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Dopamine agonists and Othello's syndrome

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Abstract

Background—Othello's syndrome (OS) is a delusion of infidelity. We describe seven cases of OS in Parkinson's disease (iPD) patients using dopamine agonists.

Methods—We searched the Mayo Clinic Medical Records System to identify all patients with OS. Clinical data abstracted include sex, age of onset of iPD, age of onset of OS, medications, effect of discontinuing the dopamine agonist, neuroimaging, and comorbidities.

Results—Seven non-demented iPD patients with dopamine agonist implementation time locked to the development and resolution of OS are reported. The average age of iPD onset was 46.6 years (Standard deviation: 5.0 years), and OS onset was 53.7 years (7.1 years). All seven patients had significant marital conflict as a result of the delusions.

Conclusions—OS can be associated with dopamine agonist use and can lead to serious consequences. Dopamine agonist cessation eliminates the delusion of infidelity and should be the first treatment option.

Keywords

Dopamine; Othello's syndrome; Parkinson's disease; Delusion

Introduction

Dopamine agonists are commonly used in young idiopathic Parkinson's disease (iPD) patients. Well described adverse effects include hypersexuality and pathological gambling[1, 2]. We recently have recognized another, less well described side effect of dopamine therapy that results in significant marital distress and conflict, Othello's syndrome (OS), which is a delusion of infidelity. Most importantly, this adverse effect is reversible by reducing or eliminating the agonist.

While delusions are common in dementia patients, and this specific delusion has been reported in dementia patients, such as dementia with Lewy bodies[3], few reported cases of OS in young, none demented, iPD patients, exist in the literature[4–7]. In order to describe our clinical experience of such patients, we report detailed clinical features of seven such patients with iPD and OS that we have encountered. These seven patients are novel and interesting because they all had a clinical diagnosis of iPD from a senior movement disorders specialist, none were demented, all had the delusion time locked to treatment with

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a dopamine agonist, all had significant marital problems, and most importantly, all responded to a reduction or discontinuation of the agonist.

Methods

Subject Selection

Using text words “Othello” or “Delusions and Infidelity” or “Delusions of Jealousy” or “Infidelity” we searched the Mayo Clinic Medical Records System to identify all patients with possible OS who were evaluated at our institution after January 1st, 1998. The search was initiated after one of the co-authors (KAJ) evaluated a patient with OS and iPD time locked to the initiation of a dopamine agonist. An institutional review board approved the project. We identified seven patients with OS having received a diagnosis of iPD[8] without any features of dementia in this time period. None of the seven patients were diagnosed with Parkinson's disease dementia or dementia with Lewy bodies[9]. All seven patients were evaluated by movement disorders specialists. We abstracted clinical data from these cases including sex, age of onset of iPD, age at onset of OS, description of the delusions, concurrent medication usage, effect of discontinuing the dopamine agonist, neuroimaging, and comorbidities. A Clinical Dementia Rating Scale (CDR) sum of boxes scores (CDR-SB) with range 0–18 for each case was retrospectively determined at the time of OS onset.

Results

All seven patients had dopamine responsive iPD[7]. The demographics are described in table 1. Average age of iPD onset was 46.6(standard deviation 5.0) years. Othello's syndrome onset was 53.7 years (7.0). With the exception of the delusion of infidelity that caused strained marriages, all continued to perform their routine activities of daily living without any difficult. The CDR-SB scores ranged from 0–1. In all seven patients, OS onset was time locked to the initiation of the agonist and in all seven discontinuation or reduction of the agonist resulted in elimination or reduction of the delusion. In 5/7, the dopamine agonist was pramipexole with ropinirole being the agonist in the other two patients.

Illustrative Case

A 42 year old male with 3 years of left sided Parkinsonism was initiated on pramipexole 0.125 mg TID. His pramipexole was titrated up to 1.5mg TID. He also was taking carbidopa/levodopa 25/100mg 1.5 tablets TID. Soon after reaching the 1.5mg TID of pramipexole, he developed the compulsion to gamble losing $3000. The compulsive gambling was also associated with a strong sexual urge, and he was at times inappropriately fixated on sex with his wife out of proportion to his usual behavior. He also reports thinking that his wife was having an affair, and he was always waiting, expecting a car to be in his driveway to pick up his wife to go off to have sex. This was also out of character for him, because he knew that his wife had always been faithful to their relationship. He also exhibited features of pathological shopping, for example, he purchased two new fishing poles despite having five at home. After hearing the hypothesis that the gambling might be associated with pramipexole, the patient quit the medication abruptly. After quitting, he noted a dramatic decline of craving to gamble and the delusion of his wife's unfaithfulness also went away.

