

# Spontaneous pneumomediastinum in COVID-19 pneumonia

Marco Loffi<sup>1</sup>, Valentina Regazzoni<sup>1</sup>, Pietro Sergio<sup>2</sup>, Enrico Martinelli<sup>3</sup>, Italo Stifani<sup>3</sup>, Filippo Quinzani<sup>1</sup>, Debora Robba<sup>1</sup>, Annunziata Cotugno<sup>4</sup>, Meghi Dede<sup>5</sup>, Gian Battista Danzi<sup>1</sup>

<sup>1</sup>Division of Cardiology; <sup>2</sup>Division of Radiology; <sup>3</sup>Division of Pneumology, Cremona Hospital; <sup>4</sup>Institute of Cardiology, Department of Medical and Surgical Specialties, Radiological Sciences, and Public Health, University of Brescia; <sup>5</sup>University of Milan, Italy

## Abstract

Spontaneous pneumomediastinum is a benign entity but can worsen the underlying condition with which it is associated. We evaluated the incidence and the clinical relevance of spontaneous pneumomediastinum in a consecutive series of 102 patients with

COVID-19 pneumonia. Six cases of pneumomediastinum were identified by high-resolution chest CT-scan. Three patients required early intubation, and one of them died, while in the remaining subjects the clinical course was benign. The presence of pneumomediastinum required some changes in the management of mechanical ventilation. In conclusion, spontaneous pneumomediastinum is a possible complication of severe COVID-19 pneumonia that can affect patient management and clinical outcomes.

Correspondence: Valentina Regazzoni, Division of Cardiology, Ospedale di Cremona, Viale Concordia 1, 26100 Cremona, Italy. Tel. +39.0372.405322. E-mail: valentina15686@hotmail.it

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## Introduction

Spontaneous pneumomediastinum (SP) is rarely diagnosed in the general population, but frequently described during bacterial and viral infection [1,2]. It usually is a benign entity but can worsen the severity of the underlying condition. Northern Italy was the first European area that faced the Coronavirus Disease 2019 (COVID-19) and our hospital located in Cremona, Lombardy Region, was early converted in a COVID-19 dedicated center [3].

This is the first study that evaluate the incidence and the clinical relevance of SP in a consecutive series of patients with severe COVID-19 pneumonia.

## Materials and Methods

We retrospectively analyzed clinical data from a sample of 187 patients admitted in our center with diagnosis of COVID-19 pneumonia between February 21<sup>st</sup> to March 1<sup>st</sup>, 2020 using a computerized data collection system. The study was approved by our Ethical Committee.

Patients were assessed for eligibility on the basis of three principal inclusion criteria: i) a confirmed clinical and radiological diagnosis of COVID-19 pneumonia [4]; ii) a positive Reverse-Transcriptase-Polymerase-Chain-Reaction assay for SARS-CoV-2 in a respiratory tract sample; iii) a high-resolution chest computed tomography scan (HRCT) within 96 hours from admission.

We identified 102 patients who represent the study population. Relevant clinical and laboratory data were obtained from medical records. CT image analysis was performed by an experienced thoracic radiologist (P.S.). Acute Respiratory Distress Syndrome (ARDS) was defined and classified based on the ratio between PaO<sub>2</sub> and FiO<sub>2</sub> ratio according to WHO criteria [5].

Pneumonia severity was classified based on the lung involvement as mild, moderate and severe as reported in Table 1. The presence and characteristics of pneumomediastinum were described qualitatively.

## Statistical analysis

Continuous variables were expressed as median with its interquartile range (IQR) and compared with the Mann-Whitney U test. Categorical variables were described as number (%), and proportions for categorical variables were compared using the Fisher exact test. A two-sided  $\alpha$  of less than 0.05 was considered statistically significant. Statistical analyses were done using the SPSS version 21.0 software (IBM, New York, USA).

## Results

Clinical characteristics, radiological data and the in-hospital outcomes of the 102 patients are reported in Table 1. Laboratory data are listed in Table 2. ARDS was present in 50% of patients at admission. SP was documented in six subjects (6%). In three cases there was a large amount of air (>20 mm) in the mediastinum surrounding all of the vascular structures, infiltrating the neck and with evidence of subcutaneous emphysema (Figure 1A). In the remaining cases the presence of air was more limited (Figure 1B). The same three patients with large SP developed severe ARDS required intubation. In two of them the accumulation of air in the mediastinum increased significantly during mechanical ventilation despite the measures taken to reduce volutrauma. In one of these patients we had to escalate the degree of support because of the presence of pneumopericardium and extensive subcutaneous emphysema (Figure 1 C,D). This same patient died during hospitalization. The remaining five patients were discharge few weeks later with documented disappearance of pneumomediastinum at control CT-scan.

