

Pulmonary Barotrauma in patient suffering from COVID-19

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ABSTRACT

Pneumothorax and pneumomediastinum are life-threatening conditions especially in critically ill patients. One of the most common situations in which they occur is prolonged invasive and non-invasive mechanical ventilation with high end-expiratory pressure. Probably due to the high number of patients with SARS-CoV-2 respiratory infection being treated with mechanical ventilation, increasing number of pulmonary barotrauma cases have been reported.

KEY WORDS: *COVID-19; SARS-CoV-2; pandemic; pneumomediastinum; pneumothorax.*

LIST OF ABBREVIATIONS

SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; COVID-19, coronavirus disease 2019; MIV, mechanical invasive ventilation; NIV, non-invasive ventilation; ICU, intensive care unit; PCR, polymerase chain reaction; BMI, body mass index; CRP, C-reactive protein; CXR, Chest X-ray; GGOs, ground glass opacities; PSV, pressure support ventilation; CT, computer tomography, PEEP, positive end-expiratory pressure; ARDS, acute respiratory distress syndrome; PaO₂/FiO₂ fraction of inspired oxygen; SARS, severe acute respiratory syndrome; PaCO₂, partial pressure of carbon dioxide.

INTRODUCTION

In December 2019, an outbreak of severe acute respiratory syndrome caused by novel coronavirus SARS-CoV-2 has been reported for the first time in Wuhan, China.¹ The rapid global spread of the infection caused a pandemic, as declared by the World Health Organization in March 2020.¹

Patients with SARS-CoV-2 infection can manifest coronavirus disease (COVID-19), with a clinical evolution that can lead in some cases to pulmonary impairment and hypoxemic respiratory failure. This may require patients to undergo mechanical invasive (MIV) or non-invasive ventilation (NIV), which has resulted in high rates of hospitalization and intensive care unit (ICU) admissions (5-37%).²

Since COVID-19 outbreak, about 750'000 patients have been hospitalized only in Italy, with ICU admission rate of 21.4%.³ Moreover, in a cohort study performed on 1591 patients in ICU, 88% required MIV and 11% underwent NIV.⁴

We here report a case of a patient affected by COVID-19, who underwent NIV for eight days, and presented a rapid clinical deterioration at ninth day, which was caused by pneumothorax and pneumomediastinum, associated with subcutaneous emphysema.

CASE REPORT

A 65-year-old man was admitted in the subintensive care unit of our hospital and informed consent form was obtained for undergoing any medical treatment. His SARS-CoV2 reverse transcription polymerase chain reaction (PCR) test was positive from two consecutive nasal swabs. He presented after 7 days of fever, severe cough and progressive dyspnea.

He was obese (BMI 32 kg/m²), with history of hypertension and smoke. At hospital admission, his laboratory tests showed a total white blood cell count of 8500 mm² [normal range (n.r): 4500-9000 mm²], with neutrophilia of 88% (n.r: 60-70%) and lymphocytopenia of 7% (n.r: 20-35%). His C-reactive protein (CRP) blood levels were elevated (4.10 mg/dl; n.r: 0-0.50mg/dl). Chest X-ray (CXR) revealed bilateral and peripheral “ground-glass” opacities (GGOs) (**Figure 1**).

He firstly received low-flow oxygen therapy and started antibiotic and steroid therapy, together with enoxaparin thromboprophylaxis. He gradually presented tachypnea and reduced SpO₂ (91%), and was subsequently ventilated with NIV using PSV (pressure support ventilation) mode, with SpO₂ improvement (stable between 94-96%).

Nine days after introduction of NIV, the patient had acute deterioration with rapid oxygen desaturation (SpO₂=88%; PaO₂/FiO₂<100) and pneumothorax was clinically suspected. Bedside CXR was performed and showed pneumothorax, bilateral

consolidations, severe subcutaneous emphysema and suspicion of pneumomediastinum (**Figure 2a**).

