

Mania with Psychotic Feature Induced by The Use of Pramipexole in Parkinson's Disease: A Case Report



Ceren MERİÇ¹, Efruz PİRDOĞAN¹, Ömür GÜNDAY TOKER¹, Atilla TEKİN¹, Bahadır BAKIM²,
Selime ÇELİK³

SUMMARY

Parkinson's disease (PD), which is frequently accompanied by psychiatric symptoms, is a neurodegenerative disease characterized by movement disorders. Psychiatric symptoms may be the direct result of PD, comorbid pathologies, or its pharmacotherapy. Pramipexole, as other dopamine agonists used in the treatment of PD, has a tendency to induce psychotic and manic symptoms due to central dopaminergic stimulation. Herein we present a PD patient that had mania with psychotic feature due to dopamine agonist treatment, which is not commonly reported.

Keywords: Parkinson's disease, psychosis, mania, pramipexole

INTRODUCTION

Parkinson's disease is the second most common neurodegenerative disorder. Although it is classified as a movement disorder, non-motor symptoms, including psychiatric complications, are commonly observed during disease progression. Mania, although not as common as depression and psychosis, also occurs in Parkinson's disease. Psychotic and manic symptoms occur in about 10% of non-treated patients with Parkinson's disease, it is predicted as these symptoms are associated with dopaminergic treatment (Engmann 2011; Ecker et al. 2009).

Dopamine receptor agonists are an effective treatment option for Parkinson's disease; however, dopamine agonists are associated with numerous side effects. The use of dopamine agonists is the most common risk factor for psychosis in Parkinson's disease. It is known that in Parkinson's disease patients who receive dopaminergic treatment the prevalence of psychosis is as high as 40% (Georgiev et al. 2010; Ecker et

al. 2009). Pramipexole, which is a dopamine receptor agonist, can be used as monotherapy or in combination with levodopa in the treatment of Parkinson's disease. It was reported that pramipexole is safe and effective for improving motor functions and daily activity in Parkinson's disease. Nevertheless, psychotic symptoms and hypomania induced by pramipexole have been reported (Friedman 2010; Singh et al. 2005; Goldberg et al. 2004; Sporn et al. 2000). Herein we present a Parkinson's disease patient who developed mania with psychotic feature following treatment with pramipexole.

CASE

History

A 67-years-old married man with a middle school education that was retired and living in the center of the city presented to a university hospital because of left hand tremor and was diagnosed as Parkinson's disease 16 years earlier. He

Received: 06.03.2013 - Accepted: 23.04.2013

¹Assist., Sisli Etfal Teaching ve Research Hospital, Department of Psychiatry, İstanbul, Turkey. ²Assist Prof., Çanakkale 18 Mart University, Medical Faculty, Department of Psychiatry, Çanakkale, Turkey. ³MD, Psychiatrist, Sisli Etfal Teaching ve Research Hospital, Department of Psychiatry, İstanbul, Turkey.

E-mail: md.atillatekin@gmail.com

has been using levodopa in combination with benserazide and other antiparkinsonian drugs such as entecapone since 1996. Approximately 3 months before presenting, pramipexole 0.5 mg d⁻¹ was added to his current treatment of levodopa + benserazide 375 mg d⁻¹ by the doctors treating him at a clinic other than ours. Then, 1 month later pramipexole was increased to 1 mg d⁻¹. Approximately 10 d after this dose increase the patient experienced an increase in sexual desire and began to think that women sitting near him would experience an orgasm if they touched his leg was defining this situation like an “original invention belongs to him”. He then presented to the Sisli Etfal Research and Teaching Hospital Psychiatry Outpatient Clinic with his wife following a referral from the clinic at which he had previously been followed-up.

Assessment and mental state examination

During his mental state examination he was conscious and fully cooperative. His mini-mental state examination (MMSE) score was 28/30—he lost 2 points for recall and drawing. His mood was elevated (he reported that he was more cheerful than he had ever been) and his affect was slightly limited (this limit, which is a parkinsonian symptom, was considered as his affect didn't participate the inner stimuli, elevated mood sufficiently). The content of his thoughts, which included statements such as, “women sitting next to me experience orgasm if they touch my leg”, was considered delusional. He didn't have insight. The quantity and speed of his speech were excessive and his thoughts were accelerated. He required less sleep and his psychomotor activity increased. He did not have suicidal or homicidal ideation. According to his wife, other than Parkinson's disease he had no other medical condition, he had not received any psychiatric treatment, he had a negative history of alcohol and substance abuse, and in terms of family history his mother had a history of antidepressant use, but no information about her diagnosis was available.

