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Case Report

Two Fulminant Tuberculosis Meningitis Cases without BCG Vaccine

Mehmet Emin Menetoğlu[1], Nihal Akçay[1], Ayşe İrem Sofuoğlu[1], Nevin Hatipoğlu[2] and Esra Şevketoğlu[1]*

[1]*Department of Pediatric Intensive Care, University of the Health Sciences, Bakirkoy Dr. Sadi Konuk Education and Research Hospital, Turkey*

[2]*Department of Pediatric Infectious Diseases, University of the Health Sciences, Bakirkoy Dr. Sadi Konuk Education and Research Hospital, Turkey*

Abstract

Tuberculosis (TB) is still an important health problem in developing countries. It is a multisystemic disease that can affect many systems, especially the respiratory system. It has been reported that the prevalence of extrapulmonary tuberculosis cases has increased in recent years. In this presentation, we aimed to draw attention to TB in the differential diagnosis of meningoencephalitis. Our first case was an immigrant child who was admitted to the pediatric intensive care unit with a pre-diagnosis of status epilepticus and meningoencephalitis, who presented with fever and convulsion. It was learned that there was no Bacille Calmette-Guerin (BCG) vaccine in the anamnesis of the patient whose clinic was compatible with meningitis / encephalitis. His cranial imaging showed hydrocephalus and thorax imaging showed signs compatible with TB. TBC-PCR test of the patient in CSF was found to be positive. Our second case was an immigrant child who presented with the complaint of vomiting for 1 week and speech disorder for 1 day. In his history, it was learned that he had a gait disturbance for the last 6 months and that the family consumed raw milk. The patient, who was unconscious at admission, was intubated and admitted to the pediatric intensive care unit. His cranial imaging was compatible with hydrocephalus and meningitis, thorax imaging was compatible with TB and spinal imaging was compatible with Pott's abscess. Mycobacterium bovis was detected in the bronchoalveolar lavage sample. Although we started TB treatment in the early period, both of our patients were discharged with severe neurological sequelae. Tuberculosis meningitis is an extrapulmonary tuberculosis infection with high mortality and morbidity. Vaccination status should be questioned for every child in the anamnesis, and TBC in our country should definitely be kept in mind in patients presenting with a change of consciousness. Early diagnosis of tuberculosis disease, screening of contacts, treatment and prophylaxis are the most important factors that can reduce morbidity and mortality.

Keywords: Tuberculosis; Central nervous system; Meningeal; Pediatric intensive care units; Childhood

Introduction

Tuberculosis (TBC) is a serious health problem in developing countries. TBC is a multisystemic disease that can affect mostly the respiratory system. In recent years, an increase in the prevalence of extrapulmonary tuberculosis cases has been reported [1,2]. In the 2018 edition of the Global Tuberculosis report, Turkey's estimated incidence rate in 2017 was 17 per hundred thousand, and the estimated mortality rate was 0.53 per hundred thousand also1.4 per hundred thousand of these patients are in age group 0-14 years [3]. Tuberculous meningitis develops by the rupture of the cerebral tuberculoma into the subarachnoid space or as a result of the hematogenous spread of the bacillus. Tuberculous lesions can be located both in the meninges and in the brain parenchyma, Isolated brain parenchyma involvement has been reported [4]. Tuberculous lesions can cause vascular occlusion, infarcts, cranial nerve paralysis and seizures. Severe obstructive hydrocephalus may develop and a Ventriculoperitoneal (VP) shunt may be needed. At the beginning of treatment, resistant mutant strains can be seen as the bacillus count is at the highest level. Therefore, the initial treatment of tuberculous meningitis includes four drugs; isoniazid, rifampicin, pyrazinamide and ethambutol for two months; maintenance therapy iincludes two drugs; isoniazid and rifampicin for 10 months [5].

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***Corresponding author:** Mehmet Emin Menetoğlu, Department of Pediatric Intensive Care, University of the Health Sciences, Bakirkoy Dr. Sadi Konuk Education and Research Hospital, Istanbul, Turkey, E-mail: menentoglu@hotmail.com

Case Presentation

The written informed consent to publications have been obtained from the parents on behalf of the patients.

Case 1

A one-year-old, foreign national, male patient was admitted to our emergency department with complaints of convulsions and crossed eyes during the febrile period. It was learned that the patient had been suffering from fever for 10 days and had been on antibiotics for seven days with a diagnosis of an upper respiratory tract infection. According to his medical history, he was not vaccinated, including the BCG (Bacillus Calmette Guerin) vaccine. His family history was negative. The patient had generalized tonic-clonic recurrent seizures in the emergency department during the febrile period. The general condition was poor, the Glaskow Coma Score (GCS) was 10, and he was lethargic. Neck stiffness, kernig's sign and brudzinski's sign were found to be positive in his physical examination. The patient was admitted to the pediatric intensive care unit for further examination and treatment with pre-diagnoses of meningitis/encephalitis and complicated febrile convulsion. At the first hour of his hospitalization, the patient was intubated due to the sudden decrease in GCS below 8. The patient's laboratory findings are summarized. The cranial imaging of the patient was consistent with hydrocephalus and meningitis. Lumbar puncture was performed. It is found that the protein levels of cerebrospinal fluid was high, glucose was low, and the cell count was

