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CASE REPORT

A Case of Tuberculous Meningitis Presenting with Non-Specific Findings

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Abstract

Tuberculosis (TB) is still a major public health problem in developing and developed countries. Extrapulmonary TB (EPTB) may mimic malignancies and many other diseases, and it should be kept in mind in the differential diagnosis. Tuberculous meningitis (TM) has high mortality and morbidity rates among EPTB forms. Mortality and morbidity rates are reduced by early diagnosis and treatment in TM.

Keywords: Child; extrapulmonary tuberculosis; meningitis; tuberculosis.

Tuberculosis (TB) is still an important public health problem with an increasing incidence despite the control strategies developed in both developing countries and developed countries due to migration[1,2]. According to the data of the World Health Organization (WHO), 650.000 (9%) of the 7.5 million TB cases in total are pediatric patients. In developing countries, this rate rises to 39%[2]. Without taking measures to improve the socioeconomic conditions of these countries, it does not seem possible to solve the TB problem in the near future with existing diagnostic and treatment methods. About 85% of all TB cases are pulmonary TB and the remaining 15% are extrapulmonary TB (EPTB) cases. The distribution of EPTB is as follows: 28% lymph node, 22% pleural, 15% genitourinary, 9% bone joint, 9% miliary, 4% meninges, 4% peritoneum, and the remaining 9% other forms of TB[3,4].

TB is still an important health problem in developing countries. While the incidence of TB in the world was 144/100.000 in 1998, this rate was 27/100.000 in our country according to 2000 data[5].

A history of close contact, clinical and radiological findings, tuberculin skin test (TST), and microbiological examinations are helpful in the diagnosis of EPTB. However, diagnosis and treatment are delayed because it is more difficult to diagnose than pulmonary TB. Because it is less common, and due to its ability to mimic many pictures from malignancies to many benign diseases seen in childhood, such as meningitis, sarcoidosis, fungus, sterile pyuria, dermatological pathologies of Crohn's disease, non-tuberculous mycobacteria, ovarian cancers, and acute abdomen, it is less recognized by physicians[6-8].

Case Report

A 16-year-old male patient, who had no known chronic disease, was admitted to the pediatric emergency service with nausea, vomiting, and inability to eat for 7 days. The

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patient was interned on detection of hyponatremia, and examination results were as follows: CRP: Negative, sodium: 125 mEq/L, potassium: 5 mEq/L, chloride: 92 mEq/L, glucose: 116 mg/dL, and magnesium: 2.3 mg/dL. Fluid therapy was initiated by calculating corrected sodium. Whole abdominal ultrasound and direct abdominal radiography obtained in a standing position were performed in the patient, which were found to be normal. Brain computed tomography (CT) was reported as normal. In the brain magnetic resonance imaging (MRI), tuberculomas with the largest diameter reaching 1.5 cm in the leptomeningeal areas were observed (Fig. 1); the third and lateral ventricles were observed to be slightly dilated. Miliary TB findings were seen on chest CT. Although sodium replacement was given according to the corrected value, the patient's hyponatremia persisted. On the 2nd day of his hospitalization, an eye consultation was performed after the neck stiffness, Kernig's and Brudzinski's signs were found to be positive. Papilledema was not detected in the eye fundus. Lumbar puncture was performed. The patient's cerebrospinal fluid (CSF) values were as follows: Glucose: 16 mg/dL (simultaneous blood glucose: 118 mg/dL), protein: 307 mg/dL, sodium: 127 mEq/l, chloride: 102 mEq/l, LDH: 52 iu/l, 301 cells/mm^3 at microscopy, and Pandy's reaction: 4 positive. Moderately dense mononuclear cells were detected in the CSF. However, no microorganism was detected. Mycobacteria polymerase chain reaction (PCR) was reported positive. TST test detected negative. Four-drug anti-TB therapy was initiated after the patient was diagnosed with tuberculous meningitis (TM) and was found susceptible to the first-generation anti- TB drugs in the CSF *M. tuberculosis* complex typing. On the 3rd day of the treatment, the general condition of the patient deteriorated, he started to breathe superficially, and he was unconscious. The patient with a Glasgow Coma Scale of 10 was transferred to the intensive care unit, was intubated, and connected to a ventilator. The patient remained in the intensive care unit for 4 days, and the patient, whose treatment was continued, recovered consciousness. The patient, whose oral intake improved, was transferred to the pediatric infection service. The patient used 1 mg/kg/day methylprednisolone for 3 weeks. The dose was reduced by 25% every week and steroid treatment was discontinued. Control lumbar puncture was performed on the 20th day of the treatment. CSF examination results were as follows: Glucose: 30 mg/dl, protein: 180 mg/dl, chloride: 114 mEq/l, CSF mycobacteria PCR: negative, Pandy's reaction: 3 positive, and 31 cells in microscopy. The patient's TB treatment still continues.

