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Original Article

Analysis of 21 Patients With Alcoholic Marchiafava–Bignami Disease in Chongqing, China

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ABSTRACT: ***Objective:*** This study aimed to investigate the characteristics and prognosis of patients with alcoholic Marchiafava–Bignami disease (MBD), a rare neurological disorder commonly associated with chronic alcoholism, in Chongqing, China. ***Methods:*** We conducted a retrospective analysis of clinical data from 21 alcoholic MBD patients treated at the First Affiliated Hospital of Chongqing University between 2012 and 2022. ***Results:*** The study included 21 patients with alcoholic MBD who had a mean age of 59 ± 9.86 years and an average drinking history of 35.48 ± 8.65 years. Acute onset was observed in 14 (66.7%) patients. The primary clinical signs observed were psychiatric disorders (66.7%), altered consciousness (61.9%), cognitive disorders (61.9%), and seizures (42.9%). Magnetic resonance imaging revealed long T1 and long T2 signal changes in the corpus callosum, with lesions predominantly found in the genu (76.2%) and splenium (71.4%) of the corpus callosum. The poor prognosis group demonstrated an increased incidence of altered consciousness (100% vs 50%, P = 0.044), pyramidal signs (80% vs 18.8%, P = 0.011), and pneumonia (100% vs 31.3%, P = 0.007). Patients with a longer drinking history (45.0 ± 10.0 years vs 32.69 ± 5.99 years, p = 0.008) and a lower thiamine dose (p = 0.035) had a poorer prognosis at 1 year. ***Conclusions:*** This study identified altered consciousness, pyramidal signs, and pneumonia as predictors of a poor prognosis in patients with alcoholic MBD. A longer duration of alcohol consumption and inadequate thiamine supplementation were associated with a poorer prognosis.

RÉSUMÉ : Analyse de 21 patients atteints de la maladie de Marchiafava-Bignami à Chongqing en Chine. ***Objectif :*** Cette étude vise à étudier les caractéristiques et le pronostic de patients de Chongqing (Chine) qui sont atteints de la maladie de Marchiafava-Bignami (MMB), un trouble neurologique rare communément associé à l'alcoolisme chronique. ***Méthodes :*** Nous avons ainsi effectué une analyse rétrospective des données cliniques de 21 patients alcooliques atteints de la MMB et traités au *First Affiliated Hospital* de l'Université Chongqing entre 2012 et 2022. ***Résultats :*** On l'a dit, l'étude a porté sur 21 patients atteints de la MMB dont l'âge moyen était de 59 ± 9,86 ans et dont l'historique de consommation d'alcool totalisait 35,48 ± 8,65 ans. Des signes cliniques apparus soudainement ont été observés chez 14 patients (66,7 %). Les principaux signes observés étaient des troubles psychiatriques (66,7 %), une altération de la conscience (61,9 %), des troubles cognitifs (61,9 %) et des crises d'épilepsie (42,9 %). Des examens d'IRM ont par ailleurs révélé des modifications du signal T1 long et T2 long dans le corps calleux avec des lésions prédominantes dans le « genou » (76,2 %) et le splénium (71,4 %) du corps calleux. Le groupe de patients dont le pronostic était mauvais a présenté une incidence accrue de troubles de la conscience (100 % contre 50 %, p = 0,044), de signes d'atteinte pyramidale (80 % contre 18,8 %, p = 0,011) et de pneumonie (100 % contre 31,3 %, p = 0,007). De plus, les patients ayant un historique de consommation d'alcool plus long (45,0 ± 10,0 ans contre 32,69 ± 5,99 ans, p = 0,008) et une dose de thiamine plus faible (p = 0,035) avaient un pronostic plus défavorable au bout d'un an. ***Conclusions :*** Cette étude a identifié les troubles de la conscience, les signes d'atteinte pyramidale et la pneumonie comme des facteurs prédictifs d'un mauvais pronostic chez les patients atteints de la MMB. Un historique plus long de consommation d'alcool ainsi qu'une supplémentation inadéquate en thiamine ont été associés à un pronostic plus défavorable.

Keywords: Marchiafava–Bignami disease; alcoholic; clinical characteristics; prognosis; MRI findings

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Introduction

Marchiafava–Bignami disease (MBD), also known as primary corpus callosum degeneration, is a rare disorder characterized by degeneration and necrosis of the corpus callosum.[1] The corpus callosum is a large bundle of nerve fibers that connects the two hemispheres of the brain and plays a critical role in transmitting information between them.[2] Damage to the corpus callosum can interfere with this communication and result in various neurological symptoms, such as altered consciousness, cognitive impairment, and changes in behavior.[3]

The clinical manifestations of MBD may overlap with those of alcoholism-related encephalopathy.[4] MBD can be divided into

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subtypes A and B based on the types of symptoms observed.[5] Additionally, MBD can be classified as acute (≤2 weeks), subacute (>2 weeks), or chronic (>3 months) based on the onset time.[6] Diagnosis heavily relies on magnetic resonance imaging (MRI), clinical presentation, histopathological examination of brain tissue, and a history of alcohol abuse.[7] Currently, there are no standard guidelines or validated treatments for managing MBD. Although MBD has been recognized for over a century since 1903, only approximately 250 cases have been reported worldwide as of 2001.[8] Most reported cases of MBD have been treated with thiamine, vitamin B complexes, and steroids.[6] The prognosis of patients varies from recovery to death.[9]

More than two billion people use alcohol worldwide, and 283 million are estimated to have disorders related to alcohol use.[10] Despite this, information on alcoholic MBD specifically is scarce. Given the potentially devastating consequences of MBD and the lack of information on the condition in China, it is essential for clinicians to be aware of the relationship between chronic alcoholism and MBD, as well as the clinical manifestations, MRI findings, treatment options, and prognosis for patients with this condition. Therefore, in this paper, we provide a comprehensive report on 21 patients with alcoholic MBD, focusing on their clinical manifestations, MRI findings, treatment options, and prognosis.

