Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Correspondence

A case of Sars-Cov-2-related mania with prominent psychosis>

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Dear Editor,

Severe Sars-Cov-2 infections have been linked to acute neuropsychiatric conditions, including delirium and worsening behavioral symptoms in cognitively impaired patients. In most cases, these clinical pictures rely upon systemic or CNS-confined inflammation. Other acute complications, like strokes, encephalitis, or seizures, could trigger behavioral changes as well. Only a few reports (Kaggwa et al., 2021; Khatib et al., 2021; Lazzari et al., 2020; Lu et al., 2020; Mawhinney et al., 2020; Noone et al., 2020; Saje et al., 2021; Sen et al., 2021; Shanmugam et al., 2021) assessed the occurrence of disrupting mood disorders with psychotic features as a possible presentation of COVID-19. All the subjects were also experiencing systemic symptoms (fever, sore throat, cough, dyspnea) except for one case (Noone et al., 2020). The present case describes a thorough diagnostic workup that may help guide neurologists and psychiatrists who may incur similar presentations.

1. Case report

On February 2nd, in a small Italian town, a 60-year-old woman underwent a Sars-Cov-2 swab since her husband had been recently found positive for COVID-19 infection. She was asymptomatic, but her swab resulted positive. The patient was the primary caregiver of her husband, affected by Mild Cognitive Impairment (MCI). The patient's medical history included hypertension, asthma, and major depression, with no manic episodes or psychotic symptoms as hallucinations or delusions. The severity of depression had always been mild to moderate, and symptoms were well under control with monotherapy (paroxetine). Her medical therapy also included perindopril, fluticasone/vilanterol spray, montelukast, and triazolam. Her family history was positive for cognitive deficits (her maternal grandmother), delusions (her mother), and major depression (two siblings). Despite the lack of ongoing respiratory symptoms, her general practitioner prescribed prednisone 1 mg/kg, which she took only for two days. On February 4th, the patient started suffering from delusions consisting of mold growing everywhere. For that reason, she threw away several pieces of furniture and bought large amounts of cleaning products to deep clean her house. She also experienced complex hallucinations in which her dead mother ordered her to clean the tombstones of all her relatives to be "…*safe from COVID-19 and rest in peace…*". The patient also reported auditory hallucinations on the same topic and went on to thoroughly clean three cemeteries. Relatives also indicated that she had become increasingly aggressive, restless, sleepless. The Sars-Cov-2 infection only lasted ten days, but behavioral symptoms persisted. In March, at a follow-up visit of her husband, the neurologist who had known her for five years noted significant behavioral disturbances so severe that a haloperidol 8 mg bid regimen was started. After two weeks, no notable changes were observed, and she was switched to clotiapine. This regimen was also ineffective, and she was admitted to the psychiatric ward. At admission, she was euphoric, exhibited accelleratied speech, racing thoughts, logorrhea, and distractibility (Young Mania Rating Scale score: 27, cut-off>20). At the same time, confusion and cognitive impairment were absent (Mini-Mental State Examination: 28/30).

The neurological exam showed no other pathological signs. Routine blood tests only revealed mild anemia. The brain Mild Cognitive Impairment MRI scan was unremarkable and showed no signs of brain atrophy. The electroencephalogram with quantitative analysis was normal. The patient also underwent a lumbar puncture for cerebrospinal fluid analysis (see Supplementary Materials, Table 1). Paroxetine and clotiapine treatment was discontinued, and lamotrigine and haloperidol were added to therapy. The patient was eventually diagnosed with mania with psychotic features triggered by Sars-Cov-2 infection. At present time, eight months after the episode, she can recall the complex hallucinations and her past delusional beliefs. Still, the increased activity, the buying sprees, and the engagement in goal-directed pursuits have disappeared.

2. Discussion

Our report describes a case of acute mania, with prominent psychotic features triggered by a Sars-Cov-2 infection in an otherwise asymptomatic patient. While the two days of inappropriate steroid therapy may have concurred in precipitating this condition, the symptoms kept worsening even after prompt drug discontinuation, thereby ruling out a steroid-dependent mechanism. A neurodegenerative cause can also be excluded as all the related biomarkers were within normal limits.

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Behavioral and mood disorders following viral infections, including other coronaviruses (Okusaga et al., 2011) and Spanish flu (Levy, 1959; Onofrj et al., 2021), have been frequently linked to an inflammatory response and autoimmune mechanisms (Stich et al., 2015). Some studies have suggested that patients who have bipolar disorders exhibit "a pro-inflammatory background" (Stich et al., 2015). It is conceivable that a transient inflammation, as well as direct neuroinvasion, had triggered - in a subject with a genetic predisposition - a cascade of events culminating in the alteration of excitatory and inhibitory circuits, ultimately leading to the onset of mania or other psychiatric disorders (DeLisi, 2021). Of note, the Sars-Cov-2-driven retrograde neuroinvasion through the olfactory pathway may favor access to the adjacent orbitofrontal cortex (Le Guennec et al., 2020), a region whose dysregulation is known to be involved in manic disorders (Cotovio et al., 2020).

In conclusion, this case underlines the possibility of severe neuropsychiatric symptoms in Sars-Cov-2 "asymptomatic" infections, with normal neuroradiological, neurophysiological, or laboratory findings. Previous outbreaks of neuropsychiatric disorders following viral epidemics were observed, thus drawing attention to a possible role for infectious disorders in so-called idiopathic conditions (DeLisi, 2021). Further studies are needed to disentangle the pathophysiological processes and neural and network imbalance underlying this peculiar condition.

Author contributions

(CRediT): SLS, MR, MVD, SC, MAD, and DC: patient's management and investigations. MR and SS: conceptualization of the manuscript and writing of the original draft. FD, CC, and MO: writing, review, and editing. SLS: writing, supervision and validation.

Declaration of Competing Interest

Nothing to disclose.

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Ethics

Written informed consent for publication was obtained.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.psychres.2021.114266.

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