Nihilism, Neurocognition, and the Novel Coronavirus: A Case of Acute Onset Cotard's Syndrome

Caitlin J. McCarthy, MD; Suraj Singh, MD

ABSTRACT

Introduction: The novel coronavirus (COVID-19) is a respiratory illness that may cause neuropsychiatric sequelae, including persistent psychotic symptoms.

Case Presentation: A 70-year-old White man with no prior psychiatric history presented with altered mental status, Cotard's syndrome, and rigid delusions of poverty and homelessness 6 weeks after recovering from a mild case of COVID-19. After extensive medical workup revealed no organic etiology, he was treated for psychotic symptoms with an atypical antipsychotic, an antidepressant, and electroconvulsive therapy, with improvement over time.

Discussion: While COVID-19 is primarily a respiratory disease, some individuals may develop new-onset psychiatric or neuropsychiatric symptoms without prior psychiatric history.

Conclusions: To our knowledge, this is the only published case of post–COVID-19 psychotic symptoms treated with electroconvulsive therapy. As the pandemic continues, the total impact of COVID-19 on psychotic symptoms remains to be seen.

INTRODUCTION

While primarily causing widespread death and devastation as a respiratory illness, several years into the COVID-19 pandemic, we now understand SARS-CoV-2 infection to cause numerous other sequelae, including psychotic symptoms. It has been established previously that other viral infections are associated with neuropsychiatric consequences. Encephalitis was seen during the 1917 Spanish flu pandemic.[1-4] Caused by similar beta-coronaviruses, severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS) were found to have increased risk of manic-depressive disorders, agitation, and delirium.[1,5,6] While coronaviruses are known to be neurotropic, the exact mechanism for neuropsychiatric symptoms is unknown.[7] Proposed theories include hypoxia, exaggerated immune response with "cytokine storm," inflammation, and invasion of the central nervous system; however, inflammatory markers were not obtained in this case.[1,3,5,7-10]

Here, we discuss the presentation and treatment course for post-COVID neuropsychiatric symptoms in a geriatric patient with minimal psychiatric history and highlight possible long-term effects of the novel coronavirus infection that are not yet fully recognized or understood. Few other case reports have demonstrated similar findings following COVID-19 infection,[5,7,9,11,12] and only 1 case report has documented Cotard's syndrome in the clinical presentation.[8]

While some studies using data from similar coronavirus pandemics suggest there is no concern for increased psychotic symptoms following COVID-19 infection,[1,10] a large retrospective analysis by Taquet et al[13] found increased risk of psychotic disorders up to 2 years after recovery. Our intent is to contribute to the limited existing literature describing psychotic symptoms secondary to COVID-19 infection and discuss treatment options, as well as highlight the importance of continued public health efforts in slowing and preventing disease spread.

CASE PRESENTATION

A 70-year-old White male with past medical history of gout, benign prostatic hyperplasia, and insomnia presented to the emergency department (ED) with altered mental status. He was brought in by family due to 2 weeks of erratic behavior, nihilistic delusions, irrational fixations on hospital bills, and delusions of outstanding debt and homelessness. His family reported that he had made statements like "I'm not going to be around very long," "It is judgement day," and "I feel like I'm out of this world." These

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Author Affiliations: Department of Psychiatry and Behavioral Medicine, Medical College of Wisconsin, Milwaukee, Wisconsin (McCarthy, Singh).

Corresponding Author: Caitlin J. McCarthy, MD, 8701 Watertown Plank Rd, Milwaukee, WI 53226; email cjmccarthy@mcw.edu; ORCID ID 0000-0002-4553-4829

behaviors had been worsening progressively over the 3 weeks leading up to admission. He had no history of substance use, was retired, and was widowed 5 years prior to admission. He reported no psychiatric history, although his mother had schizophrenia.