Methods

This retrospective study aimed to evaluate all alcoholic MBD cases hospitalized in our hospital from January 2012 to January 2022. The study was approved by the Ethics Committee of the First Affiliated Hospital of Chongqing Medical University (Research Approval No. 2021-54). Written consent was waived as this was a retrospective investigation. All records were anonymous and confidential. Alcoholic cases were identified based on the diagnosis codes and drinking history recorded in medical records. The coders encoded the alcohol dependence, alcoholism, acute alcoholism, chronic alcoholism, and alcoholic encephalopathy according to the International Classification of Diseases (ICD-10). The diagnosis of MBD relies on symmetrical lesions of the corpus callosum as observed by MRI. The typical MRI features consisted of symmetric T1-weighted low signal and T2-weighted high signal in the corpus callosum. Other diseases were excluded, such as hypoglycemia, cerebral infections, high-altitude sickness, anti-epileptic drug withdrawal, intoxication, tumorous disease, demyelinating disorders, and systemic lupus erythematosus.[9] Information such as demographics, medical history, clinical symptoms, radiographic features, laboratory-test results, therapeutic regimens, and outcomes was available in the medical records. Two specialized neurologists worked together on the diagnosis and review of medical records. Patients who present with unconsciousness, hyperintense swelling of the corpus callosum, and a poor prognosis are classified as type A, while those who exhibit opposite characteristics, such as good consciousness, few corpus callosum lesions, and a good prognosis, are classified as type B. All patients had phone call follow-ups 1 year after discharge, but one patient was lost to follow-up. The prognosis of each patient was assessed using the Glasgow Outcome Scale (GOS), which comprises five grades: Grade 5 indicates a return to normal life; Grade 4 indicates mild disability but the ability to live independently and work with support; Grade 3 indicates severe disability, being awake but dependent on daily care; Grade 2 indicates vegetative survival with minimal responsiveness, such as eyes open with sleep/wake cycles; and Grade 1 indicates death.

Data Analysis

Continuous and categorical variables are reported as the mean (standard deviation (SD), range) and number (percentage), respectively. Patients were divided into two groups (GOS ≤ 3 and GOS > 3) according to their prognosis. Comparisons across two or more groups were performed using the Kruskal–Wallis test (for continuous variables) and Pearson's chi-squared test (for categorical variables).

Analyses were performed using IBM SPSS version 25.0. Statistical significance was set at $P < 0.05$.

Results

The baseline information and characteristics of the 21 patients are shown in Table 1.

Baseline Information

In this study, 21 male patients with alcoholic MBD were included, with a mean age of 59 ± 9.86 years (range 41–82 years) and an average drinking history of 35.48 ± 8.65 years. Four of the patients (19.1%) had quit drinking before the study visit. The onset of MBD symptoms was acute in 14 patients (66.7%), subacute in 5 (23.8%), and chronic in 2 (9.5%). Based on the mode of onset and clinical manifestations, 5 patients (23.8%) were classified as type A and 16 (76.2%) were classified as type B. In addition to alcohol, 16 patients (76.2%) were also addicted to tobacco. Among the 21 included patients, 5 (23.8%) had concurrent hypertension, 2 (9.5%) had malnutrition, and 2 had diabetes (9.5%). During their hospital stay, 10 patients (47.6%) developed pneumonia. Seven patients (33.3%) had concurrent alcoholic disorders, including 4 (19.0%) with alcoholic hepatitis and 3 (14.2%) with alcoholic polyneuropathy.

Symptoms and Signs

In the 21 MBD patients, seizures were the first symptom in 5 patients (23.8%), with generalized tonic-clonic seizures occurring in 3 patients (14.2%), complex motor seizures in 1 patient (4.8%), and focal seizures in 1 patient (4.8%). The remaining patients presented with initial symptoms such as psychiatric disorders (n = 4, 19.0%), grogginess (n = 4, 19.0%), hypodynamia (n = 3, 14.2%), loss of consciousness (n = 2, 9.5%), blunted reaction (n = 1, 4.8%), insomnia (n = 1, 4.8%), and limb numbness (n = 1, 4.8%).

During hospitalization, psychiatric disorders (n = 14; 66.7%) were the most common symptom observed among the patients, followed by altered consciousness (n = 13, 61.9%), cognitive disorder (n = 13, 61.9%), seizure (n = 9, 42.9%), delirium (n = 9, 42.9%), dysarthria (n = 8, 38%), paresthesia (n = 5, 23.8%), and limb weakness (n = 2, 9.5%). Ataxia (n = 6, 28.6%), increased muscle tone (n = 7, 33.3%), increased deep tendon reflex (n = 3, 14.2%), pathological reflex (n = 4, 19.0%), and decreased deep tendon reflex (n = 1, 4.8%) were reported signs of the patients.

