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Case Report

Tocilizumab in the treatment of COVID-19 related encephalopathy with Claustrum lesion: A case report ☆,☆☆

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ABSTRACT

COVID-19-related encephalopathy is a complication of COVID-19 that affects the brain. It can present with symptoms such as altered mental status, ranging from mild confusion to deep coma. It is a major and devastating complication of the SARS-CoV-2 virus. COVID-19-related neurological symptoms may be associated with cytokine release induced by the virus, and tocilizumab targeting IL-6 receptor may provide significant benefits. We report a case of COVID-19-related encephalopathy with cerebrospinal fluid analysis revealing significantly elevated levels of IL-6. Brain magnetic resonance imaging showed a bilateral high signal in the claustrum, and treatment with tocilizumab was effective.

Case presentation

A 15-year-old previously healthy girl was admitted to the hospital due to seizures and abnormal mental behavior. Seven days before admission, she presented with fever and cough, with a maximum temperature of 39.2°C. Laboratory tests showed a decrease in white blood cells and increased lymphocyte ratio. At that time, a chest CT scan showed no significant abnormalities, and reverse transcription-polymerase chain reaction (RT-PCR) for SARS-CoV-2 RNA was negative. After antipyretic treatment, the patient's symptoms improved. The day before admission, the patient had poor short-term memory and could not remember recent events. Several hours later,

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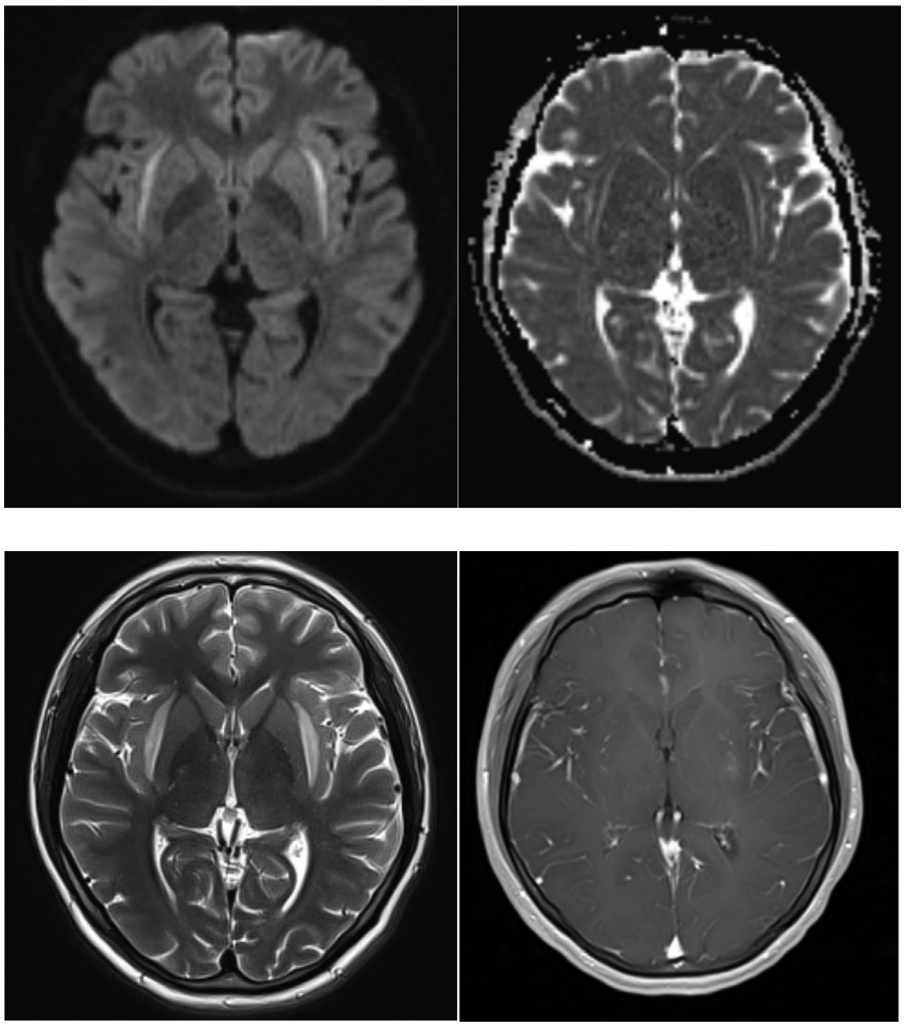

Fig. 1 – Axial DWI and T2 images reveal high signal intensity in the bilateral claustrum, which corresponds to elevated ADC values. Axial T1-contrast images show mild brain edema with linear enhancement in the bilateral claustrum.

she became unconscious and had convulsions of all 4 limbs lasting about 1 minute. The patient's medical history indicates previous good health without any prior seizure episodes. There is no record of using specific medications. The patient was born under normal circumstances without any labor complications or hypoxia. Furthermore, the patient has not received the COVID-19 vaccine previously.

On the second day of admission, the patient exhibited abnormal mental behavior and repetitive speech. Laboratory tests of blood showed no significant specific changes. Lumbar puncture was performed, and cerebrospinal fluid pressure was 350 mmH_2O. Cerebrospinal fluid protein was normal and cerebrospinal fluid cytology showed an increase in lymphocytes. HSV1, varicella-zoster virus, EB virus, and cytomegalovirus cerebrospinal fluid antibodies were all negative. Autoimmune encephalitis antibodies were also negative. However, high-throughput next-generation sequencing of cerebrospinal fluid revealed positive SARS-CoV-2 RNA with a sequence count of 3. Cerebrospinal fluid cytokine analysis showed an IL-6 level of 278.08 pg/mL, significantly higher than the normal range (0-5.3 pg/mL). Detailed examination results are provided in the supplementary table.