The patient was intubated and underwent chest-CT scan (**Figure 2b-c**) that depicted multiple and subpleural ground-glass opacities (GGOs) with bilateral parenchymal consolidations. Pneumothorax, pneumomediastinum and massive subcutaneous emphysema were also seen and the patient was transferred to ICU.

Chest drains were positioned to treat pneumothorax, and in the following days the patient underwent different ventilation strategies, to improve his respiratory function, including multiple prone positions.

Two weeks later, follow-up bedside CXR showed resolution of pneumothorax with a widening of the mediastinum and increase of bilateral consolidations, suggestive of respiratory distress syndrome (**Figure 3**). His arterial blood gas values showed a status of mild respiratory acidosis. Hydration with the administration of insulin, and adjustment of ventilation parameters were carried out with the aim to restore blood sugar levels and respiratory acidosis status (**Table 1**). However, the patient progressively deteriorated and deceased three days later.

DISCUSSION

Pneumothorax and pneumomediastinum are life-threatening conditions in critically ill patients, and they are encompassed in the spectrum of pulmonary barotrauma.⁵

Patients undergoing mechanical ventilation, may develop complications as pulmonary barotrauma with incidence ranging between 4-15%.⁶ Alveolar rupture may occur when the pressure gradient between alveoli and interstitium increases too much; this causes air entering into interstitium and determines perivascular interstitial emphysema.^{6,7}

The pressure value at which alveolar rupture occurs is associated with excessive tidal volumes during ventilation and can vary with severity of lung injury.⁷

This condition can lead to tensive pneumomediastinum through “Macklin’s phenomenon” that consists in the releasing of alveolar air after alveolar rupture, which tracks along peri-bronchial vascular sheaths into the mediastinum.⁸⁻¹⁰

Sustained lung inflammation may represent the key factor in the etiopathogenesis of pulmonary barotrauma in patients undergoing prolonged NIV.¹¹ Other risk factors include a peak inspiratory pressure of 40 cm H₂O and the use of positive end-expiratory pressure (PEEP).⁶ Diffuse alveolar damage can also cause emphysema-like changes with rupture of dilated cystic airspaces and pneumothorax.^{7,12,13}

Pneumomediastinum and pneumothorax have shown to be negative prognostic factors in intubated patients.⁸ In particular, the incidence of pulmonary barotrauma is related to duration of lung inflammation, and its occurrence has proven to increase mortality.⁷

Moreover, positive pressure ventilation in presence of an undrained pneumothorax may lead to tensive pneumothorax or pneumomediastinum. This can determine respiratory and hemodynamic failure, related to cardiac tamponade and large vessel compression, with decreased venous return to heart.^{6,8}

CXR and CT are crucial for diagnosis and typical signs of tension include mediastinal shift, displacement of anterior junction line, azygoesophageal recess, and flattening of heart.¹⁴

Since SARS-CoV-2 outbreak, increasing cases of pneumothorax and pneumomediastinum in hospitalized COVID-19 patients have been reported.^{6-8,12,15}

An increased incidence of pulmonary barotrauma has been reported also in patients who underwent mechanical ventilation (NIV/MIV) suffering from another severe acute respiratory syndrome (SARS).¹⁶ In these patients, higher respiratory rates, lower P/F, and higher PaCO₂, together with virus-induced alveolar and airways cell damage showed greater likelihood to develop pulmonary barotrauma.¹⁷

In patients suffering from COVID-19, further investigation and studies with larger patient populations are needed to better clarify the pathogenesis of this unfavorable complication. However, clinicians should be aware of complications such as pneumothorax and pneumomediastinum in patients who undergo either invasive or non-invasive mechanical ventilation, since these conditions need prompt recognition and treatment.

TABLES**Table 1**

Laboratory tests at the different time points of hospitalization: admission, during non-invasive mechanical ventilation (NIV), at the diagnosis of pneumothorax (PNX) and pneumomediastinum (PMD), during mechanical invasive mechanical ventilation (MIV), and three days before death.

