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The prevalence, characteristics and outcome of seizure in tuberculous meningitis

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Abstract

Seizures are a common finding in patients with tuberculous meningitis (TBM), and associate with four times increased risk of death and neurological disability, especially in children. It has been reported that brain inflammation, diffuse neuronal injury, and reactive gliosis may all contribute to the pathogenesis of seizures in TBM. Early seizure onset may be associated with meningeal irritation and cerebral oedema; while, the late seizures are usually due to infarction, hydrocephalus, tuberculoma and paradoxical response. Moreover, recurrent uncontrolled seizures can evolve to status epileptics resulting in an increased risk of chronic epilepsy and poor prognosis. Therefore, this review aimed to assess the frequency of seizures in patients with TBM, and discuss the etiologies, mechanisms, and characteristics of seizures in TBM. Besides, we have searched the literature to identify the prognostic factors for chronic epilepsy after TBM.

Keywords: Seizure, Tuberculous meningitis, Neuronal injury, Epilepsy

Background

Tuberculous meningitis (TBM) is the most devastating form of extrapulmonary TB, carrying significantly higher mortality and neurological disability among infected individuals, especially in low-income countries [1, 2]. The clinical characteristics of TBM include fever, headache, vomiting, impaired consciousness, focal neurological signs, and seizures [3]. Seizure is a common feature of TBM that may develop at any time point throughout the disease course, with an estimated incidence of 17 to 93% [4]. Seizures associated with TBM infection can be either acute symptomatic or unprovoked seizures. Acute symptomatic seizures usually occur within the first 2 weeks, and sometimes even later. Although they subside once the acute infection is over and may not recur; there is often an increased risk of developing subsequent epilepsy. Whereas unprovoked seizures occur later after the acute phase of TBM and have a propensity to recur [5]. Status epileptics (SE) is also not uncommon finding in patients with TBM.

The current data is showing that seizures in TBM are more common in children than adults; this may be attributed to the immaturity of the brain [4, 6–8]. Over half of children with TBM may experience seizures at any time point, but more often during the late stage [9]. There is accumulating data suggested that brain inflammation and the subsequent neuronal injury and reactivation of glial cells play an essential role in seizure induction following central nervous system (CNS) infection [10–12]. The underlying etiology of seizures in TBM is multifactorial, therefore the type and duration of treatment may vary between individual cases depending on the possible underlying cause of convulsion. In patients with CNS infections, recurrent seizures are common observation after the first seizure; therefore, these patients are probably in need of prophylactic antiepileptic drugs (AEDs) to prevent further seizure recurrence, at least during the acute phase of the disease [13].

In this review we first report the incidence and prevalence of seizures in patients with TBM, and discuss the etiological factors associated with the development of seizures. Secondly, we review the pathogenesis and mechanisms of seizure and acquired epilepsy caused by TBM; as well as the clinical and electrophysiological characteristics of these seizures. Finally, we identify the predictors of chronic epilepsy following TBM infection; and report seizure prognosis in TBM. To our knowledge this is the first paper reviewing seizures in TBM so far.

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Epidemiology

Seizure prevalence in TBM varies widely based on many factors such as the patient's age, human immunodeficiency virus (HIV) co-infection, socioeconomic status of affected individuals, study design, and the length of follow-up. Overall, seizures have been reported in 17–93% of TBM patients, and it can occur at any time point throughout the disease course [7, 8, 14–21]. Seizures in TBM can be either acute symptomatic or unprovoked seizures; the frequency of acute symptomatic seizures in TBM is estimated between 16.3 and 31.5% [20, 21]. Although acute seizures in TBM is relatively higher than that in bacterial meningitis, viral encephalitis is associated with the highest incidence of post-infection seizures, reported in 62 to 67% of the cases [22]. This is could be attributed to the fact that parenchymal involvement is often more severe in patients with encephalitis than those with meningitis [22–25]. Children with TBM are more likely to experience seizures relative to adults; this may be attributed to the immaturity of CNS, blood-brain barrier, and the immune system of this vulnerable group [4, 26]. The incidence of seizures in children with TBM has been estimated between 50 and 74% [4, 26–29]; with higher rates being reported in pediatric patients under the age of 4 years [30–33]. While the reported risk of late unprovoked seizures among CNS infection survivors in the developed countries is estimated at 6.8–8.3%, it is much higher in resource-poor countries [34]. Moreover, the highest incidence of late unprovoked seizures had been reported to occur in the first 5 years after infection [35].

