CASE REPORT

Pneumomediastinum in COVID-19: A Complication of Non-invasive Ventilation or Disease?

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Abstract

The coronavirus disease (COVID-19) is a novel infection which often necessitates the use of non-invasive ventilation (NIV) with high positive end expiratory pressures (PEEP) to maintain optimal oxygen saturation. Herein, we report two cases of severe COVID-19 who developed pneumomediastinum while receiving NIV during their course of hospital stay. The role of high PEEP and underlying COVID-19 infection in development of pneumomediastinum is discussed.

Keywords: Complication, Coronavirus, Pneumonia.

Introduction

The coronavirus disease (COVID-19), a novel infection which was first detected in Wuhan, China in December 2019 and later on transformed into a pandemic, which unfortunately continues till date. This infection has shown diverse clinical presentations and complications, some of which had not been observed previously with other diseases. The disease had a very high infectivity and often presented with severe pneumonia, high spiking fever, chills and hypoxia warranting oxygen therapy.[1] The management of hypoxia during the COVID-19 pandemic involved oxygen therapy by various modalities depending upon the required flow rates. Non-invasive ventilation (NIV) was mandated in several patients with extensive lung damage who were unable to maintain oxygen saturation despite high oxygen flow rates and had increased work of breathing. Unlike, invasive ventilation, NIV use in COVID-19 was associated with better outcomes which fostered a trend towards prolonged NIV support and an avoidance of invasive ventilation.[2] Because of extensive pulmonary involvement in COVID-19 infection, several patients who needed NIV also required high positive end expiratory pressure (PEEP).[3] Prolonged use of NIV at high PEEP was a relatively uncommon situation prior to the pandemic. This scenario has thrown up some complications which were previously very rarely reported. We report two patients with COVID-19 who developed pneumomediastinum while receiving NIV with high PEEP.

Case Description

Case 1

A 32-year-old male patient, detected to be positive for COVID-19 by RT-PCR a day prior to presentation, was hospitalized with a one-week history of fever, dry cough and breathlessness. He was a non-smoker with no known addictions or significant medical illness in the past. His body mass index (BMI) was 24 kg/m^2. On examination, his respiratory rate was 26 breaths/minute, heart rate was 96 beats/minute and blood pressure was 138/76 mm Hg. His oxygen saturation was 96% on 15 L/minute of oxygen via non-rebreathing mask. Auscultation of the chest revealed bilateral coarse crackles. Rest of the systemic examination was normal. His baseline blood investigations including hemogram, kidney and liver function tests were unremarkable. However, the C-reactive protein (7 mg/L) and d-dimer levels (0.6 µg/mL) were marginally high. The chest radiograph showed bilateral ground glass opacities in both the lungs. He was started on treatment with broad spec-trum antibiotics, steroids (dexamethasone 4 mg IV once a day), enoxaparin and pantoprazole. Awake proning was also initiated. On day 4 of the admission, his

condition deteriorated and he was found to be having a respiratory rate of 40 breaths/minute with an oxygen saturation of 86% while receiving oxygen at a rate of 15 L/minute using a non-rebreathing mask. In view of this, he was put on NIV using continuous positive airway pressure (CPAP) support at an initial PEEP setting of 10 cm H_2O and oxygen flow of 10 L/minute. Unfortunately, after initial stabilization, he deteriorated over the next two days and the PEEP had to be raised to 12 cm H_2O and the dose of intravenous steroids was increased. His CRP and d-dimer levels increased to 22 mg/L and 2.4 µg/mL respectively. A high-resolution computed tomography (HRCT) of the chest revealed bilateral ground glass opacities in all the lung zones bilaterally with a CT severity score of 21/25. A pneumomediastinum with subcutaneous emphysema with minimal left pneumothorax was detected (**Fig. 1)** for which a cardiothoracic surgery opinion was sought but conservative management was advised. In view of persistent hypoxia (oxygen saturation in the region of 80-84%), he was intubated and put on mechanical ventilation. He subsequently developed pulmonary edema and had a cardiac arrest on day 8 of admission and succumbed.

Case 2

A 54-year-old, previously healthy, male with a BMI of 28 kg/m^2 admitted with a five-day history of high-grade fever, was detected to be positive for COVID-19 infection using RT-PCR. On examination, he appeared comfortable with a respiratory rate of 20 breaths/minute with an oxygen saturation of 88% while breathing room air. He was put on oxygen therapy using a simple face mask at a rate of 5L/minute following which the oxygen saturation increased to 94%. His heart rate was 99 beats/minute and blood pressure 128/88 mm Hg. Auscultation of chest revealed scattered crepitations in right upper and left lower lobes. The CRP levels and d-dimer levels were 12 mg/L and 1.9 µg/mL respectively. He was also started on parenteral steroids (dexamethasone 6 mg IV once daily), antibiotics and low molecular weight heparin. However, he continued to worsen. On day 3 of admission, he was found to be not maintaining saturation while receiving oxygen by non-rebreather mask at 15 L/minute. The CRP and d-dimer levels continued to increase to 41 mg/L and 5.8 µg/mL respectively, necessitating an increase in the dose of systemic steroids (dexamethasone 12 mg IV once daily). He was put on NIV with a CPAP support and an initial PEEP of 10 cm H_2O and 10 L/minute oxygen. The PEEP was increased to 12 cm H_2O on day 4 of admission in view of persistent low oxygen saturation. HRCT chest revealed a CT severity score of 25/25 and evidence of pneumomediastinum (**Fig. 2**). Conservative management of pneumomediastinum was advised in this setting by the cardiothoracic surgical team. On day 5, the patient's sensorium deteriorated and a reduced spontaneous movement of the left half of the body with an extensor left plantar reflex was noted. He was intubated and non-contrast CT of head revealed a large right middle cerebral artery territory infarct. Unfortunately, he succumbed to his illness on day 6 of admission.

