

Coronavirus Pandemic

Spontaneous pneumothorax, with or without pulmonary cysts, in patients with COVID-19 pneumonia

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Abstract

Introduction: Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) affects mainly the lungs causing pneumonia and complications like acute respiratory distress syndrome. Pneumothorax is a rare manifestation of the disease. This report is a description of a series of patients with COVID-19 and spontaneous pneumothorax, some of them with associated pulmonary cysts.

Methodology: Cases were collected retrospectively. We included clinical data from medical records and described radiologic findings. Patients that developed pneumothorax during mechanical ventilation were excluded.

Results: Ten cases were included in this report, nine of them were male. The median age of our series was 62 years (IQR = 57-68). The median days since the onset of symptoms until the development of pneumothorax was 27 (IQR = 17-31), most cases developed after the second week of the diagnosis of pneumonia. Two cases required invasive mechanical ventilation, but pneumothorax occurred after ventilator weaning. Three cases showed subpleural pulmonary cysts.

Conclusions: Cysts and pneumothorax are rare manifestations of SARS-CoV-2 pneumonia with mechanisms not completely understood. This report highlights the role of CT scan in diagnosis of COVID-19 complications.

Key words: Viral pneumonia; COVID-19; pneumothorax; cysts.

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Introduction

Coronavirus disease 2019 (COVID-19) has become a health emergency worldwide causing pneumonia as its main manifestation. The most common chest computed tomography (CT) features are consolidations, ground-glass opacities, or both, with predominantly bilateral, basal, and peripheral distribution [1]. Spontaneous pneumothorax and pulmonary cystic spaces have been reported as a rare complication of COVID-19. The aim of this report is to describe cases of patients from a single-center with COVID-19 pneumonia and spontaneous pneumothorax, not related to mechanical ventilation, in some cases associated with pulmonary cysts.

Cases report

We collected retrospectively ten laboratory-confirmed COVID-19 patients that developed spontaneous pneumothorax. Patients that developed

pneumothorax during mechanical ventilation were excluded.

The median age of patients was 62 years (IQR = 57-68), nine of them were male. In all cases pneumothorax was suspected because symptoms and oxygenation acutely worsened, nine cases presented chest pain. The median days since the onset of symptoms until the development of pneumothorax was 27 (IQR = 17-31), only two patients developed this complication in the first two weeks. There were two cases with pneumothorax at the time of admission to the emergency department, one case developed pneumothorax during their inpatient admission, and seven cases developed this complication after being discharged from the first admission for COVID-19. Two cases required invasive mechanical ventilation, but pneumothoraces occurred after ventilator weaning.

Only one patient had chronic obstructive pulmonary disease (COPD) as previous chronic lung disease. One

patient had a history of HIV. No patient had thoracic trauma associated with pneumothorax.

The right side was affected in three cases, the left side in four, and three had bilateral pneumothorax. Chest X-ray failed to identify the pneumothoraces in three cases because they were loculated. Patients underwent chest CT scanning that showed multilobe subpleural consolidations or ground-glass opacities once COVID-19 was diagnosed. Three cases with CT scan follow-up showed evidence of subpleural thin-walled cystic spaces development associated with pneumothorax (Figure 1). Chest CT did not suggest pulmonary infarction or parenchymal cavitation in any case; CT pulmonary angiography was performed in six cases ruling out pulmonary embolism.

All patients required supplemental oxygen therapy; pneumothorax did not require drainage in one patient. Only one case died of respiratory failure due to COVID-19. No tissue samples were collected for pathology.

