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Differences between COVID-19 and suspected then confirmed SARS-CoV-2-negative pneumonia: a retrospective study from a single center

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Abstract

Coronavirus disease 2019 (COVID-19) broke out in Wuhan, Hubei, China in December 2019. Tens thousands of people have been infected with the disease. Our aim was to distinguish severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)-positive patients from SARS-CoV-2-negative patients. We retrospectively compared the data of COVID-19 patients with those of suspected and confirmed SARS-CoV-2-negative patients (control patients). There were 78 COVID-19 patients and 26 control patients, whose median ages were significantly different (P=0.001). The percentage of COVID-19 patients admitting exposure to Wuhan was obviously higher than that of control patients (X^2=29.130, P<0.001). Fever and cough appeared more frequently in COVID-19 patients than in the control patients. The routine blood work-up parameters of COVID-19 patients did not change much and their mean counts were in normal range. There were 38.5% of control patients had higher procalcitonin (PCT) levels than 0.5ng/ml, which was significantly higher than that percentage of COVID-19 patients (X^2=22.636, P <0.05), and COVID-19 patients were also more likely to have decreased or normal

urea and creatinine levels than control patients (X^2=24.930, 8.480, P <0.05).Younger age, exposure to Wuhan, fever, cough, and slight changes in routine blood work-up parameters, urea and creatinine were important features discriminating COVID-19 from control patients. Slightly increased, but far less than 0.5ng/ml, PCT levels also differentiated COVID-19 patients from control patients

KEYWORDS

Coronavirus disease 2019 (COVID-19), suspected then confirmed SARS-CoV-2-negative pneumonia, symptoms, laboratory test, procalcitonin

1 **INTRODUCTION**

A pneumonia-like illness with no clear etiology emerged in Wuhan, Hubei, China, in December 2019.[1] Afterwards, the Chinese Center for Disease Control and Prevention (CDC) found that the cause of this disease was a novel coronavirus named SARS-CoV-2 by the World Health Organization (WHO) in January 2020. Although patients with mild cases of coronavirus disease 2019 (COVID-19) had a good prognosis, patients with severe or critical cases rapidly deteriorated to dyspnea, acute respiratory distress syndrome (ARDS), organ failure or even death. Moreover, because of the strong infectivity of SARS-CoV-2, people in 31 provinces of China and more than 25 countries have been infected.[2,3] As of 23 March 2020, there have been 93000 cumulative patients with confirmed cases of COVID-19 and more than 10000 deaths all over the world.

As we know, the differentiation of COVID-19 and suspected but confirmed SARS-CoV-2-negative pneumonia (control patients) is difficult, and there have been few studies about it. Our aim was to compare the different aspects of the two diseases, as well as to provide some useful and supplementary indexes for the differential diagnosis of COVID-19 and SARS-CoV-2-negative pneumonia.

2 MATERIALS AND METHODS

2.1 Study subjects

On the basis of guidelines for the diagnosis and treatment of COVID-19 by the national health commission (Trial Version 5), the diagnostic criteria for patients suspected of having COVID-19 included (1) contact with Wuhan or surrounding areas of Wuhan or confirmed patient within 14 days from the onset of the diseases; (2) with symptoms of fever or respiratory; (3) with imaging features of COVID-19.[4] A total of 104 patients suspected of having SARS-CoV-2 pneumonia and hospitalized at Chongqing Three Gorges Central Hospital from 26 to 31 January 2020 were included in our study. According to WHO interim guidance, a patient can be confirmed as having COVID-19 only with a positive nucleic acid test result of high-throughput sequencing or real-time reverse-transcriptase polymerase-chain-reaction (RT-PCR) assay. All the patients in our study underwent nucleic acid tests of upper respiratory throat swab samples 2-6 times. COVID-19 could be diagnosed with two consecutive positive results. Finally, 78 patients were diagnosed with COVID-19 with positive laboratory results, and the other 26 patients were excluded as having COVID-19 because of negative results; these 26 patients were the control patients in our study.

2.2 Data collection

Data collection tables were based on electronic medical records, which included epidemic history, characteristics, symptoms, laboratory results, nucleic acid test results and chest computed tomography (CT) scans, as well as treatment measures and outcomes of all 104 patients. The epidemic history was mainly about exposure to Wuhan before the onset of the disease. The patients had a history of traveling to

Wuhan, residence in Wuhan or contact with people having fever or respiratory symptoms from Wuhan within 14 days.

