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CASE REPORT

COVID-19 patient with an incubation period of 27 d: A case report

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Abstract

BACKGROUND

As a highly contagious disease, coronavirus disease 2019 (COVID-19) is wreaking havoc around the world due to continuous spread among close contacts mainly via droplets, aerosols, contaminated hands or surfaces. Therefore, centralized isolation of close contacts and suspected patients is an important measure to prevent the transmission of COVID-19. At present, the quarantine duration in most countries is 14 d due to the fact that the incubation period of severe acute respiratory syndrome coronavirus type 2 (SARS-CoV-2) is usually identified as 1-14 d with median estimate of 4-7.5 d. Since COVID-19 patients in the incubation period are also contagious, cases with an incubation period of more than 14 d need to be evaluated.

CASE SUMMARY

A 70-year-old male patient was admitted to the Department of Respiratory Medicine of The First Affiliated Hospital of Harbin Medical University on April 5 due to a cough with sputum and shortness of breath. On April 10, the patient was transferred to the Fever Clinic for further treatment due to close contact to one confirmed COVID-19 patient in the same room. During the period from April 10 to May 6, nucleic acid and antibodies to SARS-CoV-2 were tested 7 and 4 times,

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respectively, all of which were negative. On May 7, the patient developed fever with a maximum temperature of 39°C, and his respiratory difficulties had deteriorated. The results of nucleic acid and antibody detection of SARS-CoV-2 were positive. On May 8, the nucleic acid and antibody detection of SARS-CoV-2 by Heilongjiang Provincial Center for Disease Control were also positive, and the patient was diagnosed with COVID-19 and reported to the Chinese Center for Disease Control and Prevention.

CONCLUSION

This case highlights the importance of the SARS-CoV-2 incubation period. Further epidemiological investigations and clinical observations are urgently needed to identify the optimal incubation period of SARS-CoV-2 and formulate rational and evidence-based quarantine policies for COVID-19 accordingly.

Key Words: COVID-19; Incubation period; Quarantine duration; SARS-CoV-2; Case

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Core Tip: As the quarantine duration of coronavirus disease 2019 (COVID-19) in most countries is currently 14 d, cases with an incubation period of more than 14 d in the clinic may trigger rapid spread of the epidemic, which requires us to be highly vigilant. We present a COVID-19 patient with an incubation period of 27 d confirmed in the Fever Clinic of The First Affiliated Hospital of Harbin Medical University. Further epidemiological investigations and clinical observations are urgently needed to identify the optimal incubation period of severe acute respiratory syndrome coronavirus type 2 (SARS-CoV-2) and formulate rational and evidence-based quarantine policies for COVID-19 accordingly.

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INTRODUCTION

Coronavirus disease 2019 (COVID-19), which is caused by severe acute respiratory syndrome coronavirus type 2 (SARS-CoV-2) infection, has been officially identified as a Class B infectious disease mainly involving the respiratory system. In China, the prevention and control measures for COVID-19 are required to be in accordance with Class A infectious disease[1]. SARS-CoV-2 is a novel coronavirus[2], and all individuals are susceptible to this infection. At present, no effective targeted intervention has been proposed beyond supportive treatment [3,4]. The successful experience of antiepidemic measures in China suggest that a series of multi-faceted public health interventions can effectively control the outbreak of COVID-19[5], of which centralized isolation of close contacts and suspected patients is one of the most important measures to prevent the transmission of COVID-19. The quarantine duration in most countries is 14 d based on the predicted longest incubation period of SARS-CoV-2. It is true that cases with an incubation period of more than 14 d are rare in the clinic [6]. However, it is still of great concern to avoid the rapid spread of the epidemic from cases with an incubation period of more than 14 d, since the infected person has strong infectivity in the incubation period [7,8]. We present a COVID-19 patient with an incubation period of 27 d confirmed in the Fever Clinic of The First Affiliated Hospital of Harbin Medical University.

CASE PRESENTATION

Chief complaints

A 70-year-old male patient was admitted to the Department of Respiratory Medicine of The First Affiliated Hospital of Harbin Medical University on April 5 due to a cough with sputum and shortness of breath.

History of present illness

Cough with sputum and shortness of breath appeared 2 mo ago, and the cough and dyspnea were then further aggravated.

History of past illness

The patient had a medical history of hypertension and vitiligo.

Personal and family history

The patient had no personal or family history.