BUN, Blood Urea Nitrogen; NA, Sodium; K, Potassium; CPK, creatine phosphokinase; CRP, C-reactive protein; PCT, Procalcitonin; LDH, lactate dehydrogenase; ALB, albumin; INR, International Normalized Ratio; aPPT, activated partial thromboplastin time; AST, aspartate transaminase; ALT, alanine transaminase; HB, hemoglobin; PaO₂, oxygen partial arterial pressure; FiO₂, fraction of inspired oxygen; P/F PaO₂/FiO₂ Ratio; HCO₃, Bicarbonate; PaCO₂, Partial Pressure of Carbon Dioxide.

LAB TEST	NORMAL VALUES	ADMISSION DAY	DURING NIV	PNX/PMD DAY	DURING MIV	3 DAYS BEFORE DEATH
WHITE BLOOD CELLS	4500-9000 mm ²	8500	12000	13900	29900	21800
NEUTROPHILS	60-70 %	88	82	85	88	88
LYMPHOCYTES	20-35 %	7	11	10	7	7
HEMATOCRIT	39-49 %	42,2	41,7	42,8	44,1	43,4
PLATELETS	150-400 x 10 ³ /uL	197	246	368	584	466
GLYCEMIA	60-110 mg/dL	152	415	176	207	324
BUN	15-50 mg/dL	47	46	104	130	89
CREATININE	0,7-1,4 mg/dL	0,7	0,5	0,5	1	0,6
BILIRUBIN	0,1 - 1,4 mg/dL	0,47	0,58	0,5	0,41	0,52
NA	130 - 150 mmol/L	132	134	138	135	141
K	3,6 - 5,1 mmol/L	4,3	4,6	4,6	6,2	5,1
CPK	55-170 U/L	552	510	62	139	379
CRP	0–0.5 mg/dl	4,1	3,4	16,2	13,5	19,1
PCT	<0.05 ng/ml	0,11	0,06	0,66	0,94	0,91
LDH	120 - 246 U/L	1251	1173	922	1113	888
ALB	35-55 g/L	34	31,7	24	22,4	24,4
INR	0,8 - 1,1	1,05	1,01	1,09	0,98	1,06
APPT	30 - 40 sec	34,6	33,7	23,9	28,5	30,4
AST	5-50 U/L	32	92	50	69	81
ALT	5-50 U/L	130	219	80	86	67
HB	14,4 - 18 g/dL	14,2	14	13,9	13,4	13,4
PAO2	70 - 100 mmHg	74,6	114	55	98	94
FIO2		0,2	0,7	0,55	1	0,6
P/F	> 350	373	162	99	98	135
LACTATE	0.6–1.4 mmol/L	0,9	1,1	2,4	2,4	1,5
HCO3	22–29 mmol/L	23,1	22,4	23	21	37
PACO2	38-42 mmHg	34,5	32,2	24	79	71
pH	7,35–7,45	7,43	7,45	7,43	7,10	7,30

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FIGURE LEGENDS

Figure 1

Bedside chest X-ray performed at admission in sub-intensive care unit. Typical bilateral and subpleural GGOs are shown bilaterally (*asterisks*), patient's condition was stable.

Figure 2

Bedside chest X-ray (**a**), performed after rapid deterioration of patient's clinical status, shows bilateral GGOs with peripheral distribution, basal consolidations, and suspected pneumomediastinum (*arrowheads*). Left pneumothorax (*arrows*) and diffuse subcutaneous emphysema (*asterisks*) are also seen. The patient was immediately intubated and admitted to ICU, chest-CT scan performed on the same day (**b**, **c**) confirmed the presence of multiple ground-glass opacities with typical subpleural distribution, together with bilateral parenchymal consolidations. Left pneumothorax, pneumomediastinum and subcutaneous emphysema are also shown.

Figure 3

Follow-up bedside chest X-ray performed in the ICU, thirteen days after CT scan, show resolution of pneumothorax and pneumomediastinum and demonstrates widening of mediastinum, diffuse interstitial edema, and increase of consolidations, consistent with diffuse alveolar damage and respiratory distress syndrome.

