

CASE REPORT

An Acute Disseminated Encephalomyelitis Case due to *Mycobacterium tuberculosis*

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ABSTRACT

Acute disseminated encephalomyelitis (ADEM) is an inflammatory and demyelinating disorder of the central nervous system that is characterized by multifocal involvement of the white matter. Our patient was a 27-year-old female patient who had given birth to a baby with caesarean in another hospital. After four days upon the parturition, she was admitted to our hospital's general intensive care unit with a poor general status, confusion and a fever. She was diagnosed with ADEM according to the clinical, laboratory and radiological findings. In addition to her antibiotic treatment (meropenem) that had been given in the previous health care facility, corticosteroid therapy was also started. The patient passed away due to the ventilator-associated pneumonia infection on the 10th day of her admission. *Mycobacterium tuberculosis* proliferation was observed in the cerebrospinal fluid after her death. As it is reported in literature, tuberculosis is a rare cause of ADEM. In conclusion, it should be noted that *M. tuberculosis* can be a rare cause of ADEM in regions where the disease is endemic. *J Microbiol Infect Dis* 2016;6(1): 28-31

Key words: Acute disseminated encephalomyelitis, tuberculosis

***Mycobacterium tuberculosis*'in Neden Olduğu Bir Akut Dissemine Ensefalomiyelit Olgusu**

ÖZET

Akut dissemine ensefalomiyelit (ADEM) santral sinir sisteminde beyaz cevherin multifokal tutulumuyla karakterize enflamatuvar ve demiyelizan bir hastalıdır. 27 yaşında, dört gün önce başka bir hastanede sezeryan ile doğum yapan kadın hasta genel durum kötü, bilinç konfüze ve yüksek ateş bulgularıyla genel yoğun bakım ünitesine kabul edildi. Klinik, laboratuvar ve radyolojik bulgularla ADEM tanısı kondu. Başka bir merkezde başlanan antibiyotik tedavisine (meropenem) kortikosteroid tedavisi eklendi. Yatışının onuncu gününde ventilatör ilişkili pnömoni nedeniyle hasta kaybedildi. Hasta kaybedildikten sonra beyin omurilik sıvısında *Mycobacterium tuberculosis* üredi. Tüberküloz literatürde bildirilen serilerde nadir etkenler arasında yer almaktadır. Sonuç olarak bu hastalığın endemik olduğu bölgelerde nadir bile olsa *M. tuberculosis* ADEM etkeni olarak akla gelmelidir.

Anahtar kelimeler: Akut dissemine ensefalomiyelit, tüberküloz

INTRODUCTION

Acute disseminated encephalomyelitis (ADEM) is a demyelinating central nervous system disease with an acute onset and different clinical course [1]. It is usually observed in children and young adults and sometimes it occurs following the vaccination or an infection. It has a wide spectrum of neurological signs, ranging from a normal consciousness to coma. It develops with a non-specific cerebrospinal fluid (CSF) findings, especially in case of encephalitis. The findings of the computerized tomography (CT) may be normal or shows only minimal abnormalities. The best way for the diagnosis is magnetic resonance imaging (MRI). The hallmark of magnetic

resonance imaging is bilateral, albeit asymmetrical, white matter lesions of the same age. These lesions are best demonstrated by T2 or FLAIR sequences [2]. It is a demyelinating syndrome that usually develops as a result of vaccination (postvaccination encephalomyelitis), immunization or systemic viral infection (parainfectious encephalomyelitis). The most striking clinical and pathological findings are obtained from various case reports describing the close association between the disease and a specific viral infection or vaccination. The signs and symptoms emerging upon an acute measles infection or rabies vaccination represent the prototype of this disease [1,2].

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In literature, only two cases, which were diagnosed with ADEM due to the *Mycobacterium tuberculosis* infection, have been reported [3,4]. In our study, we report here in a case diagnosed with ADEM in which the *M. tuberculosis* infection was subsequently shown to be the causative agent.

