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## Case Report

## Persistent air leak secondary to pneumothorax in COVID-19: A case report and review of literature

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## ABSTRACT

An air leak is a pathologic communication between an area of the endobronchial tree and the pleural space, causing continued air flow. The communication can originate from a distal portion of the airway, causing an alveolar-pleural fistula, or from a more proximal airway, causing a bronchopleural fistula. When the air leak persists beyond 5–7 days, it is classified as persistent air leak (PAL). PAL has serious implications on patient management and outcomes, such as prolonged chest tube maintenance, high rate of infections, ventilation-perfusion mismatch, and prolonged hospital stay with higher morbidity and mortality. There are currently no guidelines for the management of PAL in COVID-19 patients. We presented a case of PAL in a patient with COVID-19-associated pneumothorax successfully treated with a one-way endobronchial valve. We also reviewed current published cases of PAL secondary to COVID-19-associated pneumothorax and the various methods they were treated. The first line treatment was insertion of one or more chest tubes, but the persistence of an air leak then led to other treatment modalities. Initial early surgical evaluation followed by pleurodesis is recommended for the management of PAL. The most common surgical approaches include VATS or open thoracotomy with mechanical or chemical pleurodesis or pleurectomy. However, surgery is not always a feasible option for critically ill patients. In such cases, there are multiple less invasive options for the management of PAL, including implantable devices, such as Watanabe spigots and stents, and chemical agents, such as thermal treatments, hemostatic substances, and tissue adhesives.

## 1. Introduction

A persistent air leak (PAL) is a pathologic communication between an area of the endobronchial tree and the pleural space, causing continued air flow [1]. The communication can originate from the subsegmental bronchus or a more distal portion of the airway, causing an alveolar-pleural fistula, or can originate from a segmental bronchus or a more proximal airway, causing a bronchopleural fistula [1]. When the air leak persists beyond 5–7 days, it is classified as persistent or prolonged, leading to further risk of complications [2]. Several known risk factors for PAL have been previously described, including mechanical ventilation, thoracic trauma, pneumothorax, pulmonary surgery (such as lobectomy and lung volume reduction surgery), and pulmonary infection [1]. The SARS-CoV-2 virus, the causative organism of COVID-19 infection, has been a major cause of respiratory tract inflammation and subsequent pulmonary complications, including acute respiratory distress syndrome (ARDS) and pneumothorax, in recent years [3].

PAL has serious implications on patient management and outcomes, such as prolonged chest tube maintenance, high rate of

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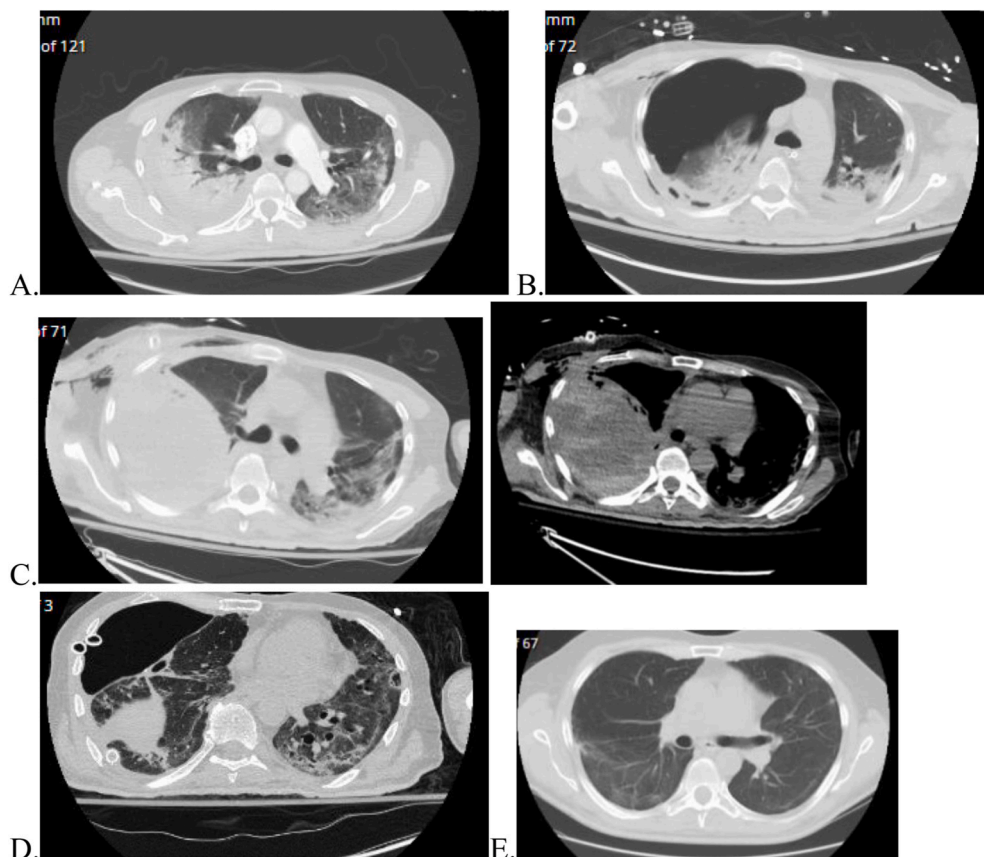
**Fig. 1.** Chest radiographs at various points during hospitalization. **A.** Day 1 of second hospitalization showing a large focal mass-like opacity involving most of the right lung. **B.** A new large right pneumothorax with mediastinal shift towards the left. **C.** Status post placement of a right basilar chest tube and decrease in size of right basilar pneumothorax. **D.** Recurrence of moderate right pneumothorax and placement of a new right apically directed chest tube. **E.** A new large right thoracic mass-like density, right apical hydropneumothorax suspected. **F.** Trace residual right pneumothorax, with interval placement of bronchial valve in right middle lobe. **G.** Resolution of pneumothorax, a few days prior to discharge. **H.** Status post removal of endobronchial valve.

