Int. J. Pharm. Investigation, 2024; 14(3):980-982.
https://www.jpionline.org

Case Report

Chlorpromazine-Induced Parkinsonism: A Case Report

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ABSTRACT

Background: The side effect of Parkinsonism due to chlorpromazine emerged three years after its approval for public use, leading to the understanding that conventional anti-psychotics could induce various Extrapyramidal Symptoms (EPS). Drug-Induced Parkinsonism (DIP) generally surfaces within days to weeks, but rare instances present delayed onset. **Case Presentation:** We present a case involving a 28-year-old male exhibiting drug-induced Parkinsonism triggered by a chlorpromazine-based regimen, three months following its initiation. Subsequent symptom relief was observed post-discontinuation.

Keywords: Antipsychotics, Parkinsonism, Drug-induced Parkinsonism, Chlorpromazine, Movement disorders, Extrapyramidal symptoms.

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Received: 04-12-2023;
Revised: 11-01-2024;
Accepted: 28-02-2024.

INTRODUCTION

Idiopathic Parkinson's Disease (IPD) stands out as the most commonly encountered subtype of parkinsonism, occurring at a rate of approximately 14.2 per 100,000 person-years.[1] Following IPD, Drug-Induced Parkinsonism (DIP) emerges as the second most prevalent cause of parkinsonism.[2] Drug-Induced Parkinsonism (DIP) is a type of drug-induced movement disorder and is primarily induced by pharmaceutical agents that affect the dopamine receptors in the brain.[3] In the 1950s, DIP was first diagnosed as a common complication of neuroleptic therapy.[4] The occurrence of parkinsonism as a side effect of chlorpromazine was initially reported three years following its introduction. However, it was quickly acknowledged that all conventional antipsychotics possessed the capability to induce Extrapyramidal Symptoms (EPS), such as acute dystonia, parkinsonism, akathisia, and Tardive Dyskinesia (TD).[5] DIP is often misdiagnosed as Parkinson's disease (PD) as the clinical manifestations of both of these diseases appear to overlap. Albeit, recovery could be attained by discontinuation of the causative agent, there are numerous instances where patients are unnecessarily prescribed antiparkinsonian medications for prolonged durations.[6] Antipsychotic-Induced Parkinsonism (AIP) typically manifests within days to weeks after initiating antipsychotic treatment. However, in rare instances, the onset delay can extend to several months or even longer.[7] In this instance, a case involving a 28-year-old male patient elucidates the patient's manifestation of DIP following the initiation of a chlorpromazine-based regimen. It outlines the temporal association between the initiation of chlorpromazine treatment and the onset of EPS, followed by substantial alleviation of symptoms after the discontinuation of the drug.

CASE PRESENTATION

A 28-year-old man presented to the emergency department of our hospital with complaints of reduced sleep and appetite, generalised weakness, and acute movement disturbances which included neck and jaw stiffness, the inability to walk, and rigidity of the lower and upper limbs and tremors. The patient's medical record revealed a history of chronic hallucinatory psychosis for 2 years, managed with a fixed-dose medication consisting of Trifluoperazine (2.5 mg) and Trihexyphenidyl (1 mg) Once Daily (OD). This treatment regimen was subsequently modified three months ago at a local private clinic, altering it to Chlorpromazine 50 mg OD and Trihexyphenidyl 2 mg Three times a Day (TID) due to reported symptoms of irritability, auditory hallucinations, and self-conversations. Following this timeline, three months later, the patient experienced acute movement disturbances.

Upon examination, the patient presented with the following vital signs: a Glasgow Coma Scale score of E4V1M2, a pulse rate of 108 beats per minute, blood pressure measuring 110/80 mmHg, oxygen saturation (Spo2) at 97% on room air, and a respiratory rate of 16 cycles per minute. Evaluation of the cardiovascular, abdominal, and respiratory systems did not reveal any abnormalities. Extra Ocular Muscle (EOM) function in both eyes was observed as normal, with equal and responsive pupils to light stimulation. The neurological examination indicated bilateral cogwheel rigidity notably more pronounced in the left upper

DOI: 10.5530/ijpi.14.3.107

limb than the right, heightened muscle tone in the lower limbs, reduced arm swing, resting tremors, and bradykinesia, along with signs of neck and jaw stiffness (Figure 1).

