

Case Report of a Critically Ill Patient with COVID-19 in Early Outbreak

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Abstract Introduction: Corona Virus Disease 2019 (COVID-19) has spread rapidly throughout the world. Many people died of this disease. We reported a case of critical illness with COVID-19 pneumonia that occurred in the early stage of viral spread in China and describe the identification, diagnosis, clinical course, and management of the case, including the patient's symptoms throughout the course. **Patient concerns:** This article describes the whole diagnosis and treatment process of a critically ill patient in a case report. **Diagnosis:** The patient was a physician and presented to a fever clinic with a history of treating a suspected patient without special protection the day before. After 5 days, a nucleic acid test for COVID-19 was positive. Then, the patient was transferred to the intensive care unit (ICU) immediately because of severe dyspnea. He was diagnosed with COVID-19 based on a history of exposure, severe acute respiratory syndrome, positive COVID-19 test and chest computed tomography (CT). **Interventions:** Various therapies were used in this critically ill patient, including anti-infection drugs, hormones, immunoglobulins, herbal medicine, noninvasive ventilation, and special plasma. **Outcomes:** The patient recovered completely and was discharged after one month of hospitalization. COVID-19 was tested negative and a chest CT showed marked improvement prior to discharge after 4 weeks admission. **Conclusion:** This study highlights the complexity of treatment and recurrent positivity of the critically ill COVID-19 pneumonia patient and aims to provide useful reference and information for our knowledge of the clinical spectrum of disease.

Keywords: COVID-19, coronavirus, pneumonia, diagnosis, treatment

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1. Introduction

In December 2019, pneumonia associated with a novel coronavirus spread rapidly throughout World [1,2]. The disease is officially named coronavirus disease-2019 (COVID-19, by the WHO on February 11, 2020) [3]. As of Mar 18, 2020, the novel coronavirus (COVID-19) has rapidly spread worldwide, with more than 180,000 laboratory-confirmed cases. In the early stages of the resultant pneumonia, severe acute respiratory infection symptoms occur, with some patients rapidly developing acute respiratory distress syndrome (ARDS), acute respiratory failure, and other serious complications [3,4,5,6]. The percentage of severe cases among all infected cases was 18.1%, and the case fatality rate of patients with COVID-19 infection was 4.3% [4]. Xiaobo Yang et al found that 61.5% (32/52) of critically ill patients with SARS-CoV-2 pneumonia had died at 28

days, and the median duration from admission to the intensive care unit (ICU) to death was 7 (3-11) days for nonsurvivors [5]. Therefore, a valid therapeutic strategy for critically ill patients will be of considerable value for individuals who are near death [6].

Previous studies have described mainly the general epidemiological findings, laboratory examinations and clinical analysis of patients with COVID-19 pneumonia [7,8,9]. Michelle L. et al reported the first case of COVID-19 in the United States [10]. Several cases of COVID-19 were reported in other countries [11,12], but there have been no cases of critically ill patients with COVID-19 infection. In this study, we report a critically ill patient with confirmed COVID-19 pneumonia who was admitted to Wuhan Jin Yin-tan Hospital. The clinical course and treatment of the case are described in detail, as well as various clinical analyses. This case will provide a valuable reference for the treatment of critically ill patients or patients who are at risk of becoming critically ill.

2. Case Report

On January 25, 2020, a 49-year-old man presented to a fever clinic in Wuhan Fourth Hospital, with a 1-day history of cough and fever. He disclosed that he was a physician and may have been infected while treating a patient who had suspected novel

coronavirus pneumonia, without special protection, the day before. In the afternoon, routine blood examination showed that his lymphocyte counts decreased to $0.8 \times 10^9/L$ (Table 1). A rapid nucleic acid amplification test for influenza and parainfluenza was negative. Chest radiography showed that bilateral lung signs increased (Figure 1A).

