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Case Study

Chlorpromazine-Induced Neurological Symptoms Mimicking Stroke in an Elderly Patient with Intractable Hiccups: A Case Report

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ABSTRACT

Background: Chlorpromazine, a widely utilized antipsychotic medication, has been recognized for its efficacy in treating intractable hiccups through its antagonistic action on histamine H1, dopamine D2, and muscarinic M1 receptors. Despite its therapeutic benefits, there is a spectrum of potential side effects, including neurological symptoms such as drug-induced stuttering, which poses diagnostic challenges and may lead to unnecessary investigations.

Objective: This case study aims to explore the paradoxical effect of chlorpromazine, which, while effectively treating an 80-year-old male patient's intractable hiccups, induced slurred speech and drowsiness, symptoms that resolved upon cessation of the drug.

Methods: A comprehensive evaluation was conducted, involving the patient's clinical presentation, treatment regimen, and the temporal relationship between medication administration and symptom onset. Investigations included a complete blood count, C-reactive protein, liver function tests, COVID-19 antigen test, cardiac workup, and brain MRI. Treatment response and side effects were meticulously documented, with follow-up to assess the resolution of symptoms.

Results: Following the administration of chlorpromazine (50mg orally), the patient's hiccups ceased, but he subsequently developed slurred speech and drowsiness. These symptoms were not present upon initial examination and resolved completely following the discontinuation of chlorpromazine. The brain MRI conducted to explore potential neurological causes was found to be insignificant, reinforcing the diagnosis of drug-induced neurological symptoms.

Conclusion: While chlorpromazine remains a valuable treatment for intractable hiccups, healthcare providers must be vigilant about its potential to induce neurological symptoms. This case highlights the importance of recognizing drug-induced side effects to avoid unnecessary diagnostic procedures and emphasizes the need for ongoing research into the mechanisms underlying such adverse reactions.

Keywords: Chlorpromazine, Intractable Hiccups, Drug-Induced Neurological Symptoms, Antipsychotic Medications, Drug-Induced Stuttering, Pharmacotherapy.

INTRODUCTION

Stuttering, characterized by interruptions in the smooth flow of speech, such as repetitive sounds, syllables, or words, prolongation of sounds, and involuntary silent pauses where the speaker is unable to produce sound, significantly affects an individual's ability to communicate effectively. These speech disruptions may be accompanied by physical manifestations of tension or struggle in the face, neck, or upper torso. The prevalence of stuttering in the general population is reported to be about 1%, with a lifetime incidence rate between 3 and 4% (1-3). The disorder exhibits a gender bias, occurring 3 to 4 times more frequently in males than in females (4). Although a universally accepted classification for stuttering is lacking, one subgroup that can be easily identified consists of individuals who start to show speech disfluencies in adulthood, termed acquired stutterers (5). This category is further divided into psychogenic and neurogenic stuttering, with the latter associated with various etiologies such as traumatic brain injury (TBI), stroke, neurodegenerative diseases like Parkinson's disease (PD) and multiple sclerosis, epilepsy, and the use of certain medications.

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The complexity of stuttering's etiology is highlighted by numerous theories aiming to explain its onset. Among the earliest neurophysiological models proposed is the theory of cerebral dominance, which posits that stuttering results from abnormal lateralization of speech in the brain. This theory suggests that speech is represented in both hemispheres of the brain, disrupting speech fluidity (6). This disruption is thought to interfere with the timing and synchronization of movements in speech muscles, thereby affecting speech production. The dopamine hypothesis is another significant theory, suggesting that stuttering may be linked to an abnormal increase in dopaminergic activity in the brain. This hypothesis is supported by evidence showing that substances like levodopa, which increase dopaminergic activity, can exacerbate stuttering symptoms (7, 13). Drug-induced stuttering is a form of acquired stuttering, with certain medications, including benzodiazepine derivatives such as Tranxene and Librium, and tricyclic antidepressants, reported to adversely affect brain function and speech behaviour (9-11). Tricyclics, even at therapeutic doses, have been observed to induce dysarthria, which resembles stuttering.

Moreover, a systemic review identified 82 instances where 27 drugs contributed to 86 episodes of stuttering, with the majority (57%) associated with antipsychotic medications, primarily clozapine, followed by central nervous system medications (11.6%) and anticonvulsants (9.3%). Most of these cases involved males aged between 31 and 40 years (14). The side effects of these medications, including extrapyramidal symptoms (EPS), can significantly impact daily life by causing movement, communication, and cognitive issues (19). Despite the known side effects, chlorpromazine remains a widely used medication, particularly beneficial in treating mental illnesses by improving symptoms and overall quality of life. However, its usage comes with potential side effects such as drowsiness, dizziness, dry mouth, constipation, blurred vision, and tardive dyskinesia, a movement disorder characterized by involuntary movements (15). The ongoing research into the efficacy and potential side effects of chlorpromazine highlights its importance in the treatment of mental disorders. It is crucial to carefully consider the benefits and risks of chlorpromazine treatment, in consultation with a healthcare professional, to determine the most appropriate course of therapy for specific conditions.

