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COMMENTARY

COVID-19 Infection May Cause Clozapine Intoxication: Case Report and Discussion

Thomas Cranshaw*,[•] and Thiyyancheri Harikumar

Cumbria, Northumberland Tyne and Wear NHS Foundation Trust, Newcastle upon Tyne, UK

*To whom correspondence should be addressed; St George's Park Hospital, Morpeth NE61 2NU, UK; tel: +44-0191-2466800, fax: +44-0167-0501883, e-mail: thomas.cranshaw@cntw.nhs.uk

We would like to describe a case of clozapine intoxication as a result of COVID-19 infection. As far as we are aware, an example of this has not yet been described.

In patients treated with clozapine, COVID-19 infection may result in complications including an increased risk of pneumonia, clozapine toxicity, and disruption to clozapine treatment by COVID-19 induced lymphopenia.[1–3]

Patients treated with clozapine are at greater risk of pneumonia and may, therefore, be at increased risk of deterioration during COVID-19 infection.[1] De Leon et al offer a thorough review of the risk of pneumonia and clozapine intoxication associated with infection, recommending clozapine dose reduction during fever and/or pneumonia including in the context of COVID-19.[2] This risk of intoxication is reflected in the RCPsych (UK) policy on clozapine and blood dyscrasias in patients with COVID-19, where it is advised that clozapine levels are taken in all patients with suspected symptoms of COVID-19.[3]

A 38-year-old male on an inpatient mental health rehabilitation ward treated with 325 mg per day of clozapine for organic psychosis developed a cough, headache, and reduced oxygen saturation of 94% on room air. COVID-19 was suspected and a nasopharyngeal swab was taken. No COVID-19 or antibiotic treatment was started.

The following day, the patient was noted to have a persistent cough and was drowsy, with markedly increased hypersalivation and myoclonus. Clozapine toxicity was suspected. After discussion with a medical registrar, a clozapine level was performed locally and it was determined that the patient was safe to remain on the ward.

Later that day, COVID-19 was confirmed by reverse transcription polymerase chain reaction (RT-PCR). Clozapine level returned as 0.73 mg/l, norclozapine 0.31 mg/l, substantially above the patient's previous stable baseline of 0.57 mg/l, norclozapine 0.22 mg/l. The most likely explanation is precipitation of clozapine toxicity by COVID-19 infection. Mechanisms for increase in plasma clozapine during infection have been shown to involve cytokine release downregulating the metabolism of clozapine in the P450 system through CYP 1A2.[2]

Clozapine was discontinued that day due to COVID-19 induced lymphopenia (0.76×10^9/l).[4] This progressed the following day to a transient mild neutropenia (1.26×10^9/l). The patient made an uncomplicated recovery from COVID-19 however experienced a relapse in psychotic symptoms as result of temporary clozapine cessation.

This case demonstrates the importance of full clinical assessment of suspected COVID-19 infection in clozapine treated patients, including assessment for features of pneumonia, clozapine toxicity, clozapine level, and full blood count. Consideration should be given to dose reduction during infection. The risks posed by clozapine treatment during the COVID-19 pandemic must, however, be balanced against the substantial benefit many patients receive from this medication and the likelihood of mental health deterioration with unplanned treatment cessation.

Consent has been obtained for the publication of this case report.

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