Ethics approval and consent to participate

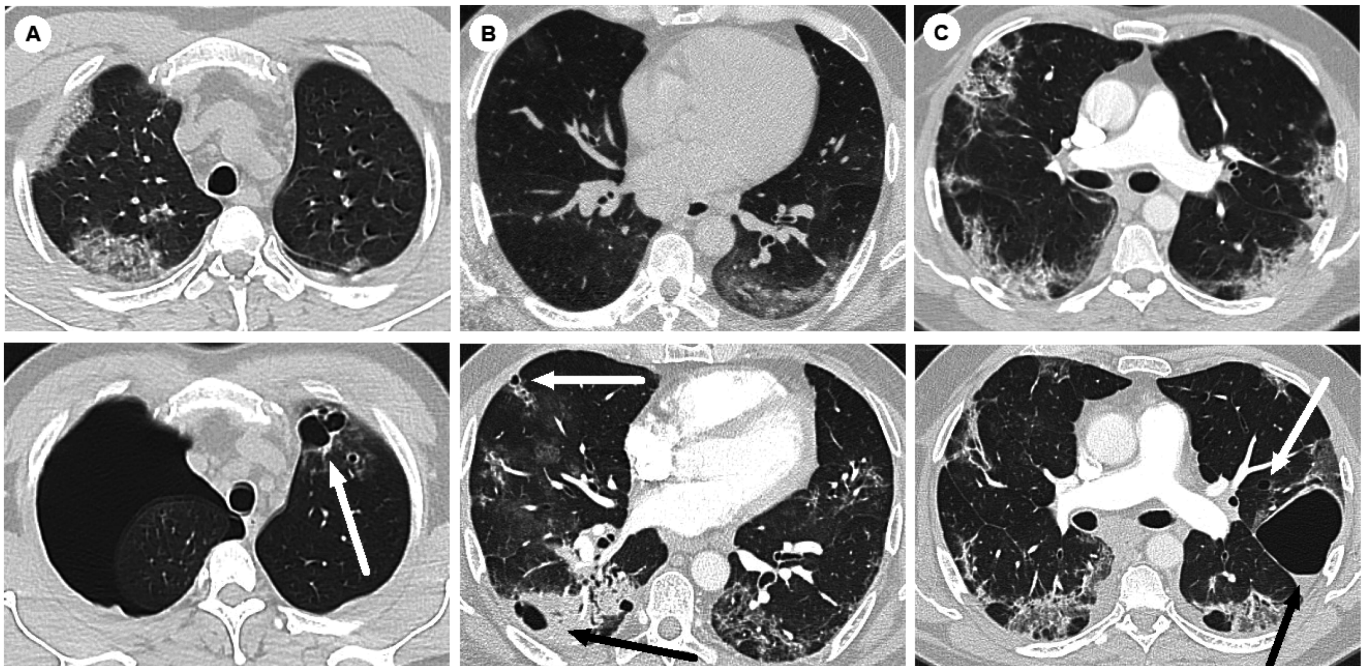
Written informed consents were taken from the patients for publication of these cases and any

accompanying images. This report was approved by the Medical Ethic Committee of Rosario University.

Discussion

We have described a case series of COVID-19 patients with pneumothorax, some related to cystic lesions. This series remarks the role of CT scan in diagnosis and identification of COVID-19 complications and the importance of clinical suspicion of pneumothorax as a potentially life-threatening complication in patients with acute worsening of symptoms. In three cases, follow-up chest CT demonstrated cysts development associated with pneumothorax, indicating its temporal relationship with COVID-19. Most of the patients did not have any risk factors for cysts or pneumothorax development, including smoking, underlying chronic lung diseases, trauma, or use of positive-pressure ventilation. Infectious diseases, such as necrotizing pneumonia and *Pneumocystis jirovecii* pneumonia, may cause air-filled spaces that sometimes lead to secondary pneumothorax. We do believe that lung damage caused by COVID-19 explains the development of these findings, and it is

Figure 1. Clinical presentation COVID-19 cases with evidence of pulmonary cysts development.



A: A 39-year-old man with a 12-day history of fever, dyspnea, cough, sore throat, vomit, and diarrhea; high-resolution CT showed multifocal upper lobe consolidations (top panel). 29 days later CT scan showed left upper lobe subpleural cystic lesions (white arrow) associated with ground-glass opacities and right pneumothorax (bottom panel). **B:** A 58-year-old with a 5-day history of fever, cough, dyspnea, and diarrhea; high-resolution CT showed multilobar ground-glass peripheral opacities (top panel). He required invasive mechanical ventilation for ten days. 31 days later CT scan showed multilobar ground-glass opacities, consolidations, parenchymal bands and loculated right pneumothorax (black arrow); middle lobe and right lower lobe had subpleural cysts (white arrow) (bottom panel). **C:** A 63-year-old man was admitted presenting with an 8-day history of cough, fever, asthenia, headache, and dyspnea; high-resolution CT showed multilobar ground-glass opacities (top panel). CT scan obtained 48 days later showed left upper lobe cystic spaces (white arrow), associated with ground-glass opacities and loculated left pneumothorax (black arrow) (bottom panel).

possible that cysts formation may play a role in the pathophysiology of pneumothorax.

The most common patterns of COVID-19 pneumonia on CT scans are ground-glass opacities (88.0%), with peripheral (76.0%) and bilateral (87.5%) distribution, and multilobe involvement (78.8%) [1]. Bronchiectasis, nodules, septal thickening, pleural effusion, and lymphadenopathy are less common and found at a later stage of the disease. Cystic spaces have been reported in up to 10% and spontaneous pneumothorax in 1% of SARS-CoV-2 pneumonia cases [2,3].

