Marchiafava-Bignami disease (MBD) is a rare neurological disorder associated with chronic, heavy alcohol consumption and/or malnutrition.

MBD was first described by two Italian pathologists who identified it in the autopsies of three patients who presented in status epilepticus and subsequently developed coma. Previously, the diagnosis could only be ascertained by autopsy. Today, neuroimaging, particularly magnetic resonance imaging (MRI) provides the opportunity for a reliable in vivo diagnosis. MBD is characterised by primary degeneration of the corpus callosum associated with chronic alcohol consumption. However, it can occur in patients who do not use alcohol. The main hypothesis for its pathogenesis is that the disease is a result of B vitamin deficiency.

MBD may present in various clinical forms. Acute MBD includes seizures, impairment of consciousness and rapid death. Subacute MBD includes variable degrees of mental confusion, dysarthria, behavioral abnormalities, memory deficits, signs of interhemispheric disconnection, and cerebellar signs. Chronic MBD is characterised by mild dementia that is progressive over years.

Below we report three cases of MBD. Each subject had a history of chronic alcoholism, different clinical presentations and MRI findings consistent with the diagnosis.

Case reports

CASE 1

A 50 year old male presented with confusion and unstable gait. The patient had a history of severe alcoholism with a high daily consumption of alcohol (35 cl/day, alcohol rate is 45%) over 30 years.
On admission, general examination showed a malnourished individual who was confused and disoriented with short- and long-term memory deficits. Examination of cranial nerves showed normal pupillary size and reaction. The fundus examination was normal. Motor examination revealed impaired motor coordination with a wide-based gait. No meningeal signs were present. Further physical examination and review of other systems was normal. Neuropsychological tests (NPT) revealed interhemispheric disconnection.

Laboratory results revealed normal haemogram and biochemical profile (gamma-glutamyl transferase: GGT=62 U/L, reference: 12-64), aspartate aminotransferase: AST=34 U/L, reference: 0-34), alanine aminotransferase: ALT=12 U/L, reference: 0-55). Serum albumin level was low (3.1 g/dl, reference: 3.5-5). Toxicology panel was negative. Serum B12 level was high (1000 pg/ml, reference: 214-914), because the test was carried out after a vitamin B12 injection.

Electrocardiography (ECG) and chest X-ray were normal. Brain MRI on T2W (Figure 1) and FLAIR (Figure 2) images showed a high signal lesion in the body and genu of the corpus callosum with relative sparing of the splenium and peripheries of the body and splenium.

On the basis of history, clinical features and imaging studies, the diagnosis of subacute MBD was made. The patient was treated with thiamine and vitamin B complex during hospitalisation. At discharge, he showed improvement in his consciousness and gait disturbance.

### CASE 2

A 64-year-old male known to be a chronic alcoholic (35 cl/day, alcohol rate is 45% and 1-2 beer/day, alcohol rate 5%) over 40 years presented with a history of fatigue and anorexia for three days. His family reported a lack of communication as well as excessive drowsiness. There was no history of fever, headache, vomiting, seizures, or head injury. Neurologically, no significant past history was present. There were no focal or lateralising neurological signs. He was confused and disoriented. He had a generalised tonic-clonic seizure in the emergency department and was taken to the Intensive Care Unit (ICU).

A diffusion-weighted MR image (DWI) obtained on admission showed a hyperintense lesion in the corpus callosum. In addition, subcortical and deep white matter lesions were observed in the bilateral fronto-parietal lobes on both DWI (Figure 3) and T2W images (Figure 4).

Laboratory test results revealed high levels of GGT and AST (GGT=105 U/L; AST=38 U/L). Sodium and potassium levels of blood were, respectively, 133 mmol/dl and 3.02 mmol/dl. Albumin level was low (2.8 g/dl). Toxicology panel was negative and ammonia level was normal (97.7 ug/dl,
reference: 27-102). Serum B12 level was raised because of vitamin B complex was commenced immediately. Cerebrospinal fluid studies revealed no abnormalities.

ECG and chest X-ray were normal. Cerebrospinal fluid studies were normal. The patient was diagnosed as having MBD, and intravenous hyperalimentation was initiated with high-dose multivitamins. His condition gradually improved. He opened his eyes on the fifth day of hospitalisation, however, due to aspiration pneumonia, he required a tracheotomy, and the patient was still in a vegetative state two months after the diagnosis.

CASE 3

A 59 years old female patient was taken to our emergency room with suspicious head trauma and confusion. She was homeless and according to information received from her relatives, she had a history of severe alcoholism with a high daily consumption of alcohol over 10 years. Neurological examination revealed loss of orientation and psychomotor slowing, disarthric speech, rigidity in her wrist and elbow joints and demonstrated gait disturbance. She was unable to perform even simple orders.

Laboratory test results revealed high level of low-density lipoprotein (LDL=150 mg/dl), high level of GGT and AST (GGT=217 U/L, AST=65 U/L). Sodium and total protein levels of blood were, respectively, 150 mmol/L and 5.53 g/dl (reference: 6.6-8.3). Toxicology panel was negative. Serum B12 level was normal (277 pg/ml).