Table 1. Clinical Laboratory Results. NB: The value in red color was above normal. The value in blue color was below normal

	1.24	1.25	1.28	1.31	2.3	2.6	2.12	2.16	2.20	2.28	3.5	3.9	3.13	3.20
Measure	Referenece range	Illness Day1	Illness Day4	Illness Day7	Illness Day10	Illness Day13	Illness Day19	Illness Day23	Illness Day27	Illness Day35	Illness Day41	Illness Day45	Illness Day49	Illness Day56
Leukocyte count ($10^9/L$)	3.5-9.5	4.97	4.45	4.08	4.59	6.19	6.57	5.68	5.09	5.72	5.44	7.16	6.01	5.99
Red-cell count ($10^{12}/L$)	4.3-5.8	4.99	4.93	4.99	4.69	4.07	4.11	4.25	4	4	4.28	4.39	4.35	4.5
Hemoglobin (g/L)	130-175	156	153	159	144	128	1.27	132	123	125	136	137	136	142
Hematocrit (%)	316-354	46.3	46.9	44.2	44	39	39.6	41.1	39	39.1	41.5	42.3	41.9	43
Platelet count ($10^9/L$)	125-350	191	162	175	171	197	268	253	206	207	221	203	211	216
Absolute neutrophil count ($10^9/L$)	1.8-6.3	3.47	2.32	3.63	3.42	5.77	5.05	3.72	2.94	3.54	3.08	3.83	3.21	2.05
Absolute lymphocyte count ($10^9/L$)	1.1-3.2	0.8	1.5	0.45	0.69	0.24	0.92	1.29	1.33	1.12	1.61	2.34	1.83	2.2
Absolute monocyte count ($10^9/L$)	0.1-0.6	0.66	0.48	0.82	0.47	0.16	0.39	0.39	0.4	0.53	0.48	0.7	0.64	0.5
Absolute eosinophil count ($10^9/L$)	0.02-0.52	0.02	0.06	0.03	0	0	0.19	0.21	0.35	0.48	0.22	0.22	0.26	0.2
Absolute basophil count ($10^9/L$)	0-0.06	0.02	0.05	0.02	0.01	0.02	0.02	0.07	0.07	0.05		0.07	0.07	0.08
International standardized ratio	0.8-1.25	--	--	0.96	0.93	1.04	0.9	--	--	--	0.98	--	1	0.97
Prothrombin time (sec)	14-21	--	--	18.8	19.1	15.9	15.1	--	--	--	18.7	--	17.6	23.1
Fibrinogen (g/L)	2-4	--	--	1.69	3.2	6.2	7.2	--	--	--	2	--	2.5	2.3
D-Dimer ($\mu g/ml$)	0-0.55	--	--	0.19	0.53	0.91	--	--	--	--	0.23	--	0.59	0.32
Total bilirubin ($\mu mol/L$)	3.4-21.3	--	7.3	15.8	10	--	11.4	8	4.5	7.2	9.9	12.1	10.1	12.9
Alanine aminotransferase (U/L)	9-50	--	24	31	30	--	91	72	30	20	65	45	30	54
Transglutaminase (U/L)	15-40	--	24	28	27	--	33	28	17	16	44	25	30	36
Total protein (g/L)	65-85	--	66.4	78.1	63	--	64.8	67.8	67	65.2	69	66.5	65	57
Albumin (g/L)	40-55	--	39.1	46.5	31.8	--	29.9	36.3	38.2	40.9	40.4	38.7	38.2	39.6
Blood urea (mmol/L)	3.1-8	--	5.52	2.62	5.5	--	7.47	4.66	5.18	6.42	4.5	5.4	5.9	6.4
Creatinine ($\mu mol/L$)	57-97	--	79.6	90.7	76.5	--	72	77	74	74	70.8	71.1	59.8	6.4
Lactate dehydrogenase (U/L)	120-250	--	--	--	280	--	303	318	223	207	--	--	189	231
Potassium (mmol/L)	3.5-5.3	--	5	4.7	4.1	--	4.9	6.1	5.2	5	--	--	4.5	4.5
Sodium (mmol/L)	137-147	--	150	142	146	--	147	144	142	144	--	--	145	144
Chlorine (mmol/L)	90-110	--	108	107	113	--	116	105	103	108	--	--	110	110
Calcium (mmol/L)	2.11-2.52	--	2.34	2.18	2.03	--	2.16	2.26	2.25	2.27	--	--	2.13	2.2
A-hydroxybutyrate dehydrogenase (U/L)	70-182	--	--	--	234	--	--	--	--	--	187	--	149	201
Total cholesterol (mmol/L)	3.3-5.2	--	--	--	3.41	--	--	--	4.31	4.28	4.16	4.34	4.17	5.1
Triglyceride (mmol/L)	0.51-1.70	--	--	--	1.13	--	1.36	1.39	1.69	1.73	3.15	1.79	1.59	1.4
High density finger protein (mmol/L)	1.16-1.42	--	--	--	0.93	--	0.61	0.63	0.65	0.79	0.91	2.96	2.79	1.18
Low density finger protein (mmol/L)	2.1-3.37	--	--	--	2.09	--	3.16	3.92	3.43	3.22	2.59	0.97	1.07	3.74
Hypersensitive C-reactive protein (mg/L)	0-3	--	1.1	5.9	8.7	--	21	3.4	0.8	1	2.1	2.4	0.8	0.8
Amyloid A (mg/L)	0-10	--	--	--	>284	--	260.66	7.28	3.98	--	--	--	<3.7	--
Ferritin determination (ng/ml)	21.8-274.56	--	--	--	--	344.64	453.99	287.18	204.61	129.34	--	113.24	78.76	--
IL-6 (pg/mL)	0-7	--	--	--	6.43	--	--	--	--	9.6	--	--	5.13	--
Procalcitonin determination	0-0.05	--	0.05	0.06	0.05	0.09	--	--	--	<0.05	--	--	--	--

