

Clinical characteristics of four cancer patients with SARS-CoV-2 infection in Wuhan, China

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Case Report

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Abstract

Background: The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) led to the outbreak of pneumonia in Wuhan, and rapidly spread throughout China. The virus is highly infectious and can infect individuals in the community, including patients in the hospital. Patients with cancer might be susceptible to the viral infection because of the immunosuppressive state cause by therapies on tumors.

Case presentation: We present the clinical features of four cancer patients who were infected with SARS-CoV-2 in the past month in our hospital. One patient with uncontrolled chronic B cell lymphocytic leukemia and many other underlying diseases was killed by the virus, and the other three patients survived. Nearly all patients showed a decrease in lymphocytes including total CD3⁺ T cells, B cells, and natural killer cells after infection of the virus.

Conclusion: This report suggests that the treatment of SARS-CoV-2 infection in cancer patients is challenged by the immunosuppressive state of these patients under chemotherapy or surgery.

Background

Since December of 2019, the outbreak of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection in Wuhan has posed significant threats to health internationally [1, 2]. The SARS-CoV-2 is highly infectious and can infect all individuals. Patients infected with the virus have suffered from the 2019 novel coronavirus disease (COVID-19), including the novel coronavirus-infected pneumonia (NCP) and have had symptoms including fever, cough, shortness of breath, diarrhea, and vomiting [3]. As of February 19, 2020, SARS-CoV-2 has infected 75,204 cases globally in 25 countries and has led to 2009 deaths due to the rapid spread of the virus [4].

The development of NCP has caused more severe cases and deaths in older people with underlying diseases, including diabetes, cardiovascular disease, and cancer [3]. There is currently no definite effective drug against the virus, although some drugs such as remdesivir, chloroquine phosphate, Arbidol, lopinavir and ritonavir have been used in clinical practice and have exerted antiviral effects in some patients [5]. However, the antiviral efficacy of these drugs needs to be verified by large-scale studies. Recent studies have demonstrated a higher frequency of severe cases and increased mortality in patients in Wuhan compared with other regions of China [6].

Patients with cancer are thought to be more susceptible to infection than the general population because of their system's immunosuppressive state cause by chemotherapy, radiotherapy, or surgery on tumors [7]. Here, we report on four cancer patients infected with SARS-CoV-2 in the past month and describe their medical history, clinical diagnosis, changes in clinical parameters, and outcomes.

Case Presentation

Case 1

A 48-year-old woman was admitted to the Department of Radiation and Medical Oncology in our hospital on 2019-12-12, because of the need for continued radiotherapy for breast cancer. She received a modified radical mastectomy of the right breast on 2019-6-25, as well as six cycles of chemotherapy with paclitaxel and doxorubicin after surgery. After four weeks of radiotherapy, the patient presented fever on 2020-1-24, and this was accompanied by cough. Chest computed tomographic (CT) scans found slight interstitial abnormalities in both lower lungs, indicating a possibility of viral pneumonia (Figure 1B). The SARS-CoV-2 infection was confirmed by positive detection of the virus in throat swab sample using the real-time reverse transcription polymerase chain reaction (RT-PCR) method. The laboratory results revealed reductions in white blood cells (WBCs) and lymphocytes in the blood, especially CD3⁺CD8⁺ T cells, B cells, and natural killer (NK) cells (Table 2). The patient was then diagnosed as suffering from NCP and transferred to an isolation ward in the Department of Infectious Diseases. The symptoms were relieved after two days in this patient. The antibiotic ceftriaxone was given as therapy (Table 1). The chest CT scan on 2020-1-30 also suggested recovery from NCP (Figure 1C). However, the virus was sustained in the throat swab samples for several days (Table 2). The patient was transferred to another isolation ward, which was arranged by the government after discharge from our hospital.

