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Case Report

Command Suicidal Hallucination as Initial Presentation of Coronavirus Disease 2019 (COVID-19): A Case Report

Junaid Mirza, M.D., Amvrine Ganguly, M.D., Alla Ostrovskaya, M.D., Ph.D., Alan Tusher, M.D., Ph.D., Ramaswamy Viswanathan, M.D., D.M.Sc.

Introduction

At the time of writing this case report in the second week of May 2020, there have been 1,409,452 confirmed cases of coronavirus disease 2019 (COVID-19) in the United States and more than 4.5 million confirmed cases worldwide.1 Most patients who have COVID-19 present initially with fever (83–99%), cough (59–82%), fatigue (44–70%), anorexia (40–84%), and shortness of breath (31–40%).2 However, as we begin to learn more about this virus and disease, we are seeing that the signs and symptoms present at illness onset may vary widely. Atypical presentations have been described in the literature, and there have been numerous cases of delayed presentation of fever and respiratory symptoms. One atypical presentation of COVID-19 has been gastrointestinal symptoms, such as diarrhea and nausea, before development of respiratory symptoms.3 Recent literature is beginning to shed light on the impact of COVID-19 on the nervous system. Common neurological features reported include headache, dizziness, anosmia, hypogeusia, and more serious complications during disease progression including seizure and stroke.4 Patients with COVID-19 can also present with encephalopathy and delirium.5 However, to our knowledge, psychiatric symptoms as the initial manifestation of COVID-19 have not been described to date. There is some literature on the relation of psychosis and previous pandemics. In drawing a comparison to the 1918 pandemic caused by the H1N1 virus, the association of influenza and psychoses in patients who were admitted to the Boston Psychopathic Hospital in 1918 was studied by Karl A. Menninger.6 The psychiatric sequelae due to COVID-19 are yet to be discovered. We present in this case report a medically healthy patient with no premorbid psychiatric history who developed command suicidal hallucination as the initial manifestation of COVID-19.

Case Report

Mr. A, a 53-year-old man with no prior medical or psychiatric history presented to the emergency department after an apparent suicide attempt, having ingested an unknown quantity from a bottle of bleach. He was alert and oriented, although mostly uncooperative owing to epigastric pain on the initial examination. He refused to answer most of the primary team’s questions.

Examination of his mouth revealed a right lower lip abrasion with no oropharyngeal injuries or erosions. Per collateral information obtained from his wife who accompanied him, she was bewildered by his action. She reported that her husband had been “healthy, normal, happy, never done anything like this before.” She also stated that he had not complained of any fever, received April 29, 2020; revised May 21, 2020; accepted May 22, 2020.

From the Department of Psychiatry (J.M., A.G.), State University of New York Downstate Health Sciences University, Brooklyn, NY; Department of Psychiatry (A.O., A.T.), Kings County Hospital Center, Brooklyn, NY; Department of Psychiatry and Behavioral Sciences (R.V.), State University of New York Downstate Health Sciences University, Brooklyn, NY. Send correspondence and reprint requests to Junaid Mirza, MD, Department of Psychiatry, State University of New York Downstate Health Sciences University, 450 Clarkson Av, MSC 127, Brooklyn, NY 11203-2098; e-mail: Junaid.mirza@downstate.edu

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cough, or recent illness. She was unsure why he would have ingested bleach. He was not cooperative with the psychiatric interview because of his apparent cultural stigma. He reiterated, “I don’t need a shrink; I’m not crazy.” His urine toxicology was negative. Our initial recommendation was psychiatric hospitalization after medical clearance. While still in the emergency department, he developed fever (temperature: 101.7°F), tachycardia (heart rate: 120 beats/min), and elevated blood urea nitrogen and transaminases. Chest X-ray revealed an opacity in the upper lobe of the right lung, indicative of a possible COVID-19 pneumonia. He was admitted to the medical service for further workup and management. He was started on ceftriaxone 1000 mg intravenous (IV) daily, azithromycin 250 mg po daily, and hydroxychloroquine 200 mg po twice daily.

During the next 5 days, he continued to be uncooperative. He refused his meals because of reported poor appetite and refused IV medications intermittently. He was observed by nursing staff to be “chanting and singing to himself” but was able to be verbally redirected. He denied suicidal ideation, intent, or plan. Infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was confirmed by COVID-19 real-time polymerase chain reaction from nasopharyngeal swab. There was no focal neurological deficit and no apparent cognitive impairment. Montreal Cognitive Assessment was performed on hospital day #6. He scored 26 out of 30, losing one point each for the modified trail making test, naming the rhinoceros, serial 7 subtractions, and delayed recall. He received a total of 3 doses of olanzapine 5 mg intramuscular injection intermittently to manage agitation on hospital day #3, 7, and 8. On hospital day #6, he developed worsening hypoxic respiratory failure due to COVID-19. He developed rigors and continued to have high-grade fevers. He began to improve on hospital day #10, requiring less supplemental oxygen and became more cooperative with examinations. Computed tomography of the head without contrast was performed on hospital day #12, and the findings were unremarkable. Lumbar puncture was not performed.

