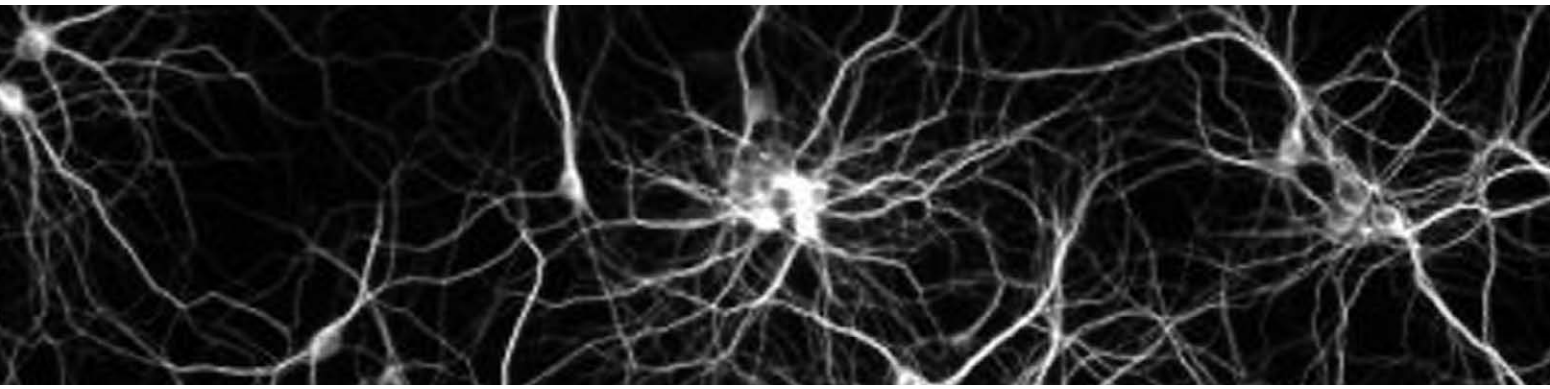

Marchiafava–Bignami disease: a rare but not forgotten complication of chronic alcoholism

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ABSTRACT – *Objectives:* To report of rare case of Marchiafava-Bignami disease (MBD), which is, to the best of our knowledge, the first to be described in Croatia. *Case description*: A 50-year-old woman, who consumed 200–500 mL hard liquor daily during a 2-year period, was admitted to hospital due to dysfunctionality, general weakness, and gradual cognitive impairment. *Results:* After her state of consciousness deteriorated to the level of sopor, urgent brain magnetic resonance imaging (MRI) was performed showing extensive lesions in the corpus callosum and subcortical white matter, bilaterally. As clinical presentation, accompanied by MRI finding, was strongly suggestive of MBD, we immediately started therapy with high-dose vitamin B complex and methylprednisolone over five days. After two weeks, a control MRI showed significant regression of the callosal and other white matter lesions. During and after treatment, the patient gradually started regaining consciousness and a natural cycle of wakefulness and sleep, but lack of verbal skill and dysphagia persisted. Further treatment focused on nutritional support, alcohol abstinence, physical and speech therapy. After a 2-year period of rehabilitation, her cognitive performance had improved markedly (MoCA was 24/30), with mild residual deficits in several cognitive domains. On examination slight gaze palsy to the left persisted, accompanied by weaker left plantar response, and mild spastic dysarthria. She moved into her own house with her sister. *Conclusion*: Although the disease is potentially fatal, a timely diagnosis based on clinical and radiological evidence and prompt treatment can result in a quite favorable final prognosis, as shown in our case.

Keywords: chronic alcoholism, corpus callosum, demyelinating disorders, Marchiafava-Bignami disease, thiamine

