Successful endobronchial occlusion in empyema with broncho-pleural fistula secondary to COVID-19 pneumonia: a case report and literature review

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Keywords
Air cyst, broncho-pleural fistula, COVID-19, empyema, endobronchial occlusion.

Abstract
A few cases of empyema secondary to coronavirus disease 2019 (COVID-19) pneumonia have been reported. Here, we report our experience of a successful endobronchial occlusion using endobronchial Watanabe spigots (EWSs) for empyema with broncho-pleural fistula secondary to COVID-19 pneumonia. A 62-year-old man was diagnosed with COVID-19 and progressed to empyema with broncho-pleural fistula. Computed tomography (CT) imaging showed cyst formation and the right B5b was presumed to be a branch dependent on the cyst. The effusion and air in the pleural cavity were well drained, although the air leak persisted. Endobronchial occlusion was performed for right B5a and B5b using 7- and 5-mm EWSs (Novatech, France), respectively, and the air leak ceased. This is the first report of successful treatment of empyema with bronchial fistula with endobronchial occlusion. Air leak secondary to COVID-19 pneumonia with a limited number of air cysts may be a good indication for endobronchial occlusion.

Introduction
Since December 2019, the outbreak of coronavirus disease 2019 (COVID-19) caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has been causing a worldwide pandemic emergency. COVID-19 is known to cause severe respiratory dysfunction. More recently, the complex respiratory pathophysiology of COVID-19 pneumonia has been increasingly reported, and it is accompanied by pneumothorax, pneumomediastinum, and empyema. A few cases of surgical interventions for empyema secondary to COVID-19 pneumonia have been reported [1–3]. However, the appropriate management of air leaks in COVID-19 has not yet been established.

Endobronchial intervention is generally considered to be a less invasive treatment for pneumothorax and empyema with broncho-pleural fistula [4]. A shortcoming of the endobronchial intervention is the difficulty in detecting the dependent bronchus to the pleural fistula causing the air leak. In an air leak secondary to COVID-19, air cyst formation arising due to pneumonia is an obvious target for endobronchial intervention. Here, we report our experience of a successful endobronchial occlusion using endobronchial Watanabe spigots (EWSs) for empyema with broncho-pleural fistula secondary to COVID-19 pneumonia.

Case Report
A 62-year-old man with diabetes mellitus was diagnosed with COVID-19 when he tested positive for SARS-CoV-2 RNA using a real-time reverse transcriptase polymerase chain reaction (RT-PCR) test. His general condition was stable at first, but his respiratory function worsened in a week, and he was transferred to the emergency department. Chest computed tomography (CT) revealed bilateral peripheral infiltrate and consolidation areas (Fig. 1A). He was intubated because of respiratory failure caused by COVID-19 pneumonia in the intensive care unit and was treated with medications, including methylprednisolone, favipiravir, RNA polymerase inhibitor, and nintedanib, an inhibitor of processes involved in lung fibrosis. On admission, his methylprednisolone dose was 1000 mg.
The methylprednisolone was tapered from 1 mg/kg on the second hospital day to 0.125 mg/kg/day on the 29th hospital day, and then discontinued. In this case, nintedanib was being administered within the context of an ongoing clinical trial examining inhibition of lung fibrosis. Neither bullae nor blebs were detected at this time (Fig. 1B).

![Figure 1. Computed tomography (CT) image of the chest. (A) CT image at initial diagnosis showed bilateral peripheral infiltrate and consolidation areas. (B) Neither bullae nor blebs were detected at initial diagnosis, including the peripheral side of B⁵b (►). (C) CT image at the onset of pneumothorax showed formation of a cyst (►) which had not been seen in previous CT image. (D) Right B⁵b was presumed to be the dependent branch to the air cyst (►).]

![Figure 2. (A) Schema of airway before performing endobronchial occlusion. (B) Endobronchial occlusion was performed at right B⁵a and B⁵b using a 7- and 5-mm endobronchial Watanabe spigot (EWS), respectively.]

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endobronchial occlusion is a less invasive method than pneumothorax, including empyema with broncho-pleural occlusion is reportedly effective for treatment of intractable these cases resulted in a good clinical course. Endobronchial occlusion performed under general anaesthesia on the day of admission to our hospital. Right B5a and B5b were occluded using 7- and 5-mm EWSs (Novatech), respectively (Fig. 2), and the air leak ceased. Antibiotics were discontinued 11 days after the intervention accompanied by SARS-CoV-1 infection, were presumed [7,14]. Air cysts in COVID-19 pneumonia have been reported to be limited in number as observed from radiological findings [7,11,12]. Considering the successful clinical course of our patient, bronchial occlusion seems to be a prioritized treatment for empyema with broncho-pleural fistula and pneumothorax secondary to COVID-19 pneumonia. SARS-CoV-2 is transferred by droplets and aerosolization [15]. Thus, endobronchial intervention has a potentially high risk of viral exposure to the medical staff, as mentioned by the Centers for Disease Control and Prevention [16]. To protect medical staff from SARS-CoV-2 infection, endobronchial intervention should not be performed as far as possible during the contagious period of SARS-CoV-2 infection, which is reported as being from four days before COVID-19 onset to eight days after [17]. In conclusion, this is the first report of successful treatment of empyema with bronchial fistula with endobronchial occlusion. Air leak secondary to COVID-19 pneumonia with a limited number of air cysts may be a good indication for endobronchial occlusion.

