Short Communication

Tuberculous Meningitis with Multiple Intracranial Tuberculomas Mimicking Neurocysticercosis Clinical and Radiological Findings

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SUMMARY: Central nervous system (CNS) tuberculosis (TB), the most dangerous form of TB, remains a public health problem, particularly in developing countries. In the differential diagnosis of intracranial tuberculomas (ICTs), images on radiological findings should be differentiated from other causes of space-occupying lesions. These lesions include malignant diseases such as glioma or lymphoma, pyogenic abscesses, toxoplasmosis, neurocysticercosis (NC), sarcoidosis, hydatidosis and late syphilitic involvement of CNS. We present a case with multiple ICTs mimicking NC with similar clinical and imaging manifestations in a young immunocompetent patient. The diagnosis was based on brain magnetic resonance imaging findings. The definitive diagnosis was confirmed mycobacteriologically in cerebrospinal fluid and sputum specimens. Adequate response to anti-TB chemotherapy was achieved while multiple ICTs in the brain disappeared slowly. In the absence of appropriate therapy, these pathologies might be fatal; the possibilities of differential diagnosis would be of great clinical importance, particularly because of the different treatment protocols required for the NC and ICTs.

Extrapulmonary tuberculosis (EPTB) is observed in approximately 20% of all tuberculosis (TB) cases, and its incidence has increased in recent years (1). Central nervous system (CNS) TB, the most dangerous form of TB, accounts for approximately 5% of EPTB cases (2). Tuberculous meningitis (TBM) is the most common form of CNS-TB; however, solitary or multiple intracranial tuberculomas (ICTs) in particular occur less frequently (2-4). Even though CNS-TB is an uncommon entity; the disease affects 0.5 to 2% of patients with systemic TB. However, ICTs account for a significant portion of intracranial masses in developing countries (5). Mortality is greatest in patients younger than 5 years of age (20%) or older than age 50 (60%), or in whom illness has been present for more than 2 months (80%) (6).

Neurocysticercosis (NC) is one of the pathologies most frequently seen by neurosurgeons from developing countries. Although brain cysticercosis is endemic in Latin America, Asia, and Africa with the exception of Muslim countries, it can be diagnosed throughout the world in patients who have migrated from endemic countries and due to the consumption of unhygienic water and foods (7). Approximately 2.5 million people worldwide carry the Taenia solium tapeworm, and not less than 20 million people are infected with T. solium cysticerci (8). Conservative estimates describe 50,000 deaths every year due to NC (9). The diagnosis of cerebral cysticercosis is based, primarily, on typical imaging characteristics in computed tomography (CT) or magnetic resonance imaging (MRI), and on clinical features. The presence of subcutaneous cysts as subcutaneous nodules usually confirms the diagnosis (7).

In this report we are presenting a case with multiple ICTs mimicking NC with similar clinical and imaging manifestations in a young patient. A 21-year-old male farmer from Southeast Anatolia was first seen in a local general healthcare center with high fever, cough, headache, weakness, pain in the neck, and loss of weight in April 2003. The initial diagnosis of this patient had been bacterial pneumonia, and the patient had superfluously received broad-spectrum antibiotics. Until August 2003, he continued seeking medical aid without any improvement, and he was then admitted to our hospital in August 2003 with a worsening condition.

In the familial history of the patient, it was noted that his father had anti-TB chemotherapy (ATCT) for pulmonary TB 4 years prior. The patient reported seizures in the last days. The patient had been smoking a packet of cigarette daily for the last 6 years. On physical examination, moderate papilledema and neck stiffness were noted on the first day of admission. Other systemic and detailed neurological examinations were normal. His urinalysis, hemogram, serum biochemical parameters and serum electrolytes were normal. The appearance of his cerebrospinal fluid (CSF) was cloudy, and was gray in color with increased opening pressure. The biochemical and cytological examination of the CSF revealed proteins at a concentration of 1,655 mg/dL, glucose at 19 mg/dL (the concordant blood glucose level was 75 mg/dL), lactate dehydrogenize at 128 U/L, and 390 mononuclear cells/mm³. Aerobic bacteria were not isolated from CSF and urine cultures. Normal nasopharyngeal flora were detected by nasopharyngeal culture.

Electroencephalogram (EEG) showed intermittent delta activity in the parieto-occipital region on the bilateral side and in the thalamus region on the right side. Routine X-rays of the skull, thigh and forearm were normal. Cranial MR revealed multiple small nodules at the gray-white junction of both the cerebral and cerebellar hemispheres, the brainstem, the right thalamus, the anterior limb of the left internal capsule and the body of the corpus callosum (Figure 1).

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streptomycin (SM), ethambutol (EMB)) was evaluated by the first-line anti-TB drugs (isoniazid (INH), rifampicin (RIF)). The chest X-ray showed signs of pulmonary TB with a triangular consolidation of the left upper lobe with blurred limits and small cavitory lesions. The mycobacterial cultures of CSF and sputum samples were found to be positive for the Mycobacterium tuberculosis complex (MTC) by conventional (Löwenstein Jensen medium; Diomed Inc., Istanbul, Turkey) and radiometric (BACTEC 460 TB culture system, Becton Dickinson Diagnostic Instruments, Sparks, Md., USA) methods. The CSF was also tested with a microscopic examination with EZN and conventional cultures; however, the results were found negative for mycobacteria. The immune status of the patient was normal. Anti-HIV antibody and Venereal Disease Research Laboratory (VDRL) tests were negative.

