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Letter to the Editor

Only in Definitive TBI According to the Marais Criteria can Differences Between Patients with and without Seizures be Reliably Assessed

[1] Sounira Mehri, [2] Josef Finsterer

[1] Laboratory of "Nutrition - Functional Food & Health", Faculty of Medicine, University of Monastir, Tunisia
[2] Neurology Department, Neurology & Neurophysiology Center, Vienna, Austria

Corresponding Author: **Josef Finsterer**

Letter to the Editor

We read with interest the article by Zulkifli *et al*. on a retrospective observational cohort study comparing the prevalence, risk factors, and treatment outcomes of 96 patients with tuberculous meningitis (TBM) with and without seizures [1]. Seizures (predominantly generalized) occurred in almost one-third of the patients. These patients more frequently exhibited a low Glasgow Coma Scale score, behavioral changes, focal neurological deficits, antiepileptic drug use, poor functional outcomes, and higher mortality compared to patients without seizures [1]. The study is interesting, but some uncertainties remain.

First, it was a retrospective study [1]. Retrospective studies have several limitations. These include low data quality, missing data, the inability to prove causality (only associations), susceptibility to memory and selection biases, difficulties in controlling confounding factors and a generally lower level of evidence compared to prospective studies [2].

The second point concerns current medication, which was not considered in the analysis [1]. Since various medications can trigger seizures, it is essential to record the number and type of medications that the included patients regularly took. Medications known to trigger seizures include bupropion, tramadol, tricyclic antidepressants, first-generation antihistamines (e.g., diphenhydramine), certain antibiotics (penicillin, cephalosporins), and stimulants such as amphetamines.

The third point concerns whether the cerebral computed tomography (CCT) or magnetic resonance imaging (MRI) was performed with or without contrast [1]. This information is crucial because meningitis may only be detectable with contrast. Furthermore, since one of the Marais criteria [3] is basal meningeal contrast enhancement, it must be ensured that all patients actually received contrast. Likewise, angiography is essential, as tuberculous meningitis can be complicated by cerebral vasculitis.

Since ischemic stroke is another feature of the Marais diagnostic criteria [3] and stroke is most reliably confirmed by MRI, it is conceivable that typical imaging features of TBM were missed in patients with TBM who only underwent CCT.

Fourth, it was not reported whether the seizures were well or poorly controlled with phenytoin, valproic acid, and levetiracetam [1]. Since treatment success in patients with TBM and seizures depends not only on the efficacy of antituberculosis therapy but also on the quality of seizure control, it is important to include this factor in the risk assessment.

Fifth, Table 1 lists one patient with a generalized seizure in the cohort of TBM patients without seizures [1]. This is inconsistent and requires clarification. It is also unclear why the number of patients in Table 1 corresponds to the number of patients without seizures (n = 67). This needs to be clarified.

The sixth point concerns patients with seizures, of whom only 46% had an electroencephalogram (EEG) [1]. To assess seizure types and the quality of seizure control, as well as to rule out non-convulsive status epilepticus, particularly in patients with behavioral abnormalities, an EEG recording would have been essential for all patients, at least those with seizures.

The seventh point concerns the number of included patients with confirmed, probable, or possible TBM according to the Marias criteria [1]. Since cerebrospinal fluid (CSF) culture was performed in only one patient in the seizure group and only two patients in the non-seizure group, since the TB PCR was positive in only 8 of 29 patients in the seizure group and in 9 of 67 patients in the non-seizure group, and since the GeneXpert test was positive in only 3 of 29 and 2 of 67 patients in the seizure and non-seizure groups, respectively, the number of patients with confirmed TBM is likely small, which calls into question the reliability of the presented data.

In summary, differences in prevalence, risk factors, and course of TBM patients with and without seizures can only be reliably assessed in patients with confirmed TBI. The classification of patients with TBM according to the Marias criteria requires

extensive clinical, cerebrospinal fluid, EEG and imaging studies to accurately assign patients with TBM to one of the three diagnostic categories.

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