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Co-occurrence of Marchiafava-Bignami Disease and Alcoholic Polyneuropathy in Chronic Alcoholic Patient Who Had Past History of Wernicke Encephalopathy: a Case Report

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Correspondence to
Mi Ja Eom
Department of Physical Medicine and Rehabilitation, Inje University Busan Paik Hospital, College of Medicine, Inje University, 75 Bokji-ro, Busanjin-gu, Busan 47392, Korea.
E-mail: reheom@inje.ac.kr

HIGHLIGHTS

- Three distinct neurologic diseases occurred in one chronic alcoholic patient.
- MBD which present poor prognosis is associated with cortical involvement.

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Mi Ja Eom
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E-mail: reheom@inje.ac.kr

ORCID iDs
Sang Hoon Jung
https://orcid.org/0000-0003-4595-0205
Nami Han
https://orcid.org/0000-0003-3651-9755
Mi ja Eom
https://orcid.org/0000-0002-3652-045X

Conflict of Interest
The authors have no potential conflicts of interest to disclose.

ABSTRACT

Marchiafava-Bignami disease (MBD), Wernicke encephalopathy (WE) and alcoholic polyneuropathy (AP) are distinct diseases and all have strong relationship with chronic alcoholism. A 70-year-old male who had altered mentality and ataxia of both lower limbs and had past history of WE 3 years previously admitted with 6 months history of impaired walking. He also had a symptom of altered sensorium by impaired consciousness for 2 days. In brain magnetic resonance imaging, the body, splenium of corpus callosum and bilateral frontal cortex were involved. The patient was diagnosed with MBD on the basis of the clinical features and the brain imaging findings. The electrodiagnostic findings implied demyelinating neuropathy in all extremities. He failed to recover his mentality and the function of the limbs remained poor finishing several treatment options including medications and physical therapy. The poor prognosis of this patient is thought to be associated with cortical involvement of MBD. We reported this very rare case who was affected by 3 distinct diseases of MBD, AP, and WE as complications of chronic alcohol abuse. Moreover, the case was relevant to a rare clinical presentation of MBD with cortical involvement which was associated with poor prognosis.

Keywords: Marchiafava-Bignami Disease; Wernicke Encephalopathy; Alcoholic Neuropathy; Magnetic Resonance Imaging; Nerve Conduction Study

INTRODUCTION

Marchiafava-Bignami disease (MBD) is a rare neurological disorder associated with long-term, heavy alcohol abuse and/or malnutrition. The patients' consciousness level generally decrease and progress to confusion and even to death. MBD has some characteristic features in the brain such as acute edema and necrosis of corpus callosum accompanying with subsequent symmetric demyelination [1,2]. When the disease progress, those lesions eventually produce the atrophy of involved structures [1,2]. One recently reported case of MBD presented that other structures of brain can also be affected and the cortical or subcortical lesions of MBD can imply the poor prognosis [3].

Meanwhile, Wernicke encephalopathy (WE) is also a neurological disorder caused by thiamine deficiency and mostly affects chronic alcohol abusers. The clinical diagnosis of WE is characterized by clinical triad of ocular signs, ataxia and altered consciousness, but the clinical presentation varies widely. WE occurs characteristically in the structures around the third ventricle, such as the medial nuclei of the thalamus, the tectal plate, the mamillary bodies and the periaqueductal gray matter [4,5]. All areas mentioned above are considered "typical" sites of involvement. Additionally, alcoholic polyneuropathy (AP) is another rare complication of chronic alcohol abuse [6].

To the best of our knowledge, MBD patient whose WE was diagnosed earlier is not previously reported in Northeast Asian population. The nervous system of this patient was affected centrally by MBD and WE and peripherally by AP. We believe that this is the first report demonstrating the features of 3 distinct disease entities in the same patient showing the clear evidences by magnetic resonance imaging (MRI) and nerve conduction studies (NCS).