220 cells/mm^3. Parenchymal findings compatible with tuberculosis were observed in thoracic imaging. The imaging findings of the patient are summarized in Figure 1. TBC-PCR test was positive in tracheal aspirate and CSF samples. Quadruple anti-TB therapy was initiated as the pre-diagnosis was TB meningitis. Anisocoria developed on the 3rd day of the patient's hospitalization. Excessive enlargement of the brain ventricules was detected in the the following cranial imaging. External Ventricular Drainage (EVD) was applied to the patient by the neurosurgery department, and a ventriculoperitoneal (V/P) shunt was inserted on the 32nd day of hospitalization. The patient was discharged from the hospital with tetraplegia and severe neurological sequelae.

Case 2

A five-year-old, foreign national, male patient was admitted to our emergency department with the complaints of vomiting 3-4 times a day for the last week and speech impairment and hearing loss since the day before. According to his medical history, he has been suffering from impaired walking. His condition had been investigated in another hospital for the last six months and an undiagnosed tumorous space-occupying lesion and destructive changes in the bones was found in the spinal region. He was not given any vaccine, including BCG vaccine, and that he frequently consumed raw milk. On clinical examination, his general condition was poor, he was unconscious, his GCS was 5, his pupils were mid-dilated and non-reactive. He was intubated and admitted to the pediatric intensive care unit for further examination and treatment. The patient's laboratory findings are summarized. His cranial imaging findings were consistent with high-pressure hydrocephalus and meningitis in his cranial imaging. An EVD was performed by the neurosurgery department at the 4th hour of his admission. The imaging findings of the patient are shown in Figure 2. The protein level of CSF was high and glucose level was low. TBC-PCR test was positive in CSF and tracheal aspirate samples. Genityping was perfomed and *Mycobacterium Bovis* was identified. His thoracic imaging was compatible with TB and his spinal imaging was compatible with Pott's abscess. The patient was diagnosed with TB and quadruple anti-TB therapy was initiated. The patient's spinal lesion was operated on the 29th day of hospitalization and ventriculostomy was performed in the same session. The patient was discharged tetraplegic with severe neurological sequelae.

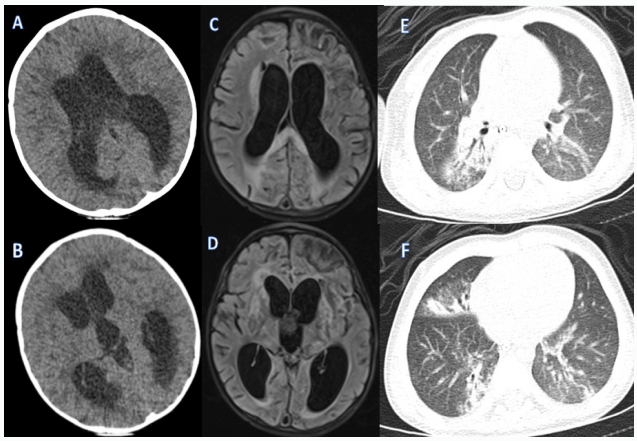

Figure 1: A.B Cranial CT: tetraventricular ventriculomegaly C,D Cranial MRI: volume loss in both periventricular deep white matter and at the level of bilateral basal ganglions, also diffuse contrast enhancement in leptomenengeal areas of basal ganglions, left frontal and left temporal sides. E,F Torax CT: the largest of which is 13 mm × 14 mm LAPs in the mediastinum, milimetrics nodules on upper lobes of lungs bilaterally, lobular atelectazic areas and ground glass apperarences in the lower lobes og lungs.

