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Spontaneous pneumothorax: An emerging complication of COVID-19 pneumonia



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ABSTRACT

Spontaneous Pneumothorax in the setting of coronavirus disease 19 (COVID-19) has been rarely described and is a potentially lethal complication. We report our institutional experience. Patients with confirmed COVID-19 who were admitted at 5 hospitals within the Inova health system between February 21 and May 2020 were included in the study. We identified 1619 patients, 22 patients (1.4%) developed spontaneous pneumothorax during their hospitalization without evidence of traumatic injury.

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The median age of the patients was 60 years and 82% were male (Table 1). The majority of the cohort was Hispanic at 95%. The median BMI was 25.4, 52% of patients had a history of hypertension, 32% had a history of diabetes mellitus and 14% were smokers. Spontaneous pneumothorax was diagnosed between the 1st and 15th day of hospitalization (median 9th day) and 100% of patients were diagnosed by chest X-ray (Fig. 1). There were 16 patients (73% of the overall population) who had a chest tube placed and the remaining 6 patients were monitored closely. Eight patients died (36% of the overall population) with fourteen patients either remaining in hospital or discharged to home. Of the 8 that remained hospitalized, 2 patients are on extracorporeal membrane oxygenation (ECMO), 2 patients remain intubated. The median length of hospitalization was 18.5 days as of May 20, 2020.

The deceased patients were more likely to be older (median age 63) and overweight (median BMI 28.3) (Table 1). As it pertains to risk factors, there was a higher prevalence of hypertension, diabetes, and congestive heart failure in the deceased patients versus patients who remain alive (75%, 50% and 25% vs. 43%, 21% and 0% respectively). At the time of diagnosis of pneumothorax, the deceased patients had higher levels of inflammatory markers (Ferritin, C-reactive protein and Fibrinogen) and white blood cell count. The deceased patients were also more likely to have required ventilator support (62.5% vs. 29%). The patients who remain alive were more likely to have received an interleukin-6 inhibitor, remdesivir or convalescent plasma as compared to the deceased patients (50%, 29%, and 29% vs. 25%, 12.5% and 0% respectively).

The most comprehensive study to date evaluating common radiographic findings associated with COVID-19 reported the incidence of pneumothorax to be 1% (1 out of 99 patients).^{1,2} A few other case reports have presented isolated cases of pneumothorax in the setting of COVID-19.^{3,4} Our case series comprehensively demonstrates this is a potentially crippling complication in COVID-19 patients as evidenced by our mortality rate of 36%, with the potential to be higher given the severity of illness in some of the patients who remain hospitalized in this study. The crude mortality of all patients admitted with COVID-19 pneumonia during this same span of time was 15.8%. The marked inflammatory response, fibrosis, and need for positive pressure ventilation in COVID-19 pneumonia are likely contributory to the development of pneumothorax in these patients. Though

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Table 1
Characteristics of 22 patients with COVID-19 and spontaneous pneumothorax.