Pneumothorax has been reported predominantly in male patients, in some cases as an early presentation of COVID-19 and in other cases as a late complication after two weeks of symptom onset, the latter sometimes associated with pulmonary cysts (Table 1) [4,13]. Cysts linked to pneumothorax in COVID-19 have been described in few case reports. Liu *et al.* [9] described a series of two men with pneumothorax and peripheral pulmonary cysts after 26 and 40 days of symptom onset; cysts decreased in number and size in the follow-up of both cases.

A multicenter case series in the UK described sixty pneumothoraces and six pneumothoraces with pneumomediastinum in patients who developed this

complication at admission or during hospitalization, regardless of the use of positive-pressure ventilation [14]. The incidence of pneumothorax was higher in males (3.3:1) and did not affect COVID-19 prognosis. In one case, CT scan showed subpleural cysts correlated to the pathology finding of a cystic space transitioning with respiratory epithelium.

The pathogenesis of pulmonary cysts in COVID-19 is not well understood. Proposed mechanisms of cystic lung disease include necrosis due to ischemia, remodeling of interstitial matrix, and bronchial obstruction with distal hyperinflation phenomenon due to a check-valve mechanism. Histopathologic features of COVID-19 may help to understand the mechanism of pneumothorax and cystic lesions; reports of autopsies have showed lung injury consistent with early acute respiratory distress syndrome as the main finding, followed by acute fibrinous and organizing pneumonia, microthrombi, vascular congestion and necrosis with microvascular damage [6,15]. Ischemia due to microvascular damage and exudates causing a check-valve mechanism within airspaces could be involved in cysts formation [9]. However, the late development of cysts suggests that alveolar wall destruction is more likely related to the healing process in areas of

Table 1. Summary of characteristics of some COVID-19 series reported with pneumothorax associated to cysts or bullae.

Reference	Age, years	Sex	Days from illness onset to pneumothorax	Smoking history	Chronic lung disease	Mechanical ventilation	Lung cysts or bullae
Aiolfi A, <i>et al.</i> [4]	56	Male	N/A	Yes	No	Yes	Yes
	70	Male	N/A	No	No	Yes	Yes
Al-Shokri, <i>et al.</i> [5]	55	Male	10	N/A	No	Yes	No
	33	Male	20	N/A	No	Yes	Yes
	50	Male	N/A	N/A	No	No	N/A
Bellini B, <i>et al.</i> [6]	58	Male	N/A	Yes	No	No	No
	53	Female	3	No	No	No	Yes
Capleton P, <i>et al.</i> [7]	64	Female	N/A	No	Bronchiectasis	Yes	Yes
Flower L, <i>et al.</i> [8]	36	Male	21	Yes	Asthma	No	Yes
Liu K, <i>et al.</i> [9]	38	Male	26	N/A	No	No	Yes
	35	Male	40	N/A	No	Yes	Yes
Mallick T, <i>et al.</i> [10]	40	Male	7	Yes	No	No	Yes
	68	Male	23	No	No	No	Yes
	58	Female	N/A	No	No	No	No
Sanivarapu RR, <i>et al.</i> [11]	40	Male	17	No	No	No	Yes
Sun R, <i>et al.</i> [12]	38	Male	39	N/A	No	Yes	Yes
Yasukawa K, <i>et al.</i> [13]	37	Male	30	N/A	No	No	Yes
	39	Male	29	Yes	No	No	Yes
Present study	58	Male	31	No	No	Yes	Yes
	71	Male	7	No	No	No	No
	62	Male	30	Yes	COPD	No	Yes
	56	Male	15	No	No	No	No
	54	Male	25	No	No	No	No
	79	Male	12	No	No	No	No
	69	Male	21	No	No	No	No
	64	Male	42	Yes	No	No	Yes
	62	Female	42	No	No	No	Yes

resorption of consolidation than to the early inflammatory damage [7].

Conclusions

There are few reports of cases to date of pneumothorax and cysts in COVID-19 to date. Mechanisms of these complications in patients with COVID-19 are not yet completely understood; further information from histopathological observations may help to elucidate them.

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Author contributions

All authors have read and approved the manuscript. JLG: Methodology, Investigation, Writing - Review and Editing. JRL, MAI and VLR: Investigation, Writing - Original Draft. JAC: Conceptualization.

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