infections due to loss of sterility of pleural space [4], ventilation-perfusion mismatches and difficulty maintaining positive end-expiratory pressure during mechanical ventilation, and overall prolonged hospital stay with higher morbidity and mortality [2]. The management of PAL is a controversial area, particularly in a critical care setting, where most patients are not ideal surgical candidates due to their tenuous status [1]. Patients tend to be treated conservatively, allowing for the gradual absorption of air. Patients can also be treated through surgical or endoscopic minimally invasive interventions, such as insertion of one-way endobronchial valves (EBV), chemical pleurodesis, or blood patch pleurodesis [1,5].

There are currently no guidelines for management of PAL in COVID-19 patients. Particularly, the treatment of PAL secondary to COVID-19 associated pneumothorax is uncertain and has mainly been described in case reports and/or series. We present a case of PAL in a patient with COVID-19-associated pneumothorax successfully treated with a one-way EBV. We also sought to review current published cases of persistent air leak secondary to COVID-19-associated pneumothorax and the various methods they were treated.

## 2. Case presentation

We present a case of a 57-year-old unvaccinated male with a medical history of hyperlipidemia who presented from an outside hospital with worsening shortness of breath and confusion of six days duration after testing positive for SARS-CoV-2 at home. The patient was hypoxemic requiring oxygen supplementation with high flow nasal cannula, eventually leading to noninvasive ventilation use. He received COVID-19 treatment with dexamethasone, remdesivir, and tocilizumab. The patient developed worsening respiratory status, and a computed tomography with angiography of the chest was performed that revealed bilateral pulmonary emboli. He was started on anticoagulation and underwent catheter directed thrombectomy of right main pulmonary artery, right lower lobe, and left



**Fig. 2.** CT chest at various points during hospitalization. **A.** Severe multifocal pneumonia, right greater than left, with small right pleural effusion. **B.** Large right pneumothorax with mediastinal shift to the left, chest tube in place, infiltrate vs atelectatic change in left lung. **C.** Dense heterogeneous mass-like opacity throughout the right lung likely represents a hematoma, air-fluid level towards right apex suggests hydropneumothorax or hemopneumothorax (correlating to Fig. 1E CXR). **D.** Moderate to large right anterior pneumothorax with chest tubes in place, findings suggestive of pulmonary fibrosis and/or interstitial lung disease. **E.** Scattered scarring throughout the lungs bilaterally, likely sequelae of prior COVID pneumonia.

pulmonary artery, leading to improvement and ultimately was transferred to an acute inpatient rehabilitation program on 3 L of oxygen.

