

Cerebral microhemorrhage in Marchiafava–Bignami disease detected by susceptibility-weighted imaging

Ryuta Kinno · Masahiro Yamamoto ·
Takahiro Yamazaki · Yoshiyuki Owan ·
Toshiya Fukui · Eriko Kinugasa

Received: 17 April 2012 / Accepted: 22 June 2012
© Springer-Verlag 2012

Abstract Marchiafava–Bignami disease (MBD) is a rare alcohol-associated disorder. Clinical features include not only disturbed consciousness, dysarthria, tetraparesis, astasia-abasia, and symptoms of interhemispheric disconnection as initial symptoms but also cognitive deficits as clinical outcomes. The clinical significance of cerebral microhemorrhage (CMH) has been recognized in patients with cognitive deficits; however, the presence of CMH in patients with MBD has not been emphasized. The aim of the present study was to clarify the relationship between CMH and MBD. For this purpose, we report four patients with MBD, who showed asymmetrical hypointense areas in multiple cortico-subcortical regions on susceptibility-weighted imaging (SWI). All cases had a history of chronic alcohol abuse and symmetrical lesions in the entire corpus callosum. These patients' clinical symptoms included not only coma, dysarthria, and astasia-abasia as initial symptoms but also dementia as a clinical outcome. SWI showed asymmetrical hypointense areas in the multiple cortico-subcortical regions, indicating the presence of CMH. Compared with patients with normal cognitive function, demented patients showed higher severity of CMH. Our report would indicate that CMH is an important factor indicating the severity of dementia in patients with MBD.

Keywords Marchiafava–Bignami disease · Cerebral microhemorrhage · Alcohol · Dementia · Susceptibility-weighted imaging

Introduction

Marchiafava–Bignami disease (MBD) is a rare alcohol-associated disorder characterized by demyelination and necrosis of the corpus callosum (CC). Clinical symptoms include not only disturbed consciousness, dysarthria, tetraparesis, astasia-abasia, and symptoms of interhemispheric disconnection as initial symptoms but also cognitive deficits as clinical outcomes [1, 2]. The clinical significance of cerebral microhemorrhage (CMH) has been recognized in cognitive deficits, with a relatively high proportion of CMH observed in patients with Alzheimer's disease (AD) or mild cognitive impairment (MCI) [3]. However, the presence of CMH in MBD has not been emphasized. The aim of the present study was to clarify the relationship between CMH and MBD. For this purpose, we report four patients with MBD who showed asymmetrical hypointense areas in multiple cortico-subcortical regions on susceptibility-weighted imaging (SWI).

Case report

The characteristics of each patient with MBD are summarized in Table 1. On admission, cases 1 and 2 showed disturbed consciousness, muscle hypertonia, and increased tendon reflexes in both upper and lower extremities. In contrast, cases 3 and 4 were alert and showed normal muscle tonus with normal tendon reflexes. Pupils, eye movements, and respiratory patterns were not remarkable in any of the cases. Laboratory examinations showed vitamin B1 deficiency and normal blood-alcohol level (<0.01 %) in all cases. Cerebrospinal fluid examinations, chest X-rays, and electrocardiograms showed no abnormalities.

After immediate treatment with intravenous thiamine administration, cases 1 and 2 regained consciousness and

R. Kinno (✉) · M. Yamamoto · T. Yamazaki · Y. Owan ·
T. Fukui · E. Kinugasa
Department of Internal Medicine, Showa University Northern
Yokohama Hospital, 35-1 Chigasaki-chuo, Tsuzuki, Yokohama,
Kanagawa 224-8503, Japan
e-mail: kinno@med.showa-u.ac.jp

