

Marchiafava - Bignami Disease – A Case Report and a Brief Review of Literature

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Abstract: *Marchiafava - Bignami disease (MBD) is a rare neurological disorder of chronic alcoholism characterized by demyelination and necrosis of corpus callosum. Here, we report the case of an alcoholic patient with highly suspicious Marchiafava - Bignami disease who developed acute neurological dysfunction and showed characteristic abnormalities in the corpus callosum on the brain MRI. A recent advance in neuroimaging has made early diagnosis of MBD possible and helps in early initiation of treatment.*

Keywords: Marchiafava - Bignami disease, Alcoholism, Corpus callosum, Sandwich sign

1. Introduction

Alcohol misuse and alcohol withdrawal are associated with a variety of neuropsychiatric syndromes, some of which are associated with significant morbidity and mortality. Marchiafava-Bignami disease is a rare neurological disease related to chronic and heavy alcohol consumption and malnutrition, and is characterized by primary demyelination and necrosis of the central part of the corpus callosum¹. Although nutritional deficiencies have been suspected, the cause is still unknown. It is a radiological diagnosis as clinical features are variable and non-specific². Over 90% of the patients with MBD exhibited a poor prognosis³. We report a case of Marchiafava-Bignami disease who had history of chronic alcoholism, different clinical presentation and MRI findings consistent with the diagnosis. Initially diagnosis of coma was unclear and only discovered with MRI and made a good recovery during hospitalization.

2. Case Report

A 50-year-old male patient presented to emergency department with the complaints of altered sensorium followed by loss of consciousness since one day. The patient then developed complex partial seizures involving left side of the body. He had history of chronic alcohol intake for about 25 years. He used to take around 1 litre (1000 ml) of country made alcohol daily. There was no history of fever, headache, vomiting, head injury, and ear or nasal bleed.

On clinical examination, the patient was found to be malnourished. Neurological examination showed a Glasgow coma scale of E2M2V3. The oculo-cephalic reflex was normal. Signs of meningeal irritation including neck rigidity and kernig sign were absent. Pupils were of normal size and normal reacting to light. The fundus examination was normal. Motor examination revealed hypotonia in all 4 limbs with exaggerated deep tendon reflexes. Bilateral extensor plantar response was present. Further physical examination and review of other system was normal.

Laboratory evaluation revealed normal haematological profile (Hb-12.5 g/dl, TLC-6500/mm³, PLT-2,20,000 /mm³). Liver function test showed increased serum gamma glutomyl transpeptidase 60 (N:10-40), bilirubin 10 (N:0.2-1), alkaline phosphatase 970 (N:80-250), and alanine transaminase 90 (0-35). Vitamin B1 level was 20 ng/ml. Cerebrospinal fluid analysis showed normal cell count and biochemistry. Values for other blood tests (serum electrolytes, kidney functions and blood sugar levels) were within normal limits. ECG and chest x ray were normal. Electroencephalogram (EEG) showed bilateral diffuse slow-wave activity. CT scan of the brain, which was performed immediately on admission in the emergency department, showed no significant abnormalities.

M R imaging showed high signal intensity in T2WI and low signal intensity in T1WI in the central portion of genu, body and splenium of corpus callosum with relative sparing of dorsal and ventral layer which give characteristic Sandwich sign (fig-1, 2).

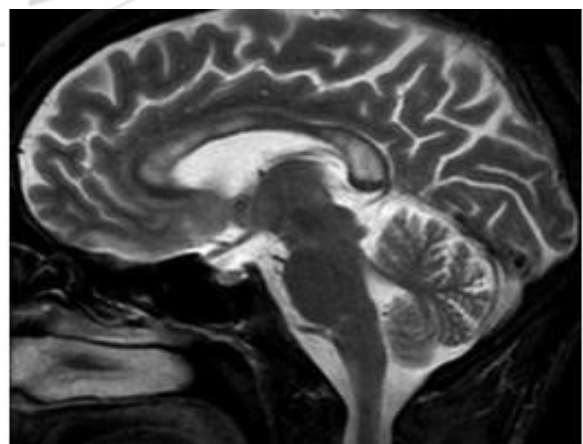


Figure 1: Sagittal T2-weighted image showed hyperintense signal in the central layer of corpus callosum with the sparing of the dorsal and ventral layers producing the ‘ sandwich sign’.

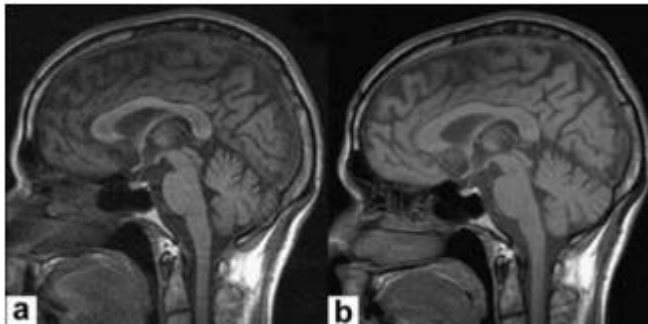


Figure 2: a) On sagittal T1- weighted image showed hypointense lesion. b) Non-enhance image after administration of contrast medium.

