

Case Report

Neuropsychiatric Presentation of COVID-19: A Case Report of Disinhibition in an Acute SARS-CoV-2 Infection

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Abstract

Description

Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) viral infection is notable for a high degree of symptom diversity. Emerging evidence suggests viral invasion of the central nervous system. Therefore, serious neurological and psychiatric manifestations are anticipated. We present the case of a 67-year-old male physician who has a history of stable bipolar disorder for decades and was recently hospitalized for persistent COVID-19 symptoms with documented positive serology. He presented with new and acute onset neuropsychiatric symptoms of disinhibition proximate to the viral infection. We postulate neuroinvasion as the putative origin of the patient's psychiatric instability. Furthermore, an investigation is needed to expand upon our understanding of the potential for neuropsychiatric morbidity related to SARS-CoV-2 for prompt diagnosis and appropriate management. There are also no current studies addressing the risks for neurological and psychiatric symptomatology in SARS-CoV-2 infected patients with persistent chronic mental illness.

Keywords

COVID-19; SARS-CoV-2; coronavirus infections; coronavirus infections/complications; virus diseases; neurologic manifestations; neurobehavioral manifestations; bipolar disorder; disinhibition; neuropsychiatric

Introduction

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) presents with commonly known symptoms of fever, cough, sore throat and, in severe cases, respiratory insufficiency or failure.¹ Emerging evidence of neurological symptoms has demonstrated the ability to affect other parts of the body. Reports now indicate associated neurological symptoms, such as anosmia, ageusia and Guillian-Barre syndrome. Other encephalopathic findings include dizziness, headache, delirium, changes in level of consciousness and seizures. Similar to other viral infections, SARS-CoV-2 is involved in the etiology of encephalitis, necrotizing hemorrhagic encephalopathies and ischemic strokes. Therefore, evidence indicates the capability of neuroinvasion.² Mechanisms of damage involve both its direct central nervous system (CNS)

invasion and its indirect effect via inflammation, hypercoagulability, receptor inhibition³ and immune cascade.⁴ The impact of SARS-CoV-2 infection on cranial nerves, blood flow and brain regulatory systems, with resultant severe inflammation and increased risk for permanent lesions, raises concern for significant psychiatric comorbidity.

Case Presentation

The patient is a 67-year-old male with a past psychiatric history of bipolar disorder type I in remission for the last 10 years. The patient had been asymptomatic and fully compliant with lithium monotherapy. His past medical history includes chronic stable small lacunar infarct, familial tremor, hyperlipidemia, benign prostatic hyperplasia (BPH), diabetes mellitus II, renal cell carcinoma and status post partial nephrec-

tomy. The patient presented to the hospital with 3 days onset of midsternal pressure, persistent dry cough, shortness of breath and lower back pain. He was found with bilateral lower lung atelectasis and positive COVID infection (confirmed with COVID IgG and IgM antibody testing). The patient also complained of mood changes that co-occurred with the respiratory symptoms. He noted unusual hyper-verbosity, amicability, sarcasm, mildly decreased impulse control and “emotional disinhibition.” Sleep, appetite and energy remained intact. Due to his concerns about potential stress, he decided to increase his home dose of lithium carbonate from 450 mg daily to 900 mg daily. The patient has always maintained a stable lithium level around 0.5 mEq/L during the previous years. During the admission, the patient denied any other neurological, medical or psychiatric symptoms. He also denied fever, chills, nausea, vomiting, diarrhea, abdominal pain and urinary symptoms. There were no indicators of lithium toxicity or other manifestations of his chronic medical conditions during this hospitalization. Physical exam and laboratory findings are presented in **Table 1**.

Treatment Plan

The patient received supportive treatment during the hospitalization; antibiotics, hydroxychloroquine and steroids were withheld due to all inflammatory markers on labs being within normal limits and chest X-ray indicating only chronic changes. Consultation Psychiatry was consulted due to his distress and disinhibition. Pseudobulbar affect and other psychiatric disorders were ruled out. Brain imaging revealed no acute changes. The patient was discharged with a prescription for lithium 450 mg twice daily, aripiprazole 5 mg daily (initiated to help address disinhibition) and benzonatate for a persistent cough.

Post-Discharge Status and Follow Up

At the 2-week post-hospitalization psychiatric follow-up, the patient reported better mood control. However, he continued to present mini episodes of emotional hypersensitivity with tearfulness, in particular when watching movies and the news or when listening to music. He was not grandiose or hypervocal. Other elements of the MSE mental status examination were unremarkable. His physical condition was notable for a persistent but improving dry

cough. He was afebrile and in no respiratory distress with a pulse oximetry reading of 98% on room air. The lithium carbonate was reduced to 625 mg per day, and aripiprazole was continued at 5 mg per day.

At the 7-week post-hospitalization psychiatric follow-up, the patient achieved complete remission of neuropsychiatric symptoms. The aripiprazole was discontinued, and the dosage of lithium was reduced to his historical dosage of 450 mg per day. The patient was able to recover gradually and successfully from the medical and psychiatric conditions after hospitalization.