Case 2

A 78-year-old woman from Wuhan came to our hospital with fatigue, malaise, and poor appetite on 2020-1-18. She was admitted to the Department of Hematology because of her past medical history of chronic B cell lymphocytic leukemia (B-CLL) for five years. She was also suffering hypertension, cardiovascular disease, and chronic obstructive pulmonary disease (COPD) for more than 10 years. She received percutaneous coronary intervention PCI on Feb. 23, 2014. She took aspirin and atorvastatin orally every day, and took nifedipine sustained-release tablets and indapamide sustained-release tablets to control blood pressure. Because of the presentation of the critical underlying diseases, she did not receive any treatment for B-CLL. The chest CT images found bilateral patchy shadowing, indicating double pneumonia in this patient on 2020-1-19 (Figure 1D). The patient was diagnosed as suffering from double pneumonia, COPD, hypertension, B-CLL, and coronary heart disease, and received antibiotic therapy with oseltamivir, cefoperazone, sulbactam, linezolid, and caspofungin. However, the pneumonia progressed, and symptoms such as fever, shortness of breath, and dyspnea appeared in the patient on 2020-1-25 (Figure 1E). The SARS-CoV-2 was found in a throat swab sample by real-time PCR. The patient was then transferred to an intensive care unit (ICU), and high flow humidification oxygen inhalation therapy and methylprednisolone (40 mg/daily) were employed as combination therapy. After five days of therapy in the ICU, symptoms of dyspnea and hypoxia improved, and the patient was transferred to an isolation ward in our department on 2020-1-31. We continued the combination therapy employed in the ICU. However, the patient died on 2020-2-10 due to respiratory failure, despite the noninvasive ventilation (Table 1). The lymphocyte subset analysis in this patient showed an increase in B cells, which may indicate uncontrolled B-CLL (Table 2). The older age, multiple underlying diseases, and severe pulmonary infection might have contributed to the death of the patient.

Case 3

A 54-year-old man from Wuhan was admitted to the Department of Colorectal and Anal Surgery on 2020-1-13. Six days before admission, a large polyp was found in his rectum by colonoscopy examination. He has been a hepatitis B surface antigen carrier for several years. He received a laparoscopic radical resection of rectal cancer on 2020-1-16, and the pathological result diagnosed rectal adenocarcinoma. On 2020-1-19, the patient presented fever, with no other symptoms. The chest CT scans suggested local patchy shadowing in the double lower lung (Figure 1G). The SARS-CoV-2 was found in a throat swab sample by real-time PCR on 2020-1-23. The patient was then diagnosed as having NCP and transferred to an isolation ward of our department. The onset of fever, antibiotic therapy with oseltamivir, meropenem, and moxifloxacin was given to the patient. The patient also received oxygen therapy by nasal catheter in the isolation ward (Table 1). The fever stopped after seven days of therapy, and the recovery of NCP was confirmed by a chest CT scan on 2020-1-30 (Figure 1H). The laboratory results also suggested a decrease in peripheral blood lymphocytes, such as B cells and NK cells, after SARS-CoV-2 infection (Table 2). The positive detection of SARS-CoV-2 in the throat swab samples of this patient lasted at least 18 days (Table 2). The patient was transferred to another isolation ward, which was arranged by the government after discharge from our hospital.

Case 4

A 37-year-old man from Wuhan had the chief complaint of upper abdominal intermittent pain for more than three months. One day before admission to the Department of Hepatobiliary Surgery, a space-occupying lesion was found in the liver of this patient by ultrasound. He has been a hepatitis B virus carrier for more than 19 years and does not take antiviral drugs or see a doctor regularly. After admission, he was diagnosed as suffering from chronic hepatitis B and hepatocellular carcinoma (HCC). On 2020-1-16, the patient received chemotherapy through transcatheter arterial chemoembolization. Multiple hepatic HCC lesions were found in this patient through a CT scan afterward (Figure 1I-J). Positron emission computerized tomography and computer tomography was performed, and no HCC lesion was found outside the liver. The patient received an allogeneic liver transplantation on 2020-1-20 for a better prognosis. A combination therapy with antibiotics, antiviral treatment with entecavir, a high dose of hepatitis B immunoglobulin, and immunosuppressive agent tacrolimus were given to the patient after surgery. However, the patient began to present a fever on 2020-1-30, and this was accompanied by a cough. SARS-CoV-2 was detected in a throat swab sample on 2020-2-1. The patient was transferred to an ICU on 2020-2-2 due to dyspnea, and the chest X-ray showed bilateral patchy shadowing, indicating NCP (Figure 1L). In the ICU, the patient was treated with a combination therapy including high-flow humidification oxygen inhalation, antibiotic therapy with oseltamivir, Arbidol, imipenem, cilastatin, moxifloxacin, caspofungin, and methylprednisolone (40 mg/daily) (Table 1). Two days later, the symptoms were relieved in this patient. The patient was transferred to an isolation ward in our

department on 2020-2-4, and received the same treatment employed in the ICU. On Feb.19, 2020, we ceased all antibiotic therapy and methylprednisolone. The lung CT images showed remission of the pneumonia despite the right pleural effusion found on 2020-2-18 (Figure 1M). Consistent with laboratory findings of other patients, the lymphocytes including T cells, B cells, and NK cells decreased after infection with SARS-CoV-2 in this patient (Table 2). The virus was persistent in the samples from throat swabs in this patient, so the patient remained in the hospital (Table 2).