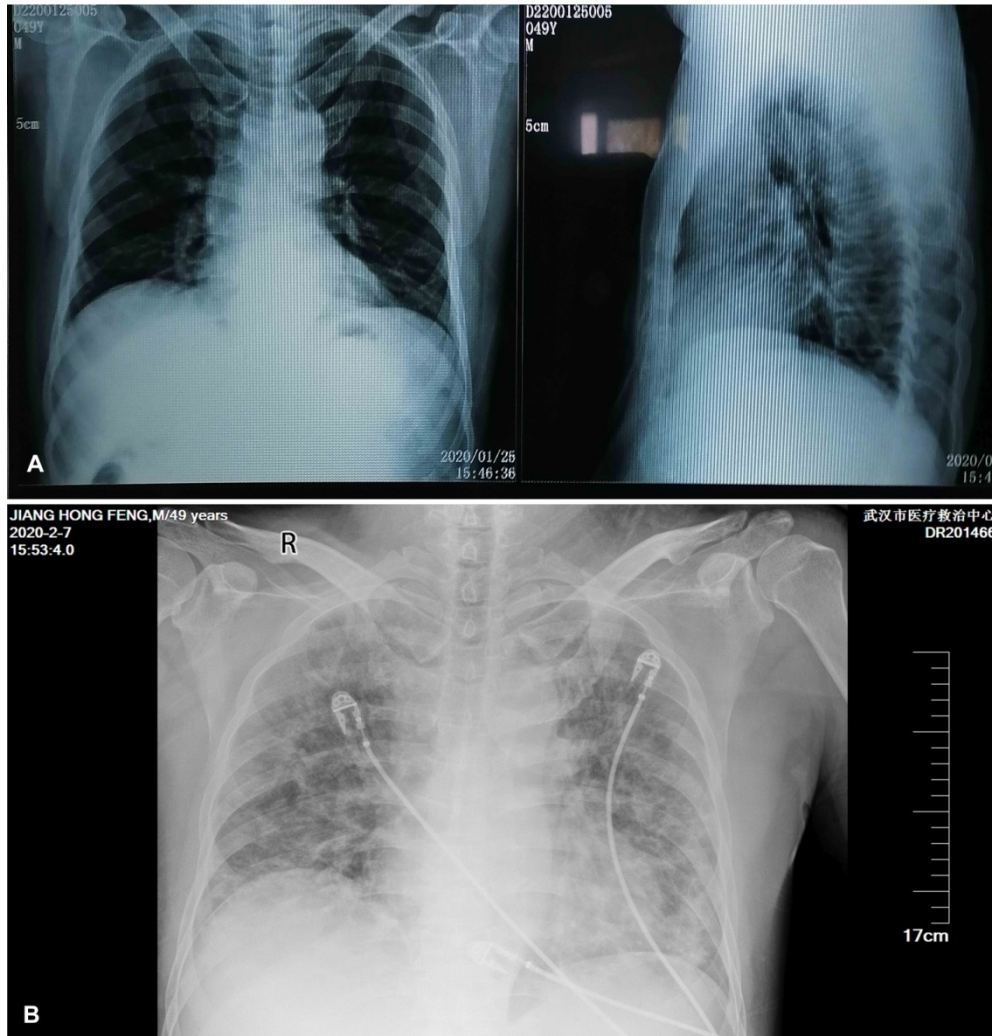


Figure 1. Chest Radiographs of patient. A. Posteroanterior and Lateral Chest Radiographs, January 25, 2020. B. Posteroanterior Chest Radiographs, February 7, 2020



Figure 2. Symptoms and Maximum Body Temperatures According to Day of Hospitalization, January 26 to March 23, 2020

