



CASE REPORT/CASO CLÍNICO

Marchiafava-Bignami Disease: The Importance of Early Diagnosis and Treatment by a Multidisciplinary Team

Doença de Marchiafava-Bignami: A Importância do Diagnóstico e Tratamento Precoces por uma Equipa Multidisciplinar

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Abstract

Marchiafava-Bignami disease is a rare condition associated with chronic alcohol consumption and/or malnutrition, characterized by demyelination of the corpus callosum, generally attributed to a deficiency in B complex vitamins. We report the case of a 34-year-old male with a 10-year history of alcohol dependence who was admitted to the hospital, after having been found lying on the floor of his house, malnourished and with pressure ulcers on his chest and knees. On clinical observation he was found to be alert but mute. He followed some simple orders. Generalized spastic hypertonia was present. Magnetic resonance imaging showed demyelination of the corpus callosum, suggesting the diagnosis of Marchiafava-Bignami disease. He was admitted to the Psychiatry Inpatient Unit and evaluated by a multidisciplinary team. He received thiamine, corticosteroids and rehabilitation. After a week, his speech was slurred but comprehensible and he could walk with aid; magnetic resonance imaging findings had improved. After three months in a Convalescence Unit, he was discharged with total autonomy.

Resumo

A doença de Marchiafava-Bignami é uma condição rara associada ao consumo crónico e abusivo de álcool e/ou desnutrição, caracterizada por desmielinização do corpo caloso, sendo geralmente atribuída a uma deficiência de vitaminas do complexo B.

Apresentamos o caso de um homem de 34 anos com 10 anos de dependência de álcool que foi trazido ao hospital, após ter sido encontrado caído no chão de sua casa em decúbito ventral, desnutrido, com úlceras de pressão no tórax e joelhos. Estava vígil, não emitia discurso, cumpria ordens simples e apresentava hipertonia espástica generalizada. Na ressonância magnética identificou-se desmielinização do corpo caloso, sendo diagnosticado com doença de Marchiafava-Bignami. Foi internado no serviço de psiquiatria e avaliado por uma equipa multidisciplinar, iniciando terapêutica com tiamina e corticosteróides e um programa de reabilitação. Após uma semana, apresentava melhoria clínica e imagiológica. Após um período de 3 meses numa Unidade de Convalescença, teve alta totalmente autónomo.

Keywords: Alcohol-Related Disorders; Corpus Callosum/diagnostic imaging; Marchiafava-Bignami Disease/diagnosis; Marchiafava-Bignami Disease/drug therapy

Palavras-chave: Corpo Caloso/diagnóstico por imagem; Doença de Marchiafava-Bignami/diagnóstico; Doença de Marchiafava-Bignami/tratamento farmacológico; Transtornos Relacionados ao Uso de Álcool

Recebido/Received: 2020-03-22

Aceite/Accepted: 2020-05-08

Publicado / Published: 2020-06-01

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INTRODUCTION

Marchiafava-Bignami disease (MBD) is a rare condition associated with chronic alcohol consumption and/or malnutrition, characterized by demyelination and necrosis of the corpus callosum that is thought to be attributed to a deficiency in the B complex vitamins.¹

CASE REPORT

A 34-year-old male was brought to the emergency room, after having been found lying on the floor of his house, where he lived alone. He was malnourished and had pressure ulcers on his chest and knees. He was alert, with no spontaneous speech. He was able to follow some simple orders and presented generalized spastic hypertonia.

He had a 10-year history of alcohol dependence, with a current daily intake of 5 L of wine. He denied other substance use. No previous psychiatric, neurologic or medical conditions were known. He had no clinically relevant

family history. He did not consult his family physician regularly nor was he on any medication.

A computed tomography-scan revealed brain atrophy. Laboratory blood testing revealed increased mean red cell corpuscular volume and leukocytosis, elevated gamma glutamyl transpeptidase and creatine kinase levels, hypokalemia and folate deficiency. After observation by a Psychiatrist and with a working hypothesis of a diagnosis of Wernicke's encephalopathy, the patient was admitted to the Internal Medicine Department and started on vitamin B complex therapy (parenteral thiamine 1500 mg and oral folic acid 5 mg daily) and diazepam.

A magnetic resonance imaging (MRI) of the brain performed two days later, showed diffuse demyelination of the corpus callosum and multifocal demyelination of the superficial and subcortical semi-oval centers of the high and medium frontal convexities with a slight anterior parietal extension, in keeping with the diagnosis of MBD in acute phase. (Fig. 1)

