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A Marchiafava-Bignami Patient with Mild Symptoms and the Role of Diffusion-Weighted Magnetic Resonance Imaging in the Diagnosis

Ilımlı Bulgular ile Seyreden bir Marchiafava-Bignami Hastasının Tanısında Diffüzyon Ağırlıklı Manyetik Rezonans Görüntülemenin Katkısı

Başar BİLGİÇ, Ali Bilgin ARSLAN*, Hüseyin BULUT**, Ali BAYRAM***, Feride GÖKBEN HIZLI****

İstanbul Üniversitesi İstanbul Tıp Fakültesi, Nöroloji Anabilim Dalı, Davranış Nörolojisi ve Hareket Bozuklukları Birimi, İstanbul, Türkiye

*Brown University Cognitive and Linguistic Sciences Department, Providence, Rhode Island, USA

**Büyükçekmece Devlet Hastanesi, Psikiyatri Bölümü, İstanbul, Türkiye

***İstanbul Nöropsikiyatri Hastanesi, Biyomedikal Birimi, İstanbul, Türkiye

****İstanbul Nöropsikiyatri Hastanesi, Psikiyatri Bölümü, İstanbul, Türkiye

ABSTRACT

Marchiafava-Bignami disease (MBD) is a rare entity associated with chronic alcoholism, with the degeneration of the corpus callosum being its most important characteristic. Clinical presentations may be in various forms, but the disorder can be divided into 2 broad clinical subtypes: a more severe type presenting with disorders of consciousness, which may lead to coma; or a second subtype with milder symptoms, easily underdiagnosed due to the similarity with alcohol withdrawal symptoms. With treatment and restoration of nutrition, the symptoms may be alleviated and the patient may even recover from the disease-induced coma. We present the case of a 40-year-old woman who was diagnosed with MBD. The patient had relatively weak symptoms and the diagnosis was made primarily on cranial imaging data. Diffusion-weighted MRI (DWI) was performed using a 1.5-Tesla MR system and it was seen to be significantly more efficient in detecting the ovoid nodular lesion of 6x10 mm size in the posterior corpus callosum, compared to FLAIR- and T1- and T2-weighted sequences. The lesion was no longer visible in the follow-up imaging studies after thiamine (100 mg/day for a week) treatment. It is concluded that DWI, a commonly used technique in the diagnosis of ischemic cerebrovascular disease, also has significant diagnostic value for MBD. In diffusion-weighted sequence, the variation from low to high intensities in apparent diffusion coefficient throughout the progression can be explained by cytotoxic edema and pure demyelination, respectively. *(Archives of Neuropsychiatry 2011;48: 277-80)*

Key words: Alcoholism, magnetic resonance imaging, Marchiafava-Bignami disease, white matter damage

ÖZET

Marchiafava-Bignami hastalığı, özellik olarak korpus kallozum dejenerasyonu ile giden kronik alkolizm ile ilişkili nadir bir hastalıktır. Klinik bulgular çeşitli olsa da iki ana klinik alt tipe indirgenebilir: bilinç değişiklikleri ile giden ve komaya neden olabilen ağır tip; ve hafif bulgular ile giden ve alkol yoksunluğu bulguları içinde kolaylıkla gözden kaçabilecek hafif tip. Bu hastalıkta beslenmenin düzeltilmesi ve tedavi ile hastalığa bağlı koma bile düzelebilmektedir. Burada 40 yaşında olan ve Marchiafava-Bignami tanısı alan bir hasta sunulmaktadır. Hastanın klinik bulguları silik olmakla birlikte tanı esas olarak görüntülüme verileri sayesinde yapılmıştır. 1.5 tesla magnet ile yapılan diffüzyon ağırlıklı manyetik rezonans görüntüleme (MRG) sekansında, korpus kallozumun arka kısmında, FLAIR, T2 ve T1 sekanslarına göre çok daha iyi seçilebilen 6x10 mm boyutlarında ovoid nodüler lezyon izlenmiştir. Tiamin tedavisi (100 mg/gün bir hafta boyunca) verilmesinin ardından takiplerde lezyon tamamen ortadan kalkmıştır. İskemik serebrovasküler hastalık tanısında sıklıkla kullanılan bir teknik olan difüzyon-ağırlıklı MRG, Machiafava-Bignami hastalığının tanısına da oldukça önemli katkı sağlamaktadır. Bu sekansta izlenen bulgular sitotoksik ödem ve demiyelinizasyon ile ilişkili olarak düşünülebilir. *(Nöropsikiyatri Arşivi 2011;48: 277-80)*

