Tuberculous Encephalopathy without Meningitis: A Rare Manifestation of Disseminated Tuberculosis

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Abstract

Tuberculous (TB) encephalopathy is a rare presentation of the central nervous system tuberculosis. Its pathophysiology is believed to have an immune mechanism without any direct invasion by the tubercular bacilli. The clinical presentation is highly variable from mild illness to a potentially fatal one. The characteristic signs of meningitis and cerebrospinal fluid findings are mild or absent. Diffuse white matter edema and demyelination have been noted. This clinical entity has been reported mainly from the pediatric population. In the adult population, it has been reported only in very few case reports. We report here a rare case of TB encephalopathy in a 21-year-old female with disseminated tuberculosis, without meningitis, responding to antitubercular therapy.

Keywords: Encephalopathy, meningitis, tuberculosis

Introduction

Central nervous system (CNS) tuberculosis is a common clinical entity, especially in the developing countries. It commonly manifests as tuberculous meningitis (TBM), brain abscess, or tuberculomas. Its manifestation as encephalopathy is a very rare entity reported commonly in children. It is described as diffuse cerebral damage reported initially by Dastur and Udani. An immune mechanism has been postulated as the underlying cause based on various clinicopathological analysis. The clinical presentation may vary from mild drowsiness to quadriplegia and coma. The characteristic meningeal signs and cerebrospinal fluid (CSF) findings of TBM are mild or absent. Diffuse or patchy involvement of white matter associated with edema and demyelination may be noted. It is imperative to make the diagnosis at the earliest so that the neurological sequelae may be prevented. While this entity has been seen commonly in the pediatric age group, it is rarely reported in the adult population. We report here a case of tuberculous (TB) encephalopathy in a 21-year-old female with disseminated tuberculosis, without meningitis, who responded to antitubercular therapy.

Case Report

A 21-years-old female presented to the medical emergency with altered sensorium and involuntary passage of urine and feces for 4 days. She had a history of low-grade fever, reduced appetite and cough without expectoration for 3 months, lower back pain, and weakness of both lower limbs for 1 month prior to the altered sensorium. There was no history of any seizure episodes or head and back trauma. On clinical examination, she was found to be in altered sensorium with flaccid lower limbs and diminished deep tendon reflexes. No response was noted on plantar reflex. The sensory examination and power of muscles could not be assessed. On investigations, her complete blood counts, serum electrolytes, and liver and renal functions were normal. Malaria, dengue, chikungunya, and enteric fever was ruled out by relevant investigations. Her blood and urine cultures were sterile. Noncontrast computed tomography (CT) scan of brain showed features suggestive of communicating hydrocephalus with periventricular ooze and hypodensity in the right occipital area. CSF analysis showed raised protein at 166 mg/dl and glucose of 31 mg/dl with <5 cells. Cartridge-based nucleic acid amplification test for...
Mycobacterium tuberculosis (MTB) was negative. A complete meningoencephalitis profile of CSF was done which turned out to be negative. Magnetic resonance imaging (MRI) brain showed multiple altered signal intensity areas appearing hyperintense on T1, T2/FLAIR symmetrically involving all the areas of both the cerebral and cerebellar hemispheres. These areas showed diffusion restriction and minimal postcontrast enhancement. Bilateral lateral, third and fourth ventricles appeared dilated [Figure 1]. A possibility of viral encephalitis was suggested which was ruled out on CSF examination. Further evaluation for fever and lower limb weakness was done. Her contrast-enhanced CT (CECT) chest revealed bilateral fibrobronchiectatic and fibrocavitatory changes involving the upper and lower lobe and multiple centrilobular nodules suggestive of active tuberculosis [Figure 2]. CECT abdomen showed multiple wedge-shaped hypodense areas involving bilateral renal cortices and multiple heterogeneously enhancing discrete mesenteric and retroperitoneal lymph nodes in paraaortic, aortocaval, and retrocaval levels [Figure 3]. MRI spine showed complete collapse of L1 vertebral body and partial destruction of L2 vertebral body, destruction of inferior endplate of T12 and superior endplate of L3 vertebra along with pre- and paravertebral bilateral psoas abscess [Figure 4]. The patient was initiated on antitubercular therapy. Four weeks later, the patient could be discharged with spontaneous eye-opening and ability to follow commands and power of 3/5 in both the lower limbs. A diagnosis of TB encephalopathy was made based on the evidence of disseminated tuberculosis in absence of meningeal signs, absence of definitive evidence of TBM on CSF examination supported by MRI findings of brain, and clinical improvement on antitubercular therapy.

**Discussion**

TB encephalopathy is a rare clinical manifestation of CNS tuberculosis and is seen commonly in the pediatric population with underlying pulmonary tuberculosis.[1] It is characterized by cerebral edema sometimes with features similar to acute disseminated encephalomyelitis (ADEM) and may manifest with a variety of symptoms ranging from focal neurological deficits to convulsions and decreased conscious state. It does not appear to be due to direct infection of the CNS by MTB.[5,6]

The clinicopathological mechanism involves heterogeneous group of immune and nonimmune conditions with diffuse or patchy cerebral edema. Contrary to pathogenesis in TBM, TB encephalopathy is believed to have a delayed type of hypersensitivity reaction to the TB protein present elsewhere in the body. This allergic or Type IV hypersensitivity is responsible for destruction of the nervous tissue mediated by the cell-mediated immunity.[2] This pathophysiology also explains mild pleocytosis in the CSF examination and diffuse involvement of the brain parenchyma. The pathological findings are also reflected in the brain imaging by MRI which shows hyperintense diffuse parenchymal lesions with contrast enhancement. Another pathogenic mechanism suggests immune-mediated white matter damage similar to ADEM.[5,6]

Although the clinical entity was described more than 50 years ago, the reported cases of TB encephalopathy have been
very few. A case of a 15-year-old with seizure and cognitive decline with white matter lesions on MRI with clinical response to antitubercular therapy has been reported by Kim et al.\textsuperscript{[4]} A case presenting with TB encephalopathy and human immunodeficiency virus infection in a 33-year-old was reported by Li et al., although the CSF was positive for interferon-gamma release assay.\textsuperscript{[7]} A case of TB encephalopathy with multiple intracranial tuberculomas by Yokoyama et al.\textsuperscript{[8]} Our case was diagnosed based on the clinical findings, MRI imaging, absence of TBM, and presence of tubercular foci in the chest, abdomen, and vertebrae.

The clinical presentation may be highly variable and may cause mild drowsiness, seizure, quadriplegia/paraplegia, cognitive decline, coma, and death. It is imperative to make an early diagnosis and initiation of ATT with steroids helps in reducing the neurological sequela and mortality.

**Declaration of patient consent**

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given her consent for her images and other clinical information to be reported in the journal. The patient understands that name and initials will not be published and due efforts will be made to conceal identity, but anonymity cannot be guaranteed.

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**Conflicts of interest**

There are no conflicts of interest.

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