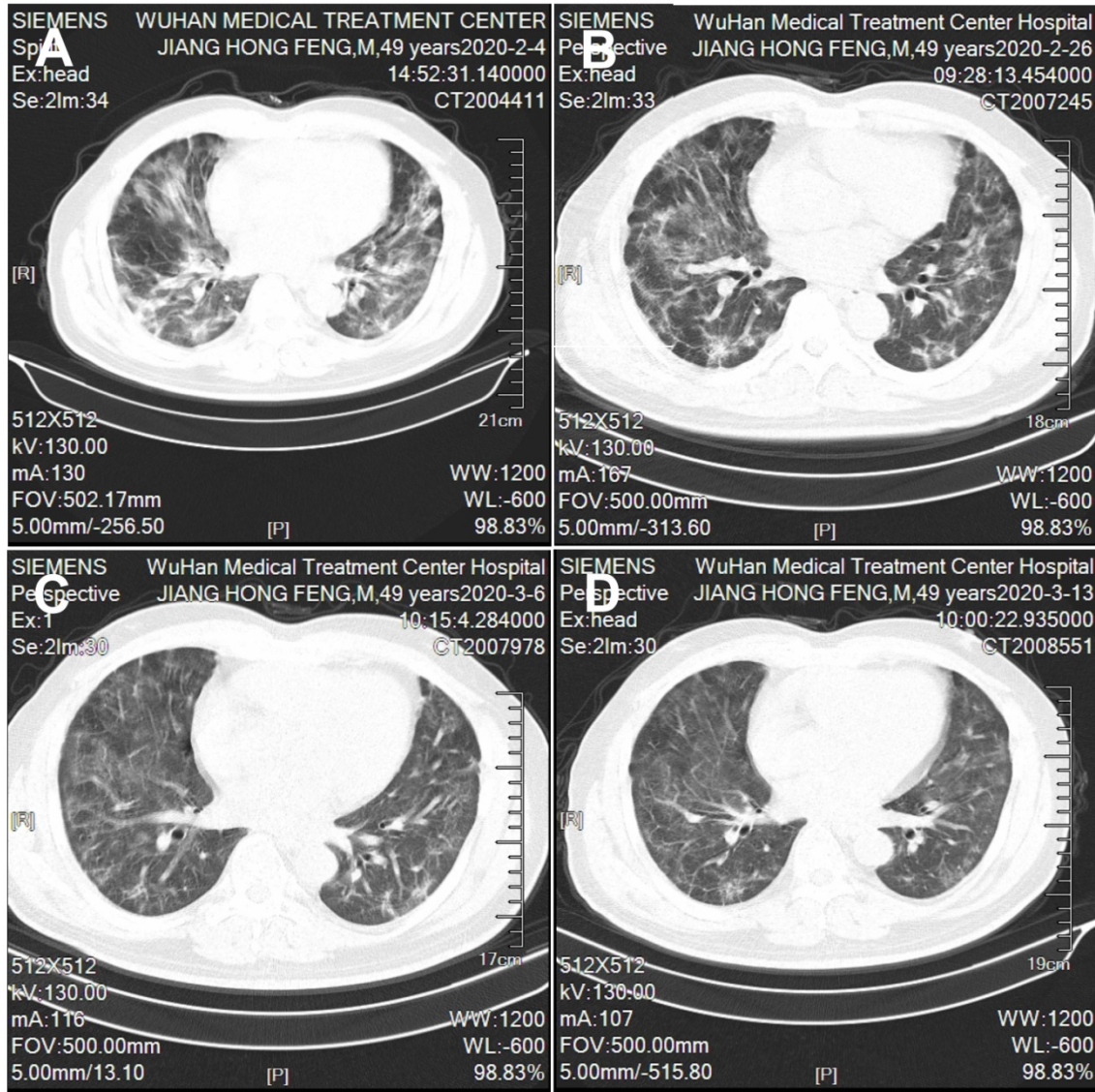


Figure 3. CT lung scanning graph of patient on different days. A. the graph on February 4, 2020. B. the graph on February 4, 2020. C. the graph on March 6, 2020. D. the graph on March 13, 2020

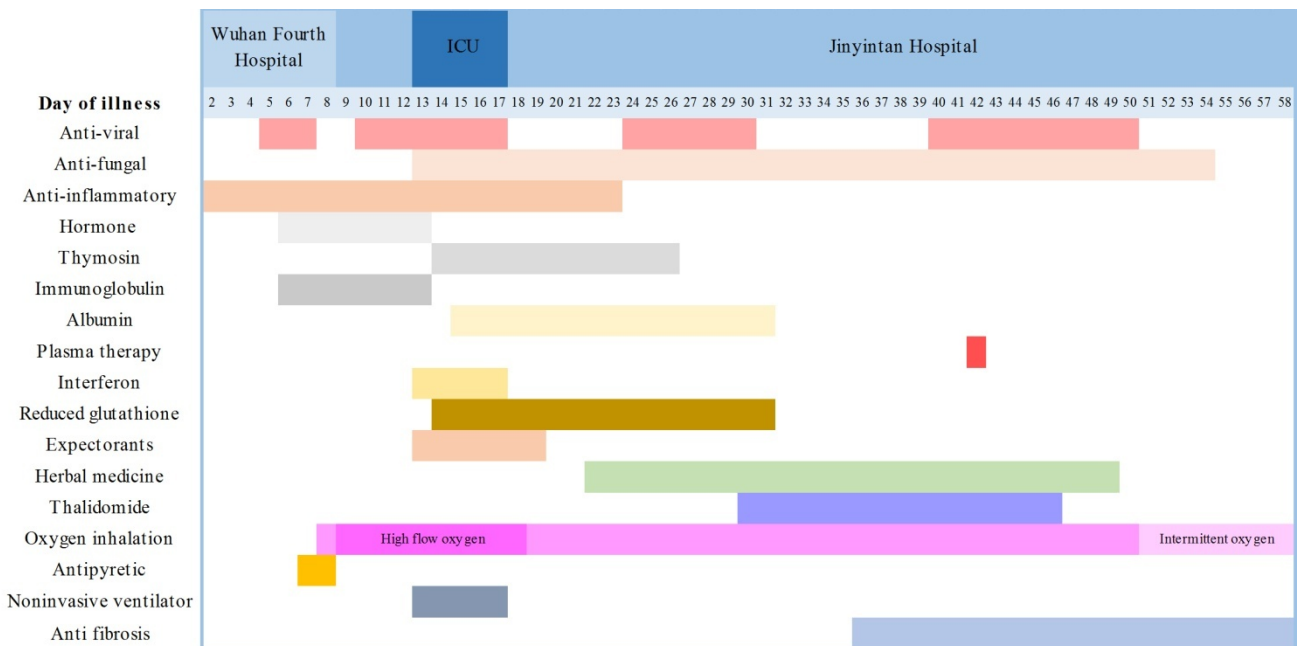


Figure 4. Therapies of patient According to Day of Hospitalization, January 26 to March 23, 2020

3. Methods

3.1. Ethics Approval and Consent to Participate

Ethics approval has been granted for the study by the Committee of Research Ethics in Wuhan Fourth Hospital & Puai Hospital (KY2020-056-01). This study protocol was performed according to the Declaration of Helsinki. The patient was required to fill a written informed consent before participating in this survey.