Anahtar kelimeler: Alkolizm, difüzyon ağırlıklı görüntüleme, manyetik rezonans görüntüleme, Marchiafava-Bignami hastalığı, ak madde hasarı

Introduction

Two Italian pathologists first defined Marchiafava-Bignami Disease (MBD) in 1903 (1). They reported alterations in the central part of corpus callosum in three alcoholic patients. While the reported cases were confined to Italy at the time it was first described, the disorder became more widely spread in other populations after 1930's. Once thought to be associated with a male gender predisposition and excessive red wine consumption, this notion has been largely abandoned due to

Yazışma Adresi/Address for Correspondence: Dr. Başar Bilgiç, İstanbul Üniversitesi İstanbul Tıp Fakültesi, Nöroloji Anabilim Dalı, Davranış Nörolojisi ve Hareket Bozuklukları Birimi, İstanbul, Türkiye Tel.: +90 212 533 85 75 E-posta: bilgicb@gmail.com

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the increased number of reported cases with more generalized demographics all over the world (2).

After the increase in the availability of magnetic resonance imaging (MRI), which is sensitive to detect even the smallest lesions in the white matter, in vivo diagnosis of the disease became more reliable. Diffusion-weighted MRI (DWI) is a new technique which has a lot of utility in the rapid diagnosis of ischemic cerebrovascular diseases, and recent studies suggest its potential role as a diagnostic tool in MBD (3-5). This paper presents a case in which the symptoms of the disease are relatively weak and where the diagnosis was made primarily on cranial imaging data.

Case Report

A 40-year-old female patient was admitted to the hospital with her consent, due to alcohol abuse and depressive symptoms.

The patient who studied anthropology in university reported getting divorced in 1999. She started using alcohol in 2000 after her divorce. Although she reported that her intake was excessive, she could not specify the exact amount. She consumed different kinds of alcoholic drinks including red wine, but she mainly drank whiskey and beer. Her daily consumption was not limited to a specific time period but spread throughout the day. As she began to use alcohol, she withdrew gradually from her usual social setting. Once a socially active individual, she became increasingly more introverted and eventually lost connections with her friends. She said that her daily activities revolved around her addiction. Her son, who was a college student, occasionally visited her to care for her needs. The patient expressed that the main source of motivations in her life were alcohol and her son. She was previously hospitalized for alcoholism in the years 2005 and 2007, but she relapsed immediately after the discharges.

The patient exhibited depressive symptoms. Her daily mood was usually depressed and with a constant state of anhedonia. Recently her attention and her ability to concentrate became impaired and she reported having trouble remembering things. She said she could not make plans and would go out only when it is absolutely necessary, spending her time alone at home. Her eating habits were also disturbed and it was told that she could miss meals during the day and was malnourished. She completely lost her appetite one or two months before the admission to the hospital. She did not want to eat anything and would vomit after her meals. She reported numbness in her feet for the past 6 months. For the last month, she was also having mild unstable gait.

In her mental state examination on admission, she was fully conscious and her place, person and time orientation was normal. She gave appropriate and relevant responses to questions. Her response time was mildly increased and the responses were relatively short. The mood was depressed (17-item Hamilton Depression Rating Scale Score was 30) (6) and her affect was wan and anxious. The negative effects of alcohol on her health, negative ideas about life occupied her thoughts. She did not report hallucinations or delusions. There was a mild psychomotor agitation in actions she exhibited.

She was assessed with a comprehensive neuropsychological battery including the Mini-Mental State Examination (MMSE), Oktem Verbal Memory Process Test, Trail Making Test, Wisconsin Card Sorting Test, Stroop Test, Boston Naming Test, Benton Facial Recognition Test, Judgment of Line Orientation Test, Digit Span Subtest of the Wechsler Adult Intelligence Scale, and phonemic and semantic fluency tests (KAS and animal naming) and, there were only mild attention deficit with a narrowed digit span and impaired vigilance. Executive, visuospatial and language functions and memory were seen to be unimpaired, except for a mild difficulty in response inhibition.

