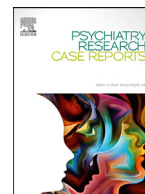




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## A rare case of catatonia associated with COVID-19 infection

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### ABSTRACT

COVID-19, caused by the SARS-CoV-2 virus, has well-documented common symptoms such as cough and fever. There is also extensive documentation on the more severe outcomes, such as sepsis and death. However, there is minimal literature regarding the neuropsychiatric effects of COVID-19. This case report outlines a patient who presented with apparent psychosis shortly after COVID-19 infection. Shortly after hospitalization, she began to develop symptoms of catatonia. Her catatonia subsequently was recognized and resolved with appropriate treatment with lorazepam. There have been a handful of similar reports regarding patients with COVID-19 developing catatonia and responding well to lorazepam. Therefore, catatonia may be associated with COVID-19. Clinicians should consider catatonia diagnosis in patients with COVID-19 who have changes in behaviour, mental status, or motor function, to prevent deterioration secondary to untreated catatonia. Furthermore, COVID-19 testing should be considered in patients with acute psychiatric presentations.

### Introduction

The SARS CoV-2 virus, which causes the coronavirus disease 2019 (COVID-19), led to a pandemic, with millions of deaths worldwide. Generally, clinical presentation varies from asymptomatic; to cough and fever; to sepsis (Grant et al., 2020; Pathophysiology, 2021). However, various reports have also highlighted neuropsychiatric sequelae of COVID-19 (Varatharaj et al., 2020; Taquet et al., 2021) (Schou et al., 2021). More recently, a limited number of reports have introduced the potential for catatonia to be related to COVID-19.

Based on the Diagnostic and Statistical Manual of Mental Disorders (DSM-5), “catatonia is a clinical picture dominated by 3 or more of the following: stupor, catalepsy, waxy flexibility, mutism, negativism, posturing, mannerism, stereotypy, agitation, grimacing, echolalia, or echopraxias” (American Psychiatric Association, 2013). One form of negativism is gegenhalten, which is resistance proportional to force used to elicit passive movement. Clinical presentation of catatonia can be heterogenous; screening and severity can be assessed using the Bush-Francis Catatonia Rating Scale (BFCRS) (Bush et al., 1996). The BFCRS has a sensitivity of between 75 and 100% and inter-rater reliability of  $r = 0.93$  (Sienaert et al., 2011). However, some of the criteria on the BFCRS, such as autonomic disturbances with deranged vital signs, can be present with other medical conditions. Therefore, the BFCRS score should be considered with the clinical picture of the patient.

Symptoms of catatonia can be subtle, leading to missed diagnosis (Llesuy et al., 2018). If untreated, catatonia is associated with high morbidity and mortality (Llesuy et al., 2018). It may lead to the development of malignant catatonia or neuroleptic malignant syndrome (NMS), with significant psychomotor agitation and potentially fatal autonomic disturbances such as hyperthermia (Rasmussen et al., 2016; Raja et al., 1994). Therefore, clinicians need to be aware of the possible causes of catatonia and appropriately screen for it to facilitate timely treatment.

Commonly known causes of catatonia include psychiatric disorders, encephalopathy, and neurocognitive changes (Llesuy et al., 2018). Medical conditions, most commonly: hyponatremia, uraemia, sepsis, and post-partum setting, have been reported to precede catatonia (Oldham, 2018). The pathophysiology of catatonia is unclear; theories postulate that it may be due to changes in gamma-aminobutyric acid and glutamate signalling (Rasmussen et al., 2016). These changes may be brought on by inflammation or anxiety (Rasmussen et al., 2016; Scheiner et al., 2021). As the COVID-19 pandemic evolves, COVID-19 infection appears to be an emerging cause of catatonia (Scheiner et al., 2021; Sakhardande et al., 2022; Torrico et al., 2021; Caan et al., 2020). The patients in these case reports have presented with varying degrees of stupor, mutism, withdrawal, posturing, negativism, autonomic instability, immobility, rigidity, and waxy flexibility. Generally, these patients responded well to lorazepam treatment. We present a further case of catatonia associated with COVID-19 infection.

