Case Report

Central nervous system tuberculosis in immunocompetent patients: Two case reports with literature review✩✩

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Abstract
Central nervous system tuberculosis (CNS) is a rare but extremely dangerous condition that has been reported in 5%-10% of extrapulmonary tuberculosis cases and accounts for approximately 1% of all tuberculosis cases. We present 2 cases of isolated central system tuberculosis in immunocompetent patients: a 57-year-old female and a 22-year-old young man, both of whom had MRI findings consistent with meningitis and tuberculomas and were complicated by cerebral ischemic infarction in the second case. Despite delaying therapy, both patients who had positive TB tests (PCR and QuantiFERON-TB Gold) nevertheless demonstrated clinical improvement. Although central nervous system tuberculosis has a high mortality rate and a high level of neurological morbidity, diagnosing it remains difficult because clinical symptoms and radiological findings can mimic other conditions such as pyogenic abscess, toxoplasmosis, sarcoidosis, and malignancy.

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Introduction
Tuberculosis of the central nervous system (CNS TB) is an uncommon consequence of Mycobacterium tuberculosis [1]. It is a rare, yet an extremely dangerous condition, reported in 5%-10% of extrapulmonary TB cases and accounting for around 1% of all TB cases with a high mortality rate and a high level of neurological morbidity.

CNS TB is frequently encountered in individuals who are already at high risk, such as those who have HIV co-infection, are using immunosuppressive drugs, are alcoholics, or have cancer [1,2].

However, it can be difficult to diagnose due to non-specific clinical symptoms and radiological findings [1]. As a result, imaging is crucial for prompt diagnosis and lowering morbidity and mortality.

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We present 2 cases of CNS TB in 2 immunocompetent patients that highlights the importance of recognizing TB in endemic areas at all times.

Case reports

Case report 1

We report a case of a 57-year-old female with a medical history of type 2 diabetes under treatment who arrived to the emergency department with severe headaches, altered consciousness, and vomiting. The patient has had these symptoms for about 2 weeks, but they have gotten worse in the previous 2 days.

There was no TB in the family or interaction with a TB patient.

MRI of the brain revealed several ring-enhancing lesions in the left cerebellum, bilateral frontal, parietal, and temporal lobes, including periventricular areas, and the left thalamus. It also shown significant leptomeningeal enhancement along sylvian fissures and basal cisterns.

The diagnosis of tuberculoma and tuberculosis meningitis was evoked. Chest CT revealed centrilobular nodules with a linear branching pattern resembling a tree-in-bud pattern, supporting the diagnosis of central nervous system tuberculosis. The QuantiFERON-TB Gold assay was positive and the patient responded favorably to anti-tuberculosis treatment, according to the follow-up (Figs. 1 and 2).

Case report 2

A 22-year-old young man was brought to the hospital for degradation of consciousness, which was preceded by headache dysarthria of progressive onset along with lower limb weakness. There had been no major previous medical or surgical history.

Given the patient’s age and the sudden onset of symptoms, he was directly referred to our department for an emergency brain MRI. The latter shows multiple focal lesions (+/- 1 cm) spread across the brain, implicating the cerebral hemispheres,
brainstem, and cerebellum. On T1, the lesions are isointense, with a low intensity center on T2/FLAIR, peripheral hyperintensity, and significant surrounding edema. They had significant ring enhancement after contrast administration. This radiological presentation was consistent with tuberculomas, and the nodules’ diffuse distribution suggested miliary cerebral tuberculosis.

The MRI also shows bilateral areas of increase signal on T2 and FLAIR and restricted diffusion, located in both frontal and parietal lobes, extending into the insular cortex, to both lenticular and caudate nucleus and the anterior part of the right thalamus. Note that MR angiography (MRA) revealed no related artery abnormalities.

The patient was diagnosed with cerebral infarcts complicating tuberculous meningitis. A Polymerase chain reaction (PCR) for M. tuberculosis and culture were performed and returned positive, confirming the initial diagnosis. Anti-tuberculosis treatment and early corticosteroid resulted in an improvement of the patient’s state (Figs. 3–5).