Discussion And Conclusions

In the present study, we collected the clinical data from four cancer patients who were infected by SARS-CoV-2 and developed NCP. The diagnosis of NCP was based on symptoms, lung X-ray/CT examination, and detection of the virus by real-time RT-PCR in throat swab samples from the patients. No patient was initially admitted to the Department of Infectious Diseases and Department of Respiration. Only Case 2 showed pneumonia on admission; however, she did not present a fever when she came to our hospital; therefore, she may have infected the virus at home. The other three patients showed normal lung images when they were admitted to our hospital. They developed a fever and other symptoms related to NCP after radiotherapy or surgery in different departments, which might indicate that the hospital acquired SARS-CoV-2 infection. This was also demonstrated by another study conducted in our hospital [3].

Early studies have demonstrated the decrease in peripheral WBCs and lymphocytes during SARS-CoV-2, and we observed the same phenomenon in these patients, except Case 2. Case 2 had an increased count of B lymphocytes in the blood, which may be attributed to her underlying disease, B-CLL. Moreover, in the other three cases, we found a reduction in all lymphocyte subsets, including CD3⁺CD4⁺ helper cells, CD3⁺CD8⁺ cytolytic cells, B cells, and NK cells. Peripheral lymphopenia was also observed during another coronavirus, SARS-CoV infection [8, 9]. During SARS-CoV infection, the severe and mortal cases had much lower CD4⁺ T and CD8⁺ T cells after viral infection [9]. The infiltration and sequestration of lymphocytes in lungs and other organs might be attributed to the reduction in blood lymphocytes due to SARS-CoV and SARS-CoV-2 infections. In a pathological study of a patient who died due to NCP, interstitial mononuclear inflammatory infiltrates, dominated by lymphocytes, were found in both lungs [10]. Moreover, the study found that the counts of peripheral CD4⁺ and CD8⁺ T cells were substantially reduced, while their status was hyperactivated [10]. Consistently, in our study, we also found that the counts of CD3⁺ CD4⁺ helper T cells were much lower in two severe cases (Cases 2 and 4) compared to patients with mild (Case 1) or common (Case 3) types of NCP. Taken together, the counts of peripheral lymphocytes, especially of CD4⁺ and CD8⁺ T cells, may be useful in predicting the severity and clinical outcomes in SARS-CoV-2 infection. However, further studies are required to test this hypothesis.

The clinical outcomes of NCP are determined by virological parameters such as age, underlying diseases, severity of the pneumonia, and admission to an ICU [3, 6]. In our four cancer patients, Cases 2 and 4 were diagnosed as severe cases of NCP according to the symptoms, results from chest X-rays, and the

admission to the ICU. Case 2 was suffering from uncontrolled B-CLL, along with many underlying diseases including COPD, hypertension, and coronary heart disease. This condition and the greater age might have caused the severity of NCP and might have led to the death of the patient. Results from the laboratory showed an elevation in markers of bacterial infection, procalcitonin, and C-reactive protein, after admission and diagnosis of NCP. Though antibiotics were used, the contaminated bacterial infection might also have contributed to the death of this patient. Case 4 was diagnosed as having NCP 10 days after liver transplantation. The immunosuppressive agent tacrolimus, which was used for anti-rejection, might have inhibited the host immune system and might have led to the severity of NCP. Consistent with this, we found an extreme reduction in lymphocytes including CD3⁺ T cells, B cells, and NK cells in this patient. However, the patient entered into remission of NCP after comprehensive therapy. Liver transplantation was also attributed to the severity of pneumonia. Cases 1 and 3 were diagnosed as mild and common NCP, respectively, according to guidelines from the Chinese Ministration of Health. These two patients had better control of their related tumors and had a low risk of immunosuppression. This might have contributed to the success in recovery from NCP after SARS-CoV-2 infection. However, the clearance of SARS-CoV-2 from these four patients was delayed for more than 12 days regardless of the clinical outcomes. Few studies have addressed the question of the amount of time that will be needed to clear the virus after the onset of symptoms in the general population. A recent study analyzed the viral loads in nasal and throat swab samples from SARS-CoV-2-infected patients. The results suggested that, in some patients, the viral RNA could be detected 15 days after symptom onset. However, the median time of viral clearance in these patients was not analyzed due to a limited number of patients [11].

