# Tuberculous meningitis and Nonconvulsive status epilepticus: a Case Report

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**Abstract**

sputum acid-fast bacilli were positive and anti-TB treatment was started. Her cerebrospinal fluid results were normal except for a positive nested polymerase chain reaction (PCR) for tuberculous. She responded to protocol for treatment of status epilepticus and anti-TBM treatment and her level of consciousness improved and she became fully aware

**Introduction:**

Nonconvulsive status epilepticus (NCSE) is a serious epileptic condition in which there is minimal or no motor activity. Electrical activity in NCSE is continuous, lasting at least 30 minutes and leads to changes in mental or behavioral status (1, 2). NCSE is relatively common and constitutes 20–25% of all status epilepticus cases (3). It is often difficult to diagnose NCSE, as there is minimal or no objective convulsive activity and many other conditions can change the mental status in predisposing conditions of NCSE. The underdiagnosis may lead to detrimental results (4).

Treatment can be delayed as mental status changes without obvious convulsions. Treatment is not simple and depends on many factors, including the etiology, electroencephalogram (EEG) findings, and the patient's clinical condition(3). Etiologies include idiopathic epilepsy syndrome, metabolic disorders, trauma, brain tumors, cerebral hypoxia, and infectious diseases (5).

Tuberculous meningoencephalitis (TBM) compromise 1% of all TB cases (6). It is a life-threatening form of central nervous system infection, with significantly higher mortality and neurological impairment among infected people. TBM has a subacute onset of symptoms with non-specific clinical signs that may persist for weeks, often making early diagnosis difficult. It is characterized by fever, headache, vomiting, focal neurological signs or coma (7).

Seizures have been reported in 17% to 93% of patients with TBM (8). The seizures in TBM can be either focal or generalized tonic-clonic seizure and convulsive or non-convulsive status epilepticus (9). The etiology of TBM seizures is multifactorial and has been identified independently or in combination due to meningeal irritation, cerebral edema, tuberculoma, infarction, hydrocephalous and hyponatremia. Seizures in TBM can occur during the active phase or as sequel of meningitis. It can even be the characteristic of CNS tuberculosis (heraldic seizure) in 10% of all patients (10).

Here we report a rare presentation of TBM where the patient presented with NCSE and tuberculous meningitis. This case highlights the importance of clinicians' awareness on unusual clinical presentations of TBM, because NCSE is hard to diagnose without having it constantly in mind and delayed diagnosis is associated with a poor prognosis.

**Case Presentation:**

A 50-year-old Iranian woman was admitted to our hospital with an exacerbation of abnormal uterine bleeding (AUB) for total abdominal hysterectomy and bilateral salpingo-oophorectomy (TAH-BSO). Her history revealed 10Kg weight loss during previous 3months, anorexia, night sweets, nausea, vomiting and several episodes of fever and cough,for which she hasn't seek any treatment. She had suffered primary biliary cirrhosis (PBC) since 1999 and had been treated with ursodeoxycholic acid (750 mg daily) without any immunosuppressive therapy. She had no significant history of pulmonary or genital tuberculosis. She had given birth to a son and a daughter. During her admission for TAH-BSO surgery she had fever. The spiral chest CT-scan showed bilateral pleural effusions without lymph node swellings with diffuse ground-glass opacities and small centrilobular nodules. Sputum acid-fast bacilli was positive and anti-TB treatment with isoniazid, rifampicin, ethambutol and pyrazinamide was started. One day after TAH-BSO surgery, she presented with acute alteration of mental status manifested with impairment of awareness, disorientation to time, place and person and bizarre behavior like undressing herself and urination in the ward. Next day she became completely unresponsive, while she was fully awake. So, she underwent neurology and psychiatry consult in the same day as it was thought to have a psychiatric origin, as well.

Examination at presentation revealed no meningeal irritation, absent neck stiffness, Kernig's and Brudzinski's signs with mental alterations in the form of unawareness and unresponsiveness. The patient was afebrile. Fundoscopy was normal with intact cranial nerves. Deep tendon reflexes were elicited and plantar reflexes were flexor. Neurological tests requiring cooperation such as cerebellar tests, muscle strength examinations, and sensorium were not performed as she ignored commands, but she moved her limbs symmetric in the bed, without any convulsive or mini convulsive signs.

