

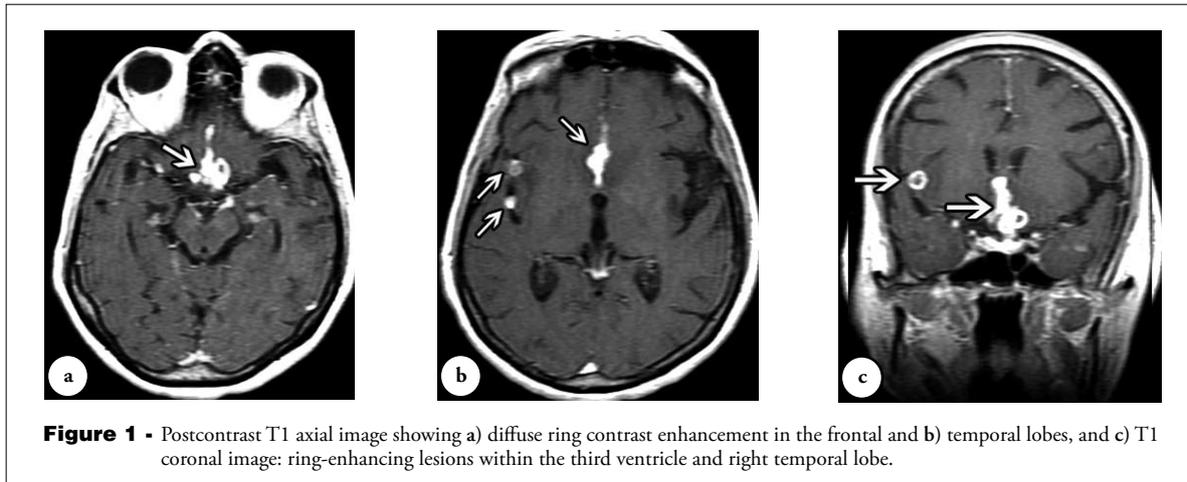
Disseminated tuberculosis complicated with tuberculous meningitis, miliary tuberculosis, and thoracic bone fracture while investigating a cervical lymphadenopathy. *Tuberculosis: a hidden enemy?*

Selda Aslan, MD, Serda Gulsum, MD, Basak Atalay, MD.

Tuberculosis (TB) is a disease that can involve every organ system. Difficulties in diagnosis and treatment of the disease make it an important health problem. Tuberculous meningitis (TBM) is not the most common, but the most serious clinical form of extra pulmonary TB. Here we describe the case of a 60-year-old woman who presented with TBM, miliary TB, and thoracic bone TB while investigating a cervical lymphadenopathy of one month's duration. Computed tomography, histopathologic, and microbiologic examinations, culture sensitivity, and clinical findings led to the diagnosis of disseminated TB. In this study, we present an unusual and interesting case. This case shows multiple unusual locations of TB and mentions the importance of physician's experience in the diagnosis and treatment process in TB. Also this case shows clinical features, diagnosis, and treatment of TB, as well as the development and rapid dissemination process of the disease.

A 60-year-old woman with no history of TB was referred to the Department of Surgery of Diyarbakir Education and Research Hospital, Diyarbakir, Turkey after one month of fever and cervical lymphadenopathy. The lymphadenopathy had been extracted in the Surgery Department and she received empiric treatment, which did not effect any improvement. On histopathologic examination, only inflammatory cells were observed. After 3 months of surgical intervention, she was readmitted to the hospital with severe back pain, fever, and fatigue complaints. With the diagnosis of thoracic spine fractures, neurosurgical operation was performed. Intraoperative specimens were referred for histopathologic examination, which proved the existence of granulomatous inflammation with caseous necrosis. She was discharged and offered outpatient visits for further investigations for TB. She did not take any medical treatment during this period and she neglected outpatient visits. After 45 days, she was admitted to the Infectious Diseases Clinic with complaints of fever, cough, weakness, loss of appetite, and weight loss. Her fever had sustained during this period. Her medical history was remarkable for taking antipsychotic drugs for 6 years due to depression. On admission, her physical examination revealed blood pressure of 90/50 mm Hg,

