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Primary Pneumothorax and Subcutaneous Emphysema in COVID-19 Disease: A Case Series

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ABSTRACT

Spontaneous pneumothorax is one of the rare complications associated with COVID-19 viral pneumonia, and its exact mechanisms are still unknown. Most often this complication occurs in the setting of mechanical ventilation. This case series reports seven patients with the first presentations of spontaneous pneumothoraxes developing in the absence of mechanical ventilation.

This case series study presents seven cases of COVID-19 with a positive COVID-19 PCR test result. A few days had passed from the onset of symptoms, and they had severe pulmonary involvement and high inflammatory markers. The patients received treatment for COVID-19; however, they developed hydropneumothorax and subcutaneous emphysema before being hospitalized or on the first day of hospitalization. A ventilator was used in the case of some patients. The mortality rate was high among these patients.

These cases confirm the hypothesis that unusual manifestations of COVID-19 can lead to life-threatening conditions. Therefore, the diagnosis and treatment of these special COVID-19 cases are highly important.

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Introduction

COVID-19 is an infectious disease and a global pandemic that has spread widely in Iran. Most viral mutations of this virus do not seem to affect its ability to cause severe symptoms; however, evidence from Britain showed that the symptoms of the disease have been more severe in some variants of COVID-19, particularly the Delta variant (1).

Pneumothorax can develop primarily in people without overt clinical lung disease or secondary to underlying lung disease. Pneumothorax has been reported as an uncommon manifestation of COVID-19 disease (2, 3). In studies conducted before the spread of new variants of COVID-19, the rate

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of pneumothorax in patients with COVID-19 has been reported to be very low and between 1% and 1.1%. A lower prevalence of 0.66% has also been reported (4, 5). Other complications, such as giant bulla, mediastinal emphysema, pneumomediastinum, subcutaneous emphysema, and cystic features were also reported in the severe cases of the disease (6-8). In all cases, pneumothorax has been associated with a worse prognosis and higher mortality (9). This study reported the highest mortality due to pneumothorax in COVID-19 patients five days after the first presentation (5).

Structural changes in terms of primary pneumothorax in severe cases of COVID-19 patients can be attributed to changes in the lung parenchyma that occur due to the direct effect of the virus on target cells, including lung cells, or to indirect damage caused by immune system stimulation and abnormal immune response related to the COVID-19 (2). Other causes of pneumothorax in COVID-19 patients include prolonged cough and the use of mechanical ventilators (3, 6-8, 10). In this study, we report COVID-19 patients with primary pneumothorax and present their experimental and radiological data.

Case reports

Case 1

A 66-year-old man without a history of underlying lung disease and smoking presented with a 10-day history of shortness of breath without cough. The patient's vital signs were stable, but he required an oxygen mask due to low oxygen saturation (70%). The nasopharyngeal swab test result for SARS CoV-2 was positive. The chest CT scan showed extensive bilateral consolidative and patchy ground-glass opacities and consolidations in a peripheral distribution (score 17/24) with large pneumothorax on the left. His laboratory findings illustrated lymphopenia along with elevated inflammatory markers, such as lactate dehydrogenase (LDH), C-reactive protein (CRP), and D-dimer. A chest tube was placed, and the patient received antibiotics, corticosteroids, remdesivir, selenium, vitamin C, and tocilizumab. His pneumothorax resolved within 6 days and the chest tube was disconnected. This patient was finally discharged in good general condition two weeks after hospitalization.

Case2

A 49-year-old man with prior history of smoking four pack -year without a history of other underlying diseases presented with 10 days' weakness and three days' history of shortness of breath without cough. There was evidence of neck swelling and subcutaneous emphysema. The nasopharyngeal swab test result for SARS CoV-2 turned positive. The laboratory findings revealed elevated inflammatory markers. His chest CT scan showed a moderate pneumothorax on the right, as well as bilateral multifocal ground glass and consolidative opacities in a peripheral distribution (score: 24/24). Extensive subcutaneous emphysema was observed in the soft tissue of the thorax, preferably anteriorly extending to the neck. He was hypoxic (oxygen saturation of 70%) needing non-invasive ventilation (NIV) upon admission. At his own request, the patient received oxygen through an oxygen mask on the first day of hospitalization, but later he accepted to use bilevel positive airway pressure (BIPAP). He received broad-spectrum antibiotics, high-dose corticosteroids, remdesivir, and tocilizumab. A chest tube was placed and was removed seven days following the resolution of the pneumothorax. After a few days, the patient's oxygen saturation decreased again. However, the patient's shortness of breath gradually improved to some extent, and vital signs were stabilized. The patient was discharged four weeks after hospitalization.