Two days post-discharge, the patient developed chest pain, shortness of breath, tachypnea and hypoxemia, requiring transfer to the emergency department and hospitalization. With initial concerns of superimposed bacterial pneumonia, the patient was started on antibiotics. However, his symptoms did not resolve, and steroids were reinitiated due to likelihood of COVID pneumonitis and organizing pneumonia. There was initial improvement, however, the patient quickly developed respiratory failure requiring intubation and mechanical ventilation. Post-intubation bedside bronchoscopy showed scant bloody secretion in bilateral distal airways with no obstructive lesion or purulence. Soon after, he developed increased peak and plateau pressures post intubation with abdominal distention and hypotension requiring vasopressor support. A chest X-ray revealed a large amount of air, likely a loculated pneumothorax in the setting of rupture of a necrotic lung segment in the right middle lobe (Fig. 1, Fig. 2). An emergent chest tube was placed for suspected tension pneumothorax, with immediate air release, drainage of 850 cc of serosanguineous output, and improvement in blood pressure and oxygen saturation.

Following patient stabilization, imaging showed improving pneumothorax (Fig. 1). However, the chest tube continued to show a large air leak, suspected to be a large bronchopleural fistula. The patient completed a course of antibiotics, and steroids were weaned off slowly. A large air leak persisted, with repeat CT chest showing a large anterior pneumothorax despite the right basilar chest tube, so an anterior chest tube was placed to achieve lung re-expansion (Fig. 2). The patient improved and was successfully extubated to nasal cannula.

A few days later, the patient became tachypneic, tachycardiac, and hypoxemic, requiring re-intubation. Initial labs revealed a hemoglobin drop and a CXR revealed a density over the right pleural space consistent with a hemothorax, further confirmed on repeat CT of the chest (Figs. 1 and 2). The patient was transfused and underwent a right video-assisted thoracoscopic surgery (VATS) decortication, hematoma evacuation and wedge resection of the RML for a ruptured bleb. He was successfully extubated a few days later, however, the chest tubes again revealed a continuous air leak while on suction. Multiple subsequent attempts at clamping the chest tubes and placing them to water seal were unsuccessful with failure of full lung expansion, thus, the decision was made to proceed with endoscopic one-way valve placement with pulmonology.

The patient underwent a bronchoscopy with sequential balloon occlusion of all airways on the right to locate the lobe/segment contributing to the persistent air leak (Fig. 3). The right middle lobe lateral (RML) segment was the only segment which decreased the pleur-evac leak and increased exhaled volume on the ventilator. A size 9 mm spiration valve was inserted into the RML lateral segment, with modest reduction in air leak noted immediately after. The patient continued to improve over the next few days, with the basilar chest tube removed, and the apical tube with a Heimlich valve placed. He still had a persistent leak through the valve but overall remained stable and was discharged to rehab. During his stay at rehab, the apical chest tube was removed, and he was ultimately discharged home. On outpatient follow-up with pulmonology, the patient received two doses of COVID-19 vaccine, completed his anticoagulation treatment for PE, and had the endobronchial valve removed.

### 3. Discussion

PAL is defined as an air leak that persists for more than 5–7 days and can be caused by either an alveolar-pleural fistula (APF) or bronchopleural fistula (BFP) [2]. The most commonly used classification system for PAL is the Cerfolio system, which relates the air leak with the phase of respiration in which it appears [5]. The most severe type of leak, a continuous (C) air leak, is one that is observed throughout the respiratory cycle and is usually seen in patients on mechanical ventilation or with a large BFP. An inspiratory (I) air leak is present only during inspiration and is also mainly seen in patients on positive pressure ventilation or with a large fistula. An expiratory (E) air leak, present only during expiration, and a forced expiration (FE) leak, present only with forced exhalation or coughing, account for >98 % of air leaks after thoracic surgery [2]. Regardless of the type, PAL represents a significant cause of morbidity, health care expenditure, and resource utilization [1]. Among the described cases of PAL in COVID-19 patients (including our case), the median length of hospital stay was approximately 48 days (Table 1).

The incidence of PAL in COVID-19 patients remains uncertain, but has been reported as up to seven times higher in patients with COVID-19 related ARDS requiring invasive mechanical ventilation as compared to non-COVID-19 ARDS [5]. The onset of PAL from the