Corresponding region in FLAIR image show hyperintense rim and hypointense core suggestive of gliotic rim with central necrosis (fig-3, 4).

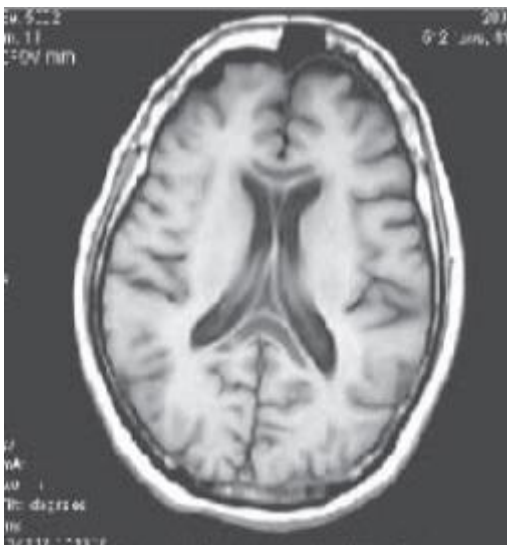


Figure 3: Axial T1 weighted M R image shows hypointense signal in the corpus callosum.

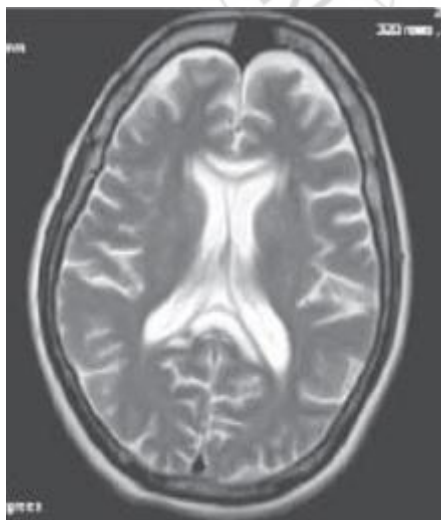


Figure 4: Axial T2 weighted M R image at the same level shows hyperintense signal in the corpus callosum.

On the basis of history, clinical features, and imaging studies, the diagnosis of Marchiafava-Bignami disease was made. However, other lesion involving corpus callosum like

multiple sclerosis, encephalitis, lymphoma, infarction, and astrocytoma were included in the differential diagnosis.

Patient was treated with intravenous B complex, oral folate, and with anticonvulsants (injectable phenytoin sodium). He also received intravenous corticosteroids (500 mg methylprednisolone) for 3 days, gradually tapered with oral and stopped over a period of 2 weeks.

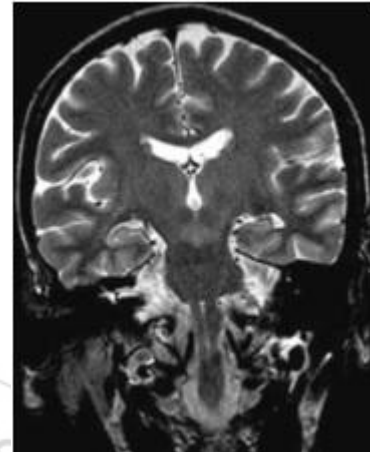


Figure 5: T2- weighted image (3 weeks following treatment) reveals complete resolution of the lesion.

Patient had marked clinical improvement with complete recovery over the next three weeks. T2- weighted images (fig-5) obtained three weeks after the treatment revealed complete resolution of imaging abnormalities. This case highlights the rare presentation of Marchiafava-Bignami disease with chronic alcoholism.

3. Discussion

The first case of MBD was described in 1898 by Carducci, in an alcoholic man who developed sudden seizures, loss of consciousness, coma and eventual death. Autopsy findings in this case revealed necrosis of corpus callosum. In 1903, Italian pathologists Marchiafava and Bignami reported similar findings in an autopsy series of three Italian wine drinkers who were found to have necrosis and cystic degeneration involving the middle layer of the corpus callosum⁴ Since then, over 200 cases of MBD have been reported in the literature⁵.

The disease is most frequently seen in middle-aged or elderly alcoholic males⁶. Most patients are male, between forty and sixty years of age and have a history of chronic alcoholism and malnutrition⁷. It is now known that Marchiafava - Bignami disease occurs worldwide and has been described in poorly nourished nondrinkers⁸. The underlying mechanism of the disease is still not understood. It is probably caused by the combination of alcohol abuse and malnutrition, leading to metabolic, toxic, and vascular disturbances⁹. The main pathologic changes seen in MBD include symmetrical demyelination and necrosis of the central part of the corpus callosum, with relative sparing of dorsal and ventral layers. Rarely, other structures of the CNS like optic chiasm and tracts, putamen, anterior commissure, cerebellar peduncles and, cortical gray matter and U fibers may be involved¹⁰.

