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LETTER TO THE EDITOR

A case of coronavirus HKU1 encephalitis

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Summary. – Coronaviruses are widespread in nature and can infect several different species, causing mainly respiratory and enteric diseases. The respiratory involvement of human coronaviruses has been clearly established since the 1960s. Three of the six coronaviruses that infect humans have been shown to be neuroinvasive and neurotropic in humans: HCoV-229E, HCoV-OC43, and SARS-CoV. No reports exist on the detection of HCoV-HKU1 in the human central nervous system (CNS). We report a case of a patient, in whose cerebrospinal fluid (CSF) was detected Coronavirus NL63/HKU1. Coronavirus HKU1 was detected in the sputum. With effective antiviral therapy and the use of glucocorticoids, the patient was eventually discharged from the hospital. This study might help understand more about coronavirus and improve the awareness of pathogen detection in patients with coronavirus encephalitis.

Keywords: coronavirus HKU1; encephalitis

Coronaviruses are widespread in nature and can infect several different species, causing mainly respiratory and enteric diseases (*1*). An estimated 200 antigenically distinct viruses can cause infection of the respiratory tract, especially in infants and children (*2*). The respiratory involvement of human coronaviruses has been clearly established since the 1960s. Three of the six coronaviruses that infect humans have been shown to be neuroinvasive and neurotropic in humans: HCoV-229E, HCoV-OC43 (*3*), and SARS-CoV (*4*). But no reports exist on the detection of HCoV-HKU1 in the human central nervous system (CNS). We report a case of a patient with coronavirus encephalitis associated with coronavirus NL63/HKU1.

A 42-year-old previously healthy, adult, male patient presented to the Department of Neurology of the Suqian First Hospital in August 2019 with 4 days of slow response. His wife and son explained that he suddenly became unresponsive, his eyes glazed over, and he was unable to answer questions from everyday life properly. The patient reported dizziness and top-heavy, unsteadiness. The patient denied visual changes, seizure, headache, swallowing difficulty, mental status changes, or bowel or bladder dysfunction. He had no history of toxin ingestion. The patient and his wife ran a restaurant and had been drinking alcohol (corresponding to 40~60 grams of ethanol daily) for about 10 years, about half a catty, which gradually decreased in the last 6 months. He smoked 25 cigarettes/day. Usually, he came in contact with people in the living area. He had no pet. Also, he denied respiratory infection in the last 2 weeks. All family members were reported to be healthy. The patient's general physical examination was unremarkable. His vital signs were stable, and he was afebrile with no ataxia or disorientation. The nervous system test was negative, and the sphincter tone was normal. The reflexes were present and symmetric in all extremities and soles of the feet. The deep and light

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Abbreviations: CNS = central nervous system; CSF = cerebrospinal fluid; HCoV = human coronavirus

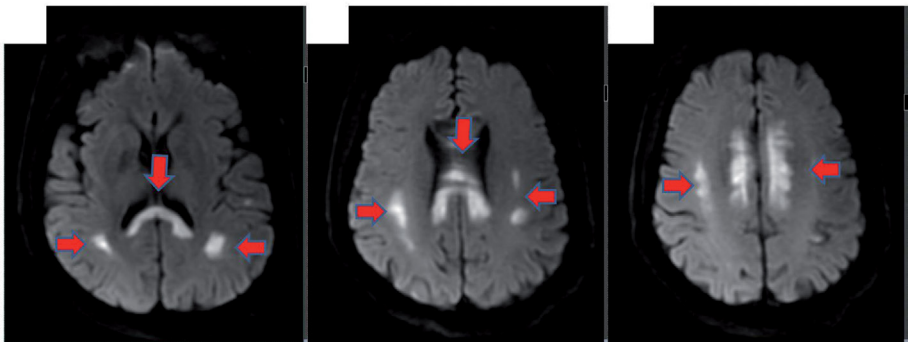

Fig. 1

DWI (TR 1794) axial image of the brain showing multiple high-signal lesions in the area of the compressors of the corpus callosum and two flanks of the corona radiata (red arrows)

feeling was normal. On the second day after admission, the patient suffered from seizures more than 10 times, with mouth spasms and limb convulsions lasting from seconds to minutes.

The computer tomography (CT) examination of brain was performed 1 day before admission and showed multiple abnormal, low-density shadows in the brain. The magnetic resonance imaging (MRI) of the brain performed 2 days after admission (Fig. 1) revealed an axial image of the brain showing multiple high-signal intensity lesions in the compressor of the corpus callosum and two flanks of the corona radiata (red arrows). On the third day, the patient experienced a prolonged seizure leading to a coma, followed by decreased blood oxygen saturation, and was transferred to the intensive care unit (ICU) for continued treatment. The chest CT scan showed a right middle lobe medial segment, a lamellar high-density shadow under both lungs, and atelectasis. The patient was treated with mannitol, immunoglobulins, ganciclovir, and methylprednisolone in the ICU. Pharyngeal swabs were negative for influenza antigen of A and B.