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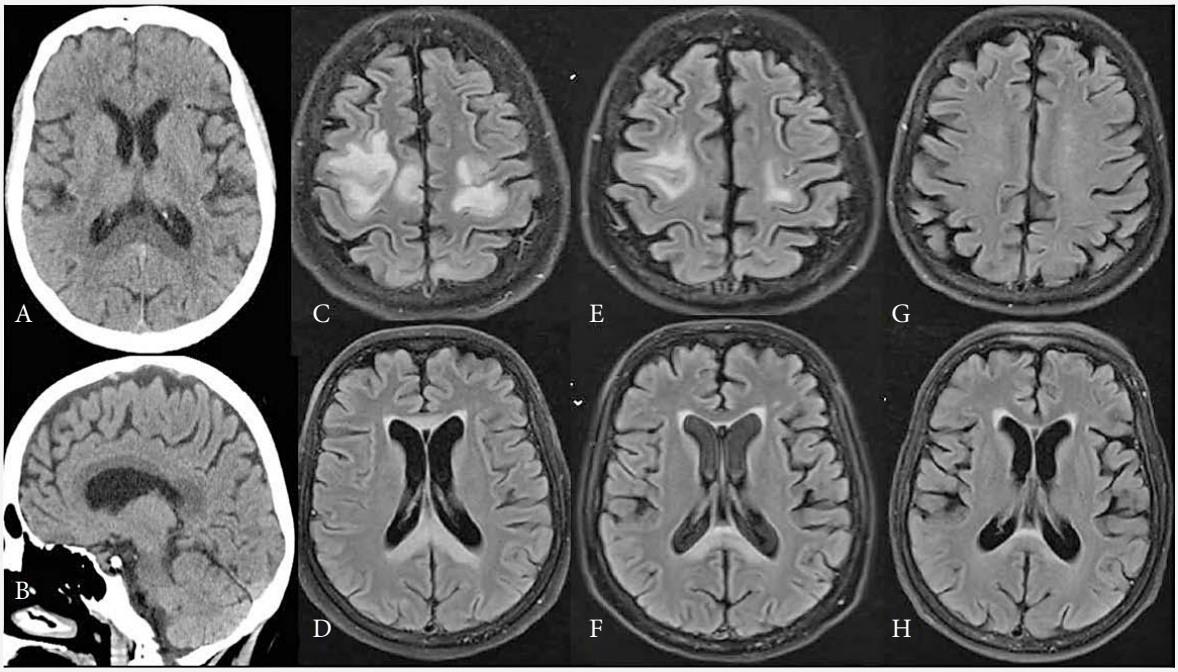

Fig. 1. *A axial, and B sagittal brain CT images showing edema of the splenium of the CC; C-H axial FLAIR images: C-D acute onset of the disease: prominent frontal bilateral white matter and CC lesions; E-F first follow-up brain MRI: moderate regression of brain lesions; G-H second follow-up brain MRI: almost complete regression of the brain lesions*

INTRODUCTION

Marchiafava–Bignami disease (MBD) is a rare demyelinating disorder associated mostly with severe and chronic alcohol abuse and/or malnutrition leading to a deficiency in vitamin B complex (1). Its incidence is higher in middle-aged men with a history of chronic alcoholism (2). The clinical presentation of MBD is nonspecific and can vary from mild motor and cognitive disturbances to coma and death; thus, early-stage MBD is difficult to diagnose or differentiate from other diseases (1,3). In addition to the clinical picture, modern brain imaging, especially magnetic resonance imaging (MRI), is crucial for prompt diagnosis, because timely treatment can remarkably increase the survival rate (1,4).

CASE DESCRIPTION

A 50-year-old woman admitted to the Department of Psychiatry for dysfunctionality and lack of motivation to abstain from chronic alcohol consumption had, during a 2-year period, consumed 200–500 mL hard liquor daily. One month before hospitalization, she started complaining of general weakness and occasional leg muscle cramps, which were accompanied by gradual cognitive impairment. As her state of consciousness deteriorated from somnolence to sopor, she was transferred to the Department of Neurology.

On admission, the patient's Glasgow coma score was 9. Dysphagia and paratonia were evident, but no signs of meningeal irritation, focal motor deficits, or pathologic reflexes were present. We performed a computed tomography (CT) scan of the brain which showed edema of the splenium of the corpus callosum (CC) bilaterally (Fig. 1, A-B). As her clinical condition was further deteriorating, we ordered a brain MRI for more detailed information. The MRI showed extensive bilateral lesions in the frontal subcortical and deep white matter region at the level of vertex and in the genu and splenium of CC, but also some lesions in the parietal and occipital regions. The lesions were hyperintense on FLAIR (Fig. 1, C-D) and T2WI images, with some signs of restricted diffusion and minor enhancement inside frontal lesions. The cerebrospinal fluid assay revealed moderate proteinorahia and just 1 leukocyte, with no signs of intrathecal immunologic activity. An electroencephalogram was remarkably slowed, without epileptiform discharges. *Escherichia coli* was isolated from urine. No deficit of folic acid or vitamin B12 was detect-

ed. Thyroid function tests were normal and antithyroid antibodies were negative.