Differential diagnosis and diagnostic process

According to SCID-1 and DSM-IV-TR criteria, he was diagnosed as substance (drug)-related mood disorder with psychotic feature (including manic features). His psychiatric scale scores were, as follows: Young Mania Rating Scale (YMRS): 26; Brief Psychiatric Rating Scale (BPRS): 38. Biochemical findings, including liver function tests, urea-creatinine, thyroid function tests, electrolyte levels, alkaline phosphatase, creatine kinase, lactate dehydrogenase, complete blood count, sedimentation rate, and C-reactive protein levels, were normal. Cranial MRI showed that the width of the cerebral cortical sulci and ventricle compartments were slightly enlarged because of diffuse atrophy related to age.

Treatment and clinical follow-up

After neurological consultation, the pramipexole dose was gradually decreased and valproate 500 mg d⁻¹ and aripiprazole 5 mg d⁻¹ were added to his treatment regimen. After 1 week of the new treatment regimen according to his mental state examination the severity of his manic and psychotic symptoms decreased significantly. Psychiatric scale scores were, as follows: YMRS: 13; BPRS: 22. Two weeks later, pramipexole was withdrawn by the neurology department and his mood was euthymic and his affect was slightly limited. The content of his thoughts was normal, grandiose delusions were no longer present, and he had good insight. The quantity and speed of his speech were normal, as was his psychomotor activity. His sleep pattern was normal. His YMRS score was 6 and BPRS score was 9.

DISCUSSION

The psychiatric conditions most frequently observed during the course of Parkinson's disease are depression, anxiety, sleep disorders, sexual dysfunction, cognitive impairment, and psychosis. Though they occur less frequently, mania and impulse control disorders (hypersexuality, pathological gambling, etc.) can occur in patients with Parkinson's disease. According to the literature, visual hallucinations are the most frequent psychotic symptoms that occur during the course of Parkinson's disease, but auditory hallucinations and paranoid delusions can be observed. These psychiatric conditions can occur as a direct result of the disease and also can occur due to the drugs used for treatment (Friedman 2010; Levenson 2007).

Although levodopa is considered the gold standard treatment for Parkinson's disease, dopamine agonists are also frequently used. It was reported that the severity of motor symptoms that can occur with levodopa alone decreased when it is used in combination with dopamine agonists. Pramipexole—a non-ergot derivative—is a dopamine agonist used in the treatment of Parkinson's disease. Its affinity to D3 receptors, which are numerous in the mesolimbic region, is greater than its affinity to D2 receptors. Pramipexole is used as a monotherapy in the treatment of Parkinson's disease and is also used in the treatment of resistant depression during the course of Parkinson's disease (Bhatia et al. 1998).

Psychosis induced by dopamine agonists in Parkinson's disease has been reported frequently, but cases of dopamine agonist-induced mania are rare. It was reported that dopamine agonists pose a greater risk of psychosis than levodopa (Antonini et al. 2009). Ecker et al. compared patients with and without psychotic symptoms during the course of Parkinson's disease, and reported that the risk of psychosis when using dopamine agonists was greater than when using levodopa in patients with psychotic symptoms during the course of Parkinson's disease. In addition, it was reported that ropinirole is the

dopamine agonist most associated with psychosis (Ecker et al. 2009).

The literature contains insufficient data regarding mania and hypomania induced by dopamine agonists in patients with Parkinson's disease. In a case reported by Singh et al. (2005) predicted hypomania induced by ropinirole and pramipexole together in a patient with Parkinson's disease. Nonetheless, it was also reported that pramipexole, which is sometimes used to treat cases of resistant depression, can cause manic or hypomanic shifts. Goldberg et al. (2004) reported that 1 of 12 patients with resistant bipolar depression treated with pramipexole and a mood stabilizer had hypomanic shift. A retrospective study by Sporn et al. (2000) observed that hypomanic shift occurred in only 1 of 12 patients with bipolar depression and 20 patients with unipolar depression that received pramipexole as an adjuvant treatment.

