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CASE REPORT

SARS Cov-2 Infection-Related Persistent Air Leaks Managed By Endobronchial Valves

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Abstract

Introduction: There have been recently documented reports of pneumothorax and persistent air leaks as complications associated with SARS CoV-2-related ARDS. Alveolar-pleural fistulas and broncho-pleural fistulas can lead to the development of pneumothorax. In more recent times, bronchoscopy-guided interventions, specifically Endobronchial Valves (EBV), have been established to serve as a treatment modality for these fistulas. In this case series, we present the first two cases of persistent pneumothorax and persistent air leak related to COVID-19 that were managed successfully with EBV placement.

Case description: Case 1- A 44-year-old female was admitted for acute hypoxic respiratory failure secondary to COVID-19 pneumonia requiring invasive mechanical ventilation. Immediate post-intubation imaging found a large right-sided pneumothorax that required emergent insertion of a chest tube. Repeat chest imaging showed worsening pneumothorax requiring additional chest tubes; however, air leaks persisted. Subsequent chest imaging showed the possibility of a fistula near the right upper lobe bronchus. Bronchoscopy-guided placement of Endobronchial Valves was performed, and follow-up imaging showed resolution of pneumothorax and improvement in clinical symptoms. Case 2- A 48-year-old male with a recent admission for COVID-19 pneumonia was diagnosed with large left-sided hydropneumothorax. A chest tube was placed and put to suction; however, it failed multiple water seal trials. Bronchoscopy with endobronchial valve placement was performed over segments of the left upper lobe. Repeat chest imaging showed the complete resolution of pneumothorax.

Conclusions: The current literature review describes only a few cases of COVID-19 related to BPF or APF. In both described cases, the diagnosis of PALs was made within 4-6 weeks of COVID-19 infection. The first case developed pneumothorax following mechanical ventilation. The etiology of the development of BPF, in this case, may be secondary to barotrauma. The second case was incidentally diagnosed with hydropneumothorax four weeks after the initial COVID infection that had not needed mechanical ventilation. This prompts the likelihood of multiple etiologies that can lead to the development of fistulas in patients with recent COVID-19 disease. Bronchoscopy is the gold standard in the management of PALs. Fistulas secondary to inflammatory processes, like a necrotizing infection, are better managed with an endobronchial intervention as lung parenchyma is too friable for surgical intervention. Recent literature has demonstrated that endobronchial valves are an effective, minimally invasive intervention for patients with PALs. We report two of the first few cases of COVID-19 complicated by PALs that were successfully managed with EBV placement. Our data search reveals six reported cases of COVID-19 that eventually developed PAL and managed with the placement of EBV and resulted in the successful resolution of the air leaks.

Introduction

Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) has dominated as a global epidemic for the past two years. There have been recently documented reports of pneumothorax and Persistent Air Leaks (PALs) as complications associated with SARS CoV-2-related infections. Broncho-pleural Fistula (BPF) is a pathological communication between the bronchus and the pleural space, and an Alveolar-pleural Fistula (APF) is a similar communication between the lung parenchyma and the

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pleural space [1]. These pathological paths can lead to air escaping from the lung into the pleural cavity, causing a pneumothorax. If the connection persists, there is the complication of worsening pneumothorax. The fistulas are associated with delayed healing processes and limited expansion of the lungs. A persistent air leak is defined as an air leak that lasts for more than five to seven days, as evidenced by air bubbling in the water seal chamber of the chest drainage system [2]. Usually, conservative treatments such as chest tube drainage and observation are the first line. Surgical management is an option in those patients with air leaks refractory to conservative management with chest tubes and observation. However, many patients either are unsuitable surgical management candidates or defer to less invasive treatments [3-5]. The other option in patients with PAL who are either not suitable for surgery or decline surgery is chemical pleurodesis with agents such as talc and tetracycline derivatives [2,4,6]. In more recent times, bronchoscopy-guided interventions, specifically Endobronchial Valves (EBV), have been established to serve as a treatment modality for APF and BPF [3,7]. EBVs have been introduced as an effective and less invasive treatment option for PAL in patients with smaller fistulas and those who are deemed poor candidates for surgery [2]. In this case series, we present the first two cases of persistent pneumothorax and persistent air leak related to COVID-19 that were managed successfully with EBV placement.

