Original Article

Generalized Dystonia Following Imipramine Use in a Male Undergraduate: A Rare Phenomenon

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Article History
Submitted: 11/01/2025; Accepted: 16/01/2025: Published: 02/02/2025

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ABSTRACT

Imipramine, a tricyclic antidepressant, is commonly used for managing nocturnal enuresis in paediatric and adolescent populations. Although it is generally well-tolerated, rare adverse effects, including movement disorders, have occasionally been reported. Generalized dystonia, however, is an exceedingly rare and unexpected complication associated with imipramine.

Keywords: Drug-induced movement disorders, Generalized dystonia, Imipramine, Rare adverse effects.

INTRODUCTION

Imipramine, a tricyclic antidepressant (TCA), has been a mainstay of pharmacological management of nocturnal enuresis for decades.[1] It acts by reducing bladder capacity and altering sleep architecture thereby providing effective symptomatic relief in many paediatric and adolescent patients.[2] Despite its established efficacy, its use is associated with drawbacks which include anticholinergic symptoms such as dry mouth, constipation, and urinary retention, as well as cardiovascular effects like orthostatic hypotension and arrhythmias.[3] Less frequently, neurological side effects, including seizures, agitation, or tremors, may occur. However, the emergence of movement disorders, particularly generalized dystonia, is highly atypical and underreported.[4]

Dystonia comprises a spectrum of movement disorders characterized by involuntary, sustained muscle contractions that cause abnormal postures or repetitive movements.[5] Dystonia is generalized when it involves multiple body regions. Its burden is huge in terms of significant impairment in the quality of life and functional independence. Drug-induced dystonia is commonly linked to dopamine-blocking agents such as antipsychotics, but cases attributed to TCAs remain exceedingly rare in the medical literature.[6] This report aims to raise awareness about this rare adverse effect, highlighting the need for early recognition and prompt intervention to prevent long-term sequelae. Furthermore, it underscores the importance of exercising caution when prescribing TCAs, particularly in young populations, where the risk-benefit ratio must be carefully considered.[7]

CASE REPORT

We present the case of a 19-year-old male undergraduate who was prescribed imipramine at a dose of 25 mg nightly for persistent nocturnal enuresis. Initially, the patient experienced symptomatic relief with no apparent worrisome adverse effects. However, about three months into his treatment therapy, he gradually developed

Article Access
Website: www.wjmbs.org
10.5281/zenodo.14816517

How to cite this article
*Nwazor E, Okeafor C, Ogbeh F. Generalized Dystonia Following Imipramine Use in a Male Undergraduate: A Rare Phenomenon. West J Med & Biomed Sci. 2025;6(1):1-3. DOI:10.5281/zenodo.14816517.

persistent generalized involuntary movements mostly affecting his face, neck, trunk and limbs, resulting in abnormal posturing and functional impairment. His symptoms were mostly provoked by physical activities especially sports. His dexterity was also impaired, affecting his writing as well as other fine movements. However, he was mostly relieved at night and sometimes, at rest. He found it difficult suppressing his abnormal movements and this would often cause him a lot of emotional distress. He is the only male and last of four children of parents in a monogamous family. He neither took alcohol or smoked cigarette. There was no history suggestive of substance abuse. He is a second-year economic undergraduate of a private university in Nigeria. Neither his parents nor siblings have movement disorders.

On examination, his skeletal muscles were intermittently contracting at rest and worse on the craniocervical region resulting in lateral head tilt. Other additional features that were demonstrated in the patient were sensory trick (*geste antagoniste*), mirroring and overflow phenomenon. However, his cranial nerves, pyramidal and sensory systems were all intact. His clinical features were in keeping with generalized dystonia.

Results of basic laboratory workup, including complete blood count, serum electrolytes, urea and creatinine, were essentially normal. His brain imaging study (MRI) did not show any structural abnormality to explain his symptoms. Dystonia genetic panels were not carried out due to their unavailability in Nigeria. The offending drug, imipramine was discontinued which resulted in partial symptomatic improvement, and he was subsequently treated with a combination of oral trihexyphenidyl (Artane), clonazepam (Rivotril) and baclofen. His symptoms have remarkedly improved over time but have not completely resolved after three months of follow up. He is still being followed up as an outpatient.

DISCUSSION

A review of the literature revealed that imipramine-induced dystonia is rare, and the underlying mechanism remains poorly understood. To the best of our knowledge, our patient might just be the first case of imipramine induced dystonia to be reported in Nigeria. More common movement disorders associated with imipramine include tremors, muscle stiffness, and other involuntary movements. The rate at which these conditions occur varies across different populations and may also be dependent on several patient factors such as age and comorbid medical conditions, to produce these adverse effects. Our patient was a teenager with absent family of movement disorders and was exposed to imipramine for about three months. It is not certain why he came down with a movement disorder, but there could be an underlying genetic predisposition.

Tricyclic antidepressants (TCAs), including imipramine, primarily act by inhibiting the reuptake of norepinephrine and serotonin, which leads to sustained neurotransmitter levels in the synaptic cleft.[8] Although this mechanism underlies their therapeutic effects, it may also contribute to dysregulation in motor control pathways, particularly in susceptible individuals.

Generalized dystonia is more frequently linked to medications that affect dopamine pathways, such as antipsychotics or antiemetics.[5] However, the pathophysiology of TCA-induced dystonia may involve secondary effects on dopamine signaling, possibly through serotonergic modulation of the basal ganglia circuits.[6] This hypothesis is supported by experimental studies demonstrating serotonergic influence on motor control, although direct evidence in humans is limited. There is also evidence that imipramine works by blocking the reuptake of serotonin (5-HT) and norepinephrine.[8] The clinical benefit that derives from this biological mechanism is the basis for their use in the treatment of mood disorders.[9]

Another potential contributing factor is genetic predisposition. Subclinical genetic susceptibilities, such as polymorphisms in dopamine receptor or transporter genes, need to be considered.[4] So, further studies are required to clarify whether specific genetic or metabolic profiles increase susceptibility to drug-induced dystonia.

Management of drug-induced dystonia is anchored

on early recognition of symptoms and withdrawal of the offending agent. In this case, the discontinuation of imipramine led to partial resolution of symptoms. Adjunctive therapies, including anticholinergics and benzodiazepines, proved effective in alleviating the patient's dystonic symptoms. This aligns with established treatment protocols for dystonia, which often emphasize the importance of targeting underlying neurotransmitter imbalances[7]

Although our patient still experiences intermittent mild dystonic posturing, he has made a remarkable clinical progress on conservative care and we hope he might be completely symptom free over time. However, in the meantime, we have continued to follow him up to see the end point of his treatment.

This case underscores the necessity of heightened clinical vigilance when prescribing imipramine, particularly in populations with limited safety data, such as adolescents and young adults. Clinicians should maintain a high index of suspicion for rare but severe adverse effects, including movement disorders, and educate patients and their families about potential warning signs. Future research should aim to identify predisposing factors and establish clear guidelines for monitoring and managing TCA-related complications.

CONCLUSION

This case highlights a rare and potentially debilitating adverse effect of imipramine. While dystonia is more commonly associated with antipsychotics or dopamine-modulating drugs, this report underscores the importance of considering tricyclic antidepressants in the differential diagnosis of drug-induced movement disorders. Early recognition and discontinuation of the offending agent are crucial for mitigating symptoms and preventing long-term complications. Clinicians should remain vigilant for rare adverse effects such as dystonia when prescribing imipramine, even in young and otherwise healthy patients.

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