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Post COVID 19 Neuro-Psychiatric complication: persistent delirium: A Case Report

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Abstract

COVID19 usually presents as severe pneumonia. Though it is different for everybody and it can cause symptoms that last weeks or months after the infection have gone. This is sometimes called Post-COVID-19 syndrome or "long COVID". One of the effects seen was Delirium. There are descriptions of neurological symptoms that can occur in this disease state, but there are few studies on the persistence of delirium for longer time. This clinical case describes a patient with no history of mental illness who developed psychotic symptoms in the context of an acute delirium due to COVID 19 and was persistent for 6 months after recovery. People who had mild symptoms at first can still have long-term problems, leaving patients with life-threatening respiratory, cardiovascular and cerebral complications. Clinicians should consider COVID 19 Neuro-psychiatric complications in the differential diagnosis of any patient with psychiatric symptoms or even the patients who are disoriented, irritable or non-cooperative.

Highlights: Patient being >60 years old and Completely Blind, this case have some specific characteristics and risk factors, including, having severe COVID-19, receiving High flow oxygen support, non-invasive mechanical ventilation, high-dose and long-term corticosteroids treatment, and delirium occurring transiently during the recovery period with negative SARS-CoV-2 results and improved laboratory results and no other organic cause in it. Blindness and physical disability could have been the reasons for delayed recovery and limitations for the management of the condition. Patient was not able to believe even after was counseled or was told about time, place or person. These detailed manifestations with dynamic changes in disease and related treatments might provide some clues to clarify the mechanism of psychiatric complications of COVID-19 and further inform targeted interventions. Although there was transient delirium during the early phase of recovery, moderate levels of fatigue, anxiety, and PTSD persisting for more than 6 months after discharge. Long-term follow-up of chronic neuropsychiatric sequel of SARS-Cov-2 infection is as important as follow-ups on acute neuropsychiatric complications.

Keywords: COVID-19, delirium, neuropsychiatric complication, long COVID, persistent delirium.

Introduction

COVID-19 is predominantly a respiratory disease. However, some cases exhibit other features including Central Nervous System symptoms. In the older adult, COVID-19 may present with atypical symptoms, including delirium and its complications.

Delirium is a clinical syndrome which is difficult to define. It is known by several terms including 'acute confusional state', 'acute confusion', 'acute on chronic confusion', and 'acute brain failure' or "acute encephalopathy" [1]. It is a relatively common acute disorder, especially in older people with physical illness, having high morbidity and mortality, often under-recognized and undertreated.

Delirium, a disorder characterized by confusion, inattentiveness, disorientation, illusions, agitation, and in some instances autonomic nervous system over activity, is common in the ICU and exceedingly challenging during the COVID-19 pandemic. However, neuropsychiatric events of COVID-19, including hyperactive and hypoactive delirium, have so far been underreported. Here we reported on a patient with severe COVID-19 who, in the absence of direct brain infection, experienced hyperactive and agitation and then hypoactive delirium during the recovery period after being transferred to the ICU and 6 months after the discharge from hospital and is still having mild symptoms.

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Case Report

A 62-year-old male with fever, drowsiness and dyspnea on exertion for five days was tested antigen and RT-PCR for Covid 19, as he just had a complaint of throat pain. Antigen test result was negative and abnormal laboratory workup included decreased lymphocytes, elevated inflammatory markers CRP, ferroprotein, elevated LDH and D dimer. Chest CT presented with typical ground-glass lesions with CT score of 11/25 and diagnosis of COVID-19 was confirmed subsequently by positive results of a throat swab for SARS-CoV-2. He was then immediately admitted to hospital. He had normal consciousness and cognition during admission and gave a history of the underlying diseases.

His medical history included well-controlled coronary heart disease, poorly-controlled type 2 diabetes with a high HbA1c. He has almost 25 years of Type II Diabetes mellitus, Ischemic heart disease and Chronic kidney disease. He had a severe Myocardial Ischemia 10 years ago and was operated CABG then, Since then he had restricted exercise due to 28% ejection fraction- left ventricular diastolic dysfunction. Patient also developed Glaucoma, Cataract and Diabetic retinopathy due to which he slowly progressed into complete blindness in both eyes.

With the diagnosis of severe COVID-19, his oxygenation index declined, which indicated ARDS. He was transferred to the ICU immediately. Unfortunately, his condition continued to deteriorate with severe respiratory symptoms, declining lymphocytes, elevating CRP, PCT, and LDH, and coagulation dysfunction. So he was given 1 dose of Tocilizumab on the same day of hospitalization, his condition became critical, with agitation and irritability with few complains of delusion of reference, he was transferred to an isolation ward and received Remdesivir 100mg -7 doses, high dose corticosteroids, supportive treatments including, anti-inflammatory and nutritional support were given. After 7 days in the ICU, He was shifted to other hospital at his home town as pulmonary function improved. At this hospital he was with his wife and son to assist as he was blind. Two days later, he was improving well. The patient had two teeth fall along with the root of tooth, which was previously not mobile. He went home and suddenly developed delirium on 4th day of hospital discharge, including confusion, disorientation and agitation, without symptoms of Peripheral Nervous System (PNS) and skeletal muscle injury, that met the delirium diagnostic criteria of Confusion Assessment Method for the Intensive Care Unit (CAM-ICU). However, except for CRP, other laboratory tests indicated improved results and the RT-PCR of the throat swab for SARS-CoV-2 came back negative. Physiotherapy was applied, unnecessary psychoactive medication was stopped, and verbal communication (consoling and reminding him of his location and the time) and family presence was encouraged. Later the delirium was intermediate with the episodes of completely normal behavior and delirium reappeared again and again almost every third day. At 3 and 5 month follow-ups after discharge, he still had moderate levels of Delirium on and off with absolutely normal episodes, fatigue and anxiety, and Post-traumatic stress disorder (PTSD).

