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Title: **Acute myelitis after SARS-CoV-2 infection: a case report**

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Acute myelitis after SARS-CoV-2 infection: a case report

Abstract

We firstly reported a case of acute myelitis in a SARS-CoV-2-infected patient. A 66-year-old man with COVID-19 was admitted with acute flaccid paralysis of bilateral lower limbs and urinary and bowel incontinence. All serum microbiological studies were negative except for SARS-CoV-2 nucleic acid testing. Clinical findings could be ascribed to a post-infectious acute myelitis. He was receiving treatment with ganciclovir, lopinavir/ritonavir, moxifloxacin, dexamethasone, human immunoglobulin and mecobalamin. With a diagnosis of post-infectious acute myelitis and comprehensive treatment, paralysis of bilateral lower extremities ameliorated. After two times negative novel coronavirus RNA nasopharyngeal swabs tests, he was discharged and transferred to a designated hospital for isolation treatment and rehabilitation therapy.

Key words: COVID-19, acute myelitis, SARS-CoV-2

Background

The coronavirus disease 2019 (COVID-19) was first reported in Wuhan, China in December 2019¹. It has been confirmed that this disease is caused by a new type of enveloped RNA coronavirus B, which is named severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)². As of March 5, 2020, there were 96643 laboratory-confirmed cases worldwide, resulting in 3313 deaths. Studies have shown that the virus has 79% homology with SARS virus³, potential intermediate animal host is still unknown, it has been demonstrated this virus did not come directly from pangolins⁴. Researchers have confirmed that SARS-CoV-2 enters the human body through ACE2 receptors on the surface of human cells and causes disease⁵. ACE2 is expected to be a possible target for intervention and treatment of the disease. There are ACE2 receptors in type II alveolar epithelial cells of human lung, so it has become the main target of SARS-CoV-2 in the pathogenesis of COVID-19⁶. However, in the process of clinical diagnosis and treatment, it has been found that many critically ill patients have symptoms of multiple organ dysfunction, in addition to the lungs, liver and kidney damage is also very prominent, which may be related to the expression of ACE2 in hepatic bile duct cells and proximal renal tubules^{7, 8}.

ACE2 receptors are also expressed on the surface of spinal cord cells^{9, 10}, whether spinal cord neurons were implicated in the Covid-19 was still unknown. We report a patient with COVID-19 who suddenly developed acute myelitis after initial high fever, suggesting central nervous system (CNS) could be also attacked by SARS-CoV-2.

Case introduction

A 66-year-old male was admitted to hospital for fever and fatigue of 2 days in Wuhan, China. He had no contact with patients with COVID-19. He developed fever without obvious cause on February 8, 2020, the highest body temperature was 39 °C, with fatigue, without cough, asthma and dyspnea. He went to the outpatient clinic of Wuhan local hospital and was treated with oral moxifloxacin hydrochloride and oseltamivir for 5 days. On February 13, he performed a chest CT in the local lung hospital and found patchy changes in both lungs (Figure 1.A&B). The test of novel coronavirus RNA nasopharyngeal swab was positive, then he was diagnosed with mild Covid-19. He was admitted to Wuhan Cabin Hospital and was treated in individual isolation. After a high fever (40 °C) at night, he developed weakness of both lower limbs with urinary and bowel incontinence, culminating in flaccid lower extremity paralysis. His condition aggravated rapidly, and he was transferred to intensive care unit for critical care and treatment. Vital signs: Oxygen

saturation < 93% at rest, T37°C, P 80 bpm, R18 times/min, BP 81/51mmHg. No obvious abnormality was found in cranial nerve examination. His neurologic examination demonstrated 3/5 power with normal reflexes in the bilateral upper extremities and 0/5 power reduction with hyporeflexia in the bilateral lower extremities. Sensation was intact to all modalities in the arms but was globally impaired in both legs. There was a sensory level at T10 to pinprick testing, with feelings of paresthesia and numbness below the level. The tendon reflex of both lower limbs decreased, and the sensation of pain and temperature and tactile sensation decreased below the level of chest 10. Bilateral pathological signs were negative.