Because the clinical presentation and MRI findings were consistent with a diagnosis of MBD, we immediately started therapy with high-dose vitamin B complex (B1, folate, B12) and intravenous methylprednisolone (1250 mg total) over five days. The urinary infection was treated with co-amoxiclav. After two weeks, total protein in the cerebrospinal fluid had decreased to almost normal, a test for JCV was negative, and follow-up MRI showed significant regression of the callosal and frontal white matter lesions (Fig. 1, E-F). During and after treatment, the patient gradually started regaining consciousness and a natural cycle of wakefulness and sleep; however, lack of verbal skill and dysphagia persisted. Further treatment focused on nutritional support and rehabilitation from alcoholism.

The patient was discharged to a long-term care facility that provided physical and intensive speech rehabilitation. Follow-up MRI of the brain 12 weeks after the initial imaging revealed almost complete regression of the brain lesions (Fig. 1, G-H). After a 2-year period of rehabilitation and alcohol abstinence, the patient's electroencephalogram was normal. Her cognitive performance had improved markedly (Montreal Cognitive Assessment: 24/30), with mild residual deficits in the areas of attention, visual–spatial skills, left–right orientation, and praxia. During a neurologic exam, her walk was unimpaired, but slight gaze palsy to the left persisted, accompanied by a brisker left patellar reflex, weaker left plantar response, and mild spastic dysarthria. She left the care facility and moved into a house with her sister.

DISCUSSION

The pathologic changes typical in MBD were first described by two Italian pathologists, Ettore Marchiafava and Amico Bignami, in 1903. The syndrome includes symmetrical demyelination and necrosis of the central part of the CC, with relative sparing of the dorsal and ventral layers (1). Later, it became evident that the pathology could additionally affect the subcortical white matter, basal ganglia, and even the brain cortex (5,6). Those changes are most frequently encountered in chronic alcoholism and other malnourishment but might also be observed in paraneoplastic syndromes or osmotic myelinolysis (2). The precise mechanism of the damage in MBD, including the selective vulnerability of the CC, is still not entirely elucidated, but synergism between ethanol-induced neurotoxic effects and hypovitaminosis B, particularly B1, is suggested to be the most plausible (7).

Although MBD occurs in both sexes, most cases are seen in men (2). The clinical spectrum of the disease is broad and lacks specificity (1). Its features can vary from mild motor and cognitive disturbances to severe motor deficits, disordered coordination, impaired consciousness, signs of interhemispheric disconnection, seizures, and ultimately death (3). Based solely on clinical manifestations, the first MBD classification (8) distinguished acute, subacute, and chronic forms. Subsequently, in 2004, with the advent of modern brain imaging, Heinrich *et al.* proposed a clinicoradiological classification of type A - with distinguishing clinical features of stupor or coma, accompanied by pyramidal signs, and imaging revealing involvement of almost the entire CC like it was in our case, or type B - normal or mildly perturbed mentation, with signs of focal callosal lesions on imaging (9). In the early 2000s, MBD was still considered a rather rare and almost invariably fatal disorder (10). But given that alcoholism is a common problem, MBD was more likely to have been underdiagnosed in the preimaging era. Data suggest that the overall outcome of MBD has improved notably in recent decades (4), partly because of increased awareness and because of the broader availability of MRI.

On MRI, a characteristic "sandwich sign" represents the involvement of the central layers of the CC body, with relative sparing of the dorsal and ventral extremes on sagittal views. In our case, the lesions were in the genu and splenium of CC, which is more common in MBD mimics but also can be seen in one-third of the MBD subjects (1). On the other hand, no lesion enhancement has been described in the MBD mimics: it is more common in real MBD like it was in our case. The CC might appear edematous in the acute phase and atrophic in the chronic phase (11). The clinical and radiologic presentations contribute equally to a quick diagnosis. The mainstay of therapy is prompt parenteral thiamine replacement (1). When MBD is suspected, disorders from the differential such as infarction of the recurrent artery of Heubner, neoplastic diseases (astrocytoma or lymphoma, for instance), demyelinating diseases such as multiple sclerosis, progressive multifocal leukoencephalopathy, or acute disseminated encephalomyelitis should first be excluded. Among the demyelinating diseases to be excluded, multiple sclerosis is the most common but occurs in a different clinical setting (11).

In our case, the diagnosis was made based on the history of chronic alcoholism and radiologic features. Diagnostic workup was limited to a certain extent as some tests like measurements of blood thiamine level or autoimmune encephalitis antibodies have not been available in our center. Although the patient initially had a severe subacute type A case of MBD, prompt treatment and long-term rehabilitation led to a favorable clinical outcome.

CONCLUSION

To the best of our knowledge, this case of MBD is the first described in Croatia. Given that the manifestations of MBD are nonspecific, early clinical suspicion coupled with timely brain imaging were crucial for effective treatment and avoiding a potentially fatal outcome in this case.

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