Laboratory Findings

Most of the 21 alcoholic MBD patients had anemia (n = 15, 71.4%), including megaloblastic anemia (n = 7, 33.3%), normocytic hypochromic anemia (n = 7, 33.3%), and microcytic anemia (n = 4, 4.8%). Over half of the patients (n = 14, 66.7%) had an increased gamma-glutamyl transferase (γ-GGT) level. The liver function indices of alcoholic MBD patients were abnormal, with hypoalbuminemia (n = 13 (61.9%)), increased total bilirubin

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Table 1: Characteristics of 21 patients with alcoholic MBD

Characteristics	Overall (n = 21)
Age, years, mean ± SD, (range)	59 ± 9.864 (41–82)
Drinking time, years, mean ± SD (range)	35.48 ± 8.65 (20–60)
Alcohol abstinence before admission	4 (19.0%)
Smoke	16 (76.2%)
Malnutrition	2 (9.5%)
Comorbidity	
Hypertension	5 (23.8%)
Diabetes	2 (9.5%)
Mode of onset	
Acute (≤ 2 weeks)	14 (66.7%)
Subacute (> 2 weeks, ≤ 3months)	5 (23.8%)
Chronic (> 3monhs)	2 (9.5%)
Symptoms of onset	
Seizure	5 (23.8%)
Generalized tonic-clonic seizure	3 (14.2%)
Complex motor seizure	1 (4.8%)
Focal seizures	1 (4.8%)
Mental behavioral abnormalities*	4 (19.0%)
Groggy	4 (19.0%)
Hypodynamia	3 (14.2%)
Loss of consciousness	2 (9.5%)
Blunted response	1 (4.8%)
Insomnia	1 (4.8%)
Numbness of limbs	1 (4.8%)
Symptoms and signs	
Psychiatric disorders*	14 (66.7%)
Altered consciousness	13 (61.9%)
Cognitive disorder	13 (61.9%)
Seizure	9 (42.9%)
Generalized tonic-clonic seizure	7 (33.3%)
Absence seizure	1 (4.8%)
Focal seizures	1 (4.8%)
Delirium	9 (42.9%)
Dysarthria	8 (38%)
Paraesthesia	5 (23.8%)
Limb weakness	2 (9.5%)
Ataxia	6 (28.6%)
Muscle tone increased	7 (33.3%)
Deep tendon reflex increased	3 (14.2%)
Deep tendon reflex decreased	1 (4.8%)
Pathological reflex	4 (19.0%)
Laboratory Findings	
Anemia	15 (71.4%)
Microcytic anemia	1 (4.8%)
Normocytic hypochromic anemia	7 (33.3%)
Megaloblastic anemia	7 (33.3%)
Hypoalbuminemia	13 (61.9%)
TBil increased	5 (23.8%)
DBil increased	8 (38%)
ALT increased	8 (38%)
AST increased	10 (47.6%)
γ-GGT increased	14 (66.7%)
Abnormal EEG	6 (28.6%)
Slow-wave activity	4 (19.0%)
θ-wave	4 (19.0%)
δ-wave	1 (4.8%)
σ-wave	1 (4.8%)
Distribution of lesions	
Periventricular	13 (61.9%)
Lobe	15 (71.4%)
Centrum semiovale	6 (28.6%)
Cerebellum	2 (9.5%)
Whole corpus callosum	13 (61.9%)
Rostrum	4 (19.0%)
Splenium	15 (71.4%)
Genu	16 (76.2%)
Body	12 (57.1%)
Complications	16 (76.2%)
Pneumonia	10 (47.6%)
Alcoholic hepatitis	4 (19.0%)
Alcoholic polyneuropathy	3 (14.2%)
Intracerebral hemorrhage	1 (4.8%)
Foot ulcer	1 (4.8%)
Skin infection	1 (4.8%)
Gastritis	1 (4.8%)
Hyperuricemia	1 (4.8%)
Undifferentiated connective tissue disease	1 (4.8%)
Treatment	
≤ 2 weeks	1 5(71.4%)
>2 weeks, ≤ 1 month	3 (14.2%)
>1 month	3 (14.2%)
Thiamine	20 (95.2%)
≤ 100 mg/d	13 (61.9%)
100 mg/d ~ 300 mg/d	3 (14.2%)
≥300 mg/d	5 (23.8%)
Steroids	1 (4.8%)
Hospitalization time, days, mean ± SD (range)	15.05 ± 9.21 (5–43)
Discharge GOS	
GOS = 3	5 (23.8%)
GOS = 4	9 (42.9%)

(*Continued*)

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Table 1: (*Continued*)

Characteristics	Overall (n = 21)
GOS = 5	7 (33.3%)
Return to regular drinking	8 (38%)
Follow-up GOS	
GOS = 1	3 (14.2%)
GOS = 3	2 (9.5%)
GOS = 4	7 (33.3%)
GOS = 5	8 (38.0%)

ALT = alanine aminotransferase; AST = aspartate aminotransferase; Crea = creatinine; DBil = direct bilirubin; GOS = Glasgow Outcome Scale; TBil = total bilirubin; γ-GGT = gamma-glutamyl transferase.
*Psychiatric disorders: disorganized speech, hallucinations, enuresis, encopresis, eating disorders, attention-deficit/hyperactivity disorder; compulsions, aggression, paranoid disorder.

(n = 5 (23.8%)), increased direct bilirubin (n = 8 (38%)), increased aspartate aminotransferase (n = 10 (47.6%)), and increased alanine aminotransferase (ALT) (n = 8 (38%)). Seven patients underwent electroencephalogram (EEG) examination, of which six patients' EEG results (28.6%) were abnormal. Four of the six patients' results (19%) revealed EEG abnormalities marked by increased slow-wave activity.

Lesion Distributions and MRI Sequences

The main MRI findings were long T1 and long T2 signal changes in the corpus callosum. T2 fluid-attenuated inversion recovery (FLAIR) sequence and diffusion-weighted imaging (DWI) showed a high signal. Two patients (9.5%) showed enhanced MRI. The typical MRI findings of alcoholic MBD patients are shown in Figure 1.

