DOI:10.4274/tnd.91328

Do Steroids Trigger Mania in Multiple Sclerosis? Not Always!

Steroidler Multipl Sklerozda Maniyi Tetikler mi? Her Zaman Değil!

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Summary

This paper consists of an unusual case history and an overview of the relationship between multiple sclerosis (MS), manic episode and corticosteroid treatment. Bipolar disorder and MS co-occur at a relatively higher rate. A 25-year old woman with a 7-year history of MS was admitted to our hospital with right side weakness. During the examination, she showed some manic behavior patterns and diagnosed as 'bipolar disorder-manic episode' by her psychiatrists. She was recommended for high dose steroids for her attack and antipsychotics for the manic episode but she refused the latter. Unexpectedly at the third day of steroid treatment, instead of being exacerbated, almost all of the manic symptoms disappeared. In the literature, this is the first report of a MS patient with bipolar disorder whose manic symptoms were cured after receiving steroids. (Turkish Journal of Neurology 2015; 21:68-70)

Key Words: Multiple sclerosis, mania, bipolar disorder, corticosteroid, treatment

Özet

Bu yazı olağan dışı bir olgu sunumu çerçevesinde multipl skleroz (MS), manik atak ve steroid kullanımı ilişkisini irdelemektedir. MS'de bipolar bozukluk görülme sıklığı normal kişilerle karşılaştırıldığında daha sıktır. Yedi yıllık MS öyküsü bulunan 25 yaşındaki kadın hastamız sağ tarafında güçsüzlük yakınması ile geldi. Muayene sırasında manik içerikli davranışları gözlendi ve psikiyatrik değerlendirme sonrası 'bipolar bozukluk-manik atak' tanısı aldı. Atak tedavisi için yüksek doz steroid ve manik semptomlar açısından antipsikotik kullanımı önerilen hasta mani tedavisini reddetti. Beklenenin aksine steroid tedavisinin üçüncü gününde, manik atak alevlenmesi olmaksızın nörolojik semptomlarda tama yakın düzelme oldu. Olgumuz manik atakla gelen ve steroid uygulaması sonrası manik semptomları tama yakın düzelen literatürdeki ilk MS hastasıdır. (Türk Nöroloji Dergisi 2015; 21:68-70)

Anahtar Kelimeler: Multipl skleroz, mani, bipolar bozukluk, kortikosteroid, tedavi

Introduction

Multiple sclerosis (MS) is a chronic, inflammatory and degenerative neurological disease of autoimmune origin. The disease has a wide variety of symptoms and clinical signs since MS plaques can be present in almost all parts of the central nervous system. In addition to the motor and sensory loss, optic neuritis, cerebellar disorders, and bladder and bowel dysfunction, more than half of the patients also show psychiatric disorders. Depression, anxiety and bipolar disorder are several times more likely in the MS populations compared to healthy people. It was also shown that psychiatric disorders are associated with treatment compliance difficulties, losses in daily functioning and quality of life (1). In 80% of the cases, MS starts with a pattern of alternating attacks and recoveries. Using high-dose corticosteroids for 3-10 days is the most common method for managing the attacks. In addition to their well-known side effects, steroids in high doses may also cause psychiatric symptoms which are mostly manic and

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Received/Geliş Tarihi: 06.11.2013 **Accepted/Kabul Tarihi:** 21.10.2014

depressive episodes It was reported that 5-18% of the patients who used high-dose corticosteroids showed psychiatric symptoms (2). However, there are other reports of MS attacks which presented with either isolated manic symptoms or other neurological findings accompanied by manic symptoms (2,3,4,5,6,7).

The motivation for presenting this case study is to comprehensively review the relatively well established MS-bipolar disorder relationship under the light of new findings, and to show that high-dose corticosteroid use which was previously associated with triggering mania actually suppressed it in our patient to a large extend.

Case Report

Our patient was a 25-year-old female who was being followed in Mersin University Neurology outpatient clinic for the past 7 years. Her visits in the last 4 years had been irregular. Her first attack occurred in 2006 with right hemiparesis and it completely subsided within 2 months. Six months after the first attack, she had a second one that started with kinetic tremor on her right arm and head, and a new cervical spinal lesion congruent with the clinical symptoms. A third attack happened in 2008 with left hemiparesis and hemihypoaesthesia. In all of the attacks, 1000 mg/day intravenous methylprednisolone treatment was administered in 5-7 day intervals. She chose not to use immunomodulatory treatment for the past 3 years. Magnetic resonance imaging (MRI) study showed periventricular, juxtacortical and spinal lesions suggesting MS. Oligoclonal band was positive in the cerebrospinal fluid and the visual evoked potentials that were repeated 3 times showed indicators of bilateral prechiasmatic optical tract demyelination. The patient did not show signs indicating vasculitis or other autoimmune diseases. Antibody studies (anti-Ro, anti-La, anti-SM, anti-DNA and anticardiolipin) and serology (syphilis, hepatitis-B and C, HIV) were negative.

Manic behaviors were observed in the exam when the patient came in for the weakness on the right arm and leg that had been going on for 3-4 days in May 2013. The exam showed right frust hemiparesis which did not exist in the earlier exams. Magnetic resonance imaging showed a lesion with a suspicious contrast-holding pattern and new lesions in addition to the cerebellar one compared to the MRI in 2008.