2.3 Statistical analysis

We described age as median (range); categorical variables were described as number (percentage), and laboratory data were described as the mean. Chi-squared and Fisher's exact tests were used to compare proportions for categorical variables. When the data of means were normally distributed, independent-group T tests were used to compare means; otherwise, Mann-Whitney tests were used. SPSS (Statistical Package for the Social Sciences) version 20 was used to perform all statistical analyses. Two-sided comparisons with a p-value less than 0.05 were considered significant.

3. RESULTS

3.1 Characteristics and symptoms of COVID-19 patients and control patients onset of the diseases

There were seventy-eight COVID-19 patients and twenty-six control cases in our study (Table 1). The median age of COVID-19 patients was 45 (from 15 to 79), which was significantly younger than that of the control patients (t=－4.686, *P*=0.001). Moreover, 83.3% (65/78) of COVID-19 patients admitted exposure to Wuhan, among whom 48 patients resided in Wuhan, 3 patients had traveled to Wuhan, and 14 patients had contact with people in Wuhan before the onset of the disease within 14 days. This percentage was obviously higher than that (26.9%) of control patients (X^2=29.130, *P*<0.05). COVID-19 patients had higher percentages of fever and cough (82.1% and 76.9%, respectively) than control patients (53.8% and 46.2%, respectively) (X^2=8.274, 8.667, P<0.05). Otherwise, in our study, control patients especially those severe patients were more prone to having underlying

diseases, and sore throat than COVID-19 patients(X^2=15.385, 4.906, P<0.05). Although no control patient had chest pain or diarrhea, only 10.3% (8/78) and 7.7% (6/78) of COVID-19 patients had these features, respectively, and these percentages were not significantly different between the two groups (P>0.05). The percentages of males in the two groups were both 50%, and all the patients had clinical symptoms, such as sputum production, fatigue, shortness of breath, headache, arthralgia and vomiting, and the percentages of patients presenting these symptoms in the two cohorts were not significantly different (P>0.05) (Table 1). Most of patients with severe cases of SARS-CoV-2-negative pneumonia had severe pneumonia and comorbidity, and we summarized the severe cases in control group in Table 2.

3.2 Laboratory results of COVID-19 patients and control patients

The mean counts of WBCs (5.8244) and neutrophils (4.08) in COVID-19 patients were in the normal range and were significantly less than the counts of control patients (Z=-3.762, -4.489, P<0.05). Moreover, COVID-19 patients were more likely to have normal or decreased WBC and neutrophil counts than the control patients (X^2=22.525, 25.474, P <0.05). Otherwise, the mean percentage of lymphocyte in COVID-19 patients was significantly higher than that in control patients (t=4.558, P<0.05), and the control patients were more likely to have decreased lymphocyte counts and percentages than the COVID-19 patients(X^2=4.464, 10.883, P <0.05) (Table 3).

The mean level of procalcitonin (PCT) in COVID-19 patients was significantly less than that in control patients (P <0.05), and there were 38.5% of control patients had higher PCT levels than 0.5ng/ml, which was significantly higher than that percentage of COVID-19 patients (X^2=22.636, P <0.05). COVID-19 patients were also more likely to have decreased or normal total bilirubin, urea and creatinine levels than control patients (X^2= 11.556, 24.930, 8.480 P <0.05). Some patients in

both groups had elevated aspartate aminotransferase (AST), alanine aminotransferase (ALT) lactate dehydrogenase (LDH) and creatine kinase levels, but the percentages of patients in both groups with elevated levels and the mean counts of both groups were not significantly different (P>0.05). Although the mean levels of C-reactive protein (CRP) of control patients were significantly higher than those of COVID-19 patients (Z=-2.008, P<0.05), but the percentages of patients with elevated levels were not significantly different (P>0.05). In light of the CT results, the percentages of patients with the presence of ground-glass opacities in the CT scans were similar in the two groups of patients (X^2=1.299, P>0.05)(Figure2.A,E) Although the presence of nodules was a specific sign of COVID-19 patients (Figure1), the percentage (12.8%) was too low to show a difference (Table 3).

3.3 Differences in variables between patients with severe and mild cases of COVID-19

The mean percentage of neutrophils, and of AST, LDH, CRP and PCT levels in patients with severe cases of COVID-19 were significantly higher than those in patients with mild cases. Otherwise, the lymphocyte count and percentage and creatinine levels in patients with mild cases of COVID-19 were significantly higher than those in patients with severe cases (Table 4).