On hospital day #12, he was able to discuss his auditory hallucinations in meaningful detail. He reported that his initial symptom was a repeated command auditory hallucination of an unrecognizable singular voice that started 1 day before he ingesting bleach. He was unsure about the gender of the voice but noted that it sounded “demonic” and stated that he heard the voice externally. The voice initially told him, “Go jump from the bridge” and later told him, “Go to the kitchen and drink bleach.” He reported feeling confused and terrified. He explained that he ultimately ingested bleach not because of suicidal intent but because “the voice got louder and more forceful.” He denied experiencing auditory hallucinations in the past and denied recurrence of hallucinations during his hospitalization. He also denied use of illicit substances, alcohol, or tobacco. He denied present or past suicidal ideation or suicidal attempts. He was goal-directed, affectively reactive, and future-oriented. He denied past or current symptoms of mood or anxiety disorders.

Since the implementation of stay-at-home directives, he reported that he had been able to continue his work remotely as an office clerk. His wife, a schoolteacher, and his 21-year-old web developer son were also working from home. Leading to his hospitalization, he noted some general anxiety about COVID-19 but stated that he felt fortunate to be at home and was trying to keep his “spirit and body occupied.” He denied other acute stressors in his relationships, employment, or finances.

Mr. A’s account of history and absence of prior psychiatric illness was supported by collateral information obtained from his wife and his primary care provider. He was psychiatrically cleared for discharge to a subacute rehabilitation center. Discharge impression was psychotic disorder owing to another medical condition.7

Discussion

The perceptual disturbance in our patient which led to the self-harm attempt meets the formal characteristics of a hallucination – (1) occurred in external objective space, (2) the voice was clearly delineated, (3) sensory elements were full and fresh, (4) the perception was constant and remained unaltered, and (5) the perception was independent of will.8 The absence of prior psychiatric illness or significant stressors, his initial experience of command auditory hallucinations, the subsequent development of COVID-19 symptoms, and the later disappearance of hallucinations suggest that the command auditory hallucinations were the first symptoms of his developing COVID-19 illness. Mr. A’s command hallucinations to ingest bleach were experienced 22 days before President Donald Trump made
comments about getting a disinfectant into the body as a potential cure for COVID-19. While there are reports of encephalopathy due to COVID-19, we are not aware of any prior report of hallucinations being the presenting symptom. Among the differential diagnoses for our case, delirium, stress-induced “reactive” psychosis, and catatonia were all considered. First, delirium, a clinical expression of encephalopathy, was plausible in our case. He had minimal cooperation initially, intermittent refusal of medications and meals, and required anti-psychotic medication for management of agitation. Earlier cognitive testing was not feasible because of patient noncooperation. However, he remained alert and oriented throughout his hospital stay. His uncooperative behavior was hypothesized to be in part due to his stigma of psychiatry with a likely component of subsyndromal delirium. Second, a stress-induced psychotic reaction was determined to be lower on the differential after review of his relatively benign account of recent psychosocial stressors. Third, there is literature on catatonia-like syndromes due to viral encephalitis and anecdotal cases of catatonia in the setting of COVID-19. This patient displayed negativism toward interventions, withdrawn behavior, and decreased oral intake, but not waxy stability, excitement, stupor, mutism, echolalia, or echopraxia.

The COVID-19 pandemic has been quite novel in its protean manifestation, including the neurological ones. Several mechanisms have been proposed for neurologic symptoms. One such mechanism is direct viral injury to the neurons akin to herpes simplex virus encephalitis. SARS-CoV-2 has the capacity to bind to angiotensin-converting enzyme 2 receptors. These receptors, although highly expressed in epithelial cells of the respiratory and digestive systems, are also expressed in neurons and glial cells in the central nervous system (CNS).

Cytokine storm may lead to acute or subacute CNS involvement, including encephalopathy. Current available evidence suggests that chronic neuro-inflammation associated with high levels of cytokines and chemokines is involved in the pathogenesis of neurodegenerative diseases such as multiple sclerosis, Parkinson disease, and Alzheimer disease. Neuro-inflammation has also been found to play a role in the pathogenesis of psychiatric diseases including affective disorders, schizophrenia spectrum disorders, and substance abuse, especially alcohol abuse. Proinflammatory cytokine dysregulation can induce changes in neurotransmitter metabolism, cause hypothalamic-pituitary-adrenal axis dysregulation, or alter neuroplasticity.

