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Restless Leg Syndrome Following Aripiprazole Discontinuation: A Case Report

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Abstract

Background: Aripiprazole is a second-generation antipsychotic known for its partial dopamine D2 agonist properties, which help reduce the risk of extrapyramidal symptoms. While effective and generally well-tolerated, withdrawal symptoms, such as Restless Legs Syndrome (RLS) and akathisia, have been observed upon abrupt discontinuation in some patients. **Objective:** To report a rare case of Restless Legs Syndrome (RLS) following the discontinuation of aripiprazole in a patient with a history of substance-induced psychosis. **Case Description:** A 39-year-old male with a history of polysubstance use in sustained remission, presented with RLS-like symptoms shortly after discontinuing aripiprazole, which he had taken consistently for the last 6 years. The symptoms, which included a pinching sensation in his thighs, involuntary leg movements during sleep, and a sense of restlessness, emerged within 2 - 3 days of medication cessation. These symptoms are resolved within an hour of reinitiating aripiprazole. The patient's clinical presentation underscores a rare but clinically significant withdrawal phenomenon associated with aripiprazole discontinuation, potentially linked to dopamine dysregulation. **Conclusions:** This case highlights the importance of recognizing and managing aripiprazole discontinuation symptoms, including RLS. Clinicians should consider a gradual tapering protocol for aripiprazole to minimize withdrawal-related movement disorders and monitor patients for emergent symptoms. Further research is recommended to establish standardized guidelines for managing similar cases.

Keywords

Aripiprazole Withdrawal, Restless Legs Syndrome, Akathisia,

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Dopamine Dysregulation

1. Introduction

Aripiprazole is a second-generation antipsychotic used in treating a wide range of psychiatric conditions, including schizophrenia and bipolar disorder. It is also approved by the FDA as an adjunctive treatment for major depressive disorder, for the treatment of irritability in autism, and Tourette's disorder in children aged 6 to 17 [1]. Aripiprazole, while acting as a partial agonist at dopamine D2 receptors, normalizes dopaminergic activity without carrying the high risks of extrapyramidal symptoms (EPS) and tardive dyskinesia associated with conventional antipsychotic drugs [1].

While generally well-tolerated, aripiprazole has been associated with several withdrawal symptoms following a reduction in dosage or complete withdrawal. These include Restless Legs Syndrome (RLS) and latent dyskinesia, both of which are thought to arise from abrupt interruption of dopamine receptor activity [2]. RLS is characterized by uncomfortable sensations within the legs, accompanied by an uncontrollable impulse to move the legs, especially during periods of rest [3]. Covert dyskinesia, another possible withdrawal effect, refers to involuntary movements that may persist if not properly managed [4].

The exact pathophysiology of RLS and dyskinesia following aripiprazole discontinuation is not fully understood, but it is likely linked to dopaminergic dysregulation [4] [5]. Aripiprazole's partial agonism helps maintain a delicate balance within the dopaminergic system. Sudden discontinuation can disrupt this balance, resulting in symptoms associated with dopamine deficiency or receptor sensitivity changes [4]. Such symptoms usually emerge from days to weeks after discontinuing the medication and present significant challenges in clinical practice.

Antipsychotic withdrawal requires careful management to prevent adverse effects. The Maudsley Prescribing Guidelines recommend gradual tapering of antipsychotics to minimize withdrawal symptoms and reduce the risk of rapid relapse [6]. Symptoms such as nausea, vomiting, loss of appetite, restlessness, increased sweating, and sleep disturbances are commonly observed during withdrawal [6]. While specific guidelines for aripiprazole withdrawal are limited, these general principles apply. This case study examines the emergence of RLS following abrupt discontinuation of aripiprazole, highlighting the need for tailored tapering strategies and further research into withdrawal effects associated with aripiprazole.

The present case report narrates the experience of a 39-year-old male with a history of polysubstance dependence who developed symptoms akin to RLS following aripiprazole discontinuation. His presentation provides valuable insights into the possible withdrawal effects of aripiprazole, highlighting the importance of recognizing and treating these symptoms appropriately.

2. Case Presentation

A 39-year-old married gentleman of an African Arab origin was receiving outpatient psychiatric care for polysubstance dependence, which had remained in sustained remission. He had been on aripiprazole since 2018 to manage substance-induced psychotic features and had successfully maintained abstinence from substances such as alprazolam, benzodiazepines, and cannabis for eight years.

His psychiatric stability was evident throughout this period, with consistent mental status examinations showing a well-groomed appearance, full orientation, stable mood, coherent thought processes, and intact judgment. While occasional financial constraints affected his clinic visits, he remained committed to his medication regimen, recognizing its role in maintaining his mental health. Regarding his medication history, the 5 mg daily dose of aripiprazole dosage was adjusted during the first few months to determine the optimal therapeutic level. Once stability was achieved, he remained on a steady 5 mg dose until the discontinuation attempt.

