Case Report

Clozapine-induced acute akathisia: A case report

Pallavi Abhilasha[1], Neena Bhatti[2], Girish Joseph[2], Ranjit J. Injety[3]

[1]Department of Psychiatry, Christian Medical College, Ludhiana, Punjab, India, [2]Department of Pharmacology, Christian Medical College, Ludhiana, Punjab, India, [3]Department of Neurology, Christian Medical College and Hospital, Ludhiana, Punjab, India

Abstract

Existing data suggest that clozapine has lesser propensity of developing akathisia as compared to first general antipsychotics. Clozapine is mostly used in patients with treatment-resistant schizophrenia, which is a second-generation antipsychotic. Akathisia is one of the rare side effects of clozapine. A 34-year-old woman with a 7-year history of schizophrenia exhibited positive and negative symptoms, initially treated with haloperidol and clonazepam. Despite relief in positive symptoms, she experienced recurring cycles of symptom exacerbation upon discontinuing medication. Because of poor compliance, she was admitted and started on clozapine, reaching 150 mg/day. Although showing symptom improvement, she developed clozapine-induced akathisia, characterized by restlessness and limb movements. Propranolol and a gradual reduction in clozapine alleviated akathisia, supplemented by lorazepam. The Barnes Akathisia Rating Scale dropped to 0 after three weeks. This case highlights the challenges of managing schizophrenia and the importance of tailored medication strategies. The use of clozapine should be customized based on each patient's needs to prevent clozapine-induced akathisia.

Keywords: Acute akathisia, case report, clozapine, psychiatry, schizophrenia

Introduction

Clozapine is highly effective for the management of treatment-resistant schizophrenia. Clozapine is an atypical antipsychotic, which acts as an antagonist at the 5HT2A and D4 receptors. It binds to both serotonin and dopamine receptors.[1] Among antipsychotics clozapine has the lowest probability of eliciting akathisia as a side effect.[2] There are case reports, which have suggested a beneficial effect of clozapine on akathisia.[3] Akathisia can be quite distressing for the patients, so understanding its prevalence with different medications is crucial for treatment decisions. The very first study compared the rates of akathisia associated with clozapine and chlorpromazine to be around 40 percent. A study conducted by Kane *et al.*[1] concluded that incidence of akathisia with clozapine is lower as compared to first-generation antipsychotics. Akathisia is defined as subjective feeling of motor restlessness and is one of the side effects arising from the use of antipsychotic medication. Akathisia is manifested in the form of need to be in constant movement. Second-generation antipsychotics have been reported to be associated with lower incidence of extrapyramidal side effects as compared to first-generation antipsychotics.[4] Restlessness, inner tension, anxiety, panic, irritability, sleeplessness, and discomfort are reported as the subjective complaints. The patient also presents with purposeful, stereotypical, repetitive movements such as pacing around, rocking while sitting, crossing, and uncrossing of the legs, and rubbing of the scalp.[5,6] Barnes akathisia rating scale is used as an assessment tool for measuring akathisia. Management of akathisia includes substitution with a drug with lesser propensity to cause akathisia or reduction of the offending agent.[7] Use of beta-blockers and benzodiazepines may also help with the reduction of akathisia. If a patient shows

Address for correspondence: Dr. Pallavi Abhilasha, Gateway Terrace No- 12, Doctors Campus, CMC Ludhiana, Punjab, India.
E-mail: pallaviabhilasha@yahoo.com

Received: 13-03-2024 **Revised:** 10-04-2024
Accepted: 22-04-2024 **Published:** 11-09-2024

Access this article online

Quick Response Code:

Website: http://journals.lww.com/JFMPC

DOI: 10.4103/jfmpc.jfmpc_421_24

How to cite this article: Abhilasha P, Bhatti N, Joseph G, Injety RJ. Clozapine-induced acute akathisia: A case report. J Family Med Prim Care 2024;13:4099-102.

signs of parkinsonism, anticholinergics can also be considered.[8] There are very few case reports, which have suggested akathisia with the use of clozapine.

Here, we report the case of clozapine-induced akathisia as a valuable tool for family physicians as they aid in recognizing, differentiating, and monitoring akathisia as a potential side effect of clozapine therapy. By understanding presentation, progression, and management strategies from these reports, physicians can develop tailored monitoring and treatment plans for their patients, improving overall care quality. Moreover, sharing such information with patients enhances their awareness of medication-related complications, fostering better communication and proactive reporting of symptoms.

