Case Report

Pneumomediastinum as patient self-inflicted lung injury in patients with acute respiratory distress syndrome due to COVID-19: a case series

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Background: In patients with coronavirus disease (COVID-19) due to severe acute respiratory syndrome coronavirus 2 infection, pneumomediastinum has been increasingly reported in cases of noninvasive oxygen therapy, including high-flow nasal cannula, and invasive mechanical ventilation. However, its pathogenesis is still not understood.

Case Presentation: We report two cases of pneumomediastinum in acute respiratory distress syndrome (ARDS) caused by COVID-19. In both cases, control of spontaneous breathing with neuromuscular blocking agents resulted in resolution of pneumoperitoneum.

Conclusion: The improvement of pneumomediastinum with control of spontaneous breathing suggested patient self-inflicted lung injury as a possible mechanism in this case series. In ARDS cases with pneumomediastinum, in addition to controlling plateau pressure with conventional lung protective ventilation, spontaneous breathing should be controlled if the patient's inspiratory effort is suspected to be strong.

Key words: Acute respiratory distress syndrome, case report, COVID-19, patient self-inflicted lung injury, pneumomediastinum

INTRODUCTION

CORONAVIRUS DISEASE (COVID-19) due to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection mainly causes lung injury in patients and requires mechanical ventilation if it leads to acute respiratory distress syndrome (ARDS). In patients with COVID-19, pneumomediastinum has been increasingly reported in cases of noninvasive oxygen therapy, including high-flow nasal cannula,[1,2] and invasive mechanical ventilation.[3,4] However, its pathogenesis is not well understood yet.

Ventilation of patients with ARDS who either had spontaneous or traumatic pneumomediastinum requires more restrictive airway pressures than usual.[5] However, when the airway pressure is decreased in the mechanical ventilator setting, inspiratory effort could become stronger in patients with spontaneous breathing. Lung injury due to strong inspiratory effort is called "patient self-inflicted lung injury" (P-SILI).[6] It has been reported in patients with COVID-19.[7]

In this study, we report two patients with ARDS due to COVID-19 whose pneumomediastinum improved due to the control of their spontaneous breathing.

CASE PRESENTATION

APPROPRIATE WRITTEN INFORMED consent was obtained from the patients for the publication of their data, and the accompanying images of this case series were anonymized.

Case 1

A 67-year-old man with a medical history of diabetes mellitus and myocardial infarction presented with cough and had a positive polymerase chain reaction result for SARS-CoV-2.

The patient received high-flow nasal cannula therapy (FiO$_2$, 100%; flow, 50 L/min) for 8 days at a local hospital, but oxygenation did not improve (SpO$_2$ 89%), and spontaneous pneumomediastinum was found on chest X-ray during high-flow oxygen therapy (Fig. 1A). He was then intubated and transferred to the intensive care unit (ICU) in our hospital. Computed tomography (CT) after intubation showed diffuse bilateral ground-glass opacities with mixed consolidation and pneumomediastinum (Fig. 1B) with air tracking along the sheath of pulmonary vasculature, which indicated the Macklin effect (Fig. 1C).

The patient underwent continuous neuromuscular blockade using rocuronium and mechanical ventilation in pressure-controlled assist/control (AC/PC) mode (FiO$_2$, 0.7; positive end-expiratory pressure [PEEP], 12 cmH$_2$O; inspiratory pressure above PEEP [PC], 16 cmH$_2$O; ventilator respiratory rate, 16 breaths/min; inspiratory time 1.0 s) with respiratory system compliance of 24.6 mL/cm H$_2$O, peak inspiratory pressure (PIP) of 28 cmH$_2$O, plateau pressure of 25 cmH$_2$O, and PaO$_2$/FiO$_2$ ratio of 187 mmHg. We monitored the esophageal pressure and transpulmonary pressure with a nasogastric catheter (Nutrivent, Sidam, Italy) and Hamilton C6 ventilator (Hamilton Medical AG, Rhäzüns, Switzerland). During the treatment, his PEEP and PIP were not strictly limited and were applied as needed for oxygenation and ventilation (Fig. 2A). Chest CT on ICU day 4 showed reduction of the pneumomediastinum (Fig. 1D). Due to scarcity of medical resources, the patient was transferred to the previous hospital on the day 11 of ICU admission.