Characteristics	Total (N = 22)	Alive (N = 14)	Deceased (N = 8)
Median Age (IQR)- yr	60 (47–67)	59 (39–63)	63 (58–78)
BMI (IQR)	25.4 (21.9–32.1)	23.7 (21.7–30.2)	28.3 (24.3–33.5)
Male Sex- no. (%)	18 (82)	11 (79)	7(88)
Ethnicity			
Hispanic	21(95)	14(100)	7(87.5)
Unavailable	1(5)	0	1 (12.5)
Risk Factors- no. (%)			
Hypertension	12(56)	6(43)	6(75)
Diabetes Mellitus	7(32)	3(21)	4(50)
Smoker	3(14)	2(14)	1(13)
Asthma	3(14)	2(14)	1(12.5)
Chronic Obstructive Pulmonary Disease	1(5)	1(7)	0
Idiopathic Pulmonary Fibrosis	0	0	0
Inflammatory disorder*	4(18)	2(14)	2(25)
Congestive Heart Failure	2(9)	0	2(25)
Malignancy	2(9)	1(7)	1(12.5)
Cirrhosis	2(9)	1(7)	1(12.5)
Home medications- no. (%)			
Aspirin	2(9)	1(7)	1(12.5)
Statin	7(32)	4(18)	3(37.5)
Inhaled Corticosteroids	2(9)	1(7)	1(12.5)
Long Acting Beta Agonists	2(9)	1(7)	1(12.5)
Long Acting Muscarinic Antagonists	2(9)	1(7)	1(12.5)
Montelukast	2(9)	1(7)	1(12.5)
Oral Steroids	3(14)	2(14)	1(12.5)
Admission symptoms- no.(%)			
Cough	7(32)	2(14)	5(62.5)
Shortness of Breath	19(86)	13(93)	6(75)
Fever	9(41)	4(29)	5(62.5)
Chills	1(5)	1(7)	0
Chest tightness	1(5)	0	1(12.5)
Altered Mental Status	1(5)	0	1(12.5)
Median Peak Inflammatory Markers. (IQR)			
Troponin I - ng/ml	0.02 (0.01–0.09)	0.02 (0.01–0.08)	0.03 (0.02–0.10)
D-Dimer – ug/ml	4.0 (3.0–10.5)	4.0 (3.0–10.7)	4.09 (3.1–10.1)
Ferritin – ng/ml	2345 (1031–3361)	2116 (952–5399)	2792 (1431–3178)
C-Reactive protein – mg/dL	28.0 (18.4–36.6)	27.7 (18.2–31.8)	33.5 (22.7–40.8)
Fibrinogen – mg/dL	812 (680–941)	740 (694–904)	873 (666–941)
LDH – U/L	723 (507–1077)	840 (559–1071)	687 (511–891)
Median Inflammatory Markers at time of pneumothorax diagnosis (IQR)			
Troponin- ng/ml	0.01(0.01–0.03)	0.01 (0.01–0.03)	0.02 (0.01–0.07)
D-dimer- ug/ml	2.6 (2.3–3.6)	2.6 (2.1–3.5)	2.9 (2.5–4.9)
Ferritin – mg/dL	1166 (697–2147)	979 (652–1680)	1857 (1222–2588)
C-Reactive protein – mg/dL	11.8(8.0–27.1)	8.7 (2.2–12.1)	27.1 (15.4–34.2)
Fibrinogen – mg/dL	659(559–725)	643 (464–706)	740 (615–866)
LDH – U/L	650 (455– 853)	658 (445–920)	624 (511–681)
Complete Blood Count			
WBC X 10 ³ /uL	7.9 (6.8–10.34)	7.22 (6.1–8.7)	9.9 (8.6–16.3)
Neutrophil- %	85.3 (78.1–88.3)	83.8 (77.2–88.2)	86.4 (82.1–88.8)
Lymphocyte- %	9.6 (5.5–13.8)	12.2 (7.7–14.4)	5.7 (4.7–7.9)
Eosinophil- %	0(0–0.08)	0(0–0.08)	0(0–0.05)
Treatments for COVID-19- no.(%)			
Intravenous Steroids	15(68)	10(71)	5(62.5)
Convalescent Plasma	4(18)	4(29)	0
Interleukin-6 inhibitor	9(41)	7(50)	2(25)
Remdesivir	5(23)	4(29)	1(12.5)
Azithromycin	18(82)	11(79)	7(87.5)
Hydroxychloroquine	9(41)	6(43)	3(37.5)
Antibiotics	12(55)	13(93)	8(100)
Inhaled Nitric Oxide	2(9)	2(14)	0
Veetri	5(23)	3(21)	2(25)
Hospital Day of pneumothorax diagnosis- median no. (IQR)	9(4–15)	7(4–16)	10.5 (4–13)
Indication for imaging- no. (%)			
Worsening Dyspnea	20(91)	13(93)	7(87.5)
Hypoxia	1(5)	0	1(12.5)
Intubation	1(5)	1(7)	0
Imaging modality for diagnosis of pneumothorax- no. (%)			
CXR	22(100)	14(100)	8(100)
CT	0.0	0	0
Respiratory Support at time of diagnosis of pneumothorax- no. (%)			
Nasal Cannula	4(18)	3(21)	1(12.5)
HFNC	5(23)	4(29)	1(12.5)
CPAP	0	0	0
BIPAP	2(9)	1(7)	1(12.5)

(continued)

Table 1 (Continued)

Characteristics	Total (N = 22)	Alive (N = 14)	Deceased (N = 8)
Ventilator	9(41)	4(29)	5(62.5)
ECMO+Ventilator	2(9)	2(14)	0
Treatment strategy- no. (%)			
Close Monitoring	6(27)	4(29)	2(25)
Chest tube placement	16(73)	10(71)	6(75)
Days until resolution	4	5	N/A
Median Duration of hospitalization (days)	18.5	21.5	11

IQR: Interquartile range.

* Inflammatory disorders included rheumatoid arthritis (2), immune-mediated necrotizing dermatomyositis (1) and Sjogren's syndrome (1).

Percentages may not total 100 because of rounding.

