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Recurrent COVID-19-related psychotic disorder with neuro-immuno-endocrine dysfunction as a possible underlying mechanism: A case report from China☆

Chenghui Yang [a,b,1], Ying He [a,b,1], Lu Yuan [a,b], Cui Yuan [a,b], Fan Chang [a,b], Wenqian Feng [a,b], Bo Zhou [a,b,*]

[a] Sichuan Provincial Center for Mental Health, Sichuan Academy of Medical Sciences&Sichuan Provincial People's Hospital, Chengdu, 610072, China
[b] Key Laboratory of Psychosomatic Medicine, Chinese Academy of Medical Sciences, Chengdu, 610072, China

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ABSTRACT

Background: SARS-CoV-2, first identified in Wuhan, China, in December 2019, has been gradually spreading worldwide since 2020. The relationship between SARS-CoV-2 infection and psychotic disorders has received much attention, and several studies have described the direct/indirect mechanisms of its effects on the brain, but no mechanism has been found to explain recurrent episodes of COVID-19-related psychotic symptoms.
Case: We report the case of an 18-year-old female patient with no family or personal psychotic disorder history with multiple hospital admissions with symptoms such as disorganized speech and behavior, hyperactivity, restlessness, and impulsive aggression during the COVID-19 recovery period. Relevant tests revealed longitudinal changes such as persistent IL-6 and IL-10 elevation, abnormal discharges on EEG, and brain and hippocampal MRI abnormal signals. The patient was treated with antipsychotics, MECT, combination therapy of hormones and antivirals, then discharged after multiple treatment rounds.
Conclusion: The case presented here outlines the possibility that the COVID-19 recovery period may be a critical period for acute psychotic episodes and that the patient's recurrent psychotic symptoms may be associated with neuro-immuno-endocrine dysfunction mediated by sustained cytokine synthesis, further causing structural and functional brain damage. Routine psychiatric evaluation and related screening should be performed at all stages of the illness to better identify, prevent, and effectively intervene in psychiatric disorders following COVID-19. Because many outcomes require long-term assessment, a clearer understanding of the impact of the COVID-19 epidemic on mental health is likely to emerge in the future.

1. Introduction

Although severe acute respiratory system coronavirus 2 (SARS-CoV-2) infection is known to affect the respiratory and cardiovascular systems, its relationship with neuropsychiatric symptoms has also received much attention. The estimated prevalence of COVID-19-related neurological and psychiatric outcomes is approximately 12.8%, which increases to 25.8% among patients admitted to the intensive care unit (ICU), Among them, the highest incidence rate is ischaemic stroke, anxiety disorder and psychotic disorder (Taquet et al., 2021). The underlying mechanisms of neuropsychiatric symptoms after SARS-CoV-2 infection are unclear. The authors of several studies have proposed that coronaviruses are neurophilic and can enter the central nervous system (CNS) through direct or indirect methods, such as hematogenous and/or neuronal retrograde dissemination (Desforges et al., 2019). Among these methods, transmission through the neuronal pathway can occur through the olfactory nerve and/or enteric nervous system (Desforges et al., 2019; Pereira, 2020). While in the blood-borne pathway, infected leukocytes can carry the virus to the brain by crossing the blood–brain barrier and directly infecting ACE-2-expressing brain

☆ Present/permanent address:32, Section 2, 1st Ring Road West, Chengdu, Sichuan, China, 610072.

* Corresponding author. Sichuan Provincial Center for Mental Health, Sichuan Academy of Medical Sciences&Sichuan Provincial People's Hospital, 32, Section 2, 1st Ring Road West, Chengdu, Sichuan, 610072, China.
E-mail address: tonyac7721@163.com (B. Zhou).

[1] Chenghui Yang and Ying He contributed equally to this work.

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microvascular endothelial cells in the brain. This receptor has been found to be expressed in various subpopulations of airway epithelium, lungs, and brain cells including endothelial cells of the brain microvascular system. The S protein covering the virus surface binds to the cell ACE-2 receptor, resulting in reduced ACE-2 expression. The down-regulation of ACE-2 triggers neutrophil infiltration into the tissue, which can enhance tissue damage (Holmes et al., 2020). However, direct viral involvement in these pathways has not been demonstrated because viral RNA and viral antigens are rarely detected in brain tissue.