The patient tested positive for COVID-19 6 weeks prior to admission and recovered without hospitalization. His predominant symptoms of COVID-19 included several weeks of gastrointestinal distress. He did not report taking any medications for his symptoms. In the ED, he had a blood pressure of 122/76 and pulse of 68 beats per minute. His oxygen saturation (Sp02) was 100%, and he was afebrile. Both complete blood cell count and comprehensive metabolic panel were within normal limits. Ammonia, thyroid-stimulating hormone, and salicylate levels were normal. Urinalysis was without infection, and urine drug screen was negative.

The patient was admitted to the inpatient medicine service with differential diagnoses of neurocognitive disorder, post-COVID encephalitis, autoimmune encephalitis, other toxicities, and primary psychiatric disorder. On physical exam, he was fully oriented and cranial nerves II-XII were intact. Both strength and sensation were intact in proximal and distal muscle groups of all extremities. His tandem walking was intact, Romberg test was negative, and he was without asterixis or tremor. He underwent comprehensive screening investigating possible organic cause for his symptoms. Computed tomography (CT) head was negative for mass effect, midline shift, hydrocephalus, or acute intracranial hemorrhage. Due to concern for underlying malignancy given his presentation and history of weight loss over the past year, a CT scan of chest, abdomen, and pelvis was performed without findings suggestive of neoplastic disease. Additional workup for paraneoplastic syndrome included amphiphysin autoantibody, CV2 antibody, and Hu autoantibody—all of which were negative. Combined with imaging, urine metanephrines testing ruled out pheochromocytoma. Magnetic resonance imaging of the brain showed abnormal increased T2/FLAIR signal intensity in the left insular cortex, which was noted to be a nonspecific finding and unclear whether related to psychosis, as well as mild chronic microvascular ischemic white matter changes. Vitamin B12 was normal, and folate was mildly low at 8.0 ng/mL. Screening for lead, mercury, and arsenic was negative. A cerebrospinal fluid examination yielded no abnormalities, which ruled out neurosyphilis and other infectious causes. Inflammatory markers were not obtained.

During initial assessment by the psychiatry consultation liaison team on day 2 of hospitalization, the patient was noted to be perseverative on having died and being in hell, stating he was being punished for the life he lived. He reported, "I wish I could kill myself, but I can't," believing to be already deceased. While his organic workup was unrevealing, his presentation and illness onset were unusual for primary psychiatric illness or neurocognitive disorder. Neuropsychological assessment showed abnormalities in executive function, abstraction, and retrieving new information on the Montreal Cognitive Assessment (MoCA version 8.2), thought to be secondary to active psychosis. He was without evidence of delirium and demonstrated intact attention on exam. He was treated with high-dose intravenous thiamine for 3 days given history of recent weight loss. Olanzapine was started and titrated to address delusions. His nihilistic delusions showed some improvement while other delusions persisted.

On day 13 of hospitalization, the patient was transferred to the inpatient psychiatric unit. He continued to express delusions of impoverishment, stating he did not have a home or family. Escitalopram was added to treat depressed mood. By day 29 of hospitalization, nihilism and Cotard's syndrome had resolved, but other delusions continued, and he noted paranoid ideas of reference regarding peers on the unit. He also struggled with simple grooming tasks, such as showering and trimming nails. As symptoms were most consistent with psychotic depression, electroconvulsive treatment (ECT) was initiated on day 40 of hospitalization and continued for 13 sessions over 5 weeks. He tolerated ECT without significant adverse effects. Olanzapine was transitioned to risperidone to further address delusions. He continued to show improvement and acknowledged owning a home and car and being without financial debts. He was without any acute agitation throughout his hospitalization and cooperative with unit staff and treatment team. Towards the end of his hospitalization, he consistently attended unit programming and group therapies. On day 74, he was discharged home with family.

During the patient's stay, collateral was collected from multiple sources. Several family members confirmed that he had never been diagnosed with psychiatric illness and that he did, indeed, own his home and had no outstanding debts. They also confirmed that prior to onset of unusual symptoms, he had been able to manage a rental property, live independently, and perform all activities of daily living (including grooming and hygiene) without issue.

