Marchiafava-Bignami Disease

S Raina*, DM Mahesh**, J Mahajan**, SS Kaushal***, D Gupta****, DS Dhiman+

Abstract
Marchiafava- Bignami disease is the symmetrical demyelination of the middle portion of the corpus callosum observed in people with chronic alcoholism. We report two male patients who had history of chronic alcoholism, different clinical presentation and MRI findings consistent with the diagnosis of Marchiafava- Bignami disease.©

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 (MBD) is a rare, alcohol associated disorder characterized by demyelination and necrosis of the corpus callosum.1 It is a radiological diagnosis as clinical features are variable and non-specific. 2 We report two cases of Marchiafava-Bignami disease who had history of chronic alcoholism, different clinical presentation and MRI findings consistent with the diagnosis. In the first case of a 35 year old male patient the diagnosis of the coma was initially unclear and only discovered with magnetic resonance imaging (MRI) and made a good recovery during hospitalization. In second case again the cause of progressively declining neurological functions was established by MRI. This patient is still in vegetative state seven months after the diagnosis.

CASE REPORT

Patient 1
A 35 year old right handed man with history of chronic alcohol abuse was admitted in medical ward with history of being found unconscious for two days. There was no history of fever, headache, vomiting, seizures, jaundice, head injury and ear or nasal bleed. Alcohol abuse was known for last 18 years and used to drink 1-2 litre of country made liquor a day. Neurologically, no significant past history was present. On admission, neurological examination showed a Glasgow Coma Scale of e2M2V4. The oculo-cephalic reflex was normal. Examination of cranial nerves showed normal pupillary size and reaction. The fundus examination was normal. Motor examination did not reveal any focal deficit. No meningeal signs were present. Further physical examination and review of other systems was normal. Laboratory results revealed normal biochemistry profile. CXR and ECG were normal. CSF studies were normal. Computer tomography (CT) of the brain, which was performed immediately on admission in the emergency department, showed no significant abnormalities. MRI brain on T2W and FLAIR images showed a high signal lesion in the body and splenium of corpus callosum (sandwich sign) with relative sparing of rostrum, genu and peripheries of body and splenium as seen on sagittal and axial view. T1W images revealed hypointensity in the same areas (Fig. 1). On apparent diffusion coefficient image (ADC) it is hypointense and hyperintense on diffusion weighted image (DWI) and these areas are showing restricted diffusion (Fig. 2). On the basis of history, clinical features and imaging studies the diagnosis of acute form of MBD was made. Patient was treated with thiamine and vitamin B complex with nutritious diet during hospitalization. At discharge he showed improvement in his consciousness, and there was residual right side hemiparesis with aphasia without cranial nerve involvement.

Patient 2
A 68 year old man with chronic alcoholism for 45 years presented with history of sudden onset right side hemiparesis of two days duration. Neurologically, no significant past history was present. Examination revealed right 7th supranuclear palsy with global aphasia in addition to features of right side UMN hemiparesis. Plain CT scan head in emergency was normal. Hemogram, biochemical profile, ECG, CXR was normal. He was managed with antiplatelets, statins, ACE inhibitors and physiotherapy. Patient showed marginal recovery in the form of improvement in weakness and was discharged after one week with the plan to get MRI done during followup. Two weeks later patient was readmitted in acute confusional state of three days duration. There was no history of seizures, fever, jaundice and trauma head. On examination patient was confused, disoriented and had focal neurological deficit in the form of right 7th
supranuclear palsy and right side UMN hemiparesis. No meningeal signs were present. Hemogram, biochemical profile, ECG, CXR was normal. MRI brain revealed multiple hyperintense areas on T2W images within the body of corpus callosum (Fig. 3) and bilateral centrum semiovale region. These hyperintense areas were hypointense on T1W and not suppressed on FLAIR sequences (Fig. 4). On DWI and ADC these areas are showing restricted diffusion. On post contrast scans no enhancement is seen in these areas. The patient was discharged in a vegetative state, which is still persisting for last seven months as observed during follow up.

**DISCUSSION**

Although first described by Carducci in 1898 in Italian red wine drinkers, it was in 1903, that the Italian pathologists Marchiafava and Bignami described a unique alteration of the corpus callosum in three alcoholic patients who died after having seizures and coma. The disease affects persons in middle and late adult life. With a few exceptions, the patients have been males and severe chronic alcoholics.1 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 disturbances.2 There are no characteristic clinical presentations of Marchiafava-Bignami disease. 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.3 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 forms.4

Acute Marchiafava-Bignami disease includes seizures, impairment of consciousness, and rapid death.

Subacute Marchiafava-Bignami disease includes variable degrees of mental confusion, dysarthria, behavioral 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 years.

Until recently, the definite diagnosis was confirmed at autopsy. However, in the era of modern imaging technology, diagnosis could be based on clinical profiles, history of alcoholism, and specific localisations of pathological lesions in the corpus callosum demonstrated by CT and MRI.4 The corpus callosum appears hypoattenuated on CT scans, with the exception of cases that are characterized by subacute bleeding, in which it may be iso-hyperattenuated.5 However, if callosal damage is mild or the lesion is small, it may not be
obvious and easily missed on CT, as in our patients. 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 splenium. 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 present.

The diagnosis of MBD rests mainly on evidence of these callosal lesions. The corpus callosum may also be affected in other diseases such as ischemic stroke, contusion, multiple sclerosis, and lymphoma. MBD, however, is distinguished from these disorders by the symmetry of the callosal lesions with relative sparing of thin upper and lower edges. Other neuropsychiatric conditions associated with chronic heavy drinking are: Wernicke's encephalopathy, Korsakoff's psychosis, alcoholic dementia, cerebellar degeneration, central pontine myelinolysis, alcoholic amytrophic, alcoholic pellagra encephalopathy and peripheral neuropathy.

Because the aetiology of the disease is uncertain, a specific therapy is not available. Cessation of alcohol intake is mandatory. Therapy with thiamine and vitamin B complex, including vitamin B-12 and folate, has been used in many patients who have recovered. However, identical therapy has been used in patients who did not recover. Seizures and coma are treated symptomatically. A favourable response has been reported after the use of corticosteroids in some cases.

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 counseling.

REFERENCES