



# Multiple sclerosis induced-mania: A Clinical challenge

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## ABSTRACT

Since its first systematic description, multiple sclerosis has been associated with cognitive and behavioral symptoms. Among psychiatric syndromes, mood disorders are highly common. Herein we report a case of a manic episode following a multiple sclerosis relapse in a young male subject without past history of psychiatric illness. The patient's psychiatric symptoms influenced negatively his adherence to treatment, possibly impacting his prognosis. Multiple sclerosis may be considered in the differential diagnosis of young adults presenting major psychiatric syndromes, including mania.

## Keywords

Multiple sclerosis, Mood Disorders, Mania, Psychosis

## Introduction

Multiple sclerosis (MS) is an autoimmune demyelinating disease of the central nervous system that may lead to severe neurological disability in early to middle adulthood. MS affects roughly 100-300 per 100,000 persons within the United States alone, and tends to be predominant among females. Besides motor, sensory and autonomic impairment, MS may determine cognitive and behavioral symptoms, impacting on patient's quality of life [1]. The high frequency of psychiatric symptoms in MS patients has led to the suggestion that MS should be routinely considered in the differential diagnosis of young patients with psychiatric complaints [2].

Bipolar disorder (BD) is a psychiatric illness characterized by alternating episodes of depression and hypomania/mania [3]. It has a worldwide prevalence of 1% and about 3% of people in the US are estimated to have BD at some point in their life [4]. The association between BD and MS has been recognized. In this report, we present an interesting case of a

patient with MS who developed an acute manic episode with psychotic features.

## Case Report

A 22 year-old Hispanic male with no previous psychiatric history was referred to our hospital due to acute behavioral changes with persecutory and grandiose ideations, and poor sleep in the last two weeks. Upon interview, he admitted that he was talking too much, and could not sleep for more than a week. He reported feelings of anxiety, sadness, and guilt. Despite denying suicidal ideations, he repeatedly admitted having thoughts of hurting himself and others, especially those "who continuously spy upon him with their cameras". The patient also exhibited persecutory ideations towards physicians who were treating him for MS and totally refused his medication. He expressed moments of personal epiphany in which he feels the ability to change the world with his powers.

Neurological examination revealed reduced sensation on both lower limbs with inability to fully stand without support. His brief psychiatric

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rating scale (BPRS) score was 57 overall. His Mini Mental Status Examination (MMSE) score was 26, with difficulty in registration and attention.

He was diagnosed with MS three years earlier, when presented with recurrent visual and gait problems. He was prescribed with Glatiramer Acetate, to which he was not compliant and discontinued due to adverse effects including generalized aches, fever and chills. In the following years, the patient experienced three other episodes of optic neuritis and gait incoordination, with complete recovery in-between them. The last episode occurred two months prior to the psychiatric hospitalization. At that time, his brain MRI showed multiple T2 hyperintense oval-shaped lesions in periventricular and deep white matter oriented perpendicularly to the ventricles. A cervical spine MRI also showed multiple T2 hyperintense lesions at the pons and the level of C3-C4.

He experienced sudden behavioral changes in the form of manic symptoms marked by insomnia, hyperactivity, talkativeness and pressed speech, few weeks after MS relapse, being responsible for his admission to our psychiatry unit.

With encouragement, he agreed to be medicated with risperidone, rejecting all mood-stabilizing drugs. He evolved with partial remission of his persecutory ideas and elated mood, but remained denying his disease. He was lost to follow-up.

### Discussion

In our case, mania seems to be the result of a MS relapse. The lack of previous personal and family history of mood disorders, and the temporal association between MS relapse (determined by clinical and neuroimaging findings) and the emergence of mania corroborate this assumption. Besides manic symptoms, the patient also exhibited psychosis, a less common neuropsychiatric feature in the context of MS.

Despite the well-known coexistence of psychopathological manifestations in MS, there are only few studies systematically addressing its associated psychiatric syndromes in contrast to the numerous reports discussing its neurological manifestations. In 1986, Schiffer and colleagues reported for the first time the potential association between MS and BD observed in 10 of their patients [5]. Later, Hutchinson and colleagues described seven patients with MS who had the diagnosis of BD prior to MS onset [6].

Interestingly, there was a report of a late diagnosis of MS in a 81-year-old woman who was treated from BD for over 30 years [7]. In 2003, the first study of its kind showed the genetic association of MS and BD based on the follow-up of a Greek family among three generation suggesting a strong association with HLA-DR2 antigen [8]. Asghar-Ali and colleagues reported two patients of MS who did not show any motor, sensory or autonomic symptoms but presented with manic symptoms (e.g. racing thoughts and pressured speech) [9]. Ybarra and colleagues also reported pure psychiatric symptoms compatible with BD in patients with MS [10]. Sidhom and colleagues described three cases of BD and MS, two of them were originally treated from manic symptoms for years before being diagnosed with MS, while the third patient was diagnosed first with MS and developed psychotic symptoms [11]. More recently, there was the report a 47 year-old woman with MS who developed a manic episode with psychotic features concomitantly to new brain lesions as detected by MRI. Her manic episode resolved with corticosteroid therapy, indicating that her mania was an acute manifestation of MS relapse [12]. Indeed, the pathogenesis of mood disorders is complex, and they may occur as part of the disease-as in this latter case and our one, secondary to treatment, due to psychosocial factors and/or combination of multiple factors.

Mania does not seem to manifest with specific features in MS, instead its psychopathology appears the same as in the general population, including excess of energy, talkativeness, disinhibited behavior, and sleeplessness, with the only difference being the neurological signs that is usually present in MS patients [10]. Occurrence of psychosis in MS is uncommon, but brief psychotic episodes mainly in the form of religious or persecutory delusions and hallucinations may occur as manifestations as well as a remission-followed onset relapse in MS [13].

Unlike our case, severe mood and/or psychotic disorders may be the presenting manifestation of MS years before the development of neurological symptoms. Previous studies addressed this possibility known as “inaugural manifestation”, which makes the diagnosis of MS easily missed [9,14,15].

In MS, damage of the white matter with subsequent disconnection of the cortical areas, mainly frontal cortices, and the basal ganglia

could be the underlying basis of the observed symptoms, including the psychiatric ones. The early course of MS is generally characterized by transitory demyelination followed by re-myelination, determining episodes of neurological dysfunction that usually recover. However, over time, the repeated inflammatory demyelinating episodes lead to cumulative axonal damage and neurodegenerative changes in brain circuits, which are clinically correlated with the progression of symptoms and disability [1]. In this scenario, the aim of current MS treatment is usually directed towards reducing the frequency of relapses to prevent the disease progression [16]. It is worth mentioning that our patient's psychiatric symptoms, especially paranoid ideation toward the treatment team, posed an additional challenge to his adherence to MS therapeutics, possibly negatively influencing his long-term clinical outcome.

## Conclusion

The actual aetiopathogenesis of the association between BD and MS, and its proper treatment are yet to be defined. Considering its potential impact on adherence to treatment and quality of life, close attention must be paid to the early diagnosis and effective management of the psychiatric aspects in MS. In addition, psychiatrists should consider MS in differential diagnosis of mental disorders in young adults, particularly in patients with atypical features, such as motor, sensory or autonomic findings, cognitive changes, and lack of response to standard treatment.

## Disclosure

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