This study emphasizes that the treatment of SARS-CoV-2 infection in cancer patients is challenged by the immunosuppressive state of patients under chemotherapy or surgery [7]. Further large-scale studies are needed to clarify whether the clearance of the virus and the recovery of NCP are delayed in tumorous patients compared to the general population.

Abbreviations

SARS-CoV-2: severe acute respiratory syndrome coronavirus 2; COVID-19: 2019 novel coronavirus disease; NCP: novel coronavirus-infected pneumonia; CT: computed tomographic; RT-PCR: reverse transcription polymerase chain reaction; WBCs: white blood cells; NK: natural killer; B-CLL: B cell lymphocytic leukemia; COPD: chronic obstructive pulmonary disease; ICU: intensive care unit; HCC: hepatocellular carcinoma;

Declarations

Ethics approval and consent to participate: This study was conducted according to the principles expressed in the Declaration of Helsinki, and was approved by the ethics committee of Zhongnan

Hospital of Wuhan University (No. 2020011). Written consent forms were obtained from the patients after gave them appropriate information.

Consent for publication: Written consent forms for publication were obtained from the patients or their clients after gave them appropriate information.

Availability of data and materials: The datasets supporting the conclusions of this article are included within the article. And further detailed datasets for the current study are available from the corresponding author on reasonable request.

Competing interests: The authors declare that they have no competing interests.

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Author Contributions: Y.X., S.S., and Z.M. conceived the original idea and led the overall study. S.S. and Z.M. wrote the paper. Y.X. carefully revised the manuscript. T.C., L.D., X.Z., P.M., W.H., and S.G. collected and analyzed the clinical data.

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Tables

Table 1 Clinical characteristics of the four cancer patients with SARS-CoV-2 infection

Clinical characteristics	Case 1	Case 2	Case 3	Case 4
Sex	Female	Female	Male	Male
Age (years)	48	78	54	37
Date of admission	2019-12-21	2020-1-18	2020-1-13	2020-1-14
Date of NCP diagnosis	2020-1-26	2020-1-25	2020-1-23	2020-2-1
Underlying diseases				
Hypertension	No	Yes	No	No
Cardiovascular disease	No	Yes	No	No
COPD	No	Yes	No	No
HBV infection	No	No	Yes	Yes
Tumor type	breast cancer	B-CLL	rectal cancer	HCC
Tumor related therapy				
Chemotherapy	Yes	No	No	Yes
Radiotherapy	Yes	No	No	No
Surgery	Yes	No	Yes	Yes
Date of surgery	2019-6-25	/	2020-1-16	2020-1-20
Dates of fever (day after admission)	Day35, Day36	Day6~Day17	Day7~Day11	Day17~Day24
Maximum temperature	38°C	39°C	39.5°C	39°C
Clinical type of NCP	Mild	Severe	Common	Severe
Anti-microbe therapy				
Antiviral	No	Oseltamivir	Oseltamivir	Oseltamivir Arbidol
Antibacterial	Ceftriaxone	Cefoperazone and sulbactam Linezolid	Meropenem Moxifloxacin	Imipenem and cilastatin Moxifloxacin
Antifungal	No	Caspofungin	No	Caspofungin
Methylprednisolone	No	40mg/day	No	40mg/day
Oxygen therapy	No	Noninvasive ventilation	Nasal catheter	High-flow oxygen
ICU admission	No	Yes	No	Yes
Clinical outcomes	Recovery of NCP; Discharge from hospital	Dead	Recovery of NCP; Discharge from hospital	Remission of NCP; Therapy in hospital

Abbreviations: SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; NCP, novel coronavirus-infected pneumonia; COPD, chronic obstructive pulmonary disease; HBV, hepatitis B virus; B-CLL, chronic B cell lymphocytic leukemia; HCC, hepatocellular carcinoma; ICU, intensive care unit

