Management of a Parkinson's disease patient with severe COVID-19 pneumonia

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***Abstract*:** Elderly populations with underlying chronic diseases are more vulnerable to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection and have higher mortality. Parkinson's disease (PD) is a neurodegenerative disease that occurs more often in elderly people. Currently, little is known about whether patients with PD are more susceptible to novel coronavirus disease 2019 (COVID-19) and whether the treatment of PD would affect the management of COVID-19 or vice versa. Here, we report a case of a PD patient with severe COVID-19 pneumonia in Wuhan, China. After diagnosis of COVID-19, this PD patient had worsening of motor symptoms, complicated with acute hypoxemic respiratory failure, urinary tract infection, and acute encephalopathy. In addition to treatment for COVID-19 and urinary tract infection, we adjusted anti-PD medicine by stepwise increasing of dose, resulting in better control of her mobility symptoms and non-motor symptoms.

Keywords: clinical manifestations, management, neurodegeneration, Parkinson's disease, SARS-CoV-2

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Introduction

Elderly populations are at high risk of novel coronavirus disease 2019 (COVID-19) pneumonia,[1] as well as neurodegenerative diseases such as Alzheimer's Disease (AD) and Parkinson's Disease (PD).[2] Currently, there is no evidence that PD increases the risk of COVID-19. On the other hand, worsening of PD symptoms associated with anxiety are commonly seen during the COVID-19 epidemic. In addition, PD patients, especially those receiving advanced therapies, such as deep brain stimulation or levodopa infusion, have a high fatality rate of 40–50%.[3] Many questions remain unanswered regarding how to care for PD patients with COVID-19 pneumonia.[4,5] Are the clinical manifestations of PD patients with COVID-19 pneumonia different from those without PD? Should the treatment of PD be adjusted for PD patients with COVID-19? How can the survival rate of PD patients with COVID-19 be improved? Here, we report a case of a PD patient with severe COVID-19 pneumonia in Wuhan, China. We would like to share our experience in successfully managing this very challenging patient population.

Case presentation

On 21 February 2020 (illness day 5 or iDay 5), an 83-year-old woman presented to our clinic in Wuhan, China with a 5-day history of fever and productive cough. She had history of hypertension for 10 years, PD for 6 years, and stroke for 2 years. She was supposed to take her PD medications of levodopa and benserazide (187.5 mg, bid) and pramipexole hydrochloride (0.25 mg, bid) tablets; however, she did not take them regularly. She had a stroke 2 years ago and took rivaroxaban tablets (10 mg, bid) regularly. At admission, she was found to have low white blood cell counts (3.24×10^9 cells per liter), low lymphocyte % (16.1%), elevated C-reactive protein (82.10 mg/l). Her oropharyngeal swab tested positive for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) by reverse-transcription polymerase-chain-reaction (RT-PCR) assay. Her chest CT images showed multiple bilateral patchy ground-glass opacities (Figure 1). She was diagnosed with severe COVID-19 pneumonia and treated with umifenovir hydrochloride (0.2 g, tid) and recombinant human interferon α-2a (5 million IU, bid). It was noticed that she had significant worsening