Case 3

An 81-year-old man referred with prior history of prostate cancer for the past year, diabetes, and hypertension. He had been hospitalized for 5 days due to COVID-19 three weeks before recent hospitalization and had received corticosteroids, remdesivir, and tocilizumab. After three weeks, he presented with shortness of breath (oxygen saturation of 55%) and loss of consciousness. Due to positive PCR for SARS CoV-2, he was admitted to COVID-19 ICU. A portable chest x-ray (CXR) revealed pneumothorax. Subsequently, a chest tube was inserted. The laboratory findings indicated lymphopenia and mildly elevated inflammatory markers.

The extensive fibrotic lesions in both lungs and large pneumothorax were observed in the chest CT scan. He was treated with antibiotics, corticosteroids, and voriconazole. Although the patient's oxygen saturation reached 85% after intubation and using mechanical ventilation, he gradually developed acute kidney injury (AKI) and expired eventually.

Case 4

47-year-old heavy smoker male referred with cough and shortness of breath. He became symptomatic two weeks prior to referring to the hospital. His COVID-19 PCR swab test result turned positive. His chest CT scan taken one week before admission demonstrated bilateral multifocal ground-glass opacities in a peripheral distribution (score: 10/24). Outpatient treatment with enoxaparin, remdesivir, and dexamethasone was started. However, the patient's shortness of breath gradually worsened despite receiving the medication. On admission, the patient was hypoxic with SpO2 of 80% requiring oxygen via NIV (BIPAP). Initial blood work revealed lymphopenia and elevated Di-dimer. The following day, his hospital course was complicated by worsening hypoxia and a decrease in the level of consciousness, necessitating invasive mechanical ventilation. Chest CT scan suggested bilateral multifocal ground glass and consolidation opacities in the peripheral lung field with a confluent view (peak phase) (score: 22/24) and mild bilateral pneumothorax and pneumomediastinum in medial anterior and posterior mediastinum. The patient was treated with corticosteroids, antibiotics, statin, and prophylactic anticoagulant. Based on surgical consultation, a chest tube was not required. He developed bradycardia and multi-organ failure two days later and died.

Case 5

A 39-year-old male without any previous underlying problems presented and reported that he had been suffering from COVID-19 symptoms from one week before hospitalization. He was admitted to the hospital due to shortness of breath and low oxygen saturation (85%). Chest CT scan demonstrated pneumopericardium, pneumomediastinum, and subcutaneous emphysema in the right thorax and thoracic muscles and mild bilateral pneumothorax in the medial anterior. Bilateral multifocal ground glass and consolidation opacities were observed in the peripheral lung (score: 18/24). A chest tube was inserted on the hospitalization day. The patient was treated with remdesivir, followed by broad-spectrum antibiotics (meropenem, vancomycin, and ciprofloxacin) and high-dose corticosteroids (three doses of 500 mg methylprednisolone followed by dexamethasone). Anticoagulation with a prophylactic dose was first prescribed followed by caspofungin. Lung CT angiography showed no evidence of embolism in the main and lobar arteries, but the lung involvement score was estimated to be 23 out of 24. The chest tube was disconnected nine days later. However, the patient's oxygen saturation decreased to 81% two days later and the chest tube was implanted again. The patient was intubated and ventilated with a ventilator. Unfortunately, the patient expired in the ICU after two days.

Case 6

A 45 years old male presented with fever and myalgia that had started 10 days earlier. Gradually, he developed shortness of breath. His COVID-19 PCR swab was positive, and he was admitted to the hospital. On the 8th day of hospitalization, his oxygen saturation dropped to 74%. A high-resolution chest CT scan (HRCT) confirmed moderate pneumothorax plus extensive subcutaneous emphysema in the soft tissue of the anterior thorax, pneumopericardium, pneumomediastinum, and extensive bilateral multifocal consolidation, and ground-glass opacities (score: 20/24). The patient was treated with corticosteroids in high doses (methylprednisone 500 mg for three days), antibiotics, and remdesivir. The chest tube was implanted .