## Discussion

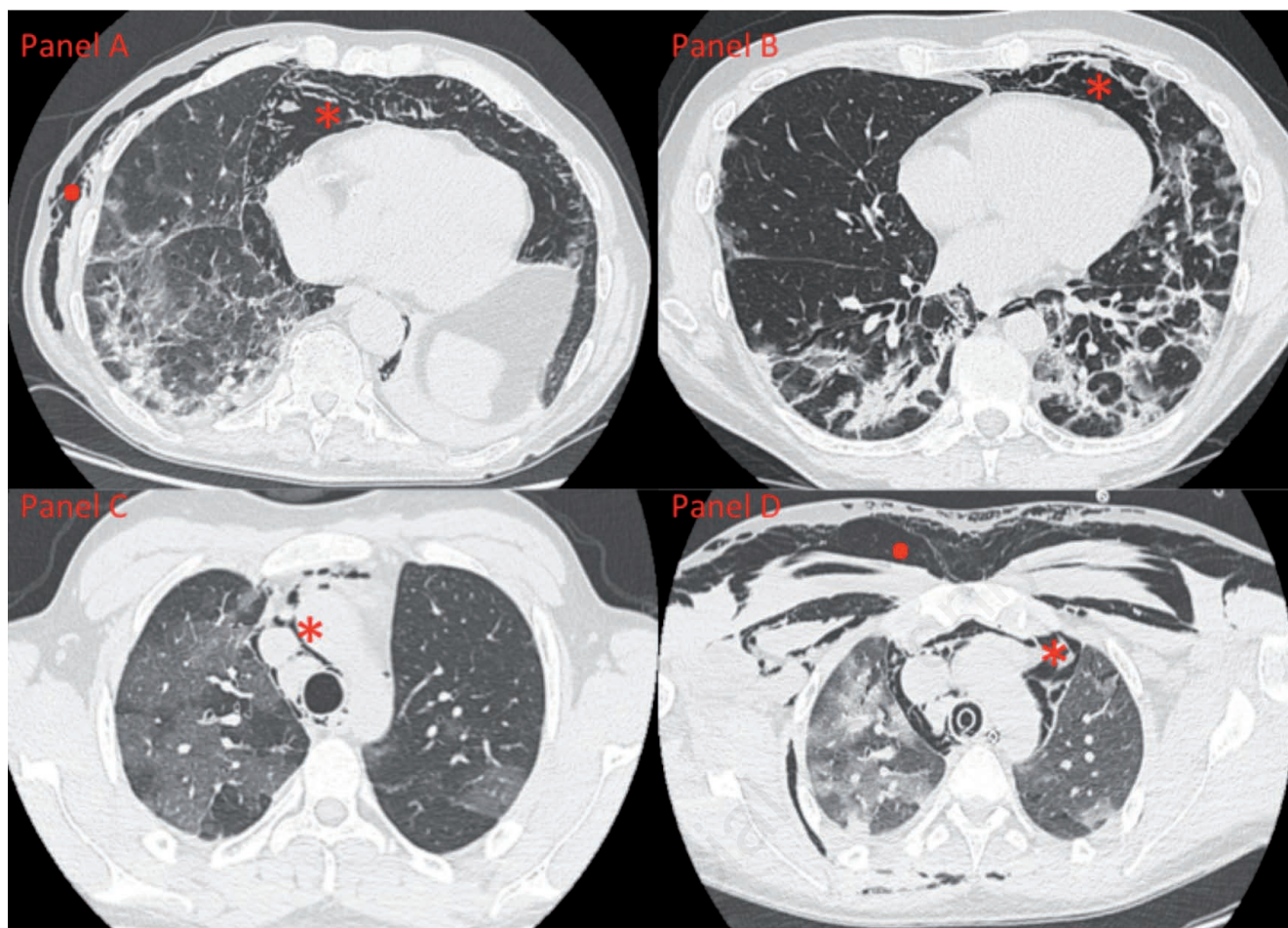
The precise mechanism underlying the development of SP during respiratory infections is unknown [1,2]. One possible explanation is that severe pneumonia can cause diffuse alveolar damage and rupture, leading to interstitial emphysema that may further progress to the mediastinal space and subcutaneous emphysema: this phenomenon is known as Macklin effect [6]. SP was documented in 11% of 123 patients during the severe acute respiratory syndrome (SARS) epidemic in 2003, and the authors concluded that the presence of SP may be related to a poor outcome [7]. In our cohort of patients with COVID-19 pneumonia, the incidence of SP seems to be lower, around 6%, possibly because COVID-19 pneumonia may have a different impact on the respiratory system from that of SARS.

