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Clinical analysis of Marchiafava-Bignami disease

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Abstract

Background Marchiafava-Bignami disease (MBD) is an exceptionally rare condition, a fact that should pique the professional curiosity of medical practitioners. In recent years, case reports of this disease have been infrequent, and no comprehensive analysis or summary of the characteristics of the published cases has been conducted.

Methods We collected the medical records of three patients treated at our hospital from March 2022 to March 2023. Furthermore, we searched PubMed for "case reports" from January 2017 to March 2023 and included 30 cases. By retrospectively analyzing these 33 cases, we summarized the characteristics of the disease.

Results Based on our analysis, we found that MBD primarily affects middle-aged men and typically has an acute or subacute onset, with the primary clinical manifestations being disturbances of consciousness, speech disorders, cognitive impairment, and psychiatric or behavioral abnormalities, often leading to misdiagnosis of psychiatric disorders. Most patients have a history of alcohol consumption or malnutrition. Head CT or MRI revealed symmetric lesions in the corpus callosum, with the splenium being the most commonly affected area. Lesions might also involve white matter outside the corpus callosum, and a wider range of lesions suggested a poor prognosis. However, the prognosis is generally favorable with timely and adequate administration of B vitamins, providing reassurance to medical professionals and patients alike.

Conclusion The early recognition and treatment of Marchiafava-Bignami disease are paramount, as they can significantly improve the prognosis. This underscores the critical need for prompt clinical intervention in the early stages of the disease, instilling a sense of urgency and significance in the work of medical professionals.

Keywords Marchiafava-Bignami disease (MBD), Corpus callosum, Neurology

Introduction

Marchiafava-Bignami disease (MBD) is a rare neurological syndrome associated with chronic alcohol abuse and malnutrition, including conditions such as post-gastrointestinal malignancy surgery, anorexia, and unbalanced diets [1]. The clinical presentation of MBD is diverse and nonspecific [2], often accompanied by psychiatric and behavioral abnormalities, leading to a misdiagnosis of mood disorders or other psychiatric illnesses, thereby complicating the clinical diagnosis. Hence, the diagnosis and treatment of MBD are challenging, and earlier studies indicate a poor prognosis for the disease [2].

Despite the limited understanding and issues in diagnosing and treating MBD in the past, recent case

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reports have contributed to a better awareness of the disease. However, whether the clinical characteristics of MBD have changed in recent years remains unclear. Given the rarity of MBD, conducting randomized trials is impractical. Thus, the only feasible research design to reveal the clinical characteristics of MBD is a retrospective analysis of published case reports. Yet, no such studies have been reported in the past nine years. We reviewed recent case reports to understand the disease in a better way, describe the key features for accurate diagnosis, summarize effective treatment methods, and predict prognosis.

Methods

We retrospectively reviewed the medical records of three patients with MBD treated at Xuanwu Hospital Hebei Hospital from March 2022 to March 2023, and each patient was followed up accordingly. Using "Marchiafava-Bignami" as the keyword, we searched PubMed for "case reports" from January 2017 to March 2023, retrieving a total of 35 case reports. Three authors (HW, BX, ST) independently reviewed these reports. Cases that were reported in more than one paper were considered only once. Eight reports were excluded because they either did not pertain to MBD or had incomplete clinical data, leaving 27 reports with 30 cases [3–29]. The present study included data from 33 cases.

All cases were diagnosed before death using either head Magnetic resonance imaging (MRI) or computed tomography (CT) scans. Most of these cases were associated with alcohol abuse, malnutrition, or both. In this study, long-term alcohol users included those described as chronic current alcohol abusers or alcohol-dependent individuals, as well as others, reported to have a long history of alcohol abuse or a habit of heavy drinking. The pattern of alcohol consumption was often reported as continuous daily drinking. The nutritional status of patients was not always defined in these reports. When reported, the definitions used encompassed malnutrition, anorexia, cachexia, or refusal to eat for several days. In this study, we considered all of these factors as indicators of malnutrition.

Results

Among the 33 cases included in the analysis, 22 were male (66.6%), and 11 were female (33.4%). The average age of onset was 52.4 years, with the average onset age being 54.9 years for males and 47.4 years for females. There were 18 cases (54.5%) with acute onset, 7 cases (21.2%) with subacute onset, and 8 cases (24.2%) with chronic onset.