All patients had corpus callosum involvement. Among the 21 patients, the proportion of total corpus callosum involvement was 61.9% (n = 13).The most common site of callosal involvement was the genu, with an involvement rate of 76.2% (n = 16), followed by the splenium with a rate of 71.4% (n = 15), the body with a rate of 57.1% (n = 12), and the rostrum with a rate of 19.0% (n = 4). In addition to the callosum, other areas of brain tissue were also affected in some cases, with a periventricular involvement rate of 61.9% (n = 13), a lobe involvement rate of 71.4% (n = 15), a centrum semiovale involvement rate of 28.6% (n = 6), and a cerebellar involvement rate of 9.5% (n = 2) (Fig. 2).

Treatment and Prognosis

One patient received methylprednisolone therapy (1000 mg per day for 3 consecutive days), and the remaining 20 out of 21 MBD patients (95.2%) received thiamine treatment, which was divided into three dosage groups: ≤ 100 mg/day (13 patients, 61.9%), 100–

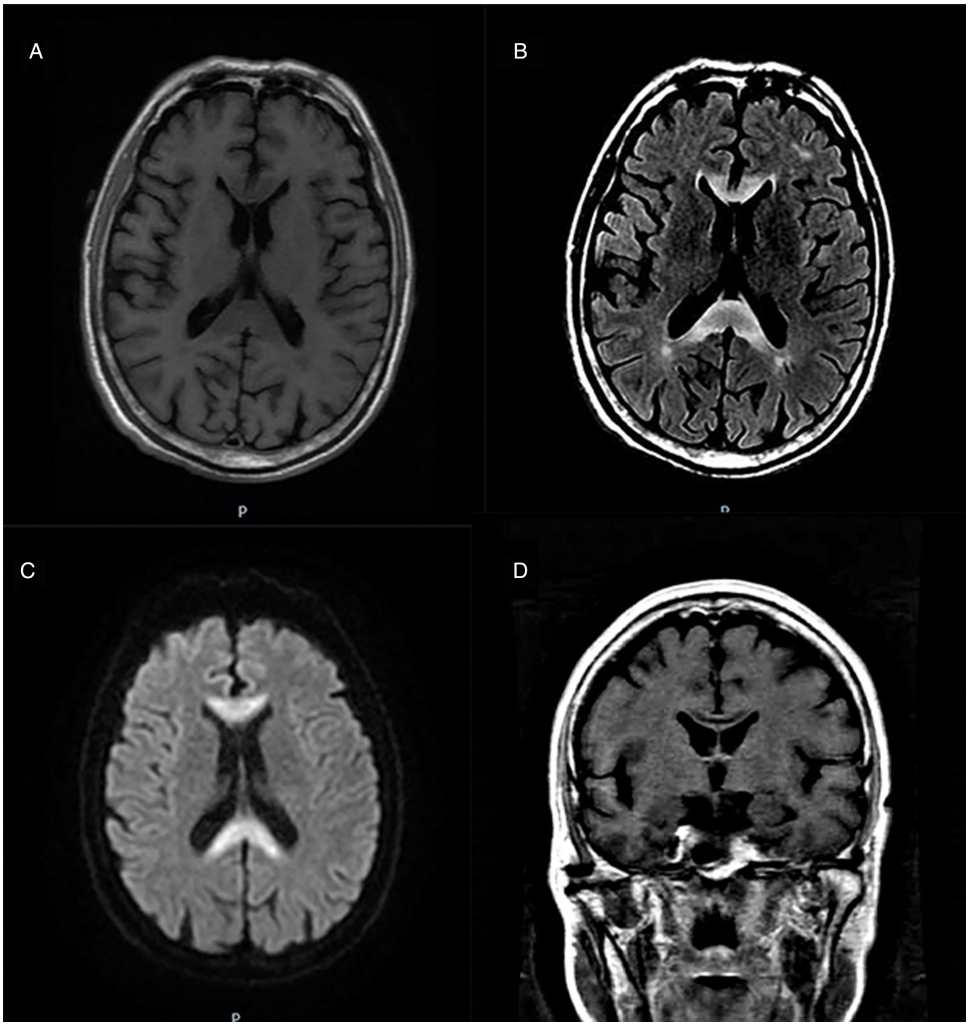

Figure 1: The typical MRI findings of alcoholic MBD patients. The MRI images reveal high signal intensities of the corpus callosum lesions on DWI and T2-weighted images (***b***, ***c***). The lesions in the corpus callosum appear as regions of low signal intensity on T1-weighted images (***a***), with the lowest signal intensity in the middle layer, presenting the "sandwich sign" (d); and no enhancement is observed in the corpus callosum lesions (***d***).

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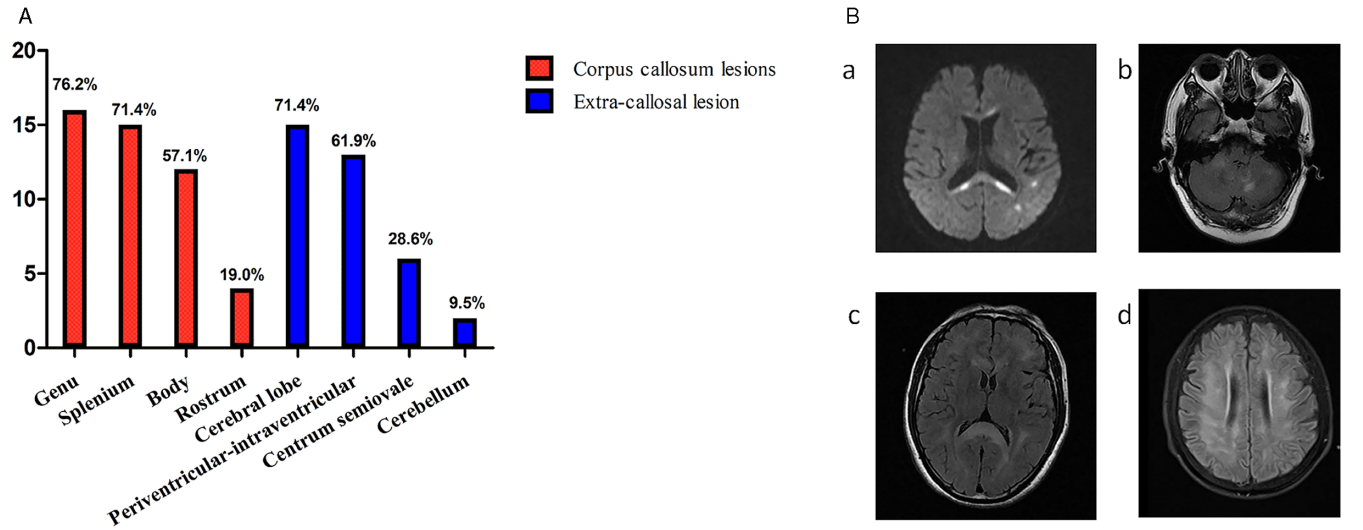

