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A Rare Case of Marchiafava-Bignami Disease Mimicking as Wernicke's Encephalopathy

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ABSTRACT

Aim: This case report aims to highlight the diagnostic challenges and management of Marchiafava-Bignami Disease (MBD) in alcohol-dependent patients, emphasizing the role of MRI in differentiating MBD from Wernicke's Encephalopathy (WE) and the importance of early, high-dose thiamine supplementation for improved outcomes. **Introduction:** Marchiafava-Bignami Disease (MBD) is a rare neurological disorder characterized by demyelination and necrosis of the corpus callosum, often associated with chronic alcohol use and malnutrition. First described in 1903, MBD typically presents with nonspecific symptoms such as confusion, ataxia, and cognitive deficits, making it difficult to distinguish from other alcohol-related conditions like Wernicke's Encephalopathy (WE). Neuroimaging, particularly MRI, plays a pivotal role in diagnosing MBD by revealing characteristic lesions in the corpus callosum. Early intervention with high-dose thiamine and supportive care is critical for improving patient outcomes. **Materials and Methods:** A 33-year-old male with chronic alcohol dependence presented with memory loss, diplopia, and ataxia. Initial tests revealed acute pancreatitis and elevated liver enzymes. Suspecting WE, standard thiamine was administered with limited improvement. Brain MRI was performed, revealing T2 hyperintensity in the corpus callosum, leading to an MBD diagnosis. Treatment was escalated to high-dose thiamine (1500 mg/day) and folic acid, alongside supportive care. **Results:** The patient demonstrated gradual clinical improvement within a week of high-dose thiamine and supportive care, achieving normal neurological function at follow-up. MRI findings, showing T2 hyperintensity in the corpus callosum, were crucial in confirming MBD and guiding effective treatment. **Conclusion:** MBD should be suspected in alcohol-dependent patients with unusual neurological symptoms, particularly if treatment fails. Early MRI diagnosis and aggressive thiamine supplementation are essential for positive outcomes, emphasizing the need for timely intervention and accurate diagnostic tools.

INTRODUCTION

Marchiafava-Bignami Disease (MBD) is a rare, yet significant, neurological disorder characterized by toxic, demyelinating, and necrotic lesions primarily affecting the corpus callosum, a crucial structure that connects the left and right cerebral hemispheres [1]. First described by Italian pathologists Ettore Marchiafava and Amico Bignami in 1903, the disease was initially observed in alcohol-dependent patients who presented with symptoms such as seizures, coma, and altered mental status, often followed by the discovery of necrotic lesions in the corpus callosum upon autopsy [2]. While traditionally linked to chronic alcohol consumption, MBD can also occur in individuals without a history of alcohol use,particularly in those who are chronically malnourished [3], such patients with diabetes, after gastric bypass surgery, or in other conditions like sepsis, cerebral malaria, and sickle cell disease. The disease primarily affects middle-aged men, possibly due to the higher incidence of alcohol-related brain damage in this population [4,5].

The exact etiology of MBD remains unclear but is believed to stem from a combination of alcohol-induced neurotoxicity, nutritional deficiencies (especially thiamine, B1), and oxidative stress. Alcohol-induced neurotoxicity leads to an impaired ability of the body to absorb and utilize essential vitamins, particularly B-vitamins, that are necessary for brain function. Thiamine deficiency, in particular, is a central factor in the development of MBD as it affects carbohydrate metabolism, resulting in impaired energy production and subsequent neuronal damage [6].

MBD is considered a progressive condition, and its clinical presentation can vary significantly depending on the severity and location of the brain lesions. Common symptoms include confusion, ataxia, dysarthria, spasticity, and, in severe cases, delirium, coma, and death. The disease can be categorized into acute, subacute, or chronic phases, with varying degrees of severity [7]. Neuroimaging, particularly magnetic resonance imaging (MRI), plays a crucial role in diagnosis. The hallmark of MBD on MRI is symmetric lesions in the corpus callosum, which may show edematous changes in the early stages and later progress to atrophy and cystic transformation if left untreated [8,9]. In some cases, the lesions extend beyond the corpus callosum, affecting other regions of the brain such as the subcortical areas, basal ganglia, and cerebral white matter. These extensive lesions are often associated with a poor prognosis, underscoring the importance of early detection and intervention [9].