Seizures are less likely to occur in HIV negative patients with TBM compared to those with HIV co-infection; with an estimated range from 4 to 11% [36–39]. A study comparing TBM patients with and without HIV infection has found that acute symptomatic seizures occurred in 30% of HIV positive cases compared to just 9.5% in those without HIV infection [40]. In addition, tuberculosis (TB) burden is significantly affected by the socio-economic gap between and within countries and communities, with the poorer groups having a higher risk of TB infection, including TBM [4, 41]. A poor socio-economic status is often associated with advanced disease stage at presentation and limited access to healthcare services; thereby, developing more complications including higher prevalence and incidence of seizures.

Seizures also can be the initial presenting symptom of TBM, even in patients with negative magnetic resonance imaging (MRI) findings at admission [3, 26]. In children, seizures are the presenting symptom in 10–20% of the affected cases, and over 50% of children with TBM develop seizures at the initial days of admission [42]. While in adults, seizures were reported as the initial presenting feature in 10–15% of TBM cases [28, 43].

Etiology

The underlying etiology of seizures in TBM is multifactorial depending on different pathophysiological changes that may simultaneously occur in the central nervous system during the disease course. Some of these pathological processes develop early after the disease onset and often response well to early management, while other pathological changes continue to damage the brain tissues resulting in devastating complications, including neurological deficits and seizures [4]. Meningeal irritation, increased intracranial pressure (ICP), cerebral oedema, tuberculoma, hydrocephalus, and cerebral ischemia were associated with convulsions in patients with TBM [3, 4]. Bharucha and colleges have also reported that TBM patients with meningeal irritation, tuberculoma, cerebral oedema, arteritis, infarction, hydrocephalus, and hyponatremia were more likely to experience seizures [44]. Moreover, in TMP patients, refractory seizures are more commonly associated with uncontrolled inflammation and severe brain injury that may eventually result in chronic epilepsy.

Drug-induced seizures in TBM have also been reported in many studies. In a randomized controlled trial, seizures were reported in 17% of patients using intensified therapy with Levofloxacin, while none of those using only the standard anti-TB regimen has developed seizures during the treatment period [45]. Furthermore, a recently published meta-analysis has also concluded that fluoroquinolones use in TBM was associated with a higher incidence of seizures [46]. Isoniazid, an anti-TB drug, was found to have seizure-inducing properties, and Isoniazid overdose has been reported to induce seizures [47]. Beside the ongoing pathological changes of TBM that play an essential role in reducing seizure threshold; these medications could further decrease the seizure threshold; thus, increasing the incidence of seizures among TBM patients receiving these particular medications.

Mechanism

Seizures can occur at different disease stages depending on the underlying pathophysiologicalmechanism. Early seizures are usually associated with meningeal irritation, cerebral oedema, and raised intracranial pressure; whereas, hydrocephalus, infarction, tuberculoma, and hyponatremia provoke late-onset seizures [4, 48]. Meningeal irritation and cerebral oedema represent the acute immune reaction in the brain as a response for *Mycobacterium tuberculosis* infiltration. The recently accumulating preclinical and clinical evidence suggest that inflammation plays a crucial role in triggering seizures [10, 11]. CNS infections often induce severe inflammatory reactions and are a major risk factor for seizures. In developed countries, it is estimated that 6.8–8.3% of CNS infection survivors develop seizures, while the rates are much higher in the developing world [34].

CNS inflammatory reaction is characterized by the activation of astrocytes, microglia, and endothelial cells of the blood-brain barrier, along with the infiltration of immune cells and plasma proteins resulting in the up-regulation of series of inflammatory mediators [49–52]. Many studies had found that pro-inflammatory mediators, such as COX-2, IL-1b, IL-6, PGE2, HMGB1, TNF-α TGF-β, TLR4, and NOX2 play essential roles in the generation and exacerbation of seizures [53–56]. Furthermore, researchers have demonstrated that seizures also can increase the permeability of blood-brain barrier (BBB), thereby intensifying the neuroinflammation via the extravasation of immune cells and inflammatory mediators from blood vessels into the brain tissue [49, 51, 52]. A recent study has also reported that neuroinflammation and reactive gliosis following diffuse neuronal injury play a major role in seizure induction; and recurrent seizures are associated with massive glial activation and inflammatory responses in the epileptogenic cortex [12].