Regarding the mechanism of SARS-CoV-2 causing neurological and psychiatric symptoms, a growing body of evidence highlights the potential role of neuroimmune networks and neuroendocrine axes. For example, SARS-CoV-2 may release a large number of cytokines through direct neuropathic effects or by promoting the host immune system, which is called "cytokine storm". It is considered to be the main cause of disease severity and death of patients with COVID-19, and this high inflammatory reaction of the body may cause abnormal performance of the nervous system. In addition to the key mechanism of the "cytokine storm" (Mehta et al., 2020), the activation of the hypothalamic pituitary-adrenocortical (HPA) axis has been observed in the pathology of immunity/inflammation (Silverman et al., 2005) and further affects the secretion of multiple neurotransmitters in the nervous system, thus causing COVID-19-related psychotic disorders.

There are currently no reports of recurrent hospital admissions in patients with COVID-19-related psychotic disorders. This paper is the first to report the case of a patient with mild COVID-19 who developed psychotic symptoms during the recovery period and was repeatedly admitted to the hospital as a result. We attempt to explain the mechanism underlying these psychotic episodes and their recurrences after SARS-CoV-2 infection. Additionally, we provide suggestions for the active diagnosis, effective treatment, a long-term follow-up and management of these patients.

2. Case report

In December 2022, an 18-year-old female presented with malaise, sore throat, cough, sputum, and fever of 38.9 °C. A COVID-19 antigen self-test showed a positive result, suggesting SARS-CoV-2 infection, and the patient's condition improved after 3–4 days of self-administration of symptomatic drugs such as ibuprofen without visiting the hospital. Approximately two weeks later, the patient became emotionally unstable after suffering some stressful events, with depressed mood most of the time, social withdrawal, reluctance to go out, and sometimes irritability, but the family did not take the patient to the hospital. In January 2023, after being diagnosed with scoliosis, the patient had another emotional outburst. After a psychotherapy session, she developed obvious disorganized speech and behavior, such as repeatedly calling her favorite boy's name, taking others' things suddenly, wearing other people's clothes, helping others make their beds, throwing clothes around, and running around. Meanwhile, She was extremely excited and talkative, having abnormally high levels of energy, staying up all night, keeping talking about previous events of which the content was disorganized and difficult to understand. She was restless, irritable, and easily provoked. She often smashed things, cursed, and even beat her parents. During the course of this episode, the patient urinated in her pants twice. The patient was poorly cooperative in the psychiatric examination, with irrelevant answers to questions, scattered thinking, disorganized speech and behavior, and psychomotor agitation. Considering the patient's prominent psychotic symptoms, excitability and irritability, significant impairment of social functioning, and complete lack of self-awareness, as well as the difficulty of her family in managing her condition, the patient was forcibly admitted to the hospital (February 16, 2023).

In a physical examination performed after admission, the patient's vital signs were stable; however, she was uncooperative. Neurological testing such as Babinski reflex were negative. The Positive and Negative Syndrome Scale (PANSS) total score was 74, and the Brief Psychiatric Rating Scale (BPRS) total score was 48.

Upon admission, the result of a nucleic acid test for SARS-CoV-2 was negative, but the results of a SARS-CoV-2 antibody test were IgM (+) and IgG (+). Cytokine test results were as follows: IL-6, 3.53 pg/ml; and IL-10, 4.31 pg/ml. Lymphocyte subset testing results showed a decreased $CD4^+$ T/CD8+ T ratio of 1.30 and a prolactin level of 2139 mIU/L. The results of a TORCH panel test were as follows: anti-rubella virus IgG antibody (RVIgG), 39.7 IU/ml; anti-cytomegalovirus IgG antibody (CMV-IgG), 90.9 U/mL. The remaining blood test results, including those for the erythrocyte sedimentation rate; calcitoninogen, lipid, and blood glucose levels; liver, kidney, coagulation, and thyroid function parameters; electrolytes; and infectious agents, were not significantly abnormal.

Regarding the patient's personal history, family history, etc. She was full term natural delivery without hypoxia or asphyxia, and the growth and development have been similar to those of her peers since childhood. She was extroverted but sensitive.