Case Description

Case 1

The patient is a 44-year-old female with a past medical history significant for hypothyroidism had presented after experiencing five days of fever, cough, myalgia, and diarrhea. She was admitted to the medical unit for acute hypoxic respiratory failure secondary to COVID-19 pneumonia. The Computed Tomography (CT) of the chest was significant for multifocal peripheral areas of consolidation with surrounding ground-glass attenuation, consistent with multifocal pneumonia. She was treated with Dexamethasone and Remdesivir. However, her hypoxia continued to worsen despite non-invasive ventilation, and she eventually required intubation. Her post-intubation imaging was suggestive of a large right-sided pneumothorax that required emergent insertion of a chest tube. The patient was also started on empiric parenteral antibiotics and was frequently placed in a prone position as per ARDS protocol. She was hypoxic while on maximum ventilator settings, and repeat chest imaging showed worsening pneumothorax. Thoracic surgery service was consulted, and a second right-sided chest tube was placed. Both chest tubes were maintained to suction but noted to have air leaks. Bronchoscopy was performed but was notable only for bronchial erythema. Pneumothorax was noted to be enlarging in size, and this led to the placement of a third right-sided chest tube. On day 22 of hospitalization, she underwent a tracheostomy due to prolonged ventilator dependence. Persistent air leaks were noticed, causing a deficit of up to 150 ml in inspiratory and expiratory volumes. Repeat CT of the chest showed the possibility of a fistula near the Right Upper Lobe (RUL) bronchus. The patient underwent a repeat bronchoscopy on day 35; a Fogarty balloon was used for occlusion of the RUL bronchus, and the air leak improved. Endobronchial valves were placed in all three RUL bronchus segments. All the valves were noted to be well seated and created a good seal. The discrepancy that was earlier noticed in inspiratory and expiratory volumes had improved after the procedure. Repeat imaging post-procedure showed resolution of pneumothorax. Chest tubes were removed 20 days after the procedure. The patient was transferred out of the intensive care unit 8 weeks after her initial presentation and successfully weaned off the trach collar. Her mental status and neurological function were preserved. Her speech returned to her baseline after decannulation. She continued to receive routine physical and speech therapy. Her rest of the hospital course remained uncomplicated, and she was discharged to a rehabilitation unit. She followed up in the pulmonary clinic two months after her discharge. The CT of the chest showed fibrosis and cystic changes over the parenchyma distal to the EBV. A shared decision was made to keep the EBV and reassess the patient with regular follow-ups.

Case 2

A 48-year-old male with a past medical history significant for Human Immunodeficiency Virus (HIV) infection, Progressive Multifocal Leukoencephalopathy (PML), seizure disorder, and recent admission for COVID-19 pneumonia was instructed to go to the Emergency Room by his primary care physician when he was noted to have left-sided pneumothorax in the outpatient chest imaging. The patient had been recently treated for COVID-19 pneumonia a month prior to his presentation, which was complicated by left parapneumonic effusion requiring left-sided thoracentesis, post-procedure chest imaging showed resolution of effusion, and there was no pneumothorax. He was discharged on antibiotics and was followed up by a primary outpatient provider two weeks after discharge, where he complained of a persistent dry cough. In the ER, he was found to be tachycardic to 120 beats per minute but otherwise hemodynamically stable with a normal oxygen saturation while breathing ambient air. Imaging reconfirmed left-sided, large, loculated hydropneumothorax with a mediastinal shift. A chest tube was placed with drainage of purulent fluid. The patient was admitted to the medical unit and started on intravenous antibiotics for broad-spectrum coverage. Pleural fluid studies were consistent with exudative

effusion; however, pleural fluid culture was negative for any growth. The etiology of hydropneumothorax was thought to be COVID-19 related. The chest tube was put to suction; however, it failed multiple water seal trials over the following week. A chest pigtail catheter was placed. The patient underwent diagnostic bronchoscopy, which showed normal bronchial mucosa on visualization, BAL fluid culture grew VRE, and Linezolid was added to the antimicrobial regimen. Repeat chest imagining continued to show loculated left pneumothorax. A diagnosis of a bronchopleural fistula or alveolar pleural fistula was suspected in the setting of persistent air leaks. Bronchoscopy was performed, and Fogarty balloon occlusion of the subsegments of the lingula and the posterior segment of the Left Upper Lobe (LUL) demonstrated resolution of the air leak. The endobronchial valves were placed over these segments and subsegments. There were no post-procedure complications, and the patient was observed for the next few days. Chest imaging was repeated, which showed the complete resolution of pneumothorax. The left-sided chest pigtail catheter was removed seven days after EBV placement. The patient was discharged to a rehabilitation center and followed up in the outpatient pulmonary clinic, where he was found to be hemodynamically stable and asymptomatic; repeat imaging showed normal pleura without effusions and pneumothorax. Endobronchial valves were subsequently removed 12 weeks after their initial placement.

Conclusions

The incidence of pneumothorax in SARS-CoV-2 is estimated at around 10% and is most associated with patients diagnosed with severe ARDS [8]. The possible mechanism of pneumothorax is related to the structural alterations in the lung parenchyma that lead to alveolar and bronchial damage. Additionally, increased intrathoracic pressure resulting from mechanical ventilation causes barotrauma [9]. Both bronchopleural and alveolar pleural fistulas can cause a pneumothorax as air escapes into the pleural cavity. Lung resection and lung volume reduction surgeries are the most common causes of the development of these abnormal fistulous tracts [10]. Other etiologies include malignancies, radiation, pulmonary drainage procedures, and necrotizing infections. The current literature review describes only a few cases of COVID-19 related to BPF or APF.