Table 2 Laboratory and radiographic findings of the four cancer patients with SARS-CoV-2 infection

Radiographic and laboratory findings	Normal Range	Case 1	Case 2	Case 3	Case 4
After admission					
White blood cell count, $\times 10^9/L$	3.5-9.5	4.21	10.91 \uparrow	4.86	5.46
Neutrophil count, $\times 10^9/L$	1.8-6.3	2.05	4.11	3.8	3.53
Lymphocyte count, $\times 10^9/L$	1.1-3.2	1.3	5.85	0.57 \downarrow	1.2
Hemoglobin, g/L	130-175	101 \downarrow	118 \downarrow	133	152
Platelet count, $\times 10^9/L$	125-350	350	202	180	182
Procalcitonin, ng/mL	<0.05	<0.05	0.1 \uparrow	<0.05	0.25
C-reactive protein, mg/L	0-10	NA	36.2 \uparrow	NA	NA
Abnormalities on chest X-ray/CT	No	No (Fig.1A)	Bilateral patchy shadowing (Fig.1D)	No (Fig.1F)	No (Fig.1K)
After fever onset					
White blood cell count, $\times 10^9/L$	3.5-9.5	2.86 \downarrow	6.67	2.7 \downarrow	9.36
Neutrophil count, $\times 10^9/L$	1.8-6.3	1.79 \downarrow	3.55	1.21 \downarrow	8.73
Lymphocyte count, $\times 10^9/L$	1.1-3.2	0.4 \downarrow	2.4	0.88 \downarrow	0.28 \downarrow
Hemoglobin, g/L	130-175	114 \downarrow	112 \downarrow	115 \downarrow	102 \downarrow
Platelet count, $\times 10^9/L$	125-350	156	177	280	50 \downarrow
Procalcitonin, ng/mL	<0.05	<0.05	0.57 \uparrow	<0.05	<0.05
C-reactive protein, mg/L	0-10	0.7	77.9 \uparrow	1.3	18.1 \uparrow
Abnormalities on chest X-ray/CT	No	Interstitial abnormalities (Fig.1B)	Progress of bilateral lung diseases (Fig.1E)	Local patchy shadowing (Fig.1G)	Bilateral patchy shadowing (Fig.1L)
Lymphocyte subsets (count/ml)					
CD3 ⁺ T cells	805-4459	435 \downarrow	297 \downarrow	865	335 \downarrow
CD3 ⁺ CD4 ⁺ T cells	345-2350	290 \downarrow	115 \downarrow	482	148 \downarrow
CD3 ⁺ CD8 ⁺ T cells	345-2350	142 \downarrow	184 \downarrow	341 \downarrow	185 \downarrow
B cells	240-1317	12 \downarrow	4213 \uparrow	44 \downarrow	41 \downarrow
NK cells	210-1514	59 \downarrow	132 \downarrow	154 \downarrow	43 \downarrow
Detection of SARS-CoV-2 in throat swab samples					
Dates of positive results	/	2020-1-26 2020-1-30 2020-2-3 2020-2-8	2020-1-25 2020-1-28 2020-2-1 2020-2-5	2020-1-23 2020-1-30 2020-2-3 2020-2-9	2020-2-1 2020-2-4 2020-2-8 2020-2-12

Abbreviations: SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; NA, not available; CT, computed tomographic; NK cells, natural killer cells