DISCUSSION

We report two cases of COVID-19 who received NIV

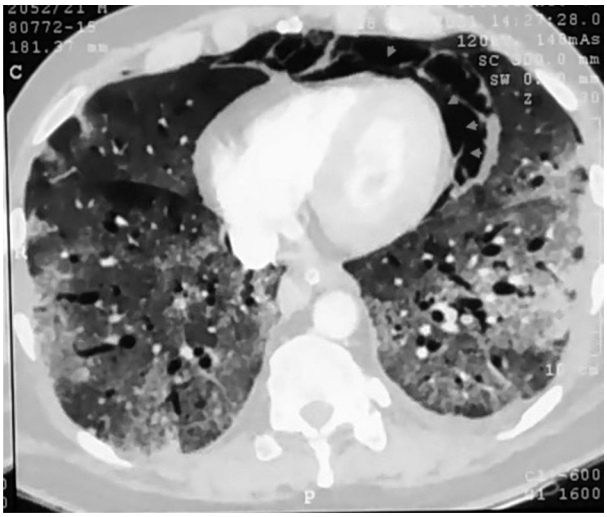

Fig.1 High resolution computed tomography of chest of case 1 showing evidence of pneumomediastinum (arrows) along with extensive ground glass opacification in lungs.

Fig. 2 High resolution computed tomography of chest of case 2 showing evidence of pneumomediastinum (arrows) along subcutaneous emphysema (arrow). Extensive ground glass opacification in lungs is visible.

support and were later detected to have a pneumomediastinum. Pneumomediastinum is a rare complication of respiratory disorders.[4] Trauma and invasive procedures of the thorax are the more common causes of pneumomediastinum. While theoretically, NIV can lead to barotrauma which in turn can cause pneumomediastinum, such reports are rare.[5] However, it must be noted that in most of these cases, NIV was used as a bridge to invasive ventilation, and hence NIV was given only briefly.[4] Further in conditions such as heart failure, NIV is initiated at lower PEEP values, usually in the range of 5-8 cm of H_2O.[6] However, in most COVID -19 cases, due to poor outcomes of invasive ventilation being observed, prolonged NIV was adopted as the preferred ventilatory strategy.[2] Further, these patients appeared to require higher PEEP with some guidelines recommending initial PEEP of 10 cm of H_2O.[2]

Pneumomediastinum has been reported in patients with COVID-19 who received NIV but there are also reports of pneumomediastinum in COVID-19 without any mechanical ventilation, suggesting that it may be a manifestation of COVID-19 per se.[7,8] This can be attributed to the extensive alveolar damage and subsequent alveolar rupture leading to leakage of air into the mediastinum. More recently, two case series of pneumomediastinum in COVID-19 have been published. In a retrospective observational study of 331 non-ICU hospitalized COVID-19 patients, Muley, *et al.* reported 48 cases of pneumomediastinum. It was more common when the CT severity score exceeded 15. Pneumomediastinum was four times more common with NIV as compared to the use of high flow nasal cannula. The patients with pneumomediastinum had greater likelihood of getting intubated and were likely to have higher mortality.[9] Kahn, *et al.* reported pneumomediastinum in 8% of COVID-19 patients receiving NIV while Rajdeep, *et al.* found it in 4.7%.[10,11]

Although pneumomediastinum, by itself, is often considered to be a relatively benign condition; very rarely a large pneumomediastinum may cause cardiac tamponade.[6] Our patients did not demonstrate any features to suggest this complication. However, in COVID-19, pneumomediastinum may represent extensive lung damage which directly causes it or necessitates high PEEP NIV, which predisposes towards it. The Hamman-Macklin mechanism states that either rapid barotrauma due to rise in intrathoracic pressure or a reduction in vascular pressure can cause rupture of the peripheral alveoli leading to pneumomediastinum. In patients with a high respiratory drive, the pressure generated by mechanical ventilation combined with the pressure generated by the spontaneous respiratory efforts can cause greater barotrauma to the alveoli resulting in "patient self-induced lung injury (P-SILI)". Watanabe, *et al.* reported two cases of pneumomediastinum in patients with COVID-19 who had acute respiratory distress syndrome (ARDS). They found that inducing paralysis by using neuromuscular blockade improved the pneumomediastinum indicating the role of SILI in these cases.[12] Elabaddi, *et al.* have reported 21 cases of pneumomediastinum in a study of 549 COVID-19 cases. They proposed that patients who developed pneumomediastinum had a delayed use of invasive ventilation and their respiratory rate oxygenation (ROX) index was higher at admission, later falling down in the days prior to the pneumothorax, it is likely that P-SILI was an important contributor to the development of pneumomediastinum.[13] The ROX index is the ratio of oxygen saturation to respiratory rate. It has been assessed as a predictor of the need for mechanical ventilation in COVID-19.