Physical examination

The patient's vital signs were stable. Rales could be heard on auscultation of both

Laboratory examinations

Laboratory tests revealed the following results on admission: White blood cell count of 9.06×10^{9} /L, neutrophil (NEUT) count of 7.34×10^{9} /L, NEUT% of 80.90%, lymphocyte (LYMPH) count of $0.47 \times 10^{\circ}/L$ and percentage of lymphocytes (LYM%) of 5.20%. During the period from April 10 to May 7, blood cell analyses were reexamined (Table 1), in which LYMPH and LYM% significantly decreased.

Imaging examinations

The initial lung computed tomography (CT) indicated pneumonia and multiple nodules in the lungs, bilateral pleural effusion and pericardial effusion. On May 7, reexamination of the lung CT showed patchy shadows and interstitial changes. On May 11, lung CT imaging showed that the lung lesions had rapidly deteriorated (Figure 1).

FINAL DIAGNOSIS

On May 7, the results of nucleic acid and antibody detection of SARS-CoV-2 were positive. On May 8, the nucleic acid and antibody detection of SARS-CoV-2 by Heilongjiang Provincial Center for Disease Control were also positive, and the patient was diagnosed with COVID-19 and reported to the Chinese Center for Disease Control and Prevention.

TREATMENT

In the initial stage of disease, the patient occasionally had shortness of breath but did not need oxygen therapy. On April 10, the patient was transferred to the Fever Clinic for further treatment due to close contact to one confirmed COVID-19 patient in the same room. During the period from April 10 to May 6, lung CT was reviewed on April 26 and 30 (Figure 1), and nucleic acid and antibody of SARS-CoV-2 were tested 7 and 4 times, respectively, all of which were negative (Table 1). Surprisingly, on May 7, the patient developed fever with a maximum temperature of 39°C, and his respiratory difficulties had deteriorated. Continuous oxygen therapy was then provided. Due to continuous deterioration of the patient's condition, a high-flow nasal cannula and invasive mechanical ventilation were given to the patient on May 7 and 11 to enhance respiratory support. In addition, comprehensive treatment measures also included antibiotic agents, analgesic and sedative drug injections, vasopressor support and immunotherapy.

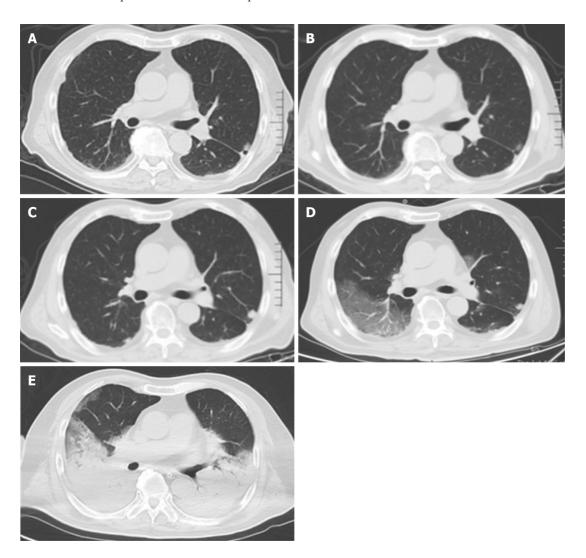


Figure 1 Lung computed tomography scan of the patient. A: April 5, 2020; B: April 26, 2020; C: April 30, 2020; D: May 5, 2020; E: May 11, 2020.

OUTCOME AND FOLLOW-UP

Unfortunately, despite timely comprehensive treatment measures were taken, the patient's immune function and condition did not improve, and he eventually died.

DISCUSSION

In April 2020, a cluster of SARS-CoV-2 infections occurred in two tertiary general hospitals in Harbin city, resulting in 66 newly confirmed patients including this case and 21 asymptomatic patients. Due to close contact to a confirmed COVID-19 patient, our patient had received relevant treatment in the Fever Clinic of our hospital for 27 d. As our hospital is the treatment center for COVID-19 in Heilongjiang Province, the ward layout, regulations, work arrangements, operation specifications and disinfection procedures in the Fever Clinic of our hospital were all in line with national regulations and standards; thus, the possibility of cross-infection in the Fever Clinic was extremely low. Therefore, by staying in the same room with a confirmed COVID-19 patient from April 5th to 10th, there was a chance of contracting SARS-CoV-2.

