Case report

Fatal serotonin syndrome in a patient with Marchiafava–Bignami disease: Combined neurological and psychiatric emergency

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ABSTRACT

Marchiafava–Bignami disease (MBD) is a rare fatal neurological disorder characterized by demyelination, primary degeneration, and necrosis of the corpus callosum. Although MBD is mostly associated with chronic alcohol consumption and malnutrition, it has been reported in non-alcoholic patients. Serotonin syndrome is a rare but potentially fatal side effect of antidepressants that results from overstimulation of both central and peripheral serotonergic receptors. In this report, we present a case with fatal serotonin syndrome happening in a non-alcoholic patient with the chronic form of MBD. To our knowledge, this case is the first report of fatal serotonin syndrome due to citalopram in an MBD patient. The present report may indicate that citalopram and other SSRIs should not be used in patients with MBD. Our case is also among few reported cases in the literature where no cause was identified in a patient with no previous history of alcohol intake.

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1. Introduction

Marchiafava–Bignami disease (MBD) is a rare fatal neurological disorder characterized by demyelination, primary degeneration, and necrosis of the corpus callosum. Although MBD is mostly associated with chronic alcohol consumption and malnutrition, it has been reported in non-alcoholic patients [1]. Serotonin syndrome is a rare but potentially fatal side effect of antidepressants that results from overstimulation of both central and peripheral serotonergic receptors [2]. This syndrome consists of a combination of mental status changes with neuromuscular and autonomic hyperactivity [3]. In this report, we present a case with fatal serotonin syndrome happening in a non-alcoholic patient with the chronic form of MBD.

2. Case report

A 52-years-old non-alcoholic previously healthy man came to our clinic complaining of subacute difficulties with daily activities, slurred speech, and depressed mood. On examina-
tion, he had dysarthria, right-left disorientation, left arm ideomotor apraxia, and appreciative agnosia. His initial magnetic resonance imaging (MRI) of the brain showed an isolated splenium lesion with restricted diffusion and subtle enhancement (Fig. 1). He refused admission, but outpatient work up including routine chemistry, autoimmune profile, viral serology including HIV, vitamin B12 level, toxicology screen, paraneoplastic studies, and cerebrospinal fluid examination was normal. Three months later, he was admitted because of worsening apathy, deteriorating mental capacities, and poor oral intake. A repeat MRI of the brain showed necrotic gliosis of the splenium lesion and a new lesion at the body of the corpus callosum limited to the central layer and sparing the dorsal and ventral layers denoting to a characteristic classical sandwich sign of MBD (Fig. 2). He was treated with high dose intravenous thiamine, vitamin B complex, and pulse steroids (1 gm methylprednisolone intravenously for 5 days) with minimal improvement. Seven days after admission, we started a small dose citalopram to treat his depression. Within 24-h, he developed symptoms and signs suggestive of serotonin syndrome with rhabdomyolysis, acute renal failure, and severe hyperkalemia, and he died before initiating hemodialysis.

3. Discussion

MBD was first described in 1903 by two Italian pathologists; Ettore Marchiafava and Amico Bignami. It typically affects males between 40 and 60 years of age with a history of chronic alcohol consumption and/or malnutrition. It is also called red wine drinkers encephalopathy [4]. Although MBD was first reported more than a hundred years ago, its etiology remains unknown. MBD has been reported in non-alcoholic diabetic patients with poorly controlled levels of blood glucose. It was predicted that long-standing untreated diabetes leads to disarrangement of energy production and osmotic stress in the corpus callosum leading to the development of MBD [5].

Pathologically, MBD is characterized by demyelination and necrosis of the central part of the corpus callosum, which is usually symmetrical and sparing the thin upper and lower layers. Necrosis eventually leads to cavitation and atrophy of the corpus callosum in chronic stages [6]. Differential diagnosis of MBD includes osmotic myelinolysis syndrome, Wernicke’s encephalopathy, vasculitis, demyelination disorders, toxic/metabolic conditions, and alcohol withdrawal syndrome [7].

There are two forms of the disease; the acute form and the subacute/chronic form. The clinical features of MBD include neuropsychiatric features with cognitive impairment, pyramidal signs, dysarthria, hypertonia, and seizures. In the acute form, symptoms and signs include alteration of levels of consciousness, seizures, and rapid death. In the subacute form, the patient may present with varying degree of confusion, dysarthria, apraxia, cognitive impairment with special involvement of memory, behavioral abnormalities, and signs of interhemispheric disconnection. The chronic form is characterized by progressive dementia [8].

Advanced diagnostic technology such as MRI (the imaging modality of choice) usually shows characteristic abnormalities even in the early stages of the disease. MRI has facilitated visualization and proper evaluation of the corpus callosum which makes premortem diagnosis feasible [9]. The early stages of the disease are characterized by symmetrical diffuse edema with/without demyelination of the corpus callosum with effect on the body of the corpus followed by the genu and the splenium. These lesions appear hypointense on T1-
weighted images and hyperintense on T2-weighted images, diffusion weighted imaging, and fluid-attenuated inversion recovery (FLAIR). In addition, corresponding hypointensity and decreased values are seen on apparent diffusion coefficient mapping. These lesions do not present with a mass effect but may show contrast enhancement. Chronic lesions may progress to necrosis and cavitation with well-defined margins (positive sandwich sign). Other areas that are possibly involved include the cortex, cerebral peduncles, internal capsule, middle cerebellar peduncles and hemispheric white matter [10]. Diffusion-tensor imaging is important in identifying the changes in the fiber tract that typically shows marked fiber disruption in the body of corpus callosum [11].

There is no definitive therapy for MBD. The treatment usually includes treating the underlying cause and supplements with thiamine, vitamin B-12, and folic acid. Seizures and coma are treated symptomatically. In addition, corticosteroids may exert some benefits in some cases by reducing brain edema and inflammation, suppressing demyelination, and stabilizing the blood-brain barrier. The prognosis of MBD is poor with most of the patients dying or surviving with long-term disability and dementia [12].

Selective serotonin reuptake inhibitors (SSRIs) are the most commonly implicated medications associated with serotonin syndrome. They are the most common antidepressant drugs used in the treatment of major depressive and anxiety disorders [13]. Citalopram is one of the most commonly used SSRIs and is significantly more effective and well-tolerated than other antidepressants [14]. However, a small dose of citalopram led to the development of serotonin syndrome in our patient within 24 h. The management of serotonin syndrome includes discontinuation of all serotonergic agents, providing supportive care, giving oxygen and intravenous fluids, providing continuous cardiac monitoring, sedating with benzodiazepines, and possibly administering serotonin antagonists. The prognosis of serotonin syndrome is usually favorable if recognized early and treated appropriately [15].

4. Conclusion

MBD is known to be associated with high morbidity and mortality. Most cases were reported in relation to malnutrition and alcoholism. However, it has been reported without these risk factors like our case. Poorly controlled diabetes and diabetic ketoacidosis may be among the major contributing factors to the development of non-alcoholic MBD. The etiology of MBD is poorly understood. To our knowledge, this case is the first report of fatal serotonin syndrome due to citalopram in an MBD patient. The present report may indicate that citalopram and other SSRIs should not be used in patients with MBD. Our case is also among few reported cases in the literature where no cause was identified in a patient with no previous history of alcohol intake.
Conflict of interest

None declared.

REFERENCES