The susceptibility testing of the MTC isolate to four first-line anti-TB drugs (isoniazid (INH), rifampicin (RIF), streptomycin (SM), ethambutol (EMB)) was evaluated by the standard protocol for the extraction of MTC-DNA was used. The result of MTC-PCR was positive. The urine was also tested with a polymerase chain reaction (PCR) assay for MTC. A repeat MRI after 4 months showed complete resolution of all the lesions (Figure 2). During this period the patient remained asymptomatic.

Multiple ICTs and parenchymal CNS involvements are not frequent TB presentations. The ICTs present a subter clinical picture than TBM, namely as space-occupying lesions that may manifest themselves with seizures. The presentation is typical for ICTs-slowly progressive headache and signs of meningeal irritation, followed by cranial nerve involvement, other neurologic deficits and progressive mental status changes over a period of weeks. These signs usually follow a subacute or chronic course leading to difficulty in differentiating the lesions, on clinical grounds, from basal carcinomatous meningitis, chemical meningitis and NC, especially in endemic countries (2-4).

Clinical manifestations of NC are varied and non-specific because of the stage, number, size, and locations of the cysticercal cysts within the CNS and the severity of the host immune response to the parasite (10). Seizures and focal neurologic signs have been described in patients with NC, particularly when the parasitic cysts are located in the parenchyma and arachnoid spaces (11). On the other hand, meningoencephalitis may result from an intense immune response to the parasite in several patients. These patients present clinically with confusion, seizures, headaches, nausea and vomiting (12). For this reason, NC and TBM must always be considered to be a part of the differential diagnosis for a new-onset of these signs in endemic areas. As in NC and ICTs, seizures were the most common symptom in our case. The physical examination findings showed signs of space-occupying lesions and edema.

Other evidence of TB (e.g., pulmonary TB) or cystercrosis (e.g., subcutaneous nodule) elsewhere is a great help in making a definite diagnosis. Some of the TBM patients and NC patients do not have pulmonary findings and subcutaneous nodules. Intracranial multiple lesions might be the only radiological findings. In our case, multiple small nodular areas of enhancement that were predominantly located at the gray-white junction.

**Fig. 1.** Axial magnetic resonance images of a 21-year-old male patient with miliary tuberculosis on admission. (A) T₁-weighted magnetic resonance image (640/14) shows nothing remarkable at the level of the midbrain. (B) Contrast-enhanced T₁-weighted magnetic resonance image (640/14) shows multiple small nodular areas of enhancement that are predominantly located at the gray-white junction.

**Fig. 2.** Axial magnetic resonance images of a 21-year-old male patient with miliary tuberculosis 4 months after antituberculosis chemotherapy. (A) T₁-weighted magnetic resonance image (640/14) shows nothing remarkable at the level of the midbrain. (B) Contrast-enhanced T₁-weighted magnetic resonance image (640/14) shows nothing remarkable at the level of the midbrain.
acteristic CT and MRI scan findings include enhancing (ring or nodular) lesions, ranging from 5 to 20 mm in diameter, which may be seen in any part of the cerebral hemisphere. A punctate eccentric high-density structure suggestive of scolex (which is pathognomonic of NC) is seen in 44% of such patients (13). Another characteristic appearance of NC is rounded hypointense non-enhancing lesions. Non-enhancing cystic lesions on CT or MRI showing scolex constitute a small fraction of patients with NC. According to reports, the majority of the patients with NC have single enhancing lesions, though multiple enhancing CT/MRI lesions are also not uncommon (14). In an epileptic patient, the characteristic CT findings along with subcutaneous nodules are virtually diagnostic of NC and usually do not require any further workup (15). These single or multiple lesions pose a challenge both to radiologists and clinicians. The imaging and clinical features of our case were exceedingly similar to those of NC, and it was difficult to differentiate between these two conditions.

The serological tests are extensively used in the diagnosis of cysticercosis. However, recent studies on serum have demonstrated a large number of false positive and false negative results. The sensitivity of these tests decreases considerably when viable parenchymal cysts are not in contact with the CSF or are calcified (16). In contrast, ELISA using CSF was 87% sensitive and 95% specific (17). On the other hand, the lumbar puncture in TBM usually shows increased opening pressure, and the CSF usually contains between 100 and 1,000 cells per mL. In approximately 65 to 75% of patients, lymphocytes predominate, whereas polymorphonuclear leukocytes predominate in the remainder of patients, generally early in the course of the CNS-TB. The protein concentration is elevated, and the glucose concentration in CSF is usually low in nearly all patients (2). In our case, all the clinical and radiological features were consistent with the diagnosis of NC; however, serological tests and CSF examination established a tuberculous etiology. The patient responded very well to anti-TB drugs, and all intracranial lesions disappeared in the second month of ATCT.

Although nearly non-existent in Western and Muslim countries, pathologies such as NC and tuberculoma are on the increase in these countries due to the increase in the immigrant population from areas in which these pathologies are endemic and due to the increase in immunosuppressed HIV patients (5). In the absence of appropriate therapy, these pathologies might be fatal; the possibilities for differential diagnosis would be of great clinical importance, particularly because of the different treatment protocols required for NC and ICT.

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REFERENCES