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Case Report

Clozapine induced pneumonitis: a case report

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ABSTRACT

Clozapine is an atypical antipsychotic used for the treatment of schizophrenia. Clozapine acts by blocking serotonin receptors in the brain, thereby reducing the symptoms of schizophrenia. Clozapine is usually restricted to the treatment of resistant cases of schizophrenia. Clozapine induced pneumonitis is a very rare adverse reaction and, one such incident in a 16-year-old Indian boy is intricated in this case report.

Keywords: Antipsychotics, Agranulocytosis, Drug induced interstitial lung diseases, Resistant-schizophrenia

INTRODUCTION

Non-infectious inflammation of lung tissue is generally termed as pneumonitis. Sometimes, the systemic use of drugs can lead to pneumonitis, which is often referred to as drug-induced interstitial lung disease (DIILD). Anticancer drugs are the leading cause of DIILD, accounting for 23-51% of cases. Psychiatric medications can also cause DIILD (1-9%).[1]

Schizophrenia is a psychiatric disorder characterized by delusions, hallucinations, and lack of insight. Clozapine is reserved for resistant schizophrenia, recurrent suicidal behaviour in schizophrenia and schizoaffective disorder. In a systematic review and meta-analysis, clozapine-treated patients showed more clinical improvement and experienced significantly fewer relapses during treatment.[2] The incidence of adverse events are more with clozapine when compared with other atypical antipsychotics. Among them, agranulocytosis is one major concern.[3] Drug-induced pneumonitis is a very rare complication of clozapine, and one such incident is stated below.

CASE REPORT

Sixteen years old male patient, who is a known case of intellectual disability with psychosis was under treatment for the same from a local mental hospital. He had history of repeated psychotic episodes and visual hallucinations of three boys trying to murder him. The patient was then taken to a tertiary care hospital in central India, where he was admitted and treated for psychotic symptoms. He started showing improvement and became stable. He was then discharged and sent home. For the next four months the patient was well maintained on haloperidol and olanzapine. Abruptly on a dreadful day, the patient started showing symptoms of psychosis again. He was anxious and restless, was squealing and screaming without provocations. He started getting visual hallucinations of those three boys again and was not able to sleep at night. The patient was then brought to the hospital and was advised admission.

On admission, general condition of the patient was not normal and he kept his neck in a hyper extended position.

Vitals were stable and no abnormalities were detected on system examinations. Central nervous system examination revealed slight rigidity and increased muscle tone. Higher mental functions and reflexes could not be elicited as the patient was non-cooperative. All routine investigations like complete blood count, liver and renal function test, HBsAg, chest X-ray, USG abdomen and pelvis, and random blood sugar were sent at the time of admission and came out to be normal. The patient was adherent to his medications while at home leading to extrapyramidal symptoms (EPS) and hence haloperidol was stopped and olanzapine 20mg twice daily was tapered to 10mg twice daily on admission. Injection promethazine 25 mg was given stat to relieve muscle rigidity and was continued in twice daily dosage for 4 days till the extra pyramidal symptoms subsided. Also, trihexyphenidyl (Benzhexol) 6mg was given for three days to relieve muscle dystonia and rigidity caused by antipsychotics.

Upon admission, he was started on clozapine 12.5 mg. The dose of clozapine was increased by 12.5 mg daily till 200 mg was attained. First day into the initiation of clozapine 200mg, the patient complained of breathing difficulties and fever. The patient was tachypnoeic, and had tachycardia. Blood pressure was on the lower side. chest was clear on auscultation; heart sounds were normal. Muscle rigidity, dyskinesia and dystonia were absent. All blood investigations were sent and found to be normal. A slight decrease in total leucocyte count (4.2×10^{-3} µL) was noted with respect to the previous (6.8×10^{-3}µL) reading. Chest X-ray showed prominent bronchial vascular markings (Figure 1). Partial pressure of O_2 (pO_2) on pulse oximetry was slightly reduced to 90%. Reverse transcriptase polymerase chain reaction (RTPCR) for COVID-19 came negative. The patient was then transferred to an intensive care unit (ICU) and was given intravenous antibiotics along with other supportive measures. Blood culture was also sent, which came out negative for any organism. Clozapine was withdrawn for the time being, considering the possibility of agranulocytosis it can produce. After one day in ICU the patient showed great improvement and was maintaining oxygen saturation at room air. Thus, he was shifted to the ward next day where, antibiotics and other supportive measures were continued. In the ward, clozapine 12.5mg was also restarted. He then developed shortness of breath and chills.

The drug was withdrawn immediately and a presumptive diagnosis of clozapine induced pneumonitis was made by the treating psychiatrist corroborated by the temporal association between development of symptoms and initiation of clozapine. Patient's symptoms subsided completely after 6-8 hours following oxygen therapy and hydrocortisone 100 mg intravenous injection single dose. The patient was closely monitored for one day after which he was sent home with olanzapine 5 mg twice daily for 2 weeks, trihexyphenidyl 2 mg once daily for 1 week. Antitussives, cefixime (200 mg BD) and pantoprazole (40 mg OD) were given for 3 days.