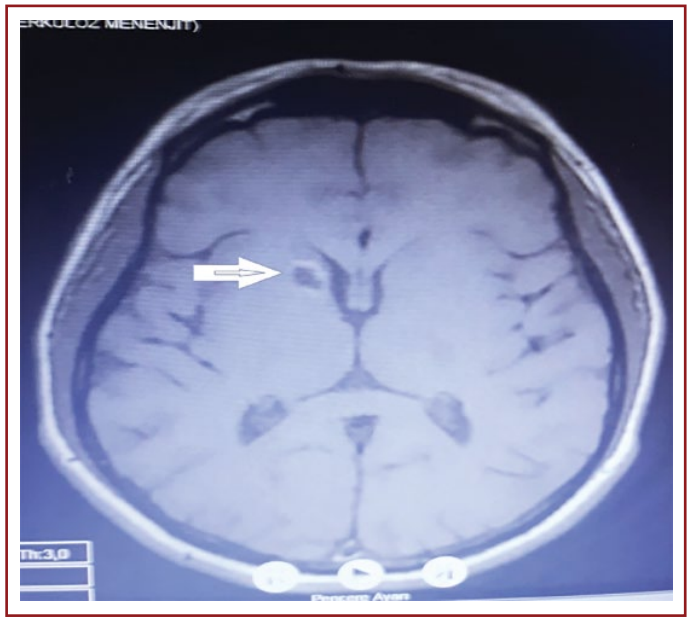

Figure 1. 1 cm × 1 cm tuberculoma.

Discussion

According to the data of the WHO, approximately 10.5 million cases of TB were seen in 2015, and 10% of them were mainly observed in countries with limited number of cases[9]. The most serious complication of TM is hydrocephalus, stroke, and tuberculoma formation and they may occur in 80% of pediatric patients[10]. Vasculitis and stroke are more common in children in TB. It has been observed that the reason for this frequency is due to the basal cisternal meningeal reaction and is most frequently associated with hemiplegia[11].

Children with TM usually have headache, diplopia, vomiting, and convulsive seizure symptoms due to increased intracranial pressure. TM is clinically defined in three stages and is important in determining the prognosis. In Stage I, there is normal state of consciousness and there are no neurological deficits. In Stage II, there may be confusion, lethargy, and focal neurological findings and cranial nerve involvement. In Stage III, multiple cranial nerve involvement, complete hemiparesis, or paralysis are observed together with stupor or coma[12,13].

Our 16-year-old male patient was brought with non-specific symptoms such as vomiting and fatigue, and hyponatremia was detected in blood examination. The patient was conscious and had no neurological deficits. Syndrome of inappropriate antidiuretic hormone secretion (SIADH) was considered due to unresolved hyponatremia, urine density, and increased urine sodium despite fluid and sodium replacement. Fluid restriction was applied. A diagnosis of

TM was made on the 2nd day of hospitalization with lumbar puncture findings due to neck stiffness and signs of meningeal irritation, as well as mycobacterium PCR positivity. Four-drug anti-TB treatment and systemic steroids were started. The patient was transferred to intensive care unit due to lethargy and signs of decompensation in blood gas. The patient, who was intubated for 3 days, was extubated and was readmitted to our service when oral intake started.