Somatic neurological examination revealed a moderate truncal ataxia and a distal stocking type hypoalgesia. Vibration sensation with C-128 tuning fork was 5 seconds in the lower limbs (medial malleolus), while it was 18 seconds in the upper limbs (distal phalanx of the middle finger). Deep tendon reflexes except for the bilateral achilles reflex were intact. Other than these findings, her somatic neurological examination was found to be normal. Electroneuromyographic examination (ENMG) revealed a peripheric sensorial type polyneuropathy, primarily affecting the axonal component.

In her routine laboratory studies including serum glucose, protein, albumin and electrolytes levels, liver, renal and thyroid function tests, complete blood count with erythrocyte sedimentation rate and C-reactive protein levels, there were low total protein and albumin values with hypochromic microcytic anemia suggesting a case of malnutrition. There was a mild elevation in liver enzyme and bilirubin levels. Cerebrospinal fluid (CSF) examination was performed on her admission and there was neither cell reaction nor protein elevation in the CSF examination. EEG showed no epileptic activity.

Cranial MRI showed a distinct ovoid nodular lesion of 6x10 mm size in the posterior parts of corpus callosum with increased signal intensity on DWI (TR/TE =3062/74, b=1000, 1.5T) and with reduced signal intensity on apparent diffusion coefficient (ADC). The lesion was less prominent on T2-weighted (TR/TE=4473/100) and fluid-attenuated inversion recovery (FLAIR) (TR/TI/TE=6000/2000/120) sequences and there was no reflection of the lesion on T1-weighted (TR/TE=596/15) images. No enhancement of the lesions after gadolinium administration was observed. A moderate cerebrocerebellar atrophy was also present.

On the basis of the clinical history, findings on physical examination and imaging features, the diagnosis of mild acute MBD was made and the patient was put on 100 mg/day thiamine treatment for 7 days. She showed a mild recovery where polyneuropathy signs were still present at the time she was discharged.

In her follow-up MRI studies after 7 days and 4 months later, the lesion was totally absent on all sequences, including DWI (Figure 1 and 2). Radiological improvement was concurrent with the alleviation of her truncal ataxia.

Discussion

MBD is a rare disease associated with chronic alcoholism. The most important characteristic of the disease is the degeneration of the corpus callosum. Clinical presentations may be in various forms, but the disorder can be divided into 2 clinical subtypes: a more severe type presenting with disorders

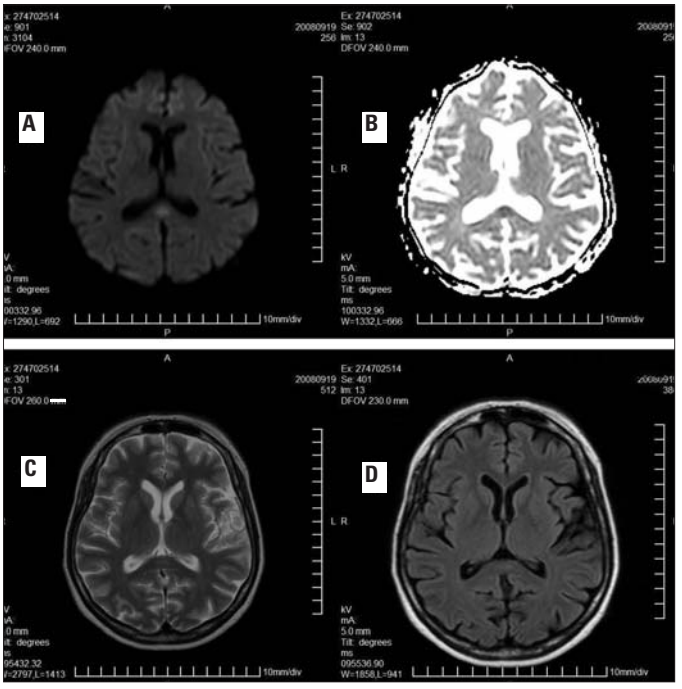

Figure 1. In the MRI scan obtained upon admission, ovoid lesion suggesting Marchiafava-Bignami disease is located in the splenium of the corpus callosum. Lesion is seen in posterior corpus callosum with increased signal in DWI (A), with low ADC values (B), with increased signal in T2 (C) and with increased signal in FLAIR (D). DWI is superior to the others in terms of lesion detecting capacity. DWI, ; ADC, Apparent Diffusion Coeifficient; FLAIR, Fluid-Attenuated Inversion Recovery