She is currently studying in college, with moderate to high academic performance and good interpersonal skills. She has no family history of psychotic disorders, and no history of psychoactive substance exposure. She had received her first dose of the COVID-19 vaccine in August 2021 and the second dose of the vaccine in September 2021, without a third dose because she was underage.

On the second day of admission, a lumbar puncture was performed, and the cerebrospinal fluid (CSF) cell count, chloride, glucose, and microglobulin total protein levels were normal. SARS-CoV-2 antibody testing of CSF showed IgG (+) and IgM (−). The CSF level of IL-6 was normal. The results of tests for autoimmune, paraneoplastic, and virus-specific antibodies in CSF were all negative.

The patient's general electroencephalogram (EEG) was normal. Brain computed tomography (CT) showed no significant abnormalities. Chest CT showed only a small nodule of approximately 3 mm in diameter in the subpleural segment of the apical segment of the right lung (TM73), which was considered an inflammatory nodule. Brain MRI was not performed because the patient was uncooperative, and the family refused.

At the time of admission, the patient could not cooperate with medication administration and was aggressive, so protective restraint was implemented, and "ziprasidone injection 20 mg bid" was administered intramuscularly for 4 days. The symptoms improved significantly. This regimen was then replaced with oral administration of "ziprasidone capsules 40 mg bid, and valproate magnesium 0.25 g bid". On the 12th day of hospitalization, the patient and her family requested discharge. At the time of discharge, the patient's answers were relevant to the questions, and her emotional responses and mental behavior were coordinated, but she was still slightly excited and talkative and could only partially recall her state at the time of illness.

After discharge, the patient returned to school and continued her studies, but she did not take her medication regularly. Five days later, the patient again had disorganized speech and laughed to herself, saying "my surname is Yang and miss my own father". She was brought to our department by her family for a second time (March 7, 2023). The patient had difficulty cooperating with the psychiatric examination, her answers were not relevant to the questions asked, she talked and laughed to herself, she was excited and talked a lot, and her thought patterns were obviously disconnected. The patient was restrained in bed because she was running around in the ward, irritable, impulsively aggressive, and smashing objects, and she urinated on the bed. She was unable to cooperate in eating and taking medication. Her PANSS total score was 147, and her BPRS total score was 86.

A SARS-CoV-2 antibody test was completed again, and the results were IgM (+) and IgG (+). Cytokine test results were as follows: IL-6, 3.55 pg/ml; and IL-10, 5.13 pg/ml. Lymphocyte subset testing results showed that the $CD4^+$ T/CD8+ T ratio had decreased by 1.34 and the $CD4^+$ T lymphocyte count had decreased by 380/μL. The remaining routine blood tests and other test results were the same as those of the

previous hospitalization without significant abnormalities. The CSF results were similar to those of the last hospitalization, with no significant abnormalities.

However, it is worth noting that the patient's general EEG at this time suggested mild to moderate abnormalities. The 24-h EEG suggested abnormalities (with epileptiform discharges and a single scattered asynchronous high-amplitude spike and spike slow-wave emission seen in the frontal, central, and temporal regions during sleep). The findings of brain and cervical-thoracic-lumbar MRI were as follows: 1. a small area of high signal intensity in the cerebral white matter of the left frontal lobe (a small, speckled, slightly T1-long, T2 signal shadow in the left frontal white matter area, with the fluid attenuation inversion recovery (FLAIR) sequence showing a slightly high signal), suggesting the need for follow-up review; 2. mild atrophy in the bilateral hippocampal MRI scan; 3. no definite abnormality in the brainstem thin layer scan; 4. an abnormal signal in the cervical medulla (at the level of the 6th and 7th vertebrae) in the form of stripes, possibly in the spinal cord cavity; 5. no definite abnormality on thoracic spine MRI; and 6. interspinous ligament edema between the 5th lumbar and 1st sacral vertebrae (see Fig. 1).