Patient experiencing jaw stiffness due to drug-induced parkinsonism, leading to the inability to close the mouth.

Laboratory evaluations including a Complete Blood Count (CBC), renal function test, liver function test, and thyroid test displayed results within normal ranges. Biochemistry reports revealed that the patient had elevated C-reactive protein levels (CRP: 28.6 mg/L). The Computed Tomography (CT) scan revealed no significant abnormalities. The Electrocardiogram (ECG) displayed a normal sinus rhythm. No organisms were isolated during microbiology tests. Cerebrospinal Fluid (CSF) analysis returned normal. A provisional diagnosis of DIP was given considering the patient's history, and clinical and laboratory data.

The medications trihexyphenidyl and chlorpromazine were discontinued. A nasogastric tube was inserted and the patient was administered a drug combination of levodopa 100 mg, carbidopa 10 mg twice a day, along with intramuscular injections of haloperidol 5 mg BD. The patient displayed signs of improvement by the 6th day, the patient was able to move his neck and jaw and gradual alleviation of resting tremors and rigidity in his limbs was noted. Following 10 days of treatment, the patient was discharged with a prescription of quetiapine 300 mg OD. During the follow-up after 15 days, the patient remained stable with an absence of Extrapyramidal Symptoms (EPS).

DISCUSSION

DIP is characterised by the development of Parkinsonian symptoms in individuals receiving medications that interfere with dopamine function. Crucially, there should be an absence of a documented history of Parkinsonism before the initiation of the specific causative drug.[8] In the presented case, the patient experienced a sudden onset of Parkinsonian symptoms after the addition of chlorpromazine to the treatment regimen, This condition had not been observed in the patient's medical history during previous medication use.

All typical antipsychotic medications have the propensity to induce EPS. Typical antipsychotics such as chlorpromazine, promazine, haloperidol, perphenazine, fluphenazine, and pimozide are among those associated with this symptoms.[9] Approximately 80% of patients consuming typical antipsychotic drugs showcase multiple types of EPS.[10] It was initially believed that atypical antipsychotics like clozapine, risperidone, olanzapine, quetiapine, and aripiprazole presented a lower risk of causing EPS. Initially, the presumed lower occurrence of associated EPS with atypical antipsychotics was attributed to their stronger antagonism toward serotonin-2A receptors compared to dopamine receptors.[11] The recent 'fast-off' theory posited that the lower risk of EPS associated with atypical antipsychotics might be explained by their rapid dissociation from D2 receptors after blocking them.[12]

Based on existing data, the efficacy of haloperidol and chlorpromazine appears comparable. However, haloperidol may present as a preferable option due to potentially lower side effects and improved tolerability.[13] In the specific clinical scenario, the patient was managed with haloperidol in the hospital and was discharged with a prescription for quetiapine.

DIP is typically managed by discontinuing the causative medications. For patients unable to cease antipsychotic drugs due to ongoing psychiatric conditions like schizophrenia or major depressive disorders, transitioning to atypical antipsychotics with a diminished risk of EPS is considered. Individuals prescribed dopamine antagonists for mild gastrointestinal disturbances, headache, dizziness, or insomnia should discontinue the causative drugs promptly. Pharmacological intervention includes the administration of levodopa and/or amantadine. Anticholinergics such as benztropine and trihexyphenidyl are also included.