CASE REPORT

A 70-year-old male was hospitalized to neurology department with 6 months history of impaired walking and weakness of upper and lower limbs. He had experienced dysarthria, altered sensorium, decreased consciousness, and ataxia for 2 days prior to the admission. He had underlying hypertension. Though he had been diagnosed with diabetes mellitus (DM) 10 years ago, he had not been treated by medications or injections. He had no history of medical consulting for the symptoms of DM complications. He smoked a pack of cigarettes a day for 25 years. He was a chronic alcoholic for 10 years with daily 5-bottle drinking history of raw rice wine, which had 6%–7% of alcohol content. The latest alcohol consumption was reported to be 7 days before the admission. Three years ago, he had admitted to our hospital with complaints of altered mentality and ataxia of both lower limbs. In brain MRI gained at the first admission, T2-weighted image (T2WI) and fluid attenuated inversion recovery (FLAIR) image showed high signal intensity in the bilateral periventricular and periaqueductal area (Fig. 1). He was treated with thiamine on the suspicion of WE on the basis of the clinical features and the brain imaging findings. At that time, he refused further hospitalization and discharged to home. Since then, follow-up was loss. His family reported that impaired walking and weakness of upper and lower limbs were getting worsen gradually after that event. Eventually he could not be sitting or lying down for last 6 months. Since then, he didn't eat food and only drank the alcohol. He abruptly stopped drinking the alcohol 7 days ago from this admission.

On the admission day, he was consulted to our department for early rehabilitation. On physical examination, he was found to be malnourished appearance and in altered sensorium (Glasgow Coma Scale [GCS]: E3V3M4). He was in drowsy mentality, and showed disoriented features in time and place. He scored 9 on the Korean version of Mini-Mental Status Examination. Psychiatric evaluation showed ideomotor apraxia presented as involuntary movements and uncontrolled motor functions, which were characteristically associated with the lesion involving the corpus callosum. Spontaneous speech was seldom observed and the speech was slurred and incomprehensible. All these signs and symptoms indicated the hemispheric disconnection.

Muscle strength was generally 3 grade in the both upper limbs and 1 to 2 grade in both lower limbs by manual muscle test. The muscle strength of bilateral ankle dorsiflexion was especially

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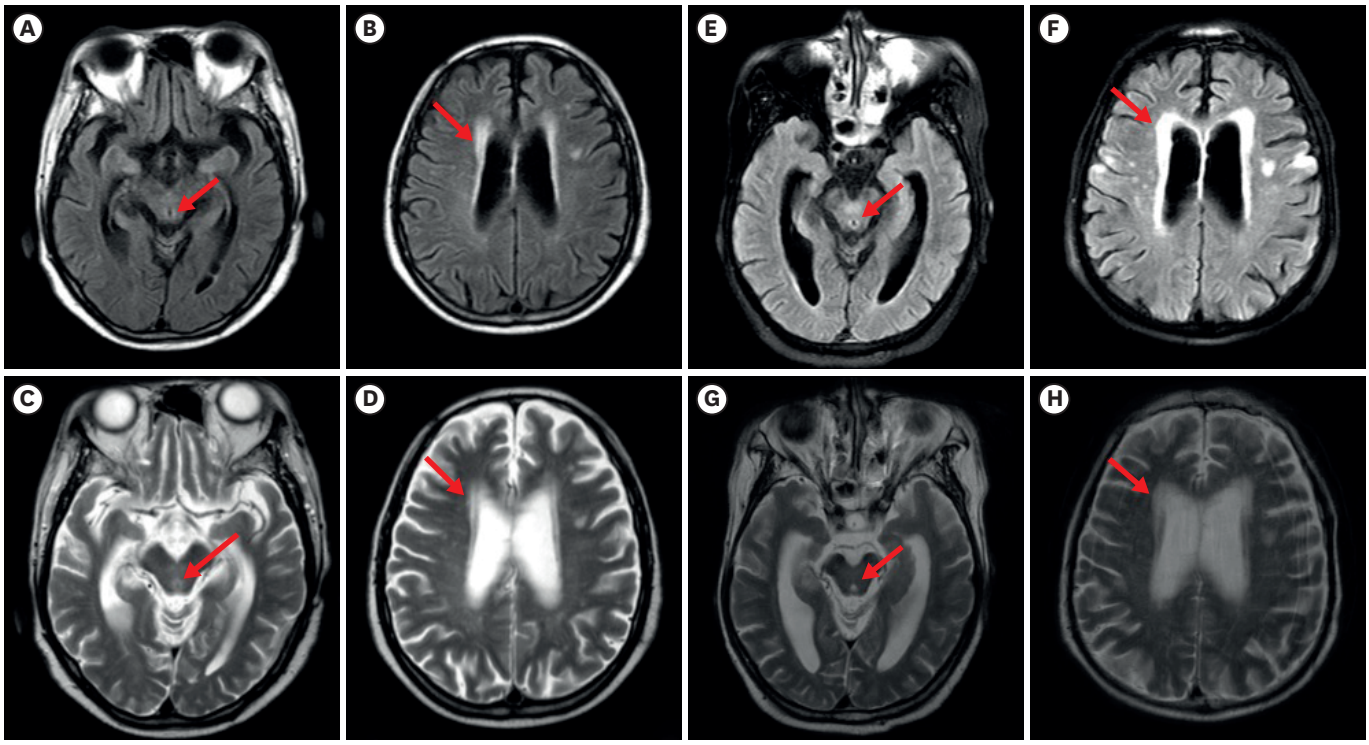