Corticosteroids were recommended due to manic behavior and psychiatric consultation was requested. Elevated mood, inappropriate jokes, amplified gestures, mild increase in libido, irritability during the exam, increasingly frequent anger and temperament attacks were seen. The rate and amount of speech were increased and hard to suppress. The patient admitted that her behavior was possibly different but refused to acknowledge her disorder. She scored 20 points on Young Mania Rating Scale (8). She was diagnosed with "mood disorder due to a general medical condition: manic episode" according to Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) and was recommended oral quetiapine 2x50 mg. She was planned to start on 1000 mg/day methylprednisolone i.v. and quetiapine and pulse steroid treatment. The patient refused quetiapine because she was breastfeeding. She was monitored for 5 days to detect any exacerbation of her manic symptoms, but they actually improved. Thus, steroid treatment was continued. She was re-evaluated on the third day of the steroid administration with Young Scale and considered within normal psychiatric status when she scored 3 points. Her hemiparesis completely improved after 5 days.

Discussion

Psychiatric disorders including manic disorder are several times more common among MS populations than healthy people. Even though mania is rare in MS, it could present either as a clinical symptom of MS or due to the use of mania-triggering medication such as steroids, baclofen, dantrolene, tizanidine.

There are no neuroanatomical studies in the literature on MS patients with bipolar disorder. Considering all of the bipolar cases as a whole, it is possible to interpret that the disorder is caused by lesions located in multiple brain regions involving limbic-thalamic-cortical loop and limbic-striatal-pallidal-cortical loop. This wide range of areas involve prefrontal cortex, basal ganglia, anterior temporal and frontal areas as well as the components of the limbic system such as amygdala, thalamus and striatum (9). It is known that especially subgenual anterior cingulate cortex lesions cause bipolar disorder. The fact that MS plaques are often seen on these regions may explain why bipolar disorder is seen at least twice as likely in MS patients than healthy populations. It is worth noting that lesions of MS patients with bipolar disorder are in very different locations.

Previous studies on this topic primarily focused on depression, anxiety and sleep in MS patients and nearly all of them found increased number of symptoms and impairment in those disorders in MS patients compared to healthy people (10). A recent study found that depression, anxiety, and bipolar disorder are more often seen in MS patients than healthy people but there was no difference in terms of schizophrenia (11).

Even though it is much more rare compared to depression, mania and hypomania can still be observed in MS patients. In addition to that, MS can develop in patients who were diagnosed with bipolar disorder and sometimes mania presents as an initial symptom of MS (3,4,5,6,7).

Eleven out of 586 MS patients that İdiman et al. followed for 12 years got diagnosed with bipolar disorder and this preceded the MS diagnosis in two of them. They concluded that manic/hypomanic episode was presented with the MS attack in two out of 11 patients and that it was related to corticosteroid use in two patients. However, stopping corticosteroids did not stop the symptoms in either of those patients and the manic findings were subsided only with antipsychotics and lithium. The authors reported that the incidence rate of bipolar disorder in MS patients is twice as much as healthy individuals (3).

We observed the manic behavioral patterns in our patients when she came to our neurology clinic with muscle weakness. Due to the motor loss and increased lesion load in MRI, we recommended hospitalization to follow the patient jointly with psychiatry department. Despite the risk of exacerbating the manic symptoms, we decided in favor of high-dose methylprednisolone treatment. We observed that the manic symptoms markedly started regressing two days after she was started on steroid even though she refused to use quetiapine recommended by the psychiatrist. In the second comprehensive psychiatric evaluation following the third dose of steroid, the manic symptoms of the patient almost

completely disappeared and she was considered psychiatrically normal.

Considering this progression, we believe that it is important to touch on the mania-inducing effects of steroids in the context of this case. The risk in the high doses is much larger than low doses. This indicates that MS patients who are experiencing an attack, much like our patient was, are in high risk. Psychiatric symptoms develop in 5-18% of the patients that receive high-dose corticosteroids. A majority of them present with manic or depressive symptoms. The duration between the start of the steroid treatment and the psychiatric symptoms is 11 days on average. However, there have been cases where this duration was 3-4 days (2). There are a few cases in the literature where the first doses of steroids cause manic symptoms and those were not MS patients. Looking at the time interval between the start of steroid treatment and the emergence of manic symptoms, it is possible to think that our patient was not under high risk, at least for the initial first doses. After the cessation of the drug, the average recovery duration for delirium is a few days. This duration is 3 weeks for mania and 4 weeks for depression. There is inconsistent data on the other risk factors but there is research suggesting that it is more commonly seen in women. Mood stabilizers like lithium, antipsychotics and antiepileptics can be used if the symptoms cannot be managed after stopping the steroids (2).

Mania is rarely reported in MS patients. In our case, the manic symptoms were possibly a part of the attack along with hemiparesis. Otherwise it would have been impossible to subdue the manic symptoms in a short amount of time by using high-dose steroid treatment only. What was striking about this case was not that mania was a symptom of the attack, but that the high-dose steroid treatment which was previously known to exacerbate mania actually completely subdued the mania symptoms in a very short time. Therefore, we can argue that mania could be a part of an MS attack or the only presenting system and that the corticosteroid treatment for the attack may actually prevent the mania symptom in some patients instead of exacerbating them. However, this should not be interpreted in a way that would suggest the steroid use permits being careless or that such conditions can be monitored without hospitalization. There are no MS cases of this kind in the literature

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Peer-review: Externally peer-reviewed

Conflict of Interest: No conflict of interest was declared by the authors

Financial Disclosure: The authors declared that this study received no financial support.

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