A CASE OF CORONAVIRUS DISEASE 2019 COMPLICATED BY VENTILATOR-ASSOCIATED PNEUMONIA, LUNG ABSCESS, AND *STAPHYLOCOCCUS AUREUS* BACTEREMIA

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Abstract

Complications of healthcare-associated infections have been reported in patients with coronavirus disease 2019 (COVID-19). We encountered a case of ventilator-associated pneumonia and lung abscess, complicated with *Staphylococcus aureus* bacteremia and multiple abscesses, in a patient with COVID-19. Streptococci and anaerobes were cultured from the sputum, which was considered to be the causative organism of the lung abscess. In the management of severe COVID-19, care should be taken to prevent complications of healthcare-associated infections; when secondary respiratory tract infections are suspected, the presence of lung abscess and anaerobic culture should be considered.

Keywords: COVID-19, lung abscess, *Staphylococcus aureus*, healthcare-associated infection

Introduction

Coronavirus disease 2019 (COVID-19) is still prevalent worldwide after first being reported in China in December 2019. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infects the lower respiratory tract and causes pneumonia. Moreover, various other complications have been reported, such as neurological symptoms[1], thrombosis[2], and bacterial infections[3]. Influenza virus has been reported to facilitate complications of bacterial infections, especially those caused by *Staphylococcus aureus* and *Streptococcus pneumoniae*[4]. However, the mechanisms of bacterial infection remain unclear in COVID-19, and a low frequency of complications with *S. aureus* infection[3] in COVID-19 has been reported.

We report a case of ventilator-associated pneumonia and lung abscess caused by oral flora, complicated with *S. aureus* bacteremia and multiple abscesses in a patient with COVID-19.

Case

A 52-year-old man with a history of treatment for unstable angina, underlying hypertension, and dyslipidemia had a fever of > 37° C and fatigue. He had no history of smoking. He underwent a SARS-CoV-2 loop-mediated isothermal amplification test, which was positive; thus, he

was diagnosed with COVID-19. The next day, the patient was admitted to the hospital. Chest radiograph revealed no infiltration shadow. Hypoxemia progressed 4 days later, and dexamethasone and favipiravir were initiated. Nine days after symptom onset, hypoxemia exacerbated, and he was transferred to our hospital.

Upon arrival at our hospital, he had severe hypoxia with SpO_2 95% (O_2 8 L/min) and an infiltrative shadow on the chest radiograph. Blood tests showed elevated levels of white blood cells (WBC) and C-reactive protein (CRP) (Table 1). He was admitted to the intensive care unit (ICU) and immediately intubated. Remdesivir and dexamethasone were administered. Oxygenation

Table 1. Laboratory test results

	on admission	Day15	on discharge
WBC (/μL)	10900	13500	8100
Hgb (g/dL)	13.0	11.1	9.5
Plt ($\times 10^4$/μL)	25.0	22.4	43.6
D-D (μg/mL)	1.6		
CRP (mg/dL)	7.27	14.39	1.06
AST (U/L)	46	25	14
ALT (U/L)	53	57	6
LDH (U/L)	433	261	196
CK (U/L)	41	46	24
BUN (mg/dL)	21	15	9
Cre (mg/dL)	0.72	0.52	0.58
Na (mEq/L)	135	133	142
K(mEq/L)	4.6	3.6	3.7
Cl (mEq/L)	104	102	103
Amy (U/L)	77	643	116

Fig.1a.

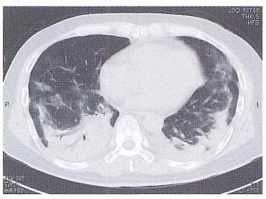

Fig.1b.

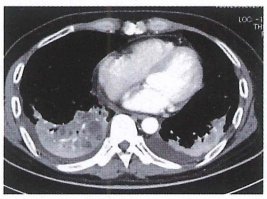

Fig.1c.

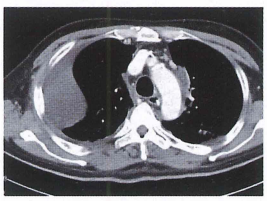

Fig.1d.