Discussion

In recent years, tuberculosis has become more prevalent in both immunocompetent and immunocompromised patients, making the disease a worldwide issue [3]. This condition is associated with high neurological morbidity and mortality and remained a major health problem, particularly since the AIDS pandemic [4].

Mycobacterium tuberculosis enters the human body by droplet inhalation, followed by macrophage phagocytosis, which triggers a cascade of inflammation, protective immunity, and the formation of a primary complex. Rich foci are formed when Mycobacterium tuberculosis bacilli spreads hematogenously to any organ, including the meninges, or when a solitary granuloma develops on the meninges, subpial surface, or subependymal of the brain or spinal cord. This tuberculosis lesion then ruptures or grows, resulting in various types of CNS TB [4]. The quantity and virulence of bacilli, as well as the host’s immunological response, determine the type and severity of the lesion. On a rare occasion, infection can spread to the CNS through a discal TB site, tuberculous otitis, or osteogenic tuberculous foci in the spine or cranial vault [3].

The diagnosis of CNS tuberculosis can be very challenging since the clinical symptoms of this condition and its radiologic manifestations might mimic other infectious and non-infectious neurological diseases including brain tumors [5,6].

CNS TB is usually preceded by a 2-4-week prodromal period with non-specific symptoms such as fatigue, malaise, myalgia, and fever. TBM causes headaches, fever, vomiting, photophobia, and rigidity of the neck if a meningitis develops (which occurs in 75% of cases). These symptoms take longer time to develop compared to bacterial meningitis, frequently more than a week [7].

Complications include cranial nerve (CN) palsies, which affect 25%-50% of patients and primarily affect the VI CN (N. abducens) and less frequently the CN III. Other symptoms include hydrocephalus, consciousness alteration and seizures in about 10%-15% of patients. Infarction secondary to vasculitis or direct inflammatory involvement of the meninges and brain parenchyma causes parenchymal damage. The most prevalent deficits after a TBM-related infarction are hemipare-

Fig. 3 – (A,B) Axial T2-weighted MRI shows a well circumscribed nodular lesion in the pons, with a low intensity center on T2 and peripheral hyperintensity. (C,D) Axial T1-weighted MRI post contrast administration demonstrates multiple nodular infratentorial nodular lesions with significant ring enhancement after contrast administration.

Fig. 4 – (A) Coronal T2 FLAIR-weighted MRI shows a well circumscribed nodular lesion in the pons, with a low intensity center and peripheral hyperintensity (yellow arrow). (B) Axial T1-weighted MRI post contrast administration demonstrates a significant leptomeningeal enhancement along basal areas (White arrows).
sis and altered awareness; however, other symptoms such as aphasia or hemianopia can also occur [7].

Intracranial TB is classified into 2 principal types: meningeal and parenchymal with a possible combination of both patterns [5].

**MRI protocol: [5]**

Mandatory sequences include: Axial precontrast T1W, T2W, FLAIR (fluid-attenuated inversion recovery sequence), DWI (diffusion-weighted imaging sequence), GRE (gradient echo sequence) or SWI (susceptibility-weighted imaging sequence) and postcontrast T1W scans in all 3 planes.

Additional sequences can be performed if the morphology or distribution of the lesions are atypical and pose a diagnostic difficulty. They include: Proton spectroscopy and magnetization transfer imaging and magnetic resonance angiography (MRA) and magnetic resonance venography (MRV) when vascular complications are suspected.

**Tuberculous meningitis**

It’s the most common manifestation of CNS tuberculosis and also the most common pattern associated with complications, seen most frequently in children and adolescents. Imaging is critical in making timely diagnoses and reducing morbidity and mortality [5,6].

Contrast-enhanced MRI is the optimal method for assessing and detecting CNS TB, as it has higher sensitivity and specificity than CT and therefore provides a specific and accurate diagnostic [7].

