Marchiafava-Bignami disease (MBD) is a rare complication of chronic alcoholism especially among the Asian people. The previous understanding of this disease relied upon roentgenographic and post-mortem pathological data and is associated with demyelination and necrosis of the corpus callosum. We report a 53-year-old chronic alcoholic Taiwanese male with clinical symptoms of MBD but presented with an atypical radiological cranial study. Based on the suspicion of possible disseminated infectious or neoplastic brain disease, the patient underwent a computer tomography-guided brain biopsy two weeks after the manifestation of disease. The pathological result did not reveal a classical picture of demyelination in MBD but that of necrosis with relatively well-preserved myelination of associated axons. We present this case study and propose a possible pathophysiology of this rare brain degenerative disease during its early stage of progression.

CASE REPORT

A 53-year-old male presented with progressive irritability, agitation and altered consciousness with associated mild right hemiparesis (grade 4/5) for ten days before arriving to our care. The patient had a history of chronic alcoholism; drank 400 to 600 ml of Taiwanese rice wine (20% ethanol) per day for more than 30 years. His past medical history included type II diabetes mellitus controlled by an unknown oral medication. He had no medical history of hypertension and stroke. History of recent headache, fever, and possible exposure to human immunodeficiency virus (HIV) infection could not be ruled out and documented because of poor mental state of the patient. On admission to our hospital, his recorded temperature was 37°C, with a regular pulse and respiratory rates of 69 and 16 per minute respectively. His systolic/diastolic blood pressure was 132/86 mmHg. The thorough physical examination of lungs, heart, and abdomen were unremarkable. His Glasgow Coma Scale (GCS) was E4V3M6. On neurological examination, the patient had truncal...
ataxia and equivocal bradykinesia. There was no dysmetria, no dysarthria, or diplopia. The examinations of cranial nerves were normal. The power of the limbs was weak (MRC 4/5) in all four limbs, but progressively recovered 10 days after the symptoms attacked. Other biochemical and hematologic investigations were normal. Enhanced computed tomography (CT) of the brain showed patches of hypodensity at the genu of the corpus callosum with extracallosal involvement (Fig. 1). The T2-weighted magnetic resonance imaging (MRI) showed irregular hyper-intense areas at the corpus callosum, paraventricular white matter, and left caudal nucleus with Gadolinium (Gd) enhancement at the anterior corpus callosum and left caudate nuclei (Fig. 2a-2d).

Although the patient’s clinical presentation painted an impression of MBD, neoplastic or infectious diseases were suspected because of the atypical Gd findings on MRI. In addition to administration of oral thiamine 400 mg per day, stereotactic CT-guided

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**Figure 1.** Enhanced brain CT scan displayed hypointense signal of the anterior corpus callosum.

**Figure 2.**

- **a.** The coronal T2-weighted MR image of the brain in the studied case displayed a hyper-intense signal at the corpus callosum, paraventricular white matters, and the left caudal nucleus (arrows).
- **b.** The FLAIR MRI displayed increased abnormal water content of the corpus callosum, paraventricular white matters, and left caudate nucleus (arrow).
- **c.** Enhanced sagittal T1-weighted MRI displayed abnormal enhancement of the genu of the corpus callosum (arrow).
- **d.** Enhanced axial T1-weighted MRI displayed abnormal enhancement of the left caudate nucleus (arrow).
biopsy of the genus of the corpus callosum was performed under local anesthesia for histo-pathological diagnosis. Macroscopically, the specimen was yellowish in color with normal vascularity. The microscopic examination revealed mild gliosis with a proliferation index of less than 1% by Ki-67 study, with no evidence of demyelination of the associated axon on Luxol Fast Blue (LFB) stain (Fig. 3a-3c).

After the appropriate investigations and treatment, the patient recovered gradually and was discharged to nursing-rehabilitation center for convalescence and care. Although his consciousness fully recovered (E4V5M6), his impairment of higher cortical function remained unchanged throughout the post-operative follow up of three years.

