Impulse control disorder associated with dopaminergic therapy in Parkinson's disease – a case report

Zaburzenia kontroli impulsów związane z leczeniem dopaminergicznym w chorobie Parkinsona – opis przypadku

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Abstract

Parkinson's disease is regularly associated with non-motor symptoms that are often not sufficiently diagnosed and treated. We describe development of an impulse control disorder in relation to the administration of dopamine agonist pramipexole to a 61 year-old male with Parkinson's disease. Behavioral disturbances in the patient evolved gradually after the initiation of pramipexole therapy in a dose of 2.1 mg pro die and disappeared within several weeks after pramipexole daily dose reduction to 0.54 mg. The case demonstrates the necessity for careful monitoring of adverse effects of dopaminergic treatment in patients with Parkinson's disease. Differential diagnosis of symptoms and treatment options are discussed.

Key words: behavioral symptoms, dopaminergic agents, impulse control disorders, Parkinson's disease, pramipexole

Streszczenie

W chorobie Parkinsona (ChP) z reguły występują objawy niedotyczące czynności ruchowych, które często nie są właściwie rozpoznane i leczone. W niniejszym artykule autorzy opisują rozwój objawów o charakterze zaburzeń kontroli impulsów, które pojawiły się w trakcie podawania agonisty dopaminy – pramipeksolu – u 61-letniego mężczyzny z ChP. Zaburzenia zachowania rozwijały się stopniowo po rozpoczęciu leczenia pramipeksolem w dawce 2,1 mg/dobę i ustąpiły w ciągu kilku tygodni po zmniejszeniu dobowej dawki pramipeksolu do 0,54 mg/dobę. Powyższy przypadek wskazuje na konieczność wnikliwego monitorowania objawów ubocznych w trakcie leczenia dopaminergicznego pacjentów z ChP. Omówiono również rozpoznanie różnicowe i opcje terapeutyczne.

Słowa kluczowe: zaburzenia zachowania, leki dopaminergiczne, zaburzenia kontroli impulsów, choroba Parkinsona, pramipeksol

Introduction

Idiopathic Parkinson's disease (PD) is the most common disorder of basal ganglia, a brain structure responsible for the control of motor function but also affecting the cognition and behavior (Philips & Breen 2007). Parkinson's disease is virtually always associated with non-motor symptoms (Table 1), which are often insufficiently diagnosed or improperly treated. Failure to identify and treat non-motor complications is associated with impaired quality of life of the patients and non-compliance. Some conditions are even life-threatening (e.g. suicidal behavior). Motor and non-motor symptoms of PD may be of intrinsic, disease-related origin, or of extrinsic origin, usually as a consequence of dopaminergic treatment. Recently, special attention has been paid to behavioral symptoms of PD (Table 1). Behavioral abnormalities associated with dopaminergic therapy can be divided into three main categories: *Impulse control disorders* (ICD), *Dopamine dysregulation syndrome*, and *Punding* (Philips & Breen 2007). ICD includes

pathological gambling, impulsive acts and hypersexuality (Voon & Fox 2007). The prevalence of pathological gambling in the common population is approximately 4% (Breo 1989). In contrast, the prevalence in the population of patients with PD ranges from 6 to 12% (Avanzi *et al.* 2006). Dopamine dysregulation syndrome is characterized by compulsive overuse of dopaminergic agents (L-dopa and dopamine agonists) (O'Sullivan *et al.* 2009). This may induce dyskinetic and/or psychotic symptoms. Behavioral symptoms are usually present in patients with an early onset of the disease and are associated with higher doses of anti-parkinson drugs, premorbid or comorbid depressive syndrome, abuse of alcohol or non-alcoholic psychotropic substances and novelty-seeking personality traits (Wolters *et al.* 2008; Isaias *et al.* 2008).

