A case report of acute Marchiafava-Bignami disease: a rare clinical entity in chronic alcoholism
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ABSTRACT
Marchiafava-Bignami disease (MBD) is a rare neurological disease often associated with a chronic consumption of alcohol and malnutrition, which is characterized by a demyelination and necrosis of the corpus callosum. We present a case of a 21-year-old male with chronic alcoholism who presented with an acute altered sensorium and seizure, which were initially treated as meningoencephalitis. His persistent poor Glasgow coma scale score and ideomotor recovery with encephalitic changes on his electroencephalogram prompted urgent magnetic resonance imaging (MRI) of his brain, which revealed extensive symmetrical hyperintensities in the corpus callosum. The diagnosis of MBD was made because of the typical MRI findings and after the exclusion of other possible diagnosis. The patient was promptly treated with a parenteral thiamine and showed a good recovery at 3 months follow-up. This case highlights the importance of diagnosing and recognizing MBD in a patient with chronic alcoholism as prompt treatment could prevent irreversible damage, which could carry high morbidity.

KEYWORDS alcoholics, case reports, corpus callosum, magnetic resonance imaging, Marchiafava-Bignami disease, Wernicke encephalopathy

CASE REPORT
We present a case of a 21-year-old Indian man with a 4-year history of alcohol abuse (average 30 standard units of alcohol/week for the past 2 years). He presented acutely with a history of altered sensorium with reduced consciousness, generalized tonic-clonic
seizures, fever, and vomiting following an episode of binge drinking. The patient was unemployed and lived with his friends in a rented house, while his family lived in a different state. His family was unaware of his drinking behavior, and his friends admitted that he had financial problems. On presentation to the emergency department, his Glasgow coma scale (GCS) score was 8 (E2 V2 M4). However, he showed no signs of meningeal irritation, had no documented fever, and had relatively normal vital signs. His pupils were normal and reactive to light. His examination revealed bilateral upper motor neuron signs in the upper and lower limbs. The patient was intubated for airway protection, given his low GCS score, and subsequently ventilated in the intensive care unit (ICU). His initial non-contrasted computed tomography (CT) of the brain was normal with the cerebrospinal fluid (CSF) showing no evidence of pleocytosis or elevated protein levels. Despite the relatively normal initial blood test and CSF results, the patient was treated for acute meningoencephalitis and Wernicke encephalopathy.

He received an infusion of thiamine 100 mg three times daily, and empirical intravenous antibiotics and an antiviral (ceftriaxone 2 g twice daily and acyclovir 500 mg three times daily). The patient’s stay in the ICU was uneventful, and he was extubated after 3 days. However, the patient showed evidence of residual neurological deficits with a poor GCS recovery, mutism, blank stares, inability to obey a command, and persistent bilateral upper motor neuron signs. His laboratory tests for thyroid function, B12, folate, retroviral screening, ceruloplasmin level, and connective tissue disease screening were within normal limits with no organism growth obtained from either CSF or blood cultures. His repeated contrasted CT of the brain after 72 hours post-extubation showed no evidence of meningeal enhancement. An electroencephalogram (EEG) was subsequently performed and showed generalized cerebral disturbances with 5–6 c/s theta activities and no alpha rhythm (Figure 1). Because of the EEG findings, we proceeded to perform magnetic resonance imaging (MRI) of the brain (Figure 2). His MRI showed bilateral symmetrical white matter T2 hyperintensities with restricted diffusion on apparent diffusion coefficient-diffusion-weighted imaging (ADC-DWI) over the corpus callosum (body and splenium) that extended to both frontal-occipital-parietal regions and the caudate nucleus. The lesions spared the thalamus, cerebellum, pons, and subcortical region. The diagnosis of MBD was made because of the typical distribution of the findings on the MRI.