DISCUSSION

Several other case reports demonstrate similar findings in patients with no prior psychiatric history who developed psychotic symptoms during acute illness or shortly after recovery from COVID-19.[2,7,9,11,12] In many cases, the patients had been treated previously with steroids, antivirals, or antibiotics.[5,11,12] To date, there is one other documented case of Cotard's syndrome following COVID-19 infection. Ignatova et al[8] described a patient with nihilistic delusions about having died (with decomposing organs) shortly after being treated for COVID-19 and pneumonia. He improved with haloperidol and showed complete recovery after several months. The authors suggested that fear of infection and impending doom related to the pandemic may be tied to onset of nihilistic or Cotard's delusions.[8]

While our patient shared some symptoms and characteristics with patients in similar case reports,[8,11] he differed in that he was not hospitalized for COVID-19 and recovered without oxygen, steroids, or antibiotics. Further, to our knowledge, this is the only

published case of post-COVID psychotic symptoms requiring ECT, though there have been other documented cases of Cotard's syndrome successfully treated with ECT.[14]

The etiology of psychotic symptoms secondary to viral illnesses is not fully understood, though several theories have been postulated. Significant inflammatory response to infection or "cytokine storm" is thought to cause cardiopulmonary complications of COVID-19 and also may contribute to neuropsychiatric symptoms.[1,7,10,15] Several previous case reports noted raised inflammatory markers (TNF-alpha, ferritin, and C-reactive protein [CRP]) in patients with similar presentations, suggesting that obtaining cytokine profiles in patients with psychiatric symptoms secondary to COVID-19 may be beneficial to inform management.[2,3,5,7,9] Other possible mechanisms include molecular mimicry and invasion of the nervous system secondary to viral "proteiform" disease.[5,9] Of note, our patient contracted COVID-19 prior to widespread use of coronavirus vaccines, thus it begs the question whether immunization would have affected or even prevented his symptom course.

In a descriptive systematic review of case reports, Smith et al[6] found delusions (92% of patients) to be the most common symptom in adults with psychotic symptoms during or after COVID-19; the authors also encouraged clinicians to acknowledge numerous confounders between COVID-19 and incident psychosis and obtain detailed clinical assessment. Later, in a retrospective analysis, Taquet et al[13] found increased risk of mood disorders, such as anxiety or depression, following COVID-19 infection that returned to baseline after several months. However, increased risk of psychotic symptoms and cognitive deficit persisted up to 2 years after initial infection. Conversely, Watson et al[4] suggested that psychosis may be a potential complication of all viral illnesses, and cases secondary to COVID-19 may seem so prevalent due to the scale of the pandemic.

While we cannot rule out the possibility that this patient's presentation was entirely related to psychological stress, it seems unlikely given the onset of symptoms and lack of psychiatric history. Was he predisposed to psychosis due to family history, coupled with the possible inflammatory insult of COVID-19 illness that led to persistent delusions? According to Watson et al,[4] the possible association between COVID-19 infection and psychotic symptoms does not meet the Bradford-Hill criteria required for determination of causality; however, there is biological plausibility to the association.

Our case describes an interesting clinical presentation possibly secondary to COVID-19, yet is limited by small sample size and lack of additional medical workup (eg, measurement of inflammatory markers such as CRP, IL-6, TNF-alpha, and other cytokines). Additionally, reliance on the patient's report and collateral information may affect the exact timeline of events. As stated by Troyer et al,[3] the neuropsychiatric burden of the COVID-19 pandemic is currently unknown but likely to be significant. This case highlights the importance of research into possible neuropsychiatric sequelae of COVID-19 infection and public health measures for disease prevention.

CONCLUSIONS

While COVID-19 is primarily a respiratory disease, some individuals may develop new-onset psychiatric symptoms without prior psychiatric history, as in this patient. Early intervention and appropriate treatment are of critical importance for effective treatment and recovery; ECT may be considered as an option if antipsychotic medications are not effective. As the worldwide coronavirus pandemic continues, it is likely that additional cases of post-COVID psychosis will manifest, requiring ongoing research into pathophysiology and treatment.

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