

[CASE REPORT]

Pneumonia Due to Human Coronavirus OC43 in an Immunocompetent Adult Detected by Multiplex Polymerase Chain Reaction

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Abstract:

A 40-year-old woman developed a fever, sore throat, and cough. Coronavirus disease 2019 (COVID-19) was suspected; chest CT showed pan-lobular ground-glass opacity in the bilateral lower lobes suggesting viral pneumonia. Although a reverse transcription loop-mediated isothermal amplification (RT-LAMP) test for COVID-19 using a nasopharyngeal swab was negative, she was hospitalized and isolated because COVID-19 could not be ruled out. After admission, multiplex polymerase chain reaction (PCR) with the FilmArray Respiratory Panel 2.1 from a nasopharyngeal swab was positive for human coronavirus (HCoV) OC43. Therefore, the diagnosis was pneumonia due to HCoV-OC43. Multiplex PCR is useful for differentiating pneumonia due to COVID-19 from that due to other viral pneumonias.

Key words: human corona virus OC43, multiplex PCR, viral pneumonia, COVID-19

(Intern Med 60: 3497-3501, 2021)

(DOI: 10.2169/internalmedicine.7450-21)

Introduction

The coronavirus disease 2019 (COVID-19) pandemic has spread around the world, causing many deaths and placing a heavy burden on healthcare providers. It is important to identify infected patients because the disease is extremely contagious, and airborne transmission can be prevented by isolating them.

Chest computed tomography (CT) is useful for screening for COVID-19 infection, as it has a high sensitivity (1, 2). However, the CT findings of viral pneumonia are nonspecific. It is thus difficult to determine whether or not a patient should be isolated if CT is positive and polymerase chain reaction (PCR) is negative.

We herein report a case of viral pneumonia caused by human coronavirus (HCoV)-OC43, which is relatively rare, that was diagnosed by multiplex PCR with the FilmArray Respiratory Panel 2.1.

Case Report

A previously healthy 40-year-old woman developed a nasal discharge and sore throat for 3 days and a fever for 1 day. Her husband's colleagues had been diagnosed with COVID-19, and he had some symptoms similar to hers. She showed decreased oxygenation and was referred to our hospital for suspected COVID-19.

She had clear consciousness, her temperature was 40.0°C, and her SpO₂ was 92% on ambient air. A physical examination showed lymphatic follicles in the posterior wall of the pharynx, but her cervical lymph nodes were not swollen. There was no wheezing or crackles on auscultation. Laboratory examinations showed increased C-reactive protein (CRP) and leukocytosis, which was neutrophil-predominant with a decreased lymphocyte percentage. There was no liver damage (Table 1).

Chest X-ray showed ground-glass opacity (GGO) in the right lower lung field, and CT showed pan-lobular GGO in the bilateral lower lobes (Fig. 1a). Although a reverse transcription loop-mediated isothermal amplification (RT-

Table 1. Laboratory Data on Admission.

Hematologic test			
White blood cells	13,200 / μ L	LDH	215 U/L
Neutrophils	90.1 %	BUN	6 mg/dL
Lymphocytes	3.9 %	Creatinine	0.6 mg/dL
Red blood cells	4.16×10^6 / μ L	Sodium	140 mmol/L
Hemoglobin	12.1 g/dL	Potassium	3.7 mmol/L
Platelet count	19.9×10^4 / μ L	Chloride	104 mmol/L
Chemistry			
Total protein	6.7 g/dL	CK	98 U/L
Albumin	3.8 g/dL	CRP	3.06 mg/dL
Total bilirubin	1.1 mg/dL	HbA1c	5.4 %
AST	19 U/L	Coagulation	
ALT	12 U/L	PT	13.9 s
ALP	62 U/L	PT-INR	1.11
γ -GTP	28 U/L	APTT	36.8 s
		D-dimer	0.8 μ g/mL