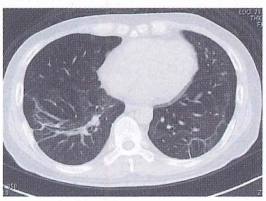

Fig. 1.
Fig.1. Chest computed tomography (CT) on day 15 (a), day 16 (b), day 22 (c), and day 115 (d).
a: Non-contrast CT showing bilateral infiltrative shadow.
b: Contrast CT showing a large number of low-density areas in the infiltrating shadows with air bronchogram.
c: Contrast chest computed tomography on day 22.
Encapsulated fluid retention on the left side of the aortic arch and pleural effusion in the right pleural cavity.
d: Chest computed tomography on day 115.
The infiltrative shadows in the bilateral lower lobes improved and low-density areas disappeared.

improved, and he was extubated on day 13 of ventilation. The infiltrative shadows seen on the bilateral lower lung fields improved but persisted at the time of transfer to a general ward.

On day 15 of hospitalization, amylase levels were elevated (Table 1), and non-enhanced computed tomography (CT) of the abdomen was performed to investigate the cause. Because the pancreatic head was enlarged, the patient was suspected to have pancreatitis, and fasting and infusion therapy were initiated. The lung field on CT showed a bilateral infiltrative shadow (Fig. 1a).

Abdominal contrast-enhanced CT was performed the following day to evaluate the severity of pancreatitis. Although the images showed an enlarged pancreatic head, pancreatitis was ruled out. However, on air bronchogram, a large number of low-densitiy areas were observed in the infiltrating shadows that could be considerd multiple abscesses (Fig. 1b). Piperacillin-tazobactam was administered (4.5 g every 6 h) after collecting sputum and blood cultures. S. aureus was detected in the blood culture. *Streptococcus dysgalactiae, Prevotella melaninogenica, Prevotella oris,* and *Fusobacterium nucleatum* were isolated from sputum samples collected at the same time. However, *S. aureus* was detected in the sputum collected the next day. On day 19 of hospitalization, he was readmitted to the ICU and reintubated. Blood cultures taken on the third day of treatment were negative. Antimicrobial drugs were changed to ampicillin-sulbactam (3 g every 6 h) based on *S. aureus* susceptibility. During the course of treatment, antimicrobial agents were changed to the following due to suspected drug side effects: cefazolin (2 g, every 8 h) against *S. aureus* and clindamycin (600 mg, every 8 h) against anaerobic bacteria. On day 23 of hospitalization, there was no worsening of the low-density areas of the lung, but a fluid collection adjacent to the aortic arch appeared to be an abscess. This was not present in the previous imaging studies (Fig. 1c). Right thoracic drainage was performed on day 24. The drained specimen culture was negative. Tracheostomy was performed and mechanical ventilation was weaned off after 22 days. On day 43 of hospitalization, he was transferred to the general ward. Antimicrobial agents were switched to oral form (cefalexin 500 mg thrice a day and clindamycin 300 mg thrice a day) after 7 weeks of intravenous infusion.

The patient was discharged on the 78th day of hospitalization. The CT before discharge and the follow-up CT 39days after discharge showed that the abscess adjacent to the aortic arch was gradually shrinking and low-density areas and infiltration in the right lower lobe had disappeared (Fig. 1d). Antimicrobial agents were administered for 7 months, and antimicrobial therapy was terminated after the absence of the low-density areas and abscess were confirmed on imaging. Analysis of the pathogen-related genes of *S. aureus* showed that the major toxin genes (enterotoxin, *TSST-1,* and *PVL*) were not retained. The coagulase gene sequence showed that it was of type Vb. Multi-locus sequence typing analysis revealed that it was ST188.

Discussion

We encountered a case of ventilator-associated pneumonia and lung abscess caused by oral flora, complicated with *S. aureus* bacteremia and multiple abscesses in a patient with COVID-19.

Secondary bacterial pneumonia following viral infection is well known in the case of influenza[5]. This is caused by damage to the airway mucosa caused by the influenza virus and usually develops 4 to 14 days after the improvement of influenza infection. The most common causative

microorganisms have been *S. pneumoniae* and *S. aureus*. Although no increase in secondary bacterial infections similar to those of influenza cases have been reported for COVID-19, COVID-19 has been associated with a high frequency of healthcare-associated infections such as ventilator-associated pneumonia and intravascular catheter-associated bloodstream infections[6,7]. In this case of severe COVID-19, ventilator-acquired pneumonia developed and a lung abscess was subsequently confirmed by contrast-enhanced chest CT. The cause of the increase in healthcare-associated infections in COVID-19 has not yet been fully studied. It is believed that in addition to needing intensive medical care in severe cases, health care workers are required to wear personal protective equipment such as gloves and gowns while performing clean and aseptic operations. Furthermore, because of this requirement, it is easy for them to neglect hand disinfection and replacement of personal protective equipment, which is thought to be one of the reasons for horizontal transmission of microorganisms and bacterial contamination of sterile areas.