Discussion

These seven patients developed OS only after starting a dopamine agonist, either pramipexole or ropinirole. The delusion resolved or improved in all seven patients after the dopamine agonist was stopped or reduced. Levodopa was co-administered in 6/7 patients

which may have potentiated the delusion of infidelity, but it should be noted that with levodopa monotherapy no patient had OS. Therefore, the timing of the delusion with dopamine agonist administration, as well as the resolution while on levodopa alone implicates the dopamine agonist as the most likely causative agent.

Othello's syndrome in iPD has been described in 2 case reports and small case series[4–7]. Similar to our results, five of the six patients in this case series developed OS on dopamine agonists including ropinirole (n=1), pramipexole (n=2), pergolide (n=1), and levodopa plus pergolide and amantadine (n=1), respectively. The sixth patient developed OS with levodopa monotherapy. Interestingly, the iPD patients in both studies tended to be young and without associated dementia. Furthermore, similar to our patients OS was successfully treated with reduction or cessation of the dopamine agonist in addition to adding an antipsychotic. In contrast to the previous reported patients of OS in iPD which included only males, our study includes two females, suggesting that this delusion is not limited to men. An additional difference between our cases and theirs is that antipsychotics were used in each of their patients to treat the delusion[5] while in our patients, OS resolved in most patients without the addition of an antipsychotic.

In our study pramipexole and ropinirole were represented amongst the dopamine agonists. Pramipexole is a direct D3 agonist[9]. Ropinirole and pergolide, implicated in the previous case report also share D3 affinity albeit less than pramipexole[9]. The neuroanatomical correlate of OS has been hypothesized to be the right frontal lobe[11]. Black et al showed that D3 selective dopamine agonists caused decreased blood flow in the orbitofrontal gyrus of baboons bilaterally but greater on the right[12]. Perhaps, stimulation of the D3 receptors in the right frontal lobe causing decreased blood flow to the region acts similar to previously described lesions in the right frontal lobe causing in OS.

Although OS have been reported in patients with dementia, it is important to recognize that these seven patients were not demented. In fact, when the delusion abated, many patients admitted that the delusion of infidelity was unfounded. Therefore, unlike delusions occurring in the context of dementia, these seven patients had the delusion in the absence of any feature suggestive of dementia. In addition, the visual hallucinations, a feature of Parkinson's disease dementia and dementia with Lewy body[9], resolved after cessation of the agonist suggesting that the hallucinations were associated with agonist use, and not spontaneous, which is typical of Parkinson's disease dementia and dementia with Lewy bodies[9].

OS is another side effect of dopamine therapy and should be added to the list of side-effect associated with agonist use. Other side effects include impulse control disorders. As described in these cases above, it can have a profound effect on marital relationships. While hypersexuality and pathological gambling are better defined side effects of dopamine agonist therapy, we report this series of OS so that it can be screened for as well when patients are on dopamine therapy. Importantly, the delusion is often completely reversible with cessation of the agonist. While this is not meant to be a prevalence study of any sort, future studies are needed to determine its prevalence.

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Table 1

Demographics and Features of iPD Patients

	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6	Case 7
Sex	M	M	F	M	M	F	M
Age at onset of iPD symptoms	49	39	53	43	50	43	49
Age at onset of Othello's Syndrome	58	42	64	49	56	56	51
Medications and doses time-locked to the development of Othello's syndrome	Pramipexole 4.5mg/day	Pramipexole 4.5mg/ day Levodopa 450mg/day	Pramipexole 4mg/ day Levodopa 200mg/day	Ropinirole 15mg/ day Levodopa 600mg/day	Pramipexole 4.5mg/ day Levodopa 1500mg/day	Pramipexole (> 6mg/ day) Levodopa 600mg/ day Eldepryl 15 mg/day	Ropinirole 16mg/ day Levodopa 1600mg/day
Intervention	Stopped pramipexole	Stopped pramipexole	Stopped pramipexole	Stopped ropinirole	Stopped pramipexole	Decreased pramipexole	Stopped ropinirole
Clinical Dementia Rating Scale sum of boxes	0	1	0.5	0	0.5	1	0
Psychiatry history	None	None	Anxiety	Depression	None	Anxiety, narcissistic personality disorder	Anxiety
Pathological Gambling	No	Yes	No	No	Yes	No	No
Pathological Shopping	No	No	Yes	No	No	No	Yes
Hypersexuality	Yes	Yes	No	Yes	Yes	Yes	Yes
Neuroimaging	None	Normal (MRI)	Normal (CT)	Normal (MRI)	None	Old right basal ganglia infarct (MRI)	Normal (MRI) Diffuse decreased activity in frontal, less so temporal & parietal lobes and caudate bilaterally (FDG-PET)