Cell-mediated immunity is important for tuberculomas' formation, and adequate response of host's immune system to Mycobacterium bacilli may lead to the development of either caseating or non-caseating granulomas at the site of dissemination; these lesions remain clinically silent until they induce a mass effect and lower seizure threshold [57–59]. In addition, raised ICP is also one of the common causes of seizures in TBM [60, 61], and various factors may contribute to the mechanism of increased ICP. In the acute phase, it could be attributed to gross cerebral oedema associated with TB inflammation [4, 62]. However, In subacute and chronic cases, hydrocephalus is the most common cause of raised ICP [4].

The pathological changes of TBM may extend to involve the brain's parenchyma and infiltrate intracranial blood vessels, causing vasculitis and subsequent infarction. These processes may lead to cytotoxicity, vasogenic oedema, and the release of inflammatory molecules. The leptomeningeal inflammatory exudates can cause hydrocephalus by either obstructing the flow of cerebrospinal fluid (CSF) or impairing its absorption, which may lead to severely high ICP and subsequent seizures.

It is also worth mentioning that isoniazid, one of the most commonly used anti-tuberculosis drugs, has seizure-inducing properties. Temmerman and colleges had reported that isoniazid overdose was associated with repetitive seizures refractory to antiepileptic drugs, metabolic acidosis, and coma [47]. Moreover, unprovoked seizures were also observed even after single conventional doses of this drug [63].

Characteristics

Although seizure is a common finding in patients with TBM, data regarding the clinical characteristics, time of onset and type of seizures remain not completely understood.

Time of onset

Seizures in TBM can occur at different time points depending on the different underlying pathologies. Early seizure onset may be attributed to meningeal irritation and cerebral oedema; while late-onset seizures are usually associated with infarction, hydrocephalus, and tuberculoma [3, 4]. Misra UK. and colleagues reported that most of the early-onset seizures were due to meningeal irritation; whereas, late-onset seizures were more commonly associated with tuberculoma, infarction, and hyponatremia [48]. In their study, 34.2% of the patients experienced seizures during the disease course, with the majority of the cases (70.4%) had late-onset convulsions [48]. Paradoxical response is also a common finding in TBM and may associate with the development of late-onset seizures. In one study, paradoxical worsening was reported in 22 (64.7%) patients, out of them 12 had experienced late-onset seizures, which were more commonly related to tuberculoma [64]. Another study from India has also found that paradoxical worsening related seizures were more frequently late-onset seizures [48].

Type of seizure

Seizure development in TBM and its type may vary based on the underlying pathologies or the affected brain regions. Seizures in TBM are either focal, that may or may not evolve to secondary generalized seizures, or generalized tonic clonic seizures (GTCS) [4]. In contrast, seizures in viral encephalitis are more likely to be GTCS or focal with secondary generalization [5]. Whether the seizure is focal or generalized, it may eventually evolve to convulsive or non-convulsive SE in some cases [26, 65]. Seizures due to meningeal irritation, cerebral oedema and raised ICP are commonly generalized seizures that emerge during the earlier phase of TBM [4]. In contrast, tuberculomas and infarctions are more likely to induce focal seizures rather than generalized ones. A study from the UK reported that out of 38 patients with TBM, 20 (50%) patients had seizures. Focal onset was noted in 15 (39.5%); whereas GTCS were observed in 5 (13.2%) patients, with all patients with isolated tuberculomas developed focal seizures [27]. Another study included 20 patients with CNS tuberculomas found that 60% of the cases have developed focal seizures with secondary generalization and only 30% of the patients presented with primary generalized seizures [66]. Furthermore, in a recent study, out of 79 Indian patients with TBM, 27 (34.2%) patients had seizures. Focal seizures were the most frequent type, reported in 12 (15.2%), followed by focal to bilateral in 8 (10.1%), and generalized seizures in 7 (8.9%) patients [48]. In this study, the common causes of seizures were tuberculoma in 33.3%, multiple associations in 33.3% and infarction in 14.8% of the cases [48].

While in another study where over 60% of TBM patients had developed hydrocephalus, among the 11 (34.4%) patients presented with clinical seizures, 9 had generalized tonic clonic seizures and 2 had partial seizures [67]. Furthermore, a study from India reported that 101 out of 136 children with TBM had seizures, and among them 57 (42%) patients experienced seizures before admission, while 44 (32%) cases developed seizure after hospitalization. In this study, GTCS were reported in 59 (43.4%) patients, followed by focal seizures (28%) and tonic spasm (3%). This is maybe attributed to the fact that cerebral oedema was found to be the most common cause of seizures (58%) followed by hyponatremia (48%) and SIADH (35%) [68].