3.2. COVID-19 Test

Clinical specimens for COVID-19 diagnostic testing were obtained in accordance with National Health Council (NHC) guideline [13]. Nasopharyngeal and oropharyngeal swab specimens were collected with synthetic fiber swabs; each swab was inserted into a separate sterile tube containing 3 ml of viral transport medium. The sputum specimens were collected in a 50 ml sterile specimen container containing 3 ml of viral transport medium. Specimens were stored between -70°C and 4°C until testing.

Clinical specimens were tested with a quantitative reverse transcription PCR (RT-qPCR) assay kit (Jiangsu Kangjian Medical Apparatus Co., Ltd.) The kit has ORF1ab and N gene targets and a positive control target. The full genetic sequence of COVID-19 could be found in the National Institutes of Health GenBank database [14] and the Global Initiative on Sharing All Influenza Data (GISAID) database [15].

3.3. Diagnosis and Treatment

The diagnosis and treatment of COVID-19 infection pneumonia was performed according to NHC guidelines [16]. Diagnostic criteria consisted of: COVID-19 detected by RT-qPCR in respiratory or blood specimen; or virus gene sequencing revealed that the virus is highly homologous to known new coronaviruses. The diagnosis of critical illness in patients met one of the following conditions: 1. respiratory failure and need for mechanical ventilation; 2. shock; or 3. ICU monitoring and treatment needed in combination with other organ failure. On the basis of symptomatic treatment, the treatment principle for critically ill patients consisted of actively preventing complications, treating basic diseases, preventing secondary infection, and supporting organ function in a timely manner.

The discharge standard was body temperature returned to normal for more than 3 days, respiratory symptoms improved significantly, pulmonary imaging showed that the inflammation was obviously absorbed, and detection of COVID-19 was negative for two consecutive tests (the sampling interval was at least 1 day).

4. Results

4.1. Pathogen Detection

The initial respiratory specimens (oropharyngeal swabs) obtained from this patient on day 9 of his illness were

positive for COVID-19 (Table 2). Nucleic acid tests were performed 18 times, including on 13 throat swabs, 1 nose swab and 4 sputum swabs. Among them, 3 were positive and 16 were negative.

4.2. Therapies

Various therapies were used in this critically ill patient, including anti-infection drugs, hormones, immunoglobulins, herbal medicine, noninvasive ventilation, and special plasma (Figure 4). At the early stage of pneumonia, the patient was treated mainly with conventional broad-spectrum antibiotics, antifungal and antiviral drugs and immunoglobulin. When the patient was in critical condition, he was transferred to the ICU and given noninvasive ventilation and special antibiotic drugs (specially formulated for hospital infection). Then, the pneumonia was effectively controlled. At the later stage, therapies were mainly symptomatic and supportive treatment.

5. Discussion

The outbreak of COVID-19 has lasted for three months since December 2019, but there is still no effective method to control COVID-19 spread except for strict isolation [17]. Human-to-human transmission can occur by droplets or contact, and if there is no strict infection control or appropriate personal protective equipment, it may endanger the front-line medical staff [18]. This patient was a front-line medical staffs who was infected when rescuing a patient of suspected COVID-19 without effective protective equipment.