Figure 2: Distribution of lesions in patients with alcoholic MBD. Percentage distribution of corpus callosum and extracallosal lesions in 21 patients (***a***); extracallosal lesions on MRI (***b***). DWI (diffusion-weighted imaging, ep2d_diff_2scan_trace) (a); T2-FLAIR (b, c); T2_tirm_tra_dark_fluid (d).

300 mg/day (3 patients, 14.2%), and > 300 mg/day (5 patients, 14.2%), for a duration of 5–20 days. Upon discharge, the patients were evaluated using the GOS, with 16 patients (76.2%) having a good prognosis, including 9 patients (42.9%) with a GOS score of 4 and 7 patients (33.3%) with a GOS score of 5, while the remaining 5 patients had a poor prognosis with a GOS score of 3. One year later, follow-up showed that 15 out of 20 patients (75%) had a good prognosis, while the remaining 5 patients (25%) had a poor prognosis. The groups with good and poor prognoses were compared.

Table 2 presents a comparison of the clinical characteristics of alcoholic MBD patients with good prognosis (GOS > 3) and poor prognosis (GOS ≤ 3) at discharge and during the follow-up period. The poor prognosis group had a higher incidence of altered consciousness (100% vs 50%, $P = 0.044$), pyramidal signs (80% vs 18.8%, $P = 0.011$), and pneumonia (100% vs 31.3%, $P = 0.007$) at discharge, indicating statistically significant differences between the two groups ($P < 0.05$).

However, there were no statistically significant differences between the two groups in terms of anemia (100% vs. 66.7%, $p = 0.136$), liver function (total bilirubin, direct bilirubin, ALT, and γ-GGT, $p > 0.1$), lesion location (periventricular, lobes, or whole corpus callosum, $p > 0.1$), time of treatment initiation (≤2 weeks, 1 week–2 weeks, over 1 month, $p > 0.1$), or dose of thiamine (≤100 mg/d, 100 mg/d ~ 300 mg/d, ≥300 mg/d, $p > 0.1$) (Table 2). In the 1-year follow-up period, the main differences between the poor prognosis group and the good prognosis group were the time of alcohol consumption (45.0 ± 10.0 years vs 32.69 ± 5.99 years, $p = 0.008$) and a low thiamine dose (≤100 mg/d, $p = 0.035$) (Table 2).

Discussion

Alcoholic MBD is an uncommon alcohol-induced illness characterized by corpus callosum degeneration and necrosis.[11] In this paper, we present a comprehensive analysis of 21 cases of alcoholic MBD treated at our hospital over a span of 10 years. Acute symptoms were the predominant feature of alcoholic MBD, with type B patients being more prevalent. The main clinical manifestations observed in these patients included psychiatric disorders, altered consciousness, and cognitive impairment. MRI revealed corpus callosum lesions, with the genu being the most commonly affected region. Additionally, we found that patients with a poor prognosis upon discharge demonstrated an increased incidence of altered consciousness, pyramidal signs, and pneumonia. Our study further emphasized the significance of long-term alcohol consumption and lower thiamine supplementation as factors associated with a worse prognosis.

Based on the study conducted by Hillbom et al., we classified the 21 patients into three categories: acute, subacute, and chronic presentations. Consistent with previous findings, our analysis revealed that patients with alcoholic MBD predominantly experienced an acute onset.[6] The acute onset of MBD can likely be attributed to alcohol-induced neurotoxicity, which leads to degeneration and necrosis of the corpus callosum.[12] This, in turn, disrupts neuronal function and impairs neural transmission, resulting in the emergence of acute symptoms. Additionally, thiamine deficiency, often associated with long-term alcohol consumption, may further contribute to acute onset.[13] Acute alcoholic MBD typically manifests with psychiatric disorders, altered consciousness, and seizures.[14] The impairment of the corpus callosum plays a crucial role in disrupting the transmission of motor, sensory, visual, spatial, and proprioceptive information between the hemispheres.[15] Moreover, the 21 patients also exhibited pyramidal signs, such as increased reflexes or abnormal tendon reflexes in the limbs, as well as extrapyramidal signs like ataxia and dystonia. Other reported symptoms include headaches, disturbances in gait, urinary incontinence, and visual impairments.[16]

MRI findings of corpus callosum involvement provide valuable diagnostic information for MBD. The corpus callosum lesions appeared as hyperintense signals on T2-weighted and FLAIR sequences and showed restricted diffusion on DWI. These findings are in line with the typical radiological features described in the literature.[17–18] The corpus callosum is a large bundle of nerve fibers connecting the two cerebral hemispheres, and its degeneration and necrosis are key pathological features of MBD.[19] The genu, which is the anterior part of the corpus callosum, appears to be particularly susceptible to damage in MBD cases.[5] This observation aligns with previous studies, which have consistently reported genu