On initial presentation, routine blood tests revealed a normal white blood cell count of 8,700/$mm^3$, low erythrocyte count of 3,630,000/$mm^3$ and hemoglobin level of 8.3 g/dL, high C-reactive protein level of 95 mg/L (normal: <6), glucose level of 190 mg/dL and low sodium level of 130 mmol/L. She had negative results for human immunodeficiency virus. Other laboratory findings had no remarkable changes.

cerebrospinal fluid (CSF) was taken immediately after neurology consult, which is about a weak after initiation of treatment for TB. The opening pressure was 25cmH2O, the leukocyte count was 0/μL, the protein level was 36.1 mg/dL, and the glucose level was 57 mg/dL (corresponding blood glucose level, 130 mg/dL). Tuberculous DNA polymerase chain reaction (PCR) of CSF showed negative results, but nested PCR assay yielded a positive result. Adenosine deaminase level was 32.4 IU/L (normal <10 IU/L).

The EEG showed generalized 1.5- to 2-Hz continuous sharp and slow wave activities. (figure 1), that had improved significantly after administration of diazepam (figure 2) and after antiepileptic treatment significant improvement in EEG trace is seen together with normal alpha background and correction of periodic discharge waves (figure 3).

Magnetic Resonance Imaging (MRI) of the brain revealed multiple lesions which were iso signal in T1 and low signal at center in T2, with ring enhancement in supra and infratentorial regions of both hemispheres, at the subcortical, white-gray matter junction. Some of them had nodular enhancement, with moderate vasogenic edema around lesions. All of the findings in the context of clinical features were in favor of TB (figure 4).

The patient was diagnosed as having TBM presenting with NCSE, and treatment was started for NCSE. The protocol for treatment of status epilepticus comprised diazepam and levetiracetam infusion, and then treatment with the oral antiepileptic drugs. Anti-TBM treatment consisted of four anti-tuberculosis drugs continued. The patient's consciousness and clinical picture improved completely after the loading dose of

levetiracetam and she became entirely aware and oriented. Her follow-up EEG improved significantly. No reoccurrence of cognitive decline happened.

**Discussion:**

In this study, a TBM patient with NCSE is reported. The frequency of status epilepticus in TB patients is 7.6%.(9) However, to the best of our knowledge, only 4 cases of TBM presenting with NCSE have been reported in the literature (11-14). Seizures are reported in 50-73% of children, and 10-38% of adults in the clinical course of TBM (15-17).

Both febrile and afebrile seizures can be the presenting feature of TBM in children. The frequency of status epilepticus in TBM patients is 7.6%. It is reported that Convulsions are a significant predictor of mortality (18). Our patient presented with altered level of consciousness and unresponsiveness and persistent seizure activity on the EEG that comprised 1 to 2-Hz continuous sharp and slow wave activity. Inconsistent with our study, a study by Arman study et al. (11) has reported a patient with NCSE due to tuberculosis meningitis who had right frontal 1.5- to 2-Hz continuous focal sharp and slow waves. In contrast in Oka study et al. (13), EEG showed left frontal 2.5- to 3-Hz repetitive focal sharp wave activity compatible with NCSE.

Continuous epileptiform EEG activity in NCSE is expected to be higher than 2.5 Hz, whereby when epileptiform discharges are less than 2.5Hz, one out of three other criteria is needed to confirm the diagnosis of NCSE including presence of mini-convulsive signs, evolution in amplitude or frequency of discharges and responsiveness to intravenous administration of benzodiazepines (19). Our patient had no mini-convulsive signs but she had an obvious response to intravenous diazepam and levetiracetam, both clinically and electrically. The patient in Arman study et al. (11) responded to diazepam and phenytoin, followed by midazolam infusion. In Oka study et al. (13) after anticonvulsant treatment with levetiracetam, persistent EEG activity ceased with the recovery of consciousness

In our study, recovery of consciousness and normalization of subsequent EEGs with antiepileptic therapy have happened. A study by Kalita et al. (19) on the 32 patients with highly probable tuberculous meningitis have done. Evidence of extra-CNS tuberculosis were present in 6 patients; all had pulmonary tuberculosis. The main abnormality in their EEG was diffuse slowing of the background activity (69%).