Head magnetic resonance imaging (MRI) showed a high signal in the bilateral Claustrum on DWI, T2, and Flair sequences with a corresponding high signal on ADC. T1-contrast showed mild brain edema with linear enhancement of the pia mater at the top of the bilateral frontal and temporal lobes, suggesting inflammation (Fig. 1). Electroencephalogram (EEG) showed asynchronous sharp slow waves in the bilateral temporal regions during sleep.

Based on the positive COVID-19 RNA and increased IL-6 level in cerebrospinal fluid, the patient was diagnosed as parainfectious encephalopathy related to COVID-19. Immediate treatment with methylprednisolone 500mg/d for 5 days was initiated, followed by a gradual reduction in steroid dosage. Tocilizumab (4 mg/kg, used twice) was also administered. The patient's symptoms improved, and abnormal mental behavior disappeared. Cognitive function improved with a Montreal Cognitive Assessment (MOCA) score of 18 at admission and 26

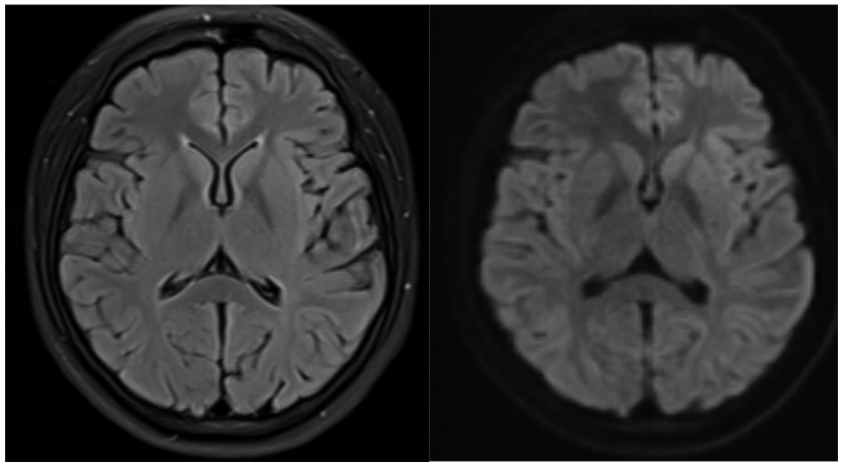

Fig. 2 – Axial Flair and DWI show Claustrum sign disappeared 3 months later.

after 14 days. Three months later, the patient's imaging results returned to normal and were generally good (Fig. 2).

Discussion

The pathogenesis of encephalopathy associated with COVID-19 may be multifactorial. the mechanisms include para-infectious inflammation induced by the intense cytokine storm [1]. Multiple studies have demonstrated a direct correlation between the severity of cytokine storm and the severity of neurological manifestations in COVID-19-related encephalopathy [2,3]. patients with COVID-19 related cytokine storm had a lower average serum cytokine load which may be the reason for the lower incidence of encephalopathy in the COVID-19.

Claustrum sign are associated with refractory epileptic syndrome, which may predict a poor outcome. Claustrum sign have been widely reported in febrile infection-related epileptic syndrome (FIRES) and new-onset refractory status epilepticus (NORSE), which may represent a subclass of newly intractable epileptic states induced by cytokine storm [4,5]. Interleukin-6 is an important member of the cytokine network. It plays a key role in the body's anti-infection immune response. Excessively elevated IL-6 levels maybe a marker of cytokine storm. Tocilizumab is a recombinant humanized monoclonal antibody that binds to interleukin-6 (IL-6) receptors, thereby blocking the activity of pro-inflammatory cytokines [6]. Several clinical trials have indicated that tocilizumab may ameliorate the symptoms and outcomes of patients with COVID-19 by attenuating cytokine release syndrome [7,8]. Anti-interleukin-6 receptor monoclonal antibody may be a potential therapeutic option for this condition.

In this case, there was a significant increase in the level of IL-6 in the cerebrospinal fluid and the presence of imaging changes in the bilateral claustrum. Given the uncertain long-term outcomes of COVID-19-related encephalopathy and claustrum signs may cause potentially severe clinical manifestations, tocilizumab therapy was initiated for this patient, resulting in a significant improvement of her symptoms. Tocilizumab may have a significant short-term effect on COVID-19 patients with encephalopathy, and further follow-up observation is required for long-term treatment.

Conclusion

Acute encephalopathy with claustrum sign may be one of the clinical phenotypes of inflammatory neurological complication of COVID-19. Tocilizumab may have a therapeutic effect on this condition and warrants further study.

Patient consent

Verbal and written informed consent were obtained from the patient.

Author contributions

CH.L: performed data analysis and drafted the manuscript. N.W and QQ.H: performed data analysis and prepared the manuscript. XC.L and MM.Z: prepared the manuscript. HZ.G: drafted the manuscript, reviewed the article critically for important intellectual content. GQ.Y: reviewed the article critically for important intellectual content. All authors contributed to the article and approved the submitted version.

Professor Hongzhi Guan and Gaiqing Yang served as a co-corresponding author for this article.

Data availability statement

The data used and analyzed during the present study are available from the corresponding author on reasonable request.

Ethical approval

We confirm that we have read the journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines. As this is a case report describing clinical observations, ethics approval was waived.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.radcr.2024.09.092.

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