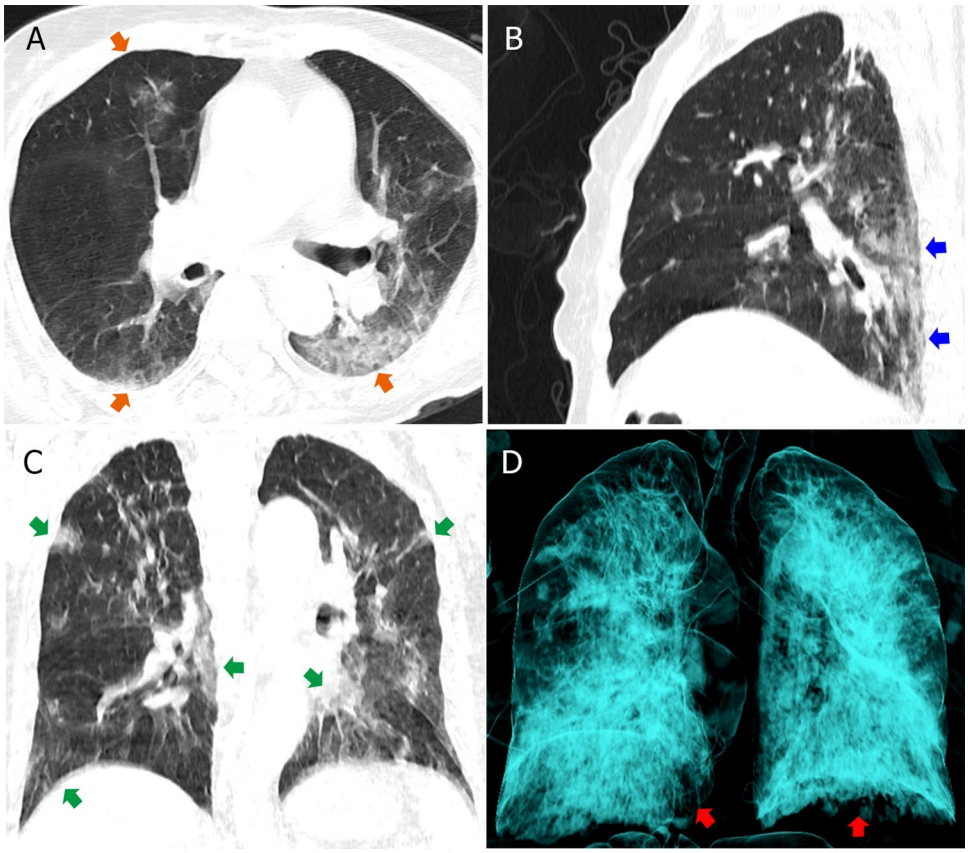

Figure 1. Chest CT of a PD patient with COVID-19. (A) axis scan; (B) sagittal scan; (C) coronal scan; (D) three-dimensional reconstruction.
CT images showed multifocal bilateral (marked by arrows) in the middle lobe of the right lung, upper and lower lobes of both lungs, mainly in the left lower lobe, consistent with COVID-19 pneumonia.
COVID-19, novel coronavirus disease 2019; CT, computed tomography; GGO, ground-glass opacities; PD, Parkinson's disease.

of her motor symptoms, including persistent tremor and rigidity, also she was unable to speak coherently. As she was not taking her PD medications regularly at home, we started at lower doses with levodopa and benserazide at 62.5 mg tid and pramipexole hydrochloride at 0.25 mg tid. At 3 days later (iDay 8), the patient became more anxious, agitated and delirious; her motor symptoms were not improved and she had persistent tremor and rigidity of her right hand. Her levodopa and benserazide was increased in dose to 125 mg tid, resulting in improvement of her motor symptoms.

On iDays 25 and 27, her nasopharyngeal and oropharyngeal swabs became negative for SARS-CoV-2. However, on iDay 32, her oxygen saturation at room air dropped suddenly and she became more confused, with worsening of her mobility again. She started with oxygen therapy for acute hypoxemic respiratory failure. Her levodopa and benserazide was further increased in dose to 187.5 mg tid, along with pramipexole hydrochloride at 0.25 mg tid. The next day (iDay 33), she developed symptoms of urinary tract infection, for which antibiotics was started. In the following 3 days, her acute hypoxemic respiratory failure improved. Her acute encephalopathy resolved after her urinary tract infection was treated. Her motor symptoms and non-motor symptoms improved as well. Moreover, her COVID-19 IgM/IgG antibody tests (INNOVITA Biotechnology Company; Chengdu Precision Medicine Industrial Technology Research Institute Co. Ltd. of West China) were both positive. On iDay 41, her overall condition improved

and her repeated nasopharyngeal swab remained negative for SARS-CoV-2. After meeting our discharge criteria, she was discharged home on iDay 42. At discharge, she was taking levodopa and benserazide each at 187.5 mg, tid and pramipexole hydrochloride at 0.25 mg, tid. Her motor symptoms were well-controlled and her ability to speak coherently had improved significantly.