3.4 Outcome and complications of the COVID-19 patients

We performed active treatments for almost all of the COVID-19 patients, such as antiviral therapy, nebulization inhalation and antibiotic therapy (Figure 2). Consequently, the discharge rate, admission rate of intensive care units (ICUs) and prevalence of acute respiratory distress syndrome (ARDS) and acute respiratory injury were not different between the two groups (Table 5).

4 DISCUSSION

COVID-19 has spread rapidly throughout China and the world, and the morbidity of COVID-19 has increased worldwide. Although RT-PCR tests with throat and nose swabs or lower airway secretion were the gold standard and the most reliable method for the differentiation of COVID-19 and from SARS-CoV2-negative pneumonia, all the steps would take a long time, occupy and exhaust limited medical resources; moreover, in the early stage of the disease, the positive rate of the test was relatively low. Our aim was to find other useful laboratory indicators to assist RT-PCR tests and to help physicians differentiate the two diseases more effectively.

To determine useful indexes for the COVID-19 diagnosis, we compared the clinical characteristics, laboratory test results and outcomes of the 78 COVID-19 patients with those of 26 control patients. In our study, the median age of COVID-19 patients was 45, which was generally consistent with previous reports[5] and significantly younger than that of the control patients. More COVID-19 patients admitted having contact with Wuhan. In addition, fever and cough appeared more frequently in COVID-19 patients than in the control patients; therefore, we confirmed that exposure to Wuhan, fever and cough were not only characteristics of COVID-19 patients but also factors for the differentiation of COVID-19 from other types of pneumonia. The percentages of males in the two groups were both 50%, and this result was different from earlier results, in that males accounted for a greater proportion of COVID-19 patients.[6] A probable explanation was that earlier COVID-19 was related to exposure to the South China Seafood Market, and most of the patients affected were male workers. In addition, some symptoms such as sputum production, fatigue, shortness of breath, dyspnea and headache, presented in COVID-19 patients and the control patients with similar percentages. Consequently, the sex of patients and the symptoms mentioned above had limited effects on the

differentiation of COVID-19 from other types of pneumonia. It was reported that more than 20% of patients with MERS-CoV or SARS-CoV infection had diarrhea, [7] and in our study, we also found that 7.7% of COVID-19 patients had this symptom, but no control patients had the symptom. Diarrhea may be a potential index for the discrimination of COVID-19 from other types of pneumonia. However, because of limited patient numbers or the low percentage of patients with diarrhea in our study, the differences between the two diseases were not significant; therefore, we need further studies or more specimens to identify the role of diarrhea in discriminating COVID-19 from other types of pneumonia. It was interesting that the percentage of patients with underlying diseases in our COVID-19 group was significantly lower than that in the control group because the majority (80.8%) of COVID-19 patients had mild cases were younger in our study. Finally, fewer patients with COVID-19 had sore throats, which might be because SARS-CoV-2 preferentially attacks the lower airway.[1]

Tissue damage due to infection or malignant diseases could lead to changes in WBC counts, and neutrophils and lymphocytes were peripheral WBCs. Neutrophils were mainly involved in nonspecific immunity, and their increased counts were mainly due to decreased adhesion, delayed apoptosis and the stimulation of growth factor.[8] Lymphocytic reduction was a sign of low immunity, and its mechanism was mainly related to increased lymphocyte wall attachment and accelerated apoptosis. In our study, the elevated mean counts of WBCs and neutrophils of control patients, and the decreased counts and percentages of lymphocytes in the control patients as well as in 41% and 35.9%, respectively, of COVID-19 patients were consistent with the above views. However, the routine blood work-up parameters of COVID-19 patients did not change much and were in normal range mainly due to the following aspects. First, because of the increased vigilance of the masses, many asymptomatic patients with a history of contact in Wuhan came to see a doctor, thus, the patients

saw a doctor earlier. Since inflammation was a time-depend process, the routine blood work-up parameters of COVID-19 patients had not change in such a short time.[9] Second, because the changes of routine blood work-up parameters, especially the decrease of lymphocyte count and its percentage were more common in patients with severe cases than patients with mild cases of COVID-19 (Table 4), and patients with mild diseases accounted for the most patients(80.8%), changes were not common in our study(Table 1). Third, the patients in our study were COVID-19 patients at Chongqing Three Gorges Central Hospital from 26 to 31, January 2020. The possibility cannot be excluded that there was variation between the virus that infected our patients and the virus that infected the patients in Wuhan reported previously. Last, some patients may have already used drugs before admission, resulting in interference with the results of routine blood tests. Our results also reminded doctors not to rely on the decrease in lymphocytes to speculate whether patients have COVID-19.