ALP: alkaline phosphatase, ALT: alanine aminotransferase, APTT: activated partial thromboplastin time, AST: aspartate aminotransferase, BUN: blood urea nitrogen, CK: creatine kinase, CRP: C-reactive protein, γ -GTP: γ -glutamyl transpeptidase, HbA1c: hemoglobin A1c, LDH: lactate dehydrogenase, PT: prothrombin time, PT-INR: prothrombin time-international normalized ratio

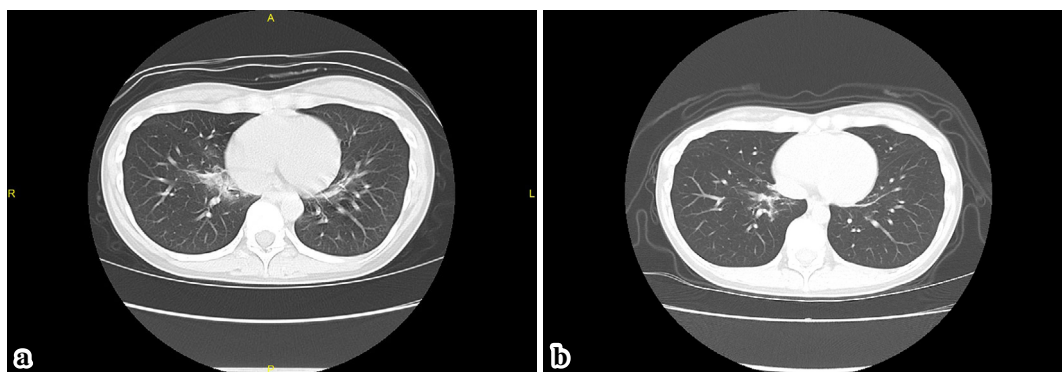


Figure 1. Chest CT (a) shows pan-lobular GGO in the bilateral lower lobes on the day of admission. GGO in the bilateral lower lobes had disappeared on chest CT (b) on day 14 after leaving the hospital.

LAMP) test of a nasopharyngeal swab was negative, COVID-19 could not be ruled out given the patient's history and symptoms; therefore, the patient was hospitalized and isolated. After admission, she was given acetaminophen for her fever but no antimicrobial agents. Multiplex PCR with a nasopharyngeal swab was performed on the second day after admission, and HCoV-OC43 was detected (Table 2). Her oxygenation and general condition were relatively good; therefore, isolation was lifted, and she was discharged from our hospital. At the outpatient visit on the 14th day after leaving our hospital, the sore throat and cough had improved, and the GGO in the bilateral lower lobes had disappeared on chest CT (Fig. 1b).

At a later date, to confirm the diagnosis, the specimens that tested positive for HCoV-OC43 in the FilmArray Respiratory Panel 2.1 and the RT-LAMP specimens that tested negative for severe acute respiratory syndrome coronavirus 2 (SARS-CoV2) at the time of admission were sent to the Department of Virology III, the National Institute of Infectious

Diseases of Japan, for real-time reverse transcription (RT)-PCR. Real-time RT-PCR for the detection of the four HCoVs (HCoV-229E, HCoV-OC43, HCoV-NL63, and HCoV-HKU1) was performed using the same specimen in which HCoV-OC43 had been detected by multiplex PCR. Ribonucleic acid (RNA) extraction was performed using the QIAamp Viral RNA mini kit (Qiagen, Hilden, Germany) and confirmed to be positive for HCoV-OC43. In addition, real-time RT-PCR using the QIAamp Viral RNA mini kit for RNA extraction was also conducted to detect SARS-CoV-2 and confirmed negative (Fig. 2, 3).