Case 2

A 65-year-old man who was overweight (body mass index 29.7 kg/m^2) and had hypertension was admitted to another hospital for COVID-19. The patient was intubated, with mechanical ventilation initiated using synchronized intermittent mandatory ventilation (SIMV) mode with PEEP of 15 cmH$_2$O, PC 6 cmH$_2$O, pressure support 6 cmH$_2$O, and FiO$_2$ of 50%. After 7 days of ventilator use, subcutaneous
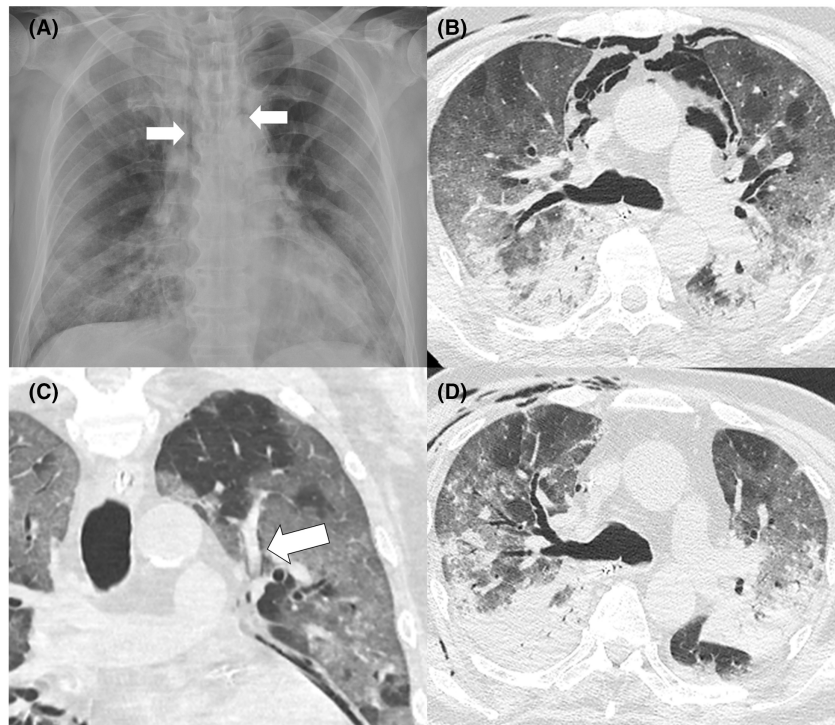