Case report

Presented patient is a 61 year-old male, with no personal history of serious diseases and no remarkable family history of neurological or psychiatric disorders. He works as a tinsmith and has five children. He has been treated for Parkinson's disease since 2002. His daily drug regimen consisted of 500 mg levodopa, 200 mg amantadine and 10 mg donepezil (due to mild cognitive impairment) per day. Additionally, pramipexole was initiated in 2006 in a dose of 0.7 mg three times daily. It was about that time, when patient's family members first realized the changes in the patient's behavior. He started treating his wife and children disrespectfully. Despite having no money to spare, he financially supported their 23 year-old female neighbor who was living in poor socioeconomic conditions and was drinking alcohol excessively. He even took two loans for her sake, though he had always had a negative attitude towards loans and liabilities. At the same time, he didn't pay his bills, had no money even for food and his family was almost cut off power supplies because of his debts. He started forcing his wife into sexual activities and was physically abusive towards her. He started being suspicious. Once he followed his wife to Poland, where she wanted to visit her relatives. At the other time, he suddenly left for a car drive at 4.00 a.m. The family members were frightened by his behavior and described it as markedly different from the patient's previous standard. The patient himself admitted retrospectively that it "was not him". He said that he was "sexually energized" and that he didn't care for the money. Due to apparent changes in the patient's behavior, the dose of pramipexole was reduced in the spring 2008 to 0.18 mg three times daily and the dose of amantadine was reduced to 100 mg daily. Behavioral symptoms disappeared within several weeks after dose adjustment, leaving only stable mild cognitive deficit. Motor symptoms did not worsen significantly. The patient continues to live in a family setting and is followed up by neurologist as an outpatient.

Table 1. Behavioral symptoms and other non-motor symptoms of Parkinson's disease (PD)

Behavioral symptoms of PD	Other non-motor symptoms of PD
Impulse control disorders • gambling • hypersexuality • compulsive shopping • compulsive eating Punding Dopamine dysregulation syndrome	Autonomic dysfunction • orthostatic hypotension • genitourinary dysfunction • constipation • thermoregulatory disorder • excess or reduced sweating Sleep disorders • sleep fragmentation • sleeplessness • excess diurnal somnolence • REM-related sleep disorder • restless legs syndrome • periodic limb movement in sleep Sensory disorders • hyposmia • disorders of color vision • vestibular deficit • pain • paresthesia and dysesthesia Neuropsychiatric symptoms† • fatigue • apathy and anhedonia • depressive and anxious symptoms • cognitive dysfunction and dementia • psychotic disorders

†*Behavioral symptoms are considered as a part of neuropsychiatric symptoms of PD*

Discussion

In this case report, we describe an occurrence of behavioral symptoms in a patient on dopaminergic therapy. Patient's symptoms were not a part of an affective disorder and were probably not related to the patient's mild cognitive deficit. The fact that the appearance of behavioral changes coincided with the initiation of pramipexole therapy and they resolved after the dose reduction of pramipexole

and amantadine suggests drug-related etiology. In addition, the mild cognitive disorder was stationary all the time. Impulse disorders, including hypersexuality, could represent an undesirable effect of dopaminergic therapy (Voon & Fox 2007). However, since many other exogenous factors may play a role in their etiology, symptoms should be considered as multifactorial. A typical example is addictive behavior, which can result from dysphoria related to a dopamine deficit combined with euphoric effects of levodopa, cholinergic denervation due to the progression of PD and aging, as well as factors related to psychosocial conditions (Wolters *et al.* 2008). Undoubtedly, patient's dispositions for addictive behavior may have played important role and administration of a dopaminergic agent could have served as a trigger. Dopamine is responsible not only for the control of voluntary movements but also plays an important role in the brain reward system and behavioral regulation. Therefore the majority of patients with PD have clinical symptoms of dysphoria, which leads to a reward-seeking behavior. Some patients take higher doses of drugs for the treatment of motor symptoms than required, resulting in the development of dopamine dependence. Presented complications may have been caused by receptor changes after the administration of dopamine agonists. Treatment of impulse disorders is related to the underlying pathology. If extrinsic factors are involved, dopaminergic therapy should be reduced (Wolters *et al.* 2008). Antidepressants from the group of Selective Serotonin Reuptake Inhibitors (SSRIs) or small doses of atypical antipsychotic agents should also pose some benefit (Lader 2008). If the causes of dopamine deficiency syndrome are intrinsic, treatment with levodopa can be successful. In the case of multifactorial etiology, the addictive behavior should be preferably managed by psychosocial strategies, while punding should be treated by continual stimulation of dopaminergic receptors to decrease hypersensitization (Wolters *et al*. 2008). In the majority of cases, a multi-disciplinary cooperation among the neurologist, psychiatrist and psychologist, as well as communication with patient's family, is required.

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