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Table 2: Comparison of the clinical traits between the groups with good and bad prognosis

	GOS at discharge			GOS at follow-up		
Characteristics	GOS ≤ 3 (n = 5)	GOS>3 (n = 16)	P1	GOS ≤ 3 (n = 5)	GOS>3 (n = 15)	P2
Age, years, mean ± SD	61.60 ± 2.97	58.19 ± 11.16	0.514	66.80 ± 9.284	57.27 ± 8.795	0.053
Drinking time, years, mean ± SD	38.0 ± 4.47	34.69 ± 9.57	0.469	44.0 ± 8.944	33.67 ± 6.114	**0.009**
Hospitalization time, days, mean ± SD	15.40 ± 8.08	14.94 ± 9.77	0.925	16.40 ± 8.532	14.67 ± 9.969	0.732
Alcohol abstinence before admission	2 (40%)	2 (12.5%)	0.172	1 (20%)	3 (23.1%)	0.937
Smoke	4 (80%)	12 (75.0%)	0.819	5 (100%)	10 (66.7%)	0.136
Malnutrition	0	2 (12.5%)	/	0	2 (13.3%)	/
Comorbidity						
Hypertension	1 (20%)	4 (25.0%)	0.819	1 (20.0%)	4 (26.7%)	0.766
Diabetes	1 (20%)	1 (6.3%)	0.361	1 (20.0%)	1 (6.7%)	0.389
Mode of onset						
Acute (≤ 2 weeks)	4 (80%)	10 (62.5%)	0.469	3 (60.0%)	11 (73.3%)	0.573
Subacute (> 2 weeks, ≤ 3 months)	1 (20%)	4 (25.0%)	0.819	2 (40.0%)	2 (13.3%)	0.197
Chronic (> 3 months)	0	2 (12.5%)	/	0	2 (13.3%)	/
Symptoms and signs						
Psychiatric disorders*	3 (60.0%)	11 (68.8%)	0.717	2 (40.0%)	11 (73.3%)	0.176
Altered consciousness	5 (100%)	8 (50%)	**0.044**	3 (60.0%)	9 (60.0%)	1.000
Cognitive disorder	1 (20%)	2 (12.5%)	0.027	1 (20%)	11 (73.3%)	0.109
Seizure	2	7 (43.8%)	0.882	2 (40.0%)	6 (40.0%)	1.000
Generalized tonic-clonic seizure	2 (40%)	5 (31.3%)	0.717	2 (50.0%)	4 (30.8%)	0.482
Delirium	3 (60.0%)	6 (37.5%)	0.375	1 (20%)	7 (46.7%)	0.292
Dysarthria	0	8 (50%)	/	0	8 (53.3%)	/
Paraesthesia	1 (20%)	4 (25.0%)	0.819	2 (40.0%)	3 (20%)	0.371
Ataxia	2 (40%)	4 (25.0%)	0.517	1 (20%)	4 (26.7%)	0.766
Pyramidal signs	4 (80%)	3 (18.8%)	**0.011**	2 (40.0%)	5 (33.3%)	0.787
Laboratory findings						
Anemia	5 (100%)	10 (62.5%)	0.105	5 (100%)	10 (66.7%)	0.136
Normocytic hypochromic anemia	2 (40%)	5 (31.3%)	0.717	3 (60.0%)	4 (26.7%)	0.176
Megaloblastic anemia	2 (40%)	5 (31.3%)	0.717	2 (40%)	5 (33.3%)	0.787
Hypoalbuminemia	3 (60.0%)	10 (62.5%)	0.920	3 (60.0%)	10 (66.7%)	0.787
Crea decreased	2 (40%)	7 (43.8%)	0.882	2 (40%)	7 (46.7%)	0.795
Hypopotassemia	2 (40%)	2 (12.5%)	0.172	2 (40%)	2 (13.3%)	0.197
TBil increased	2 (40%)	3 (18.8%)	0.330	2 (40%)	3 (20%)	0.371
DBil increased	3 (60.0%)	5 (31.3%)	0.248	2 (40%)	6 (40%)	1.000
ALT increased	2 (40%)	6 (37.5%)	0.920	2 (40%)	6 (40%)	1.000
AST increased	2 (40%)	8 (50%)	0.696	3 (60.0%)	7 (46.7%)	0.606
GGT increased	4 (80%)	10 (62.5%)	0.469	3 (60.0%)	11 (73.3%)	0.573
Abnormal EEG	2 (40%)	4 (25.0%)	0.517	1 (20.0%)	4 (26.7%)	0.766
Distribution of lesions						
Periventricular	4 (80%)	9 (56.3%);	0.340	3 (60.0%)	9 (60%)	1.000
Lobe	3 (60.0%)	12 (75.0%)	0.517	3 (60.0%)	12 (80.0%)	0.371
Whole corpus callosum	3 (60.0%)	10 (62.5%)	0.920	2 (40.0%)	10 (66.7%)	0.292
Complications						
Pneumonia	5 (100%)	5 (31.3%)	**0.007**	4 (80.0%)	6 (40.0%)	0.121

(*Continued*)

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Table 2: (*Continued*)