The patient was completely unable to cooperate with eating and oral medication administration and was given "ziprasidone injection 20 mg bid" intramuscularly, which was changed to oral "aripiprazole oral solution (gradually increased to 5 ml bid) and quetiapine 0.2 qn" after she was able to cooperate with oral medication administration. The patient was restless and irritable, so she was given "magnesium valproate 0.5 bid" to stabilize her mood. The patient's symptoms still did not improve significantly, and she showed poor cooperation with oral medication administration, so she was treated with modified electroconvulsive treatment (MECT) on the 7th day of admission, but her symptoms still did not improve significantly, so she was treated with a methylprednisolone sodium succinate 1.0 g qd intravenous drip (1.0 g intravenous drip for 3 days, 0.5 g intravenous drip for 2 days, changed to prednisone tablets 45 mg qd orally) on the 10th day of admission, and following combined treatment with nematovir/ritonavir tablets 3 co q12h orally for 5 days, the above symptoms gradually improved. The patient no longer needed forced restraint. Her impulsive agitation, excitement and restlessness gradually decreased, but she still showed significant disconnected thought patterns. On the basis of treatment with aripiprazole and quetiapine combined with magnesium valproate, her symptoms were largely relieved after hormone combined with antiviral therapy was started on day 10 and MECT was administer 6 times.

The patient complained of poor memory and slow response; her Mini-Mental State Examination (MMSE) score was 28, and her Montreal Cognitive Assessment (MoCA) score was 23. On the 23rd day of hospitalization, the patient was reexamined. The results for serum IgM antibodies to SARS-CoV-2 turned negative, while the results for IgG antibodies remained positive. Her cytokine levels were elevated again, and her white blood cell count and neutrophil count were elevated (the possibility of this being related to hormone use was considered, as no other basis for infection was found). On the 29th day of hospitalization, the patient and her family requested discharge from the hospital. At discharge, the oral medications were aripiprazole oral solution 5 ml bid, quetiapine 0.2 qn, magnesium valproate 0.5 bid, and prednisone 40 mg qd.

After discharge from the hospital, the patient returned to school without significant disorganized speech or behavior but experienced poor memory and mental unresponsiveness. On April 14, 2023, the patient was admitted to the hospital for a third time and again showed completely disorganized speech and behavior, disconnected thought patterns, and manic-like symptoms.

During this hospitalization, the family refused lumbar puncture and 24-h EEG review. A re-evaluation of head and neck MRI showed the following: 1. small ischemic foci in the left frontal and biparietal lobes (a punctate long T2 signal seen in the left frontal and biparietal lobes with high signal on FLAIR); and 2. a striated long T2 signal seen in the spinal cord in the plane of the 6th cervical vertebra, possibly with an enlarged central canal or other finding. Cytokine test results showed that IL-6 levels were even higher than in the previous hospitalization and the leukocyte counts were higher than normal (the patient's leukocyte counts continue to be higher than normal after the use of hormones), but the remaining test results were not significantly abnormal. For treatment, the family refused gammaglobulin shock therapy, so the treatment plan was adjusted to aripiprazole 15 mg qd+10 mg qn; clozapine 150 mg bid; valproate 500 mg qn; and benzhexol hydrochloride 2 mg bid, with a reduction of the prednisone dose as planned. The patient was again discharged after 25 days of treatment, and her IL-6 level at discharge was even higher than before, at 7.56 pg/ml (see Tables 1 and 2).