5.1. Laboratory Tests' Characteristic of Critically Ill Patients

For the laboratory tests, lymphopenia (75.4%) and eosinopenia (52.9%) have been observed in most patients infected with COVID-19 [19]. Li LQ, et al. showed that the lymphocytopenia (64.5%), increase of C-reactive protein (44.3%), increase of lactic dehydrogenase (28.3%), and leukocytopenia (29.4%) were more common laboratory abnormality [20]. Lymphocytopenia occurred in more than 80% of critically ill patients infected with SARS-CoV-2, while 35% of patients had only mild lymphocytopenia among noncritically ill patients, suggesting that the severity of lymphocytopenia reflects the severity of SARS-CoV-2 infection [5]. Zhang JJ et al. reported that blood eosinophil counts correlated positively with lymphocyte counts in severe ($r = .486, P < .001$) and nonsevere ($r = .469, P < .001$) patients after hospital admission. Significantly higher levels of D-dimer, C-reactive protein, and procalcitonin were associated with severe patients than with nonsevere patients (all $P < .001$) [19]. Xiong Y et al. showed that the C-reactive protein level, erythrocyte sedimentation rate and lactate dehydrogenase level showed significantly positive correlations with the severity of pneumonia assessed on initial CT (R range.36-.75, $p < .05$) [21]. The patient's laboratory examination revealed a marked decrease in lymphocytes, with abnormalities in hypersensitive C-reactive protein, alanine aminotransferase and ferritin.

It was reported that some discharged patients with COVID-19 had reoccurrence of fever and a positive nucleic acid test soon after [22]. This phenomenon might be due to the biological characteristics of COVID-19, might also be related to the basic disease, clinical status, glucocorticoid use, specimen sampling, processing and detection of patients, and some even related to reinfection or secondary bacterial or virus infection [22]. On February 29, 2020, the patient's symptoms improved significantly without fever, and the next two COVID-19 tests were negative. The CT image indicated that inflammation was absorbed, which almost met the discharge standard. However, two days later, the patient fell discomfort again, with low fever and runny nose, and then a sputum COVID-19 test returned positive again. This case indicated that more attention should be paid to re-positivity of COVID-19 in critically ill patients. As a result, three consecutive COVID-19 tests are the discharge standard in many hospitals. Furthermore, the patient should be isolated for two weeks after discharge from the hospital.

5.2. Therapies

Unfortunately, there are still no specific antiviral medicines or vaccines recommended for COVID-19 infection. At present, our understanding of the clinical spectrum of COVID-19 infection is very limited. For patients with severe clinical manifestations, an effective clinical treatment scheme is of great importance [23]. Because there is no good treatment for critical pneumonia caused by COVID-19 infection, many drugs and treatments were tried in this case.

5.2.1. Antiviral Drugs

Since the outbreak of COVID-19 pneumonia, various antiviral drugs have been used to treat patients. However, antiviral drugs commonly used in clinical practice, including neuraminidase inhibitors (oseltamivir, paramivir, zanamivir, etc.), ganciclovir, acyclovir and ribavirin are invalid for COVID-19 and not recommended [24]. Moreover, most of them have obvious side effects on the body [25]. Four of 5 patients treated with lopinavir-ritonavir developed nausea, vomiting, and/or diarrhea, and 3 developed abnormal liver function test results [8]. Therefore, the antiviral efficacy of such agents needs to be assessed in clinical studies [26]. Ribavirin and chloroquine are regarded as potential effective drugs and are currently undergoing clinical trials [27]. An approved immune modulator, chloroquine shows inhibitory effects against COVID-19 (EC₅₀ = 1.13 μM in Vero E6 cells) and is being evaluated in an open-label trial (ChiCTR2000029609) [27]. In this case, the patient was treated with various antiviral drugs (such as arbidol, klizhi, and Lianhuaqingwen capsule), which showed no obvious effect on COVID-19 pneumonia. In addition, the heart rate decreased gradually when taking coriolus.

5.2.2. Antibiotic Drugs

Prompt administration of antibiotics to prevent infection and strengthen immune support might reduce complications and mortality [16]. It is generally believed that secondary

bacterial infection will occur after virus infection in pneumonia patients, including that by pneumococcus, Haemophilus influenzae, and Pseudomonas aeruginosa [28]. Therefore, antibacterial drugs are commonly used for COVID-19 pneumonia patients, such as moxifloxacin, cefoperazone/sulbactam sodium, and ceftriaxone. It is well known that the infection of COVID-19 will decrease the function of lymphocytes and induce obvious immune deficiency [19,20], which may result in respiratory fungal infection. Therefore, it is also necessary to administer antifungal drugs to severe patients, especially in the ICU. Broad-spectrum antibiotics need to be used to eliminate bacterial or fungal infection as soon as possible for critically ill patients, which could help control the disease. In this case, moxifloxacin, ceftriaxone and cefoperazone/sulbactam sodium were used successively, but the symptoms of high fever and cough were not relieved significantly. It was not until the use of meropenem and micafungin that the symptoms of the patient were relieved, which indicated that the patient may have been infected by a very rare bacterium or fungus.