Narrative

A 34-year-old woman presented with a history suggestive of schizophrenia for 7 years duration. She first developed symptoms of auditory hallucinations, suspiciousness, fearfulness, decreased interaction with family members, decreased self-care, muttering, and smiling to self, and social withdrawal. Family history did not reveal any psychiatric illness. Before the onset of the illness, no psychosocial stressors were identified. No pre-existing medical illness or conditions such as anemia, diabetes, neuropathy, substance use, and renal failure were found. All systemic examinations are within normal limits. There was no diurnal variation that ruled out restless leg syndrome. No family history of RLS was found. It was supported admission, and consent was obtained by the parents.

There was no significant medical or psychiatric history. Her laboratory data revealed no abnormalities, including no anemia and normal biochemical tests. Six months after the onset of the illness, she was treated with T. haloperidol 10 mg/day along with clonazepam 3 mg/day with which her positive symptoms subsided, but negative symptoms continued. However, a month later, she discontinued the medications and had a relapse of the same symptoms earlier mentioned after 30 to 45 days. She was then treated with clonazepam 0.5 mg/day and risperidone 2 mg per day. Over the years, she developed a pattern in which she would have florid-positive symptoms for 3–6 months, after which treatment of clonazepam 0.5 mg/day and risperidone 2 mg/day. The patient would then discontinue medication when the symptoms would reduce. This cycle would repeat every over varying periods of 6 months to 2 years. Because of poor compliance and repeated relapse of symptoms, she was admitted and was started on clozapine 25 mg/day. Clozapine was started because the patient developed menstrual irregularities and weight gain as mentioned by parents.

The dosage incrementally was increased over 3 weeks to 150 mg/day. She showed improvement in symptoms, although she started to complain of feeling restless and would have a tingling sensation in her hands and feet; continuously felt an urge to move about and would not be able to sit at a place. But when she sat in one place, she would keep on moving her feet and regularly shift positions. There was no evidence of tremors, rigidity, drooling of saliva, or any orofacial movements. During the mental status examination, she was restless throughout the interview and kept on moving both her upper and lower limbs. She would get up every few minutes during the interview and reported inner restlessness.

On Barnes Akathisia Rating Scale, her total score was 13. Her routine investigations did not reveal any abnormality, and magnetic resonance imaging of the brain did not reveal any abnormality.

A diagnosis of schizophrenia with akathisia (possibly clozapine-induced) was considered. The diagnosis of restless leg syndrome was considered but ruled out because of diurnal variation. All the investigations were within the normal limits.

She was treated with tab. propranolol 40 mg/day, clozapine (regular decrement from 150 mg/day to 50 mg/day). Reduction of clozapine led to subsidence of akathisia with Barnes Akathisia Rating Scale scores coming down to 0 after 3 weeks of reduction of clozapine to 50 mg/day and the addition of lorazepam 2 mg/day (divided doses). Prognosis in this case is poor as the patient had a poor insight regarding her illness, and it was likely that she would discontinue her medications.

On follow-up, her positive and negative symptoms subsided. Her interactions with family members have improved, suspiciousness toward family members, and people around has also reduced. Her restlessness was also reduced, and she was comfortable sitting at one place. Barnes Akathisia Scale was administered, which came out to be zero. Despite knowing the outcomes about her condition, the patient is still hesitant to take medications. Parents are psycho-educated regarding the illness and the need for drug compliance.

Patient's Perspective

I was brought up in a state where I did not know what was happening to me. I was working very well and had no problems. I did not continue medications as I felt I was completely okay. People around me were trying to do some harm against me, and my father and brother also tried to rape me. I could hear voices talking to me and asking me to do things. I was forcefully brought to the hospital. I never wanted to interact with anyone as I never felt the need to. Whenever I felt like taking bath, I took bath. I did not enter the bathroom because I knew my father my keeping a watch over me and would do something inappropriate. After weeks of being in the hospital, I think these medications have helped me with my self-care, eating habits, hearing voices, and sleep. But, these medications are causing side effect as I was unable to sit at one place and was feeling very restless. I was constantly moving, and these medications are making me feel uncomfortable. After reduction of the dose, I felt much better, and I was able to sit comfortably at one place.

Discussion

A study performed by Kane *et al.*[1] suggested that the incidence of akathisia with first-generation antipsychotics was more than with clozapine. A comparison of clozapine with other various second-generation antipsychotics was studied in a recent meta-analysis study in which the rate of akathisia with clozapine was more than ziprasidone but was similar with risperidone and olanzapine.[9] A similar case report has described acute nocturnal akathisia induced by clozapine.[10] There is also evidence where clozapine has been used in treating children with schizophrenia, which has led to akathisia.[11] Incidence of akathisia with clozapine is very less compared with any other antipsychotics. Tapering down the dose of clozapine can help manage akathisia while balancing the therapeutic benefits of the medication. In our study, we have used both the modalities.