There are no characteristic clinical presentations of Marchiafava-Bignami disease¹¹. Clinical clues for the disease are reduced consciousness, psychotic and emotional symptoms, depression and apathy, aggression, seizures, hemiparesis, ataxia, apraxia and frequently leading to coma and death. The course of the disease may be acute, subacute or chronic and may lead to death within weeks to months. Marchiafava-Bignami disease may present in various clinical forms¹².

Acute Marchiafava - Bignami disease includes seizures, impairment of consciousness, and rapid death. Subacute Marchiafava - Bignami disease includes variable degrees of mental confusion, dysarthria, behavioural abnormalities, memory deficits, signs of interhemispheric disconnection, and impairment of gait. Chronic Marchiafava - Bignami disease, which is less common, is characterized by mild dementia that is progressive over years¹³.

Diagnosis is made on the basis of clinical findings in combination with radiological imaging features. Diagnosis is now much easier with MRI imaging. Most patients presenting with the acute type of MBD will go into coma and eventually die, some survive¹⁴.

Diagnosis is made on the basis of clinical findings in combination with radiological imaging features. The corpus callosum appears hypoattenuated on CT, with the exception of cases that are characterized by subacute bleeding, in which it may be iso or hyperattenuated¹⁵.

MRI is currently the most sensitive diagnostic tool. Conventional MRI typically detects lesions as hyperintense on T2- phase and FLAIR signal intensity, and hypointense on T1-weighted images in the body of the corpus callosum, sometimes extending into the genu, and the splenium¹⁶. Mainly the central layers of the corpus callosum are affected, with sparing of the dorsal and ventral layers (sandwich sign on MRI). The entire corpus callosum is rarely involved. Similar lesions may also be found in the middle cerebellar peduncles and in the hemispheric white matter involving the centrum semiovale and extending, in some cases, into the adjacent convolutional white matter. These lesions usually do not have mass effect and may show peripheral contrast enhancement during the acute phase. As lesions become chronic, cystic lesions are likely to develop. Pathology may also be seen on diffusion-weighted imaging and ADC as areas of restricted diffusion. Greater the restriction, worst the prognosis. After a few months, signal intensity alterations become less evident but residual atrophy of the involved structure usually is present¹⁷.

Lesions show high signal intensity on DWI with reduced or increased apparent diffusion coefficient (ADC) values depending on the progression of the disease. In early stage, cytotoxic oedema may be the underlying mechanism where the lesions are seen as hyperintense on DWI with reduced ADC. In the later stages, increased ADC may be due to the pure demyelination without axonal injury¹⁸.

Other imaging modalities include MR spectroscopy (MRS) which shows increase in choline, increased choline/creatine (Cho/ Cr) ratio in acute phase. Lactate peak is usually seen

in the acute/subacute phase of demyelination. SPECT studies shows bilateral reduction in cerebral blood flow¹⁹. The recent clinical and neuroradiological classification of MBD describes two subtypes. Type A: acute to subacute onset of consciousness impairment, pyramidal tract signs, limb hypertonia, seizures, hyperintense swelling of the corpus callosum on T2weighted MR sequences and is associated with poor prognosis. Type B: normal or slightly impaired level of consciousness, dysarthria, gait disturbance, signs of interhemispheric disconnection and hyperintense lesions on T2-weighted MR sequences partially involving the corpus callosum. Type B has favourable prognosis and lesions may reverse suggesting an underlying oedema rather than demyelination²⁰.

Differential diagnosis includes infarction of recurrent artery of Heubner, neoplastic disease such as astrocytoma or lymphoma, demyelinating disease such as multiple sclerosis (MS), progressive multifocal leukoencephalopathy, or acute disseminated encephalomyelitis. MS is by far the most common and needs to be ruled out. Compared to MS, MBD has symmetric and oedematous spots restricted in corpus callosum on brain CT scans or MRI²¹.

No standardized treatment protocols have been established in MBD. Because the aetiology of the disease is uncertain, a specific therapy is not available. Cessation of alcohol intake is mandatory. However, most often patients are treated with thiamine, vitamin B-complex and folate, with good clinical recovery in many patients. Staszewski *et al.* treated a patient with thiamine, vitamin B-12 and folate and amantadine with improvement²². Seizures and coma are treated symptomatically. Clinical improvement has been documented using high dose of corticosteroids²³. The available evidence suggests that an effective and aggressive early treatment is often associated with marked clinical improvement. Early diagnosis and prompt appropriate management are critical in reversing the underlying pathophysiology in the early stage²⁴. Some patients survive for many years in a demented condition or occasionally even show partial or complete recovery. Patients who survive should stop alcohol consumption, receive rehabilitation and nutritional counselling.

4. Conclusion

MBD is considered a radiological and medical emergency and early recognition is critical for good clinical outcome. Marchiafava-Bignami disease is a complication of chronic alcoholism with various clinical manifestations which is often misdiagnosed and mistreated. But recent advance in neuroimaging has made early diagnosis of MBD possible & helps in early initiation of treatment. Recognition of the imaging features of MBD is essential for radiologist for proper diagnosis.

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