Fig. 1. Axial images of brain MRI when WE was diagnosed 3 years ago (left) and MBD was diagnosed at current admission (right). MRI showed hyperintensities in FLAIR (A, B, E, and F) & T2WI (C, D, G, and H) in the bilateral periaqueductal area and periventricular area (arrow in A-H).
MRI, magnetic resonance; WE, Wernicke encephalopathy; MBD, Marchiafava-Bignami disease; AP, alcoholic polyneuropathy; FLAIR, fluid attenuated inversion recovery; T2WI, T2-weighted image.

low as 1 grade. Atrophy of both lower limb muscles was generally observed. Limitation of motion was observed at both ankle dorsiflexion about −5°. Modified Ashworth scales indicated mildly increased spasticity in bilateral legs, scored 1 in both knees. Sensory impairment was uncheckable because of poor cooperation. Babinski's sign, ankle clonus, and Hoffman's sign were not detected. Hypoactive deep tendon reflexes were observed in bilateral knees and ankles. He couldn't move to the sitting posture by himself and poor sitting balance was checked at static position. The patient scored 0 on the Korean version of modified Barthel index which was suggestive of total dependency of activities of daily living (ADL).

The initial nutrition evaluation was conducted and revealed high risk of malnutrition. His height was 160 cm and his body weight was 37.0 kg, that means 67 percentages of ideal body weight and low body mass index (14.5kg/m^2).

The laboratory data revealed hypoproteinemia and hypoalbuminemia (total protein, 5.3 g/dL; albumin, 2.8 g/dL). The patient had been diagnosed with DM 10 years ago, but he didn't take oral hypoglycemic agent. Serum glucose level was not poorly controlled without complications such as diabetic retinopathy or neuropathy. HbA_1C level was in the normal range (HbA_1C 5.0%). The patient' liver and renal functions were slightly abnormal (aspartate transaminase/alanine aminotransferase, 57/34 U/L; blood urea nitrogen 59 mg/dL; creatinine 1.22 mg/dL; estimated glomerular filtration rate 59.7 mL/min/1.73 m^2), but serum ammonia level was in normal range. Serum level of creatine phosphokinase (CPK) was also elevated (CPK 817 U/L). C-reactive protein (CRP) was elevated because of 6 × 6 cm sized coccyx sore with grade 3 (CRP 8.97 mg/dL). However, his serum level of vitamin B1 and vitamin B12 was

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in the normal range (vitamin B1 7.6 μg/dL; vitamin B12 1,016 pg/mL). Serum electrolytes and thyroid stimulating hormones were in normal range. Blood alcohol and drugs were negative. Urinalysis showed ketone bodies. Chest X-ray was negative and the computed tomography (CT) of abdomen and pelvis didn't show any relevant alteration.

Brain CT scan was performed and revealed a lesion of hypodensities in the body, splenium of corpus callosum and both frontal cortex, without perilesional edema (Fig. 2). MRI showed hypointensities in T1 weighted image (T1WI) and hyperintensities in T2WI in the body, splenium of corpus callosum, both precentral gyrus and both frontal cortex. Corresponding region in axial diffusion-weighted magnetic resonance (MR) image (DWI) and FLAIR image showed hyperintensities with a decreased apparent diffusion coefficient (ADC) image (Fig. 2). Abnormal findings associated with previous WE showed no significant change and additional lesion compatible to WE was not noted (Fig. 1). The patient was eventually diagnosed with MBD on the basis of the clinical features and the imaging (CT and MRI) findings.