DECLARATIONS

AUTHOR CONTRIBUTION STATEMENT

All listed authors have significantly contributed to this article.

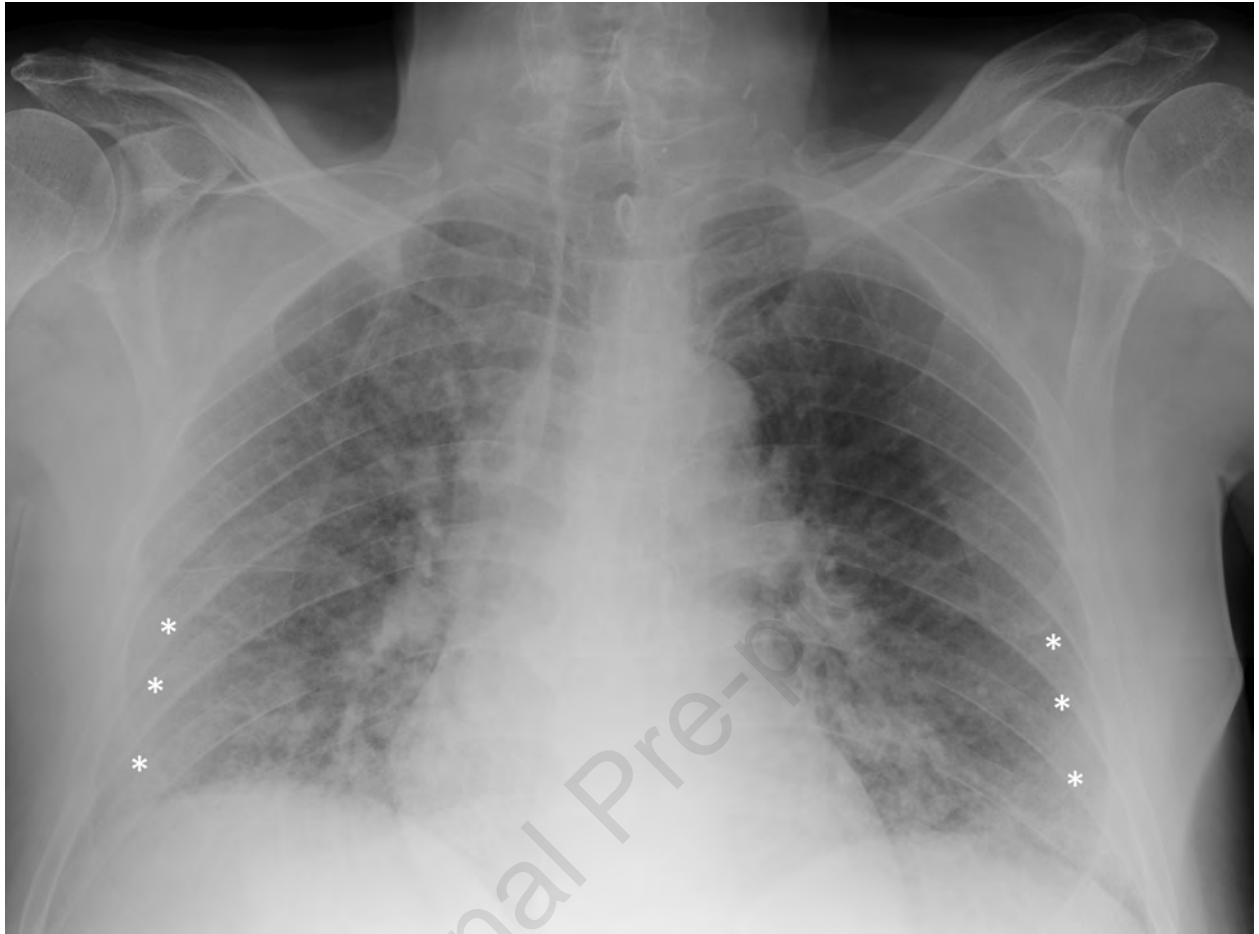
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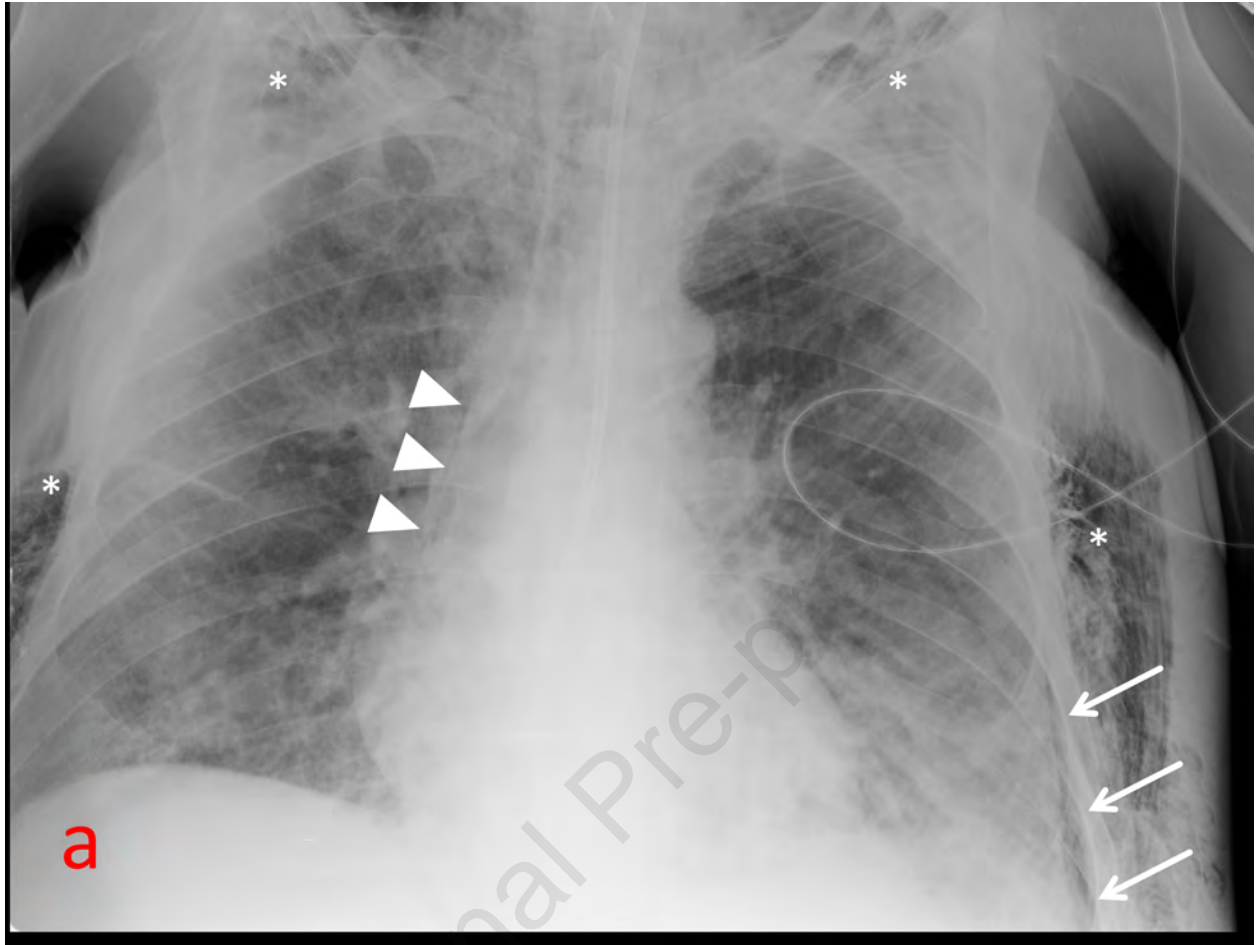