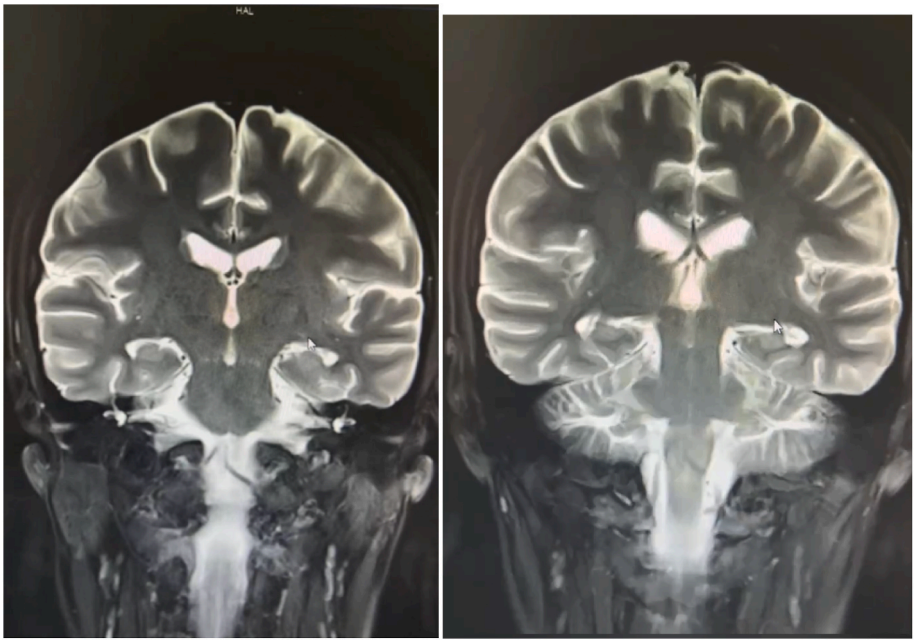

Fig. 1. Brain magnetic resonance imaging showing mild atrophy in the bilateral hippocampal on March 25, 2023 (Illness Day Over 2 months).

Table 1
Serum SARS-CoV-2 antibody test.

	IgM	IgG
2023.2.17	+	+
2023.3.13	+	+
2023.3.30	–	+

Table 2
Longitudinal changes in peripheral blood cytokine detection.

	2023.2.17	2023.3.8	2023.3.20	2023.5.9
IL-6 (pg/ml)	3.53	3.55	6.74	7.56
IL-10 (pg/ml)	4.31	5.13	6.51	9.5

3. Discussion

In this article, we report a new case of a female patient with no personal or familial history of psychosis who presented initially with a psychotic disorder dominated by schizophrenia-like symptoms such as disorganized speech and behavior, disconnected thought patterns, and mania-like symptoms such as impulsive aggression and excitement and talkativeness during the COVID-19 recovery period. Episodes recurred despite symptomatic treatment. Progressive cytokine elevation and EEG and MRI abnormalities were observed. In our case, tests for many infectious agents associated with encephalitis in the CSF were performed, as well as tests for paraneoplastic and autoimmune antibodies, but the results were negative; thus, these factors were excluded as being responsible for the pathogenesis.

The present case is similar to the results reported by Carroll et al. who found that neuropsychiatric symptoms were present not only in patients in the acute phase of COVID-19 but also in the later stages of recovery in asymptomatic or mildly ill patients with COVID-19 (Carroll et al., 2020; Chaudhary et al., 2022; Wu et al., 2020.) The recurrence of psychotic symptoms after COVID-19 and the longitudinal variability of test results make sense for the patient in this case report.

The immune system can be considered a link between SARS-CoV-2 infection and psychiatric disorders. There is growing evidence that altered local cytokine levels in the brain affect the synthesis, release, and reuptake of several neurotransmitters, including monoamine neurotransmitters such as dopamine, norepinephrine, and serotonin (Miller et al., 2013). Furthermore, the dysregulation of the monoamine system is associated with the pathophysiology of various psychiatric disorders, such as depression, anxiety, posttraumatic stress disorder, obsessive-compulsive disorder, and certain behavioral deficits (Bandelow et al., 2017; Grace, 2016). We noticed a progressive increase in the levels of IL-6 and IL-10 in this patient with recurrent episodes and multiple admissions; therefore, we hypothesized that the persistent elevation of cytokines correlated with the progression of her condition. IL-6 is a well-known pleiotropic cytokine whose synthesis is strictly regulated by transcriptional and posttranscriptional mechanisms. When infection and tissue damage occur, IL-6 synthesis is rapidly induced, contributing to bursting signals for host defense. After environmental stressors are removed from the host, IL-6 production is terminated (Moore and June, 2020). However, in some cases, the levels of IL-6 can remain elevated and cause disease even after the removal of stressors (Balschun et al., 2004; Tanaka et al., 2014). Regarding the mechanisms of dysregulated IL-6 synthesis, researchers have recently discovered two regulatory factors that play important roles. One is regulatory RNase-1 (Regnase-1), whose nuclease disrupts the stability of IL-6 mRNA. The other is AT-rich interaction domain 5A (Arid5a), which is binds to the 3′- UTR of IL-6 mRNA, leading to selective stabilization of IL-6. Arid5a offsets the unstable function of Regnase-1 on IL-6 mRNA, thus the imbalance between Arid5a and Regnase1can promote inflammatory processes and possibly induce the development of inflammatory autoimmune diseases (Masuda et al., 2013). More importantly, evidence is available that the dysregulation of cytokine expression can lead to the development of psychiatric disorders (Wiener et al., 2019).