His family reported that the mood of the patient rapidly fluctuated and he often look anxious and agitated. He had been suffered from insomnia and intermittent tremor. Under strong suspicion of psychiatric features of alcoholic disorder, he was consulted at psychiatry department. The psychiatrist recommended treatments for alcohol withdrawal symptoms such as anxiety, agitation, sweating and tremor.

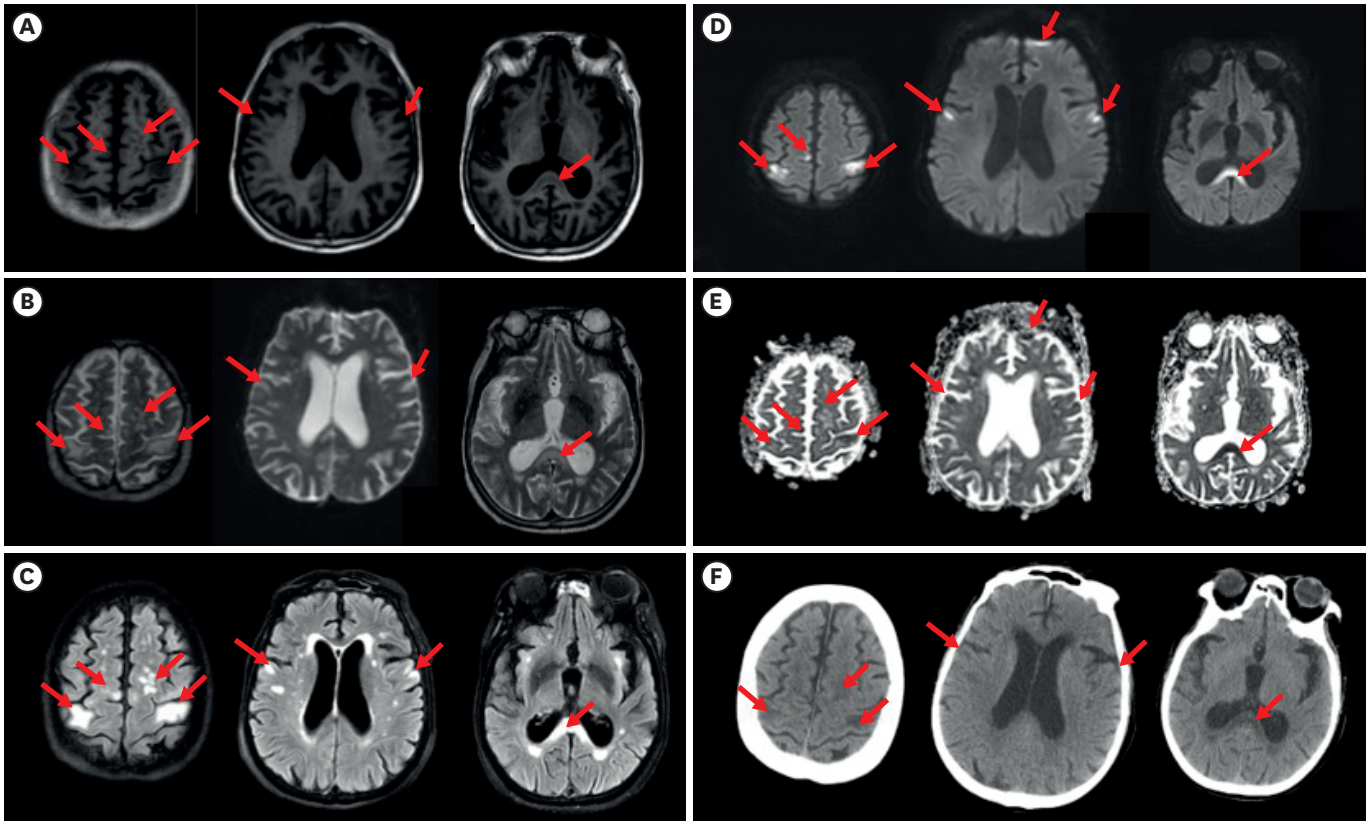

Fig. 2. Axial images of brain MRI and CT when MBD was diagnosed. MRI showed hypointensities in T1WI (A), hyperintensities in T2WI (B) and hyperintensities in T2 FLAIR (C) in the body, splenium of corpus callosum, both precentral gyrus and both frontal cortex. Corresponding region in DWI (D) showed hyperintensities with a decreased ADC image (E). Corresponding region in CT (F) showed hypointensities (arrow in A-F).
MRI, magnetic resonance; CT, computed tomography; MBD, Marchiafava-Bignami disease; T1WI, T1-weighted image; T2WI, T2-weighted image; FLAIR, fluid attenuated inversion recovery; DWI, diffusion-weighted magnetic resonance image; ADC, apparent diffusion coefficient.