The patient was continued on oral thiamine 100 mg once daily, oral vitamin B12 500 mcg once daily, and oral folate 5 mg once daily. He was discharged after 3 weeks of hospitalization, but with only mild improvement regarding speech and ideomotor performance. He showed a marked improvement within 4 weeks when he could obey commands and be independent with daily activities at the follow-up. However, he continued to have a limitation regarding speech with emotional

Figure 1. Electroencephalogram (EEG) of the patient showing generalized cerebral disturbances with 5–6 c/s theta waves and no alpha rhythm
lability. He received counseling on nutritional requirements and alcohol cessation during this stage. Subsequently, he had full neurological recovery at 3 months follow-up and no longer consumes alcohol.

**DISCUSSION**

This case highlights the importance of the prompt recognition and treatment of a potentially fatal, albeit reversible condition in a patient with chronic alcoholism. MBD is a rare demyelinating disease characterized by necrosis of the corpus callosum. It occurs as a complication of chronic alcoholism and malnutrition with a poorly understood etiology.¹,⁴ In our case, MBD was suspected because of a poor GCS score, and speech, ideomotor, and neurophysiological symptoms that may be suggestive of interhemispheric disconnection with encephalopathy changes on EEG despite the institution of appropriate initial treatment. Persistent encephalitic changes prompted a brain MRI after two normal CT brain findings, which showed the characteristic features of MBD, i.e., extensive involvement of the corpus callosum with the relative sparing of subcortical and brain stem structures. However, MBD must be differentiated from other mimics by careful assessment of clinical and radiological findings. Wernicke’s encephalopathy (WE), commonly also seen in individuals with chronic alcoholism, usually presents with less severe signs and symptoms of altered cognition or consciousness and with faster recovery. Furthermore, the MRI findings in WE usually shows symmetrical lesions in the thalamus and brainstem.⁵ WE is also commonly seen associated with a nutritional deficiency and anemia that are not prominent in this patient. Also, multiple sclerosis (MS) could mimic this condition, especially in young patients with no history of alcohol intake. However, MS usually presents with a relapsing-remitting course with MRI lesions that are relatively small and confined to the periventricular white matter with relative sparing of the corpus callosum.⁶ Paraneoplastic, e.g., limbic encephalitis, might present similarly; however, the CSF would exhibit elevated protein with pleocytosis.⁷ This patient’s CSF was normal, and his MRI findings were not suggestive of either paraneoplastic syndrome or MS. Other demyelinating diseases need to be excluded in the differential diagnosis with the use of neuroimaging in particular MRI. For example, central pontine myelinolysis⁸ with lesions confined to the pons, Morel’s laminar sclerosis in which the MRI shows diffuse cortical lesions,⁹ and progressive demyelinating multifocal leukoencephalopathy with the MRI showing non-symmetrical subcortical white matter lesions.¹⁰

![Figure 2. Brain MRI examination of the patient with Marchiafava-Bignami disease. T2-weighted imaging showing hyperintensities in (a) the frontoparietal region, (b) the caudate nucleus and the corpus callosum, and (c) over the corpus callosum (body and splenium) (arrowhead). T2 fluid-attenuated inversion recovery images showing hyperintensities in (d) the frontoparietal region and (e) the caudate nucleus and the corpus callosum (arrowhead). Diffusion-weighted imaging (DWI) showing restricted diffusion over (f) the frontoparietal region and (g) the caudate nucleus and the corpus callosum (arrowhead).](image-url)
The underlying pathophysiology in MBD remains unknown. Studies have shown that high consumption of alcohol leads to ethanol-induced neurotoxicity with vitamin B deficiency, especially thiamine, which interrupts myelin production. Furthermore, thiamine deficiency may lead to further alteration in neurotransmitter synthesis, such as reducing the production of acetylcholine, glutamate, and aspartate while increasing the dopamine level, which may contribute to the neurophysiological symptoms. Although it was postulated that vitamin B deficiencies were due to an ethanol toxicity, cases were also seen among patients without alcohol abuse, after chemotherapy, with sickle cell disease and Plasmodium falciparum co-infection, and with carbon monoxide poisoning. These metabolic disturbances in these relatively immunosuppressed patients predisposed them to cytotoxic edema, which leads to demyelinating and degenerative changes, mainly in the corpus callosum. The corpus callosum is the most extensive commissural fiber system and has a relatively high myelin content, although extra-callosal changes could occur in more severe condition. Moreover, in our case, the patient is relatively young to have an alcohol-related complication that may suggest other contributing factors, such as insufficient dietary intake of thiamine. A report had shown that a deficiency in thiamine might predispose individuals to complications, in particular, WE, even if the deficiency is of a short duration of time. This deficiency occurs due to the increased thiamine requirement because of the high carbohydrate intake (alcohol) as the body could only store around 30 to 50 mg of thiamine.