The pathophysiology of MBD remains an area of ongoing investigation. However, several key mechanisms have been proposed. Ethanol itself is thought to contribute to the development of MBD through a combination of direct neurotoxicity and impairment of myelin synthesis. Chronic alcohol consumption results in oxidative stress, mitochondrial dysfunction, and damage to the blood-brain barrier. This process leads to cytotoxic edema, which initially affects the corpus callosum due to its high myelin content. In the later stages, the damage progresses to focal demye-lination and necrosis. The loss of myelin in these regions disrupts the normal exchange of information between the hemispheres of the brain, contributing to the cognitive and motor deficits seen in patients with MBD [6,10].

Additionally, Thiamine deficiency plays a crucial role in the pathogenesis of Marchiafava-Bignami Disease (MBD). Thiamine is essential for carbohydrate metabolism, particularly in converting pyruvate to acetyl-CoA, a key step in ATP production. Insufficient thiamine impairs neuronal energy production, leading to oxidative stress and brain damage, especially in the myelin-rich corpus callosum. Thiamine deficiency also increases catecholamine activation, contributing to psychiatric symptoms like delirium and hallucinations. While alcohol and thiamine deficiency are primary causes, MBD can also arise from non-alcohol-related conditions such as diabetic ketoacidosis, carbon monoxide poisoning, and sepsis. These conditions highlight that MBD can develop in various contexts involving malnutrition or metabolic disturbances [11].

The clinical presentation of Marchiafava-Bignami Disease (MBD) is often nonspecific, making diagnosis challenging, especially in the acute phase. In chronic alcohol users, these symptoms are frequently mistaken for other alcohol-related disorders like 's encephalopathy due to overlapping features such as confusion, ataxia, and ophthalmoplegia. As MBD progresses, patients may develop cognitive deficits, dem-entia, and signs of interhemispheric disconnection, such as apraxia and abnormal gait [12].

Neuroimaging, especially MRI, is crucial for diagnosing Marchiafava-Bignami Disease (MBD). Typical findings include symmetric lesions in the corpus callosum, visible as edema with increased signal intensity on T2-weighted and diffusion-weighted imaging (DWI) in early stages. Over time, lesions may resolve or lead to permanent myelin damage, atrophy,and cystic changes. Advanced cases can involve other brain regions, resulting in severe neurological dysfunction and a poorer prognosis [13].

Treatment focuses on addressing underlying causes, such as alcohol cessation, nutritional support, and vitamin supplementation. Early thiamine (B1) supplementation is critical, often requiring high doses (e.g., 1500 mg/day) for optimal recovery. Folic acid and supportive care, including benzodiazepines for agitation and physical therapy, are also important [14].

Prognosis depends on the extent of brain damage, timing of diagnosis, and treatment effectiveness. Early intervention can lead to significant recovery, but extensive damage, particularly to cortical regions, often results in persistent neurological deficits or poor outcomes [9].

CASE DESCRIPTION

A 33-year-old male with a 25-year history of alcohol dependence presented with a one-week history of memory impairment, diplopia (double vision), and an unsteady gait. He had developed tremors and vomiting over the past two days. Upon clinical examination, the patient was conscious and oriented but exhibited decreased attention and impaired recent memory. Neurological examination revealed brisk reflexes, coarse tremors, and ataxia.

Blood tests indicated elevated total count, impaired liver function tests (LFT), and raised pancreatic enzymes, while an abdominal ultrasound confirmed the diagnosis of acute pancreatitis. In response to his symptoms, the patient was admitted and started on parenteral antibiotics and detoxification. Despite an ophthalmology evaluation that ruled out other causes of his diplopia, he developed agitation, visual hallucinations, and confused behavior after two days of hospitalization.

Given the clinical presentation, Wernicke's Encephalopathy (WE) was initially suspected and the patient was treated with the standard dose of parenteral thiamine. However, only mild improvement was observed. Further investigation with brain MRI revealed T2 hyperintensity in the corpus callosum, leading to a revised diagnosis of Marchiafava-Bignami Disease (MBD), a rare neurological disorder associated with chronic alcohol use.