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Despite the normal level of serum vitamins, the patient was treated with intravenous high-dose vitamin treatments (500 mg 3 times for 2 days and 250 mg 1 time for an additional 5 days intravenously, in combination with other B vitamins) and inserted Levin-tube for hyperalimentation. In addition, physical therapy was carried out for strengthening of upper and lower limbs at bedside.

On the second day of admission, the NCS and electromyography (EMG) was executed for evaluating the weakness of upper and lower limbs and electrophysiological findings were suggestive of axonal demyelinating sensorimotor polyneuropathy, compatible with AP (Tables 1 and 2). EMG was not sufficiently done in bilateral tibialis anterior, peroneus longus and gastrocnemius because of poor cooperation. No abnormal spontaneous activity was observed in tested muscles and proper volitional contractions for analysis were not provoked. Somatosensory evoked potentials of bilateral median and tibial nerves were not obtained in the cortex (Table 3). On the basis of history, clinical features, imaging findings, and electrodiagnostic findings, patient was diagnosed as having MBD combined with AP.

On the fifth day of admission, electroencephalography was performed and revealed diffuse cerebral dysfunction. After the scheduled vitamin treatment, no further medical treatment was done.

On the eighth day of admission, the patient was transferred to secondary referral hospital. At discharge, his general condition was slightly improved but his mentality remained drowsy as the GCS score was similar (E4V3M4) with that of admission. His ADL function showed minimal improvement in sitting balance, but was persistently poor, and weakness of upper and lower limbs was stationary. One week later, the family visited our hospital and reported

Table 1. Nerve conduction studies and later responses in upper extremities

Characteristics	Stimulation site	Recording site	Latency (msec or msec, peak)	Amplitude (mV or μV)	NCV (m/sec)
Motor (side, nerve)					
Right					
Median	Wrist/elbow	APB	4.3/9.5	8.2/7.5	44.6
Ulnar	Wrist/below elbow	ADM	3.5/8.1	9.6/8.9	51.4
Radial	Forearm/lateral brachium	EIP	1.2/5.0	4.6/4.4	47.3
Left					
Median	Wrist/elbow	APB	4.1/8.8	14.1/12.9	45.6
Ulnar	Wrist/below elbow	ADM	3.4/8.3	9.9/8.1	44.8
Radial	Forearm/lateral brachium	EIP	1.1/4.6	5.6/4.4	51.4
Sensory (side, nerve)					
Right					
Median	Wrist	Finger	3.8	3.7	32.5
Ulnar	Wrist	Finger	2.9	0.7	33.4
Radial	Forearm	Wrist	3.0	5.0	37.2
Left					
Median	Wrist	Finger	4.7	5.4	26.5
Ulnar	Wrist	Finger	2.8	9.3	36.6
Radial	Forearm	Wrist	2.5	6.5	34.9
Late responses					
Right median F-wave			33.7		
Left median F-wave			30.8		
Right ulnar F-wave			35.2		
Left ulnar F-wave			30.6		
Right median H-reflex			27.7	0.6	
Left median H-reflex			25.6	0.3	

NCV, nerve conduction velocity; APB, abductor pollicis brevis; ADM, abductor digiti minimi; EIP, extensor indicis proprius.