Our patient had diffused sharp and wave activity with slow background which is compatible with status epilepticus (20). Several reports establish that 84% of CNS tuberculoma clearly showed low signal on T2- weight images and 16% had lesions with central high signal thought to represent caseating necrosis or tuberculous abscesses (21-23).

At an early stage of tuberculoma formation, the mass is isointense on T1- and T2-weighted images and shows some contrast enhancement, that is secondary to occurrence of inflammatory reactions and excess of giant cells in the mass and a poor collagen capsule, that it becomes rich in collagen, later in the course of disease. They give low signal on T2-weighted images because of fibrosis, scar tissue (24). Rarely, tuberculomas show calcification on CT, but it can appear as low signal on MRI. All tuberculomas show ring or nodular contrast enhancement.

Almost one third of tuberculomas are multiple (25). Various differential diagnosis should be considered in a patient presented with altered level of consciousness and multiple ring-enhancing lesions, especially neoplasms either metastasis or primary lymphoma and other infectious diseases like fungus or bacterial endocarditis. Moreover, Tuberculomas have a variety of different features that can mimic other space-occupying lesions, such as neoplasms.

Metastases, multiple gliomata or meningiomas excluded by further evaluations. No space occupying lesion was found in the chest and abdominopelvic CT-scan. The pathology of her surgery was in favor of diffuse granulomatous involvement.

The normal CSF glucose and protein levels are unusual but not incompatible with the diagnosis of TB (26). Acid-fast bacilli are seen in only 40% cases on initial CSF examination (27). The tuberculin test is negative in

50% cases at presentation (28). Similar to Arman study et al. (11) in this study, PCR of CSF was negative, but nested PCR assay was positive. Nested PCR is a technique that reduces nonspecific amplification of the DNA template. It increases the sensitivity and specificity of the reaction and is useful on suboptimal nucleic acid samples (29).

The presence of a low signal lesion on T2-weighted images that shows ring or nodular contrast enhancement in a patient who has tuberculosis elsewhere in the body and from a region in which tuberculosis is endemic should suggest CNS tuberculoma.

The patient's clinical findings, unexplained acute change of consciousness, together with chest involvement, diffuse granulomatous infiltration in uterus and ovaries, and multiple ring enhancement lesions in brain MRI, led to the diagnosis of TBM. The positive response of the patient to antituberculosis treatment also supported the diagnosis.

**Conclusion:**

The varied manifestations of CNS tuberculosis, that used to be a common neurological disorder in developing countries, have now become relevant worldwide. Early diagnosis and timely treatment of the disease are critical. TBM and NCSE constitute a diagnostic challenge and both should be considered by clinicians among the many presentations of tuberculosis.

**Data Availability Statement (DAS)** :

The data that support the findings of this study are available from the corresponding author, [Mostafa Almasi-Dooghaee ,Neurology Department, Firoozgar Hospital, School of Medicine, Iran University of Medical Sciences, Tehran, Iran. Email: A_mostafa108@yahoo.com , Tell: +98 98 915 180 1384], upon reasonable request.

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Figure 1: EEG trace; transverse montage (7μv/mm, 30mm/s), Generalized periodic discharges with 1-2 Hz frequency superimposed on slow background.

Figure 2: EEG trace; transverse montage (7µv/mm, 30mm/s), after administration of 10mg IV Diazepam, significant improvement with some transient sharp waves at left hemisphere and normalization of background.

Figure 3: EEG trace; transverse montage (7µv/mm, 30mm/s), after antiepileptic treatment significant improvement in EEG trace is seen, with normal alpha background and omission of periodic discharges. In this trace C3 & F4 lead artifact is seen.

Figure 4: Brain MRI revealed multiple T1-weighted hyposignal (3-a) and T2-weighted hypo/hypersignal (3-b, 3-c) lesions with ring-like gadolinium enhancement at cerebellum and throughout the cerebellum ( 3-d, 3-e, 3-f), predominantly at gray matter-white matter junction.