Fig. 1. Time series of radiographic results of a 67-year-old man with acute respiratory distress syndrome caused by COVID-19 with pneumomediastinum (case 1). (A) Chest X-ray 2 days before admission to the intensive care unit (ICU) showing pneumomediastinum (white arrows). (B) Computed tomography (CT) on the day of ICU admission after intubation showing diffuse bilateral ground-glass opacities with mixed consolidation and pneumomediastinum. (C) CT on the day of ICU admission after intubation showing pneumomediastinum with air tracking along the sheath of pulmonary vasculature, indicating the Macklin effect (white arrow). (D) CT on ICU day 4 showing improvement in pneumomediastinum by controlling spontaneous breathing.
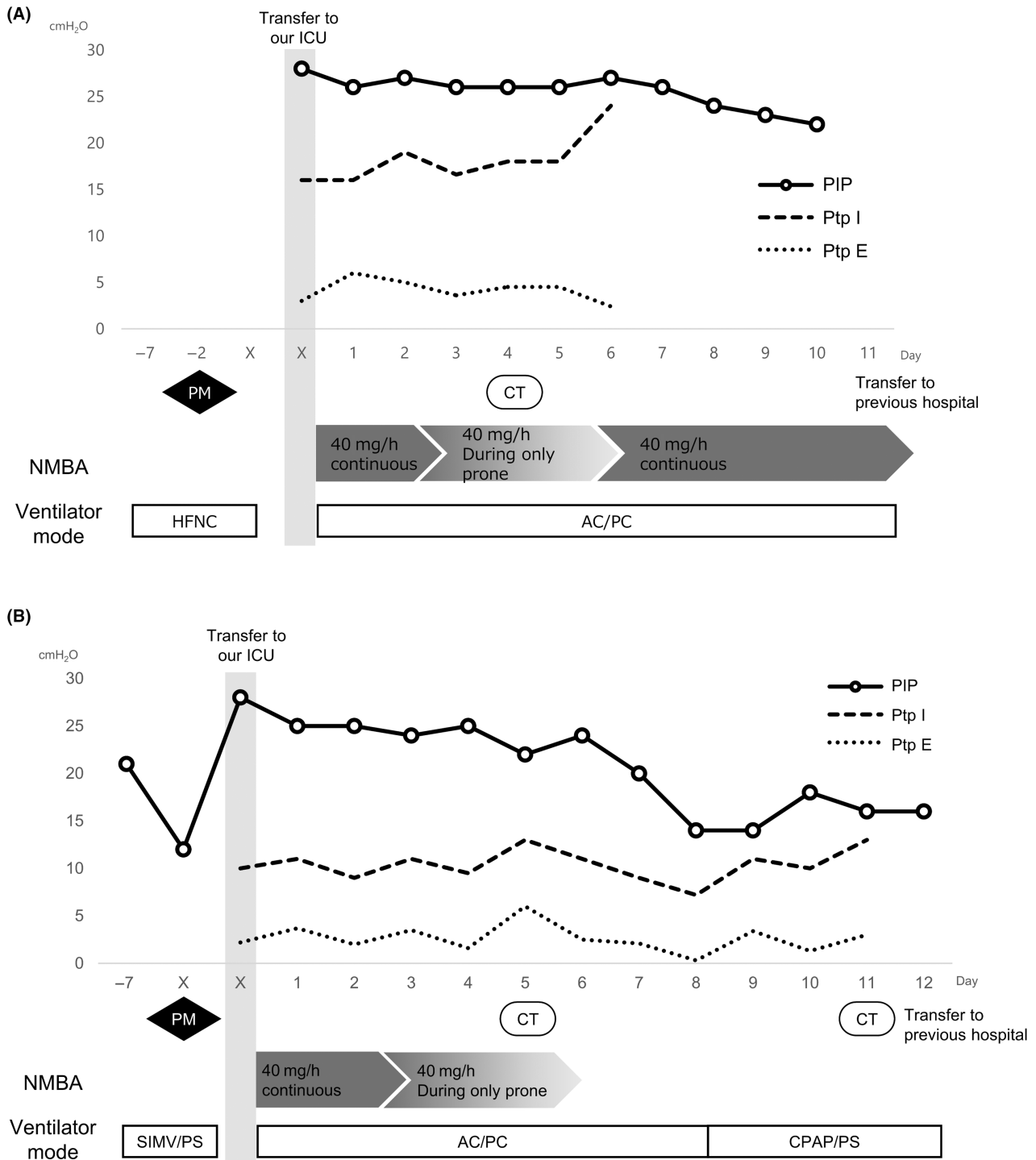
Fig. 2. (A) Clinical course and ventilation settings of a 67-year-old man with acute respiratory distress syndrome caused by COVID-19 with pneumomediastinum (case 1). (B) Clinical course and ventilation settings of a 65-year-old man with acute respiratory distress syndrome caused by COVID-19 with pneumomediastinum (case 2). AC/PC, assist control/pressure control ventilation; CPAP/PS, continuous positive airway pressure/pressure support; CT, computed tomography; HFNC, high-flow nasal cannula; ICU, intensive care unit; NMBA, neuromuscular blocking agents; PIP, peak inspiratory pressure; PM, pneumomediastinum; Ptp E, transpulmonary pressure on expiration; Ptp I, transpulmonary pressure on inhalation; SIMV/PS, synchronized intermittent mandatory ventilation/pressure support.
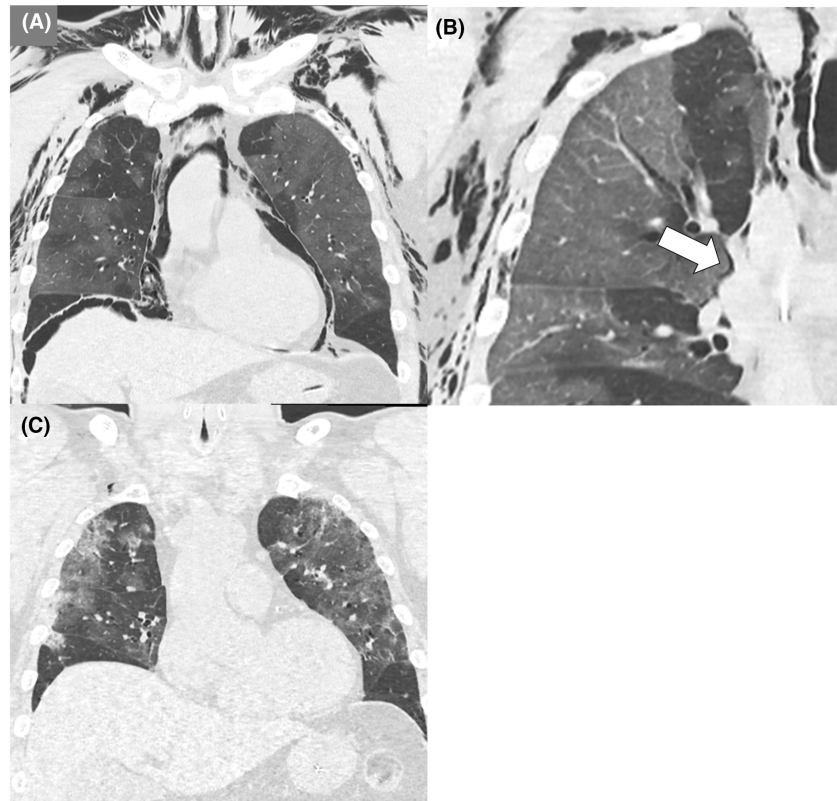
Fig. 3. Time series of radiographic results of a 65-year-old man with acute respiratory distress syndrome caused by COVID-19 with pneumomediastinum (case 2). (A) Computed tomography (CT) on the day of intensive care unit (ICU) admission showing pneumomediastinum, subcutaneous emphysema from neck to abdomen, and bilateral ground-glass infiltrates. (B) CT on the day of ICU admission showing pneumomediastinum with air tracking along the sheath of pulmonary vasculature, implicating the Macklin effect (white arrow). (C) CT scan at ICU day11 showing complete resolution of pneumomediastinum by controlling spontaneous breathing.