SP is usually benign, as in a recent case that occurred during the COVID-19 epidemic in China [8]. The prognosis usually depends on the underlying conditions but it could represent a potential indicator of worsening disease. In our experience, the concomitant presentation of SP and diffuse COVID-19 pneumonia was associated with a severe clinical course characterized by sudden ARDS that required aggressive management and early intubation in three patients [9]. Furthermore, the presence of pneumomediastinum required some changes in the management of mechanical ventilation in order to minimize volutrauma and prevent its expansion. Avoidance of overventilation, adoptions of measures to limit hyperinflation and the cautious use of high levels of positive end-expiratory pressure was required but, despite these precautions, mechanical ventilation had the effect of increasing the size of the pneumomediastinum, as observed in two of our patients.

**Table 1. Clinical characteristics, radiological data and in-hospital outcomes.**

	Total (n=102)	SP (n=6)	Non-SP (n=96)
Age (years)	65 (56-73)	72 (49-80)	64 (53-75)
Gender, male	73 (71%)	5 (83%)	68 (71%)
Temperature at admission (°C)	37.4 (36.7-38)	38 (37.3-38.5)	37.4 (39.7-37.8)
Days of fever	5 (3-7)	6 (5-7)	5 (3-7)
Comorbidities			
Hypertension	38 (37%)	1 (17%)	37 (38%)
Smoke	27 (26%)	2 (33%)	25 (26%)
Diabetes	11 (10%)	0	11 (12%)
Chronic heart disease	9 (8%)	0	9 (9%)
ARDS at admission	51 (50%)	4 (67%)	47 (49%)
Mild (PaO <sub>2</sub> /FiO <sub>2</sub> 200-300)	44 (43%)	3 (50%)	41 (43%)
Moderate (PaO <sub>2</sub> /FiO <sub>2</sub> 100-200)	6 (6%)	1 (17%)	5 (5%)
Severe (PaO <sub>2</sub> /FiO <sub>2</sub> <100)	1 (1%)	0	1 (1%)
CT-scan pneumonia severity			
Mild	16 (15%)	1 (17%)	15 (16%)
Moderate	25 (25%)	2 (33%)	23 (24%)
Severe	61 (60%)	3 (50%)	58 (60%)
In-hospital outcome			
Intubation	12 (12%)	3 (50%)	9 (9%)
Death	12 (12%)	1 (17%)	11 (12%)
Discharged	90 (88%)	5 (83%)	85 (88%)

Data are median (IQR) or n (%). SP, Spontaneous pneumomediastinum; ARDS, acute respiratory distress syndrome; PaO<sub>2</sub>, arterial oxygen partial pressure; FiO<sub>2</sub>, fraction of inspired oxygen; CT, computer tomography.



**Figure 1.** Axial CT-images. A) Peripheral airspace consolidations and ground glass densities in the right lower lobe, a large pneumomediastinum around the heart, and diffuse subcutaneous emphysema on the right side. B) Multiple patchy linear opacities with a perilobular pattern in both lungs, and a moderate amount of air in the anterior mediastinum. C) Extensive patchy ground glass density in the right upper lobe, less extensive similar densities in the left upper lobe, and a moderate pneumomediastinum. D) Chest CT-scan after two days of endotracheal intubation showing ground glass densities progressing to consolidation in the right upper lobe, diffuse subcutaneous emphysema, and more evident mediastinal emphysema than in the previous scan.

**Table 2.** Laboratory data at admission.

	Normal range	SP (n=6)	Non-SP (n=96)
D-dimer (mcg/ml)	0-0.5	3 (2.1-7.2)	0.9 (0.7-6.3)
Tn (ng/L)	0-34	10.5 (5.1-134)	9.2 (4.7-25)
CRP (mg/L)	0-5	109 (38-263)	50 (16-117)
WBC ( $\times 10^3/\text{mm}^3$ )	3.9-10.6	10560 (4920-20255)	5265 (4692-8100)
LC (%)	20-45	16 (8-41)	11 (8-15)
Hb (g/dL)	13.7-17.5	14.4 (12.2-15.4)	14.1 (13.1-15.1)
PTL ( $\times 10^3/\text{mm}^3$ )	150-400	156 (127-200)	183 (139-252)
ALT (U/L)	0-41	37 (19-92)	18 (38-44)
AST (U/L)	10-40	60 (32-91)	36 (26-59)
INR	0.8-1.2	1 (0.9-1.2)	1 (0.7-1.1)
LDH (U/L)	<248	236 (167-305)	367 (235-487)
Creatinine (mg/dL)	0.7-1.18	0.87 (0.7-1.2)	0.96 (0.8-1.2)

Data are median (IQR) or n (%). SP, Spontaneous pneumomediastinum; Tn, troponin; CRP, C-reactive protein; WBC, white blood cell count; LC, lymphocyte count; PTL, platelets; ALT, alanine aminotransferase; AST, aspartate transaminase; INR, international normalized ratio; LDH, lactate dehydrogenase; EGFR, estimated glomerular filtration rate.

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## Conclusions

In conclusion, SP is a possible complication of severe COVID-19 pneumonia that can affect patient management and clinical outcomes.

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