Clinical characteristics

The primary clinical manifestations observed in the 33 cases are as follows: Among the 33 cases in this study, the primary clinical manifestations were dyskinesia (22 cases,66.7%), which included 11 cases of ataxia, 3 cases of decreased muscle strength of both lower limbs, 3 cases of decreased muscle strength of limbs, 2 cases of ataxia and decreased muscle strength of both lower limbs, 1 case of tremor and and 2 cases unspecified types. Speech disorders were observed in 19 cases (57.6%), such as dysarthria (11 cases), aphasia (3 cases), mixed aphasia (2 cases), complete aphasia (1 case), and unspecified types of speech disorders (2 cases).Consciousness disorders were present in 18 cases (54.5%), such as coma (7 cases), agitation (4 cases), somnolence (4 cases), and other types (3 cases).Cognitive impairment was found in 15 cases (45.5%).Other clinical manifestations included emotional or personality changes (10 cases, 30.3%), seizures (4 cases, 12.1%), sensory disturbances (3 cases), neglect (2 cases), corpus callosum disconnection (2 cases), apraxia (4 cases), and combined neglect and apraxia (1 case). Table 1 presents detailed information on clinical manifestations.

Among the 18 patients with acute onset, the primary clinical manifestations are as follows: Consciousness disorders were observed in 14 cases (77.8%), such as coma (4 cases), somnolence (4 cases), agitation (3 cases), and other types (3 cases).Speech disorders were found in 12 cases (66.7%), such as aphasia (2 cases), dysarthria (6 cases), unspecified types (2 cases), mixed aphasia (1 case), and complete aphasia (1 case).Movement disorders were present in 11 cases (61.1%), such as ataxia (4 cases), decreased muscle strength (4 cases), unspecified types (2 cases), and combined ataxia and decreased muscle strength (1 case).

Among the seven patients with subacute onset, the primary clinical manifestations are as follows: Movement disorders were observed in 5 cases (71.4%), such as ataxia (3 cases) and decreased muscle strength (2 cases). Apraxia/disconnection syndrome was seen in 3 cases, such as neglect (1 case) and apraxia (2 cases).Consciousness disorders were present in 3 cases, in which all were coma.

Among the eight patients with chronic onset, the primary clinical manifestations are as follows: Movement disorders were seen in 6 cases (75.0%), such as ataxia (4 cases), tremor (1 case), and combined ataxia and decreased muscle strength (1 case). Speech disorders were found in 5 cases (62.5%), such as dysarthria (3 cases), aphasia (1 case), and mixed aphasia (1 case). Cognitive impairment was observed in 5 cases (62.5%). Emotional or personality changes were present in 4 cases (50%).

Table 1 Clinical data analysis of 33 patients with MBD

Case Number	Reference	Age(year)	Onset form	Symptom							
				Consciousness disorder	Movement disorder	Sensory disturbance	Speech disorder	Neglect/apraxia	Seizure	Cognitive impairment	Personality/ mood change
1	3	31-40	acute	agitation	—	—	—	—	—	—	—
2	4	31-40	acute	agitation	unknown type	—	unknown type	neglect、apraxia	—	+	—
3	4	51-60	acute	—	—	—	—	—	—	+	—
4	5	51-60	chronic	agitation	ataxia	+	—	—	—	+	—
5	6	41-50	chronic	—	ataxia	—	aphasia	—	+	+	+
6	7	41-50	subacute	coma	ataxia	—	—	—	—	+	—
7	7	61-70	acute	somnolence	—	—	—	—	+	—	—
8	7	51-60	acute	others	ataxia	—	aphasia	—	—	—	—
9	8	71-80	acute	others	—	—	dysarthria	—	—	+	—
10	9	51-60	chronic	—	—	—	—	disconnection	—	+	+
11	10	51-60	acute	coma	muscle weakness	—	aphasia	—	—	—	+
12	11	31-40	subacute	—	ataxia	—	—	—	—	—	—
13	12	51-60	acute	coma	—		—	—	—	—	—
14	13	51-60	acute	coma	—	—	—	—	—	—	—
15	14	81-90	acute	somnolence	muscle weakness	—	unknown type	—	—	+	—
16	15	51-60	subacute	coma	—	—	—	—	—	—	—
17	16	21-30	acute	—	unknown type	—	dysarthria	—	—	—	—
18	17	31-40	chronic	—	tremor	—	mixed aphasia	apraxia	—	+	—
19	18	61-70	acute	—	ataxia	—	dysarthria	—	—	+	—
20	19	31-40	subacute	—	ataxia	—	dysarthria	apraxia	—	+	+
21	20	31-40	acute	others	muscle weakness、ataxia	—	—	—	—	+	+
22	21	51-60	subacute	—	—	—	dysarthria	apraxia	—	—	+
23	22	41-50	acute	coma	—	—	complete aphasia	—	—	—	—
24	23	31-40	acute	agitation	ataxia	—	dysarthria	—	—	—	—
25	24	31-40	acute	—	ataxia	—	dysarthria	—	—	—	—
26	25	41-50	chronic	—	—	—	dysarthria	—	+	—	—
27	26	71-80	subacute	—	muscle weakness	+		neglect	—	—	
28	27	31-40	chronic	—	ataxia	—	dysarthria	disconnection	—	—	+
29	28	61-70	subacute	coma	muscle weakness	—	—	—	+	—	+
30	29	61-70	acute	somnolence	muscle weakness	—	dysarthria	apraxia	—	+	—
31	—	51-60	acute	somnolence	muscle weakness	—	mixed aphasia	—	—	+	+
32	—	51-60	chronic	—	muscle weakness、ataxia	+	dysarthria	—	—	+	+
33	—	71-80	chronic	—	ataxia	—	—	—	—	—	—