Characteristics	GOS at discharge			GOS at follow-up		
	GOS ≤ 3 (n = 5)	GOS>3 (n = 16)	P1	GOS ≤ 3 (n = 5)	GOS>3 (n = 15)	P2
Alcoholic hepatitis	1 (20%)	3 (18.8%)	0.950	1 (20.0%)	3 (20.0%)	1.000
Alcoholic polyneuropathy	1 (20%)	2 (12.5%)	0.676	1 (20.0%)	2 (13.3%)	0.718
Treatment						
≤ 2 weeks	3 (60.0%)	12 (75.0%)	0.517	3 (60.0%)	11 (73.3%)	0.573
>2 weeks, ≤ 1 month	2 (40%)	1 (6.3%)	0.06	2 (40.0%)	2 (13.3%)	0.197
>1 month	0	3 (18.8%)	/	1 (20.0%)	1 (6.7%)	0.347
Thiamine						
≤ 100 mg/d	4 (80%)	9 (56.3%);	0.340	5 (100%)	7 (46.7%)	**0.035**
100 mg/d ~ 300 mg/d	0	3 (18.8%)	0.296	0	3 (20.0%)	/
≥ 300 mg/d	1 (20%)	4 (25.0%)	0.819	0	5 (33.3%)	/
Discharge GOS						0.142
GOS = 3	/	/	/			
GOS = 4	/	/	/			
GOS = 5	/	/	/			
Return to regular drinking	1 (20%)	7 (43.8%)	0.312	1 (33.3%)	7 (46.7%)	0.671

ALT = alanine aminotransferase; AST = aspartate aminotransferase; Crea = creatinine; DBil = direct bilirubin; GOS = Glasgow Outcome Scale; TBil = total bilirubin; γ-GGT = gamma-glutamyl transferase.
Bold numbers represents statistical significance.
*Psychiatric disorders: disorganized speech, hallucinations, enuresis, encopresis, eating disorders, attention-deficit/hyperactivity disorder; compulsions, aggression, paranoid disorder.

involvement as a prominent feature in MBD-related corpus callosum lesions.[15] Extracallosal lesions, such as those found in the white matter of the lobes, periventricular and centrum semiovale, are frequently observed in cases of alcoholic MBD.[18] The presence of extracallosal lesions during the early stages of the disease substantiates their association with the primary pathogenic processes triggered by alcohol intoxication and malnutrition in MBD.[20]. In our study, it was observed that more than 61.9% of the patients displayed extracallosal lesions in the brain, which is a higher proportion compared to the findings reported by Hillbom et al. (49.6%).[6] This difference can be attributed, at least in part, to the fact that the majority of our patients had acute alcoholic MBD. It has been reported that lesions outside the corpus callosum tend to diminish rapidly with appropriate treatment.[21]

In our study, it was observed that over 70% of the 21 alcoholic MBD patients had a favorable prognosis, which is higher than the reported rates in northern China (Shenyang, 55.5%).[22] The severity and duration of alcohol abuse can vary across different geographical areas, leading to variations in the extent of corpus callosum damage and overall disease progression.

Our analysis revealed that patients with a poor prognosis upon discharge demonstrated a higher incidence of altered consciousness, pyramidal signs, and pneumonia. The presence of altered consciousness may reflect severe neurological damage and is indicative of a more advanced stage of the disease.[23] The presence of pyramidal signs in MBD patients with a poor prognosis suggests more extensive involvement of the central nervous system. These signs may be associated with significant impairment of motor function and overall neurological deterioration. Pneumonia is a common respiratory complication observed in individuals with severe neurological conditions. It is particularly relevant in the context of MBD, as patients with alcohol use disorder are often predisposed to respiratory infections due to compromised immune function and aspiration pneumonia related to altered consciousness.[24] The increased incidence of pneumonia in patients with a poor prognosis underscores the importance of appropriate respiratory care and infection prevention strategies in managing MBD.

Moreover, our study emphasized the importance of long-term alcohol consumption and inadequate thiamine (vitamin B1) supplementation as factors significantly associated with a poor prognosis. Long-term alcohol abuse is a well-established risk factor for the development of MBD.[12] Prolonged alcohol abuse can lead to more severe corpus callosum lesions and neurological dysfunction, ultimately resulting in a poorer prognosis. Thiamine deficiency, often seen in individuals with chronic alcohol abuse, is another critical factor that impacts the prognosis of MBD. Thiamine is essential for normal neurological functioning, and its deficiency can exacerbate the neurotoxic effects of alcohol.[13] Our findings revealed that a lower dosage of thiamine was associated with a worse long-term prognosis, while no significant difference was observed in the short term. These results suggest that the effects of thiamine deficiency in patients with alcoholic MBD are long lasting and may take time to become apparent. Consequently, continuous and long-term thiamine supplementation is essential for individuals with alcoholic MBD to alleviate the enduring effects of thiamine deficiency and potentially improve their prognosis.

It is important to acknowledge the limitations of our retrospective study. Due to the rarity of alcoholic MBD, the sample size of our study was small. However, to the best of our knowledge, our study represents the largest sample size reported to date. Furthermore, we did not assess the long-term effects of treatment on cognitive function, quality of life, and daily activities

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using objective scales. Further research is needed to address these limitations and provide a more comprehensive understanding of alcoholic MBD.

Conclusion

In conclusion, our study sheds light on the clinical characteristics and outcomes of alcoholic MBD, emphasizing the importance of timely and appropriate treatment to achieve better patient outcomes. Long-term alcohol consumption and lower thiamine supplementation were associated with a worse prognosis in the long term. Early diagnosis and treatment are critical for improving the prognosis of MBD. Further studies are needed to elucidate the underlying mechanisms of the disease and to develop more effective treatments.

Data availability statement. The data used in this study are available upon request.

