

# Pisa syndrome with clozapine therapy in a young patient with schizoaffective disorder

Shreyas Aneja<sup>1</sup>, Sharanya B. Shetty<sup>1</sup>, Aayush Srivastav<sup>1</sup>, Keshava Pai<sup>1</sup>,  
Priyanka D'Souza<sup>1</sup> & Sunil Kumar<sup>2</sup>

<sup>1</sup> Department of Psychiatry, Kasturba Medical College Mangalore, Manipal Academy of Higher Education, Manipal, India

<sup>2</sup> Wenlock Government Hospital, Mangalore, India

received: 15. 04. 2024;

revised: 07. 05. 2025;

accepted: 23. 07. 2025

\* \* \* \* \*

## INTRODUCTION

Antipsychotics, though effective agents in treating schizophrenia, can lead to the development of side effects ranging from metabolic to hematologic, and affecting the CNS as well (Franza et al., 2017). One such rare effect is Pisa syndrome. Pisa syndrome is a tonic flexion of the trunk and leaning of patient's head to one side with some degree of body rotation, which resolves in supine position (Zhao et al., 2020). The risk factors include female gender, older age groups, and neurodegenerative disorders such as Parkinson's disease (Yokochi, 2006). It is associated with the use of neuroleptics, including typical and atypical antipsychotics, antidepressants, mood stabilizers like lithium, benzodiazepines, and anticholinergic drugs. Limited literature exists on clozapine-induced Pisa syndrome, with few reported cases to date. Here, we present a case of a young patient with schizoaffective disorder who developed Pisa syndrome while being treated with clozapine.

## CASE PRESENTATION

A male patient presented in his early 20s, from an urban background, middle socioeconomic status of Mangalore. Premorbidly patient was well adjusted with a family history of psychiatric illness and death by suicide in the mother when the patient was one year old.

The patient has had a history of illness for 10 years characterized by seven episodes of persistent sadness, easy fatigability, reduced interest in activities, deliberate self-harm attempts, poor academic performance, disturbed sleep, and appetite along with hearing the voice of his neighbour and delusion of persecution towards the neighbour. The patient also had two episodes of excessive talking, irritability, and grandiose delusions, lasting for 1-2 months. The patient was diagnosed with schizoaffective disorder and treated with atypical antipsychotics

and mood stabilizers (figure. 1). The recent episode was 6 months back, characterised by 2 months of low mood, tiredness, disinterest in activities, hearing the voice of his neighbour, with a feeling that thoughts are being put in and taken out from his mind by the neighbour, guilt about his mother's death, suicidal ideation, fearfulness, impaired biological and socio-occupational functioning. Mental status examination showed decreased psychomotor activity, decreased tone of speech, thought withdrawal, thought insertion, delusion of persecution and guilt, being responsible for everything happening to him and people around him including his mother, low mood, depressed affect, restricted range, auditory hallucination of a single male, neighbour, threatening and commanding him to attempt an act of self-harm, present both during the day and night, distressful, with impaired social judgement and grade 3 insight. The patient had a failed trial of two atypical antipsychotics along with adequate doses of sodium valproate and lithium during the previous episodes. As the patient did not respond adequately to the medications and had a breakthrough episode, the patient was started on the tablet clozapine and responded well to the dose of 300mg/day.

The patient was on regular follow-up for 6 months, and the patient's psychotic symptoms had improved. After being on clozapine therapy for 6 months, the patient presented with complaints of feeling as if he was about to fall on one side for 1 week, with friends and family noticing a change in his posture. The general physical examination showed forward and rightward bending of the trunk, and rightward turning of the neck, especially while walking and standing. The patient's posture was found to improve while in the supine position (figure 1). Other systemic examinations were within normal limits. On mental status examination, the patient was well-kempt, with normal psychomotor activity, and speech output, with being preoccupied with thoughts about the recent difficulties with the posture and anxious affect. The x-ray of – whole spine and cervical spine (Antero-posterior and Lateral views) were taken and the findings were clinically

corroborated as shown (figure 1). The Adverse Drug Reaction probability scale (using the Naranjo Algorithm) gave a score of 7, a probable temporal association of adverse events with drug use.

The patient was started on trihexyphenidyl 4 mg/day and the dose of clozapine was reduced to 250 mg/day. On follow-up after 1 month of starting the medication, patient's posture had improved. On subsequent follow-up at 2 months, no posture-related abnormalities were noted.

## DISCUSSION AND CONCLUSION

Pisa syndrome was first reported by Ekblom et al as a side-effect of antipsychotic drugs in 1972. It was described as an involuntary posture where the trunk was biased towards one side of the body (Zhao et al., 2020). It is an atypical 'Tardive dystonia' called pleurothotonus (Yokochi, 2006). Dystonia, defined as involuntary movement disorders that are distressing and can be painful is hypothesised to be caused due to excessive compensatory activity following dopaminergic antagonism (Fariba & Estevez, 2025).