Discussion

To our knowledge, case reports with CT images of pneumonia caused by HCoV-OC43 in immunocompetent adults are rare. If viral pneumonia is suspected, multiplex PCR of a nasopharyngeal swab specimen is useful, as we can differentiate COVID-19 from infections with other respiratory or-

Table 2. Viral and Bacterial Respiratory Organism Test

Multiplex PCR		LAMP	
Adenovirus	Negative	Parainfluenza virus 1	Negative
HCoV 229E	Negative	Parainfluenza virus 2	Negative
HCoV HKU1	Negative	Parainfluenza virus 3	Negative
HCoV NL63	Negative	Parainfluenza virus 4	Negative
HCoV OC43	Positive	Respiratory syncytial virus	Negative
SARS-CoV-2	Negative	Bordetella parapertussis	Negative
Human metapneumovirus	Negative	Bordetella pertussis	Negative
Human rhinovirus/Enterovirus	Negative	Chlamydia pneumoniae	Negative
Influenza A	Negative	Mycoplasma pneumoniae	Negative
Influenza B	Negative		

HCoV: human coronavirus, LAMP: loop-mediated isothermal amplification, SARS-CoV-2: severe acute respiratory syndrome coronavirus 2

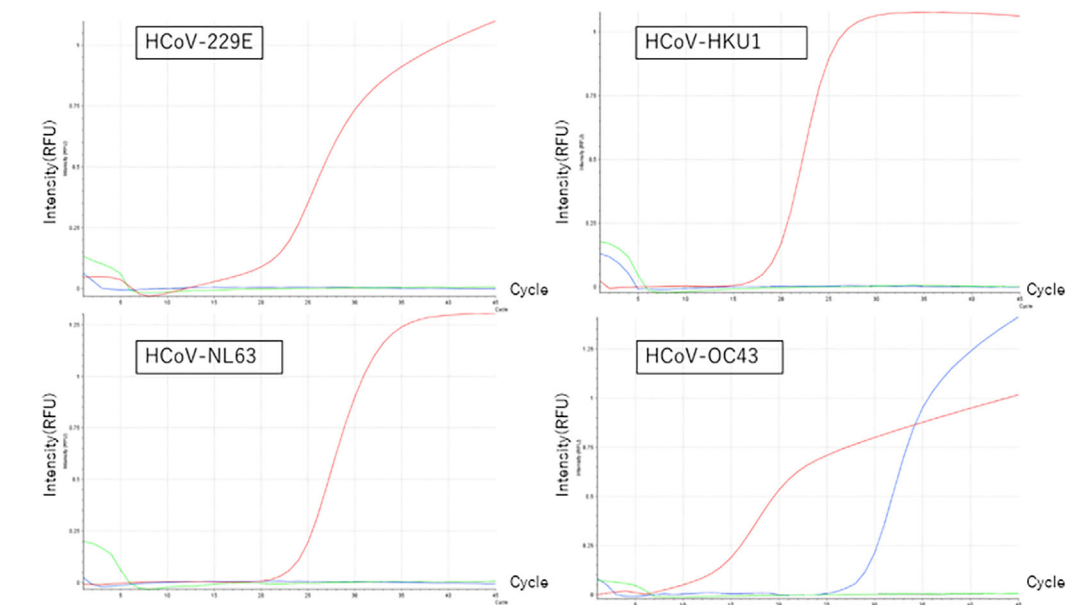


Figure 2. Real-time reverse transcription polymerase chain reaction for four HCoVs (HCoV-229E, HCoV-HKU1, HCoV-NL63, and HCoV-OC43). The blue line shows the findings for the present specimen. The red line indicates a positive control, and the green line indicates a negative control. HCoV-OC43 was detected in the nasopharyngeal swab of the patient.

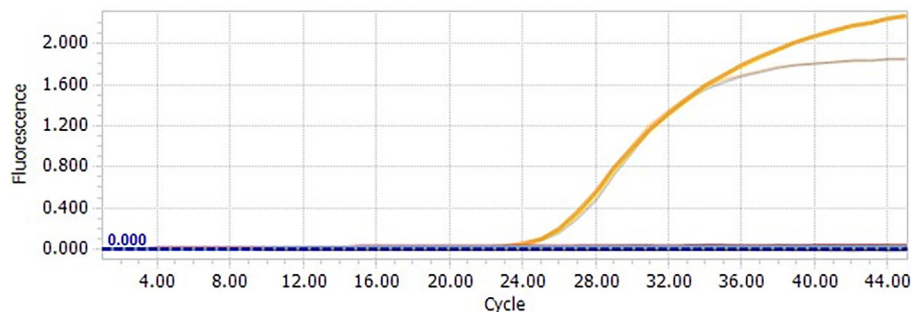


Figure 3. Real-time reverse transcription polymerase chain reaction for SARS-CoV-2. The blue line shows the negative control, the gray shows the specimen of this case, and the upper two yellow lines show the positive control. SARS-CoV-2 was not detected in the nasopharyngeal swabs of the patient.

ganisms, allowing us to decide whether or not a patient should be isolated.