5.2.3. Corticosteroid Treatment

The topic of corticosteroid use in patients with COVID-19 has been a matter of debate [29]. Systemic corticosteroid treatment (methylprednisolone, <1~2mg per kg body weight for 3~5 days) was recommended as an adjuvant therapy for severe cases [16]. However, the potential risks associated with high-dose corticosteroids in treating COVID-19 pneumonia include secondary infections, long-term complications, and prolonged virus shedding [30]. This patient was treated with prednisone for one week when he became endangered by severe pneumonia. No obvious effect was found.

5.2.4. Convalescent Plasma Therapy

Therapy with plasma of convalescent patients was helpful for the recovery of SARS patients and reduced the mortality rate [31]. Convalescent plasma therapy for serious patients with COVID-19 was first attempted in Wuhan [32]. The therapy plays a certain role in the entire treatment and is helpful for serious patients. Therapy with plasma of convalescent patients was recommended for COVID-19 patients with rapid progress and severe and critical illness on February 19, 2020 [33]. This critically ill patient was given convalescent plasma therapy shortly after recurrent positivity, and his symptoms ameliorated immediately, which means that convalescent plasma therapy is a potential effective treatment for seriously ill patients with COVID-19.

5.2.5. Other Therapies

Since the first autopsy results showed that the formation of phlegm thrombi in the lung may be an important cause of death [34], clinical physicians began to pay more attention to expectorant treatment. Ordinary sputum aspirators can only aspirate the sputum in the trachea above the bronchus and cannot remove sputum in the small bronchus. Therefore, sputum aspiration with fiberoptic bronchoscopy is the first choice for critically ill patients. This patient was treated with expectorant drugs, such as acetylcysteine effervescent tablets, loquat cream

and Lanqin oral liquid, which have a good effect on phlegm thrombi.

Hypoalbuminemia is one of the most common laboratory abnormalities of COVID-19 pneumonia, which is a potent, dose-dependent predictor of poor outcome [35]. The causes of hypoalbuminemia in COVID-19 may be related to the following reasons: first, liver damage caused by the virus; second, an increase in globulin content inhibits the production of albumin; third, fibrin and coagulation factors are consumed in the body [36]. Hypoalbuminemia in COVID-19 pneumonia patients does not mean a real decrease in albumin concentration. When the condition of the patient is improved, serum albumin levels return to normal. In contrast, a large amount of albumin supplementation will lead to excessive deposition of albumin in the alveolar stroma, which will delay the patient's remission. In this case, the patient had obvious hypoalbuminemia and was treated with albumin infusion. After a long-term supplement, albumin infusion stopped on February 24, 2020, which may be one factor contributing to the improvement in the patient's symptoms.

The patient was in the hospital for almost two months and was treated with various treatments, which indicated that the course of critical COVID-19 pneumonia can last very long and that its treatment is extremely complex and difficult. Currently, COVID-19 has become a pandemic. Patients should be treated as soon as possible to prevent severe or critical pneumonia development. This case may be helpful for the treatment of patients with COVID-19 pneumonia.

A List of Abbreviations

Corona virus disease 2019 (COVID-19)
 Acute respiratory distress syndrome (ARDS)
 Intensive care unit (ICU)
 Computed tomography (CT)
 Quantitative reverse transcription PCR(RT-qPCR)
 National Health Council (NHC)

Author Contributions

CL Z wrote the article and performed all of the necessary literature searches and data compilation. HH C performed the necessary literature searches and data compilation. DH H performed data analysis, revised the article and give valuable suggestions. HF J designed the review, reviewed it, and approved the submitted manuscript. All authors have read and approved the final manuscript.

Declaration of interests

We declare no competing interests.

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