PCT levels have been reported to increase to more than 0.5ng/ml in the presence of a bacterial infection, such as bacterial pneumonia or sepsis, in the body .[10] When the body is invaded by a virus, the value levels of PCT generally do not increase or only slightly increase.[11] Some of our patients in the control group had bacterial infection; therefore, 38.5% of them had PCT values higher than 0.5ng/ml, which was significantly higher than those of COVID-19 patients. The reason PCT levels were also higher than 0.5ng/ml in 2.8% of COVID-19 patients may be that these patients had comorbid bacterial infections. A slight increase in PCT levels, but much less than 0.5ng/ml is an important indicator to distinguish COVID-19 patients from SARS-CoV-2-negative patients.

It had been reported that in 6.7% (36/536) of patients with severe acute respiratory syndrome (SARS), creatinine would rise at a median of 20 days after admission.[12]

Renal injury might not have occurred at the time of admission, and the number of patients with COVID-19 was only seventy-eight in our study, which was why the mean counts of indicators reflecting renal injury, such as creatine kinase and urea, were within the normal range. Clinically, kidney injury caused by bacterial infection is more common than that caused by viral infection and streptococcal glomerulonephritis was the most typical.[13]The constituent percentage of the patients with bacterial infection in the control group was probably higher than that in the COVID-19 group, which might also be the reason that the mean levels of urea and creatinine in the control patients were significantly higher than those in COVID-19 patients. Furthermore, patients with COVID-19 more frequently had decreased or normal urea and creatinine compared than control patients. If a person has pneumonia symptoms and has normal or decreased creatinine levels, doctors should pay attention.

Bile duct cells express angiotensin converting enzyme 2 receptor with high specificity, and SARS-CoV-2 and SARS-CoV both enter human cells through the receptor angiotensin converting enzyme 2 receptor. The damage to liver function might be due to the dysfunction of bile duct cells, drug-induced, systemic inflammation and other causes.[14] It has been reported that some patients with COVID-19 had elevated AST, ALT and total bilirubin levels, but the mean value was within the normal range,[1,6] which was consistent with our results. Moreover, Huang et al [1] showed that patients with severe cases of COVID19 were more likely to have liver injury, which was confirmed by our studies. Since most patients in our study had mild cases, the liver function indexes were within the normal range. It has been reported that only 13.75% of patients with community-acquired pneumonia also suffer from liver injury, and most of them have normal liver function, which was consistent with our results. Although some patients with COVID-19 had abnormal liver function, the results were not different from those of the control patients;

therefore, the indexes of liver function were not suitable for the differentiation of the two diseases. Moreover elevated CRP and LDH levels as well as presence of ground-glass opacities and nodules were important indexes for the diagnosis of COVID-19, but they were not useful to differentiate COVID-19 from SARS-CoV-2-negative pneumonia.

In conclusion, younger age, exposure to Wuhan, fever and cough were important features discriminating COVID-19 from control patients. In addition, COVID-19 patients more frequently had slight changes in routine blood work-up parameters, urea and creatinine than control patients. Furthermore, slightly increased, but far less than 0.5ng/ml, PCT levels also differentiated COVID-19 patients from control patients.

There were some limitations in our study. First, there were relatively few research subjects. Second, many patients were still in the hospital at the end of the study; therefore, so the prognosis information of patients was not very comprehensive. Finally, the majority of control patients did not undergo cytokine tests; consequently, we could not compare the cytokine test results of the two groups in our study.

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CONFLICTS OF INTERESTS

All the authors declare that there are no conflicts of interest.

