

PSYCHOTIC DEPRESSION WITH PERSISTENT COGNITIVE DEFICITS ASSOCIATED WITH COVID-19 - A CASE REPORT

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INTRODUCTION

Coronavirus Disease 2019 (COVID-19) may impact many different organ systems, including the central nervous system. Evidence suggests that adults have approximately doubled risk of being newly diagnosed with a psychiatric disorder, including depression, in the 3 months following COVID-19 infection (Taquet et al. 2021).

In this case report, we present a man who developed psychotic depression with suicidal behaviour and persistent cognitive deficits following a COVID-19 infection. We will discuss the role of SARS-CoV-2 and psychological factors in the pathophysiology of the manifested symptoms.

CASE REPORT

A 57-year-old man, with no past or family history of mental illness, was admitted to Clinic for psychiatry after a suicide attempt. According to his family, the patient was fully functional until the COVID-19 infection two months prior to admission, when he became "anxious, depressed, and disconnected from reality". During the COVID-19 infection, the patient had only a fever and his laboratory values were in the normal range, except for slightly elevated monocytes and lymphocytes. The patient emphasised that he did not cope well with either the personal diagnosis of COVID-19 or the quarantine. He was preoccupied with the idea that he had inadvertently transmitted the virus to others. At that time, the patient began to suffer from insomnia, loss of interest, abulia, and anhedonia. He also noticed difficulty concentrating, especially when playing chess. Finally, before his admission, he attempted suicide by cutting his wrists.

During the initial psychiatric evaluation, the patient was speaking slowly and his movements were decreased. Orientation was intact. He was feeling tense and his mood was low with reduced affect modulation. The patient's thinking was circumstantial with hyper-tenacity and he exhibited paranoid delusions and delusions of guilt. The patient denied auditory or other sensory hallucinations. Physical examination revealed no acute findings other than wrist lacerations.

The only remarkable finding in blood analysis were anaemia with haemoglobin 133 g/L (Ref: 119-157 g/L), MCV 81.2 fL (Ref: 83.0-97.2), MCH 28.1 pg (Ref:

27.4-33.9), MCHC 346 g/L (Ref: 320-345) and mildly low lymphocytes 19.7% (Ref: 20-46). During hospitalisation he was also tested for COVID-19 and the test was negative. Because of the patient's symptoms and age, a computed tomography (CT) of the head was performed, which revealed bilateral cortical atrophy in the parietal area and to a lesser extent in the frontal area; not observing intracranial acute pathology. A psychological assessment showed depressive features in functioning and cognitive deficits in learning and verbal memory, suggestive of organicity. Considering the totality of his symptoms, major depressive disorder with psychotic features was diagnosed.

The patient was offered reassurance and support from our psychiatric team. After one month of hospitalisation, he no longer had psychotic symptoms, he endorsed some improvement in mood symptoms, but cognitive disturbances persisted. The patient was discharged from the hospital with the recommended therapy: olanzapine 5 mg/day, vortioxetine 15 mg/day and diazepam 5 mg PRN. The patient saw the psychiatrist regularly over the next few months and his psychiatric status and general functioning continued to improve. Seven months after the initial psychological assessment, another was performed by the same trained psychologist. It showed the resolution of depressive symptoms, but the cognitive deficits persisted.

DISCUSSION

SARS-CoV-2 continues to present an international public health problem (Mohammadkhanizadeh & Nikbakht 2021). COVID-19, the disease caused by SARS-CoV-2, is asymptomatic in some, some have mild symptoms similar to the common cold, while others develop severe symptoms requiring ventilator treatment (Østergaard 2021). It was quickly recognised that SARS-CoV-2 can be associated with various neuropsychiatric manifestations (Mohammadkhanizadeh & Nikbakht 2021, Jakovljević et al. 2020). Taquet et al. showed that 5.8% of COVID-19 survivors had their first recorded diagnosis of a psychiatric illness such as depression within 90 days of coronavirus diagnosis (Taquet et al. 2021).

Here we report the case of a patient with no history of mental illness who presented with psychotic depression after testing positive for COVID-19. The patho-

genesis of psychotic depression is unknown in general, although various neurobiological approaches have been pursued. Decreased plasma levels of dopamine-beta-hydroxylase and dysregulation of the HPA axis have been observed, the latter being the most consistent finding that differentiates it from non-psychotic depression (Keller et al. 2017, Neufeld et al. 2020).

