

Bipolar Mania Rapidly Induced by Low Dose Pramipexole in a Japanese Bipolar I Disorder

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Abstract

Dopaminergic agonists are widely used in the treatment of Parkinson's disease and bipolar disorder. Psychosis induced by dopaminergic agonists in Parkinson's disease has been reported frequently, but cases of mania induced by dopaminergic agonist are rare. Here we report the case of bipolar mania induced by pramipexole, which was used for the treatment of Parkinson's disease. The patient was a 59-year-old male with bipolar disorder type I. He presented with an exacerbated hand tremors. Physical examinations revealed that he presented symptoms of Parkinson's disease (i.e., hand tremors, stiffness, rigidness, and postural reflex impediment). After using a week of pramipexole (0.25 mg d⁻¹), his hand tremors improved markedly. However, at the same time, he developed hyperthymia, irritability, aggression, hyperlogia, and the flight of ideas. He was diagnosed as bipolar mania. Most manic symptoms were resolved within 4 weeks by using valproic acid, olanzapine, and levomepromazine. Our case is unique in that pramipexole induced bipolar mania rapidly (i.e., within a week) even in minimum doses (i.e., 0.25 mg d⁻¹). Dopaminergic agonists are often used to treat bipolar disorder, for example, in cases complicated with Parkinson's disease and cases of refractory/recurrent bipolar depression. When dopaminergic agonists are used in patients with bipolar disorder, as in this case, mood should be assessed and checked for signs of bipolar mania.

Introduction

The dopaminergic neurons are widely distributed across the brain and have diverse and significant roles in physical activities and mental state. Quantitative changes in dopamine levels are known to cause Parkinson's disease and mood disorder, and control of dopamine levels using drugs is significant as a therapeutic strategy. Dopamine agonists such as pramipexole, L-DOPA, and bromocriptine are effective in Parkinson's disease, RLS, and recurrent/refractory bipolar depression.

On the other hand, there are some reports that dopaminergic agonists cause psychosis [1]. Ecker et al. [2] compared patients with and without psychotic symptoms during the course of Parkinson's disease, and reported that the risk of psychosis when using dopaminergic agonists was greater than when using L-DOPA in patients with psychotic symptoms during the course of Parkinson's disease. However, there are few reports on the association between dopaminergic agonists and psychiatric symptoms in bipolar disorder [3,4]. Here, we report the first case of bipolar mania induced by pramipexole in Asia.

Case Presentation

A 59-year-old man with bipolar disorder type I had been referred to our hospital. He had suffered from hand tremors for approximately 10 years and presented akinesis, stiffness, and postural reflex impediment from 2 years earlier. His hand tremors had been gradually worsening for 4 months. His mood was neutral, and blood test, urine test, and electroencephalogram revealed no abnormalities. However, neurological examination revealed hands tremors, stiffness, rigidness, and postural reflex impediment. His maintenance medications were lithium carbonate 400 mg d⁻¹, levomepromazine 50 mg d⁻¹ (Figure 1). A switch lithium carbonate to valproic acid 400 mg d⁻¹ did not affect hand tremors. Using biperiden 3 mg d⁻¹ also did not improve his hand tremors. From these observations, we diagnosed with Parkinson's disease. We then switched biperiden to pramipexole 0.25 mg d⁻¹ and increased dose to 0.5 mg d⁻¹ over a 1 week. At a week after the use of pramipexole, symptoms of Parkinson's disease were improved. However, he developed manic symptoms such as hyperthymia, irritability, aggression, hyperlogia, the flight of ideas, and the decrease of the sleep requirement. We diagnosed with bipolar mania and discontinued pramipexole and added olanzapine 10 mg d⁻¹,

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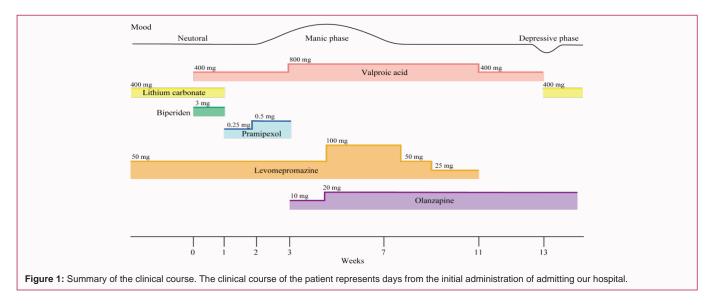
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which was increased to 20 mg d $^{-1}$ over 4 weeks. Levomepromazine and valproic acid dosage were also increased to 100 mg d $^{-1}$, 800 mg d $^{-1}$, respectively. It took 4-weeks to be back in a neutral mood after discontinuing pramipexole. However, 2 weeks after recovering a neutral mood, he developed depression, inhibition, micromania, anorexia, and loss of motivation. We then diagnosed with bipolar depression. We added lithium carbonate 400 mg d $^{-1}$, and his mood was re-shifting to a neutral mood a month later. Since then, his mood has been neutral.

Discussion

In the treatment of the bipolar disorder, using Lithium and other mood stabilizers are the most effective treatments. Since antipsychotics are also effective in both the manic and depressive phases, the standard protocols are to use mood stabilizers and antipsychotic medications in combination. Dopaminergic agonists have been reported to be effective in bipolar depression [5,6]. On the other hand, psychosis induced by dopaminergic agonists has been reported frequently; there are rare cases that show dopaminergic agonists can induce mania like our case. Goldberg et al. [5] reported that patient with resistant bipolar depression treated with pramipexole and a mood stabilizer had hypomanic symptoms. Sporn et al. [4] observed that hypomanic symptoms occurred in only 1 of 12 patients with bipolar depression and 20 patients with unipolar depression that received pramipexole as an adjuvant treatment.

Our case is the lowest dose (i.e., 0.5 mg d^{-1}) and most rapid (i.e., one week) of any reported case to date. In addition, our study was the first report from the Asian region, including Japan. Therefore, the induction of bipolar mania by pramipexole occurs independently of race.

Dopaminergic agonists are also used to treat Parkinson's disease. Bipolar disorder is known to be at a higher risk for idiopathic Parkinson's disease [7]. Thus, even when using dopamine agonists for Parkinson's disease, we should recognize that there is a risk of induction of bipolar mania.

Conclusion

Dopaminergic agonists such as pramipexole, which are used frequently in the treatment of Parkinson's disease, can cause manic symptoms. When dopaminergic agonists are used in patients with bipolar disorder, mood should be assessed and checked for signs of bipolar mania.

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