Discussion

The association of various viral infections to neuropsychiatric illness is well established. Data supports the association between respiratory viruses, particularly influenza, and neuropsychiatric conditions, including acute encephalopathy (seizures and coma, with or without multiorgan failure) and transient neuropsychiatric disorders (delirium and abnormal behaviors)⁵ such as schizophrenia.^{6,7} Prenatal influenza exposure shows a subsequent heightened risk for the development of schizophrenia, bipolar disorder, autism and mood disorders.⁸ SARS-CoV, the strain responsible for the initial SARS outbreak in 2003, had reported psychiatric morbidities, including persistent depression, anxiety, panic attacks, psychomotor excitement, psychotic symptoms, delirium and suicidality.⁹ Additionally, previous studies have also demonstrated that exposure to the coronavirus may be a comorbid risk factor in neuropsychiatric disease due to the presence of immunoglobulin G (IgG) response in patients with recent onset of psychotic symptoms.¹⁰

SARS-CoV-2 is one of many strains of coronavirus, all of which share the same large, enveloped, nonpigmented positive-sense ribonucleic acid structure and pathway, clinically manifesting most typically in the gastrointestinal and respiratory tracts.¹¹ More recent evidence indicates neurological manifestations, including, but not limited to, headache, disturbed consciousness and paresthesia, in about a third of the affected population.¹² Initially, fatalities were attributed to multiorgan failure with homeostatic dysregulation. Studies now show that CNS involvement, with subsequent brainstem damage-induced respiratory distress, is

Table 1. Physical examination with laboratory findings of the patient with pertinent laboratory values on admission and upon discharge.

Physical Exam		
General Assessment	Awake, alert and oriented. No acute distress.	
Vital Signs	Heart rate: 67 beats per minute	
	Blood pressure: 135/88 mmHg	
	Temperature: 98.1° F	
	Respiratory rate: 16 breaths per minute	
	O ₂ saturation: 98% (ranged from 93%–99%)	
	Body mass index: 28.4 kg/m ²	
Labs	Admission	Discharge
	Platelet count: 141 u/L	Platelet count: 155 u/L
	D-dimer: <200 ng/mLDDU	
	Procalcitonin: <0.05 ng/mL	
	Lipase: 122 U/L	
	C-reactive protein: <0.05 mg/dL	
	Ferritin: 117 ng/mL	
	Troponin: <0.012 ng/mL	
	CMP: unremarkable	
	BUN: 18 mg/dl	BUN: 17 mg/dl
	CR: 0.9 mg/dl	CR: 0.9 mg/dl
	AST: 21 Units/L	AST: 25 Units/L
	ALT: 21 Units/L	ALT: 25 Units/L
	Lithium level: 0.9 mmol/L	
	COVID-19 PCR: Positive	
ECG	Prolonged QTc: 472 ms	
Imaging	Chest X-ray: Bibasilar infiltrates, likely secondary to atelectasis	
Physical Exam	Unremarkable	
Mental Status Exam	Patient is alter, fully oriented, with no confusion, delirium, obsessions, compulsions, hallucinations nor internal stimuli noted.	

potentially one of the major contributors to mortality with CNS involvement leading to advanced mortality rates.^{11,13}

Previous strains of the coronavirus have shown neurotropic potential.¹⁴ The neurotropic nature of the virus is suspected to be most likely via circulatory system exploitation and host cell entrance through the utilization of cellular receptor angiotensin-converting enzyme 2 (ACE2). ACE2 is widespread within the human body, including airway epithelia, vascular endothelia, lung parenchyma, small intestine cells and kidney cells with expression noted in glial cells and neurons. Although common

pathophysiology to all strains of the coronavirus, SARS-CoV-2 holds a 10- to 20-fold higher binding affinity to the ACE2. These factors likely contribute to the neuronal damage, cerebral capillary endothelial rupture and brain bleeding seen in many patients affected by COVID-19.^{11,13,15,16} The similar neurotropic pathophysiology between the two strains with an exacerbated response along with previously reported psychiatric sequelae of SARS-CoV, deem neuroinvasion a plausible postulation of the patient’s psychiatric instability in this case presentation. Our final diagnosis is disinhibition in the context of acute SARS-CoV-2 infection.

Conclusion

We describe neuropsychiatric instability proximate to SARS-CoV-2 infection in a patient with bipolar disorder who had been stable for decades. As he recovered from the infection and his physical symptoms resolved, so too did his psychiatric findings. The authors postulate neuroinvasion and neuroinflammation as the putative origin of the patient's acute psychiatric mood instability. Current clinical guidelines and effective treatment for patients with COVID-19-induced psychiatric disorders do not exist. Continued investigation is needed to expand upon our understanding of the potential for psychiatric morbidity related to SARS-CoV-2 infection for prompt and appropriate diagnosis and management. Furthermore, respiratory symptomatology has been the focus of diagnosis and management in patients infected with SARS-CoV-2. Appropriate comprehensive screening and clinical examination that includes the psychiatric and neurological systems in patients infected with SARS-CoV-2 is imperative and perhaps mandatory in patients with previous neuropsychiatric complaints.

Conflicts of Interest

The authors declare they have no conflicts of interest.

Drs. Abramson, Alvarez, and Fisher are employees of Aventura Hospital and Medical Center, a hospital affiliated with the journal's publisher.

This research was supported (in whole or in part) by HCA Healthcare and/or an HCA Healthcare affiliated entity. The views expressed in this publication represent those of the author(s) and do not necessarily represent the official views of HCA Healthcare or any of its affiliated entities.

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