

Clinical and neuroradiological features of 15 patients diagnosed with Marchiafava-Bignami disease

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To the Editor: Marchiafava-Bignami disease (MBD), a rare neurological disorder frequently associated with alcoholism, is characterized by demyelination and necrosis of the central layer of the corpus callosum (CC).^[1] A wide spectrum of clinical manifestations of MBD has been described in the literature, including altered mental state, impaired walking, dysarthria, mutism, signs of disconnection syndrome, incontinence, seizures, and dementia. Conventional magnetic resonance imaging (MRI) sequences are useful in diagnosing MBD, which demonstrate a symmetrical involvement of the CC, with hyperintense signal on T2-weighted and fluid-attenuated inversion recovery (FLAIR) images. However, the lesions in patients with MBD were not only limited to the CC. The aim of this study was to demonstrate the clinical and radiological characteristics of MBD.

We retrospectively reviewed the clinical data of 15 patients with MBD who visited at The Affiliated Hospital of Jiujiang University and The Third Affiliated Hospital of Nanchang University between January 2014 and December 2018. The diagnosis of MBD was made based on the following criteria: (1) a history of chronic alcoholism or malnutrition; (2) acute or sub-acute onset of neuropsychiatric symptoms; (3) symmetrical hyperintensity of the CC on T2-weighted and FLAIR images; (4) exclusion of other diseases including Wernicke encephalopathy (WE), reversible splenic lesion syndrome, intra-cranial infections, cerebrovascular diseases, and demyelinating diseases of the central nervous system. Clinical data, including demographics (gender and onset age), risk factors, types of onset, clinical presentations, MRI findings, treatment and outcome, were collected. At the time of follow-up (time range: 1–2 months), the treatment outcomes were classified

as complete, partial, and bad according to the objective improvement in neurological findings during drug therapy (death, apathetic state, or vegetative state was considered as a bad outcome).

All these 15 patients were male with average age at presentation of 54 years (range 40–85 years). Among these 15 patients, 14 had risk factor of chronic alcoholism, complicated with malnutrition in two patients. Types of onset included acute ($n = 8$) and sub-acute onset ($n = 7$). On admission, disturbance of consciousness (10/15) was the most common symptom. Other clinical presentations included ataxia gait ($n = 5$), aphasia ($n = 5$), impaired cognition ($n = 4$), seizure ($n = 4$), tetraparesis ($n = 4$), dysarthria ($n = 2$), positive pyramidal sign ($n = 1$), psychiatric symptoms ($n = 1$), and muscular hypertonia ($n = 1$). Eleven patients only received vitamins, and three patients were treated with vitamins combined with glucocorticoid [Supplementary Table 1, <http://links.lww.com/CM9/A64>]. At the time of follow-up, seven patients completely recovered from all symptoms, three patients had slight sequelae, and five with bad outcomes. On admission, MRI revealed symmetric hyperintense changes in the CC on T2-weighted imaging (T2WI) and diffusion-weighted imaging (DWI) [Figure 1]. The lesions were located in different parts of the CC, including entire ($n = 6$), genu + splenium ($n = 4$), body + splenium ($n = 2$), and isolated splenium ($n = 3$). In addition, more than half of the patients (8/15) had extra-callosal lesions, including cortical gray matter (4/8), sub-cortical white matters (SCWM; 2/8), periventricular white matters (PVWM; 2/8), and middle cerebellar peduncles (MCPs; 2/8), which demonstrated symmetrically hyperintense changes on T2WI, FLAIR, and DWI [Figure 1].

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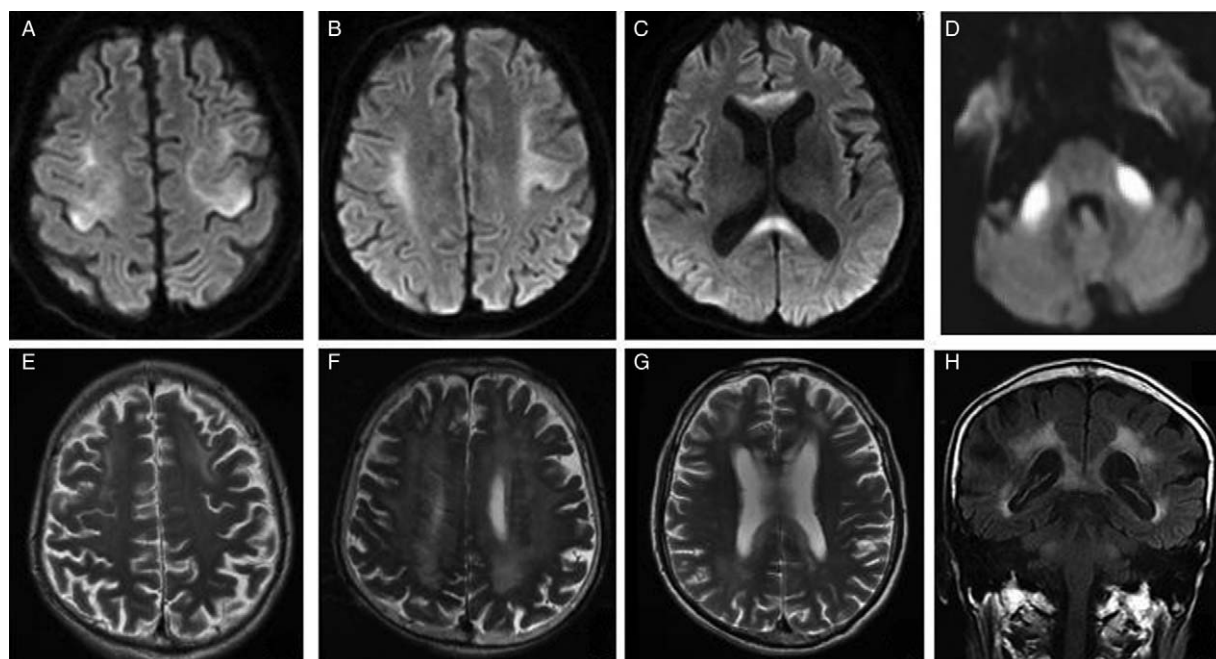