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Table 2. Nerve conduction studies and late responses in lower extremities

Characteristics	Stimulation site	Recording site	Latency (msec or msec, peak)	Amplitude (mV or μV)	NCV (m/sec)
Motor (side, nerve)					
Right					
Peroneal	Ankle/fibular head	EDB	NR	NR	NR
Peroneal	Fibular head	TA	3.1	4.2	
Tibial	Ankle/popliteal fossa	AH	4.0/11.4	3.3/2.4	44.1
Left					
Peroneal	Ankle/fibular head	EDB	3.9/10.6	0.7/0.4	45.1
Peroneal	Fibular head	TA	3.2	1.3	
Tibial	Ankle/popliteal fossa	AH	3.4/10.8	4.8/3.9	46.0
Sensory (side, nerve)					
Right					
Superficial peroneal	Shin	Ankle	2.2	2.5	50.9
Sural	Calf	Ankle	3.2	5.7	36.6
Left					
Superficial peroneal	Shin	Ankle	2.4	1.6	41.5
Sural	Calf	Ankle	2.7	2.7	37.0
Late responses					
Right peroneal F-wave			NR		
Left peroneal F-wave			NR		
Right tibial F-wave			55.5		
Left tibial F-wave			55.0		
Right tibial H-reflex			NR	NR	
Left tibial H-reflex			NR	NR	

NCV, nerve conduction velocity; EDB, extensor digitorum brevis; NR, no response; TA, tibialis anterior; AH, adductor halluces.

Table 3. Scalp somatosensory evoked potentials

Nerve	Latency (msec)			Amplitude (μV)
	EP or PF	N20 or P37	P25 or N45	
Right median	13.1	NR	NR	NR
Left median	12.4	NR	NR	NR
Right tibial	14.8	NR	NR	NR
Left tibial	13.3	NR	NR	NR

EP, erb point; PF, popliteal fossa; NR, no response.

that his physical and mental status showed no interval change. Follow-up MRI couldn't be obtained because further visit was not achieved.

DISCUSSION

MBD, WE and AP are distinct diseases and all have strong relationship with chronic alcoholism. MBD is a rare idiopathic syndrome observed at 0.01% of patients with alcohol related diseases. The pathologic findings of the MBD are characterized by symmetrical demyelination and necrosis of the corpus callosum. No more than 300 cases of MBD have been reported so far, and most of the patients in the MBD cases had history of alcohol abuse or chronic alcoholism [7,8]. Although the first case of MBD symptoms was described by Carducci in 1898, the disease was finally named after Marchifava and Bignami, who originally suggested the relation between the disease and increased consumption of alcohol, which was mass produced red wine in that case [1].

The exact underlying etiology and pathophysiology of MBD still remain unclear. It has been hypothesized that a toxin in the alcohol may cause demyelination, encephalopathy, and callosal edema [7]. New reports also discussed MBD to be a paraneoplastic syndrome or to

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be related to operations [1]. Other risk factors including lead toxicity, neoplasm, vitamin B complex deficiency, or osmotic disorders were suggested to have association with MBD [2]. Alcoholism, however, remains the most frequently reported underlying manifestation and considered to be the greatest risk factor for MBD alongside malnutrition [1].

MBD has not a typical clinical presentation. The disorder may present severe neuropsychiatric symptoms, including non-specific mental disorders such as confusion, delirium, unconsciousness, impaired memory and/or disorientation. Physical symptoms can appear in various part of body according to the affected structures of the brain. Gait disturbance, limb hypertonia occasionally worsen to rigidity, signs of disconnection or split brain syndrome, seizures, pyramidal signs, incontinence, sensory disturbance, and orofacial symptoms such as dysarthria and gaze palsy were reported in previous cases. Split brain syndrome has been proposed as a unique feature of MBD. However, it is difficult to be recognized because of the poor cooperation and the lower level of consciousness [1,7]. In our patient, impaired walking and limb weakness appeared as the first symptom and then unconsciousness, impaired memory, disorientation, dysarthria, spasticity, signs of interhemispheric disconnection were followed.

Nowadays, the accessibility to brain MRI has been improved surprisingly, so that the early detected mild cases of MBD with partial callosal involvement often present favorable outcomes [3]. Typical findings in patients with acute MBD include symmetric hyperintensities at the swollen parts or the whole corpus callosum in T2WI with hypointensities in T1WI [1]. The signal change observed in T2WI gradually normalizes after the acute stage. Later on, symmetric atrophy appears at the corresponding sites of the corpus callosum, which indicates the ongoing pathologic change of progressive demyelination, regional necrosis, and cyst formations. DWI frequently shows an increased signal intensity of the corpus callosum extending into the adjacent white matter usually sparing the subcortical U-fibers [1]. A reduced value in ADC image is often observed and are considered to reflect the risk of developing necrosis [9].