Table 1 (continued)

Case Number	Previous history	Auxiliary examination	Treatment	Prognosis					
	Nalnutrition	Drinking	Vitamin B deficiency	Lumbar puncture	EEG	CT lesions	MR lesions		
1	—	—	VitB12 normal	Glu↑	extensive slow waves	<MR	④	vitamin B	improvement
2	—	+	VitB1↓	N	NA	NA	③	vitamin B+hormone+amantadine	improvement
3	—	+	NA	NA	NA	NA	⑤	amantadine	lost to follow up
4	—	+	VitB12↓	NA	NA	N	②	vitamin B	improvement
5	+	+	VitB6、VitB12↓	NA	NA	NA	⑥	vitamin B	no improvement
6	+	+	VitB12↑	NA	NA	NA	①	vitamin B	improvement
7	—	+	VitB12↑	N	NA	NA	④	vitamin B	vegetative state
8	—	+	VitB12 normal	Pro↑	extensive slow waves	N	②	vitamin B	no improvement
9	+	+	VitB1↓、VitB12↑、folate normal	NA	NA	<MR	⑥	vitamin B	improvement
10	—	+	VitB12 normal	NA	N	NA	⑧	vitamin B	improvement
11	—	+	NA	NA	NA	NA	⑨	vitamin B	improvement
12	+	—	VitB12 and folate normal	N	N	NA	⑥	vitamin B+hormone	improvement
13	—	+	NA	N	N	NA	②	vitamin B	improvement
14	—	+	VitB1 normal	N	NCSE	NA	④	vitamin B	improvement
15	+	—	VitB1、B12↓	Pro↑	NA	NA	⑪	vitamin B+hormone	no improvement
16	—	+	NA	N	extensive slow waves	NA	⑤	vitamin B	improvement
17	+	—	NA	NA	NA	NA	②	NA	improvement
18	+	+	VitB1↓	nucleated cell: 1; RBC: 4	NA	NA	③	vitamin B+hormone	improvement
19	—	—	NA	NA	NA	NA	③	vitamin B	improvement
20	—	+	VitB12↑、VitB1↓	RBC:4, nucleated cell: 1	NA	NA	③	vitamin B+hormone	improvement
21	+	+	VitB12 and folate normal	NA	N	N	⑩	vitamin B	improvement
22	—	—	VitB12 normal	N	NA	NA	②	vitamin B+hormone	death
23	—	+	folate↓	NA	NA	NA	④	vitamin B+hormone	improvement
24	+	—	NA	NA	NA	consistent with MR	②	NA	lost to follow up
25	—	—	NA	WBC: 10; RBC: 1	NA	N	④	vitamin B+hormone	improvement
26	—	+	NA	not check	NA	NA	⑦	vitamin B	improvement
27	—	—	NA	NA	NA	NA	④	vitamin B+hormone	death
28	—	+	VitB12 normal	NA	NA	NA	⑧	NA	lost to follow up

Table 1 (continued)

Case Number	Previous history	Auxiliary examination	Treatment	Prognosis					
	Nalnutrition	Drinking	Vitamin B deficiency	Lumbar puncture	EEG	CT lesions	MR lesions		
29	—	—	NA	Pro↑,WBC↑	NA	N	⑪	vitamin B	improvement
30	+	+	VitB1、B12 normal	NA	extensive slow waves	consistent with MR	⑥	vitamin B	lost to follow up
31	+	+	VitB12、folatenormal	not check	not check	consistent with MR	④	vitamin B	improvement
32	+	+	NA	not check	not check	N	③	vitamin B	improvement
33	—	+	NA	not check	not check	NA	⑤	vitamin B	improvement