Both our cases presented with severe COVID-19. In both cases, initial management was with supplemental oxygen, and within a few days, NIV had to be initiated. The disease worsened in both cases whereby higher PEEP had to be used. Case 1 had received NIV for 3 days prior to the CT scan in which pneumomediastinum was documented. The role of P-SILI in this case may have been important. In case 2, the worsening of disease was much quicker and the CT severity was very high. The pneumomediastinum was noted in the CT on the 2nd day after starting NIV. In this case, extensive lung damage appears to be a bigger contributor to pneumomediastinum.

Pneumomediastinum seems to be a marker of poor prognosis in COVID-19. It is often not diagnosed on chest radiographs but is readily noticed on CT scans. Hence, CT imaging should be sought if pneumomediastinum is suspected. Considering the present scenario, it may be worthwhile for clinicians to suspect pneumomediastinum early in predisposed patients.

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REFERENCES

1. Hu B, Guo H, Zhou P, Shi ZL. Characteristics of SARS-CoV-2 and COVID-19. *Nat Rev Microbiol*. 2021;19(3): 141-154. doi: 10.1038/s41579-020-00459-7.
2. National Health Service. Guidance for the role and use of non-invasive respiratory support in adult patients with COVID-19 (confirmed or suspected), 26 March 2020, Version 2. Accessed on April 16, 2023. *https://amhp.org.uk /app/uploads/2020/03/Guidance-Respiratory-Support.pdf*
3. Mittermaier M, Pickerodt P, Kurth F, *et al*. Evaluation of PEEP and prone positioning in early COVID-19 ARDS.

EClinicalMedicine. 2020;28:100579. doi: 10.1016/j.eclinm. 2020.100579.
4. Chu CM, Leung YY, Hui JY, *et al*. Spontaneous pneumomediastinum in patients with severe acute respiratory syndrome. *Eur Respir J*. 2004;23(6):802-804. doi: 10.1183/09031936.04.00096404.
5. Ruggeri P, Girbino G. Fatal pneumomediastinum associated with use of noninvasive mechanical ventilation. *Respirol Case Rep*. 2014;2(4):126-128. doi: 10.1002/rcr2.73.
6. Maraffi T, Brambilla AM, Cosentini R. Non-invasive ventilation in acute cardiogenic pulmonary edema: how to do it. *Intern Emerg Med.* 2018;13(1):107-111.doi:10.1007/s11739- 017-1751-4.
7. Thein OS, Niazi M, Ali A, Sahal A. Pneumomediastinum in patients with SARS-CoV-2 treated with non-invasive ventilation. *BMJ Case Rep*. 2021;14(3):e241809. doi: 10.1136/bcr-2021-241809.
8. Zhou C, Gao C, Xie Y, Xu M COVID-19 with spontaneous pneumomediastinum. *Lancet Infect Dis*. 2020;20(4):510. doi: 10.1016/S1473-3099(20)30156-0.
9. Muley M, Finamore P, Pedone C, *et al*. Incidence and Outcome of Pneumomediastinum in Non-ICU Hospitalized COVID-19 Patients. *Crit Care Med*. 2023;51(1):47-56. doi: 10.1097/CCM. 0000000 000005680.
10. Kahn MR, Watson RL, Thetford JT, *et al*.: High incidence of barotrauma in patients with severe coronavirus disease 2019. *J Intensive Care Med*. 2021;36(9):646-654. doi: 10.1177/0885066621989959.
11. Rajdev K, Spanel AJ, McMillan S, *et al*. Pulmonary barotrauma in covid-19 patients with ARDS on invasive and non-invasive positive pressure ventilation. *J Intensive Care Med*.2021;36(6):1013-1017.doi:10.1177/08850666211019719.
12. Watanabe R, Nakayama R, Bunya N, *et al*. Pneumomediastinum as patient self-inflicted lung injury in patients with acute respiratory distress syndrome due to COVID-19: a case series. *Acute Med Surg*. 2022;30(9):e796. doi: 10.1002/ams2.796.
13. Elabbadi A, Urbina T, Berti E, *et al*. Spontaneous pneumomediastinum: a surrogate of P-SILI in critically ill COVID-19 patients. *Crit Care.*2022;26(1):350.doi:10.1186/s13054-022-04228-1.