Limitations

The other modalities of treatment such as gabapentin and use of other benzodiazepines such as clonazepam/diazepam could also be used for further research purposes. Use of neuroradiological approach could also be used for further research purposes. Gabapentin's influence on neurotransmitters involved in movement and mood regulation can indeed be beneficial for alleviating the inner restlessness associated with akathisia. Gabapentin enacarbil, the prodrug of gabapentin used specifically for restless leg syndrome, targets similar symptoms to akathisia such as discomfort in legs.

There's ongoing research and some reported cases indicating gabapentin's success in treating akathisia, and it's essential to note that individual responses to medications can vary. It's crucial for individuals experiencing akathisia to consult healthcare professionals for proper diagnosis and treatment options tailored to their specific needs.[12,13] Absolutely, propranolol, a beta-blocker commonly used for various conditions such as high blood pressure and anxiety, has a substantial body of evidence supporting its efficacy in managing akathisia. Its mechanism of action involves blocking the effects of adrenaline, which can help alleviate the physical symptoms of akathisia, such as restlessness and tremors.

When adjusting the treatment for akathisia, especially when dose reduction or changing the antipsychotic medication is not feasible or effective, adding a medication such as propranolol can be an excellent choice. Its effectiveness and tolerability make it a preferred option in many cases.

However, the choice of treatment should always be made based on individual circumstances, medical history, and the overall response to previous medications. Healthcare professionals can best determine the most suitable approach for managing akathisia in each specific case.[14]

Thus, existing literature corroborates our findings that akathisia is a rare side effect of clozapine. Treatment protocols that include clozapine should be customized to the therapeutic response and adverse effects experienced.

Conclusion

Adjuvant medicines should not be used in the treatment of antipsychotic-induced akathisia; instead, antipsychotic dose reduction, stopping antipsychotic polypharmacy, and switching to an antipsychotic with a perceived lower risk for akathisia should be taken into consideration.

When selecting adjuvant drugs, the more well-proven therapies should be given preference, and side effects and contraindications should be carefully considered. Prompt cautious prescribing is necessary, especially when it comes to the length of time that adjuvant drugs are used.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients 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.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Kane JM, Fleischhacker WW, Hansen L, Perlis R, Pikalov A 3rd, Assunção-Talbott S. Akathisia: An updated review focusing on second-generation antipsychotics. J Clin Psychiatry 2009;70:627-43.
2. Weiden PJ. EPS profiles: The atypical antipsychotics are not all the same. J Psychiatr Pract 2007;13:13-24.
3. Chengappa KN, Shelton MD, Baker RW, Schooler NR, Baird J, Delaney J. The prevalence of akathisia in patients receiving stable doses of clozapine. J Clin Psychiatry 1994;55:142-5.
4. Grover S, Sahoo S. Clozapine induced akathisia: A case report and review of the evidence. Indian J Pharmacol 2015;47:234-5. doi: 10.4103/0253-7613.153441.
5. Kern D, Lange A, Friedman J. Acute Akathisia. Cambridge: Cambridge University Press; 2015.
6. Koliscak LP, Makela EH. Selective serotonin reuptake inhibitor-induced akathisia. J Am Pharm Assoc (2003) 2009;49:e28-36.
7. Barnes TR. A rating scale for drug-induced akathisia. Br J Psychiatry 1989;154:672-6.
8. Iqbal N, Lambert T, Masand P. Akathisia: Problem of history or concern of today. CNS Spectr 2007;12:1-13.
9. Rummel-Kluge C, Komossa K, Schwarz S, Hunger H, Schmid F, Kissling W, *et al.* Second-generation antipsychotic

drugs and extrapyramidal side effects: A systematic review and meta-analysis of head-to-head comparisons. Schizophr Bull 2012;38:167-77.

10. Sahoo, S, Ameen, S. Acute nocturnal akathisia induced by clozapine. J Clin Psychopharmacol 2007;27:205.
11. Gogtay N, Sporn A, Alfaro CL, Mulqueen A, Rapoport JL. Clozapine-induced akathisia in children with schizophrenia. J Child Adolesc Psychopharmacol 2002;12:347-9.
12. Pfeffer G, Chouinard G, Margolese HC. Gabapentin in the treatment of antipsychotic-induced akathisia in schizophrenia. Int Clin Psychopharmacol 2005;20:179-81.
13. Sullivan MA, Wilbur R. Gabapentin pharmacotherapy for antipsychotic-induced akathisia: Single-patient experiment and case report. Ther Adv Psychopharmacol 2014;4:100-2.
14. Pringsheim T, Gardner D, Addington D, Martino D, Morgante F, Ricciardi L, *et al.* The assessment and treatment of antipsychotic-induced akathisia. Can J Psychiatry 2018;63:719-29.