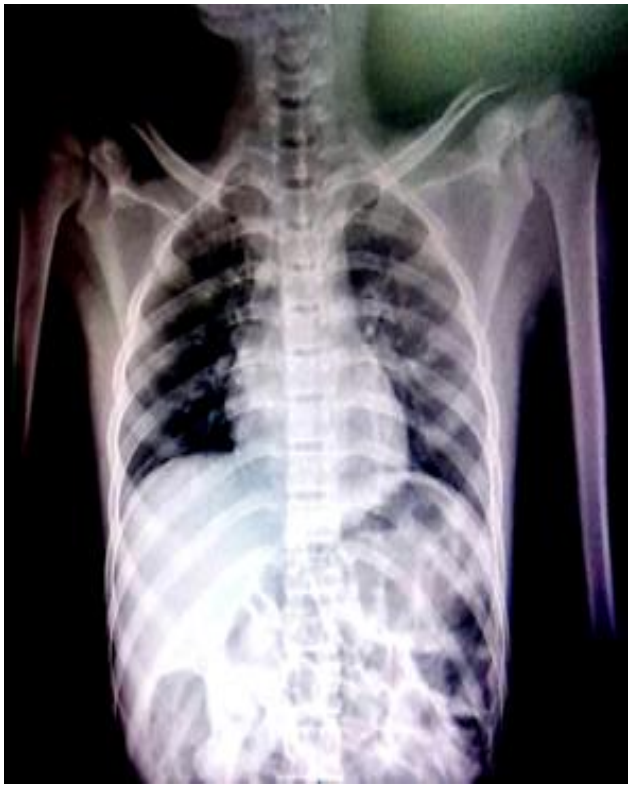

Figure 1: Prominent (left) bronchial vascular markings.

DISCUSSION

Clozapine is an atypical antipsychotic which is limited to the usage in resistant schizophrenia. Even though we are aware of many adverse effects of clozapine, pneumonitis seldom occurs and is rarely reported. This case report suggests a strong association between clozapine and pneumonitis observed in a patient. On an extensive search for the association between clozapine and pneumonitis, we could find few other research articles and case reports suggesting the same.[4,5,7] Neutropenia with increased risk of lung infection is far more commonly associated with clozapine than non-infectious lung injury.[6] It is also important to note that the symptoms of clozapine induced pneumonitis resemble sepsis. In a study conducted by Schoretsanitis et al clozapine appears to attenuate the defensive mechanisms against infection and aggravates the lethality of pneumonia.[8] Diagnosis of clozapine-induced pneumonitis is based on the temporal association between onset of symptoms and administration of the drug, which resolves in most cases by withdrawal of clozapine.

CONCLUSION

Drug-induced pneumonitis is an exceptional adverse effect of clozapine. This case report throws some light into such an isolated incident and thereby helping clinicians get acquainted to this rare adverse event. Pneumonitis should be suspected when a patient with ongoing clozapine treatment suddenly shows respiratory symptoms mimicking sepsis.

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REFERENCES

1. Skeoch S, Weatherley N, Swift AJ, Oldroyd A, Johns C, Hayton C, et al. Drug-Induced Interstitial Lung Disease: A Systematic Review. J Clin Med. 2018;7(10):356.
2. Wahlbeck K, Cheine M, Essali A, Adams C. Evidence of Clozapine's Effectiveness in Schizophrenia: A Systematic Review and Meta-Analysis of Randomized Trials. Am J Psychiatry. 1999;156(7):990-9.
3. Meyer JM. Chapter 16: Pharmacotherapy of psychosis and mania in Goodman and Gilman's The pharmacological basis of therapeutics. McGraw Hill. 2011;442.
4. Aldridge G, Collins C, Croucher M. Clozapine-induced pneumonitis. Aust N Z J Psychiatry. 2013;47(12):1215-6.
5. Lewis A, Gibbs A, Hope-Gill B. Probable occupational pneumonitis caused by inhalation of crushed clozapine. Occup Med. 2012;62(5):385-7.
6. Torrico T, Crandall RO, Meza C, Abdijadid S. Clozapine-Induced Pneumonitis: A Case Report. Front Psychiatry. 2020;11:572102.
7. Bugge E, Nissen T, Wynn R. Probable clozapine-induced parenchymal lung disease and perimyocarditis: a case report. BMC Psychiatry. 2016;16:438.
8. Schoretsanitis G, Can-Jun R, Christopher R, Hélène V, De Las Cuevas C, Edoardo S et al. An update on the complex relationship between clozapine and pneumonia. Expert Rev Clin Pharmacol. 2021;14(2):145-9.

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