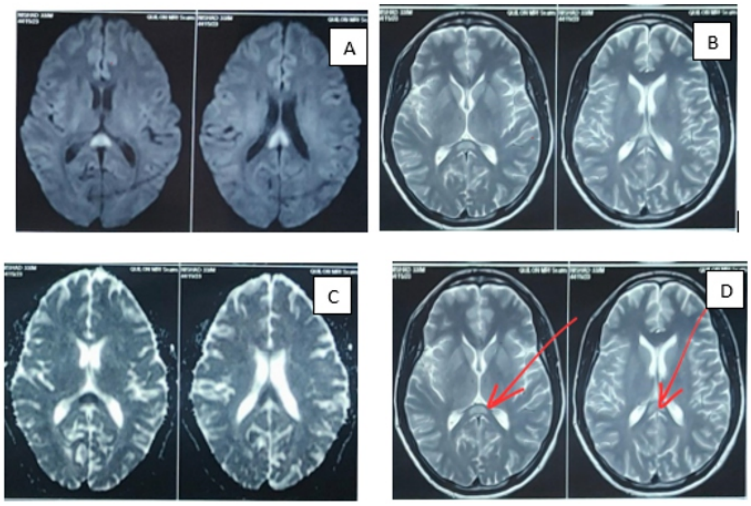

Figure 1: MRI Brain Imaging Showing T2 Hyperintensity in the Corpus Callosum: Diagnostic Hallmark of Marchiafava-Bignami Disease (MBD)

In response, the patient's thiamine dose was adjusted to 1500 mg/day, and folic acid was added to the treatment regimen. Benzodiazepines and other supportive measures were continued. Over the course of the following week, the patient demonstrated gradual clinical improvement. Upon discharge, he was switched to oral thiamine (300 mg/day) and followed up one month later, where he was clinically stable, abstinent from alcohol, and his neurological tests were normal.

This case underscores the importance of considering MBD in alcohol-dependent patients who present with symptoms such as ataxia, diplopia, and confusion, especially when initial diagnoses such as Wernicke's Encephalopathy fail to fully explain the clinical picture. MRI plays a crucial role in identifying MBD, which can lead to more effective treatment and better outcomes.

DISCUSSION

This case highlights a critical and often overlooked diagnosis in alcohol-dependent individuals Marchiafava-Bignami Disease (MBD), which should be considered when patients present with neurological symptoms that resemble other alcohol-related conditions like Wernicke's enceph alopathy (WE). The patient described here, a 33-year-old male with a long history of alcohol dependence, presented with an acute onset of memory impairment, diplopia, tremors, and unsteady gait, which evolved over the course of one week. Initial diagnosis suggested Wernicke's encep halopathy, given the patient's alcohol history and typical presentation of ataxia and confusion. However, the sub sequent lack of substantial improvement after standard thiamine treatment prompted further investigation, which revealed typical MRI findings of MBD, leading to a revision of the diagnosis.

In MBD, the onset of symptoms can vary, with cases presenting acutely, subacutely, or chronically. As seen in this patient, the acute form of MBD can include severe disturbances in consciousness, seizures, and limb hypertonia, while the subacute form may manifest as confusion, dysarthria, somnolence, and visual disturbances [15]. Our patient's presentation, characterized by cognitive impairment, visual disturbances (diplopia), and ataxia, aligns with the subacute form of MBD. The clinical signs, such as coarse tremors, ataxia, and cognitive deficits, reflect the typical progression of the disease, which can evolve rapidly if not promptly treated.

However, the nonspecific nature of MBD symptoms often leads to challenges in diagnosis, especially when other conditions like alcohol withdrawal syndrome, delirium, and encephalitis can present with similar signs and symptoms [16]. Early misdiagnosis is common, but it is crucial to differentiate MBD from conditions like WE or other alcohol-related disorders, which are also characterized by ataxia, ophthalmoplegia, and confusion. This is particularly important since treatment strategies, although overlapping in some cases, may differ in their specifics, particularly in the use of thiamine and other vitamins.

A key diagnostic tool in the identification of MBD is neuroimaging, specifically magnetic resonance imaging (MRI). MBD lesions are most commonly detected in the corpus callosum, with the hallmark feature being bilateral hyperintensities on T2-weighted imaging and diffusion-weighted imaging (DWI), particularly in the central part of the corpus callosum. As highlighted by several studies, MRI plays a pivotal role in diagnosing MBD, especially when other clinical features and conditions are not fully explanatory [10,17]. In our case, MRI revealed the characteristic T2 hyperintensity in the corpus callosum, which led to the correct diagnosis. Importantly, this finding, along with the patient's poor response to initial Wernicke's treatment, guided clinicians to reconsider the diagnosis. Additionally, the presence of extra-callosal lesions, such as those in the cerebral lobes and basal ganglia, can indicate more severe cases with a poorer prognosis [18].

