Catatonia After COVID-19
A Case Series

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Abstract: Coronavirus disease 2019 (COVID-19) has affected more than a hundred million people worldwide. In addition to the devastating number of deaths caused by this disease, it can cause significant morbidity in some survivors. The understanding of the morbidity associated with COVID-19 is rapidly evolving. This report describes 3 cases of catatonia associated with COVID-19. Catatonia is easily confused with other forms of delirium but if recognized can be effectively treated. We hope that awareness gained from these cases would help clinicians better recognize and diagnose catatonia following COVID-19 infection.

Key Words: catatonia, COVID-19, ECT, SARS-CoV-2

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Coronavirus disease 2019 (COVID-19), which is caused by the SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2) virus, has thus far infected many millions of people over the world and has had a drastic social and economic impact.

As medical knowledge has grown, it has become apparent that COVID-19 has significant impacts on the brain. These neuropsychiatric symptoms can include cognitive deficits (often described as "brain fog"), cerebrovascular events, encephalopathy, anxiety, depression, and psychosis.[1] There is some case-report level evidence that the development of catatonia may be an additional risk.[2]

The *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition* defines catatonia as the presence of 3 or more of the following symptoms: catalepsy, waxy flexibility, stupor, agitation, mutism, negativism, posturing, mannerisms, stereotypies, grimacing, echolalia, and echopraxia. Catatonia is a complex neuropsychiatric syndrome that can be secondary to psychiatric illness or medical condition. Some patients with catatonia respond to benzodiazepines, and electroconvulsive therapy (ECT) is usually considered as the second line of treatment.

Catatonia may often be confused with similarly presenting disorders, such as delirium or akinetic mutism, resulting in underreporting of a treatable syndrome. It is crucial that cases of catatonia are recognized early and treated appropriately to avoid unnecessary morbidity and mortality. We describe 3 cases of catatonia associated with COVID-19 and each patient's treatment course.

CASE 1

A 36-year-old woman with a history of bipolar disorder, posttraumatic stress disorder, and chronic kidney disease presented with suicidal ideation. She had no respiratory symptoms but tested positive on a SARS-CoV-2 polymerase chain reaction test. Once admitted, she was uncooperative with care and minimally verbal and had minimal oral intake. Her laboratory test results were unremarkable other than a low thiamine level, which was treated with intravenous (IV) thiamine. On day 3, she became obtunded with nystagmus, not responsive to noxious stimuli. Computed tomography of the head was unremarkable. Because of suspicion for catatonia, lorazepam challenge was done, and within 15 minutes, she was sitting up and speaking. At this time, she was noted to display negativism, posturing, poor oral intake, mutism, and tachycardia, and a presumptive diagnosis of catatonia was made. She was started on lorazepam IV and valproate IV, which improved her oral intake and posturing.

She had no respiratory symptoms or elevation in inflammatory markers; thus, on day 14, she was transferred to inpatient psychiatry, and her lorazepam was increased to 8 mg/d. She was also treated with olanzapine to target underlying psychosis. Because of lack of improvement, a lumbar puncture was performed on day 31 with unremarkable results, including paraneoplastic and autoimmune panels. She did not show clear improvement until day 50 and slowly began to be able to communicate verbally and have adequate oral intake, and the mutism, negativism, posturing, poor intake, and tachycardia resolved. She was continued on valproate and a standing dose of 6 mg of lorazepam and was discharged nearly 2 months after admission.

CASE 2

A 69-year-old woman with a history of bipolar II disorder was hospitalized for 10 days due to COVID-19 pneumonia, treated with remdesivir and dexamethasone and discharged to a rehabilitation facility. Patient then developed an altered mental status, became nonverbal and incontinent, and was transferred to our facility for further workup. Patient underwent an extensive workup, including cerebrospinal fluid with autoimmune and paraneoplastic panels. No pathological findings were detected.

During hospitalization, patient had waxing and waning of mental status and manifested paranoid thought content and auditory and visual hallucinations. COVID encephalitis and seronegative autoimmune encephalitis were both considered, and patient was treated with a course of IV immunoglobulin without any notable improvement.

Upon initial psychiatric evaluation, patient was thought to have delirium but subsequently showed signs of catatonia including echolalia, staring, posturing, stereotypy, mannerisms, and negativism. A lorazepam challenge was done, which produced improvements in the posturing and stereotypy, and IV lorazepam treatment was continued. Despite some improvement in catatonic symptoms, her executive function remained poor, and she additionally manifested a labile affect, pressured speech, hypersexuality, and poor judgment. Bitemporal ECT using a MECTA 5000Q device (MECTA Corporation, Tualatin, OR) with a pulse width of 0.5 millisecond was added with rapid and significant improvement in executive function and mood symptoms for a total of 6 treatments. She was discharged on day 45 having returned to her baseline.