MATERIAL AND METHODS

The case study follows a retrospective analysis of the clinical presentation, treatment, and outcomes of an 80-year-old male patient with a medical history significant for hypertension and diabetes, who presented to the emergency department (ED) with persistent hiccups, sore throat, and itching. The patient's medical regimen included amlodipine (5mg daily) and metformin (500mg twice daily) for the past ten years. Upon presentation, vital signs were recorded, and a comprehensive physical examination was conducted to assess the patient's overall condition and identify any immediate concerns (14).

Baseline investigations were initiated to explore the underlying cause of the hiccups and associated symptoms, including a complete blood count (CBC), C-reactive protein (CRP), liver function tests (LFTs), and a COVID-19 antigen test. Given the patient's age and symptoms, a cardiac workup was also performed, comprising troponin I levels, electrocardiogram (ECG), and chest X-ray, to rule out any cardiac-related events. The treatment regimen consisted of intravenous Omeprazole (40mg), injection Metoclopramide (10mg), and oral Chlorpromazine (50mg) (18, 19).

Following the onset of additional symptoms, namely slurred speech and drowsiness, the patient and his family were counselled regarding the potential side effects of the administered medications. Due to the family's concerns for an underlying neurological cause, a brain MRI was performed, which yielded insignificant findings. The patient was observed in the ED for two hours before being discharged with instructions for follow-up. The patient's condition, including the resolution of symptoms, was evaluated during a follow-up visit the subsequent day.

Data collection for this case study was performed through a review of the patient's medical records, including clinical notes, laboratory results, imaging studies, and follow-up findings. This case study aims to contribute to the existing literature on the management and differential diagnosis of persistent hiccups in elderly patients, emphasizing the importance of considering medication side effects in the clinical assessment.

RESULTS

An 80-year-old male was admitted to the emergency department (ED) with complaints of persistent hiccups lasting five days, accompanied by a sore throat and itching. The patient, with a medical history of hypertension and diabetes managed with amlodipine (5mg daily) and metformin (500mg twice daily) for the past ten years, expressed significant anxiety and exhaustion due to the continuous use of accessory muscles for hiccupping. Upon presentation, his vital signs were stable, with a heart rate of 85 beats per minute, blood pressure at 150/80 mmHg, and an oxygen saturation of 96% on room air. His random blood sugar level was 150 mg/dl. The patient was fully oriented, with a Glasgow Coma Scale (GCS) score of 15/15. A primary survey revealed an intact airway, symmetrical chest rise without any visible deformity or neurological deficits.

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The systemic examination showed no signs of jaundice, anemia, or visible pulsations, although the patient's throat appeared hyperemic. Auscultation of the chest revealed no abnormalities, and the abdomen was soft and non-tender. Neurologically, muscle power and sensation in all limbs were preserved. Given the patient's symptoms and examination findings, a working diagnosis of pharyngitis or viral infection was considered. Baseline investigations including a complete blood count, C-reactive protein, liver function tests, COVID-19 antigen test, along with cardiac workup comprising troponin I levels, electrocardiogram (ECG), and chest X-ray were ordered.

Treatment was initiated with intravenous Omeprazole (40 mg), injection Metoclopramide (10mg), and oral Chlorpromazine (50mg). Shortly after the administration of these medications, the patient's hiccups ceased, but he developed slurred speech and drowsiness, though his vitals remained stable without any signs of tachycardia, tachypnea, shortness of breath, or focal neurological deficits.