**OPERATIVE PROCEDURE**

The Brown-Roberts-Wells (BRW) head ring with localizer was firmly fixed to patient’s skull with screws after subcutaneous injections of adequate amount of 2% xylocain. Brain CT scan was done with the localizer securely fixed on the table. The Coordinates of genus of the edematous corpus callosum were calculated by commercial computer program. Right anterior frontal burred hole was drilled for passage of the brain biopsy needle that was targeted to the genus of corpus callosum according to the relevant coordinates. Four quadrant brain biopsies were taken and the tissues were sent for histo-pathological study. The wound was

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**Figure 3.**

- **a.** Hematoxlylin-Eosin stain (400x) revealed the necrosis and gliosis of the biopsy brain tissue.
- **b.** Immunohistochemical stain with anti-Ki-67 (400x) showed a proliferation index of less than 1% with a low possibility of neoplasia.
- **c.** The luxol fast blue (LFB) stain (100x) revealed well preserved myelination of associated axons.
promptly closed and BRW head ring removed. The entire procedure was uneventful.

DISCUSSION

MBD was first described in 1903 and thought to be as a result of chronic alcoholism [4]. Reviewing the cases reports of MBD in the English literature, most of them were reports from European countries or the United States. Until now, there is only a single case reported in Taiwan.[3]. MBD is diagnosed clinically by the neurological deficits such as discontinuous affect coupled with specific radiological features such as edema or necrosis of the corpus callosum via brain CT scans or MRI [5-7]. The primary treatment of MBD is administration of high dose intravenous thiamine at the early stage of the disease [8, 9]. However, extracallosal involvements occur in 30-40% of patients. Other differential diagnosis including infarction of recurrent artery of Heubner, neoplastic disease such as astrocytoma or lymphoma, demyelinating disease such as multiple sclerosis (MS), progressive multifocal leukoencephalopathy, or acute disseminated encephalomyelitis[10-13]. Of all the differentials listed above, MS is by far the most common and needs to be ruled out for MBD to be considered. When differentiating from MS, MBD has symmetric and edematous spots restricted in corpus callosum on brain CT scans or MRI [5, 12]. On histologic examination, acute MS displays partial or complete destruction of myelin with sparing of the axon cylinders and are usually permanent in the chronic stage [14]. In previous autopsy reports of MBD, the portion of the brain that is involved displays intense destruction of myelin and axon combined with a picture similar to that of a vascular infarction. The pathological pictures of specimens from protracted MBD are reported as complete demyelination, without axon involvement or necrosis [2]. Some studies mentioned that the degeneration of the corpus callosum may display different degrees of the damages, ranging from destruction of myelin sheath only to demyelination associated with axonal necrosis [1]. These pathologic features were mainly observed from post mortem tissues. In our present study, the atypical enhanced extracallosal involvement raised the suspicion of neoplastic infiltration, infection process or other more common inflammatory brain disease, which highlights the importance of a histologic diagnosis[15].

In our present case, there was no evidence of the myelin loss on LFB stain. The finding conflicts with those of previous reports gained from postmortem examination which displayed destruction of myelins as well as axons. It can be hypothesized that the relatively intact myelin sheath may represent a mild form of MBD or an acute disease process with potential progression. Further studies with creation of a representative animal model will help us better understand the etiology, evolution, and potential prognostic factors associated with this rare disease.

The current treatment regimens for MBD include thiamine, vitamin B complex, and corticosteroid [8, 16]. According to previous experience, high-dose intravenous thiamine in acute stage could lead to clinical and radiographic improvement, but the time of administration and the therapeutic dose remains controversial [9,17]. In present case, acute intravenous vitamin B complex administration followed by oral 400 mg thiamine per day for one-month showed minimal improvement and the patient did not regain full cognitive function thereafter. Delay administration of treatment (the patient transferred to our hospital 10 days after the onset of the disease) may be the main reason why this was unsuccessful. The administration of the vitamin B complex during the early phase of the disease is highly
recommended to circumvent disease progression and reverse the cognitive function.

**REFERENCE**

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罕見胼胝體變性病患之病例報告

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胼胝體變性（Marchiafava-Bignami disease）是一種慢性酒精濫用造成的罕見疾病，且絕大部分的報告病例都在歐美國家。過去此疾病的診斷均藉由屍體解剖及電腦斷層或核磁共振之影像診斷，認為其病理是因為胼胝體的脫鞘及溶解造成。作者在此報導一位五十三歲台灣男性，在臨床症狀及影像檢查上皆高度懷疑胼胝體變性，在病發十六天後，我們安排電腦斷層導引切片欲做確定診斷，卻意外發現胼胝體的髓鞘是完整的，和過去脫鞘的認知完全相反。據我們所知，此病患是唯一一位活體切片之病例，因此這樣特殊的發現值得提出討論做為此疾病往後神經病理機轉探討的參考。