The reference values for laboratory markers are listed below:

Troponin I level: <0.05 ng/ml

D-Dimer: <0.7 ug/ml

Ferritin: 4.6 – 204 ng/ml

C-Reactive protein: <0.8 mg/dL

Fibrinogen: 189– 458 mg/dL

Lactic Acid Dehydrogenase: 125–331 U/L

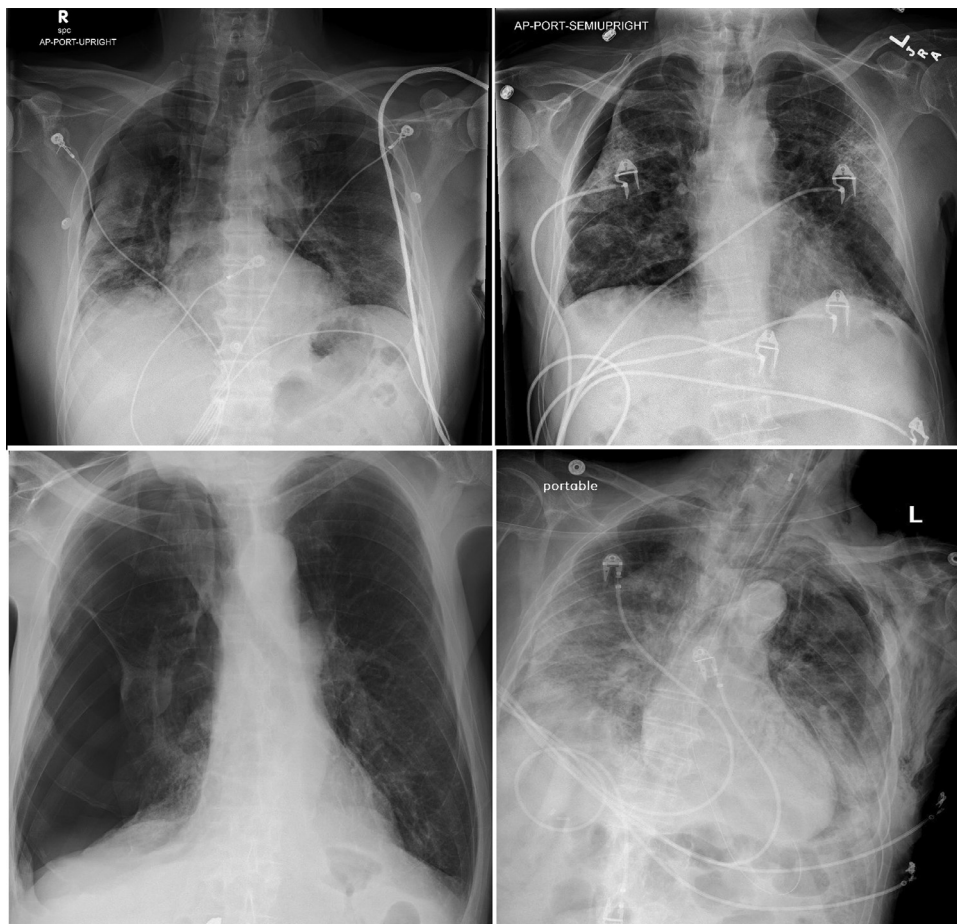


Fig. 1. Chest x-rays of four patients demonstrating pneumothoraces.

classically, pneumothorax is more likely to develop in patients with underlying lung disease, the prevalence of COPD and asthma was only 19% in this study. Additionally, 50% of the patients were not on a ventilator when pneumothorax was diagnosed with 4 patients (18% of the population) only on nasal cannula. This suggests that there are factors uniquely associated with COVID-19 that contribute to the incidence of spontaneous pneumothorax. Additionally, we believe that the development of spontaneous pneumothorax likely reflects the severity of disease which is why the mortality is high in this

cohort. Review of the chest x-rays and CT scans, the latter only obtained in 2 patients, demonstrated variable incidence of cystic and bullous disease (Fig. 2). Cross sectional imaging may be of value in this population as bullous disease may develop rapidly with progression resulting in misplaced chest tubes.

To our knowledge, this is the largest and most comprehensive description of the findings associated with spontaneous pneumothorax in COVID-19. Clinicians should be attuned to the possibility of this complication as it portends a poor prognosis.

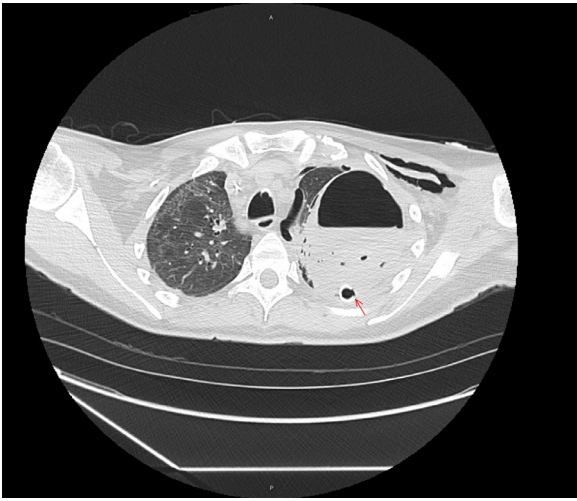


Fig. 2. CT chest without contrast showing small left anterior pneumothorax, pneumomediastinum and large lateral collection of gas and blood within the left chest. A left chest tube is present with tip at the posterior left lung apex.

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Declaration of Competing Interest

None.

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