Clozapine, an atypical antipsychotic, acts by antagonism at dopamine receptors D2 and D4 with a higher affinity towards D4 than D2. This makes the causation of extrapyramidal symptoms by clozapine a rarity. However, a case report on massive consumption of clozapine, the patient presented with facial grimacing and choreatic movements but no such feature was seen with therapeutic doses (Turk et al., 2020).

Other side effects such as sedation, constipation, sialorrhea can also occur due to clozapine's action on serotonin and muscarinic receptors (Kırşavoğlu & Odabaşı, 2023).

The exact mechanism of the development of Pisa syndrome is not known, it has been hypothesized that it is caused by dopamine-cholinergic imbalance in the patient (Jankovic & Tolosa, 2015). This imbalance is hypothesised to be asymmetrical, leading to lateral flexion on one side (Pandey & Mehndiratta, 2011). Some studies also suggest impairment in proprioceptive integration during spatial orientation in Parkinson's disease, which leads to postural change (Marchione et al., 2014).

No consensus has been drawn on the diagnostic criteria of Pisa syndrome, but a bend of 10° on one side of the body is considered diagnostic by a few studies. The bend is increased when the patient stands, sits, or walks but reduces in the supine position (Zhao et al., 2020).

Many cases of Pisa syndrome have been reported in patients suffering from Parkinson's disease, and a few in

cases of Alzheimer's disease (Fariba & Estevez, 2025) and in a single case of subdural hematoma. As per recent studies, drugs such as dopamine agonists, and antiepileptics such as sodium valproate have been implicated in causing Pisa syndrome as well (Jankovic & Tolosa, 2015). Some of the other case reports have implicated the use of acetylcholinesterase inhibitors in the causation of the condition apart from first and second-generation antipsychotics (Kwak et al., 2000).

As there is no specific guideline for treating Pisa syndrome, our approach focused on restoring this balance by starting anticholinergic medication and reducing the neuroleptics. In this case, the patient belonged to a young age group and did not have an adequate response to multiple antipsychotic medications but on clozapine, the patient's psychotic symptoms had improved. Despite clozapine's tendency to cause fewer extrapyramidal side effects, the patient developed a change in posture only after treatment with clozapine for 6 months.

Considering the above findings, it can be concluded that our case presented a rare side effect of an atypical antipsychotic clozapine in young age group. This is one of the unique and rare cases adding to the existing literature emphasising the need for clinicians to be aware of this side effect. Further efforts are needed to understand its pathophysiology, its association with neuroleptic medications and evidence-based treatment approaches.

**Ethical Considerations:** Does this study include human subjects? YES

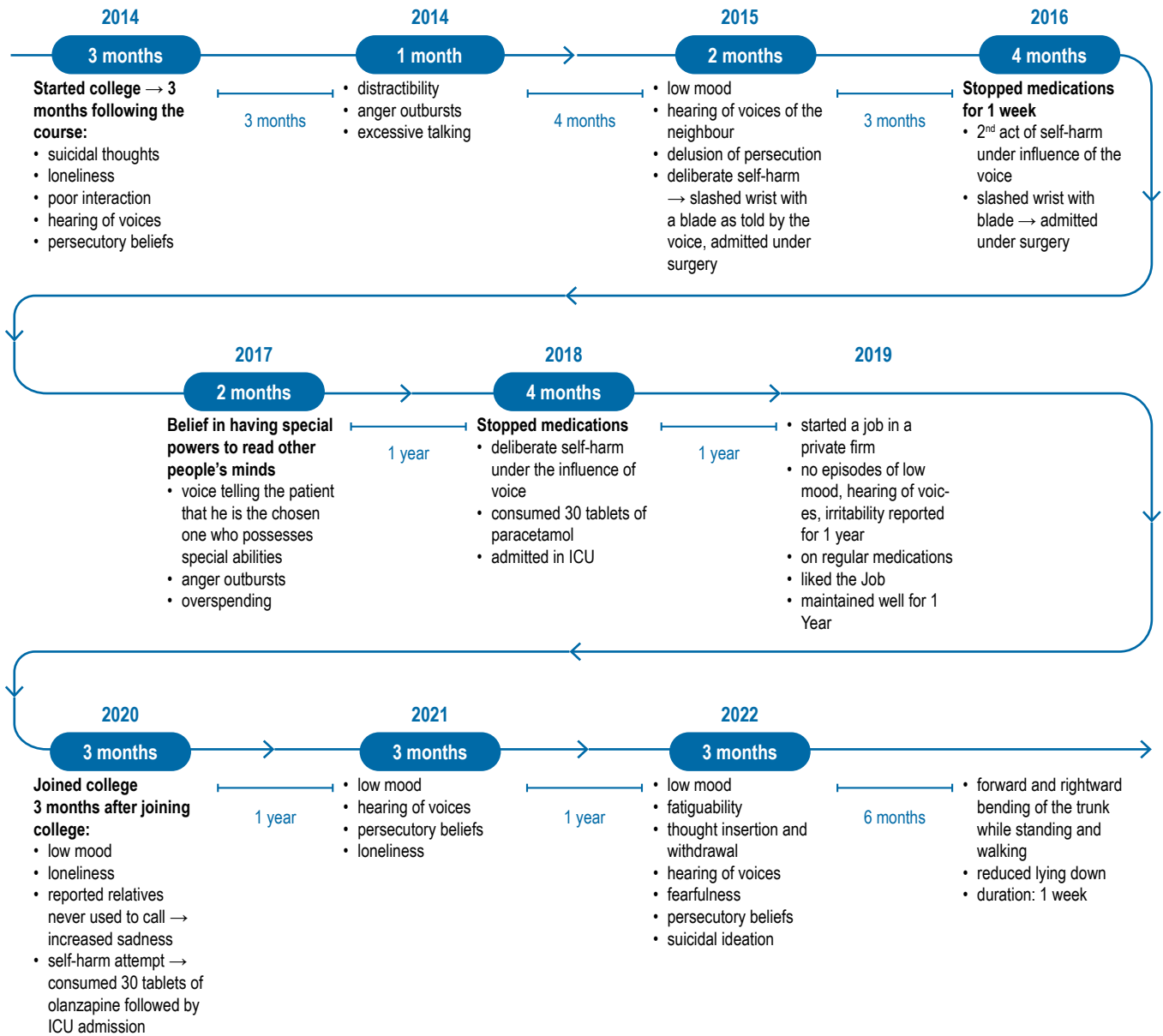
Authors confirmed the compliance with all relevant ethical regulations.