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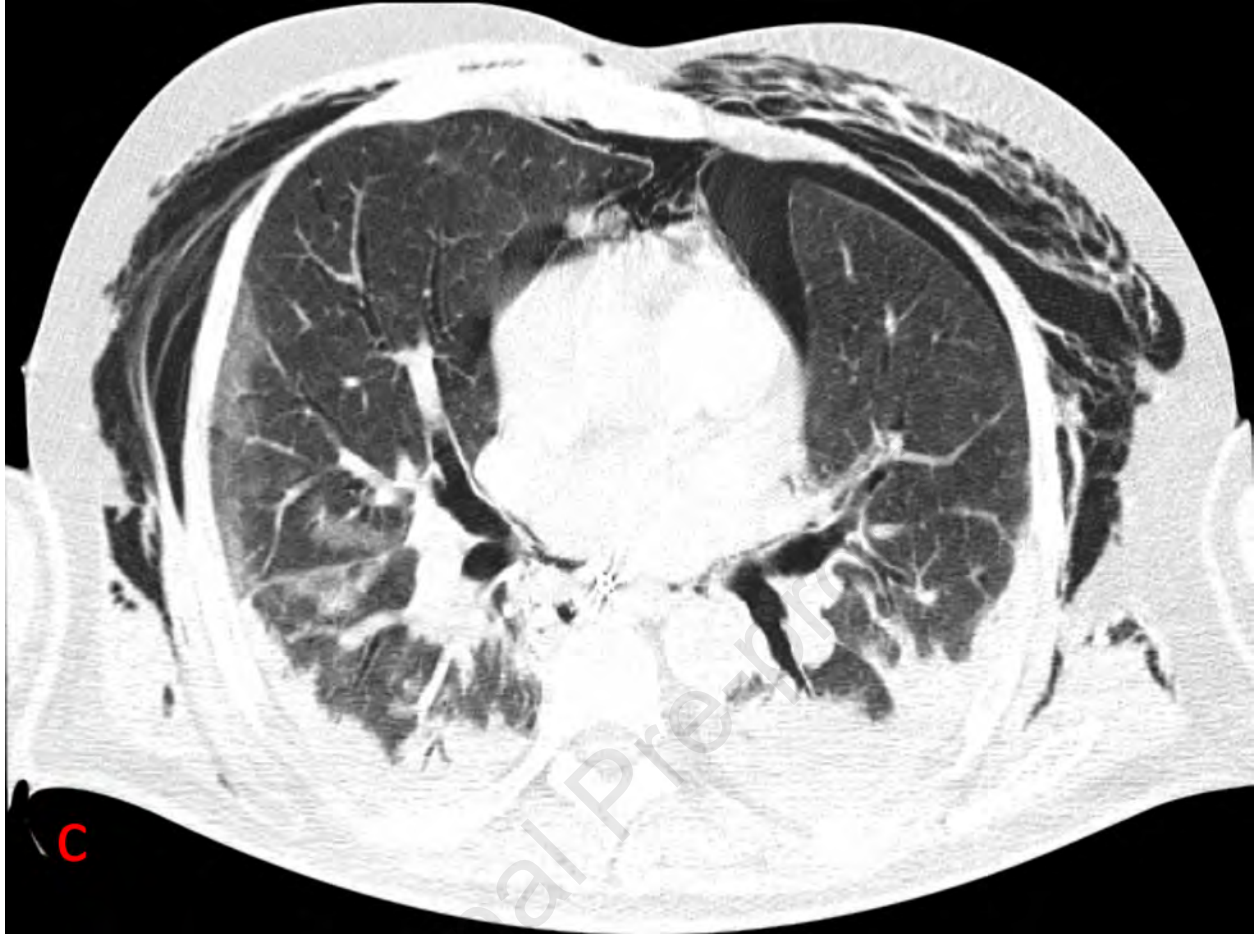
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