In this case, we found a sustained increase in peripheral blood white blood cells and neutrophils, but the patient showed no signs of infection. We consider this change to be related to the use of steroid hormone therapy. For patients on GC therapy, the effects of GCs on white blood cells are similar to the effects of bacterial infections on white blood cells, which may lead to misdiagnosis of patients suffering from infection and overuse of antibiotics. The mechanism of GC action on leukocytes is very complex. Several researchers selected 44 articles for analysis and summary, and summarized the relevant research on the effects of GCs on leukocytes in recent decades. Glucocorticoids (GCs) increase peripheral blood neutrophil counts through genomic and non-genomic actions and reduce the numbers of lymphocytes, eosinophils, basophils, and monocytes. GCs increase the neutrophil count in peripheral blood through a variety of mechanisms of action: (1) They promote neutrophil attachment to the blood vessel walls to enter the blood circulation (the marginal pool enters the circulating pool); (2) They reduce neutrophil outflow from the circulating pool; (3) They inhibit the apoptosis of neutrophils and delay their clearance in peripheral blood; and (4) They stimulate hematopoiesis in the bone marrow and increase the production of neutrophils in the peripheral blood (Jia and Zhang, 2022).

Currently, a growing body of data confirms the direct effects of SARS-CoV-2 on the limbic system of the brain and its immune-mediated damage (Bridwell et al., 2020; Lu et al., 2020; Paterson et al., 2020). In addition, there are many studies describing the cases of patients with COVID-19 presenting with symptoms such as cognitive impairment, anxiety/depression disorders, and sometimes aggressive psychotic behavior, which, combined with information from patients' clinical examinations such as EEG, MRI, and CSF analysis, suggest that most patients with COVID-19 fit the profile of having limbic encephalitis (Machhi et al., 2020; Troyer et al., 2020). Due to the absence of viral RNA or specific antibodies in the CSF, some authors have suggested that the development of SARS-CoV-2-associated parainfluenza limbic encephalitis is caused by a secondary hyperinflammatory syndrome with a massive release of proinflammatory cytokines and chemokines from the limbic system of the brain (Mehta et al., 2020; Pizzanelli et al., 2021; Perrin et al., 2021). Therefore, the nature of this pathological process can be described as paracontagious, and MRI of limbic structures can be considered an important method for the diagnosis of paracontagious limbic encephalitis associated with SARS-CoV-2 infection (Pizzanelli et al., 2021; Zambreanu et al., 2020.). According to MRI, in most cases, damage to the limbic system in patients with COVID-19 is bilateral, manifesting as high T2 and FLAIR signals (Lu et al., 2020; Zambreanu et al., 2020). In addition, the presence of abnormal activity in the EEG in the temporal lobe during seizures or (more commonly) during interictal periods should be considered an important factor (Kurd et al., 2021). Similarly, the patient whose case is reported here continued to present with schizophrenia-like and mania-like symptoms such as disorganized speech, behavior and cognitive decline after the second admission. With the abnormal discharges showed in EEG, suggesting that the patient's condition may be consistent with parainfluenza limbic encephalitis in the context of a persistently dysregulated immune response. However, there is no imaging or CSF evidence of limbic system damage at this time, so long-term follow-up of the patient is particularly important.

SARS-CoV-2-mediated neurogenic alterations and neuroinflammation may be associated with abnormal hippocampal plasticity. Hippocampus plays an important role in the regulation of mood and cognitive functions, and hippocampal atrophy caused by some viral infections leads to neurocognitive impairment and memory loss (Kandasamy et al., 2020; Popkirov et al., 2017). Douaud et al.'s investigation found SARS-CoV-2 had a significant longitudinal impact on the brain of infected people, including a greater reduction in the thickness of gray matter and tissue contrast in the orbitofrontal cortex and parahippocampal gyrus as well as a greater reduction in the overall brain

volume. Also, these infected participants showed more pronounced cognitive decline (Douaud et al., 2022). This is similar to the clinical features of the case, who not only showed subjective cognitive decline, but MRI also revealed mild atrophy of the hippocampus bilaterally.