Cranial CT was normal. An MRI demonstrated a hyperintense lesion in the splenium of corpus callosum on DWI and T2W images (Figure 5 and 6).

Cerebrospinal fluid studies revealed high protein level (70.95 mg/dl) and no lymphocytes. EEG showed diffuse slow waves of 6-7 Hz frequency. Intravenous hyperalimentation was initiated with high-dose multivitamins. Due to respiratory failure she was taken to the intensive care unit. Based on her history of chronic alcoholism and specific brain MRI findings MBD was diagnosed. She had myoclonic jerks and agitation in her clinical follow-up and was commenced on valproic acid and clonazepam.

After treatment there was no improvement in her medical condition. She needed care while being discharged from hospital.

Discussion

MBD results in acute demyelination and necrosis of the corpus callosum; it is associated with chronic alcohol consumption but is occasionally seen in non-alcoholic patients.

The disease may present in two major clinical forms: acute and chronic. The acute form, with severe impairment of consciousness, seizures and muscle rigidity, often results in death after several days7. In the chronic form, an interhemispheric disconnection syndrome is a typical clinical feature of the disease, but it may easily remain undetected if not sought out, and it may even be misdiagnosed as Wernicke encephalopathy, alcohol withdrawal syndrome, or encephalitis. The early diagnosis depends on MRI8. MRI is currently the most sensitive diagnostic tool. Conventional MRI typically detects lesions as hyperintense on T2 and FLAIR, and hypointense on T1-weighted images in the body of the corpus callosum, sometimes extending into the genu and the splenium. The central layers of the corpus callosum are mainly affected, with sparing of the dorsal and ventral layers. The entire corpus callosum is rarely involved. DWI, in the acute phase, shows restricted diffusion because of cytotoxic edema. DWI reveals the earliest signs of lesions and can identify more extensive callosal lesions in MBD than FLAIR. Apparent diffusion coefficient was the low apparent diffusion coefficient6, 8.

Two clinicoradiologic subtypes of MBD may be differentiated: Type A is characterized by major impairment of consciousness, T2-hyperintense swelling of the entire corpus callosum on early MRI and poor outcome. Type B shows at most slight impairment of consciousness, partial callosal
lesions on MRI and a favorable outcome. Differentiation of these clinicoradiologic subtypes may help resolve inconsistencies of the established clinical classification resulting from new insights into the clinical course and prognosis of MBD by structural neuroimaging3, 6.

The diagnosis of MBD rests mainly on evidence of these callosal lesions. The corpus callosum may also be affected in other diseases such as ischaemic stroke, contusion, multiple sclerosis and lymphoma. MBD, however, is distinguished from these disorders by the symmetry of the callosal lesions. 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. The main pathologic change associated with MBD is a degeneration of the corpus callosum with different degrees of damage from demyelination to necrosis5, 9, 10. Cortical radiological abnormalities have been explained as Morel’s laminar sclerosis in MBD. Reduced apparent diffusion coefficient (ADC) in the cortical lesions is cytotoxic oedema and suggests the acute phase of Morel’s laminar sclerosis. This cortical lesion, mainly in the third layer and especially in the lateral-frontal cortex, is associated with the callosal lesions of MBD7, 9, 11.

Although the direct toxic effect of alcohol is thought to be responsible in the aetiology of the disease, the significantly low incidence rate of the disease among alcoholic populations raises questions. Similar clinical cases were also reported with non-alcoholic patients, therefore, alcohol addiction cannot be considered as the sole cause of the disease12, 13. The pathogenesis is still unclear. Thiamine deficiency is often seen in patients with alcoholism and contributes to the neurologic complications, however, the exact mechanism of how thiamine treatment may be effective for MBD remains unclear. Early diagnosis and thiamine administration may result in a better prognosis5, 14.

Above, we have reported on three cases of MBD. In the first and third patients with focal abnormalities of the corpus callosum on MRI, the clinical outcome was satisfactory. In the second patient, the MRI showed acute cortical abnormalities in addition to callosal lesions. The clinical evolution in this patient was worse, with definite residual neurological signs. It has been suggested that cortical lesions on MRI are occasionally associated with MBD, especially in cases with poor prognosis and severe cognitive decline; our patient also had a poor prognosis.

The diagnosis of MBD is based on the callosal lesions. Differentiation of MBD from infarction of the corpus callosum or multiple sclerosis may be difficult13, however, selective involvement of the entire length of the corpus callosum and focal cytotoxic necrosis confined to its central layer are more likely to be due to MBD. The combination of chronic alcoholism, other clinical features, and MRI findings support the correct diagnosis.

It is concluded that chronic alcoholism with malnutrition may lead to damage in both the central and peripheral nervous systems. In such cases, cranial MRI with DWI carry significant diagnostic value and it can help the physician to plan out the appropriate treatment for the patient suffering from a potentially fatal disease.

REFERENCES