MBD can be classified into two subtypes, type A and type B, based on clinical and neuroradiological findings. The type A subtype, which carries a poorer prognosis, is characterized by an acute to subacute onset of an altered level of consciousness, language, and cognitive deficits, and memory impairment. It is accompanied by the presence of seizures, hemispheric disconnection signs, and pyramidal tract signs with the MRI findings showing edema of the entire corpus callosum and frequently extra-callosal involvement. Patients may also present with a prodromal stage of neuropsychiatric symptoms and gait disturbances, which may be mistaken for alcohol consumption or intoxication. Type B, on the other hand, has a more insidious to chronic onset. It carries a relatively better prognosis when patients manifest with a slight impairment in consciousness with gait disturbances, dysarthria, and signs of interhemispheric disconnection. The MRI brain findings (T2-weighted) in these patients are characterized by partial involvement of the corpus callosum with extra-callosal involvements being less frequently seen. However, a few documented cases showed the progression of symptoms with deterioration in consciousness and neuroimaging, which support the notion that type B may progress into type A. In our case, the patient presented acutely with an extensive involvement in both the corpus callosum and extra-callosal involvement, which may suggest the subtype with a poorer prognosis (type A).

Management of MBD has proven to be challenging with variable results. First-line early treatment with thiamine may translate to better outcomes as MBD may be associated with WE in 15% to 20% of patients. A recent review demonstrated the complete recovery in 15.4% of patients with alcohol-related MBD compared with those with 43.5% of those with a non-alcoholic etiology. Other treatment options include corticosteroids; however, their usage remains controversial. Previous reports showed improvement in symptoms for their ability to reduce brain edema and suppress inflammation and demyelination. Nevertheless, a recent review paper did not observe any net benefit, although no adverse effects were reported. The prognosis of this condition is highly variable. It depends on the extent and location of the lesions on the MRI and the concomitant presentation of a mimic, in particular, WE, coupled potentially with the timing of thiamine administration. A study showed that patient with an early treatment of thiamine, non-alcoholics and patient with DWI images demonstrates splenial lesions (typical findings of WE in subjects with MBD) carries a better prognosis. The interesting aspect of our patient was despite the extensive involvement on MRI, he ashowed marked improvement upon follow-up. The development of an early recovery emphasized the importance of early treatment with thiamine in all patients with alcoholism to halt the demyelinating process plus possible concomitant WE at his presentation, which further translates into a better recovery. Furthermore, an early rehabilitation with both alcohol and nutritional counseling should be the cornerstone in the management of patients with alcoholism to avoid recurrence and aid in recovery.
In conclusion, MBD is a potentially reversible condition if prompt action and awareness among clinicians, especially in recognizing its clinical features with the careful exclusion of mimics coupled with the early use of MRI to establish the diagnosis and make a prognosis. Although commonly seen in patients with a history of alcohol abuse, patients who are malnourished due to other illnesses without a drinking history are also susceptible to this illness and must be timely diagnosed to prevent irreversible damage.

Conflict of Interest
The authors affirm no conflict of interest in this study.

Acknowledgment
We would like to thank the patient for his consent to this case report publication and Director General of Health Malaysia for permission in publishing this case report.

Funding Sources
None.

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