Molecular mimicry leading to bystander effect such as Guillain-Barre syndrome is another proposed mechanism. In susceptible individuals, an aberrant immune response may become cross-reactive with both viral antigens and self-antigens. Systemic illness leading to CNS manifestations may also be contributory. An example of such a mechanism would be peripheral myeloid cells infected by SARS-CoV-2 which can subsequently transmigrate to the CNS under conditions of increased blood-brain barrier permeability due to inflammation and psychological stress.

Our case indicates that what appeared as a sudden onset of a psychiatric illness in the current context may have been an initial manifestation of a developing COVID-19 illness. Testing for COVID-19 and a period of observation in the medical setting before psychiatric hospitalization may be warranted in such cases. Considerations should be made for delirium, encephalopathy, catatonia, and stress-induced psychotic reaction. Management of such patients may benefit from neurology consultation, neuroimaging, electroencephalogram, formal neuropsychological testing, and lumbar puncture. In addition, the neuropathological mechanisms of such cases need to be explored.

Conflicts of Interest: The authors declare that they have no conflict of interest.

References
1. World Health Organization: Coronavirus Disease 2019 (COVID-19): Situation Report, 118. 2020. Available from: https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200517-covid-19-sitrep-118.pdf?sfvrsn=21c0dafe_6.

2. Cennimo DJ, Bergman SJ: Coronavirus Disease 2019 (COVID-19): Clinical Presentation. Medscape 2020. Available from: https://emedicine.medscape.com/article/2500114-clinical.

3. Wong SH, Lui RN, Sung JJ: COVID-19 and the digestive system. J Gastroenterol Hepatol 2020; 35:744–748.
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4. Mao L, Jin H, Wang M, et al: Neurologic manifestations of hospitalized patients with coronavirus disease 2019 in Wuhan, China. JAMA Neurol 2020:e201127
5. Filatov A, Sharma P, Hindi F, Espinosa PS: Neurological complications of coronavirus disease (COVID-19): encephalopathy. Cureus 2020; 12:e7352
6. Yudoñsky SC: Contracting schizophrenia: lessons from the influenza epidemic of 1918-1919. JAMA 2009; 301:324–326
7. American Psychiatric Association: Diagnostic and Statistical Manual of Mental Disorders: DSM-5, 5th ed. Washington, DC: American Psychiatric Association; 2013. p. 115
8. Sims A: Symptoms in the mind: an introduction to descriptive psychopathology, 3rd ed. London: Elsevier Science Limited; 2003. p. 99
9. Rogers K, Hauser C, Yuhas A, Haberman M: Trump’s suggestion that disinfectants could be used to treat coronavirus prompts aggressive pushback. The New York Times 2020. Available from: https://www.nytimes.com/2020/04/24/us/politics/trump-inject-disinfectant-bleach-coronavirus.html.
10. American Psychiatric Association: Diagnostic and Statistical Manual of Mental Disorders: DSM-5, 5th ed. Washington, DC: American Psychiatric Association; 2013. p. 596–602
11. Levkoff SE, Liptzin B, Cleary PD, et al: Subsyndromal delirium. Am J Geriatr Psychiatry 1996; 4:320–329
12. Stoudemire A: The differential diagnosis of catatonic states. Psychosomatics 1982; 23:245–246, 248, 250-252
13. American Psychiatric Association: Diagnostic and Statistical Manual of Mental Disorders: DSM-5, 5th ed. Washington, DC: American Psychiatric Association; 2013. p. 119–120
14. Troyer EA, Kohn JN, Hong S: Are we facing a crashing wave of neuropsychiatric sequelae of COVID-19? Neuropsychiatric symptoms and potential immunologic mechanisms. Brain Behav Immun 2020. https://doi.org/10.1016/j.bbi.2020.04.027
15. Serrano-Castro PJ, Estivill-Torrus G, Cabezudo-Garcia P, et al: Impact of SARS-CoV-2 infection on neurodegenerative and neuropsychiatric diseases: a delayed pandemic? Neurologia 2020. https://doi.org/10.1016/j.nrleng.2020.04.002
16. Frank-Cannon TC, Alto LT, McAlpine FE, Tansey MG: Does neuroinflammation fan the flame in neurodegenerative diseases? Mol Neurodegener 2009; 4:47
17. Rhie SJ, Jung EY, Shim I: The role of neuroinflammation on pathogenesis of affective disorders. J Exerc Rehabil 2020; 16:2–9
18. Tsai LK, Hsieh ST, Chao CC: Neuromuscular disorders in severe acute respiratory syndrome. Arch Neurol 2004; 61:1669–1673
19. Desforges M, Coupance AL, Dubeau P, et al: Human coronavirus and other respiratory viruses: underestimated opportunistic pathogens of the central nervous system? Viruses 2019; 12:14