NA Not available, *N* normal, *NCSE* Non-Convusive Status Epilepicus, *Pro* protein, *RBC* red blood cell, *WBC* white blood cell, *Glu* glucose

Lesion Locations:

① Genu of the corpus callosum

② Splenium of the corpus callosum

③ Genu and splenium of the corpus callosum

④ Genu, splenium of the corpus callosum, and white matter lesions

⑤ Genu of the corpus callosum and white matter

⑥ Splenium of the corpus callosum and white matter

⑦ Splenium of the corpus callosum and cerebellum

⑧ Entire corpus callosum

⑨ Body of the corpus callosum

⑩ Splenium of the corpus callosum and brainstem

⑪ Splenium of the corpus callosum, cerebellum, and white matter

Table 2 Comparison of clinical data between long-term alcohol users and non-alcohol users

Clinical features	Long-term alcohol (*n*= 23)				Non-alcohol (*n* = 10)		
	Total	Acute onset = 12	Subacute onset = 3	Chronic onset = 8	Total	Acute onset = 6	Subacute onset = 4
Symptom							
Consciousness disorder	13(56.52%)	10(83.33%)	2(66.67%)	1(12.50%)	4(40.00%)	3(50.00%)	1(25.00%)
Movement disorder	13(56.52%)	6(50.00%)	2(66.67%)	5(62.50%)	8(80.00%)	5(83.33%)	3(75.00%)
Speech disorder	12(52.17%)	7(58.33%)	0	5(62.50%)	6(60.00%)	5(83.33%)	1(25.00%)
Cognitive impairment	11(47.83%)	6(50.00%)	0	5(62.50%)	2(20.00%)	2(33.33%)	0
Personality/mood change	7(30.43%)	3(25.00%)	0	4(50.00%)	2(20.00%)	0	2(50.00%)
MR lesions							
①+⑤	5(21.74%)	1(8.33%)	3(100.00%)	1(12.50%)	0	0	0
②+⑥+⑦+⑩+⑪	8(34.78%)	5(41.67%)	0	3(37.50)	6(60.00%)	3(50.00%)	3(75.00%)
③+④	9(39.13%)	5(41.67%)	0	4(50.00%)	4(40.00%)	3(50.00%)	1(25.00%)
⑨	1(4.35%)	1(8.33%)	0	0	0	0	0
Treatment							
Vitamin B	17(73.91%)	9(75.00%)	2(66.67%)	6(75.00%)	3(30.00%)	2(33.33%)	1(25.00%)
Vitamin B+hormone	3(13.04%)	1(8.33%)	1(33.33%)	1(12.50%)	5(50.00%)	2(33.33%)	3(75.00%)
Amantadine	1(4.35%)	1(8.33%)	0	0	0	0	0
Vitamin B+hormone+amantadine	1(4.35%)	1(8.33%)	0	0	0	0	0
NA	1(4.35%)	0	0	1(12.50%)	2(20.00%)	2(33.33%)	0
Prognosis							
Improvement	17(73.91%)	8(66.67%)	3(100.00%)	6(75.00%)	6(60.00%)	4(66.67%)	2(50.00%)
No improvement	2(8.70%)	1(8.33%)	0	1(12.50%)	1(10.00%)	1(16.67%)	0
Vegetative state	1(4.35%)	1(8.33%)	0	0	0	0	0
Death	0	0	0	0	2(20.00%)	0	2(50.00%)
Lost to follow up	3(13.04%)	2(16.67%)	0	1(12.50%)	1(10.00%)	1(16.67%)	0

NA Not available

Lesion Locations:

① Genu of the corpus callosum

② Splenium of the corpus callosum

③ Genu and splenium of the corpus callosum

④ Genu, splenium of the corpus callosum, and white matter lesions

⑤ Genu of the corpus callosum and white matter

⑥ Splenium of the corpus callosum and white matter

⑦ Splenium of the corpus callosum and cerebellum

⑧ Entire corpus callosum

⑨ Body of the corpus callosum

⑩ Splenium of the corpus callosum and brainstem

⑪ Splenium of the corpus callosum, cerebellum, and white matter

Out of the 33 cases analyzed, 23 (69.6%) had a history of long-term alcohol consumption, whereas the other 10 cases (30.4%) did not. Among the patients with a history of long-term alcohol consumption, the primary clinical manifestations were consciousness disorders (13 cases, 56.5%), movement disorders (13 cases, 56.5%), and speech disorders (12 cases, 52.2%). Among those who did not have a history of long-term alcohol consumption, the primary clinical manifestations were movement disorders (8 cases, 80%) and speech disorders (6 cases, 60%). Table 2 provides detailed information.