Figure 1: Imaging findings of patients with MBD. Transverse diffusion-weighted imaging revealed hyperintense lesions in bilateral frontal lobes, SCWM, the CC and the MCPs (A–D). Transverse T2-weighted and coronal fluid-attenuated inversion recovery images showed hyperintense lesions in SCWM, PVWM, the entire CC, and the MCPs (E–H). CC: Corpus callosum; MBD: Marchiafava-Bignami disease; MCP: Middle cerebellar peduncle; PVWM: Periventricular white matter; SCWM: Sub-cortical white matter.

Hillbom *et al*^[2] systematically reviewed 153 subjects with confirmed MBD. Altered mental state (80.4%) and impaired walking (68.0%) were the most frequent symptoms. Loss of consciousness, dysarthria, impaired memory, signs of disconnection, pyramidal signs, and were also frequently found in MBD. In our study, disturbance of consciousness was the most common symptom, followed by ataxia gait, aphasia, dementia, seizure, and tetraparesis.

In patients with MBD, the lesions are located in different parts of the CC, even the entire. Extra-callosal regions, such as SCWM or frontal cortex, have been infrequently described; other extra-callosal lesions including internal capsules, cerebral peduncles, MCPs, and hippocampus have also been rarely documented.^[3,4] In this study, the incidence of extra-callosal involvement was estimated to be 53.3%. Among eight patients with extra-callosal involvement, four had cortical gray matter lesions. Other extra-callosal lesions included SCWM, PVWM, and MCPs. The cortical lesion, also known as Morel's laminar sclerosis, is mainly located in the third layer, especially in the lateral-frontal cortex.^[5] A possible explanation for the co-existence of cortical and callosal lesions is accompanied by WE or extra-pontine myelinolysis. Advanced neuroimaging techniques are helpful for understanding the pathophysiologic processes of MBD. In magnetic resonance spectroscopy studies, the increased choline/creatine ratio and reduced N-acetyl aspartate/creatine ratio suggested myelin destruction and secondary neuronal loss, respectively. In addition, decreased cerebral blood flow and cerebral blood volume in each lesion on perfusion-weighted MRI suggested that ischemia might be the cause of pathogenesis.^[6] Furthermore, positron emission tomography scan showed reduced glucose metabolism in CC, cerebral hemispheres and hemispheric

white matter, indicating that in MBD, perfusion and metabolism defects may affect structures beyond the CC.^[7]

The treatment of MBD is still a challenge in clinical practice. Efficacy of high-dose vitamins and corticosteroids in MBD has been well-documented. Corticosteroids are administered because it may stabilize the blood-brain barrier, diminish inflammatory edema, and decrease the formation of leucocytes, especially of lymphocytes. Moreover, some researchers suggested that patients could completely recover with adequate thiamine therapy.^[2] However, the outcomes of MBD may vary. Different predictors of poor prognosis have been proposed including cortical lesions, low apparent diffusion coefficient values of the CC, entire CC involvement, and severe disturbances of consciousness. In our series, 4/6 patients with the whole CC involvement had good recovery, suggesting that the entire CC lesions did not seem to be correlated to bad outcome. As for extra-callosal involvement, the vast majority of the patients (87.5%) had unfavorable prognosis. We, therefore, speculated that extra-callosal lesions may be associated with poor prognosis.

In summary, MBD is mainly seen in middle-aged men and always related to alcohol consumption. In patients with MBD, extra-callosal lesions are not rare, especially for cortical gray matter. Both clinician and radiologist should maintain a high level of awareness of extra-callosal involvement in this entity.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patients have given his/her/their consent for their images and other clinical

information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Conflicts of interest

None.

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