In an attempt to discontinue aripiprazole, a tapering trial was initiated. Within 2 - 3 days of stopping his 5 mg daily dose, he experienced progressively worsening withdrawal symptoms. The onset was rapid, with symptoms intensifying over the 2 - 3 days. He described a persistent pinching sensation in his right thigh and an uncomfortable crawling sensation in his legs and hips, coupled with an involuntary urge to move his legs. These sensations were most intense during rest and sleep, disrupting his ability to relax and contributing to heightened anxiety. The pinching sensation resembled intermittent sharp pressure in the lower limb region, akin to mild electrical shocks or deep tissue compression, while the crawling sensation was a creeping, tingling discomfort that moved across the legs and hips, intensifying at night both of which closely align with classic descriptions of RLS. The decision to reinitiate aripiprazole was made following counselling with the patient. Alternative treatment options were considered. However, given the rapid and distressing onset of symptoms, the patient opted to restart aripiprazole, which led to a rapid resolution of symptoms within hours.

3. Discussion

This case represents a rare but clinically significant development of RLS following the abrupt discontinuation of aripiprazole. While aripiprazole is greatly treasured for its benign side effect profile [7], there have been reports both of RLS and even other movement disorders following its withdrawal, pointing to the complex effects that dopamine modulation has on the central nervous system [8].

Aripiprazole's partial agonist activity at dopamine D2 receptors may contribute to a unique withdrawal profile compared to other antipsychotics. While common withdrawal symptoms across antipsychotics include nausea, vomiting, loss of appetite, restlessness, increased sweating, and sleep disturbances, aripiprazole withdrawal has been associated with specific symptoms such as RLS. This case suggests

the necessity for clinicians to monitor for such atypical withdrawal symptoms when discontinuing aripiprazole [8].

3.1. Comparison with Literature

Similarly, Dokuz *et al.* (2022) present a case wherein, following the discontinuation of aripiprazole, a patient developed RLS [5]. In both cases, the onset of symptoms was within days of discontinuation, and they resolved upon re-institution of the medication, suggesting a possible causative role of aripiprazole discontinuation for symptoms appearing in RLS. These observations are, however, further extended by the current case through the inclusion of akathisia-like motor symptoms, adding to the clinical complexity of the aripiprazole withdrawal phenomena.

Currently, there is limited literature specifically addressing aripiprazole withdrawal symptoms like RLS. The absence of extensive clinical trials highlights the need for further research to better understand the withdrawal effects associated with aripiprazole and to develop comprehensive guidelines for its discontinuation.

3.2. Pathophysiological Mechanism

The pathophysiology of the exact occurrence of RLS post-withdrawal of aripiprazole is not fully comprehended but presumably involves dysregulation of dopamine. Aripiprazole, as a partial agonist at the dopamine D2 receptors, does have an overall stabilizing effect on dopaminergic transmission [9]. Discontinuation may disrupt this further, leading to symptoms associated with dopamine deficiency, such as RLS and dyskinetic movements. Furthermore, antagonism in serotonin 5-HT2A receptors and partial agonism in 5-HT1A receptors by aripiprazole may promote symptoms of withdrawal through changes in the serotonin-dopamine interaction that is integral to the regulation of movement [10].

3.3. Clinical Implications

These findings of RLS symptoms following discontinuation with aripiprazole would support the idea that tapering the dosage gradually is important to minimize such withdrawal-type effects. These complications may alert clinicians to the possible onset of various withdrawal-induced movement disorders and inform patients about symptoms they might experience with abrupt discontinuation. If withdrawal symptoms develop, reinstitution of aripiprazole as soon as possible or supportive pharmacotherapy, including the addition of propranolol, is an option for symptom management.

3.4. Limitations and Future Directions

Although this case gives valuable insights, it is a case report; thus, the generalization of results is limited. Further studies are warranted to establish the prevalence and mechanisms of movement disorders due to aripiprazole withdrawal. Prospec-

tive studies would establish guidelines with evidence-based practice on how aripiprazole can be withdrawn safely, probably with other medications during tapering to prevent withdrawal symptoms.

4. Conclusion

This case underscores the potential for RLS to develop as withdrawal symptoms following the discontinuation of aripiprazole, particularly in patients with a long-standing treatment history. The swift resolution of symptoms upon reintroduction of aripiprazole suggests a strong link between abrupt dopamine modulation and these movement disorders. Clinicians should be vigilant about withdrawal symptoms when tapering aripiprazole and consider gradual dose reduction to mitigate these risks. Future research is needed to better understand the mechanisms behind aripiprazole withdrawal-induced movement disorders and to establish evidence-based protocols for safely discontinuing treatment in clinical practice.

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Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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