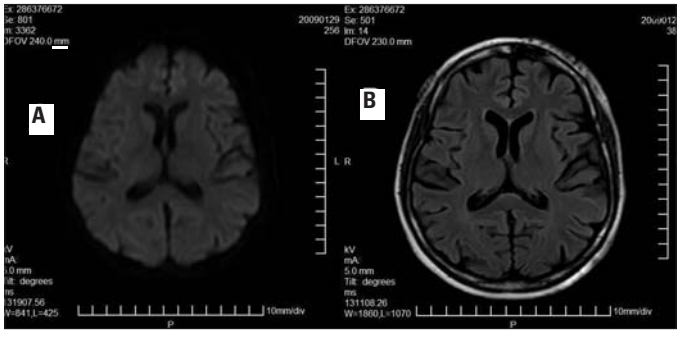

Figure 2. MRI during follow-up (after 7 days). Lesion disappeared in all sequences including DWI. Slices from axial DWI (A) and FLAIR (B) sequences of the same patient are shown

of consciousness, which may lead to coma; or a second subtype with milder symptoms such as irritability and impairment of gait, easily underdiagnosed due to the similarity with alcohol withdrawal symptoms (7). Apathy, violent tendencies, inappropriate sexual demands, disarthria, apraxia, transitory sfincter disorders, hemiparesis and aphasia may co-exist in the clinical presentations of the disease. Rare cases of progression suggesting purely frontal lobe dysfunctions have also been reported (2). With treatment and restoration of the nutrition, the symptoms may be alleviated and the patient may even recover from the disease-induced coma.

The histopathological examination of corpus callosum shows tissue loss and a change of color varying between yellow and red, depending on the duration of the disease. In addition to microscopically visible demyelination, the tissue may contain macrophages with fatty particles. There are no inflammatory changes. Aside from corpus callosum, these abnormalities may also reside in commissural fibers such as anterior and posterior commissure, but less frequently. The reason why this disease is selective of commissural structures is currently unknown.

Although the direct toxic effect of alcohol is thought to be responsible in the etiology of the disease, the significantly low incidence rate of the disease among alcoholic population raises questions. Similar clinical cases were reported also with non-alcoholic patients (8,9). Therefore, the alcohol addiction cannot be considered as the sole cause of the disease.

In acute MBD, MRI reveals focal callosal lesions of high T2-weight and FLAIR signals with hypoattenuation and low T1-weight signals. Generally, there is no sign of a mass effect (3). Lesions demonstrate high signal intensity on DWI with reduced or increased apparent diffusion coefficient (ADC) values depending on the progression of the disease (10). DWI technique is sensitive to random water movements in spatial scales defined as Brownian motion and any lesion with restriction in the Brownian motion of the water molecules is seen as hyperintense signal on DWI. In early stage of MBD, cytotoxic edema may be the underlying mechanism where the lesions are seen as hyperintense on DWI with reduced ADC. In the later stages, increased ADC may be due to the pure demyelination without axonal injury (10). In this patient's case, the most prominent finding was on the DWI. T2-weighted and FLAIR images revealed mild hyperintensities that one can easily overlook. Similar lesions may appear in the course of the other diseases such as encephalitis (especially influenza encephalitis), cerebrovascular disease, traumatic diffuse axonal injury, multiple sclerosis, electrolyte disturbances, some primary central nerve system tumors, and after the epileptic seizures. The course of the disease and laboratory findings in the reported patient was not suggestive of any other condition.

Except for a moderate truncal ataxia and polyneuropathy signs, there were no abnormalities in somatic neurological examination. In terms of cognitive capacities, her neuropsychological examination did not show a distinctive loss of function other than attention and response inhibition impairment, which is not specifically associated with MBD. In contrast, her cranial MRI and, especially DWI, revealed a robust finding which reflects the corpus callosum involvement as a characteristic of the disease.

It is concluded that chronic alcoholism with malnutrition may lead to damage in both central and peripheral nervous system. MBD with mild symptoms may exhibit symptoms associated with alcohol withdrawal such as anxiety, ataxia and attention deficit, as it is seen in the case of this patient. In such cases, cranial MRI with DWI carry significant diagnostic value and it can help the physician to plan out the appropriate treatment for the patient suffering from a potentially fatal disease.

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