In a few cases of MBD, cortical involvement was observed as a major finding in MRI. The case of cortical involvement predominantly in bifrontal area who exhibited very poor prognosis was recently reported [3]. In that report, the authors suggested that the cortical lesions may be a marker of poor outcomes. Moreover, cortical lesions accompanying with the lower ADC values of the corpus callosum, like observed in our case, are reported to be associated with a higher mortality rate [1]. This cortical lesion, called Morel's laminar sclerosis, is a unique pathological finding in the brains of chronic alcoholics. It is characterized by cortical laminar necrosis and gliosis, mainly in the third layer and especially in the lateral-frontal cortex [10] and considered to be associated with or secondary to the callosal lesions of MBD [9,10]. The pathophysiology of the alcoholic cortical lesion is not clearly defined. Decreased glutamate uptake in the precentral cortex was revealed to be associated with thiamine deficiency not with chronic alcohol consumption itself, in animal model [11]. However, the MRI findings, which are hyperintense on DWI with relatively reduced ADC value in the cortical lesions of MBD, suggest that the pathologic change of Morel's laminar sclerosis can be caused secondarily by a cytotoxic edema in acute phase [10]. The abnormalities in our patient's MR images also presented similar patterns in DWI and ADC, and were observed mainly in both precentral gyrus and both frontal cortex, so that the findings were compatible with Morel's laminar sclerosis. Considering that his thiamin level was in normal range, thiamine deficiency cannot be pointed as the major cause of Morel's laminar sclerosis and his poor outcome is assumed to have little relation with thiamine level.

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In WE, the structures around the third ventricle are most commonly damaged, which includes the medial nuclei of the thalamus, the tegmentum, the periaqueductal, gray matter, the tectal plate of the midbrain and the mamillary bodies. These regions are known to have high oxidative metabolism and can be sensitively affected by thiamine deficiency [4,7].

On the recent visit, our patient's clinical features and the imaging (CT and MRI) findings presented MBD rather than WE. The imaging findings were far different from those of 3 years ago when he was diagnosed with WE, with the fact that the involvement of periaqueductal and paraventricular area was obvious in the previous MR image.

In our case, the NCS-EMG was also carried out to differentiate the weakness of both upper and lower limbs because it was the first sign among many symptoms of patient and accompanied with muscle atrophy of both lower limbs. The result was suggestive of axonal demyelinating sensorimotor polyneuropathy, compatible with AP. Diabetic polyneuropathy was also considered with the electrodiagnostic findings. However, the risk of DM polyneuropathy was assessed to be low noting that his HbA_1C level was normal and he had not experienced any DM complications. Without any hypoglycemic agent, his glucose level was fairly controlled under 200mg/dl during the whole admission period. AP is another neurologic disease recognized as a complication of chronic alcohol abuse and has compatible features with this case. According to a report of meta-analysis, AP frequently and more severely involves the lower limbs and NCS findings include the reduced amplitude pattern [12]. The weakness of our patient was more severe in both legs and the reduced amplitudes of nerves were more prominent in both lower extremities. Despite the several researches, the impact of alcohol to peripheral nervous system is not fully understood [2,12]. With the electrodiagnostic results of our patient, it cannot be clearly concluded that which component influenced more to peripheral nervous system between cytotoxicity of alcohol or malnutrition.

In our literature search, we could find just one study that reported co-occurrence of MBD with WE and co-occurrence of MBD with AP, respectively [2,6]. This case was unique in several aspects that typical imaging features of MBD including cortical involvement were observed and 3 distinct neurologic diseases appear in the same person. Considering that his liver function was not seriously depleted, the repeated and definite impact on the nervous system arise the question about the fundamental cause. Surprisingly, the co-occurrence of MBD and AP in chronic alcoholic patient whose WE was diagnosed earlier has not been reported in the previous literatures.

The treatment of suspected MBD is similar to the treatment of the Wernicke-Korsakoff syndrome. For WE treatment, B-group vitamins, including folate (B9), thiamine (B1), and vitamin B12, are most commonly applied. A high-dose corticosteroid therapy has been presented to have strong evidences to improve the clinical symptoms. However, there is no proven treatment established specifically for MBD [1,7], and vitamin supplement and steroid therapy are adopted for treating MBD. Although laboratory tests of this case did not show vitamin B deficiency, high-dose vitamin treatment was executed. Remarkable clinical improvement wasn't observed after vitamin supplement treatment. Mentality and general condition of patient were slightly improved but weren't conspicuously effective in this patient. It has been postulated that the co-occurrence of MBD involving cortical involvement and past history of WE affected the prognosis.