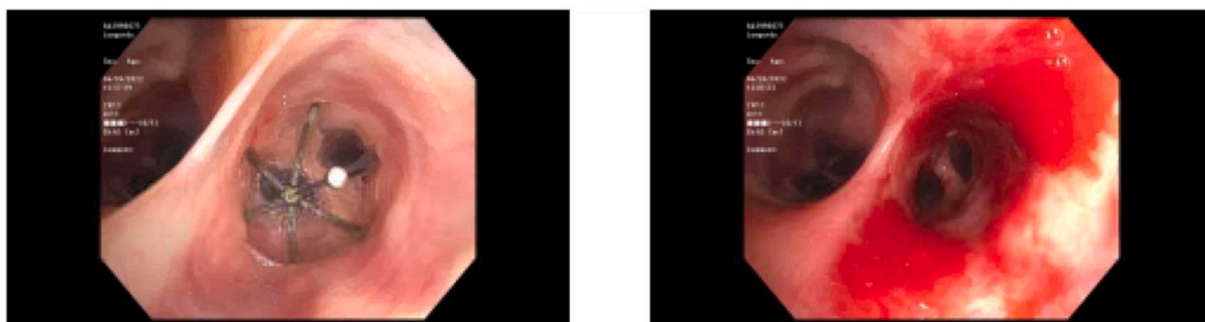


Fig. 3. Bronchoscopy showing A. insertion of a size 9 spiration valve into the RML lateral segment; followed by B. removal of endobronchial valve months later.

**Table 1**

A review of cases with persistent air leak secondary to pneumothorax in patients with COVID-19.

Cases/Reference	Age/ Sex	COVID-19 treatment	COVID-19 vaccination status	PTX location	PTX initial treatment	Other pulmonary complications	Mechanical ventilation required	PAL treatment	Length of hospital stay	Outcome
<b>Durrance et al. 2022 [10]</b>	65/ M	Steroids, IL-6 inhibitor	N/A	Right	Two chest tubes	ARDS, ipsilateral hemothorax	Yes	Autologous endobronchial blood patch with occlusion of B4 segment of RML	N/A	Chest tube removal 16 days post procedure
<b>Ali 2021 [11]</b>	80/ M	Oral favipiravir, Dexamethasone, empiric antibiotics	N/A	Right	Two chest tubes	N/A	No	Autologous blood pleurodesis (2 doses)	At least 28 days	Chest tubes removed 1- and 4-days post procedure
<b>Morita et al. 2022 [12]</b>	77/F	Dexamethasone, Remdesivir, Methylprednisolone, Sulfamethoxazole/trimethoprim, Antifungals	N/A	Right	Chest tube	COVID-19 associated pulmonary aspergillosis	Yes	Autologous blood pleurodesis, followed by 6 mm EWS and 1:1 mixture of lipiodol and NBCA	N/A	Chest tube removed 3 days post procedure
<b>Morita et al. 2022 [12]</b>	52/ M	Dexamethasone, Remdesivir, Methylprednisolone	N/A	Right	Chest tube	N/A	Yes	Autologous blood pleurodesis, followed by 2 attempts at EWS and 1:1 mixture of lipiodol and NBCA	N/A	Chest tube removed 3 days post procedure
<b>Nakano et al. 2021 [13]</b>	62/ M	Methylprednisolone, Favipiravir, Nintedanib (clinical trial)	N/A	Right	Chest tube	Secondary bacterial pneumonia, empyema	Yes	Chemical pleurodesis (3 doses minocycline and talc powder), followed by two EWSs (7 mm in B5a and 5 mm in B5b)	N/A	Chest tubes removed 14 days post procedure
<b>Aiolfi et al. 2020 [6]</b>	56/ M	N/A	N/A	Left	Pleural drain	ARDS	Yes	Left-sided 3-port thoracoscopy with bleb resection, followed by mechanical pleurodesis	N/A	Chest tube removal
<b>Aiolfi et al. 2020 [6]</b>	72/ M	N/A	N/A	Left	Chest tube	ARDS	Yes	Left-sided 3-port thoracoscopy with bleb resection, followed by mechanical pleurodesis	N/A	Chest tubes removal 2 days post procedure
<b>Caviezel et al. 2020 [7]</b>	58/ M	Tocilizumab	N/A	Left, then right 16 days later	Three chest tubes	N/A	No	Left thoracoscopy with hematoma resection, followed by same procedure on right side 6 days later, then left redo-thoracoscopy, wedge resection and permanent pleura catheter placement 18 days later	At least 2 months	Removal of pleura catheter 30 days after discharge
<b>Malkoc et al. 2022 [8]</b>	77/ M	Dexamethasone, Remdesivir, oral baricitinib	Moderna 2 doses prior to presentation	Right	Chest tube	N/A	No	Right-sided VATS and talc pleurodesis	17 days	Chest tube removal 16 days post operatively
<b>Pantazopoulos et al. 2022 [9]</b>	23/ M	Ceftriaxone	N/A	Right	Chest tube	Associated pleural effusion	No	VATS bullectomy and talc pleurodesis	N/A	Resolution and discharge
<b>Puthak et al. 2020 [19]</b>	55/ M	Tocilizumab (2 doses), Remdesivir	N/A	Right	Chest tube	ARDS, secondary bacterial pneumonia	Yes	Four Spiration EBVs (9 mm in RML lateral, RML medial, RLL superior segments, 7 mm in RLL medial basilar segment), followed by two more 4 days later (9 mm in anterolateral and posterior basilar segments)	N/A	Chest tube removed 1 week post procedure