Auxiliary examination results

Blood tests indicated a decrease in vitamin B1 in 4 out of 20 cases (20.0%) and a decrease in vitamin B12 in 3 out of 20 cases (15.0%). Folate levels were reduced in 1 out of 20 cases. Electroencephalograms (EEG) were performed on 9 patients (27.3%); 4 patients exhibited generalized slow waves, 1 indicated nonconvulsive status epilepticus, and 4 showed no abnormalities. Lumbar puncture examinations were completed in 14 cases, with 7 showing abnormalities. Among these, 3 cases had mildly elevated protein levels (70.95–76 mg/dl), and 1 had a mild

increase in white blood cell count. Head CT scans were performed on 11 patients, where 6 showed no abnormal lesions in the corpus callosum, 3 had findings consistent with MRI results, and 2 showed smaller lesion areas compared to MRI findings.

All 33 cases underwent MRI scans of the head, revealing lesions in the corpus callosum. Lesions in the splenium of the corpus callosum were observed in 28 cases (84.9%), whereas lesions in the genu of the corpus callosum were found in 18 cases (54.6%). Combined lesions in both the genu and splenium of the corpus callosum were observed in 5 cases (15.2%). Lesions involving the genu, splenium, and white matter were observed in 7 cases (21.2%), of which 6 had an acute onset and 1 had a subacute onset. Furthermore, 18 cases (54.6%) had lesions outside the corpus callosum, 16 cases (48.5%) had involvement of the subcortical white matter, and 3 cases (9.10%) had cerebellar involvement.

Treatment and prognosis

Out of 33 cases, 20 cases (60.6%) were treated with B vitamins, and the prognosis was improved in 16 cases. Vitamin B1 was used in 12 cases, and in 1 case 200 mg of vitamin B1 was injected intravenously daily for 28 days, then changed to 30 mg/day orally. Six cases received intravenous injections of vitamin B1 no less than 500 mg/day, and most of the application time was longer than half a month. Among these, 2 cases received intravenous injections of vitamin B1 500 mg/day, where the effect was not good, and the symptoms improved after the dosage was increased to 1000 mg/day or 1500 mg/day. Vitamin B12 was used in 6 cases and 1 mg/day in 2 cases, all of which were used for 7 days or more. Two patients were treated with oral vitamin B12 at 0.5 mg/day for more than 14 days. Folic acid was used in 4 cases, and 1 case, was given an intravenous injection of 1 mg/day; the specific course of treatment was not mentioned. One case received an intravenous injection of 5 mg/day; 1 case was treated with 5 mg orally three times a day.

Eight cases (24.2%) were treated with B vitamins combined with hormone, 6 cases were treated with intravenous high-dose hormone, and 4 cases were treated with intravenous methylprednone 1 g/day (3 cases were treated for 5 days, and their symptoms were improved; 1 case did not mention the course of treatment and the patient died). Symptoms improved in 4 cases; in 2 cases, symptoms did not improve, and the patient died in 2 cases.

Two cases (6.1%) were treated with amantadine, and one case was treated with 100 mg orally twice a day for 2 weeks, and then the symptoms improved. One patient took 100 mg orally twice daily, and the symptoms improved after 3 days of application. The dosage was then increased to 200 mg each time, three times a day. After that, the drug was discontinued due to auditory and visual hallucinations, and then the follow-up was lost.

Three cases (9.1%) did not explicitly mention the treatment method.

Regarding overall outcomes among the 33 cases, 23 patients (69.7%) showed improvement, 3 (9.1%) showed no improvement, 1 (3.0%) remained in a vegetative state, 2 (6.1%) died, and 4 (12.1%) were lost to follow-up (detailed in Table 1). The 6 patients with poor prognosis may have been affected by factors such as difficult-to-correct nutritional deficiencies (2 cases), the presence of consciousness disorders (2 cases), and comorbidities, particularly epilepsy, associated with a worse outcome. No deaths occurred among those with a history of long-term alcohol consumption. Out of the two patients who did not have a history of long-term alcohol consumption and died, one succumbed to a hematologic disease while the other as a result of the tumor.