The present case was diagnosed as multiple lung abscesses on chest CT on the 27th day of COVID-19. Although the patient was on ventilator management from the ninth day to the 20th day of the disease, he was mananged without antimicrobial agents because he originally had abnormal shadows in the lung fields caused by COVID-19, and a portable chest radiograph did not reveal any new lung lesions.

Plain chest CT showed infiltrative shadows with pleural effusion and air bronchograms in both dorsal lower lung fields, and contrast-enhanced CT showed multiple abscesses. Clancy et al. summarized 75 studies including 621 cases with autopsies in COVID-19 and reported that 3.5% had lung abscesses[8].

Blonz et al. reported in a review of 188 ventilator-associated pneumonia cases that 1.4% had lung abscesses[9]. Similarly, Beaucoté et al. reported that out of the 57% of ventilator-requiring COVID-19 patients who underwent chest CT, 14% had lung abscesses[10].

It is possible that the actual incidence of lung abscesses may be lower than that estimated because contrast-enhanced CT of the chest may be required for its diagnosis, as in this case. COVID-19 may be difficult to evaluate on chest imaging because of the presence of abnormal chest shadows due to the primary disease, COVID-19. If a lung abscess is present, the duration of antimicrobial therapy should be extended, and chest imaging should be carefully evaluated. Chest contrast-enhanced CT should be considered to exclude lung abscesses, especially in the case of recurrent or refractory pneumonia.

Beaucoté et al. reported that *Pseudomonas aeruginosa*, *Enterobacteriaceae*, and *S. aureus were* the most common bacteria detected in a study of 17 lung abscesses complicated by COVID-19[10]. Ippolito et al. conducted a systematic review and meta-analysis of studies on ventilator-associated pneumonia among COVID-19 patients and reported that the most common bacteria detected were *Enterobacteriaceae* and glucose non-fermenting bacteria. In our case, in addition to *Streptococcus dysgalactiae equisimilis*, two species of *Prevotella spp.* and anaerobic bacteria, such as *Fusobacterium nucleatum*, were detected.

It is well known that lung abscesses are caused by commensal bacteria in the oral cavity such as streptococci and anaerobes; anaerobic culture is not performed in some hospital clinical laboratories, and this may have been underestimated in the study of causative microorgan-

isms in pneumonia complicated with COVID-19. Rattanaburi et al. reported that patients with COVID-19 had a wider variety of oral flora, including *Streptococcus species* and *Prevotella species*, than patients with influenza infection[11].

It has also been reported that the amount of *Prevotella spp.* correlates with the severity of COVID-19[12]. Based on these findings, it is important to consider the involvement of anaerobic bacteria in addition to *Enterobacteriaceae*, non-fermenting gram-negative bacteria, and *S. aureus*, which are reported to be common in severe COVID-19 ventilator-associated pneumonia and lung abscess in particular.

This case was also complicated with *S. aureus* bacteremia. Although *S. aureus* was only initially detected in the blood culture, it was later detected in the aspirated sputum. It is possible that colonization of *S. aureus* was horizonatlly transmitted during the course of the disease, first causing bacteremia and subsequently invading the respiratory tract to allow detection in the respiratory specimen; however, it is also possible that *S. aureus* migrated from the blood vessels into the alveolar space in conditions such as septic pulmonary embolism and became one of the microorganisms causing lung abscess. It is also possible that *S. aureus* is a microorganism that causes lung abscesses. In this case, lesions that appeared to be abscesses on the chest wall and aortic arch suggested multiple abscesses associated with *S. aureus* bacteremia. The ST type of *S. aureus* detected in this case was ST188, which is relatively common in Southeast Asia and does not produce toxins such as TSST-1 or PVL, but it is important to note that multiple abscess formation is a common characteristic of *S. aureus* infection[13].

In conclusion, we encountered a case of severe COVID-19 complicated with a pulmonary abscess caused by oral commensal bacteria, including anaerobic bacteria, after ventilator management that was further complicated with *S. aureus* bacteremia and multiple abscesses. In the management of severe COVID-19, care should always be taken to prevent complications of healthcare-associated infections; furthermore, when respiratory infections are suspected, the presence of lung abscesses and bacteremia should be noted.

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Declaration of competing interest

None.

Ethics statement and informed consent

Written consent for case reports is obtained from the patient.

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