SE is more common in resource-limited countries, thus contributing to the higher prevalence and incidence of epilepsy after cerebral infection in the developing world. Moreover, the frequency of SE among children in these countries is three times higher than adults [5].

SE including convulsive and non-convulsive, has also been reported in TBM [26, 65, 69–71]. In a recent study from India, SE occurred in 22.2% of TBM patients presented with seizures [48]. Interestingly, all these patients had multiple causes, including tuberculomas, infarctions, and hydrocephalus.

EEG findings

TBM has been reported to induce more abnormalities on Electroencephalography (EEG) than other meningitis [72], especially in children [73]. The EEG changes in patients with TBM vary according to the site of the ongoing inflammatory process [74]. In patients with TBM, EEG may demonstrate diffuse slowing with or without focal changes and epileptic discharges, depending on the severity of TBM symptoms [3, 21]. Researchers have also found that the involvement of meninges and cerebral cortex often results in a typical pattern of diffuse slowing on EEG [3, 67]. Furthermore, the absence of well-defined lateralization on EEG is a sign of a widespread meningeal inflammation as the most likely cause of the seizure in these patients [3]. Patwari and colleagues found that TBM patients presented with GTCS had generalized dysrhythmia with slow activity, and multiple spike and wave pattern; while those presented with focal seizures had interhemispheric asymmetry and focal spike and wave pattern, which were more likely due to focal intracranial lesions such as tuberculoma and infarction [4]. This study has also suggested that the presence of epileptiform discharges on EEG may predict chronic epilepsy [4]. Gunawan and colleagues have reported abnormal EEG activity in 75% of the patients, out of them 77% had epileptogenic activities; moreover, they found a strong correlation between epileptic spikes on EEG and the development of clinical seizures [30]. However, a recent study from China has concluded that the presence of epileptiform discharge on EEG was not associated with poorer outcome [75]. In TBM patients with convulsions, epilepitform discharges are less common finding relative to slow activity, especially in adult patients. Although Kalita J. et al. has reported clinical seizures in 11 adult patients with TBM, epileptiform activity was noted in only 4 patients [67]. EEG is often more sensitive in children than adults; In a study included 12 children with TBM, epileptic activity was detected in 8 out of the 10 (83.3%) children presented with clinical seizures [30]. It is also worth mentioning that EEG recording in TBM patients with non-convulsive SE often shows continuous rhythmic activity. Arman et al. had reported a case presented with impaired consciousness and persistent seizure activity on EEG; particularly, continuous sharp and slow-wave activity that was suppressed after SE therapy and the patients regain her consciousness [26].

EEG can be used to detect the underlying seizure activity and predict the risk of secondary epilepsy in patients with TBM [4, 30]. Moreover, EEG may help to localize the underlying lesions, exclude non-convulsive SE, and provide a rough guide to the degree of cortical and subcortical dysfunction in TBM patients [76, 77].

Predictors of chronic epilepsy

The mechanisms of chronic epilepsy following TBM are not well established. However, prolonged inflammatory stimulation by either chronic inflammation or by seizures themselves and structural damage of brain tissues resulting from infarction, space-occupying lesions, and gliosis may all constitute to epileptogenesis. Several factors have been reported to associate with increased risk of epilepsy following TBM infection including the patient's age, recurrent seizures and SE, tuberculoma, infarction, hippocampal sclerosis, and persistent epileptic activity on EEG.

Young age

Children with TBM are more likely to develop seizures during the disease course compared to adults; this could be attributed to the immaturity of the brain in these patients [4, 26]. The younger the age, the higher is the incidence of seizures and subsequent epilepsy [4]. Moreover, the frequency of SE after cerebral infection in children can be 3-fold higher than adults, thus contributing to the higher incidence and prevalence of epilepsy in this vulnerable group [5, 78]. In addition, many studies had found that the occurrence of meningitis at early-life is associated with mesial temporal sclerosis and chronic epilepsy [33, 79, 80], especially before the age of 4 years; authors have proposed that mesial temporal region is generally vulnerable and more sensitive to epileptogenic

damage at a young age; while at an older age, the region is more mature and thereby more resistant to damage [31].

