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Case Report

A Case of Concurrent Delirium and Catatonia in a Woman With Coronavirus Disease 2019

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Introduction

Delirium is a syndrome of acute brain dysfunction caused by an underlying medical condition or toxic exposure and characterized by deficits in attention, awareness, and cognition.\(^1\) Because it is the most common psychiatric syndrome observed in medically hospitalized patients\(^2\) and a known predictor of excess mortality, length of stay, long-term cognitive impairment, and increased cost of care in critically ill patients,\(^3\)–\(^6\) delirium is routinely screened for in intensive care unit (ICU) settings.

Catatonia\(^7\) is a potentially lethal syndrome characterized by prominent motor, behavioral, and affective abnormalities that can occur in a wide range of both psychiatric and medical illnesses; however, it is an underrecognized cause of altered mental status in the medically ill population.\(^8\) Many have recognized the presence of catatonic signs in patients with delirium,\(^9\)–\(^11\) and there is increasing evidence suggesting that delirium and catatonia can co-occur in up to one-third of critically ill patients.\(^9\)\(^,\)\(^11\)

The novel coronavirus, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), causes the coronavirus disease 2019 (COVID-19), which is primarily characterized by acute pneumonia; however, central nervous system insults have been described.\(^12\)\(^,\)\(^13\) In patients with COVID-19 who present with respiratory distress, around half require intensive care.\(^14\) In addition to respiratory failure, many hospitalized patients with COVID-19 will develop delirium and other neurological and neuropsychiatric complications,\(^13\)\(^,\)\(^15\)–\(^17\) sequelae which may be downstream effects of direct nervous system involvement by SARS-CoV-2.\(^18\) One case report has described catatonia in a man with COVID-19\(^19\); however, to our knowledge, COVID-19 has not previously been associated with co-occurring delirium and catatonia. We present a case of concurrent delirium and catatonia in a woman hospitalized with COVID-19 pneumonia.

Case

Mrs. K is a 70-year-old female with no prior psychiatric history and prior medical history of diabetes mellitus type 2, end-stage renal disease on hemodialysis, hypertension, coronary artery disease previously complicated by non-ST segment elevation myocardial infarction, heart failure with preserved ejection fraction, hypothyroidism, and a history of transient ischemic attack who presented to the hospital with a 4- to 5-day history of cough, fatigue, fever, and recent positive test result for SARS-CoV-2 at a local clinic. Upon presentation, her workup was concerning for COVID-19 pneumonia, and she was admitted medically for management. Her hospital course was...
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complicated by acute hypoxemic respiratory failure, non-ST segment elevation myocardial infarction, physical deconditioning, fever, and altered mental status. On hospital days (HD) 2 and 3, she was noted to appear slightly confused. A computed tomography scan of her head was obtained for evaluation of altered mental status, which did not reveal any acute intracranial pathology. By HD 4, she reportedly was more somnolent, less interactive, and disoriented; had delayed responses to questions; and was noted to be febrile that night, which prompted her team to obtain blood cultures and to initiate broad-spectrum antibiotics on HD 5. Between HD 5 and 8, her level of consciousness fluctuated, and she was intermittently febrile and had increased oxygen requirement. On HD 8, she was no longer febrile, her oxygen requirement had stabilized, and the blood cultures were negative, so broad-spectrum antibiotics were discontinued. She remained disoriented and less interactive, and on HD 10, she refused oxygen supplementation without clear explanation. Her disorientation and difficulty with engagement continued, and on HD 12, she refused her morning medications, removed her intravenous line, and refused to participate in the physical examination or answer questions. On HD 12, the psychiatry consultation-liaison (C-L) service was consulted to evaluate for the presence of catatonia, given her persistent altered mental status, withdrawal, and refusal of medications and treatment. Notably, upon review of her medical chart, there had been no prior mention of the term “delirium,” nor was there documentation of any Confusion Assessment Method (CAM) assessments, despite the use of language in notations in her chart describing features of delirium throughout her hospitalization. This could be due to failure to recognize less overt delirium or more likely a failure to document that the condition was present.