Disclosure Statement
Appropriate written informed consent was obtained for publication of this case report and accompanying images.

Table 1. Summary of previous reports on empyema with BPF secondary to COVID-19 pneumonia.

| No | Author | Age, sex | Cyst formation | Intervention for BPF | Prognosis |
|----|--------|----------|----------------|---------------------|-----------|
| 1  | Placki [1] | 49, M | + | Surgery (lung resection) | Dead |
| 2  | Tessitore [2] | 72, M | Not described | Surgery (lung resection and decortication) | Alive |
| 3  | Our case | 62, M | + | Endobronchial occlusion | Alive |

BPF, broncho-pleural fistula; COVID-19, coronavirus disease 2019.

On the 17th hospital day, right pneumothorax occurred, and a chest tube was placed for drainage of the air. CT imaging on the same day showed cyst formation, which was not seen in the previous CT scan (Fig. 1C). Right B5b was presumed to be a branch dependent on the cyst (Fig. 1D). Bacteriological inspections of sputum and pleural effusion revealed infection by Pseudomonas aeruginosa, and tazobactam/piperacillin was administered on the 20th hospital day to treat secondary bacterial pneumonia and empyema. The general condition and laboratory findings improved, and the effusion and air in the pleural cavity were well drained, although the air leak persisted. Repeat RT-PCR tests for SARS-CoV-2 resulted negative on the 28th and 31st hospital days. After three cycles of chemical pleurodoses using 200 mg of minocycline on the 33rd hospital day, 400 mg of minocycline on the 39th hospital day, and 4 g of sterile talc powder on the 41st hospital day, he was transferred to our hospital to treat the air leak on the 54th hospital day.

Endobronchial occlusion was performed under general anaesthesia on the day of admission to our hospital. Right B5a and B5b were occluded using 7- and 5-mm EWSs (Novatech), respectively (Fig. 2), and the air leak ceased. Antibiotics were discontinued 11 days after the endobronchial occlusion. The chest tubes were completely removed 14 days after the endobronchial occlusion, and the patient was transferred to a rehabilitation hospital 28 days after the endobronchial occlusion.

Discussion
Bilateral multiple pneumonia is a common clinical presentation in COVID-19 cases [5,6] and some cases with complex respiratory pathophysiology, such as pneumothorax, pneumomediastinum, and empyema, have been reported [7,8]. To our knowledge, five cases of empyema secondary to COVID-19 have been reported to date, including two cases of pleural fistula (Table 1) [1–3]. All five patients were treated with surgical intervention, such as decortication, and four of these cases resulted in a good clinical course. Endobronchial occlusion is reportedly effective for treatment of intractable pneumothorax, including empyema with broncho-pleural fistula [9]. For the treatment of broncho-pleural fistula, endobronchial occlusion is a less invasive method than thoracic surgery [4,10]. However, it has not been reported for pneumothorax or empyema with bronchial fistula secondary to COVID-19 pneumonia. In our case, a simple pleural cavity without a septal wall was well drained by the chest tube. Thus, surgical debridement of the pleural cavity was considered unnecessary. In addition, a dependent bronchus to the pleural fistula was obvious on chest CT because of air cyst formation. Thus, endobronchial occlusion was performed at the right middle lobe bronchus and it successfully stopped the air leak.

As in our case, air cyst formation has been reported in COVID-19 pneumonia, especially secondary pneumothorax [7,11,12]. The mechanism of air cyst formation is presumed to be barotrauma caused by positive pressure ventilation [13]. On the other hand, cases of pneumothorax with air cyst secondary to COVID-19 pneumonia which were not treated with positive pressure were also reported, for which other mechanisms, such as check-valve due to bronchial inflammation accompanied by SARS-CoV-1 infection, were presumed [7,14]. Air cysts in COVID-19 pneumonia have been reported to be limited in number as observed from radiological findings [7,11,12]. Considering the successful clinical course of our patient, bronchial occlusion seems to be a prioritized treatment for empyema with broncho-pleural fistula and pneumothorax secondary to COVID-19 pneumonia.

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**Author Contribution Statement**

Takahito Nakano prepared the data and drafted the manuscript. Masahiro Kawada and Kensuke Minami supported the data collection. Hiroyuki Kaneda revised and edited the manuscript. All authors read and approved the final manuscript.

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