emphysema was noted in his neck, chest, and arms. The ventilator setting was changed to PEEP 8 cmH$_2$O, PC 4 cmH$_2$O, PS 4 cmH$_2$O, supporting 8 breaths/min, and FiO$_2$ 0.65 in SIMV mode. However, it was difficult to maintain oxygenation and ventilator management. Thus, he was transferred to the ICU in our hospital.

The patient had tachypnea (24 breaths/min) with activation of respiratory accessory muscles such as sternocleidomastoid muscle, which indicated high inspiratory effort, and SpO$_2$ was 99% (FiO$_2$ 1.0) on ICU admission. Computed tomography scan revealed extensive pneumomediastinum, subcutaneous emphysema from the neck to the abdomen, and bilateral ground-glass infiltrates (Fig. 3A). In order to control spontaneous breathing, the patient underwent continuous neuromuscular blockade by rocuronium and the mechanical ventilator setting in AC/PC mode with PEEP 15 cmH$_2$O, PC 13 cmH$_2$O, FiO$_2$ 0.4, inspiratory time 1.0 s, and 18 breaths/min while monitoring the esophageal pressure using a nasogastric catheter (Nutrivent) and Hamilton

C6® ventilator (Hamilton Medical AG). During the treatment, his PEEP and PIP were not strictly limited and applied as necessary for oxygenation and ventilation; his PIP was 28 cmH$_2$O on the day of admission to our ICU, compared to 12 cmH$_2$O in the previous hospital (Fig. 2B). The patient underwent CT scan on day 11 of ICU admission; the scan showed complete resolution of pneumomediastinum (Fig. 3B). Spontaneous breathing was monitored using tidal change in esophageal pressure with a target of 10 cmH$_2$O or less (Fig. S1). He was weaned off the ventilator to ensure that there was no lung injury or exacerbation of the pneumomediastinum. As his hypoxemia and pneumomediastinum had improved, the patient was transferred to the previous hospital after 12 days of ICU admission and weaned off the ventilator.