**Ethical clearance:** The case report was approved and cleared by the ethics committee of the institute (Protocol number: IEC KMC MLR 11/2023/462)

**Conflict of interest:** No conflict of Interest

**Funding sources:** The authors received no funding from an external source

**Authors Contributions:** Dr. Shreyas Aneja: conceptualization, Investigation, Resources, Manuscript Writing – original draft, review and editing. Dr. Sharanya Shetty: conceptualization, Investigation, Supervision, Manuscript Writing – original draft, Writing- review and editing. Dr. Aayush Srivastav: conceptualization, Investigation, Manuscript Writing – review and editing. Dr. Keshava Pai: conceptualization, Manuscript Writing- review and editing. Dr. Priyanka D'Souza: manuscript Writing- review and editing. Dr. Sunil Kumar: investigation, Manuscript Writing- review and editing.



STANDING



SUPINE



X-Ray – spine

Figure 1

## References

- Fariba, K. A., & Estevez, R. (2025). Tardive dystonia. In *StatPearls*. StatPearls Publishing.
- Franza, F., Solomita, B., Aldi, G., & Del Buono, G. (2017). Assessing the critical issues of atypical antipsychotics in schizophrenic inpatients. *PubMed*, 29(Suppl 3), 405–408.
- Jankovic, J., & Tolosa, E. (2015). *Parkinson's disease and movement disorders* (6th ed.). Lippincott Williams and Wilkins.
- Kırşavoğlu, B., & Odabaşı, O. (2023). An unexpected side effect related to the use of clozapine: Neutrophilic leukocytosis and brief review of the literature. *Psychiatry Research Case Reports*, 2(1). <https://doi.org/10.1016/j.psy-cr.2022.100101>
- Kwak, Y. T., Han, I. W., Baik, J., & Koo, M. S. (2000). Relation between cholinesterase inhibitor and Pisa syndrome. *Lancet*, 355(9222). [https://doi.org/10.1016/S0140-6736\(00\)02412-0](https://doi.org/10.1016/S0140-6736(00)02412-0)
- Marchione, P., Spallone, A., Valente, M., Giannone, C., De Angelis, F., & Meco, G. (2014). Reversible Pisa syndrome associated to subdural haematoma: Case-report. *BMC Neurology*, 14(1). <https://doi.org/10.1186/1471-2377-14-149>
- Pandey, S., & Mehndiratta, M. (2011). Concomitant appearance of Pisa syndrome and striatal hand in Parkinson's disease. *Journal of Movement Disorders*, 4(2). <https://doi.org/10.14802/jmd.11017>
- Turk, V. E., Kucan, M., & Vitezic, D. (2020). Massive clozapine overdose: What to expect? *Psychiatria Danubina*, 32(3–4), 431–433. <https://doi.org/10.24869/psyd.2020.431>
- Yokochi, F. (2006). Lateral flexion in Parkinson's disease and Pisa syndrome. In *Journal of Neurology* (Vol. 253, Suppl 7). <https://doi.org/10.1007/s00415-006-7005-4>
- Zhao, J., Wang, Q., Sun, H., Liu, X., Leng, B., & Wang, T. (2020). Quetiapine relieved Pisa syndrome in patient with Parkinson disease. *Clinical Neuropharmacology*, 43(6). <https://doi.org/10.1097/WNF.0000000000000416>

### Correspondence:

Sharanya B. Shetty, Assistant Professor, Department of Psychiatry, Kasturba Medical College Mangalore, Manipal Academy of Higher Education, Manipal, 576 104, India  
[sharanyabshetty@gmail.com](mailto:sharanyabshetty@gmail.com)

Published under



<https://creativecommons.org/licenses/by-nc-nd/4.0/>