Table 1 Characteristics of each patient with MBD

	Case 1	Case 2	Case 3	Case 4
Age/gender	63/M	62/M	60/M	68/M
Initial GCS	E1V1M1	E1V1M5	E4V5M6	E4V5M6
Initial symptom (duration of symptoms)	Coma (2 days)	Semicoma (2 days)	Dysarthria (5 days)	Astasia–abasia (7 days)
Medical history	Chronic alcoholism, NIDDM	Chronic alcoholism	Chronic alcoholism, NIDDM	Chronic alcoholism, hypertension
Serum vitamin B1 (ng/ml)	13.6	11.2	11.4	12.1
Therapy	Intravenous thiamine	Intravenous thiamine	Intravenous thiamine	Intravenous thiamine
MMSE score	7 (on day 17) 28 (on day 182)	24 (on day 16) 30 (on day 180)	24 (on day 14) 17 (on day 172)	22 (on day 12) 14 (on day 181)
Outcome	Slight cognitive impairment	Normal	Dementia (memory disturbance, agnosia)	Dementia (memory disturbance, agnosia, disturbance in executive functioning)
Number of CMH	11	14	26	22
GD of CMH (mm)	3.8	3.5	6.2	6.8

GCS Glasgow coma scale, GD greatest diameter, M male, F female, NIDDM non-insulin-dependent diabetes mellitus, MMSE mini-mental state examination

their general condition improved rapidly. Based on a medical interview after the regained consciousness, no cases had a history of neurological or psychological disorders. All cases had been consuming alcohol mainly in the form of beer (alcohol content of about 5 %) and shochu (a Japanese traditional spirit; alcohol content of about 25 %) daily for 40 years. Neurological examination after the regained consciousness showed severe dementia with delirium in case 1, whereas there were no apparent signs of dementia in cases 2, 3, or 4 in the acute phase. Case 1 was transferred to a psychiatric hospital for treatment of his psychiatric symptoms. With treatment, his psychiatric problems were gradually resolved, and he was discharged. On day 182, he showed normal cognitive function. Case 2 became able to look after himself and was discharged. Dysarthria in case 3 and astasia–abasia in case 4 resolved after rehabilitation, and these two cases were discharged. However, they became demented, which resulted in impaired in social functioning.

T2-weighted imaging (T2WI) or fluid attenuated inversion recovery imaging (FLAIR) in the acute phase showed symmetrical hyperintense areas in the entire CC in all cases (Fig. 1a). Diffusion-weighted imaging (DWI) showed hyperintense areas in the genu of the CC in case 1, which diminished in the chronic phase. To assess patients for the presence of CMH, an SWI scan was performed (Fig. 1b). SWI showed asymmetrical hypointense areas in multiple cortico-subcortical regions. These lesions were not detected on T2WI or FLAIR, indicating the presence of CMH. The extent of CMH was estimated by counting the number of hypointense areas on SWI and measuring the greatest diameter (GD) of the areas. Compared with patients with

normal cognitive function in the chronic phase (cases 1 and 2), demented patients (cases 3 and 4) showed higher severity of CMH (i.e., the larger GD and larger number of hypointense areas on SWI).

Discussion

Our cases had a history of chronic alcohol abuse and symmetrical lesions in the CC (Fig. 1a). Clinical symptoms included not only coma, dysarthria, and astasia-abasia as initial symptoms but also dementia as clinical outcomes (Table 1). These clinical features were compatible with classical MBD [2]. It was notable that all cases showed asymmetrical hypointense areas in multiple cortico-subcortical regions on SWI (Fig. 1b). In the differential diagnosis of hypointense areas on SWI, vascular flow voids of small vessels, calcium or iron deposits, or cerebral cavernous malformations would be considered [4]. A recent study showed that the detection of CMH with MRI in the cortico-subcortical regions is more reliable than that in the cerebellum or brainstem when comparing the pathological findings of post-mortem brain slices with those of T2*WI [5]. Moreover, the previous histological examination of a patient with MBD showed astrocytes filled with iron-positive granules in the centrum semiovale [6]. These findings, when taken together, suggest that the SWI findings in our cases represent CMH.

