New-Onset Psychosis Secondary to COVID-19 Infection

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Virus-borne infections play a significant role in neuropsychiatric manifestations, with delirium being a systemic infection's most common secondary complication.[1] HIV, herpes simplex virus, varicella-zoster virus, influenza A and other influenza viruses, and hepatitis C virus are viruses that result in infections associated with depression and anxiety. HIV infection may also result in psychosis and mania.[2] Respiratory viruses have been associated with psychosis since the 1918 influenza (Spanish flu) pandemic.[3] In 1919, Menninger published a case series of 100 patients with neuropsychiatric sequelae associated with influenza infection, including 23 patients with "other psychosis."[3,4]

About one-third of the patients with SARS-CoV-2 develop neuropsychiatric symptoms, such as anxiety, depression, psychosis, brain fog, and suicidal behavior.[5] Recently, several cases have reported new-onset psychotic symptoms in individuals following an infection with SARS-CoV-2.[5,6] The possible etiologic factors are viral exposure, treatment modality (possibly steroids), and psychosocial stress.[7,8] From studying recently published case reports,[9–11] the psychotic symptoms develop approximately 2 weeks after the remission of fever and flu-like and upper respiratory symptoms. However, these symptoms can develop within the week of the onset of upper respiratory symptoms.[4]

Besides the respiratory system, SARS-CoV-2 targets the central nervous system (CNS), which can lead to cerebrovascular diseases, encephalopathy, and encephalitis.[12] Acute psychosis is a rare CNS condition possibly triggered by the inflammatory response to a SARS-CoV-2 infection.[7,9] Direct viral infiltration in the CNS triggers the neuroinflammatory reaction, and the microglial-induced demyelinating process causes encephalopathy. Peripheral hypercytokinemia triggers a noninflammatory response, disrupting the blood-brain barrier. The transmigration of the peripheral immune cell into the CNS causes an imbalance in neurotransmitters, which may be responsible for neuropsychiatric manifestations.[13] Although it is commonly thought that psychosis related to COVID-19 is due to inflammation, sometimes the inflammatory markers are normal.[14]

To better understand the neuropsychiatric symptoms and their management following a COVID-19 infection, we reviewed some case reports in the pediatric and adult population. One report[15] was of a 15-year-old girl with no known psychiatric history who presented with visual and tactile hallucinations, delusions, and paranoia 2.5 weeks after being infected with COVID-19. She was treated with dexamethasone 4 mg for 5 days for COVID-19, with all her laboratory results being within normal limits except for a positive SARS-CoV-2 serology. Her psychosis was treated with olanzapine 5 mg, which was increased to 7.5 mg, to which she responded. Her symptoms improved, and she was discharged within 5 days.[15] In March 2021, a 69-year-old woman presented with symptoms of catatonia, bizarre behavior, visual hallucinations, and paranoid delusions following a resolved COVID-19 infection.[16] Her catatonia responded to a trial of therapeutic lorazepam. Other case reports[4,9–11] reveal persecutory delusions, auditory and visual hallucinations, disorganized behavior, and agitation as some of the most commonly presenting symptoms. COVID-19–related psychosis tends to respond well to antipsychotics, mood stabilizers, and benzodiazepines. The widely used antipsychotics are haloperidol, risperidone, aripiprazole, and olanzapine.[4,9–11]

A study from China[17] demonstrated the relationship between psychosis-like experiences (PLEs) and COVID-19–related psychological symptoms, including depression, anxiety, neurasthenia, fear, obsession-compulsion, and hypochondriasis. The study[17] suggested the predictive value of PLEs for measuring the psychological impact of a public health emergency. The PLEs are associated with many psychosocial factors, such as ethnic minority, urbanization, perceived stress, and childhood trauma.[17] In addition, there is evidence of coronavirus-associated psychosis through neuroinflammation, with linked factors including stress, isolation, and uncertainty, further showing how pandemics can increase the risk of psychosis.[18]

As neuropsychiatric complications can develop within weeks of a COVID-19 infection, health care providers should consider COVID-19 a causative agent of sudden and new-onset psychotic disorders. We propose well-designed and large-scale research studies to explore the pathophysiology behind SARS-CoV-2 and other coronaviruses altering neuronal activity and neurotransmission.

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