Discussion

Marchiafava–Bignami disease (MBD) refers to primary degeneration of the corpus callosum characterized by symmetrical demyelination, central necrosis, and corpus callosum atrophy. The MBD presents a wide range of clinical symptoms, none specific to the disease [2]. In the acute phase, symptoms may include seizures, consciousness disturbances, and rapid death. Subacute symptoms involve varying degrees of confusion, dysarthria, psychiatric and behavioral abnormalities, memory loss, interhemispheric disconnection syndrome, and gait instability. The chronic phase is marked by progressive dementia [30].

The corpus callosum is located at the base of the longitudinal fissure of the brain, and it is divided into four parts from anterior to posterior: the rostrum, genu, body, and splenium [31]. The white matter fibers of the corpus callosum radiate throughout the hemispheres, connecting with the frontal, parietal, occipital, and temporal lobes, forming the anterior and posterior forceps and the fibers that extend to the centrum semiovale on both sides. The blood supply to the corpus callosum comes from the anterior cerebral artery, the anterior communicating artery, and the posterior cerebral artery. The anterior part comprising four-fifths of the corpus callosum is primarily supplied by the anterior cerebral artery, anterior communicating artery, pericallosal artery, and their respective branches, whereas the posterior one-fifth is supplied by the posterior cerebral artery and posterior choroidal arteries. The splenium of the corpus callosum receives blood from three arteries: the terminal branches of the anterior cerebral artery (the anterior pericallosal artery), branches of the posterior cerebral artery (the

posterior pericallosal artery), and the posterior accessory pericallosal artery [32, 33].

The corpus callosum connects corresponding regions of both cerebral hemispheres, allowing the brain to function as a unified entity. Its primary role is facilitating communication between the hemispheres, integrating bilateral motor, sensory, and language functions, coordinating motor skills, and contributing to cognitive functions such as memory and calculation. The corpus callosum is especially crucial for integrating cognitive information between the hemispheres. When any part of the corpus callosum is damaged, the integrity of these fiber connections is compromised, disrupting communication between the hemispheres and resulting in various clinical manifestations [34].

The present study showed that the splenium was involved in 28 cases (84.9%) and the genu in 18 cases (54.6%), as lesions in MBD primarily affect the corpus callosum. Furthermore, MBD can involve extensive areas of the brain's white matter, as detailed in Table 1. Lesions in different areas may lead to varying symptoms. Researchers indicated that the genu is connected to the prefrontal lobe, premotor, and supplementary motor areas, while the body connects to the primary motor and sensory cortex. The splenium (posterior) is associated with the parietal, occipital, and temporal lobes [35]. The genu primarily facilitates neural conduction, and damage to this area can result in motor, speech, and cognitive dysfunctions. The splenium transmits visuospatial information, language, reading, arithmetic, intelligence quotient behavior, and consciousness [31]. Therefore, the symptoms of MBD are expected to vary depending on the affected corpus callosum region. However, the present study did not show a clear relationship between symptoms and lesion location, possibly because many MBD patients also exhibit cognitive impairments and psychiatric symptoms, making it challenging to distinguish symptoms and arrive at a clinical diagnosis.

This study demonstrated that when the splenium of the corpus callosum is involved, it is often accompanied by concurrent white matter involvement, resulting in a more extensive range of lesions and diverse clinical manifestations. Conversely, lesions involving the genu of the corpus callosum tend to be smaller and associated with fewer clinical symptoms.

Although it is challenging to distinguish lesion sites based solely on symptoms, differences in lesion locations do exist. Our research indicates that in non-alcoholic patients, lesions primarily involve the splenium of the corpus callosum. Conversely, in chronic alcoholics, there is widespread involvement of the corpus callosum, often accompanied by lesions in the white matter outside the corpus callosum, as well as in the cerebellum and brainstem. The corpus callosum is primarily composed of white matter, with myelin being a key component. The integrity and function of white matter myelin depend on adequate levels of vitamin B1 [36, 37]. Therefore, lacking vitamin B1 can lead to MBD in patients with nutritional deficiencies. Moreover, due to the distribution of blood vessels, the splenium has a relatively poor blood supply, as it is situated in a watershed area between multiple arteries [31, 38], making the splenium more vulnerable to damage when nutritional deficiencies are present. Furthermore, the splenium is characterized by high metabolic activity [39], making it more susceptible to damage when the microenvironment of the corpus callosum is altered. These factors likely explain why the splenium of the corpus callosum is particularly prone to involvement in MBD patients.