Subsequently, a lumbar puncture was performed to collect the CSF at a rate of about 100 drops/min. The CSF examination demonstrated no red blood cells, 41 × 10^6/l karyocytes, 85% polykaryocytes, and 15% monocytes. The protein concentration was 0.53 g/l, and the glucose level was 5.7 mmol/l. The CSF culture for bacteria was negative. The Pandy test was weakly positive (+–). The specimen of the patient's CSF was sent to Shanghai GeneoDx Biotechnology Co., Ltd. The nucleic acids were extracted from the CSF specimen (including double-distilled H2O as control samples) with a QIAamp cador Pathogen Mini Kit (Qiagen) following the manufacturer's instructions. The extracted nucleic acid samples were tested for viruses and bacteria by PCR using a RespiFinder Smart 22 kit (PathoFinder BV) (including internal and amplification controls) and a LightCycler 480 real-time PCR system, following the manufacturer's instructions (*5*). The specimen was analyzed for 22 pathogens (18 viruses and 4 bacteria) as detailed in the Supplementary Appendix. Coronavirus NL63/HKU1 was detected in the CSF. However, the RespiFinder Smart 22 kit could not further differentiate between coronavirus NL63 and HKU1. At the same time, we switched to ribavirin antiviral therapy and sent pharyngeal swab of the patient to Jiangsu Provincial Center for Disease Control and Prevention (Jiangsu Provincial CDC). Jiangsu Provincial CDC further completed virus typing. Coronavirus HKU1 was detected in the sputum. (The result was recorded in the patient's progress report in the Supplementary Appendix).

On the fifth day after admission, the patient developed fever and released a large amount of white watery sputum. The chest CT of both lungs suggested exudation. After 1 week, the Glasgow Coma Scale ranged from 3 to 10. After 10 days, the CSF protein concentration was normal. On MRI enhanced scanning, the lesion showed obvious annular enhancement. After 3 weeks of admission, the head CT scan suggested disappearance of the acute lesion. About 1 month later, the patient's nerve function recovered, and he could take care of himself.

This study was novel in reporting a case of coronavirus HKU1 associated with encephalitis disease in an adult patient. The patient's presumed diagnosis was coronavirus HKU1 encephalitis, although the lesions in the corpus callosum might be caused by demyelination due to long-term alcohol consumption. Central infection caused by the coronavirus is rare in adults. The presence of coronavirus HKU1 in the patient's sputum suggested the coronavirus was likely to infect CNS via the patient's respiratory tract. We were surprised at the rapid progression of the disease. Also, whether the severity of the disease is due to the difference in the viruses or the neurotropic nature of

the viruses cannot be differentiated. Effective drugs for treating coronavirus encephalitis are not available. Also, whether the antiviral drugs and glucocorticoids can help alleviate the symptoms of patients is not clear. A previous study based on a mouse model of herpes simplex virus encephalitis reported that 72 h after infection, mice that received glucocorticoids (56%) had a higher average life expectancy compared with those that did not receive glucocorticoids (44%) or those that received glucocorticoids early (13%) ($P < 0.05$) (*6*).

Neurological etiology examination is not common in clinic, and hence pathogenic microorganisms are not identified in many CNS infections. The detection of HCoV-HKU1 in human central nervous system has not been previously reported. The findings of this study might help clinicians understand more about coronavirus and improve their awareness of pathogen detection in patients with coronavirus encephalitis.

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References

1. Weiss SR, Leibowitz JL., Adv. Virus Res. 81, 85, 2011. https://doi.org/10.1016/B978-0-12-385885-6.00009-2

2. Zeng ZQ, Chen DH, Tan WP, Qiu SY, Xu D, Liang HX, Chen MX, Li X, Lin ZS, Liu WK., Eur. J. Clin. Microbiol. Infect. Dis. 37, 363–369, 2018. https://doi.org/10.1007/s10096-017-3144-z

3. Arbour N, Cote G, Lachance C, Tardieu M, Cashman NR, Talbot PJ., J. Virol 73, 3338–3350, 1999. https://doi.org/10.1128/JVI.73.4.3338-3350.1999

4. Gu J, Gong E, Zhang B, Zheng J, Gao Z, Zhong Y, Zou W, Zhan J, Wang S, Xie Z, Zhuang H, Wu B, Zhong H, Shao H, Fang W, Gao D, Pei F, Li X, He Z, Xu D, Shi X, Anderson VM, Leong AS., J. Exp. Med. 202, 415–424, 2005. https://doi.org/10.1084/jem.20050828

5. Zhu N, Zhang D, Wang W, Li X, Yang B, Song J, Zhao X, Huang B, Shi W, Lu R, Niu P, Zhan F, Ma X, Wang D, Xu W, Wu G, Gao GF, Tan W., N. Engl. J. Med. 382, 727–733, 2020. https://doi.org/10.1056/NEJMoa2001017

6. Yan S, Guy B, David G, Serge R., J. Infect. Dis. 195, 817–825, 2007. https://doi.org/10.1086/511987