On examination, Mrs. K exhibited several signs of catatonia, including immobility, mutism, grimacing, catalepsy, echolalia, stereotypy, verbigeration, rigidity, negativism, waxy flexibility, automatic obedience, and gegenhalten. She also exhibited labile blood pressure throughout that day not attributable to another cause. The Bush-Francis Catatonia Rating Scale (BFCRS) was administered. The Bush-Francis Catatonia Screening Instrument comprises the first 14 items of the 23-item BFCRS. The Bush-Francis Catatonia Screening Instrument score is reported as a tally of the number of items present in items 1–14, while the BFCRS is reported as the total severity score of all 23 items. Mrs. K’s initial Bush-Francis Catatonia Screening Instrument/BFCRS score was 11/21, indicating the presence of catatonia. Administration of the Confusion Assessment Method for the ICU was positive for features of fluctuating course of mental status, inattention, altered level of consciousness, and disorganized thinking, indicating the concurrent presence of delirium. Indeed, Mrs. K met Diagnostic and Statistical Manual of Mental Disorders Fifth Edition (DSM-5) criteria for delirium, based on disturbances in attention and awareness which developed over days, represented a change from her baseline, and fluctuated during the course of a day, as well as disturbance in cognition. It should be noted that Mrs. K also met DSM-5 criteria for Catatonic Disorder Due to Another Medical Condition, except for criterion D which specifies that the catatonia does not occur exclusively during the course of a delirium. A trial dose of 0.5 mg of intramuscular lorazepam was administered and resulted in modest improvement in Bush-Francis Catatonia Screening Instrument/BFCRS score to 7/12, with most notable improvements in mutism, echolalia, rigidity, waxy flexibility, and automatic obedience, as well as mild improvements in features of delirium, most notably attention and level of consciousness. She notably did not exhibit any worsening signs of delirium after administration of lorazepam. With presumed diagnoses of both catatonia and delirium, Mrs. K was treated with scheduled 0.5 mg of oral or intravenous lorazepam q8h. She received 8 total doses of lorazepam 0.5 mg between HD 12 and 15 with a corresponding improvement in signs of both delirium and catatonia. She did not receive neuroleptics during her hospitalization.

When she was reassessed by the psychiatry C-L service on HD 14, catatonia was noted to have improved, although she still exhibited negativism and mutism and continued to exhibit features of delirium including reduced arousal and inattention. As such, lorazepam was tapered to 0.5 mg BID on HD 14, which led to small improvements in delirium on HD 15, as evidenced by improving alertness and orientation, and her mild symptoms of catatonia remained stable. Lorazepam was subsequently discontinued on HD 16, without the return of catatonic signs; however, she continued to exhibit evidence of resolving delirium, primarily inattention, throughout the remainder of her 17-day hospitalization. Given continued physical
deconditioning, it was recommended that Mrs. K was discharged to a skilled nursing facility, but both she and her family preferred for her to be discharged home where she would receive 24-hour care and supervision. Mrs. K was able to be discharged home on HD 17.

**Discussion**

We describe a case of co-occurring delirium and catatonia in a woman with COVID-19, who responded favorably to repeated doses of low-dose lorazepam. While delirium is routinely screened for in medically ill patients, catatonia is often underrecognized in this population, despite a recent refocus on the co-occurrence of these 2 conditions.9-11 The ramifications of unrecognized and untreated catatonia can be serious. In some cases, untreated catatonia can progress to its most severe form, malignant catatonia, which is characterized by fever, severe autonomic instability, significant muscle rigidity, and altered mental status, which may result in multiorgan dysfunction and death.20 It is therefore crucial that catatonia remain on the differential diagnosis of altered mental status in patients with COVID-19 and that formal evaluation for catatonia be performed when it is suspected (e.g., prominent motor abnormalities, mutism, withdrawal, or acute worsening of symptoms after exposure to a neuroleptic, and so on). Evidence suggests there is overlap of delirium and catatonia in the medically ill population that up to one-third of critically ill patients meet criteria for both delirium and catatonia9,11 and that delirious patients may be particularly vulnerable to the development of catatonia.21 In the case of a patient with persistent delirium, suspicion for comorbid catatonia should increase, and a BFCRS should be performed.

We are aware of one prior case report of catatonia in a man hospitalized for COVID-19 with no prior psychiatric history.19 To our knowledge, we describe the first case of COVID-19 associated with co-occurring delirium and catatonia. In addition to a positive Confusion Assessment Method ICU with features of fluctuating mental status, inattention, altered level of consciousness, and disorganized thinking. Mrs. K met DSM-5 criteria for delirium. She also exhibited multiple signs and symptoms of catatonia, with a BFCRS score of 11/21, indicating the concurrent presence of catatonia. Were it not for the exclusionary criterion D, which specifies that the catatonia cannot occur exclusively during the course of a delirium, Mrs. K would have also met DSM-5 criteria for the diagnosis of Catatonic Disorder Due to Another Medical Condition.