Evidence from studies on human brain tissue and animal models (rodents) suggests a synergistic effect between alcohol-induced neurotoxicity and vitamin B deficiency, particularly vitamin B1. Both chronic alcohol consumption and malnutrition can lead to vitamin B1 deficiency. Therefore, in alcoholics, the damage to the corpus callosum may result from the combined effects of nutritional deficiencies and direct alcohol-induced damage to the corpus callosum. Thus, alcoholic patients with concurrent malnutrition tend to have more extensive lesions and severe symptoms.

The etiology of Wernicke's encephalopathy is also related to vitamin deficiency, particularly vitamin B1, suggesting that MBD and Wernicke's encephalopathy may share similar underlying pathophysiological mechanisms [6]. However, there are differences between the two regarding symptoms, imaging, and lesion locations. Wernicke's encephalopathy is characterized by a classic triad of symptoms: ophthalmoplegia, ataxia, and mental confusion [40]. On brain MRI, lesions typically show symmetrical distribution along the midline, primarily involving the mammillary bodies, medial thalamus, the periaqueductal gray matter of the midbrain, the areas surrounding the third and fourth ventricles, and the corpora quadrigemina [40], all of which are gray matter structures. Conversely, MBD lacks specific clinical manifestations. The MRI findings predominantly showed involvement of the corpus callosum and white matter outside the corpus callosum, with little or no involvement of gray matter [1]. Thus, the exact differences in the pathophysiological mechanisms between the two conditions require further investigation.

The diagnosis of MBD mostly depends on a thorough patient history, with particular attention to any history of chronic alcohol abuse or malnutrition, as well as clinical symptoms and imaging studies [30]. Advances in imaging techniques have significantly facilitated the

recognition and accurate diagnosis of MBD. The MBD often presents as symmetric low-density lesions in the splenium, body, and genu of the corpus callosum on head CT scans [41], typically showing an expansive appearance with blurred boundaries. However, CT has limited sensitivity in detecting MBD. In this study, the positive rate of CT for MBD was only 27.3% (3 out of 11 cases). Conversely, MRI is crucial for diagnosing MBD. Characteristically, MRI scans revealed abnormal signals within the corpus callosum without mass effect, often accompanied by swelling of the genu and splenium of the corpus callosum. During the acute and early subacute phases, MRI findings showed cytotoxic edema and demyelination within the lesions, with the corpus callosum appearing expansile thickening. These lesions typically showed low signal intensity on T1-weighted images and high signal intensity on T2-weighted, FLAIR, and Diffusion-weighted imaging (DWI) sequences without enhancement on contrast scans. In the chronic phase, the splenium, body, and genu of the corpus callosum showed cystic degeneration and atrophy, with T1 hypointense and T2 hyperintense signals [41]. Figure 1 depicts a typical MRI image of a patient with MBD treated at our hospital.

Once diagnosed, it is essential to administer B vitamins, particularly vitamin B1, promptly. Previous studies have indicated a generally poor prognosis for MBD. Nevertheless, our research suggests a significant enhancement in recent years, as evidenced by 69.7% of patients showing improvement. This positive shift is likely due to increased awareness and earlier diagnosis and treatment of the disease by clinicians. In the present study, only six patients had poor outcomes attributed to other diseases beyond corpus callosum degeneration.

This study has the following limitations. First, the number of cases included was relatively small due to the scarcity of related research in recent years. Second, in some of the literature included in this study, the descriptions of clinical symptoms were unclear, and the information on auxiliary examinations was incomplete, leading to gaps in the data. Third, the classification of clinical manifestations in this study was insufficient, and the limited data prevented us from establishing a clear relationship between clinical manifestations and lesion locations. Finally, the data