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## Case

AA, a 49-year-old woman, was diagnosed on PCR with COVID-19 as an outpatient at a local hospital. According to collateral information from her sister, AA had chronic sleep problems and anxiety secondary to a separation from her husband. However, with the COVID-19 diagnosis, this intensified and she had increasing paranoia. On this particular day, AA was particularly distractible, disorganized, and expressed that “the COVID is back”, “I’m going to die”, and “the microchips are controlling me”. Her sister became worried and called 911. An ambulance then brought AA voluntarily to the emergency department.

On presentation, AA was agitated, crying, and asking for help. She expressed persecutory delusion, delusion of monitoring, passivity, delusion of thought reading, and bizarre delusions. Her thought content included: “they are trying to kill me”, “they insert chips into my body”, “they insert COVID-19 into me”, and “they want to change me into a robot”. She believed that “they” were monitoring her and could read her thoughts. She believed cold showers would “kill them” and so she had been taking cold showers for several days. She believed that “they” had planted a black square in the ambulance to monitor her. She reported that her thoughts were moving very quickly “in a race against time”. AA reported several days of insomnia, poor energy, and low mood. AA reported feeling this way for “a few days” and her sister confirmed the same. AA had ongoing cough, diarrhoea, and fatigue which she attributed to COVID-19.

Her past psychiatric and medical history revealed potential undiagnosed anxiety, resolved postpartum depression, and hypertension. Her sister suffered postpartum psychosis but otherwise, there was no other contributory family history that would place her at risk of developing psychosis.

On presentation, AA was tachycardic with a heart rate of 140 beats per minute (BPM). The rest of her vital signs (temperature, respiratory rate, oxygen saturation) were unremarkable and within normal limits.

In terms of the mental status exam, AA appeared fatigued, confused, and distracted. Her speech was slow, monotone, and robotic, with regular rhythm and volume. She was not objectively pressured. There were no neologisms, verbigeration, or clang associations. Her mood was distressed and dysphoric, although with a blunted affect. Thought stream was normal. Thought form was disorganized with loose associations. She denied suicidal and homicidal ideation. She exhibited thought reading, persecutory delusions, bizarre delusions, delusion of monitoring, passivity, and delusions of reference. She denied auditory hallucinations and was not seen responding to internal auditory stimuli. Her insight was negligible, and her judgement was poor.

The provisional diagnosis was unspecified mania with psychotic features due to her lack of sleep, racing thoughts, and significant delusions. As this was her first psychiatric presentation at an atypical age, so an extensive medical workup was completed per hospital standard practice. MRI head, CT head, CXR, EEG, and extensive laboratory investigations were unremarkable including autoimmune encephalitis antibodies (anti-NMDA, anti-DPPX, anti-VGKC profile, anti-GABAB, and anti-AMPA).

The BFCRS score was not assessed daily during hospitalization because catatonia was not suspected during the initial days of admission.

On Day 1 of admission, AA endorsed ongoing psychotic symptoms similar to presentation. Her heart rate was elevated at 131 BPM. The rest of her vital signs were within normal limits. She had a repeat COVID-19 PCR test which was positive. She was started on olanzapine 10 mg oral (p.o.) daily for treatment of psychosis.

On Day 2, AA continued to exhibit psychotic symptoms. Further, AA had been checking the prescribed olanzapine. She thought “they” had given her the medication. She also exhibited clang associations and verbigeration, stating “the chips and the tricks” repeatedly. She behaved inappropriately and blew a kiss at the end of the interview. Her heart rate was elevated at 140 BPM. The rest of her vital signs were within normal limits. Medication was changed to olanzapine oral dissolving

(Zyprexa Zydis) 10 mg p.o. nightly (qHS) with the option to use intramuscular (i.m.) if she refused oral (which she did). She also received lorazepam 2 mg i.m. and loxapine 20 mg i.m. for agitation.

On Day 3 AA’s psychotic symptoms persisted. She was awake overnight insisting that “I am dying”. She continued to have tangential speech with clang associations. She continued to exhibit perseveration of “the chips”. Her heart rate was elevated at 113 BPM. The rest of her vital signs were within normal limits. Olanzapine dosage was increased to 15 mg p.o./i.m. qHS due to ongoing psychotic symptoms, which she accepted orally.