Discussion

Mortality rates can rise up to 55%-75% in patients with tuberculous meningitis [6]. Although hydrocephalus is the most common complication of tuberculous meningitis; complications such as quadriplegia, monoplegia, paraplegia, symptoms of cerebral dysfunction can be seen. In the terminal period; coma, decerebral, decorticated posture, extensor rigidity and spasms are also observed. Hydrocephalus was present at the time of admission in both cases. In addition, both cases were admitted to our emergency department with paraplegia and coma. Studies have shown that 80% of TB meningitis cases are accompanied by hydrocephalus. In two studies conducted in a large study population, it was observed that 75% of TB meningitis cases had hydrocephalus and 38% had basillary meningeal involvement on MR images. In both cases we discussed, basilar meningeal involvement was accompanying hydrocephalus [7]. Although parenchymal abnormalities were seen in thoracic tomography, at the time of diagnosis in both of our patients, lung sounds were normal on auscultation. In the study conducted by Uniyal et al. [8] 81 TB patients with meningitis were evaluated. Centrilobular nodules were the most common pulmonary parenchymal abnormality seen in thoracic CT in 2/3 of the cases. Asymptomatic miliary lung lesions were reported in many case. In the clinical presentation of our second case, Pott abscess was accompanied by psoas abscess. In the study of Trunç et al. [7], TB was found in 33% of psoas abscess cases. In the presence of a destructive mass in the spinal region, tuberculosis should definitely be taken into consideration. In patients with psoas abscess, sepsis and tuberculous meningitis increase the mortality case [6]. Mycobacterium Bovis causes chronic progressive disease in animals, especially in cattles. It cannot be distinguished radiologically and pathologically from infections of other TB agents. In our patient's case, mycobacterium bovis meningitis was severe and our patient continues his life as tetraplegic with V/P shunt. Therefore, it is important to take precautions against it and to determine the transmission routes and risk factors of zoonotic TB infections [9]. In the treatment of TB meningitis, the initial therapy is quadruple therapy regimen including isoniazid, rifampicin, pyrazinamide, ethambutol which continues for two months. Then maintenance treatment is given. We started the initial anti-TB therapy in our patients, and dexamethasone treatment was added concurrently. Since both had hydrocephalus, EVD was applied in the acute period and a V/P shunt was inserted in the following period. Mycobacterium bovis is naturally resistant to pyrazinamide [10]. Pyrazinamide treatment was discontinued as a result of the detection of M. Bovis in our first case. The treatment protocol of the disease varies according to the tuberculosis agent. Therefore, determining the agent in patients diagnosed with tuberculosis shapes the treatment. Tuberculous meningitis has a broad spectrum of clinical presentations from chronic headache to altered consciousness, progressive meningitis and coma. TB disease is usually silent at the beginning, but our patients had neurological symptoms at the time of the first presentation. Since the GCS of the patients was below eight, they were intubated and connected to a mechanical ventilator. The neuromotor functions were severely affected when the patients were discharged. Both of our patients were tetraplegic. Tuberculous meningitis is a disease with high mortality and morbidity rates and it is still seen in our country. Studies have shown that the neurological complications are severe, as

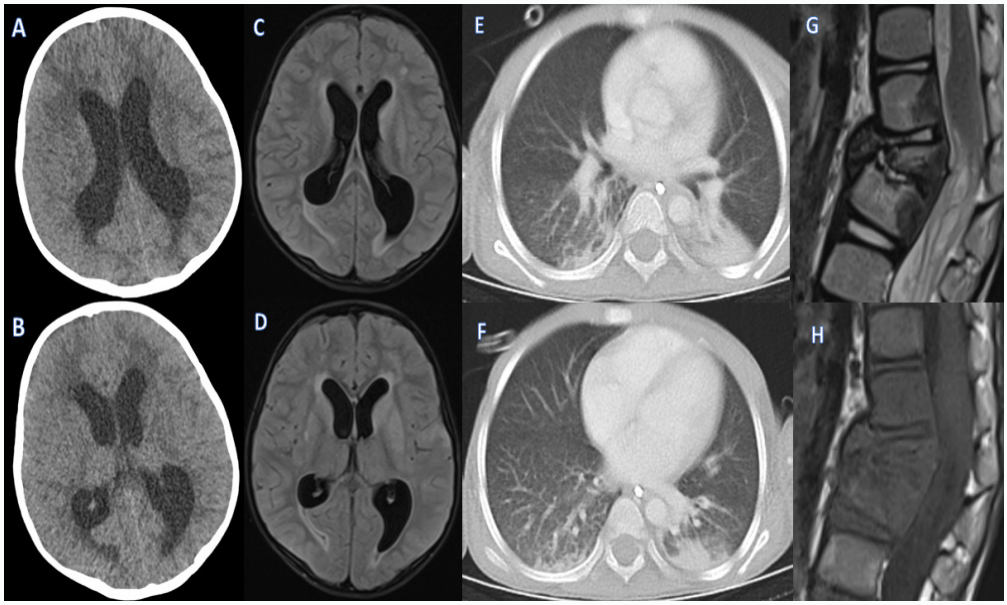

Figure 2: A.B Cranial CT: Hydrosefalic dilatations in the 3rd ventricule and lateral ventricules. C,D Cranial MRI: Hyperintense areas on the basal ganglions, temporal lobes and discrimination line of gray-white matter on the right frontal lobe, also in the FLAIR secans and diffusional series. Gyral type contrast enhencements in the bilateral cerebral hemispheres and basal cisternas. E,F Torax CT: atelectasis and consolidations on the parenchymal sites and superior segments of lower lobes of lungs. H,G: Lomber MRI : Paraspinal abscess which is started at the level of posterior sides of f L1, L2, L3 vertebras reaches by the transeverse processes.

in our cases, the disease leaves patients with serious sequelae even after treatment. We observed in two cases that tuberculosis had a severe course and caused severe neurological complications in unvaccinated children. Although early diagnosis and treatment of the disease are important; vaccination, determining the sources of transmission and transmission routes in the pediatric population, starting prophylaxis are the most effective methods in preventing tuberculous meningitis.

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