The function of the hypothalamic-pituitary-adrenal (HPA) axis could be affected by COVID-19 through various mechanisms (Mohammadkhanizadeh & Nikbakht 2021). Since angiotensin-converting enzyme 2 (ACE-2) is a SARS-CoV-2 entry receptor, SARS-CoV-2 affects the ACE/ACE-2 balance associated with HPA axis dysregulation (Conejero et al. 2021). The hippocampus, a part of the brain that has a close anatomophysiological relationship with the HPA, has been shown to be particularly vulnerable to coronavirus infection (Mohammadkhanizadeh & Nikbakht 2021). It could also be affected by compromised neuroplasticity and neurogenesis resulting from the decrease levels of BDNF that can occur in COVID-19 infection. In particular, BDNF levels could be downregulated by SARS-CoV-2 infection directly (Perlmutter 2021) or by psychological stressors (Miao et al. 2020). Regarding psychological stressors, our patient stated that he did not cope well with either the diagnosis of COVID-19 or quarantine, both of which are associated with elevated stress and other psychological complications (Mohammadkhanizadeh & Nikbakht 2021, Perlmutter 2021). Finally, dysregulation of the HPA axis can lead to persistently high cortisol levels, mediating vulnerability to depression (Mohammadkhanizadeh & Nikbakht 2021). It may also be associated with disturbed dopaminergic activity which could explain our patient's psychotic symptoms (Busatto 2013).

Our patient manifested suicidal behaviour. In addition to the psychological stress mentioned earlier, the increased vulnerability to suicidal behaviour may be mediated by SARS-CoV-2 affecting several biological pathways, including the renin-angiotensin system (i.e., the HPA axis), inflammation system, and nicotine receptors (Conejero et al. 2021).

The patient was most concerned about his cognitive difficulties, which were noted in both psychological assessments. Poorer cognitive performance in some cognitive domains is associated with psychosis during the course of major depression, and some findings link this to dysregulation of the HPA axis (Zaninotto et al. 2015). Importantly, the patient's psychological assessments indicated an organic background of cognitive deficits. This could be related to the cortical atrophy found on his brain CT scan (Aljondi et al. 2019). However, the patient and his family reported that the patient's cognitive dysfunction began at the onset of COVID-19 infection and did not resolve even 10 months later. In addition, there is emerging evidence that a substantial proportion of COVID-19 patients have persistent cognitive problems with memory and

concentration difficulties for several months after recovery from the infection. (Miskowiak et al. 2021). The literature suggests that cognitive dysfunction is likely the result of multiple causes, particularly direct neuronal damage by SARS-CoV-2, indirect damage from systemic impairment, and psychological distress (Ritchie et al. 2020). Accordingly, multiple interacting causes could be responsible for the cognitive decline in this patient, particularly cortical atrophy, the course of psychotic depression, COVID-19 associated organic and psychological factors.

With the exception of impairments in some cognitive domains, our patient showed resolution of his symptoms when treated with pharmacological treatment and psychological support. Several studies have reported the advantage of combined treatment of antidepressants and antipsychotics in depression with psychotic features (Gabriel et al. 2020). The patient was treated with the antipsychotic olanzapine due to its established efficacy in the acute treatment of psychotic depression (Flint et al. 2019). The antidepressant vortioxetine was added to the therapy as it has been shown to significantly improve depression, cognitive function, and functionality (Mahableshwarkar et al. 2015).

While this case report adds to previous reports and studies pointing out COVID-19 impact on mental health, it also raises questions about the aetiology of psychotic depression in general. This disorder is not as well-researched as other, more common psychological disorders and its pathophysiology is poorly understood (Neufeld et al. 2020). Although psychotic depression is still included in the category of depressive disorders in both ICD-10 and DSM-V, some studies suggest that it should be a distinctive diagnostic entity (Park et al. 2014). Moreover, COVID-19 associated depression seems distinct from the classical presentation of major depressive disorder in many characteristics, such as a higher incidence of psychotic features and clear neurocognitive deterioration (Steardo et al. 2021), as reported in this case. It is therefore possible that further research on the effects of SARS-CoV-2 on the brain may also help to clarify the aetiology of psychotic depression.

CONCLUSION

We report on the case of a 57-year-old man who manifested psychotic depression and suicidal behaviour with significant cognitive disturbances following a COVID-19 infection. We suggest this case may represent a manifestation of COVID-19 infection and discuss possible mechanisms. Elucidating the biology of COVID-19 associated depressive disorder that appears in many aspects atypical could help in understanding the pathophysiology of psychotic depression in general. Overall, this case should make clinicians working with COVID-19 patients cautious of possible cognitive consequences and psychiatric manifestations (especially suicidal risk).

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Contribution of individual authors:

Tonka Borovina was involved in the conception and design, data collection, analysis and interpretation of the data, preparation of the manuscript and writing of the article.

Tonći Mastelić & Mirjana Sučević Ercegovac were involved in patient's care and data collection, reviewing the draft manuscript and manuscript preparation.

Trpimir Glavina was involved in with the patient's care, critically reviewed the paper for important intellectual content.

Duška Krnić was involved in the patient's care, critically reviewed the manuscript for important intellectual content.

All authors were approved the final version.

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