DISCUSSION

HEREIN, WE PRESENT cases of pneumomediastinum in patients with ARDS due to COVID-19, which

improved by controlling their spontaneous breathing. These cases show that spontaneous breathing could cause pneumomediastinum.

This case series showed that controlling spontaneous breathing with neuromuscular blockade was effective for pneumomediastinum associated with ARDS. Because the etiology of pneumomediastinum during mechanical ventilation has been classified as traumatic, PIP and PEEP are commonly restricted in cases of pneumomediastinum under mechanical ventilation.[5] In both cases, however, PEEP and PIP were applied as necessary for oxygenation and ventilation; these were not strictly restricted beyond the usual lung protection strategy. Furthermore, in case 2, although the PIP was higher than that in the previous hospital, there was a noticeable improvement in the pneumomediastinum. Sekhon *et al.*[2] reported a case of ARDS due to COVID-19 with improvement in the pneumomediastinum using extracorporeal membrane oxygenation and suggested the possibility of lung injury due to P-SILI. The previous study showed that neuromuscular blocking agent could reduce barotrauma, including pneumothorax and pneumomediastinum for ARDS patients.[8] Therefore, we propose that the pneumomediastinum in these cases was caused by P-SILI and improved by spontaneous respiratory control with neuromuscular blocking. Additionally, in case 2, we adjusted the ventilator settings toward weaning off while confirming that tidal change in esophageal pressure (ΔPes) was lower than 10 cmH$_2$O to avoid strong inspiratory effort.[9]

In these cases, the Macklin effect was seen in CT scan as a linear air image contiguous to the bronchovascular sheaths. It is one of the mechanisms of spontaneous pneumomediastinum. Macklin *et al.*[10] reported that pneumomediastinum is induced when a strong pressure gradient occurs between the marginal alveoli and the lung interstitium, and the air is drawn into the bronchovascular sheath. Thus, the cause of pneumomediastinum is not only pulmonary damage caused by COVID-19, but also a pressure gradient between the alveoli and the lung interstitium. This results in the alveolar rupture and movement of air into the bronchovascular sheath.[10,11] As neuromuscular blockade improved pneumomediastinum, the pressure gradient that caused the Macklin effect could be due to spontaneous breathing in both cases, and the mechanism was considered as P-SILI.

CONCLUSION

THE IMPROVEMENT OF pneumomediastinum with control of spontaneous breathing suggested P-SILI as a possible mechanism in this case series. In ARDS cases with pneumomediastinum, in addition to controlling plateau pressure with conventional lung protective ventilation, spontaneous breathing should be controlled if the patient's inspiratory effort is suspected to be strong.

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DISCLOSURE

APPROVAL OF THE research protocol with approval no. and committee name: N/A.

Informed consent: Informed consent was obtained from the patients.

Registry and the registration no. of the study/trial: N/A.

Animal studies: N/A.

Conflict of interest: None.

Data sharing and accessibility: N/A.

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SUPPORTING INFORMATION

Additional Supporting Information may be found in the online version of this article at the publisher's web-site:

Fig. S1. Ventilator waveforms of a 65-year-old man (case 2). The upper waveform shows airway pressure (Paw), the middle waveform shows esophageal pressure (Pes), and the lower waveform shows transpulmonary pressure (P_L). P_L is defined as the following formula: Paw – Pes. The ventilator settings were continuous positive airway pressure/pressure support (CPAP/PS) with pressure support of 6 cmH_2O, positive end-expiratory pressure of 8 cmH_2O, tidal change in esophageal pressure (ΔPes) of 7, and tidal change in dynamic transpulmonary pressure (ΔP_L) of 12.