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References

1. Youn M, Lee JJ, Park JM, et al. A case of cortical involvement in Marchiafava-Bignami disease accompanying Wernicke's encephalopathy. J Clin Neurol. 2021;17:499–500. DOI: 10.3988/jcn.2021.17.3.499.
2. De León Reyes NS, Bragg-Gonzalo L, Nieto M. Development and plasticity of the corpus callosum. Development. 2020;147:dev189738. DOI: 10.1242/dev.189738.
3. Degraeve B, Sequeira H, Mecheri H, Lenne B. Corpus callosum damage to account for cognitive, affective, and social-cognitive dysfunctions in multiple sclerosis: a model of callosal disconnection syndrome? Mult Scler. 2023;29:160–8. DOI: 10.1177/13524585221091067.
4. Boloursaz S, Nekooei S, Seilanian Toosi F, et al. Marchiafava-Bignami and alcohol related acute polyneuropathy: the cooccurrence of two rare entities. Case Rep Neurol Med. 2016;2016:5848572–3. DOI: 10.1155/2016/5848572.
5. Hofman J, Hutny M, Sztuba K, Paprocka J. Corpus callosum agenesis: an insight into the etiology and spectrum of symptoms. Brain Sci. 2020;10:625. DOI: 10.3390/brainsci10090625.
6. Hillbom M, Saloheimo P, Fujioka S, Wszolek ZK, Juvela S, Leone MA. Diagnosis and management of Marchiafava-Bignami disease: a review of CT/MRI confirmed cases. J Neurol Neurosurg Psychiatry. 2014;85:168–73. DOI: 10.1136/jnnp-2013-305979.
7. Matsuura H, Shindo K. Marchiafava-Bignami disease. QJM. 2018;111:755–755. DOI: 10.1093/qjmed/hcy101.
8. Helenius J, Tatlisumak T, Soinne L, Valanne L, Kaste M. Marchiafava-Bignami disease: two cases with favourable outcome. Eur J Neurol. 2001;8:269–72. DOI: 10.1046/j.1468-1331.2001.00212.x.
9. Singh S, Wagh V. Marchiafava Bignami disease: a rare neurological complication of long-term alcohol abuse. Cureus. 2022;14:e30863. DOI: 10.7759/cureus.30863.
10. Benson S, Verster JC, Scholey A. Consumption patterns of alcohol and alcohol mixed with energy drinks in Australian students and non-students. Nutrients. 2020;12:149. DOI: 10.3390/nu12010149.
11. Al-Witri A, Vialatte AL, Tan KL, Dexter MAJ. Antemortem histopathology and imaging findings in a case of Marchiafava-Bignami disease. J Clin Neurosci. 2019;66:273–5. DOI: 10.1016/j.jocn.2019.05.009.
12. Tapia-Rojas C, Torres AK, Quintanilla RA. Adolescence binge alcohol consumption induces hippocampal mitochondrial impairment that persists during the adulthood. Neuroscience. 2019;406:356–68. DOI: 10.1016/j.neuroscience.2019.03.018.
13. Fernandes LMP, Bezerra FR, Monteiro MC, et al. Thiamine deficiency, oxidative metabolic pathways and ethanol-induced neurotoxicity: how poor nutrition contributes to the alcoholic syndrome, as Marchiafava-Bignami disease. Eur J Clin Nutr. 2017;71:580–6. DOI: 10.1038/ejcn.2016.267.
14. De Ryck H, Van Cauter S, Bekelaar K. From mild gait difficulties to a sudden coma: a rare case of Marchiafava-Bignami disease. Top Magn Reson Imaging. 2023;32:1–4. DOI: 10.1097/RMR.0000000000000301.
15. Quintas-Neves M, Amorim JM, Soares-Fernandes JP. Marchiafava-Bignami disease: two chronologically distinct stages in the same patient. Can J Neurol Sci. 2020;47:689–90. DOI: 10.1017/cjn.2020.86.
16. Barz H, Schreiber A, Barz U. Demyelinating diseases as a result of cerebral edema? Med Hypotheses. 2017;104:10–4. DOI: 10.1016/j.mehy.2017.05.010.
17. Li W, Ran C, Ma J. Diverse MRI findings and clinical outcomes of acute Marchiafava-Bignami disease. Acta Radiol. 2021;62:904–8. DOI: 10.1177/0284185120943040.
18. Zhao P, Zhang H, Zhang Y, Sun L. Marchiafava-Bignami disease with cortical involvement. Clin Lab. 2018;64:1055–9. DOI: 10.7754/Clin. Lab.2018.171220.
19. Innocenti GM, Schmidt K, Milleret C, et al. The functional characterization of callosal connections. Prog Neurobiol. 2022;208:102186. DOI: 10.1016/j.pneurobio.2021.102186.
20. Kinsley S, Giovane RA, Daly S, Shulman D. Rare case of Marchiafava-Bignami disease due to thiamine deficiency and malnutrition. BMJ Case Rep. 2020;13:e238187. DOI: 10.1136/bcr-2020-238187.
21. Yang L, Liu J, Yin Y, Yu H. Simultaneous acute Marchiafava-Bignami disease and posterior reversible encephalopathy syndrome: a case almost misdiagnosed. Quant Imaging Med Surg. 2020;10:1392–5. DOI: 10.21037/qims-19-967.
22. Dong X, Bai C, Nao J. Clinical and radiological features of Marchiafava-Bignami disease. Medicine (Baltimore). 2018;97:e9626. DOI: 10.1097/MD.0000000000009626.
23. Jung SH, Han N, Eom MJ. Co-occurrence of Marchiafava-Bignami disease and alcoholic polyneuropathy in chronic alcoholic patient who had past history of Wernicke encephalopathy: a case report. Brain Neurorehabil. 2021;14:e19. DOI: 10.12786/bn.2021.14.e19.
24. Carrilho PE, Santos MB, Piasecki L, Jorge AC. Marchiafava-Bignami disease: a rare entity with a poor outcome. Rev Bras Ter Intensiva. 2013;25:68–72. DOI: 10.1590/s0103-507x2013000100013.