CASE

A 27-year-old female patient, who had delivered a baby with caesarean, was admitted to our hospital four days after the birth. She had a 2-month fever history. Additionally, both the consciousness and the diplopia were observed ten days before the delivery, but they lasted nearly in two hours and she was recovered spontaneously. She had again the altered confusion three days later and she was consulted by neurologists. She was admitted to our hospital to an intensive care unit. The general status of the patient was poor and she was confused. Her body temperature was 38.5°C, pulse rate was 84 bpm, and blood pressure was 140/90 mmHg. She had meaningful motor and verbal responses to verbal stimuli in the neurological examination. Her pupils were anisocoric. The left-sided light reflex was diminished. There was no neck stiffness. There was a muscle weakness in her left leg. The muscle strength was 4/5 in her four extremities. Compared to the right side, her deep tendon reflexes were mildly increased in the left side. Babinski reflex was indifferent in the left side. Sensory and cerebellar examination could not be performed clearly because the patient was not cooperative. Her fundus and systemic examinations were normal. She had no previous history of tuberculosis or pneumonia. She did not have BCG scar. The three divided doses of meropenem (6g/day intravenously) and mannitol (20%) treatments, which was started in the previous institution, were continued also in our hospital. The laboratory results were as follows: leukocyte count: 9200/mm³; hemoglobin level: 10.8 g/dL; thrombocyte count: 288.000/mm³; C-reactive protein: 51 mg/L, erythrocyte sedimentation rate: 72 mm/hour. The liver and renal function tests, serum calcium and phosphorus levels were normal. Electrocardiogram and chest X-ray roentgenogram were also normal. The patient was HIV-negative. An abdominal ultrasonography was normal. A nodular hyperdense appearance was detected in the thalamus on the right side according to the results of the computerized brain tomography. Brain Magnetic Resonance Imaging showed a lesion in the right temporal capsular and external capsular regions starting from the level of pons and involving bilateral mesencephalon-thalamus-posterior leg of capsula interna on the right side. This le-

sion was evaluated as an ADEM lesion (Figure 1). A lumbar puncture was performed. According to the CSF analysis, there were 220 leukocyte/mm³ (80% lymphocyte), protein 213 mg/dL, glucose 5 mg/dL (simultaneous blood glucose: 98 mg/dL). There was no microorganism according to the CSF gram staining results. There was no proliferation in CSF and the acid-fast bacilli (AFB) examination was also negative. Upon the recommendation of the neurology department, the intravenous methylprednisolone (1 g/day for the first 3 days followed by 0.5 g/day) treatment was started and then the 1500 mg/day parenteral acyclovir (30 mg/kg/day) was also given to the patient. The patient was intubated and connected to a ventilator unit four days after her admission. She had again fever two days after the ventilator connection. *Acinetobacter baumannii* proliferation was observed in the deep tracheal aspirate culture. The microorganism was found to be meropenem-resistant whereas it was sensitive to cefoperazone-sulbactam. Then, meropenem therapy was stopped and cefoperazone-sulbactam treatment was started at a dose of 4 g/day. The general condition of the patient deteriorated progressively and she passed away due to the nosocomial sepsis 10 days after her admission. *M. tuberculosis* proliferated in BACTEC and Lowenstein-Jansen cultures in the CSF sample four weeks after the sampling. The microorganism was observed to be sensitive to antimicrobial drugs (isoniazid, rifampin, ethambutol, and pyrazinamide). The tuberculosis PCR and Herpes PCR results of the CSF sample were negative. The written consents of the patient's relatives were obtained in order to publish her data.

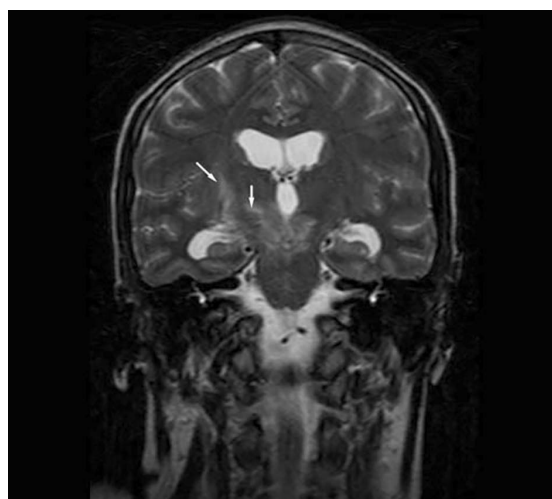


Figure 1. Brain MRI showed a lesion in the right temporal capsular and external capsular regions starting from the level of pons and involving bilateral mesencephalon-thalamus-posterior leg of capsula interna on the right side.

DISCUSSION

ADEM is a disease of central nervous system that is characterized by multifocal demyelinated areas. It is an autoimmune disorder in which a cross reaction develops between the triggering infectious agents and the neural tissue [5]. Retrospective studies have shown that the 50-75% of ADEM cases in adults is a result of infections or vaccination [6]. The causative infections are either viral or bacterial. Although the underlying pathogens cannot be always identified, ADEM can occur upon a non-specific upper airway or gastrointestinal disease. The viruses that lead to ADEM include measles, rubella, mumps, varicella, chicken pox, Epstein-Barr virus, Herpes Simplex virus, Human Herpes virus-6, influenza, Human immunodeficiency virus. Besides, the bacterial agents that induce ADEM include Group A beta-hemolytic streptococci, *Mycoplasma pneumoniae*, Chlamydia, Rickettsia, and Leptospira infections [7]. ADEM usually develops in children and young adults. Although the age range of adults is known as 18 to 82 years, the median age has been reported 33-41 years [7]. Our case was 27 years old. In the previous reports, one of the tuberculosis-induced ADEM patient was 35 whereas the other one was 50 years old [3,4].