It was notable that demented patients showed higher severity of CMH when compared with patients with normal cognitive function (Table 1). Therefore, our report would indicate that CMH is an important factor indicating the

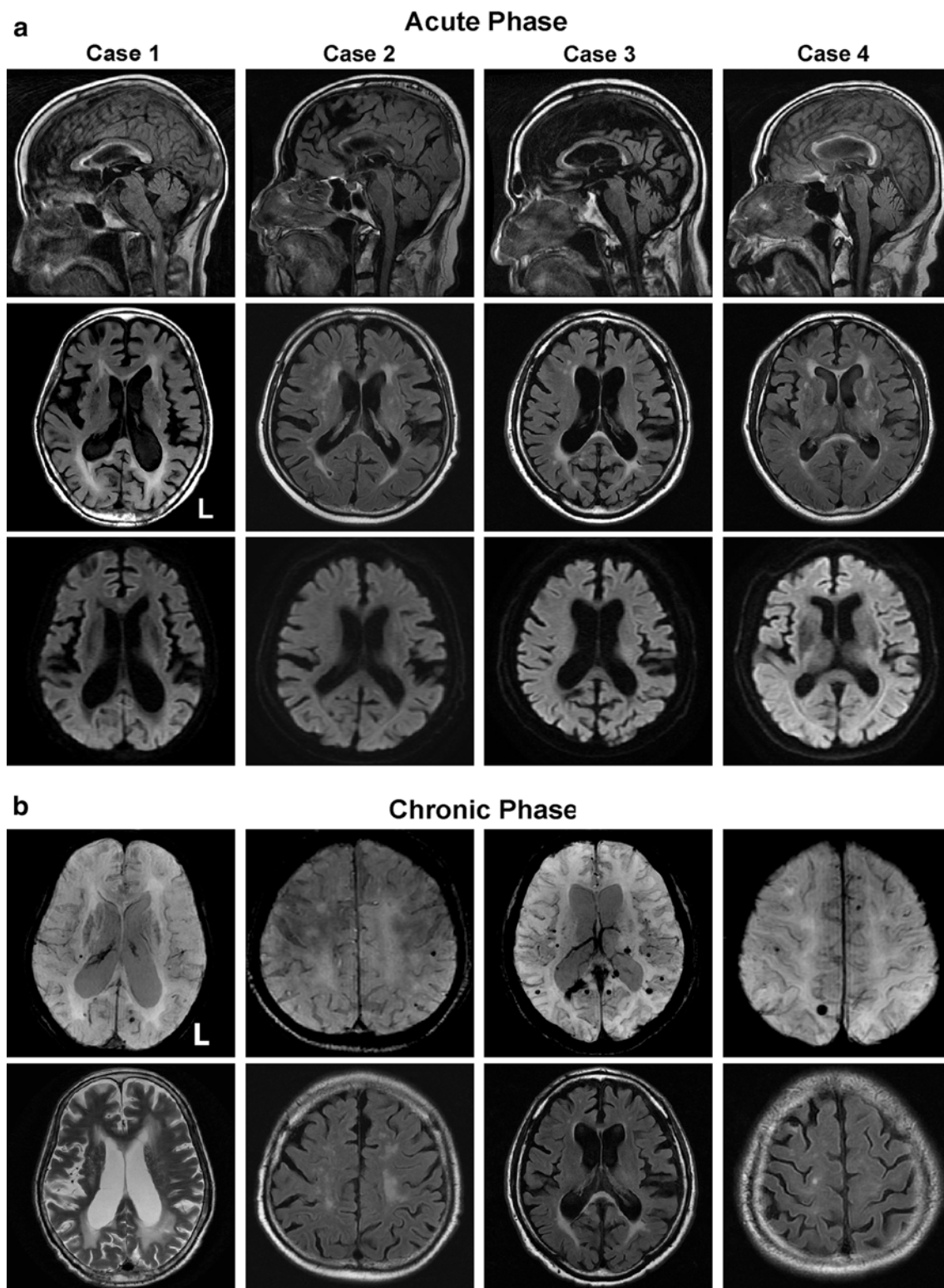


Fig. 1 MRI findings of each patient. **a** MRI findings in the acute phase (within 5 days after admission). Sagittal (*upper*) and axial FLAIR images (*middle*), and axial DWI (*lower*) are shown. Note the symmetrical hyperintense areas in the CC for all cases. **b** MRI findings in the chronic phase (approximately 6 months after

admission). SWI (*upper*) and axial FLAIR images (*lower*) are shown. For case 1, an axial T2WI is shown instead of axial FLAIR image. Note the asymmetrical hypointense areas in the multiple cortico-subcortical regions which were not detected on T2WI or FLAIR images, indicating the presence of CMH

severity of dementia in patients with MBD. A previous study demonstrated a relatively high proportion of CMH in patients with AD and MCI, which provides further evidence of the involvement of vascular factors in neurodegenerative diseases [3]. Vascular factors might affect the presence of dementia as a clinical outcome of MBD.