Discussion

There were more than 80,000 COVID-19 patients in China but only a few of them were reported with PD. To our knowledge, this is the first report of any PD patients with severe COVID-19 pneumonia in China. After diagnosis of COVID-19, the PD patient had worsening motor symptoms and non-motor symptoms, including disorders of consciousness, cognitive dysfunction, and psychiatric symptoms, complicated with urinary tract infection. This patient required multiple adjustments of her PD medications (larger dosage of levodopa) during hospitalization. From this case, three lessons thus can be learned, in terms of early diagnosis, complications, and medication adjustment.

Early diagnosis of PD patients with COVID-19 can be challenging. First, elderly populations with underlying chronic diseases are more susceptible to SARS-CoV-2[6]; however, they may not be able to describe symptoms clearly. Second, PD patients may have a variety of complex symptoms, such as motion fluctuations and hallucinations, which may interfere with the timely diagnosis of COVID-19. Third, dysosmia is one of the early symptoms of COVID-19 infection.[7,8] In PD patients, olfactory dysfunction is one of the non-motor symptoms, which could mask early symptoms of COVID-19.

PD patients are prone to develop non-motor symptoms such as depression, anxiety, and sleep disorders.[9] Relevant treatment should be continued and positive psychology management is beneficial.[10] More importantly, urinary urge/incontinence and increased motor fluctuations are commonly observed in PD patients, perhaps partly due to pharmacokinetic issues.[11] In our case, the patient was not able to tell the difference in her urinary symptoms but she had a urinary tract infection. She subsequently had acute encephalopathy secondary to urinary tract infection, which further complicated this very challenging case. After antibiotic treatment, her acute encephalopathy resolved and her PD symptoms also improved to some extent.

Close monitoring and adjustment of anti-PD medicine doses are essential to control PD symptoms in COVID-19 pneumonia patients. Motor symptoms from PD may affect respiratory effort and secretion clearance.[6] In our case, the patient's motor symptoms did not improve initially after we restarted her PD medications. She went into acute hypoxemic respiratory failure for 4 weeks after she was diagnosed with COVID-19 pneumonia. At that time, her nasopharyngeal swabs for SARS-CoV-2 had already turned negative. Thus, we continued to increase the dosage of her anti-PD medications and her motor symptoms improved significantly.

The mechanism of the exacerbation of PD symptoms after COVID-19 infection remains unclear. A recent survey showed 10% of PD patients reported that their motor symptoms were worsened, including increased tremor and stiffness during the COVID-19 pandemic.[12] Increasing evidence suggests that SARS-Cov-2 may use the brain as a reservoir organ.[13,14] The cytokine storm caused by COVID-19 may result in disturbance of the micro-environment in the brain.[15] The interaction between SARS-CoV-2 and ACE2 protein interferes with the physiological function of ACE2.[16] SARS-CoV-2 may cross the blood-brain barrier (BBB) and directly damage neurons,[17] causing exacerbation of PD symptoms.

We provide our experience in management of an elderly PD patient with severe COVID-19 pneumonia, complicated with uncontrolled PD symptoms, acute hypoxemic respiratory failure, acute urinary tract infection, and acute encephalopathy. Her disease course of severe COVID-19 pneumonia lasted for 6 weeks with a favorable outcome after aggressive management of PD symptoms. Longitudinal studies, larger cohorts and different social settings would help to better understand the prognosis for this comorbidity.

Author contributions

JWL, XL, CZ, RW, SH, and NX collected the epidemiological and clinical data and processed statistical data. JWL, XL, and CZ drafted the manuscript and share first authorship. TW, NX, JHL, and ZL revised the final manuscript. NX is

responsible for summarizing all epidemiological and clinical data.

Availability of data and material

All data included in this study are available upon request by contact with the corresponding author. The lead authors and manuscript's guarantor affirm that the manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned have been explained.

Conflict of interest statement

The authors declare that there is no conflict of interest.

Ethics approval statement

This study was approved by the Ethics Committee of the Wuhan Red Cross Hospital (Approval Number 2020017).

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Informed consent statement

The patient provided written informed consent for the publication of her information.

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Supplemental material

Supplemental material for this article is available online.

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