Repetitive seizures and status epileptics

In TBM patients, the occurrence of repetitive seizures despite adequate and appropriate medical management is associated with a higher incidence of structural abnormalities and an increased risk of chronic epilepsy [68]. Furthermore, recurrent seizures increase the permeability of BBB and intensify neuroinflammation resulting in severe neuronal injury and gliosis. These changes contribute to epileptogenesis and chronic epilepsy. SE is also a common life-threatening condition in TBM and is associated with increased risk of mortality, disability, and epilepsy [5, 65, 71, 81], especially in developing countries [5, 34, 82]. The role of inflammation in the pathogenesis of epilepsy and seizure-induced brain injury has been recently confirmed by many studies [83, 84]. SE itself provokes brain inflammation resulting in an increased tendency for seizures, severe brain injury, thus constitute a major risk for chronic epilepsy [44, 85]. It is estimated that SE has a 3-fold higher risk of acquired epilepsy compared with a single self-limited seizure [86]. Kim and colleagues had found that SE was the only significant clinical predictor of drug-resistance epilepsy at long-term follow-up [22].

Tuberculoma

Tuberculomas can occur at any age and can be either single or multiple, with the incidence being higher in pediatrics [87]. Parenchymal invasion in TBM followed by the development of tuberculoma(s) may induce chronic epilepsy with a latency period [88, 89], especially in HIV positive patients [90]. Bahemuka, M. et al. also has found that CNS tuberculoma was associated with refractory epilepsy [91]. In a study included 93 TBM patients with tuberculomas, seizures occurred in 22 (23.6%) patients, and out of 63 followed patients, 35% had concomitant epilepsy [92].

Infarction

In most of the reported studies, the frequency of stroke in TBM varied from 20 to 66% [93–97]. The strokes associated with TBM are often ischemic and multifocal [96, 97]. These infarcts usually occur in areas supplied by the deep penetrating arteries such as internal capsules, basal ganglia, and thalamus, but infarctions in the cortical and subcortical regions are not uncommon [94, 96, 97]. However, many studies had reported that cortical and subcortical infarctions were more likely to induce convulsions compared to other regions [48, 67]. Furthermore, cerebral infarctions tend to occur more commonly in children and more frequently result in generalized seizures rather than focal seizures [4]. A recently conducted study has detected infarction in 39% of TBM patients, seizures had occurred in half of them, with only cortical and subcortical infarctions were significantly associated with seizure induction [48].

Hippocampal sclerosis

The involvement of mesial temporal lobe during CNS infection is common and has been reported in 64.3% of epilepsy patients after surgery [98]. In a study, hippocampal sclerosis was confirmed in most of the cases (76.5%) with repetitive seizures or SE during the acute phase of encephalitis [99]. In a recent study, hippocampal sclerosis alone was reported in 30% of patients with chronic epilepsy as a sequel of TBM; while hippocampal sclerosis in combination with encephalomalacia was detected in 65% of the cases; with a latency period ranges from 5.3 to 6.5 years [88]. Therefore, hippocampal sclerosis could function as a prognostic factor for CNS infection-related epilepsy.

Epileptic activity on EEG

EEG is a valuable diagnostic tool for predicting further seizures following a first-unprovoked seizure [22]. EEG has been found to have a role in assessing the gravity of lesions and even to help in predicting the outcomes [100]. Focal spikes on EEG are more often associated with brain abnormalities that may induce recurrent seizures and chronic epilepsy [4]. Gunawan et al. have found a strong correlation between clinical seizures and EEG abnormalities; this study has also reported that EEG can be used to detect seizure activity and assess the risk of epilepsy in patients with TBM [30]. Therefore, a severe and persistent epileptic activity on EEG may predict recurrent seizures and chronic epilepsy.

Treatment

Early treatment of TBM with appropriate anti-TB drugs could reduce complications such as infarction, tuberculoma, or hydrocephalus; thereby decrease the incidence of late-onset seizures and acquired epilepsy. Beside the recommended anti-TB treatment and restoring internal homeostasis, TBM patients with seizures are in need of either short or long-term antiepileptic drugs (AEDs). After the first acute seizure, patients with TBM commonly experience recurrent seizure attacks unless treated with AEDs prophylaxis; or in the acute phase with benzodiazepines, then phenytoin/ fosphenytoin and subsequent maintenance therapy. Many epidemiological studies concluded that regardless of the etiology of seizure, the number of seizures occurring before adequate treatment is a paramount prognostic factor for predicting the patients' response to AEDs. Therefore, early treatment with AEDs is crucial and may significantly reduce the risk of chronic epilepsy following TBM infection [101–103].