The limitation of this report is that we couldn't get the follow-up MRI image because the family refused further image evaluation and follow-up was failed. With adequate follow-up,

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changes of the brain lesions on serial MRI could be compared with images of previously reported cases which showed complete resolution [2]. During an NCS-EMG, abnormal spontaneous activity was noted, but motor unit action potentials couldn't be analyzed because the volitional recruitment was not elicited under patient's poor cooperation.

The influence of chronic heavy alcoholic consumption on nervous system is not fully investigated. We report one person affected by 3 distinct neurologic complications of alcoholic abuse and assumed that the individual's vulnerability of nervous system can arouse the repetitive insult to nervous system. More cases and further controlled studies are needed to establish the effect of heavy alcoholic consumption to the nervous system.

REFERENCES

1. Wenz H, Eisele P, Artemis D, Förster A, Brockmann MA. Acute Marchiafava-Bignami disease with extensive diffusion restriction and early recovery: case report and review of the literature. J Neuroimaging 2014;24:421-424.
PUBMED | CROSSREF
2. Boloursaz S, Nekooei S, Seilanian Toosi F, Rezaei-Dalouei H, Davachi B, Kazemi S, Abbasi B. Marchiafava-Bignami and alcohol related acute polyneuropathy: the cooccurrence of two rare entities. Case Rep Neurol Med 2016;2016:5848572.
PUBMED | CROSSREF
3. Namekawa M, Nakamura Y, Nakano I. Cortical involvement in Marchiafava-Bignami disease can be a predictor of a poor prognosis: a case report and review of the literature. Intern Med 2013;52:811-813.
PUBMED | CROSSREF
4. Cerase A, Rubenni E, Rufa A, Vallone I, Galluzzi P, Coratti G, Franchi F, Giannini F, Venturi C. CT and MRI of Wernicke's encephalopathy. Radiol Med 2011;116:319-333.
PUBMED | CROSSREF
5. Zuccoli G, Pipitone N. Neuroimaging findings in acute Wernicke's encephalopathy: review of the literature. AJR Am J Roentgenol 2009;192:501-508.
PUBMED | CROSSREF
6. Tsui E, Man B, Fu M, Chan J, Yuen M, Ng S. Coexistence of Marchiafava–Bignami disease, Wernicke encephalopathy and central pontine myelinolysis in a patient with chronic alcoholism. Eur J Radiol Extra 2003;48:74-77.
CROSSREF
7. Gramaglia C, Feggi A, Vecchi C, Di Marco S, Venesia A, Delicato C, Chieppa N, De Marchi F, Cantello R, Zeppegno P. Marchiafava-Bignami disease with frontal cortex involvement and late onset, long-lasting psychiatric symptoms: a case report. Riv Psichiatr 2016;51:79-82.
PUBMED
8. Chen X, Wang Y, Wang Y, Tong D, Zhu B. Alcoholic and non-alcoholic Marchiafava-Bignami disease: a comparative study. Neurosci Med 2016;7:99-105.
CROSSREF
9. Lee SH, Kim SS, Kim SH, Lee SY. Acute Marchiafava-Bignami disease with selective involvement of the precentral cortex and splenium: a serial magnetic resonance imaging study. Neurologist 2011;17:213-217.
PUBMED | CROSSREF
10. Johkura K, Naito M, Naka T. Cortical involvement in Marchiafava-Bignami disease. AJNR Am J Neuroradiol 2005;26:670-673.
PUBMED
11. Carvalho FM, Pereira SR, Pires RG, Ferraz VP, Romano-Silva MA, Oliveira-Silva IF, Ribeiro AM. Thiamine deficiency decreases glutamate uptake in the prefrontal cortex and impairs spatial memory performance in a water maze test. Pharmacol Biochem Behav 2006;83:481-489.
PUBMED | CROSSREF
12. Julian T, Glascow N, Syeed R, Zis P. Alcohol-related peripheral neuropathy: a systematic review and meta-analysis. J Neurol 2019;266:2907-2919.
PUBMED | CROSSREF