Figures

Figure 1

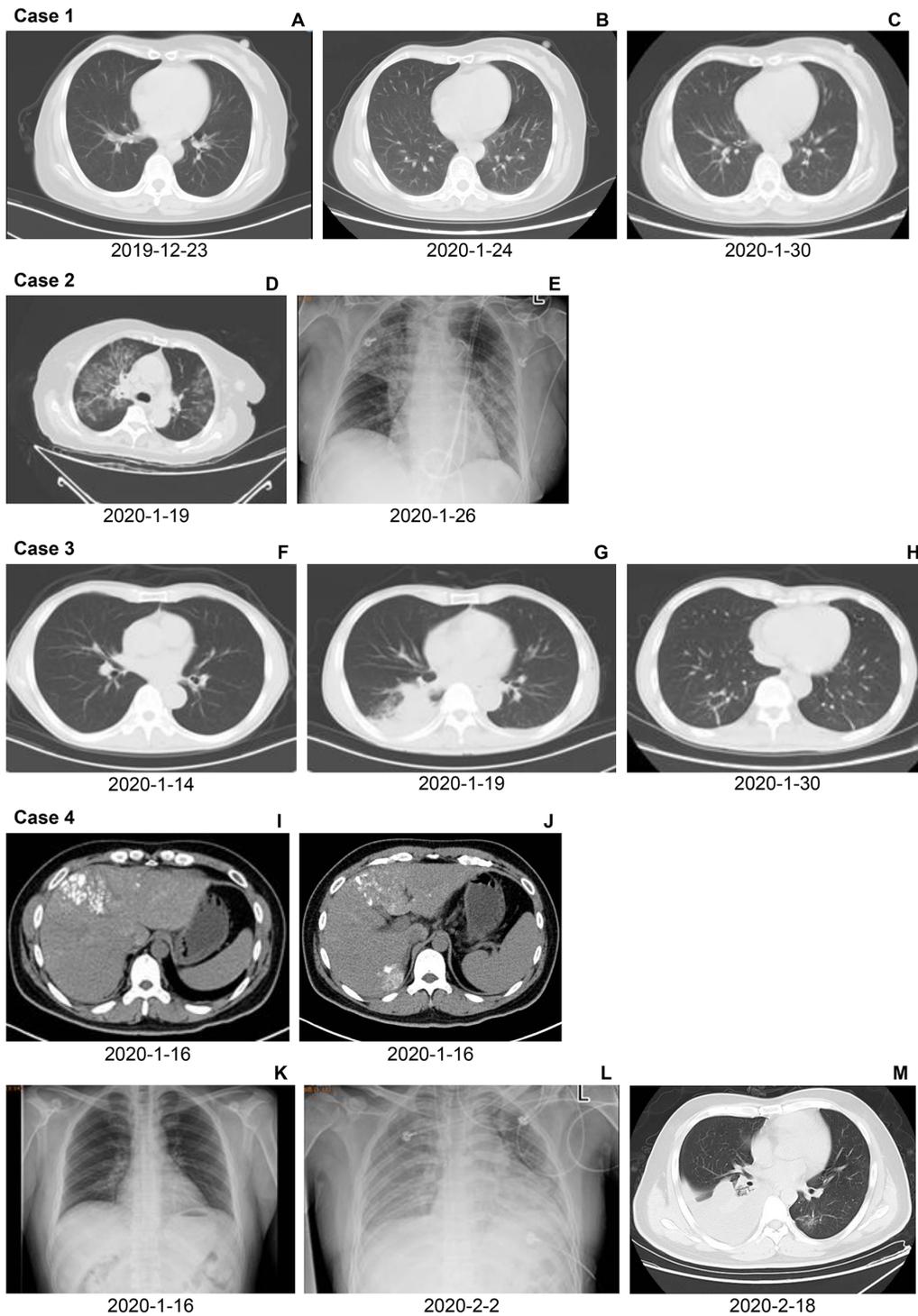


Figure 1

The chest X-ray/computed tomographic (CT) images of the four patients on different time points. (A-C) Images from Case 1. The patient had normal CT images on 2019-12-23 after admission (A). However, on 2020-1-24, after onset of fever, CT scan showed interstitial abnormalities in both lower lung, which

revealed the possibility of viral pneumonia (B). And these changes were ameliorated after treatment and showed on 2020-1-30 (C). (D-E) Images from Case 2. The CT images showed bilateral patchy shadowing in the patient after admission (D), and the lesion progressed one week later (E). (F-H) Images from Case 3. The CT scans taken on different time points, showed local patchy shadowing in right lung 6 days after admission (G), which is the time point of fever onset in this patient. And the lesion was recovered after treatment and showed on 2020-1-30 (H). (I-M) Images from Case 4. (I-J) The CT scans showed the multiple HCC lesions in the liver after transcatheter arterial chemoembolization therapy. The X-ray examination of the patient revealed normal lung after admission (K). However, on 2020-2-2 the images from X-ray showed bilateral patchy shadowing, indicating viral pneumonia (L). The patient has been in remission of the pneumonia despite right pleural effusion was showed by CT scan on 2020-2-18 (M).