Valproic acid and Levetiracetam are commonly used alternative agents [104–106], and AEDs use may be continued for a period of 3 to 6 months if the risk of

recurrence is relatively high [107]. However, it is suggested to withhold Valproic acid use in TBM patients if possible due to the increased risk of hepatotoxicity [13]. The treatment of post-TBM epilepsy is usually similar to other symptomatic epilepsies. The choice of AED should be based on the seizure semiology [5]. But, drug interactions must always be considered in each individual case, as it may lead to either decreased efficacy or toxicity.

Since seizure generation is associated with an inflammatory response, the use of anti-inflammatory agents may reduce or suppress seizures [5]. A Cochrane meta-analysis has also concluded that adding 6–8 weeks' course of steroids may reduce TBM complications, including seizures, and improve the outcomes [108]. Moreover, neuroimaging is warranted in all cases to guide treatment, monitor progress, and assess the need for further intervention. Physicians should also be aware that although fluoroquinolones are a good alternative for the current anti-TB medications, they are known to exacerbate seizures and should be avoided in TBM patients with documented seizures [109]. A recently published meta-analysis has reported similar findings [46].

Prognosis

Although very limited data regarding the prognosis of TBM patients presented with seizures is available so far, seizure occurrence has been considered as a significant predictor of mortality [110], especially in children and HIV-positive patients [40, 111]. Seizures increase the burden of disability among TBM patients and produce neurological deficits, thereby, increase the mortality and require a long-term antiepileptic treatment [110]. TBM Patients with seizures often have a worse prognosis relative to those without seizures [70]. A study from India found that TBM patients presented with seizures had a 2-fold increased risk of subsequent mechanical ventilation, and high mortality compared to those without seizures [112]. Another study included 478 TBM patients, has found that new-onset seizures were associated with a 4-fold risk of death and neurological disability [113]; many other studies had also reported relatively similar findings [21, 70, 114].

TBM related seizures are more likely to associate with a better prognosis compared with viral encephalitis-induced seizures. Patients with viral encephalitis are approximately 16-fold more likely to develop chronic epilepsy relative to the general population [115]. Furthermore, it is estimated that up to 60% of patients with viral encephalitis continue to have recurrent seizures and epilepsy [116] compared to around 20% of those with TBM [117–119]. Regardless of the etiology, aggressive control of clinical and subclinical seizures, especially prolonged or repetitive ones such as SE, is the mainstay approach that may improve the therapeutic outcomes and prevent the development of chronic epilepsy in patients with TBM.

Conclusion

Seizures are a common finding in patients with TBM, and can occur at any time point of the disease course, especially in children. Neuroinflammation, diffuse brain injury, reactive gliosis, and mass effect contribute to the pathogenesis of seizures in TBM. The early-onset seizures in TBM patients may be attributed to meningeal irritation and cerebral oedema; while, the late seizures are usually associated with infarction, hydrocephalus, tuberculoma, and paradoxical response. Seizures in TBM are plonic seizures based on the underlying pathologies. The patient's age, repetitive seizures and SE, tuberculoma, infarction, hippocampal sclerosis, and persistent epileptic activity were reported to associate with increased risk of chronic epilepsy following TBM infection. Therefore, adequate treatment of TB infection along with early identification and management of seizures and other complications may reduce the risk of developing chronic epilepsy and improve the overall outcome in TBM patients.

Abbreviations

AEDs: Antiepileptic drugs; BBB: Blood-brain barrier; CNS: Central nervous system; CSF: Cerebrospinal fluid; EEG: Electroencephalography; GTCS: Generalized tonic clonic seizures; HIV: Human immunodeficiency virus; ICP: Intracranial pressure; MRI: Magnetic resonance imaging; SE: Status epileptics; TB: Tuberculosis; TBM: Tuberculous meningitis

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Authors' contributions

AMTA: made substantial contributions to the conception and content of the study, drafted and revised the manuscript, read and approved the final manuscript. JML: drafted and revised the manuscript, read and approved the final manuscript. DZ: made substantial contributions to the conception and content of the study, revised the manuscript, read and approved the final manuscript.

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Competing interests

The authors declare that they have no competing interest.

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