heart rate of 100 breath/min, and temperature of 37.8°C. Chest auscultation was significant for bilateral diffuse crackles. The other physical examination findings were normal. A complete blood count showed hemoglobin of 11.9 g/L (normal range [NR] 12.3-15.3), hematocrit 33.9% (NR 38-54), white blood cell count 10.3 k/ul, platelet count of 298,000, aspartate aminotransferase of 16 U/L, alanine amino transferase of 14 U/L, gamma-glutamyl transferase of 25 U/L, sodium of 119 mmol/L (NR 136-146), chloride of 81 mmol/L (NR 98-110), excessive urine sodium excretion (UNa 40 mEq/L). Biochemistry testing showed mild elevation of the erythrocyte sedimentation rate. Serological tests for many pathogens and tumor markers, were all negative. The x-ray showed bilateral diffuse infiltrations. She was hospitalized with the diagnosis of miliary TB and Inappropriate Antidiuretic Hormone Secretion Syndrome. Chest CT scan showed bilateral diffuse nodular lesions and multiple paratracheal and right hilar lymph nodes with peripheral contrast areas. All blood, urine, and sputum cultures taken on the day of admission were reported to be sterile. Repeat routine and fungal blood cultures were negative throughout her hospitalization. After 5 days of hospitalization, vomiting, headache, and disorientation appeared. Then she lost consciousness. A lumbar puncture was performed and microbiological features revealed a CSF glucose of 42 mg/dl (blood glucose 143 mg/dl), CSF chlorine level of 100 mg/dl, elevated protein at 200 mg/dl with positive pandy reaction, white blood cells per microliter were 40/mm³ (70% mononuclear). Direct microscopy of the Ehrlich Ziehl Nielsen staining of the lumbar puncture fluid confirmed the presence of an acidoresistant bacillus. A CT of the brain revealed solid nodules (tuberculomas) located in the frontal and temporal lobes (Figures 1a-c). The specimen culture on solid egg based agar (Löwenstein Jensen) showed the growth of *Mycobacterium tuberculosis*. A diagnosis of miliary TB with TBM was made based on chest x-ray, CT findings, histopathologic, and microbiologic findings. Anti-tuberculous drugs were prescribed. She was treated with isoniazid (300 mg/day), rifampicin (600 mg/day), ethambutol (1200 mg/day), and pyrazinamide (1 g/day) for 2 months. Combination therapy with isoniazid and rifampicin was maintained for 12 months. The fever resolved gradually and she became afebrile on the eighteenth day of the treatment. Her general condition improved. The absence of miliary lesions on chest radiography began to appear after 3 months of treatment. Fever did not recur again during the 20 month follow-up. She mobilized quickly and appeared to make a complete recovery without adverse sequelae.



If not treated, TB is associated with high morbidity and mortality. Retrospective studies confirm that at least 75% of individuals have a tuberculous infection at least 12 months before admission for meningitis, and it is said to be rare that cervical lymph node swelling is seen in the early stages of disseminated TB as seen in our case report.¹ It is also obvious with this case report that physician's experience and correlation with patients is vital for TB especially in endemic regions. Khan et al² showed that physician experience and use of directly observed therapy positively influences the survival of patients with active TB. Thus, patients survival is influenced not only by patient characteristics, but also by features of the treating physician. They studied a total of 1154 active tuberculose patients and 178 physicians. Extrapulmonary TB occurred in 57% of adolescents, which may have contributed to this diagnostic delay. Additionally, we emphasized the importance of the correlation with patients for TB especially in endemic regions. Tuberculosis patients should be traced by telephone call or visit to their homes to identify reasons for non-adherence, identification of patients who are at high risk, psychological counseling and health education, and social supports are some of their recommendations.³ In our case, bacteriologic yield and physical examination findings were obvious, but hematological abnormalities were few. Generally, the correct diagnosis was possible from the history, physical examination or routine laboratory tests. In our study, failure to utilize findings correctly, delay in ordering appropriate tests, and misinterpretation of test results have all contributed to missed diagnoses.

In Turkey, TB is the final diagnosis of fever of unknown origin with infectious etiology in 15-65% of cases.⁴ Tuberculosis should be borne in mind in the differential diagnosis of cases with granulomatous lymphadenitis presenting as prolonged or recurrent fever, even if the cultures and polymerase chain reaction for *Mycobacterium tuberculosis* are negative, especially in endemic areas such as Turkey.

Received 25th August 2009. Accepted 15th December 2009.

From the Division of Infectious Diseases and Clinical Microbiology (Aslan, Gulsun), Division of Radiology Clinic (Atalay), Department of Medicine, Diyarbakir Education and Research Hospital, Turkey. Address correspondence and reprint requests to: Dr. Serda Gulsun, Division of Infectious Diseases and Clinical Microbiology, Department of Medicine, Diyarbakir Education and Research Hospital, PO Box 21100, Dagkapi, Diyarbakir, Turkey. Tel. +90 (505) 3848993. E-mail: serdagulsun@gmail.com

References

1. Parsons M, editor. Tuberculosis meningitis: A Handbook for Clinicians. Oxford (UK): Oxford University Press, 1979. p. 2-4.
2. Khan K, Campbell A, Wallington T, Gardam M. The impact of physician training and experience on the survival of patients with active tuberculosis. *CMAJ* 2006; 175: 749-753.
3. Jakubowiak W, Bogorodskaya E, Borisov S, Danilova I, Kourbatova E. Treatment options and duration associated with default among new patients with tuberculosis in six regions of Russia. *Int J Infect Dis* 2009; 13: 362-368.
4. Yasar B, Yuksel S. Approach to the Patient with Fever of Unknown Origin [article in Turkish]. *Medical Sciences & Doctor* 2002; 8: 304-308.