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TABLE1: Characteristics and symptoms of COVID-19 patients and control cases

Variables No (%)	COVID-19 patients (n=78)	control cases (n=26)	X^2/t	p value
Sever diseases	15(19.2)	6(23.1)	0.179	0.672
Age, median (range)	45(15-79)	61(28-95)	−4.686	0.001*
Male	39(50.0)	13(50.0)	0.000	1.000
Exposure to Wuhan	65(83.3)	7(26.9)	29.130	<0.001 *
Underlying diseases	12(15.4)	14(53.8)	15.385	<0.001 *
Fever	64(82.1)	14(53.8)	8.274	0.004 *
Cough	60(76.9)	12(46.2)	8.667	0.003 *

Sputum production	28(35.9)	8(35.8)	0.227	0.634
Fatigue	17(21.8)	5(19.2)	0.077	0.782
Shortness of breath	16(20.5)	10(32.3)	1.685	0.194
Dyspnea	13(16.7)	5(19.2)	0.090	0.765
Headache	12(15.4)	2(7.7)	0.990	0.509
Chest pain	8(10.3)	0(0)	2.889	0.196
Arthralgia	7(9.0)	1(3.8)	0.722	0.395
Diarrhea	6(7.7)	0(0)	2.122	0.145
Sore throat	4(5.1)	5(19.2)	4.906	0.027*
Vomit	4(5.1)	2(7.7)	0.236	0.627

Abbreviations: COVID-19=coronavirus disease 2019; *p<0.05

TABLE 2 Severe cases in the control group

Case	Age	Sex	CT description	Main disease	Comorbidity
1	60	Female	Bilobed *Schistosoma* exudates with a small amount of pleural effusion	Severe pneumonia (probably bacterial infection)	1. Anemia (HB: 60 g/L) 2. Occupying lesions adjacent to the lumbar vertebrae (tumor or abscess was not confirmed after data collection)
2	83	Male	Patchy exudation in the middle lobe of the right lung and in the lower lobe of both lungs; patchy consolidation in the middle lobe of the right lung.	CAP	Intracranial hemorrhage
3	60	Female	Patchy shadow in the upper lobe of the right lung and the lower and upper lobe of the left lung accompanied by atelectasis in the middle lobe of the right lung.	CAP	Coma because of diabetes mellitus ketoacidosis
4	58	Male	Multiform ground-glass opacity with blurred margin and interstitial alteration in both lungs.	CAP	Coma with unknown cause
5	56	Female	0.3 cm ground-glass nodule in the lingual lobe of the left lung.	CAP	Subarachnoid hemorrhage
6	95	Female	Infections in both lungs and obvious bilateral pleural effusion in the lower lobe of both lungs.	CAP	1. Type I respiratory failure 2. Heart failure

CT=computer tomography, CAP=community acquired pneumonia, HB=hemoglobin

TABLE3 Laboratory results of COVID-19 patients and control cases

Variables (normal range)	COVID-19 patients (n=78)	Control cases (n=26)	Z/t/ X^2	P
Blood routine				
White blood cell count(3.5-9.5×10⁹/L)	5.8244	9.6885	-3.762	0.000*
≤9.5, No(%)	73(93.6)	14(53.8)	22.525	<0.001*
Neutrophil count(1.8-6.3× 10^9/L)	4.08	8.6	-4.489	<0.001*
≤6.3, No(%)	70(89.7)	11(42.3)	25.474	<0.001*
Lymphocyte count (1.1-3.2×10⁹/L)	1.2917	1.0658	1.723	0.88
<1.1, No(%)	32(41)	17(65.4)	4.644	0.031*
Neutrophil% (40-75%)	67.02%	78.28%	-4.047	0.001*
≤75, No(%)	62(79.5)	10(38.5)	15.407	<0.001*
Lymphocyte% (20-50%)	24.41%	13.81%	4.558	<0.001*
<20, No(%)	28(35.9)	19(73.1)	10.883	0.001*

Blood biochemistry				
Total bilirubin(0-21umol/L)	9.9078	14.3538	-2.270	0.029*
≤21, No(%)	76(97.4)	20（76.9）	11.556	0.001*
ALT（7-40 U/L）	28.4103	23.5308	-1.333	0.183
＞40, No(%)	17（21.8）	5（19.2）	0.077	0.782
AST（13-35 U/L）	28.9744	31.7808	-0.634	0.526
＞35, No(%)	18（23.1）	5（19.2）	0.692	0.581
LDH（120-250IU/L）	256.7410	248.2962	-1.19	0.234
≤250, No(%)	67(64.4)	18(69.2)	0.212	0.414
Creatine kinase（40-200U/L）	102.3936	263.7615	-1.104	0.270
≤200, No(%)	72(93.5)	23(88.5)	0.691	0.406
Urea（2.6-7.5mmol/L）	3.959	6.4654	-3.174	0.004*
≤7.5, No(%)	77(98.7)	17(65.4)	24.930	＜0.001*
Creatinine（41-73μmol/L）	62.4721	78.6154	-2.235	0.033*
≤73, No(%)	67(76.1)	12(46.2)	8.480	0.004*
Infection-related biomarkers				