Respiratory viruses are the second leading cause of pneumonia after bacteria (3). Pneumonia caused by human coronaviruses, such as HCoV-229E, HCoV-HKU1, HCoV-NL63, and HCoV-OC43, is less common than that caused by other viruses, including COVID-19 (4, 5). However, HCoV-OC43 is an important differential diagnosis because it causes severe pneumonia and neurological disease in pediatric and immunocompromised patients (6, 7). Although cases of lower respiratory tract infections in HCoV-OC43 have been reported in immunocompromised patients, there are few reports of the CT findings. Chest CT has a high sensitivity but no specificity for detecting COVID-19 pneumonia (1). The major CT findings of COVID-19 are GGO, a crazy-paving pattern, and consolidation predominantly in subpleural locations in the lower lobes (8). CT findings of coronavirus infections other than COVID-19 typically show consolidation and GGO in a peripheral distribution (9). Although there are characteristic CT findings depending on the time course of COVID-19, it is difficult to distinguish COVID-19 from other viral pneumonias by CT findings alone.

The patient was suspected of having COVID-19 and tested negative on nasopharyngeal swab RT-LAMP. Since COVID-19 could not be ruled out based on her history and imaging findings, she was admitted to the hospital. Multiplex PCR for nasopharyngeal swab fluid was positive for HCoV-OC43, leading to the final diagnosis. Although HCoV-OC43 can also occur as a co-infection with other viruses (10), the negative percent agreement of multiplex PCR was very high (11), and the possibility of a false-negative result or other viral pneumonia was considered to be low. In addition, real-time RT-PCR using the QIAamp Viral RNA mini kit for RNA extraction was performed on the same specimen and confirmed to be positive for HCoV-OC43 (Fig. 2). On multiplex PCR, HCoV-OC43 showed cross-reactivity with HCoV-HKU1 and no cross-reactivity with SARS-CoV-2 (11, 12). Therefore, given the results of real-time RT-PCR, cross-reactivity was considered unlikely in this case. Furthermore, real-time RT-PCR for SARS-CoV-2 was performed on the nasopharyngeal swab of the same day and confirmed to be negative (Fig. 3). False-negative results for SARS-CoV-2 were also considered unlikely. Co-infection with bacterial pneumonia cannot be ruled out in elderly or immunocompromised patients (13). However, in the present case, the symptoms and laboratory findings, including imaging, improved spontaneously without antimicrobial treatment, suggesting that the patient was suffering from a viral pneumonia. It is also possible that HCoV-OC43 was present in the nasopharynx and therefore tested positive. Although it is difficult to completely rule it out, it was considered reasonable to assume that the infection had been caused by HCoV-OC43 based on the symptoms and course of spontaneous resolution. Based on the present findings, we believe that multiplex PCR is valuable when COVID-19 cannot be ruled out and gene tests including LAMP are negative.

In conclusion, a relatively rare case of pneumonia due to HCoV-OC43 in an immunocompetent adult was presented. Multiplex PCR was useful in this case because COVID-19 was able to be differentiated from infection with other respiratory organisms. The diagnosis of viral infection other than COVID-19 using multiplex PCR may be useful for preserving medical resources, including human resources, such as ward isolation.

The authors state that they have no Conflict of Interest (COI).

Acknowledgements

The authors thank Dr. Kazuya Shirato of the Department of Virology III, National Institute of Infectious Diseases of Japan, for performing real-time RT-PCR.

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Intern Med 60: 3497-3501, 2021