There have been several described neuropsychiatric sequelae of COVID-19 illness.15,17 While the pathophysiology of catatonia and delirium remains unclear, potential mechanisms leading to both patients with COVID-19 might include direct neurotoxic effects from the virus22,23; lack of effective blood oxygenation due to acute hypoxemic respiratory failure, leading to brain tissue hypoxia24-26; circulating cytokines and acute phase proteins in systemic inflammation activating the vasculature, increasing blood-brain barrier permeability, and activating microglial cells, resulting in neuroinflammation27-29; and inflammation promoting hypercoagulation, resulting in cerebrovascular disease and other organ system failure.30-32 Iatrogenic and environmental factors such as prolonged mechanical ventilation, the use of sedatives, immobilization, and social isolation and separation from family members only further increase the risk of development of delirium and therefore catatonia in these patients.16 Mrs. K’s lingering inattention was likely multifactorial. Given her age and vascular risk factors, it is likely that she had premorbid cognitive impairment, increasing her risk for a prolonged course of delirium, which in turn increases the likelihood that she will experience further cognitive decline. In addition, new cognitive impairment has been associated with COVID-19 infection.33

It is important to note that management of delirium versus catatonia in medically ill patients is distinct with regard to the use of psychopharmacologic agents. Delirium is primarily managed by treatment of the underlying medical conditions, optimization of environmental factors, and avoidance of benzodiazepines and other psychoactive medications. Antipsychotics are frequently used for the management of agitation or psychotic symptoms of delirium (e.g., hallucinations, delusions, and so on), but most studies show that the use of antipsychotics does not alter the duration or severity of delirium.34-36 In the ICU, the ABCDEF bundle (Assess, prevent, and manage pain; Both spontaneous awakening and breathing trials: Choice of analgesia and sedation; Delirium assess, prevent, and manage; Early mobility and exercise; Family engagement/empowerment) is a multicomponent safety intervention that has been shown in
over 20,000 patients to yield significant improvements in clinical outcomes such as mortality, length of stay, and effective reductions in delirium duration.37,38

The treatment of catatonia includes the use of benzodiazepines as first-line agents as well as a general avoidance of antipsychotics, given their potential to worsen catatonia and precipitate malignant catatonia. As the use of benzodiazepines can worsen delirium, electroconvulsive therapy is another treatment option to consider in patients with comorbid catatonia and delirium.39 Similar to delirium, the management of catatonia often involves a medical workup and treatment of any underlying medical or neurologic causes.10 Nonpharmacologic treatments for delirium may also improve symptoms of catatonia, given their frequent comorbidity, although this has not been studied. Because Mrs. K exhibited persistent altered mental status, withdrawal, and refusal of medications despite treatment of her underlying medical conditions, there was concern from her primary medical team for the presence of catatonia. As her examination was unequivocally positive for features of both delirium and catatonia, the decision was made to perform a lorazepam challenge with low-dose lorazepam so as not to potentially worsen her symptoms of delirium. Interestingly, symptoms of both catatonia and delirium improved with the lorazepam challenge, and her catatonia fully resolved with scheduled treatment with lorazepam over several days. While certain features of delirium also improved while she received scheduled lorazepam, primarily fluctuations in mental status, level of consciousness, and disorganized thinking, her inattention was slower to improve and still present by the time she was discharged. While it may seem counterintuitive that features of her delirium improved with treatment with lorazepam, one possible explanation for this could be that by treating the catatonia with lorazepam, the delirium was indirectly being treated, given that catatonia and delirium co-occur frequently and that the mechanisms underlying the 2 conditions may be shared. The exact mechanism(s) by which administration of lorazepam improves catatonia is not fully understood. One possibility is that at least in stuporous or akinetic catatonia, there is orbitofrontal cortex dysfunction which leads to poor connectivity in the medial prefrontal cortices, which is partially reversed by lorazepam administration.40,41 In medically ill patients, during heightened periods of physiological stress (systemic, neuroinflammation, and so on), there is activation of the sympathetic nervous system, leading to increased noradrenergic tone. Under such stress, there is activation of the amygdala, which in turn activates the locus coeruleus, triggering elevated noradrenergic tone, which has been implicated in (at least partially) the inattention frequently seen in patients with delirium.42 Theoretically, by decreasing this physiological fear response (and overall noradrenergic tone) through administration of lorazepam to treat her catatonia, her attention and other nonspecific symptoms of delirium were indirectly improved, although further research is needed to clarify the exact pathological drivers of delirium and catatonia, and therefore their treatment(s), in patients with COVID-19.

**Conclusion**

Mrs. K’s case highlights that delirium and catatonia represent 2 manifestations of acute brain dysfunction that can co-occur in the context of acute COVID-19 illness. Features specific to COVID-19, both pathophysiological and environmental, create a unique set of conditions that predispose patients to co-occurring delirium and catatonia. Catatonia and co-occurring delirium may improve with administration of low-dose lorazepam in selected patients.

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