On Day 4, psychotic symptoms persisted with poor insight. AA was suspicious that staff wanted to “reintroduce the chips” into her and refused to leave her room. She insisted that she should be discharged. She perseverated on “you will let me go home” and “you did not start me on these medications”. AA was examined for side effects of olanzapine, including muscle tone. AA exhibited negativism of her right arm when examined. Further, she exhibited intense staring. Her heart rate was elevated at 122 BPM. The rest of her vital signs were within normal limits. Lorazepam 1 mg p.o./sublingual (s.l.) twice daily (BID) was initiated for agitation.

On Day 5, psychotic symptoms and lingering cough from COVID-19 persisted. She had similar perseveration to the prior day. Her heart rate was elevated at 141 BPM and her blood pressure was elevated at 133/94 millimeters of mercury (mmHg). The rest of her vital signs were within normal limits. Olanzapine was titrated down to 10 mg p.o. qHS in favor of a switch to haloperidol as psychotic symptoms were not improving. Haloperidol 2 mg p.o./i.m. was added for the treatment of psychosis.

On Day 6, AA remained isolated and refused to leave her room. She also refused medical imaging and medications; she specifically did not want to take lorazepam. This was possibly due to persecutory delusions. Furthermore, she was seen holding a cup at 60° horizontal by nursing staff and when they tried to take it from her, she stiffened her arm. This could have been posturing, rigidity, and negativism. Furthermore, she reached out with her other hand in an exaggerated gesture to shake the nurse’s hand, exhibiting automatic obedience. Her heart rate was elevated at 139 BPM. The rest of her vital signs were within normal limits. The cross taper of olanzapine and haloperidol continued by decreasing olanzapine to 5 mg p.o. qHS and increasing haloperidol to 4 mg p.o./i.m. as the patient continued to exhibit psychotic symptoms.

On Day 7, psychotic symptoms persisted. Her heart rate was elevated at 138 BPM and her blood pressure was elevated at 139/92 mmHg. The rest of her vital signs were within normal limits. Olanzapine was discontinued. Haloperidol was continued at 4 mg p.o./i.m. for psychotic symptoms and lorazepam 1 mg p.o./s.l./i.m. BID was continued for agitation.

On Day 8 there was seemingly no change to AA’s psychotic symptoms. AA’s heart rate was elevated at 128 BPM. The rest of her vital signs were within normal limits. AA was observed sitting at a table in front of food and not eating nor moving; she then stood up, turned around in a circle and sat back down. She had minimal oral intake this day. Haloperidol continued at 4 mg p.o./i.m. for psychotic symptoms and lorazepam 1 mg p.o./s.l./i.m. BID for agitation.

On Day 9, AA was formally diagnosed with catatonia. In retrospect, AA was exhibiting various catatonic symptoms throughout days 1-8 of her admission, including manneristic speech (speaking in a robotic-like fashion), perseveration, verbigeration, rigidity, negativism, withdrawal, ambitendency, and gegenhalten; all of which resolved by Day 9 with the regular lorazepam. However, on Day 9 she continued to have somewhat deranged vital signs with an elevated heart rate at 150 BPM and elevated blood pressure at 145/93 mmHg. The rest of her vital signs were within normal limits. The remaining antipsychotic was discontinued as it can worsen catatonia and is a risk factor for NMS. Additional lorazepam at 1–2 mg s.l. every 1 to 2 h (q1–2H) was added as needed (PRN) for symptoms of catatonia. She received one dose of 1 mg in addition to her BID dosing, making a total of 3 mg of lorazepam in 24 h.

On Day 10, AA's psychotic symptoms resolved, with catatonic symptoms appearing to have nearly completely resolved; her heart rate was elevated at 110 BPM and her blood pressure was elevated at 145/100 mmHg. The rest of her vital signs were within normal limits. Lorazepam 1 mg p.o./i.m. three times daily (TID) was initiated for ongoing treatment of catatonia, and she did not require any PRN doses. BFCRS was 2 for tachycardia and elevated blood pressure.

On Day 11, aside from an elevated heart rate at 108 BPM, no other symptoms or signs of catatonia were appreciated. No psychosis was present. The rest of her vital signs were within normal limits. Lorazepam was continued at 1 mg p.o./i.m. TID. BFCRS was 1 for tachycardia.

On Day 12, aside from an elevated heart rate between 110 and 147 BPM, no signs or symptoms of psychosis or catatonia were appreciated. The rest of her vital signs were within normal limits. Lorazepam was increased to 1 mg p.o./i.m./s.l. BID and 2 mg p.o./i.m./s.l. qHS to prevent further breakthrough catatonic symptoms. BFCRS was 1 due to tachycardia.