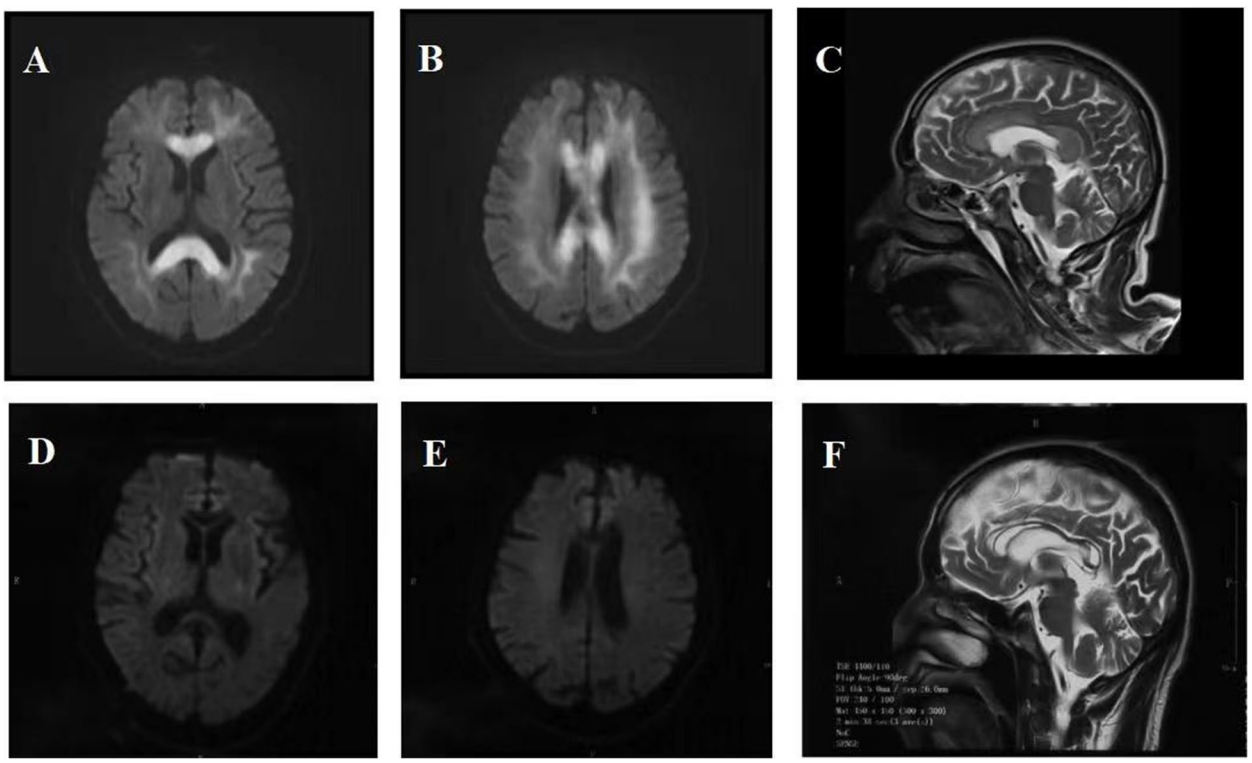

Fig. 1 MRI imaging of a patient with MBD**A** DWI of the brain MRI shows hyperintense signals in the genu and splenium of the corpus callosum five days after MBD onset; **B** DWI of the brain MRI shows hyperintense signals in the periventricular white matter five days after MBD onset; **C** Sagittal T1-weighted MRI shows swelling of the splenium of the corpus callosum five days after MBD onset; **D** DWI of the brain MRI shows hypointense signals in the genu and splenium of the corpus callosum 84 days after MBD onset; **E** DWI of the brain MRI shows isointense signals in the periventricular white matter 84 days after MBD onset; **F** Sagittal T1-weighted MRI shows atrophy of the splenium of the corpus callosum 84 days after MBD onset

analysis methods were relatively simple, and no in-depth analysis was conducted.

In summary, primary corpus callosum degeneration is more common in middle-aged individuals, predominantly males, and often presents with acute or subacute onset. The primary clinical manifestations include consciousness disturbances, speech disorders, cognitive impairments, and psychiatric or behavioral abnormalities, which can easily be misdiagnosed as psychiatric disorders. The CT or MRI scans of the brain often reveal symmetric lesions in the corpus callosum, which might be mistaken for ischemic cerebrovascular disease. In clinical practice, the diagnosis should be supported by the patient's medical history, especially if they have a history of chronic alcohol abuse or long-term nutritional deficiencies, and brain MRI can assist in the diagnosis. With timely and adequate administration of B vitamins, the prognosis for this condition is generally favorable. Despite its prevalence in clinical settings, the lack of extensive study has resulted in inadequate clinical awareness, necessitating increased attention from clinicians.

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Authors' contributions
CL: analysis and interpretation of data, drafting the work and revising it critically for important intellectual content. YD: interpretation of data, drafting the work and revising it critically for important intellectual content. HW, BX and ST: analysis and interpretation of data, revising it critically for important intellectual content. All authors contributed to and have approved the final manuscript.

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Availability of data and materials
The data that support the findings of this study are available from the corresponding author upon reasonable request.

Declarations

Ethics approval and consent to participate
This study was conducted in accordance with the guidelines of the World Medical Association Declaration of Helsinki (2000) and was approved and supervised by the Ethics Committee of the first hospital of Hebei medical university hospital. All participants at the First Hospital of Hebei Medical University obtained written informed consent from their cognitively normal legal guardians.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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