Treatment of underlying etiology and chest tube insertion remains the mainstay for the management of pneumothorax. The passage of air bubbles into the chest drainage system after insertion of a chest tube indicates an air leak. Air leaks are initially managed with watchful waiting as the majority will heal spontaneously. Persistent air leak is defined as the persistence of air leakage in the chest drainage system that lasts more than five to seven days. The incidence of PALs can be as high as 40% [8]. The uninterrupted flow of air through the fistula into the pleural space delays healing and also inhibits lung expansion [2]. It also increases the risk of superadded infection in the unexpanded lung and prolongs the length of hospital stay [11].

In both our cases, the diagnosis of PALs was made within 4-6 weeks of COVID infection. Both the patients had illnesses complicated by severe multifocal pneumonia and pleural effusion. Our first case developed pneumothorax following mechanical ventilation. The etiology of the development of BPF, in this case, may be secondary to barotrauma to an already inflamed lung parenchyma. Interestingly, the second case was incidentally diagnosed with hydropneumothorax four weeks after the initial COVID infection that did not need mechanical ventilation. This prompts the likelihood of multiple etiologies that can lead to the development of fistulas in patients with recent COVID-19 infection. Also, both cases were coincidentally associated with superadded bacterial or fungal infections that may have enhanced the inflammatory process. Another case series observed a similar hospital course in their patients, where it was found that both reported cases had superadded bacterial pneumonia [12].

Contrast-enhanced CT helps diagnose large BPF, as was seen in our first case. However, small BPF (< 8 mm) and APFs are unlikely to be visualized on imaging. Bronchoscopy is the gold standard in the management of PALs. Localization of PALs can be challenging when the fistulas are often too small to be observed with bronchoscopy. Hence, the Fogarty balloon dilation method is popularly used to isolate PALs. The balloon is sequentially advanced over the bronchus and dilated to cause occlusion. Cessation of an air leak after occlusion indicates successful localization of air leak.

Large BPFs that are described as more than 8 mm in size and fistulas secondary to lung surgery are usually managed with surgical closure. Endobronchial interventions are preferred in high-risk surgical candidates to avoid complications and in the management of smaller fistulas [13]. Also, fistulas secondary to inflammatory processes, like a necrotizing infection, are better managed with an endobronchial intervention as lung parenchyma is too friable for surgical intervention. Recent literature has demonstrated that endobronchial valves are an effective, minimally invasive intervention for patients with PALs. They work as one-way valves that are placed over the airways proximal to air leaks [13,14]. This prevents entry of air distal to the valve causing segmental atelectasis and resolution of pneumothorax. Reduced airflow across the fistula allows healing of the abnormal fistulous tract [16]. EBV is the best procedure to manage PALs when surgical options are not feasible or anatomically impossible. The Food and Drug Administration has approved EBV to

treat PALs. In a large multicenter study, EBV placement was shown as an effective minimally invasive procedure that led to the complete resolution of PALs in more than half the study population [14]. We report two of the first few cases of COVID-19 complicated by PALs that were successfully managed with Endobronchial Valve placement. Our data search reveals six reported cases of COVID-19 that eventually developed PAL and managed with the placement of EBV and resulted in the successful resolution of the air leak [8,12,15-17]. The ages of the cases in the patient group ranged from 42 to 73 years old. All reported cases have been males, making our case the only female patient who has received EBV for PALs after a COVID infection. Two of the six reported cases were not mechanically ventilated, which coincides with our second case that had developed pneumothorax and PAL in the absence of prior mechanical ventilation. Hence, multifactorial etiology needs to be considered when assessing the etiology of PALs in patients with recent COVID infections.

All the reported cases had successful outcomes with the resolution of PALs after placement of EBV, followed by removal of the chest tubes 1-6 weeks after the procedure. Our first case had her tube removed three weeks after the procedure, whereas the second case had tube removal seven days after EBV placement. EBVs were eventually removed in all patients 6-13 weeks after the procedure. Our first case has not had the EBV removed because of non-functional and fibrotic tissue distal to the valves, and this occurred as an outcome of shared decision-making between the physician and the patient. Our second case had outpatient bronchoscopy with EBV removal 12 weeks after the initial placement. So far, the reported experiences in COVID-19 patients with PALs refractory to conservative strategy have demonstrated that the EBV procedure is safe, less invasive, and effective. However, some drawbacks and risks of the procedure need consideration. In patients with bacterial super-infection, valve placement may facilitate post-obstructive pneumonia. Also, the guidelines have been unclear about the timing of removal of EBV after PAL resolution. Hence, there is a theoretical risk of pneumothorax recurrence after EBV removal.

Author's Contribution

Author MT was involved in writing case descriptions and conclusions. Author NT wrote the introduction. Authors ASN and KP reviewed and proof-read the manuscript, and helped in editing the conclusions.

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