In the presented case grandiose delusions with elevated mood, increased psychomotor activity and quantity of speech, acceleration of thoughts, and decreased need for sleep indicated mania. The diagnosis was differentiated from hypomania based on a clinical picture that persisted for >1 week, presence of a psychotic sign, and more severe clinical course. The patient's negative history of psychiatric disease, the onset of symptoms after pramipexole was added to the treatment, and regression of symptoms after pramipexole was withdrawn and a mood stabilizer with an atypical antipsychotic were added to the treatment, all indicated that the symptoms were induced by pramipexole. Accordingly, it is necessary to differentiate pathological hypersexuality caused by dopamine agonists from mania. According to Kaplan et al. (1994), pathological hypersexuality was defined like because of the need for uncontrollable sexual behaviour, the patient's spending money, time, concentration and energy, insistent and undesirable paraphilic thoughts' preventing necessary concentration for the other requirements of life and creating resource for anxiety and the orgasm's not satisfying enough for the age typically. As mentioned above, the diagnosis was differentiated from pathological hypersexuality by the patient's elevated mood and delusions that were adjusted with mood, decreased need for sleep, and increase in sexual desire in the absence of uncontrollable sexual behavior and persistent paraphilic thoughts.

The literature is limited in terms of the treatment of psychotic and manic symptoms during the course of Parkinson's

disease. It was reported that lithium can exacerbate motor symptoms; however, valproate is more a reliable mood stabilizer (Engmann 2011). It was also reported that clozapine and quetiapine exacerbate extrapyramidal symptoms, although to a lesser extent than the other antipsychotic drugs, but that aripiprazole and olanzapine could be effective in some patients (Karakuş et al. 2012; Engmann 2011; Zahodne and Fernandez 2008). In the presented case psychotic and affective symptoms disappeared entirely following treatment with valproate and aripiprazole, and any deterioration was observed in motor symptoms.

In conclusion, dopamine agonists such as pramipexole, which are used frequently in the treatment of Parkinson's disease, can cause psychiatric symptoms. The outcome of psychiatric symptoms induced by pharmacotherapy is not well known; therefore, additional relevant research is required.

REFERENCES

- Antonini A, Tolosa E, Mizuno Y et al (2009) A reassessment of risks and benefits of dopamine agonists in Parkinson's disease. *Lancet Neurol* 8:929–37.
- Bhatia K, Brooks DJ, Burn DJ et al (1998) Guidelines for the management of Parkinson's disease. The Parkinson's Disease Consensus Working Group. *Hosp Med* 59: 469– 80.
- Ecker D, Unrath A, Kassubek J et al (2009) Dopamine agonists and their risk to induce psychotic episodes in Parkinson's disease: a case-control study. *BMC Neurol* 9:23
- Engmann B (2011) Bipolar affective disorder and Parkinson's disease. *Case Report. Case Rep Med* 154165.
- Friedman JH (2010) Parkinson's disease psychosis 2010: A review article. *Parkinsonism Relat Disord* 16:553–60.
- Georgiev D, Danieli A, Ocepik L et al (2010) Othello syndrome in patients with Parkinson's disease. *Psychiatr Danub* 22:94–8.
- Goldberg JF, Burdick KE, Endick CJ (2004) Preliminary randomized, double-blind, placebo-controlled trial of pramipexole added to mood stabilizers for treatment-resistant bipolar depression. *Am J Psychiatry* 161:564–6.
- Kaplan HI, Saddock BJ, Grebb JA (1994) *Synopsis of Psychiatry*. 7th Ed. Baltimore(MD): Williams&Wilkins.
- Karakuş G, Özpoyraz N, Zengin M et al (2012) Parkinson hastalığı sırasında ortaya çıkan psikotik özellikli manik atak: olgu sunumu. *Klinik Psikiyatri* 15:248–51.
- Levenson JL (2007) Parkinson's Disease and Multiple Sclerosis. *Psychiatric Issues in Neurology* 14:35–9
- Singh A, Althoff R, Martineau J et al (2005) Pramipexole, ropinirole and mania in Parkinson's disease. *Am J Psychiatry* 162:814–5.
- Sporn J, Ghaemi SN, Sambur MR et al (2000) Pramipexole augmentation in the treatment of unipolar and bipolar depression: A retrospective chart review. *Ann Clin Psychiatry* 12:137–40.
- Zahodne LB, Fernandez HH (2008) A review of the pathophysiology and treatment of psychosis in Parkinson's disease. *Drugs Aging* 25:665–82.