Discussion

This is yet another detailed report of delirium in severe COVID-19 patients during the recovery period with negative SARS-CoV-2 results and improved laboratory

findings. Delirium is very common in critical illness, especially in the ICU, with a high prevalence of up to 85% [2]. However, the incidence of delirium in COVID-19 is unknown. Mao *et al.* [3] reported that “impaired consciousness” occurred in only 14.8% of patients with severe COVID-19. A recent study of 58 patients with COVID-19 reported agitation in 40 (69%) patients after the withdrawal of sedation and neuromuscular blockades in the ICU [4]. Similarly, agitation, confusion, and hallucinations occurred in 61% of patients in the acute stage of SARS [5]. Underreporting of delirium may be common because it is hard to screen delirium and other mental illness under a heavy workload and epidemiologic precautions during this pandemic [6]. In the post-illness stage of SARS and MERS, persistent psychiatric impairment, including depression, anxiety, Post-traumatic stress disorder, and fatigue, are rather common, but there is little data yet on COVID-19 [7]. More attention should be paid to the long-term psychological prognosis related to COVID-19 recovery. Potential mechanisms of delirium in COVID-19 might be heterogeneous and multifactorial, including direct effects of the virus infiltration, hypoxia, and/or the subsequent host immunologic response, medical interventions and Tocilizumab, and so on. Direct CNS invasion by the virus appears to occur rarely and might be not the related factor in this case because of the absence of manifestations of brain infection. Our guess may be further supported by the negative SARS-CoV-2 results and improved laboratory results during delirium. Although the patient's experienced severe hypoxia and high inflammatory reactions complicated with coagulation dysfunctions and heart failure, delirium occurred after leaving the ICU. Correspondingly, we speculated that the possible mechanism of delirium in this case might not be the direct effect of viral infection, but might be a post-infection immunologic response and immunomodulatory treatment (corticosteroid therapy, Tocilizumab). It is reported that steroid-induced psychotic disorder occurred in 13 (0.7%) of 1,744 patients with SARS in the acute stage [1]. In addition, the environment factors caused by being isolated from family and limited support from healthcare workers contributed to the occurrence of delirium. Thus, from the case, more exploration on psychoneuroimmunology mechanisms, including the characterization of immune host responses, exploration of genetic associations, and comparison with different medical interventions, especially immunomodulatory treatments, might be useful.

Although data about the acute effects of the illness on neuropsychiatric complications are limited, the evidence from SARS and MERS suggested the high mortality might be linked with poor prognosis of psychosis [8, 9]. So far, no medical intervention can be routinely recommended to apply for prevention and management [10, 11]. Non-pharmacological interventions, such as comfort and regular orientation from family, friends, and healthcare workers, have proven to be safe and effective methods for treating delirium [12, 13].

There are several limitations in our case reports. First, the patient has CKD and therefore we could not go for contrast CT, MRI angiography contrast, which is necessary to elucidate the causality and etiopathogenic mechanisms. Second, we here reported single patient and his delirium, information obtained on a recent follow-up period of 6 months after discharge, which is not enough to evaluate the

neuropsychiatric impact of COVID-19. Population-based multi-center research about delirium and longitudinal monitoring of neuropsychiatric complications of COVID-19 is still needed. During the period of the COVID-19 outbreak, in order to avoid cross-infection and reduce the burden on front-line health workers, advanced neuroimaging techniques were purposefully avoided.

Conclusion

In summary, we reported a COVID-19 patient who experienced delirium in hospital and persistent psychiatric impairment for longest period known after discharge. Those detailed manifestations during the dynamic changes of disease and related treatments might provide some clues to clarify the psychoneuroimmunological mechanism of psychiatric complications of COVID-19 and further contribute toward targeted interventions. Long-term follow-ups of chronic neuropsychiatric sequel of SARS-Cov-2 infection are as important as follow-ups of acute neuropsychiatric complication.

Ethics Statement

The patients/participants provided their written informed consent to participate in this study. Written informed consent was obtained from the individual(s) for the publication of any potentially identifiable images or data included in this article.

Author Contributions

Suraj Dhankikar: Acquired, analyzed patient data, design and conceptualized the report and drafted the manuscript.

Akansha Arewar: Interpreted clinical data and revised manuscript.

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