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CASE 3

A 74-year-old man with a history of major depressive disorder, diabetes mellitus, splenomegaly, and Barrett esophagus presented to our emergency room with a recent decrease in appetite, increased fatigue, dysphoria, dyspnea, and cough and was diagnosed with COVID-19.

Patient was treated with remdesivir and dexamethasone. He developed hyponatremia attributed to syndrome of inappropriate secretion of antidiuretic hormone secondary to COVID pneumonia. Patient was later found to have increased opacities on chest radiograph, which was treated with antibiotics, and he was discharged.

Patient was admitted 3 days later because of suicidal ideation; he was found with a suicide note, holding a knife to his wrist. Patient was only able to provide brief and vague responses to questions. On subsequent days, he started to verbalize paranoid ideation, endorsed auditory hallucinations, and had poor sleep. He then started to become lethargic with poor eye contact. Low-dose second-generation antipsychotics were started for the patient. Patient then developed symptoms of catatonia, including negativism, stupor, mutism, and rigidity. A few hours after a lorazepam challenge patient became responsive, able to converse and follow commands, and denied any memory of the earlier events. Lorazepam treatment continued, and ECT using a MECTA 5000Q device (MECTA Corporation, Tualatin, OR) was initiated because of only a partial response. He received a total of 8 bitemporal treatments with a pulse width of 0.5 millisecond. Patient showed dramatic improvement and had remission of all catatonic and mood symptoms and was discharged after 16 days.

DISCUSSION

Catatonia has been associated with a wide variety of psychiatric and medical conditions.[1] Its diagnosis can be challenging, and it is often underdiagnosed. This problem may be exacerbated in case of COVID-19, as many of the features and complications of the disease are still unknown. As the medical community understands more about COVID-19, the presence of neuropsychiatric sequelae is becoming evident.

In each of the cases presented, the patient had a psychiatric history but no history of psychiatric hospitalization or catatonia, suggesting a deviation from their typical psychiatric presentation potentially attributable to COVID-19. However, these cases presented with varying degrees of respiratory symptoms, ranging from no symptoms to hospitalization. Prior studies have reported primarily on neuropsychiatric illness in those patients with COVID-19 respiratory symptoms requiring hospitalization.[2] However, COVID-19 is also associated with many mild and asymptomatic infections. These cases present the possibility that neuropsychiatric manifestations of COVID-19 may manifest independent of the severity of respiratory illness or the possibility of coincidental infection with the virus.

Certain treatments for COVID-19 may also complicate neuropsychiatric presentations. For example, dexamethasone treatment may be associated with neuropsychiatric adverse effects. In this series, one patient did not receive dexamethasone at all, and the other two had neuropsychiatric symptoms that lasted well beyond the administration of dexamethasone. As such, it is unlikely that these cases can be explained by steroid induction alone.

The overlapping features of catatonia and delirium may play a role in the limited recognition of catatonia in medically ill patients. Delirium is often considered when a medically ill patient presents with a waxing-and-waning mental status. However, catatonia may have a similar presentation in regard to mental status. It may be comorbid or distinct from delirium and cannot be distinguished without a thorough assessment and workup. An important distinction, however, is that lorazepam and ECT are highly effective in the treatment of catatonia. Underdiagnoses may result in prolonged illness for individuals with a highly treatable disorder.

While the available cases emphasize the importance of considering catatonia in the setting of COVID-19, the data are insufficient to draw any conclusions about the frequency of catatonia in patients with COVID-19, or whether COVID-19 is a specific risk factor for catatonia. Given the large number of patients suffering from COVID-19 and its severity, one possibility is that COVID-19 can trigger catatonia as a nonspecific stressor in patients who are otherwise susceptible to develop catatonia. However, potential mechanisms have been proposed connecting coronavirus and neuropsychiatric symptoms. This virus may have direct neurotoxic effects as glial cells and neurons express angiotensin-converting enzyme 2 receptors providing a way for the virus to spread.[3] There is also a significant inflammatory response to the COVID-19 virus, which may precipitate neuroinflammatory processes and/or compromise the blood-brain barrier leading to central nervous system dysfunction.[4] Additional theories have also been proposed including postinfectious autoimmunity, immune cell transmigration, and hypoxic brain injury. There are also numerous reports of cross-reacting antibodies against host antigens, particularly the development of anti–*N*-methyl-D-aspartate receptor encephalitis both with and without respiratory involvement, making it imperative that autoimmune and paraneoplastic panels are performed.[5] Further studies are needed to provide complete information regarding prevalence, risk factors, and mechanisms for the relationship between COVID-19 and catatonia. However, the current data demonstrate that it is imperative that catatonia be a part of the differential diagnosis for patients with COVID-19 and altered mental status to ensure that a highly treatable condition does not go unrecognized.

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