There are 2 main radiologic features:

- Enhancing exudate in the basal cisterns, which is the most prevalent and relatively specific manifestation of leptomeningeal tuberculosis
- Meningeal enhancement on post contrast T1W images: occurring in up to 90% of cases and considered to be the most sensitive feature of tubercular meningitis

The subpial exudate is primarily located in the inferomedial surface of the frontal lobes, the anteromedial surface of the temporal lobes, the superior aspect of the cerebellum, and the floor of the third ventricle. Extension to suprasellar, interpeduncular and ponto-mesencephalic cisterns may also occur. In most cases, some degree of meningeal involvement is seen within the sulci over the cerebral convexities, the Sylvian fissures, and also the ependymal surfaces of the ventricles; the latter usually occurs in the advanced stages of the disease [6].

The most common consequence of tuberculous meningitis is communicating hydrocephalus. It is usually caused by an obstruction of cerebrospinal fluid (CSF) flow in the basal cisterns. In other situations, the hydrocephalus may be non-communicative, due to obstruction caused by tuberculoma or, in rare cases, a tuberculous abscess [6]. Other complications include:

- Ischemic infarct: which is another common complication, occurring in 20%-41% of patients, mostly in the basal ganglia or internal capsule regions, and caused by vascular compression and occlusion of small perforating vessels (necrotizing arteritis), particularly the lenticulostriate and thalamoperforating arteries.
- Dural venous sinus thrombosis and hemorrhagic infarction
- Cranial nerve involvement: occurring in 17%-40% of cases, most typically affecting the second, third, fourth, and seventh cranial nerves. MRI shows a thick aspect of the nerve especially in their proximal segments, with high signal intensity on T2-weighted images and important enhancement on postcontrast imaging.

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Fig. 5 – Coronal T2 FLAIR (A) and Axial diffusion-weighted images (B,C) demonstrating bilateral areas of increase signal on T2 FLAIR and restricted diffusion, located in both frontal and parietal lobes, extending into the insular cortex, to both lenticular and caudate nucleus and the anterior part of the right thalamus (White arrows).
**Tuberculomas**

Tuberculous granuloma or tuberculoma are the most common parenchymal lesion in CNS TB. They may be solitary or multiple and may be associated with meningitis. They are more common in children who tend to have infratentorial tuberculoma while adults present with supratentorial tuberculoma. They can occur anywhere within the brain but they are commonly located at corticomedullary junction and periventricular regions [3].

Histologically, mature tuberculoma is formed of a necrotic caseous center surrounded by a capsule containing fibroblasts, epithelioid cells, Langhans giant cells, and lymphocytes [6].

Because of its high specificity and sensitivity, MR imaging was chosen as the method of choice for the diagnosis of tuberculomas. The radiologic findings depend on the type of the lesion [1]:

- Non-caseating tuberculomas demonstrate an iso or high signal intensity on T1WI sequences, while they are hyperintense on T2WI with a homogeneous enhancement on post contrast images.
- Caseating solid tuberculomas appear hypo-intense on T1WI and T2WI, which is assumed to be due to granulation tissue and compressed glial tissue in the central core, which has a higher cellular density than the brain parenchyma. These lesions show ring enhancement or heterogeneous central enhancement.
- Tuberculoma with central liquefaction are hypointense on T1, hyperintense on T2 with a peripheral hypo-intense rim on T2W images and ring enhancement on post contrast images. This peripheral low signal intensity on T2 may be attributable to a layer of collagenous fibers with a high protein concentration and low water content, as well as an outer layer of inflammatory cells.

Neoplasms, primary lymphoma of the CNS (central nervous system), pyogenic abscess, fungal infection, cysticercosis, and toxoplasmosis should all be considered in the differential diagnosis of CNS tuberculoma [7]. MR spectroscopy is a valuable method for distinguishing tuberculomas from other intracranial mass lesions and should be performed at the slightest doubt [1].

**Conclusion**

Tuberculosis remains a major cause of infectious disease morbidity and mortality around the world, notably in South Asian and North African countries. The central nervous system (CNS) is a less common location of involvement, but it can be lethal if not diagnosed and treated early.

As a result, radiologists must be aware of the various manifestations and patterns of this condition in order to make an early diagnosis and guide an appropriate management.

**Patient consent**

Written informed consent for publication was obtained from patient.

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