After admission, the laboratory test such as blood routine, C-reactive protein, serum amyloid protein, procalcitonin and large biochemistry were shown in Table 1. On admission, CEA was normal, serum ferritin > 2000 (normal range 21.81-274.6ng/ml), electrolytes: no obvious abnormality except serum iron (see Table 1). Hypersensitive troponin was normal. Blood lipid showed low high-density lipoproteinemia, high density lipoprotein cholesterol (HDL-C) 0.51 (1.16-1.42mmol/L). Interleukin 6 56.72 (0-7pg/ml). Detection of pathogenic microbes: chlamydia pneumoniae IgM, Epstein-Barr (EBV) antibody IgM, influenza B virus IgM, adenovirus IgM, coxsackievirus IgM, mycoplasma pneumoniae IgM, influenza A virus IgM, parainfluenza virus IgM, cytomegalovirus (CMV) IgM, respiratory syncytial virus IgM were all negative. T cells of tuberculosis infection were negative. The results of novel coronavirus RNA nasopharyngeal swab were shown in Table 2. Before treatment on February 15th, chest CT showed patchy high-density blurred shadow in the upper lobe of the left lung (figure 1A) and patchy ground glass shadow in the anterior segment of the upper lobe of the right lung (figure 1B), considering viral pneumonia. Cranial CT revealed bilateral basal ganglia and paraventricular lacunar infarction, brain atrophy (figure 2). CSF serological testing and MRI of spinal cord were not performed for pandemic during hospitalization.

Table 1 Characteristics of blood routine and biochemical tests after admission

| Indicators (normal rang) | Detection time | | | |
|--|----------------|-------------|-------------|-------------|
| | February 15 | February 18 | February 23 | February 27 |
| White blood cell ($3.5-9.5 \times 10^9/L$) | 11.81 ↑ | 16.15 ↑ | 11.93 ↑ | 10.61 |
| Neutrophil ($1.8-6.3 \times 10^9/L$) | 10.77 | 14.65 | 11.04 | 84.3 |
| Lymphocyte ($1.1-3.2 \times 10^9/L$) | 0.55 ↓ | 0.75 ↓ | 0.53 ↓ | 1.21 |
| Eosinophils ($0.02-0.52 \times 10^9/L$) | 0 ↓ | 0 ↓ | 0 ↓ | 0.02 |
| Red blood cell ($4.3-5.8 \times 10^9/L$) | 4.18 ↓ | 3.67 ↓ | 3.93 ↓ | 3.63 ↓ |
| Hemoglobin (130-175g/L) | 139 | 120 ↓ | 127 ↓ | 117 ↓ |
| C-Reactive Protein (0-5mg/L) | 277.76 ↑ | 162.4 ↑ | 19.94 ↑ | 7.16 ↑ |
| Serum amyloid protein (0.1-10mg/L) | 1843.8 ↑ | 980.75 ↑ | 232.65 ↑ | 99.09 ↑ |
| Procalcitonin (0.04-0.25ng/mL) | 4.33 ↑ | 0.52 ↑ | 0.08 | - |
| Alanine aminotransferase (5-40U/L) | 56.4 ↑ | 59.8 ↑ | 98.9 ↑ | 64.8 ↑ |
| Aspartate aminotransferase (8-40U/L) | 50 ↑ | 56.6 ↑ | 93.6 ↑ | 48 ↑ |
| Serum total protein (60-83g/L) | 67.7 | 49.1 ↓ | 55 ↓ | 55.5 ↓ |
| Serum albumin (34-54g/L) | 34.7 | 26.1 ↓ | 25.1 ↓ | 25.9 ↓ |
| Creatine kinase (25-200U/L) | 102 | 853 ↑ | 2476 ↑ | 441 ↑ |
| Lactic dehydrogenase (109-245U/L) | 183 | 160 | 241 | 220 |

| | | | | |
|-----------------------------------|--------|--------|-------|-------|
| Blood urea nitrogen (3-9.2mmol/L) | 7.38 | 7.1 | 8.3 | 7.3 |
| Creatinine (44-120umol/L) | 78 | 86 | 78 | 68 |
| Serum iron (10.6-36.7umol/L) | 1.80 ↓ | 6.16 ↓ | 17.56 | 13.35 |

Table 2 2019-nCoV RNA nasopharyngeal swabs tests in the patient with COVID-19

| 2019-nCoV detection time | February 13 | February 19 | February 21 | February 23 | February 26 | February 28 |
|-----------------------------|-------------|-------------|-------------|-------------|-------------|-------------|
| Results | Positive | Negative | Negative | Positive | Negative | Negative |