In addition, we found that this patient had a certain level of social and psychological stress before every onset of an episode. Could it be that psychological and behavioral factors, in addition to biological processes, may similarly influence these immune dynamics and ultimately the course of viral infection? Research in psychoneuroimmunology (PNI) has documented the close connection between the brain and the immune system, which together protect the organism from infection and injury. The persistence of psychosocial stress leads to elevated circulating levels of stress hormones such as cortisol, corticosteroid-releasing hormone (CRH), epinephrine, and norepinephrine, which may alter HPA axis signaling, exacerbate neuroinflammation, and worsen neuroplasticity in the brain (Herman et al., 2016). There are no studies on the link between psychosocial factors and immunity in SARS-CoV-2-infected individuals. However, there is evidence that patients with mental disorders are at increased risk of hospitalization and death associated with COVID-19 (Vai et al., 2021; Wang et al., 2021), which supports the relevance of negative mental states to SARS-CoV-2 immune defense.

For this patient, we considered that early hormonal therapy and antiviral therapy at the first admission might be more effective in suppressing the excessive immune response in the body, interfering with the progression of her condition and shortening her treatment course. Considering that persistently elevated IL-6 may be a key factor in the recurrent episodes in this patient, the rationale for the use of immunomodulatory agents such as anti-IL-6 antibodies in such patients would be worth exploring. There is evidence that the inflammatory status of psychiatric patients plays a role in their response to treatment (Baumeister et al., 2016). For example, patients diagnosed with inflammatory diseases (rheumatoid arthritis, asthma, lupus, and ulcerative colitis) often present with depressive symptoms that can be ameliorated by immunomodulatory medications. In addition, studies have found that anti-IL-12/23 antibodies and anti-IL-6 antibodies have antidepressant effects (Wittenberg et al., 2020). Thus, these study findings highlight that the addition of anti-inflammatory agents may be an important approach to treating psychiatric disorders, especially in patients who are in an inflammatory state at baseline. Indeed, in a recent review, Areaga Henríquez et al. (Arteaga-Henríquez et al., 2019) noted that the use of infliximab (an anti-TNFα agent), dimethylaminotetracycline (a tetracycline antibiotic), or eicosapentaenoic acid (ω3 fatty acid) improved depression in patients with elevated CRP/IL6 levels at baseline.

4. Conclusion

Although COVID-19 is considered a respiratory disease, its relationship with neuropsychiatric symptoms needs to be emphasized. In addition, impaired concentration, headache, sensory disturbances, mood disorders, and even psychiatric disorders may persist for months after infection as part of a spectrum of symptoms now known as long COVID. With millions of people infected, neuropsychiatric complications pose a public health challenge in terms of recovery, rehabilitation, and workforce disruption due to an inability to work. There is an urgent need to understand the pathophysiology of these conditions and to develop methods to effectively diagnose and treat them. Here, the case of a patient who was repeatedly admitted to the hospital because of recurrent psychotic symptoms in recovery from COVID-19 is reported. Her acute psychotic episodes are described, and the possible mechanisms underlying recurrent episodes are discussed. The report of this case provides ideas for clinical correct identification, active intervention, prevention of recurrence and long-term follow-up of patients with psychotic symptoms after COVID-19. It is suggested to clarify the time interval between COVID-19 infection and the onset of psychosis, detect cytokines, electroencephalogram, brain imaging and other aspects of patients, and early immunotherapy is possibly beneficial to the prognosis of the disease.

CRediT authorship contribution statement

Chenghui Yang: Conceptualization, Data curation, Formal analysis, Methodology, Writing – original draft. **Ying He:** Conceptualization, Funding acquisition, Validation. **Lu Yuan:** Resources. **Cui Yuan:** Conceptualization, Supervision, Writing – review & editing. **Fan Chang:** Resources. **Wenqian Feng:** Resources, Software. **Bo Zhou:** Conceptualization, Writing – review & editing.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

No data was used for the research described in the article.

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