ADEM syndrome develops within 6 days to 6 weeks following an infectious disease. Ozhan et al. have reported a case diagnosed with ADEM at the third week of the anti-tuberculosis therapy [4]. On the other hand, our patient had a 2-month history of the disease and we diagnosed the tuberculosis after the patient passed away.

The headache, fever, nausea, and vomiting are observed in cases with ADEM. In 20-52% of adult ADEM patients, the mental status changes in the form of irritability, confusion, psychosis, somnolence, and even coma [7]. In case of our patient, she had predominantly fever and confusion as well as diplopia. In the study performed by Ozhan et al., they also observed diplopia [4]. However, the general status of our patient was more severe compared to the cases in the other two studies [3,4]. In 1947, the "British Medical Council" described the signs and symptoms of central nervous system tuberculosis in three stages. In the first stage, the patient has conscious and there exists no neurological symptoms. Stage two is characterized by the signs of meningeal irritation and mild mental status changes. In the third stage, the severe mental status changes, stupor, coma, convulsions, and marked paresia are present [8]. Our patient was in the third stage. It was considered to be an unfortunate status

for both the patient and us because the patient was admitted to our hospital in the third stage and she could not be diagnosed previously despite having high fever for the previous two months.

Apart from the central nervous system, we did not detect any sign of tuberculosis in the lungs or abdomen. Similarly, Masoodi et al. also did not find any focus of tuberculosis except the central nervous system [3]. In the case of Ozhan et al., they only diagnosed the lung tuberculosis [4].

The CSF findings vary in ADEM cases. The 50% to 80% percent of cases has abnormal CSF findings [6,7]. Lymphocytosis is present in CSF samples. The leukocyte count is usually less than 100 cells and the protein level is mildly elevated (<70 mg/dL) [7]. In central nervous system tuberculosis, the CSF samples are characterized by pleocytosis (more than 20 cells and lymphocyte percentage over 60%), an increased protein content (over 100 mg/dL) and a low glucose level (less than 60% of the simultaneously measured blood glucose level) [9]. Our patient's CSF sample was characterized with a leukocyte count of 220 cells/mm³ (80% lymphocyte), protein content of 213 mg/dL, and a glucose level of 5 mg/dL (simultaneous blood glucose 98 mg/dL). Ozhan et al. have reported normal CSF findings in their case with ADEM developed after the lung tuberculosis [4]. Masoodi et al. have reported similar CSF results to ours (210 leukocyte/mm³; 85% lymphocyte; protein 542 mg/dL, glucose 28 mg/dL) and they have also isolated *M. tuberculosis* in the CSF sample of their case it was in our patient [3]. In our case, the biggest handicap was the negative tuberculosis PCR test results. PCR methods are regarded as early diagnostic tools in order to search for *M. tuberculosis* DNA. However, the sensitivity and the specificity of the test are 56% and of 98%; respectively [9].

The differential diagnosis of ADEM includes multiple sclerosis, infectious meningoencephalitis, antiphospholipid antibody syndrome, primary isolated central nervous system angiitis, vasculitis, central nervous system metastasis, and neurosarcoïdosis. The classical lesions on MRI and the temporary profile are diagnostic [3]. The mainstay of the therapy is immunosuppression. High dose intravenous glucocorticoids are recommended in the first step treatment [10]. They can be started simultaneously with antibiotics [7]. In our case, we added also high dose methylprednisolone therapy in addition to the antibiotic therapy, but we could not assess the success of steroid therapy since we lost our patient. In the two previously reported tuberculosis-induced

ADEM cases, the high dose glucocorticoids were used successfully [3,4].

The complete remission rate has been reported as 10% to 46% in adult cases diagnosed with ADEM. The mortality rate of particularly the fulminant cases is between 4% and 12% [6,7]. On the other hand, the mortality rate has been reported as 25% in ADEM cases who are followed in an intensive care unit [11]. Our patient died due to the nosocomial sepsis while being treated in the intensive care unit, whereas the other two cases had complete remission [3,4].

In conclusion, it should be noted that *M. tuberculosis* can be a rare cause of ADEM in regions where the disease is endemic.

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