The pathophysiology of MBD remains poorly understood but several hypotheses have been proposed. It is widely believed that alcohol-induced neurotoxicity, particularly

through mechanisms of oxidative stress and impaired blood-brain barrier integrity, plays a central role in the development of MBD. The corpus callosum is particularly vulnerable due to its high myelin content, making it susceptible to cytotoxic edema and subsequent demyelination and necrosis [19]. In this case, the patient's prolonged alcohol use, combined with his malnutrition and subsequent thiamine deficiency, likely contributed to the development of the lesions in the corpus callosum, manifesting clinically as ataxia, tremors, and cognitive deficits. This fits the hypothesis that the neurotoxic effects of alcohol combined with deficiencies in vital nutrients like thiamine result in significant brain injury, especially in structures with high metabolic demands like the corpus callosum .

Furthermore, the cortical lesions found in some patients are likely due to Morel's laminar sclerosis, which has been noted in postmortem studies and suggests a more extensive pathophysiological involvement in MBD, possibly linked to thiamine deficiency [20]. These cortical lesions may not directly be caused by alcohol toxicity but rather by a lack of thiamine, which impairs neuronal function and contributes to neural degeneration.

Treatment for MBD primarily involves the administration of thiamine, given its crucial role in neuronal energy metabolism. In this case, the patient's initial response to the standard dose of thiamine was minimal, prompting a significant dose escalation to 1500 mg/day, which resulted in clinical improvement. The addition of folic acid, along with continued supportive care, likely contributed to the patient's gradual recovery. This case supports the findings of other reports suggesting that high-dose thiamine, especially in patients with chronic alcohol use, may be necessary for optimal recovery [21].This aligns with current clinical practice, which emphasizes high-dose thiamine in cases of alcohol-related neurological disorders, particularly when MBD is suspected [22].

The prognosis for MBD varies significantly depending on the severity of the brain lesions, the timing of diagnosis, and the promptness of treatment. As noted in previous studies, patients with severe cognitive impairment and extra-callosal lesions tend to have a poor prognosis [23]. Conversely, those with limited damage confined to the corpus callosum may experience significant recovery if treated early [24]. In this case, the patient demonstrated significant improvement within a week of starting high-dose thiamine and supportive care, leading to normal neurological function at follow-up. This suggests that early and aggressive treatment can greatly improve outcomes for MBD, particularly when the disease is confined to the corpus callosum.

Given the overlap in clinical presentations, MBD must be differentiated from several other conditions. As discussed, Wernicke's encephalopathy is a major differential diagnosis, with both diseases presenting similarly in alcohol-dependent individuals. The key difference lies in the specific . neuroimaging findings: while WE typically affects the thalamus, mammillary bodies, and other deep brain structures, MBD presents with symmetric lesions in the corpus callosum [10,25]. Additionally, conditions such as pontine myelinolysis and multiple sclerosis must also be considered in the differential diagnosis, though MBD's characteristic MRI findings and clinical course help distinguish it from these disorders [26].

This case, while informative, does have limitations inherent to single-center reports and small sample sizes. The relatively small cohort limits the generalizability of the findings, and further studies with larger populations are needed to better understand the full spectrum of MBD's clinical manifestations and long-term outcomes. Additio nally, while the clinical features of MBD are well-described in the literature, further research into the exact patho physiological mechanisms remains necessary to fully elucidate the disease process.

CONCLUSION

This case underscores the importance of considering Marchiafava-Bignami Disease in alcohol-dependent patients who present with atypical neurological symptoms such as ataxia, diplopia, and confusion, especially when initial diagnoses like Wernicke's encephalopathy fail to fully explain the clinical picture. High-dose thiamine, along with other supportive measures, remains the cornerstone of treatment, and early intervention can lead to favorable outcomes. MRI plays a crucial role in confirming the diagnosis and guiding management, and should be consi dered in any alcohol-dependent patient with neuro logical symptoms that do not resolve with conv-entional treatment for other alcohol-related diseases.

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