CRP（0-11mg/L）	30.9746	49.5392	-2.008	0.045
＞11, No(%)	42(53.8)	18(69.2)	1.891	0.169
PCT（<0.046 ng/ml）	0.098	1.9735	-4.495	＜0.001*
≥0.5, No(%)	2(2.8)	10(38.5)	22.636	＜0.001*
CT				
ground glass opacity, No(%)	37(47.4)	9(34.6)	1.299	0.254
nodule, No(%)	10(12.8)	0(0)	3.688	0.063

Abbreviations: COVID-19=coronavirus disease 2019, Lymphocyte%, the rate of Lymphocyte; Neutrophil %, the rate of Neutrophil; AST, aspartate aminotransferase; ALT, alanine aminotransferase; LDH, lactose dehydrogenase; CRP, C-reactive protein; PCT, procalcitonin; CT, chest computed tomographic;*p<0.05

TABLE 4 Laboratory results of patients with severe and mild cases of COVID-19

Variables（normal range)	Mild case of COVID-19	Severe cases of COVID-19	Z/t	P
Blood routine				
White blood cell count(	5.6556	6.5333	-0.786	0.432

3.5-9.5×10⁹/L)				
Neutrophil count(1.8-6.3× 10^9 /L)	3.8334	5.1273	-0.038	0.97
Lymphocyte count (1.1-3.2×10^9/L)	1.3736	0.948	2.713	0.008
Neutrophil% (40-75%)	65.62%	72.91%	-2.233	0.029
Lymphocyte% (20-50%)	25.75%	18.77%	2.505	0.014
Blood biochemistry				
Total bilirubin(0-21umol/L)	9.755	10.2667	-0.248	0.805
ALT (7-40 U/L)	27.9683	30.2667	-0.336	0.737
AST (13-35 U/L)	25.7968	42.3200	-2.937	0.009
LDH (120-250IU/L)	227.0127	381.6000	-3.203	0.006
creatnne kinase (40-200U/L)	97.8629	123.9467	-5.532	0.596
Urea (2.6-7.5mmol/L)	3.9127	4.1533	-0.462	0.65
Creatinine (41-73μmol/L)	64.4992	54	2.004	0.049
Infection-related biomarkers				
CRP (0-11mg/L)	19.3375	75.8507	-4.615	0

PTC (<0.046 ng/ml)	0.0496	0.2835	-3.465	0.001

TABLE 5 Outcomes and complications of COVID-19 and control cases

Outcomes	COVID-19 patients No (%) (n=78)	Control cases No (%) (n=26)	p value
Discharge	34(43.6)	16(61.5)	0.113
Admission to ICU	9(11.5)	0(0)	0.108
ARDS	10(12.8)	1(3.8)	0.284
Acute respiratory injury	10(12.8)	2(7.7)	0.726

Abbreviations: COVID-19, 2019 novel coronavirus–infected pneumonia; ICU, Intensive Care Unit; ARDS, acute respiratory distress syndrome

FIGURE1 Chest computed tomography (CT) scans for coronavirus disease 2019 (COVID-19) patients and SARS-CoV-2-negative pneumonia. Case 1: chest CT obtained on Jan-30 (A) Mostly floc and ground glass opacities were located in the right lower lobe of lung and left and upper lobe of the left lung and partly located

under the pleura and inter lobar fissure. The fiber focus was scattered in the right lung, and the pulmonary bubble was located under the pleura of the upper lobe of the right lung. Right lateral pleural was thickening with adhesion. Chest CT obtained on Mar-01 (B) Multiple infectious lesions in both lungs had been absorbed. The subpleural pulmonary bullae were located in the upper lobe of the right lung, and the right local pleura was thickened and adherent. Case 2: chest CT obtained on Jan-30 (C) Multiple spots, patchy ground glass shadows were in each lobe of both lungs, considering infectious diseases. Chest CT obtained on Feb-10(D) Multiple foci were in two lungs, roughly the same as before, and local adhesion was in bilateral pleura. Case 3: chest CT obtained on Jan-30(E) patchy and indistinct ground glass was on the edge of the lower lobe of the right lung. Chest CT obtained on Feb-8(F) More lesions in the basal segment of the right inferior lobe of right lung by comparison with chest CT obtained on Jan-30

