Case Report

Diagnostic & Management Dilemma in Atropine induced Psychosis with Restless Leg Syndrome – A Case Report

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ABSTRACT:

Anticholinergic medications are commonly used yet frequently overlooked as potential causes of isolated neuropsychiatric symptoms. While acute atropine toxicity produces a characteristic peripheral and central anticholinergic toxidrome, chronic low-dose exposure may manifest exclusively with psychotic symptoms. We present a case of a 48-year-old male who developed persistent auditory hallucinations and delusional beliefs following prolonged use of diphenoxylate–atropine. Symptoms resolved rapidly after discontinuation of the medication and initiation of pregabalin for co-existing Restless Leg Syndrome (RLS). This case highlights the importance of considering anticholinergic-induced psychosis in patients presenting with new-onset hallucinations and emphasizes the need for careful review of chronic anticholinergic use before initiating antipsychotic therapy.

KEY WORDS: Anticholinergic Psychosis, Atropine, Restless Leg Syndrome, Substance-Induced Psychosis, Diphenoxylate–Atropine

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INTRODUCTION:

Anticholinergic toxicity classically presents with a constellation of cognitive, autonomic, and neuromuscular features summarized by the mnemonic "mad as a hatter, blind as a bat, red as a beet, dry as a bone, hot as a hare".[1] While these symptoms are well documented in acute overdose, prolonged low-dose exposure may result primarily in central effects such as hallucinations, agitation, delusions, and confusion, often without typical peripheral signs.[2-4]

Atropine-induced psychosis remains under-recognized and may mimic primary psychiatric disorders, delaying accurate diagnosis and leading to unnecessary antipsychotic treatment. Additionally, misuse of anticholinergic-containing medications has been increasingly reported in individuals with substance dependence or chronic uncomfortable sensory states such as Restless Leg Syndrome (RLS).[5] This case highlights a rare presentation of chronic atropine-associated psychosis with co-existing RLS.

CASE REPORT:

A 48-year-old male presented with a six-month history of auditory hallucinations, predominantly hearing a female voice at night, which he misattributed to his wife. This progressed to a fixed delusion of infidelity, causing interpersonal distress. There were no features of delirium, confusion, or fluctuating sensorium.

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Past History and Medication Use:

He had a previous history of opioid use disorder (2014–2018), currently abstinent. Since 2019, he had been self-administering diphenoxylate–atropine (Lomotil), starting at ~10 tablets/day and tapering to 4 tablets/day over the past several years. He reported taking it for relief of uncomfortable sensations in the legs consistent with Restless Leg Syndrome, which worsened when the medication was withheld.

Mental Status Examination:

- Auditory hallucinations (third-person running commentary)
- Delusion of infidelity
- No visual hallucinations
- No autonomic features of anticholinergic syndrome
- No cognitive impairment or disorientation

DIAGNOSIS:

Based on symptom chronology and medication history, he was diagnosed with Substance/ Medication-Induced Psychotic Disorder, likely attributable to chronic anticholinergic exposure.

MANAGEMENT:

Diphenoxylate–atropine was discontinued immediately. He was started on pregabalin 75 mg at bedtime for RLS.

OUTCOME:

Within seven days, there was:

- Complete resolution of hallucinations
- Significant reduction in delusional beliefs
- Marked improvement in RLS symptoms without recurrence

He remained stable on follow-up, without requiring antipsychotic medication.

DISCUSSION

Anticholinergic psychosis is mediated primarily through central muscarinic receptor blockade, disrupting cholinergic–dopaminergic balance in the cortex and limbic structures.[6,7] While acute atropine intoxication is well described, there is growing recognition that chronic exposure to low doses of anticholinergic agents-including atropine, trihexyphenidyl, and diphenoxylate—may produce primarily psychiatric symptoms such as hallucinations, agitation, affective instability, or delusions.[8–10]

In this case, the patient presented with pure psychotic symptoms without typical anticholinergic signs such as mydriasis, tachycardia, hyperthermia, urinary retention, or dry mucous membranes. Similar cases of isolated atropine-induced psychosis have been documented in the literature.[11–12]

Relationship with Restless Leg Syndrome (RLS):

Although diphenoxylate–atropine is not an established therapy for RLS, patients may self-medicate due to sedative or anxiolytic effects. RLS is associated with dopaminergic dysfunction, and anticholinergic medications may transiently modulate sensory symptoms, explaining the patient's perceived benefit.[13]

Effective treatment of RLS with pregabalin is consistent with evidence showing benefit of alpha-2-delta ligands in sensorimotor symptoms.[14]

Clinical Importance:

This case demonstrates several key points:

1. Chronic anticholinergic use can cause isolated psychosis in the absence of classic toxidrome.
2. Stopping the offending agent is often sufficient, preventing unnecessary exposure to antipsychotics.
3. Anticholinergic medications frequently used in psychiatry (e.g., trihexyphenidyl) may worsen psychosis and should be monitored closely.[15]
4. Detailed medication history remains essential in evaluating first-episode psychosis.

CONCLUSION:

Chronic use of anticholinergic medications such as diphenoxylate–atropine can lead to isolated psychosis without peripheral toxicity. Clinicians must maintain a high index of suspicion for medication-induced psychosis, particularly in individuals with prolonged exposure. Prompt discontinuation and targeted treatment of underlying symptoms such as RLS can result in rapid and complete recovery.

DECLARATION OF PATIENT CONSENT:

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s)/guardian has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients/guardian understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of Interest
There are no conflicts of interest.

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