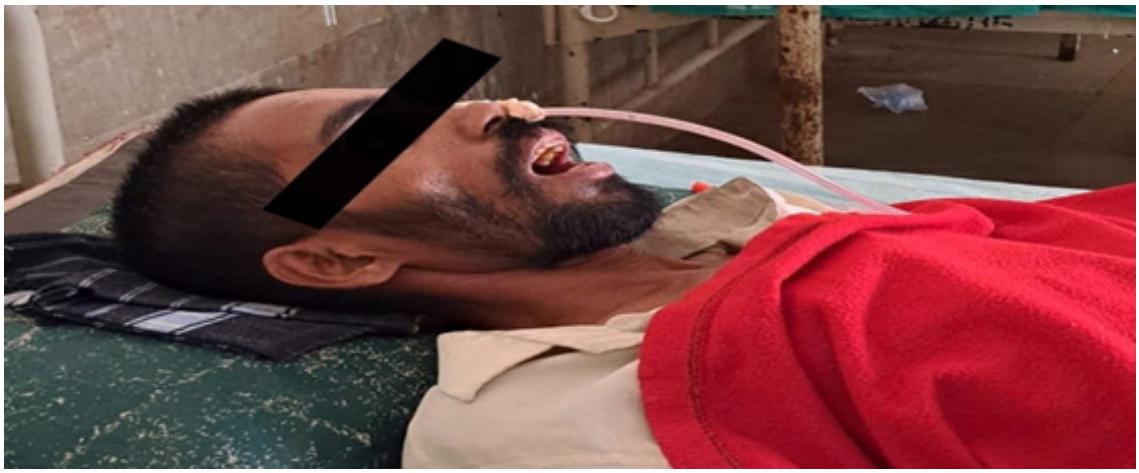

Figure 1: Patient experiencing jaw stiffness due to drug-induced parkinsonism, leading to the inability to close the mouth.

These drugs can alleviate the symptoms of DIP, typically within weeks to months following the discontinuation of the causative medication.[3,14]

This case report highlights the patient's development of DIP upon the initiation of a chlorpromazine-based regimen. The temporal association between the commencement of chlorpromazine treatment and the onset of EPS was determined using the Naranjo scale. Upon assessment, a score of 7 was obtained, indicating DIP as a "probable" adverse reaction attributed to the administration of an antipsychotic medication (chlorpromazine).

CONCLUSION

From the provided case report, it can be deduced that Chlorpromazine may contribute to the emergence of Extrapyramidal Symptoms (EPS), notably Drug-Induced Parkinsonism (DIP) in patients. Thorough clinical assessment and vigilant observation assist the attending clinician in diagnosing and managing the patient. Early prevention or timely identification and treatment of EPS can significantly enhance patient compliance, thus positively impacting the overall prognosis. This case highlights the importance of thorough clinical assessment and medication history to identify potential drug-induced adverse effects. The prompt withdrawal of chlorpromazine and initiation of alternative therapies, like levodopa-carbidopa, was crucial in improving the patient's symptoms. Hence, balancing symptom control while minimizing adverse effects was key to optimizing patient care and management outcomes.

ACKNOWLEDGEMENT

The authors would like to thank the invaluable contributions of Dr. Bharati Kangrali (MBBS, MD, General Medicine) in the thorough clinical assessment and clerking of the case presented in this case report.

ETHICS STATEMENT

A single case report is exempt from ethical approval in our institution. Written informed consent was obtained from the patient for the publication of this report and the accompanying images.

AUTHORS' CONTRIBUTION

All authors contributed equally to conceptualising the study and conducting the literature review, and they collaborated in writing and revising the manuscript. All the authors have read and approved the final version of the manuscript and agreed to be accountable for all aspects of the work.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

ABBREVIATIONS

AIP: Antipsychotic-induced Parkinsonism; **DIP:** Drug-induced Parkinsonism; **EOM:** Extra Ocular Muscle; **EPS:** Extrapyramidal symptoms; **IPD:** Idiopathic Parkinson's disease; **TD:** Tardive dyskinesia.

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Cite this article: Hegde M, Raj S, Tikadar D, Nyamagoud SB, Nawab S, Padgutti M, *et al*. Chlorpromazine-Induced Parkinsonism: A Case Report. Int. J. Pharm. Investigation. 2024;14(3):980-2.