Design: EŞ, AMŞ

Analysis/Interpretation: All of authors

Data acquisition: AMŞ

Writing: AMŞ

Clinical Revision: EŞ

Final Approval: EŞ, AMŞ

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