Symmetrical lesions in the CC suggest that the most probable diagnosis of our cases was MBD. However, the clinical course of our cases suggests a possible differential diagnosis with Wernicke–Korsakoff Syndrome (WKS). WKS is also alcohol-related encephalopathy, clinically characterized by confusion, ataxia, nystagmus, and ophthalmoplegia in the acute phase as well as memory disturbance in the chronic phase [7]. The characteristic neuropathology involves CMH as well as neuronal loss and gliosis in the paraventricular and periaqueductal grey matter [8]. As several features are shared by the two diseases, our case presents further evidence that CMH may be a common feature of alcohol-related encephalopathy.

Data from population-based MRI analyses suggest connections between normal ageing and asymptomatic stages of age-associated small-vessel diseases, such as hypertensive vasculopathy and cerebral amyloid angiopathy (CAA) [9]. The prevalence of CMH is lowest in healthy individuals (3–6 %) and highest in individuals with intracerebral hemorrhage or CAA (54–74 %) [4]. Considering these prevalence rates, it was notable that all of our cases had CMH, although the coexistence of CAA or hypertensive CMH cannot be completely ruled out. Because of the small number of patients in the present study, further study will be required to establish a relationship between CMH and alcohol-related encephalopathy.

Acknowledgments This research was partly supported by a Grant-in-Aid for Young Scientists (B) (No. 24720190) from the Ministry of Education, Culture, Sports, Science and Technology of Japan (to RK).

References

1. Canaple S, Rosa A, Mizon JP (1992) Marchiafava–Bignami disease. Interhemispheric disconnection, favourable outcome, neurological aspect. *Rev Neurol (Paris)* 148:638–640
2. Heinrich A, Runge U, Khaw AV (2004) Clinicoradiologic subtypes of Marchiafava–Bignami disease. *J Neurol* 251:1050–1059
3. Cordonnier C, van der Flier WM, Sluimer JD, Leys D, Barkhof F, Scheltens P (2006) Prevalence and severity of microbleeds in a memory clinic setting. *Neurology* 66:1356–1360
4. Viswanathan A, Chabriet H (2006) Cerebral microhemorrhage. *Stroke* 37:550–555
5. De Reuck J, Auger F, Cordonnier C, Deramecourt V, Durieux N, Pasquier F, Bordet R, Maurage CA, Leys D (2011) Comparison of 7.0-T T_2^* -magnetic resonance imaging of cerebral bleeds in post-mortem brain sections of Alzheimer patients with their neuropathological correlates. *Cerebrovasc Dis* 31:511–517
6. Shiota JY, Nakano I, Kawamura M, Hirayama K (1996) An autopsy case of Marchiafava–Bignami disease with peculiar chronological CT changes in the corpus callosum: neuroradiopathological correlations. *J Neurol Sci* 136:90–93
7. Kopelman MD, Thomson AD, Guerrini I, Marshall EJ (2009) The Korsakoff syndrome: clinical aspects, psychology and treatment. *Alcohol Alcohol* 44:148–154
8. Victor M, Adams RD, Collins GH (1971) The Wernicke–Korsakoff syndrome. A clinical and pathological study of 245 patients, 82 with post-mortem examinations. *Contemp Neurol Ser* 7:1–206
9. Greenberg SM, Vernooij MW, Cordonnier C, Viswanathan A, Al-Shahi Salman R, Warach S, Launer LJ, Van Buchem MA, Breteler MM, Group MS (2009) Cerebral microbleeds: a guide to detection and interpretation. *Lancet Neurol* 8:165–174