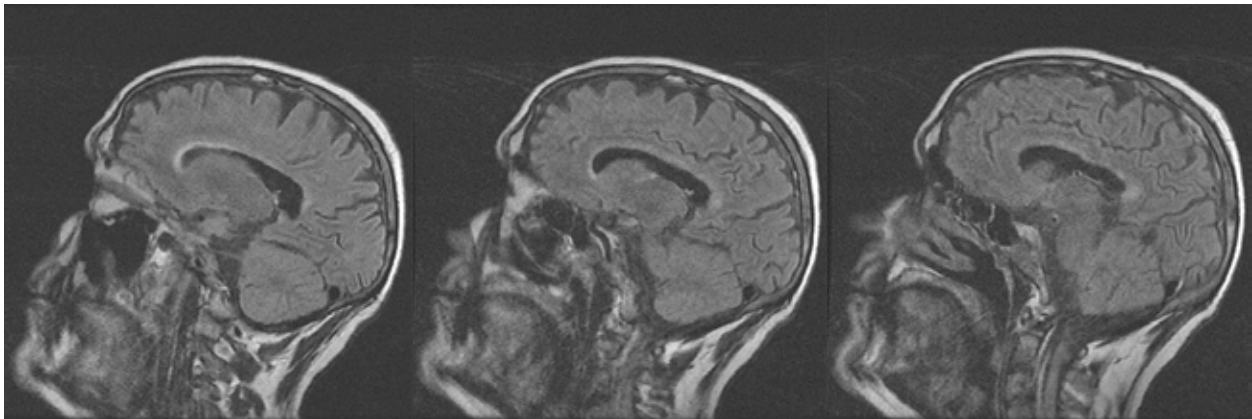


Figure.1 - Diffuse hyperintensity of the corpus callosum on T2/FLAIR - “sandwich sign”

An electroencephalogram showed moderately slow (6 Hz) electrogenicity without asymmetries or paroxysmal activity, possibly in the context of a metabolic encephalopathic dysfunction. After a consultation with a Neurologist, he received corticosteroids (parenteral methylprednisolone 1000 mg daily) for three days. Thiamine was then reduced to 600 mg daily for 5 days, after which he remained on a 200 mg daily oral dose.

The patient remained in the Internal Medicine Department for one week, for hydration and correction of hydroelectrolytic disorders, after which he was transferred to the Psychiatry ward. On admission, he was alert, partially oriented to place and time, with focused and sustained attention. His speech was slow and poor (with moderate dysarthria and hypophonia). His mood was neutral with flattening of affect. His thought process appeared to be organized but he had behaviour suggestive of illusions or hallucinations. Despite showing psychomotor delay, he could now move himself on the bed and take small steps with aid. A brief neuropsychological evaluation was performed that additionally showed ideomotor and ideational apraxia,

perceptive alterations (suggesting alteration of the body scheme) and marked changes in executive functioning.

By indication of the Physical Medicine and Rehabilitation Department, the patient started a program of physiotherapy and occupational therapy, as well as antispasmodic therapy. The Dietary and Nutrition Service initiated a personalized diet. The Social Service was contacted to arrange a future referencing to a Convalescence Unit.

A control MRI, performed two weeks after admission, revealed decreased thickness of the corpus callosum, reported as being due to a diffuse decrease of brain parenchyma or as consequence of the diffuse demyelination previously detected, alterations consistent with MBD in subacute phase. (Fig. 2)



Figure. 2 - Small hyperintense T2/FLAIR foci in the splenium of the corpus callosum

Two weeks after the brief neuropsychological evaluation the patient underwent a comprehensive one, which described changes in speech (poor, hypophonic and moderate dysarthria), difficulties in maintaining memory after interference, deficits in various areas such as sustained attention, immediate retention, logical reasoning, conceptual organization, the ability to criticize absurd situations, verbal initiative, mental flexibility, and the ability to resist interference, along with apraxia (ideomotor and ideational), perceptual alterations and slow processing speed (mental and motor). Compared to the previous evaluation there was a favorable cognitive evolution. Nevertheless, the overall picture suggested a strong impairment in executive domains.

The patient was then admitted to a Convalescence Unit, medicated with a daily oral dose of 200 mg thiamine. After 3 months he was discharged with total autonomy for the activities of daily living, referenced to an addiction recovery center. Unfortunately, he suffered a relapse of his alcohol consumption.

DISCUSSION

MBD is a rare condition characterized by demyelination and necrosis of the corpus callosum.¹ First reported in 1903 in Italian alcoholics,² it is associated with patients who have a history of chronic alcohol ingestion; however, it has also been reported in diabetic and malnourished non-alcoholic patients.³⁻⁵ It mainly affects the male population, in the age group between 40 and 60 years. The actual pathogenesis of the disease remains uncertain, but it is thought to be attributed to a deficiency in the B complex vitamins.⁶

There is no standard clinical picture in MBD and the possible initial manifestations are non-specific of the condition.⁷ According to the clinical classification of Brion *et al*, MBD may present in an acute form, with impairment of consciousness, seizures, and rapid death; a subacute form,

with variable degrees of mental confusion, dysarthria, behavioral abnormalities, memory deficits and impairment of gait; and a chronic form, characterized by progressive dementia, behavioral abnormalities and signs of interhemispheric disconnection. If diagnosis and treatment are not timely, MBD may progress to coma or even death.^{6,8,9}

With advances in neuroimaging techniques, early diagnosis of MBD has become possible on the basis of clinical findings in combination with radiological imaging features demonstrated by computed tomography (CT) and/or MRI.^{10,11}