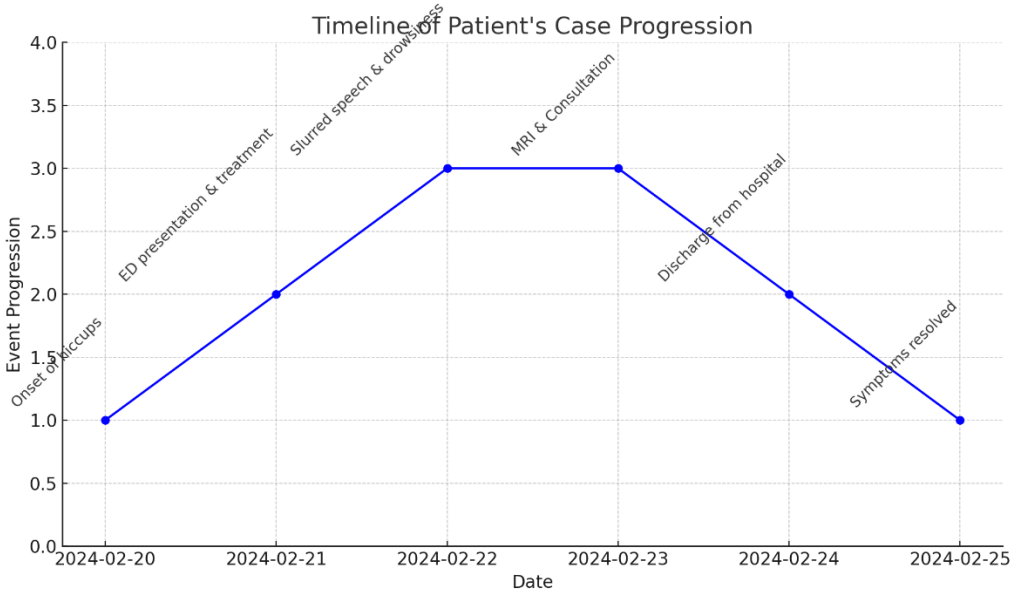

Figure 1 Progression of the Patient's case over Time

The patient and his family were informed that these new symptoms could be a known side effect of Chlorpromazine, which was effective in halting his hiccups. Despite reassurances from the ED team, the patient's family was highly concerned about the possibility of an underlying condition causing these symptoms. In response to the family's request for further evaluation, a neurology consultation was arranged, and a brain MRI was performed, which showed no significant abnormalities. Following a two-hour observation period, the patient was discharged with advice for follow-up.

At the follow-up visit the next day, the patient's symptoms of slurring and drowsiness had completely resolved, and he experienced no further episodes of hiccups. This case illustrates the importance of considering drug side effects in differential diagnosis and underscores the necessity of effective communication and reassurance in managing patient and family concerns.

DISCUSSION

The pharmacological efficacy of chlorpromazine in the management of intractable hiccups is attributed to its antagonistic action on histamine H1, dopamine D2, and muscarinic M1 receptors within the vomiting centre, marking it as the most extensively researched and FDA-approved medication for this condition. Its preference as a treatment option is well-documented, with intravenous (IV) or intramuscular (IM) administrations of 25 to 50 milligrams achieving success in approximately 80% of cases (16). However, the case presented herein illustrates a paradoxical scenario where chlorpromazine, typically effective in alleviating hiccups, induced stuttering in a patient, a side effect that resolved upon cessation of the drug. This incident underscores the complexity of drug-induced neurological symptoms and highlights the need for thorough patient assessment prior to medication administration.

The occurrence of drug-induced stuttering, potentially as a manifestation of akathisia, presents a significant challenge in clinical practice (17). It prompts a revaluation of the dopaminergic system's role in both the therapeutic effects and adverse reactions of antipsychotic medications. The primary hypothesis for the aetiology of stuttering suggests that increased dopaminergic activity disrupts striatal metabolism. The effectiveness of dopamine antagonist drugs like chlorpromazine, risperidone, and olanzapine in treating stuttering lends support to this theory. Nonetheless, the case discussed demonstrates that chlorpromazine can also act as a precipitant for stuttering, thereby complicating the clinical picture and treatment approach.

The incident highlights the imperative for healthcare professionals to possess a comprehensive understanding of the potential side effects associated with medications. A lack of awareness can lead to misinterpretation of symptoms, unnecessary diagnostic

procedures, and potentially harmful interventions, exacerbating the patient's condition. It underscores the importance of informed prescribing practices and patient education to mitigate the risks associated with drug therapy.

The strength of this case study lies in its detailed account of an uncommon adverse effect of chlorpromazine, providing valuable insights into the nuanced relationship between antipsychotic medications and neurological symptoms. However, it also reveals the limitations inherent in diagnosing and managing drug-induced conditions, particularly in the absence of extensive etiological research. This case underscores the need for further investigation into the mechanisms underlying drug-induced neurological symptoms to enhance clinical decision-making and patient safety.

CONCLUSION

In conclusion, while antipsychotic-induced slurring is a rare side effect that may mimic more serious conditions such as stroke, prompting unwarranted investigations, it highlights the critical need for etiological studies to elucidate the underlying mechanisms. This case serves as a reminder of the complexity of pharmacotherapy, emphasizing the necessity for vigilance, comprehensive patient assessment, and a judicious approach to medication use in clinical practice. Future research should aim to unravel the intricate pathways involved in drug-induced neurological symptoms, facilitating the development of targeted treatment strategies and minimizing the risk of adverse effects.

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