Currently, the diagnosis of COVID-19 mainly depends on detection of SARS-CoV-2 nucleic acid on oropharyngeal and/or nasopharyngeal swabs by real-time polymerase chain reaction (RT-PCR)[9,10], although there is still a possibility of false-positive and false-negative results[11-13]. Therefore, lung CT has been proposed as an auxiliary method for the rapid diagnosis of COVID-19 due to its low rate of missed diagnosis [14]. In addition to a CT scan, abnormal findings on fluorodeoxyglucose-positron emission tomography/CT scans may confirm or exclude the presence of SARS-CoV-2 infection[15]. Bilateral and peripheral ground-glass opacities and consolidation are the

Table 1 Timeline of the disease course (April 5 to May 11, 2020)																	
Day of illness		1	2	3	6	7	8	10	11	13	17	20	21	27			
Disease Course	Hospitalization	Close contact	The Fever Clinic											Positive PCR			
White blood cell count (× $10^9/L$)	9			6.87					8.67					8.62		9.69	6.63
Lymphocyte count (× 10 ⁹ /L)	0.47			0.55					0.73					0.24		0.18	0.12
Lymphocyte percentage (%)	5.2			8					8.42					2.82		1.92	1.8
Nucleic acid detection		Negative		Negative		Negative		Negative		Negative	Negative	Negative		Positive		Positive	
Antibody detection IgM				Negative	Negative		Negative						Negative	Positive		Positive	
Antibody detection IgG				Negative	Negative		Negative						Negative	Positive		Positive	
Oxygen therapy															Oxygen therapy	HFNC	Invasive mechanical ventilation
CT	CT										CT		CT		CT		CT
Date	Apri l5	April 10	April 11	April 12	April 15	April 16	April 17	April 19	April 20	April 22	April 26	April 29	April 30	May 6	May 7	May 8	May 11

CT: Computed tomography; HFNC: High-flow nasal cannula; PCR: Polymerase chain reaction.

most common features of COVID-19 on lung CT imaging[16-18], which were not found in the three lung CT examinations before our patient was diagnosed with COVID-19. In addition, the patient's seven nucleic acid tests and four antibody tests for SARS-CoV-2 were all negative during the quarantine period. Following the diagnosis of COVID-19, CT imaging revealed rapid deterioration of the lungs with the typical imaging characteristics of COVID-19 over a short period of time compared with the previous CT scans[19]. Based on the above history, it was concluded that the patient had acquired SARS-CoV-2 infection due to sharing the same room with a confirmed COVID-19 patient from April 5th to 10th, he then developed worse symptoms on May 7th and was confirmed to have COVID-19 on May 8th. Thus, the incubation period was 27 d, which is very rare in clinical practice.

The prerequisite for determining the optimal quarantine duration is a good understanding of the incubation period. The incubation period usually refers to the time between infection and the onset of corresponding symptoms and signs or when the disease is confirmed [20], which determines the adjustment in quarantine policies.

The mainstream view is that the incubation period of SARS-CoV-2 is usually identified as 1-14 d with a median estimate of 4-7.5 d[6,21-23], and thus the current clinical practice of 14-d quarantine duration in most countries seems reasonable. However, there is a different opinion that a small proportion of COVID-19 patients have an incubation period of more than 14 d based on the estimated incubation distribution [6, 20], which will be an enormous figure considering the surge in COVID-19 patients and its rising trend. Age may be one of the explanations for the longer incubation period of COVID-19[24], while the other mechanisms are still unclear.

Definitive close contact, as shown in this case report, and some extreme cases should be considered to extend the quarantine duration during the outbreak stage of the epidemic[25,26]. When the epidemic recurred in Heilongjiang Province in April 2020, the quarantine duration was extended and the SARS-CoV-2 nucleic acid test was popularized for entry personnel, referred to as "14 + 7 + 14". Fourteen days of centralized isolation and 2 nucleic acid tests, and 7 d of centralized isolation and one nucleic acid test should be carried out at the entry point and the local region, respectively, and then 14 d of home isolation and observation should be carried out and incorporated into the grid management of the local community[27]. Prolonged quarantine duration can effectively prevent SARS-CoV-2 from spreading during the incubation period. Obviously, an extension of quarantine duration will make the already overwhelmed medical system even more overstretched, and increase the burden on society and individuals during the COVID-19 epidemic. Further epidemiological investigations and clinical observations are urgently needed to identify the optimal incubation period of SARS-CoV-2 and formulate rational and evidence-based quarantine policies for COVID-19 accordingly.

CONCLUSION

As the quarantine duration for COVID-19 in most countries is currently 14 d, cases with an incubation period of more than 14 d in the clinic may trigger rapid spread of the epidemic, which requires us to be highly vigilant. Further studies are needed to determine the proportion of COVID-19 patients with an incubation period of more than 14 d, and weigh the costs of extending quarantine duration and the potential risks and consequences of the spread of the epidemic during the incubation period. These findings will have important implications for optimal prevention and control of COVID-19.

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