On CT, the corpus callosum is hypodense, except in cases characterized by subacute hemorrhage, in which the lesions may be isodense or hyperdense. Because CT has a lower sensitivity than MRI, it may show no alterations when the lesions are small.^{9,11}

On MRI, the typical changes seen in acute MBD include symmetric T2W-hyperintense and T1W-hypointense lesions of the central part of the body of the corpus callosum (with relative sparing of thin upper and lower edges – this being known as the “sandwich sign”). After the acute stage, the T2-signal of the corpus callosum (related with edema), normalizes and, later on, symmetric atrophy of the corpus callosum with focal hypointensities on T1WI with corresponding focal hyperintensities on T2WI (consistent with progressive demyelination, regional necrosis, and cyst formations), develop.^{1,12} Lesions may also be found in other regions of the brain, such as the cerebral lobes, the hemispheric white matter, and the basal ganglia; such extracallosal lesions are found primarily in patients with a poor prognosis and severe cognitive impairment.¹³⁻¹⁶ Our patient had the classical “sandwich sign” involving the corpus callosum (Fig. 1) and also extracallosal lesions. According to Wang *et al*, it is likely that gadolinium enhancement during acute stage of MBD indicates severe damage and may lead to necrosis in the chronic stage, which is associated with poorer clinical outcome.¹⁷

According to the more recent clinical-radiologic classification by Heinrich *et al*, there are two subtypes of MBD. Type A is characterized by an acutely altered state of consciousness, cognitive deterioration and language deficits, focal neurological deficits, T2-WI hyperintense swelling of the entire corpus callosum, frequently with extracallosal lesions and a poor prognosis. Type B evolves with insidious clinical onset and progression, less severe and disabling clinical symptoms and less long-term disabilities; T2-WI hyperintense lesions only partially involve the corpus callosum with extracallosal lesions being less frequently seen, and a better outcome.¹⁸ Considering our patient's clinical-radiologic picture, he should be categorized into type A, but his clinical progression was not as poor as would be expected.

The treatment of MBD is still controversial. Assuming the implication of nutritional factors in its pathogenesis, in a way similar to Wernicke's encephalopathy, it is suggested that vitamin B complex replenishment should be instituted, with parenteral administration of thiamine being carried out until behavioral symptoms are reversed.⁶ There are variable reports of doses used (between 75 and 1000 mg/kg) and duration of treatment (between 1 and 12 weeks) until clinical improvement.^{5,6,10,13,20-22}

Some authors also propose the co-administration of corticosteroids in the acute phase to reduce cerebral edema, suppress demyelination, stabilize of the blood-brain barrier and reduce inflammation, contributing to improvement

of clinical response.^{4,5,6,23,24} This is controversial because most cases were treated with thiamine and corticosteroids concomitantly and it was difficult to assess which of the two had the preponderant role in recovery.¹⁰ We made the clinical decision to follow both strategies in our case with partial clinical and radiological recovery.

Concerning the prognosis of MBD, it tends to be worse in alcoholic patients, but can be improved if promptly diagnosed and expeditiously treated.²⁵ According to an analysis of 153 cases by Hillbom *et al*, early initiation (within two weeks after the onset of the clinical picture) of thiamine replacement improves MBD prognosis and represents the only limiting factor in patient outcome.¹⁰ More recently, the results of an observational study by Dong *et al*, established some factors of poor prognosis in patients with an acute or subacute onset: having heavy alcoholic habits, extracallosal lesions, cerebral lobe impairment and severe disturbances of consciousness.⁷

CONCLUSION

Considering the initial clinical-radiologic picture, we consider that a prompt diagnosis and initiation of treatment (with thiamine and high-dose corticosteroids) by a dedicated multidisciplinary team resulted in a better than expected improvement for our patient. We hypothesize that the patient's young age and the absence of comorbidities also contributed to this favorable outcome.

Acknowledgments / Agradecimentos: The authors would like to thank Camila Nóbrega (Attending Neurologist, Centro Hospitalar Psiquiátrico de Lisboa, Portugal) and José Palma Góis (Attending Psychiatrist, Psychiatry and Mental Health Department, Hospital do Espírito Santo de Évora, Portugal)

Responsabilidades Éticas

Conflitos de Interesse: Os autores declaram a inexistência de conflitos de interesse na realização do presente trabalho.

Fontes de Financiamento: Não existiram fontes externas de financiamento para a realização deste artigo.

Confidencialidade dos Dados: Os autores declaram ter seguido os protocolos da sua instituição acerca da publicação dos dados de doentes.

Consentimento: Consentimento do doente para publicação obtido.

Proveniência e Revisão por Pares: Não comissionado; revisão externa por pares.

Ethical Disclosures

Conflicts of Interest: The authors have no conflicts of interest to declare.

Financing Support: This work has not received any contribution, grant or scholarship.

Confidentiality of Data: The authors declare that they have followed the protocols of their work center on the publication of data from patients.

Patient Consent: Consent for publication was obtained.

Provenance and Peer Review: Not commissioned; externally peer reviewed.

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