An Agitated Patient With COVID-19 Infection and Early-onset Alzheimer Disease

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Abstract: Encephalopathy, delirium, and agitation are documented symptoms of coronavirus disease (COVID-19) infection, but research into the management of agitation in the setting of COVID-19 and pre-existing neuropsychiatric disease is ongoing. We present a 55-year-old male patient with early-onset Alzheimer disease and deteriorating mental and functional status who presented to our institution with agitation and persistent COVID-19 positivity on polymerase chain reaction testing. His agitation was improved through pharmacologic optimization including the avoidance of benzodiazepines and initiation of clonidine and prazosin, which temporally coincided with the resolution of his nearly 2-month-long COVID-19 positivity.

Key Words: early-onset Alzheimer disease, agitation, aggression, sedation, COVID-19, encephalopathy

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Preliminary studies have described the neurological manifestations of coronavirus disease (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS CoV-2), as encephalopathy or altered sensorium.1 An even more uncharted territory is the intersection between COVID-19 and pre-existing neuropsychiatric comorbidities. Patients with dementia are not only at high risk for morbidity and mortality, but are also more susceptible to mental health sequelae of COVID-19.2–3 We present a patient with early-onset Alzheimer disease (AD) who presented to our institution with agitation and COVID-19 infection.

CASE DESCRIPTION

Mr R. is a 55-year-old male with early-onset AD diagnosed in 2014 on the basis of history, exam, brain magnetic resonance imaging, fluorodeoxyglucose-positron emission tomography pattern typical of AD, and cerebral spinal fluid amyloid and tau protein markers after ruling out several metabolic, autoimmune, infectious, and other etiologies. Genetic testing did not demonstrate any known mutations in genes associated with early-onset AD and his disease was thus suspected to be sporadic. Because of progressive cognitive and functional decline, as of August 2019 his Short Test of Mental Status score was 15/38 and he was living in a group home. In September 2020, he was hospitalized in a geropsychiatric unit for new onset aggression, where he was found to be positive for SARS CoV-2, though asymptomatic from a respiratory perspective. However, after his COVID-19 infection, his mentation continued to worsen and he was minimally responsive with disorganized, flailing movements. He had paradoxical reactions to quetiapine, olanzapine, and ketamine, manifesting as aggression and akathisia. He was discharged to a new group home on dextromethorphan-quinidine, galantamine, lorazepam, and trazodone.

In November 2020, 1 week after his discharge, he once again became aggressive and presented to our emergency department. He was afibrile and hemodynamically stable but attempted to strike staff members. His SARS CoV-2 polymerase chain reaction (PCR) test at our institution was positive. Other laboratory studies showed only mild stable normocytic anemia. Computed tomography imaging of his brain without intravenous contrast demonstrated moderate diffuse parenchymal atrophy with enlarged ventricles and sulci, which were slightly increased from 1 year prior, but with no acute intracranial abnormality (Fig. 1). His home medications were continued with lorazepam ordered as needed for agitation.

The patient’s hospital course lasted 23 days. He experienced significant combative behavior soon after admission and required soft restraints and frequent lorazepam administration which was minimally effective. After consultation with neurology and psychiatry, he was started on clonidine 0.1 mg twice daily for agitation. Trazodone was initially continued but mirtazapine and trazodone were alternated several times during his admission with no major symptom relief. He responded favorably to clonidine 0.1 mg bid and experienced about 1 h of sedation and anxiolysis. Clonidine was therefore increased to 0.2 mg bid which he could not tolerate because of hypotension.

Pharmacologic interventions had thus far proved insufficient to control his agitation and he had another episode of aggression to nursing staff, resulting in denial of his transfer to memory care. Citalopram was initiated for long-term agitation control. We prescribed prazosin 1 mg nightly with plans to increase this dose every 2 to 3 days until reaching a target dose of 6 mg nightly. Unfortunately, because of hypotension, prazosin dose could not be increased further. Lorazepam was discontinued.

With discontinuation of lorazepam and initiation of prazosin, his agitation improved and soft restraints were removed. The patient underwent evaluation by local memory care units. During his stay, he had 3 SARS CoV-2 PCR tests which were positive and a fourth final negative PCR (over 2 months after his original infection), eliminating the last barrier to discharge. At the conclusion of his hospital course, his psychiatric regimen included citalopram, clonidine, galantamine, melatonin, dextromethorphan-quinidine, and prazosin. Upon discharge to a memory care unit, he was sleeping 6 hours per night, ambulatory, but requiring full assistance with activities of daily living.

DISCUSSION

As the manifestations of COVID-19 infection include widely distributed physiological effects, so does the care of patients with severe infection require familiarity with rapidly evolving research. Management of agitation is an indispensable part of care for patients with AD. Here we present our management of a patient with early-onset AD who subsequently experienced COVID-19 infection with persistent PCR positivity, a lack of hallmark disease symptoms, and worsening agitation.

Citalopram was initiated off-label during hospitalization based on its demonstrated calming effect in patients with AD, but a more rapid anxiolytic and sedating strategy was needed.4 His previous adverse reactions to antipsychotics and ketamine complicated our management. While antipsychotics are beneficial and mortality, but are also more susceptible to mental health sequelae of COVID-19 and pre-existing neuropsychiatric comorbidities.

An even more uncharted territory is the intersection between COVID-19 and pre-existing neuropsychiatric comorbidities. Patients with dementia are not only at high risk for morbidity and mortality, but are also more susceptible to mental health sequelae of COVID-19.2–3 We present a patient with early-onset Alzheimer disease (AD) who presented to our institution with agitation and COVID-19 infection.
of his poor tolerance of antipsychotic medications. We do maintain that a trial was clinically reasonable because the recommendations proposed by Baller et al. Clonidine is sometimes used off-label in intensive care units as an alternative sedative agent, particularly when transitioning from dexmedetomidine. It has successfully been adopted for this purpose in mechanically ventilated patients with COVID-19. Our patient responded favorably to clonidine experiencing a marked improvement in agitation and sleep, and the ability to further clarify the extent of central nervous system involvement of COVID-19 is limited. Despite this fact, the resolution on PCR of the patient’s COVID-19 infection also temporally coincided with the improvement of his symptoms, so we attribute his improvement to the combined resolution of his COVID-19 infection and appropriate adjunctive psychiatric medications.

CONCLUSION

As global understanding of the pathophysiology of the neuropsychiatric symptoms of COVID-19 infection evolves, formulation of standardized and validated guidelines will be essential to address new symptoms which arise in patients with underlying dementia and to manage existing symptoms in the setting of acute illness. Further research is required to determine the best approach for treating agitation or delirium in patients with COVID-19 and comorbid neuropsychiatric disease.

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FIGURE 1. Computed tomography of the brain without intravenous contrast obtained on admission demonstrated moderate diffuse parenchymal atrophy with enlarged ventricles and sulci, which were slightly increased from 1 year prior, but with no acute intracranial abnormality.