Ulusoy et al.[14] found that the number of cells in the CSF was below 500/mm^3 in 79% of 43 cases of TM, and Taflova et al.[15] found it between 100 and 200/mm^3 in 58.2% of the cases. The number of cells in CSF was found to be 7–4000/mm^3 in the study of Kent et al.[16] Yechoor et al.[17] reported the mean number of cells in the CSF as 426/mm^3. In our case, the number of cells in the CSF was found to be 301/mm^3. In this respect, the characteristics of our case are similar to the presented publications.

In the studies of Ulusoy et al.[14] and Taflova et al.[15], ARB positivity was reported as 2% and 29.4%, respectively, and culture positivity was reported as 21% and 11.8%, respectively. In foreign sources, both ARB and culture positivity are at much higher rates[16,9]. Even if treatment is initiated, it has been reported that ARB can be seen in CSF smears performed consecutively in the 1st days[16]. In our case, ARB was negative at the first CSF evaluation. ARB positivity could not be detected in the CSF in the serial lumbar punctures performed later. This can be explained by the presence of a small number of bacilli and/or technical deficiencies.

In the literature, it has been reported that TST is positive in 50% of the cases with TM[18]. Yaramış et al.[10] reported in 1998 that 30% of 214 children with TM were found to be TST positive and 64% were anergic. TST was also anergic in our patient. TST may be negative in severe forms of TB.

Ulusoy et al.[14] found a patient (2%) with a normal CSF glucose level; and they reported that the protein level was between 60 and 700 mg/dl in all of their cases. Taflova et al.[15] found CSF glucose level below 45 mg/dl in 64.7% of cases and CSF protein level above 100 mg/dl in all cases. In our case, the initial CSF protein level was 307 mg/dl, glucose was 16 mg/dl, and control CSF protein was 187 mg/dl, and glucose was 47 mg/dl. Our data were consistent with the classical findings of TM.

Some authors reported that prognosis is related with CT features, especially at the time of diagnosis, but some secondary complications that develop after diagnosis may negatively affect the prognosis. Hydrocephalus is the most common secondary problem in TM and is associated with permanent disability and poor prognosis[12,19]. In our case, although cranial CT was normal, hydrocephalus was detected in cranial MRI. The intracranial findings of our case were compatible with the literature.

Van Well et al.[20] found the risk of mortality as high, when corticosteroids are not used in the treatment of patients with TM. One milligram/kilogram/day methylprednisolone was administered to our patient for 3 weeks, then the dose was reduced by 25% each week and discontinued in a total of 7 weeks.

Our case was 16 years old and was outside the 2-4 age range, when TM is most common. The presenting symptoms were non-specific findings such as vomiting and fatigue. He is a lucky case whose hyponatremia could not be corrected and cranial MRI was performed considering SIADH, and lumbar puncture was performed due to neck stiffness and meningeal irritation findings, was quickly diagnosed with CSF findings and PCR, and anti-TB treatment was initiated. If the diagnosis was delayed, the disease could result in death or disability. The treatment of the patient still continues. Clinically, he has no neurological deficits. Cognitive functions are normal. It should be kept in mind that TM may present with SIADH in Stage I or Stage II, it should be considered in the differential diagnosis of uncorrected hyponatremia, and death or disability can only be avoided by rapid diagnosis and treatment process.

Although the level of health services is praiseworthy in Turkey, a 16-year-old young boy developing TM and tuberculoma suggests that TB still exhibits serious threat, physicians should be cautious, and cases with TB should be followed closely and people around them should be protected.

Informed Consent: Written informed consent was obtained from the patients' family for the publication of the case report and the accompanying images.

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Conflict of Interest: None declared.

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