For positive 2019-nCoV test, COVID-19 was diagnosed. Based on the acute flaccid myelitis of lower limbs, urinary and bowel incontinence, and sensory level at T10, diagnosis of acute myelitis was more likely. After admission, oxygen inhalation treatment with high-flow nasal catheters was given. Meanwhile, the patient was treated with comprehensive drug therapies: ganciclovir(0.5g once daily) for 14 days, lopinavir/ritonavir (500mg twice daily) for 5 days, moxifloxacin(400mg once daily) for 6 days, meropenem (1g twice daily) for 8 days, glutathione(1.8g once daily) for 14 days, dexamethasone (10mg once daily) for 10 days; human immunoglobulin (15g once daily) for 7 days, mecobalamin (1000ug once daily) for 14days; pantoprazole(80mg once daily) for 10 days. On the second day after admission, the patient's body temperature basically returned to normal, and the oxygen saturation was more than 93% at rest. There was no occurrence of adverse drug reactions and contraindications. The muscle strength of both upper limbs recovered to grade 4/5, and the muscle strength of both lower limbs was grade 1/5. Two times novel coronavirus RNA nasopharyngeal swabs tests were negative with an interval of more than one day. Re-examination of pulmonary CT showed that the lesions were absorbed and met the discharge criteria of COVID-19. Then, he was discharged and transferred to a designated hospital for isolation treatment and rehabilitation therapy.

Discussion

Our study firstly reported a post-infectious myelitis case in the world, indicating acute myelitis might be the neurological complication of 2019-nCov. It had been demonstrated that microbes including mycoplasma pneumoniae, EBV, CMV, rhinovirus and measles were implicated in post-infectious acute myelitis¹¹⁻¹³. Mycoplasma pneumoniae was thought to be one of the most recognized infections. Probable hypothesis was that infectious organism was targeted against by immunologic system which also attacked central nervous system (CNS) tissue because of structural similarities between the microbial cellular wall components and neuronal receptors¹⁴. In this study, the IgM antibody of common infectious organisms including mycoplasma pneumoniae, EBV and CMV were negative, and the symptoms of acute myelitis occurred after high fever and diagnosis of COVID-19, suggesting 2019-nCov might be the pathogenic virus. Moreover, recent study showed that SARS-CoV-2 could enter the human body through ACE2 receptors on the surface of human cells and causes disease⁵. It was intriguing that ACE2 receptors were also expressed on the membrane of spinal cord neurons^{9,10}, furtherly suggesting that SARS-CoV-2 was implicated in acute myelitis by the specific ACE2 receptors on the surface of spinal cord neurons.

Based on our study, acute paralysis was the novel neurological symptom of COVID-19. Analysis of the clinical characteristics of 1099 patients with COVID-19 showed that the common symptoms at the onset of disease were fever (43.8% of the patients appeared on admission, while 88.7% of the patients occurred after admission), cough (67.8%), and neurological symptoms were rare². However, severe patients with COVID-19 were likely to have neurological symptoms (such as headache, dizziness, hypogeusia, and neuralgia) and complications including acute cerebrovascular diseases, impaired consciousness and skeletal muscular injury¹⁵.

According to the laboratory testing, we found that lymphopenia and eosinopenia happened in the early stage of COVID-19. The decrease of red blood cell and hemoglobin showed that bone marrow hematopoietic system was affected by SARS-CoV-2, which was expected to be further confirmed by large-scale retrospective analysis. It had been reported that ACE2 was expressed in hepatic bile duct cells and proximal renal tubules^{7, 8}, hepatic and renal dysfunctions were also detected in the patients with COVID-19¹⁶. Liver function of this patient in this study was obviously damaged with normal renal function, the elevated levels of alanine aminotransferase and aspartate aminotransferase reached the peak on the 15th day after the onset of disease, and then recovered gradually. At the same time, the level of total protein, albumin and HDL-C significantly decreased with the process of the disease, suggesting that metabolic abnormalities contributed to the pathogenesis of COVID-19. However, the renal function was normal in this study, which was inconsistent with previous study. It had been reported that the decreased level of serum iron in patients with pneumonia was an independent risk factor for hospital death¹⁷. The mechanism may be related to the influence of pathogenic microorganism infection on iron uptake. In this patient, on the 7th day of the onset of the disease, the level of serum iron was only 1.8 $\mu\text{mol/L}$, and gradually increased with the treatment. The level of serum iron returned to normal when the nucleic acid test of 2019-nCov turned into negative. The possible role of serum iron in the 2019-nCov infection deserved further research in the future. We believed that overactive inflammation response and immune damage occurred in COVID-19 for the high level of C-reactive protein, SAA, IL-6 and ferritin in the patient. Immune damage and cytokines released by inflammatory storms at the early stage of COVID might interpret and explain why spinal cord was implicated in the disease.

