

Pathological Gambling in a Patient on a Dopamine Agonist

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INTRODUCTION

Restless leg syndrome (RLS) is a common and disabling disorder with four essential criteria that establish the diagnosis: (1) an urge to move that is often associated with paresthesias, (2) onset or exacerbation of symptoms at rest, (3) symptom relief with movement, and (4) manifestation of symptoms in a circadian pattern.¹ Although the underlying mechanism is not understood, RLS symptoms are thought to occur in part due to abnormal signaling in dopaminergic and gamma aminobutyric acid (GABA) pathways, as both dopaminergic agents and gabapentinoid drugs have been proven to be effective in treating RLS.^{1,2} Dopamine agonists (DAs), such as pramipexole and ropinirole, are medications commonly prescribed to patients with Parkinson's disease (PD) and RLS for symptom control. In the past decade, the use of DAs has been frequently associated with impulse control disorders (ICDs) such as pathological gambling (PG), compulsive shopping, compulsive eating, hypersexuality, and punding, a term used to describe compulsive performance of repetitive, mechanical tasks.³

Pathological gambling is characterized by persistent and recurrent maladaptive gambling behavior. This is most common in patients with Parkinson's disease (PD), where the incidence of ICD is between 10–14% of patients taking a dopamine agonist.⁴ Patients with PD take much higher doses, in general, than those used in RLS. There are numerous case reports in the literature suggesting that DAs can cause ICDs, particularly PG in patients with RLS. d'Orsi et al. reported the case of a 71-year-old man who developed PG following 5 months of daily 0.18 mg pramipexole, a small yet unconventional dose.⁵ Symptoms of PG resolved after pramipexole was discontinued.⁵ Kolla et al. described two patients with RLS treated with pramipexole: one presented with depression and one presented following a suicide attempt, both in the context of compulsive gambling.⁶ In a survey of patients diagnosed with RLS using DAs, 6% of the respondents reported increased gambling and 4% reported increased sexual desire after beginning treatment.⁷ In another study, the frequency of PG was 5% and any ICD was 17% in RLS patients receiving treatment with DAs; these percentages were statistically significant compared with RLS patients not receiving dopaminergic treatment.⁸

Among patients with prolactinomas, treatment with DAs has also been associated with ICDs. A prospective study

of 25 patients with prolactinomas reported two new cases (8%) of ICD associated with DAs; both cases presented with hypersexuality which was reversed upon discontinuation of the drug.⁹ One case-control study found that males with prolactinomas treated with DAs were 9.9 times more likely to develop an ICD than those with nonfunctioning pituitary adenomas,³ and a cross-sectional study found that the prevalence of DA-induced ICDs among patients with prolactinomas was 17%.¹⁰

Herein we report a patient with RLS seen in a psychiatric setting who presented with suicidal ideation, depression, and PG.

CASE REPORT

A 47-year-old woman with a past medical history significant for gastric bypass, rheumatoid arthritis, latent tuberculosis, hypertension, gastroesophageal reflux disease, and RLS, and a psychiatric history of depression and PG presented to the Rhode Island Hospital Emergency Department (ED) after attempting to cut her wrists in a suicide attempt. Upon admittance the patient endorsed severely depressed mood, anhedonia, anergia, poor sleep, and poor appetite, and reported feeling hopeless and helpless, with "no way out other than suicide." Over the past several years the patient had experienced worsening depression as her pathological gambling depleted her family's financial resources, causing her to resort to borrowing and begging for money. The patient's gambling addiction eventually became severe enough to cause intense feelings of shame and embarrassment, and led to divorce from her husband. On several occasions the patient visited a therapist for pathological gambling but did not seek treatment for her depression. During this time period the patient was taking pramipexole prescribed by a neurologist for RLS. The patient reported that she had started taking high-dose pramipexole (2-3 mg BID) in 2014 and that the gambling behavior began during the same time period. The only significant family psychiatric history was depression in the patient's sister.

The patient saw gradual improvement throughout the course of her hospital stay as fluoxetine and gabapentin were prescribed and pramipexole discontinued. She reported improved mood and expressed greater hopefulness for the future, and was discharged after several days with plans

to follow up with an outpatient psychiatrist and gambling support resources. On follow-up two months after discharge, the patient reported full remission of symptoms. Though the patient initially desired to gamble following discharge, she was able to abstain. The patient resumed the relationship with her husband and began working full time. On follow-up 18 months after discharge, the patient reported that she has not engaged in any gambling activity, continues to work full time, remains psychiatrically stable, and has maintained good relationships with her husband and children. The patient discontinued fluoxetine and remained on gabapentin for RLS, which was eventually uptitrated to 600 mg TID. She reported that her current treatment regimen has unfortunately provided modest, if any, relief of RLS symptoms.

DISCUSSION

Until recently, DAs were considered the sole first-line treatment for RLS due to their acute efficacy.¹¹ When used for RLS, the typical DA doses are extremely low compared with those used in the treatment of PD, and, for pramipexole, range from 0.125 mg to 0.75 mg daily, whereas in PD doses usually range from 1.5 to 4.5 mg daily.² In our case, the patient had been prescribed a significantly higher dose of pramipexole than the maximum recommended dose for PD, which is 4.5 mg daily.¹²

The pathophysiology underlying DA-induced compulsive behaviors remains poorly understood. Although excess stimulation of the dopamine D3 receptor by DAs has been considered a possible mechanism, this theory fails to account for the wide array of compulsive behaviors patients may develop, which often includes gambling, hypersexuality, excessive spending, or consumerism, and does not explain why DAs with greater D3 agonism are seemingly no more likely to cause compulsive behaviors than agonists with predominant activity at other dopamine receptors.⁸ In addition, though various atypical antipsychotics have been implicated in the development of compulsive disorders,¹³ these medications have also been used in the treatment of compulsive symptoms,¹⁴ further obscuring the role of D3 receptors in the pathogenesis of these disorders. Although antipsychotics and SSRIs have been considered therapeutic options for the treatment of PG, their efficacy is limited,¹⁵ and dose reduction or discontinuation of DAs may be a more reliable strategy for the treatment of DA-induced compulsive behaviors.¹⁶ It is worth noting that, in addition to compulsive gambling behavior, patients with PG have been suggested to have possible associations with high impulsiveness, low disorderliness, and high exploratory excitability.¹⁷

Correlations exist between RLS and depressive symptoms; in one study, RLS subjects had a higher risk of developing anxiety and depressive disorders compared to controls,¹⁸ and RLS patients in another study reported significantly higher

rates of depressive symptoms versus controls.¹⁹ Despite our patient's lack of improvement in RLS symptoms, we believe that treatment with gabapentin was an appropriate clinical decision; in addition to its effects on RLS symptoms, gabapentin has been shown to target features of impulsivity, anxiety, and craving, which could potentially alleviate PG.²⁰ Similar to our case, cessation of dopaminergic treatment led to improvement or resolution of PG in most reported cases.⁵ In conclusion, our case adds to the growing literature of RLS patients developing PG following use of DAs. Further studies are needed to elucidate the exact mechanism of DAs in the development of compulsive disorders, and caregivers who prescribe DAs should closely monitor patients for serious adverse events such as PG.

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