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Table 1 (continued)

Cases/Reference	Age/ Sex	COVID-19 treatment	COVID-19 vaccination status	PTX location	PTX initial treatment	Other pulmonary complications	Mechanical ventilation required	PAL treatment	Length of hospital stay	Outcome
<b>Saha et al. 2021</b> [3]	42/ M	Dexamethasone, Remdesivir, Empiric antibiotics	N/A	Left	Three chest tubes	Bilateral apical bullous emphysema	No	Three 9 mm EBVs in apicoposterior, anterior and lingular bronchi	N/A	Chest tubes removed 36 hours post procedure
<b>Talon et al. 2021</b> [14]	64/ M	N/A	N/A	Right	Chest tube	Recurrent right- sided empyema	No	9 mm EBV (Spiration) in RML	N/A	Chest tube removed 6 weeks post procedure
<b>Donatelli et al.</b> <b>2021</b> [4]	67/ M	Hydroxychloroquine, azithromycin, Darunavir- cobicistat, ceftazidime, Tocilizumab	N/A	Right	Chest tube	ARDS, Associated pleural effusion and secondary bacterial pneumonia	Yes	Two 5 mm EBVs in RML segmental bronchi	N/A	Resolution of PAL and removal of chest tube 3 days and 1 week post procedure, respectively
<b>Donatelli et al.</b> <b>2021</b> [4]	73/ M	Hydroxychloroquine, azithromycin, ceftriaxone, Tocilizumab	N/A	Right	Chest tube	ARDS, Associated pleural effusion and secondary bacterial pneumonia	Yes	Three 5 mm EBVs in segmental bronchi of RLL, followed by one in the apical segment of RLL bronchus 1 week later	N/A	Chest tube removed at least 4 months after admission
<b>Styvoký et al.</b> <b>2022</b> [15]	67/ M	Remdesivir, Dexamethasone	N/A	Right	Multiple chest tubes (>2)	ARDS, empyema	Yes	Two 7 mm Spiration EBVs in medial and lateral RML and a 9 mm in proximal RML	88 days	Chest tubes removal within 1 week post procedure
<b>Nugent et al.</b> <b>2022</b> [16]	71/ M	Hydroxychloroquine	N/A	Right	Chest tube	PE	Yes	Three 4.0 Zephyr EBVs in RUL, RML, RLL	N/A	Chest tube removal 24 hours post procedure
<b>Bar-Shai et al.</b> <b>2022</b> [18]	81/ M	N/A	N/A	Right	Chest tube	N/A	Yes	Four Spiration EBVs in apical, anterior segments of RUL, lateral and medial segmental bronchi of RML	N/A	Chest tube removed 5 days post procedure
<b>Umar et al. 2022</b> [17]	86/ M	Remdesivir, Dexamethasone, Azithromycin, Tocilizumab	J&J vaccine 6 months prior to presentation	Right	Two chest tubes	N/A	No	EBV and blood patch placement to apical segment of RUL, followed by two EBVs in apical and posterior segments of RUL 10 days later	N/A	Chest tube removal at least 3 days post procedure
<b>2022</b>	57/ M	Dexamethasone, Remdesivir, Tocilizumab, Antibiotics, Methylprednisolone	Unvaccinated prior to presentation	Right	Two chest tubes	ARDS, secondary bacterial pneumonia, hemothorax	Yes	Right VATS, hematoma evacuation and wedge resection of RML for ruptured bleb, followed by one 9 mm Spiration EBV to lateral segment of RML	48 days	Chest tubes removed 4- and 16-days post EBV, EBV removed 55 days post- insertion

M: Male, F: Female, ARDS: Acute respiratory distress syndrome, PTX: Pneumothorax, PAL: Persistent air leak, RUL: Right upper lobe, RML: Right middle lobe, RLL: Right lower lobe, VATS: video assisted thoracoscopic surgery, EBV: Endobronchial valve, EWS: Endobronchial Watanabe spigot; NBCA: N-butyl-2-cyanoacrylate.

time of COVID-19 symptoms is highly variable, with a mean presentation of approximately 19.6 days from symptom onset [5]. There are currently no guidelines for the management of PAL in COVID-19 patients. Approximately 30 % of COVID-19 patients who develop a pneumothorax can be managed conservatively, but the remaining patients often require further intervention [5]. Among all described COVID-19 patients with pneumothoraces, the first line treatment was insertion of one or more chest tubes (Table 1). The persistence of an air leak then led to one or more other treatment modalities.