On Day 13, aside from tachycardia of 103 BPM, all psychotic and catatonic symptoms remained in remission. The rest of her vital signs were within normal limits. BFCRS was 1 due to tachycardia. AA's final diagnosis was unspecified psychosis and unspecified catatonia. The patient was discharged home on lorazepam at 1 mg p.o./i.m./s.l. BID and 2 mg p.o./i.m./s.l. qHS. The risk of dependence and tolerance with long-term benzodiazepine use was discussed with AA.

The lorazepam dose was slowly titrated down over 3 months in the community. Initially, this period was planned to be 1-month, but AA was worried about returning catatonia. AA reached out to her general practitioner for another prescription of lorazepam 1 mg p.o. b.i.d. after one month of tapering. Therefore, her outpatient psychiatrist restarted the tapering process. During this period, she was also maintained on quetiapine 25–50 mg p.o. b.i.d. PRN for lingering anxiety and related difficulty initiating sleep. At the 4-month follow-up, she remained in remission from catatonia and psychosis with a successful taper of lorazepam.

## Discussion

This report describes a case of catatonia associated with COVID-19 treated with lorazepam. To the authors' understanding, there have only been seven other reports globally on this emerging clinical presentation (Scheiner et al., 2021; Sakhardande et al., 2022; Torrico et al., 2021; Caan et al., 2020). The patient initially presented with symptoms of psychosis that did not respond to antipsychotics. Although it was not initially realized, in retrospect, the patient had been demonstrating catatonic symptoms throughout the initial days of her admission, including manneristic speech, perseveration, verbigeration, rigidity, negativism, withdrawal, ambivalence, and gegenhalten. With increasing clinical suspicion due to evolving signs and symptoms, she was subsequently diagnosed with and successfully treated for catatonia. The catatonia and psychosis resolved with the withdrawal of antipsychotics and initiation of lorazepam. We believe her past psychiatric history (notably undiagnosed anxiety) and family psychiatric history may have predisposed her to catatonia post COVID-19 infection.

Previously, discussions regarding neuropsychiatric sequelae of COVID-19 have focused on depression, anxiety, post-traumatic stress disorder, fatigue, and sleep disturbances (Schou et al., 2021). There has been a systematic review regarding neuropsychiatric sequelae of COVID-19, however, this has largely shown an increased incidence of anxiety and depression (Schou et al., 2021). Interestingly, there have been some reports showing increased insomnia and psychotic diagnosis following COVID-19 (Schou et al., 2021). Overall, patients with more severe disease and longer symptom duration are at a higher risk of these psychiatric sequelae (Schou et al., 2021). In this case, our patient was female and had symptoms for well over three weeks, which may have put her at higher risk.

This case illustrates two important points. First, clinicians caring for patients with acute psychiatric conditions should exclude recent COVID-19 infection. Hospital screening for COVID-19 focuses on reducing the spread of infection to limit serious disease and death, reduce healthcare demand, and limit the need for more restrictive public health measures (Government of Canada, 2022). Generally, common symptoms such as fever, cough, runny nose, myalgia, and fatigue, are used to screen patients for COVID-19 (Government of Canada, 2022). Therefore, patients with presentations that are seemingly exclusively psychiatric may be missed by these screening measures. Second, clinicians caring for patients diagnosed with COVID-19 should consider a diagnosis of catatonia on the differential if there is a recent change in behaviour, motor function, or mental status. As the saying goes, hindsight is 20/20. In this case, the team found many signs of catatonia when reviewing the patient's presentation and daily progress in retrospect. Therefore, a high index of suspicion is necessary for the correct diagnosis and treatment of catatonia as a sequela of COVID-19. As previously discussed, many patients with COVID-19 infection have neuropsychiatric sequelae and atypical presentation.

We add to the literature indicating catatonia as a potential neuropsychiatric sequela of COVID-19. Delayed catatonia diagnosis is associated with higher morbidity and mortality (Llesuy et al., 2018). Therefore, increased awareness of this potential association will be important for early identification and treatment.

## Patient consent

All identifying patient information has been removed/altered.

## Declarations of Competing Interest

The authors of this paper have no conflict of interest to declare.

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