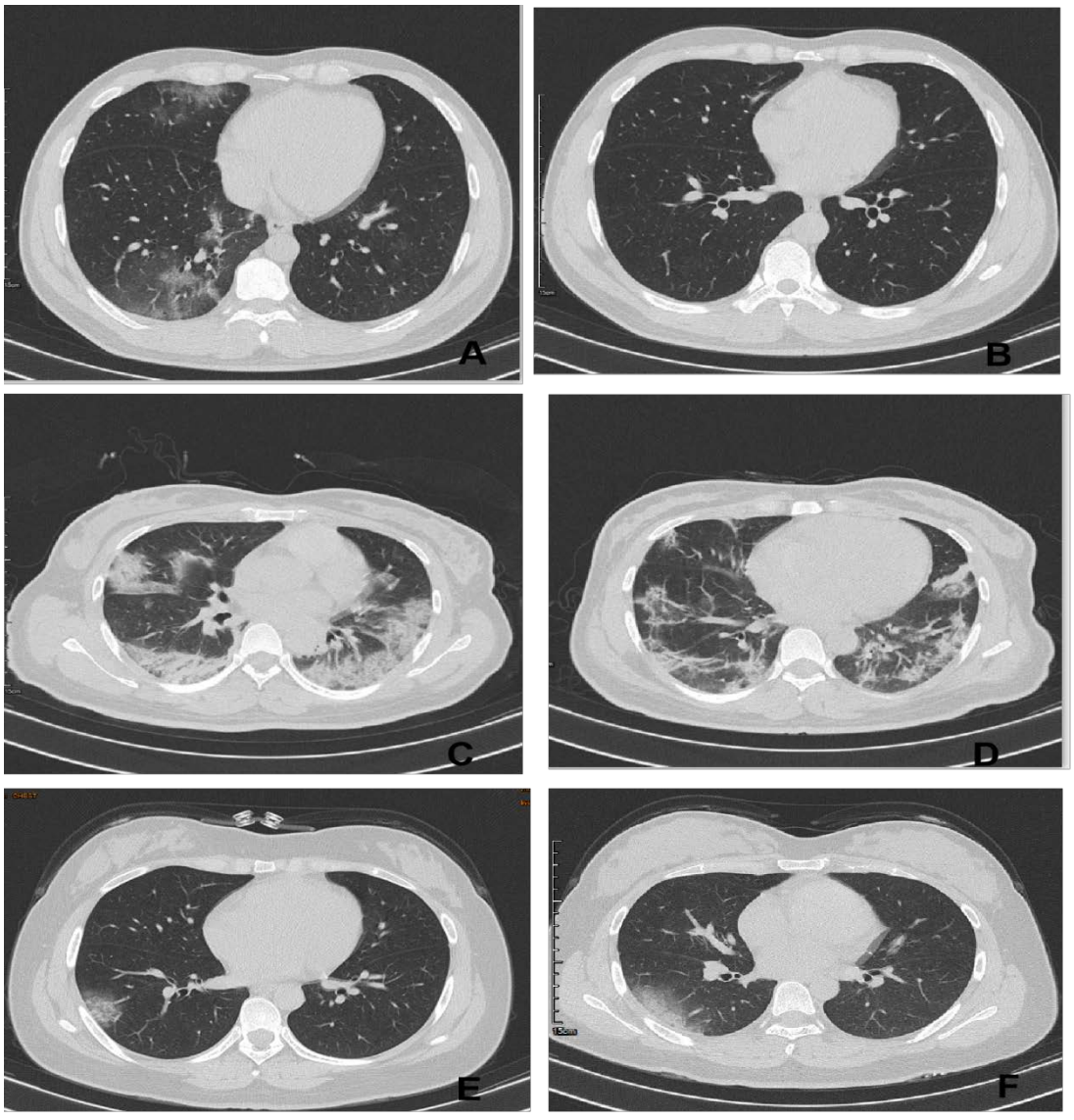

FIGURE2 Treatment of coronavirus disease 2019 (COVID-19). Abscissa represented the treatment method, and ordinates represented the percentage of a treatment used. Almost all the COVID-19 patients underwent antiviral therapy and nebulization inhalation.