Conclusion

Our study firstly presented a COVID-19 case with spinal cord involvement 1 week after the onset of fever, clinical findings could be ascribed to a post-infectious acute myelitis. Acute myelitis might be the neurological complication of 2019-nCov.

Contribution: KZ and S-KN conceptualized the paper. S-KN analyzed the data, with input from KZ, J-CH and Y-WF. S-KN and L-ML wrote the initial draft with all authors providing critical feedback and edits to subsequent revisions. All authors approved the final draft of the manuscript.

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Ethical approval: This study was approved by the Third people's Hospital of Hubei province.

Patient consent: Consent was obtained from the patients.

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Legend.

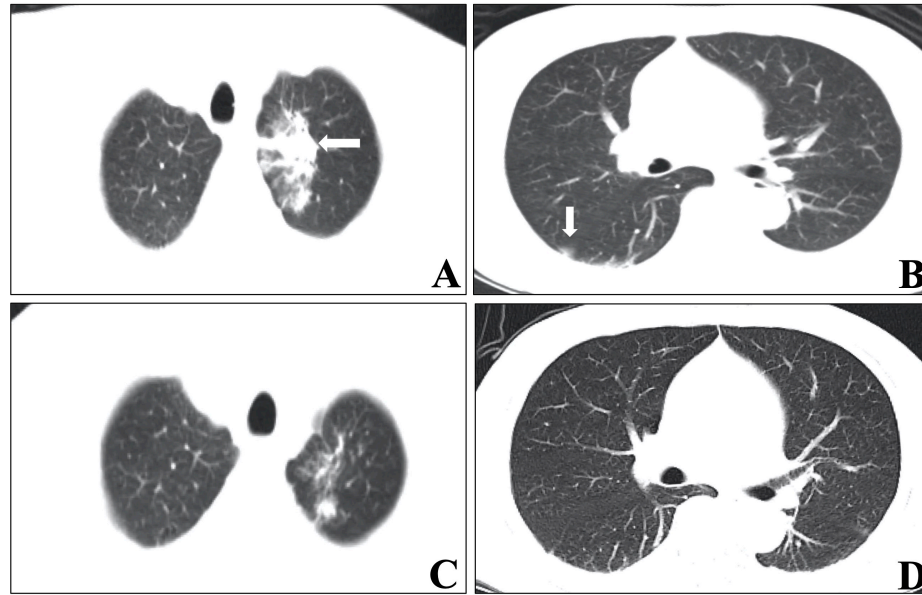


Figure 1. Chest CT imaging of the patient with COVID-19. Chest CT showed patchy high-density blurred shadow in the upper lobe of the left lung (Figure 1A) and patchy ground glass shadow in the anterior segment of the upper lobe of the right lung (Figure 1B). After treatment, chest CT showed that the previous lesions were almost absorbed.

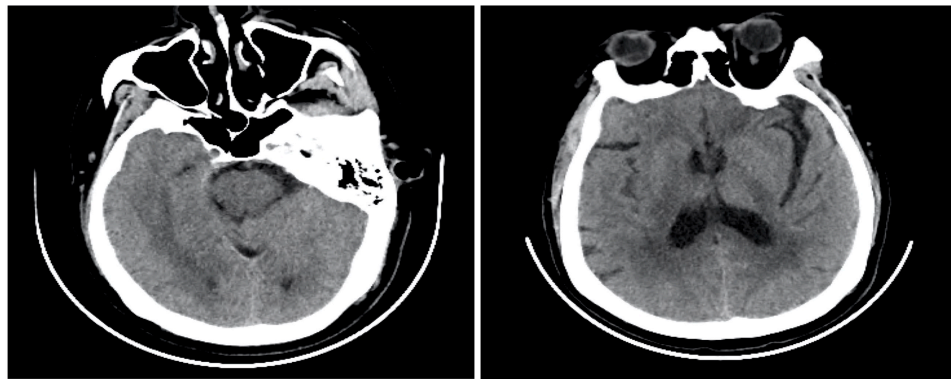


Figure 2. Cranial CT imaging of the patient with COVID-19. Cranial CT revealed bilateral basal ganglia and paraventricular lacunar infarction, brain atrophy (Figure 2).