The 2001 American College of Chest Physicians and 2010 British Thoracic Society guidelines recommend initial early surgical evaluation followed by pleurodesis for the management of PAL [2]. The most common surgical approaches include VATS or open thoracotomy with either mechanical or chemical pleurodesis or pleurectomy [2]. Among the published cases of PAL secondary to pneumothorax in COVID-19 patients, two cases were treated with thoracoscopy and mechanical pleurodesis [6], one case was treated with thoracoscopy and resection [7], and two cases were treated with VATS and talc pleurodesis [8,9] (Table 1).

However, surgery is not always a feasible option for all patients, particularly critically ill patients. The 2001 American College of Chest Physicians and 2010 British Thoracic Society guidelines made no specific recommendations for such situations where surgery is not an option. Surgical repair in critically ill patients with COVID-19 can lead to further morbidity and mortality [5]. In such cases, there are multiple less invasive options for the management of PAL, including implantable devices, such as Watanabe spigots and stents, and chemical agents, such as thermal treatments, hemostatic substances, and tissue adhesives [1].

Chemical pleurodesis involves instilling sclerosants into the pleural space to cause an inflammatory reaction to achieve pleurodesis. This can be done using talc, doxycycline, bleomycin, minocycline, and tetracycline [1]. Autologous blood patch pleurodesis involves instilling peripheral venous blood into an existing tube thoracostomy, allowing the blood to cover the pleural defect and create a seal [1]. Among the reported cases of PAL in COVID-19 patients, two cases were treated with only autologous blood pleurodesis [10,11] (Table 1). Two cases were treated with a combination of autologous blood pleurodesis, endobronchial Watanabe spigots (EWS), and chemical pleurodesis with a mixture of lipiodol and NBCA (*N*-butyl-2-cyanoacrylate) [12], and one case was treated with chemical pleurodesis (with minocycline and talc) and EWS [13] (Table 1).

The only bronchoscopic modality with US FDA approval for treatment of PAL are one-way endobronchial valves (EBV). These valves allow air to move proximally into the central airways but block distal ventilation, thus limiting airflow through the fistula to allow for the pleural defect to heal [1]. There are currently nine published cases of PAL in COVID-19 patients treated with EBVs (Table 1). The number of EBVs inserted varied; one case was treated with a single EBV [14], one case was treated with two EBVs [4], four cases were treated with three EBVs (3, 15–17), two with four EBVs [4,18], and one with six EBVs [19].

The outcome for all these published cases of PAL in COVID-19 patients was similar, with a resultant removal of chest tube(s). The time to removal of chest tubes post-procedure was not specified in all cases, however, the data available revealed removal of chest tubes after a median time of 6 days post-EBV insertion, 16 days post-surgical intervention with or without pleurodesis, 3 days post-autologous blood pleurodesis with or without EWS, and 14 days post-chemical pleurodesis followed by EWS.

Our case is the first reported case of PAL secondary to pneumothorax in a COVID-19 patient that was treated with a combination of VATS and EBV placement. Our patient had a complicated hospital course, treated initially with two chest tubes for his pneumothoraces, followed by VATS and resection, and finally placement of an EBV. His chest tubes were successfully removed up to 16 days post-insertion, with good outcomes.

#### 4. Conclusion

The incidence of PAL in patients with COVID-19 remains uncertain. The lack of up-to-date guidelines regarding treatment of these cases has led to variability in management amongst the published cases. Surgical treatment, chemical pleurodesis, autologous blood patch pleurodesis, implantable devices such as Watanabe spigots or endobronchial valves all seem to be viable management strategies. However, larger studies are required to develop more standardized management approaches for these cases.

#### Author contributions

H.A. conceived the study, H.A, C.G, and S.A. wrote the main manuscript and prepared the tables and figures. C.D. edited the manuscript. All authors reviewed the manuscript.

#### Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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