Three days later, due to low oxygen saturation of about 65% and failure to respond to non-invasive oxygenation with BIPAP, the patient was intubated and connected to a ventilator. Unfortunately, the patient died three days later.

Case7

A 67-year-old male without previous history of diabetes, hypertension, and smoking presented with seven days history of fatigue, cough, and shortness of breath. The nasopharyngeal swab detected SARS-CoV-2. He was admitted to a hospital and was discharged after four days from that center. After three days of rest at home, he presented with shortness of breath, hypoxic, and cervical and thorax emphysema indicating the need for an oxygen mask. He was admitted to our tertiary teaching hospital and reported no history of neck trauma, intubation, or recurrent severe coughing. Computed tomography (CT) of the lung indicated evidence of extensive subcutaneous emphysema in the soft tissue of the thorax and neck and mild pneumothorax on both sides and diffuse large areas of mixed patchy ground-glass consolidation in the peripheral lung regions (lung involvement score: 22/24). He was treated with antibiotics (ceftriaxone), corticosteroids (dexamethasone), and mask oxygenation. Due to the limited amount of pneumothorax, the chest tube was not implanted. He was discharged after five days of hospitalization in good general condition with oxygen saturation of 95% and an improved emphysema.

The laboratory data of the seven cases are presented in Table 1, and the history and related risk factors are tabulated in Table 2. Figure 1 presents the diagnostic images of the presented cases.

Discussion

The presentation of COVID-19 disease may be asymptomatic or associated with a range of life-threatening symptoms. The COVID-19 disease is mostly presented with pulmonary manifestations that may lead to acute respiratory distress syndrome (ARDS). The most characteristic findings in the chest CT scan of COVID-19 patients include consolidated, ground-glass opacities, and septa thickening. In the late stages of lung involvement in the COVID-19 patents, fibrotic changes can occur (5, 11).

Table 1. Laboratory data related to the presented cases.

Variable	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6	Case 7
WBC (T/Cumm)	10.5	10.2	12.1	14	13	5.2	17.3
Lymphocyte (%)	5.9	8	4	4	3.1	4.1	5.9
Neutrophils (%)	89	90	91	92	93.5	89	90.2
Hemoglobin (g/dL)	16.4	17	12.3	16.8	18.5	14.9	13.4
platelet (ng/mL)	255	303	124	340	200	144	588
LDH (units/L)	1666	1470	997	777	1123	2314	
CRP (IU/mL)	34	64.1	1.3	101	11.5	120	47.5
ESR (mm/h)	38		51	58	40	83	74
AST (IU/L)	90	46	20	30	34	182	36
Alt (IU/L)	53	35	31	65	38	130	31
ALP (U/L)					112	285	243
Urea (mg/dL)	66	46	185	36	75	69	39
Creatinine (mg/dL)	1.1	0.9	71	0.6	0.9	1.5	0.9
Procalcitonin ng/mL	0.08	0.07	1.6	-			0.03
D-dimer (ng/mL)	9760	250	-	2560	370		822
Ferritin (µg/L)		>1000	-	-		807	

Abbreviations: WBC: White blood cell, **PLT:** platelet, **ESR:** Erythrocyte sedimentation rate, **CRP:** C-reactive protein, **LDH:** lactate dehydrogenase, **AST:** Aspartate aminotransferase, **ALT:** Alanine aminotransferase, **ALP:** Alkaline phosphatase.

Based on the evidence, some patients with a severe type of the disease experience complications such as pneumothorax, mediastinal emphysema (pneumomediastinum), and subcutaneous emphysema (3, 6-8, 12-14). Along with the use of mechanical ventilators due to respiratory failure, changes in lung parenchyma can put patients at risk of developing pneumothorax (11).

Although the definite mechanism of pneumomediastinum and pneumothorax in COVID-19 patients is unknown, evidence from previous studies suggests that the most common cause of pneumothorax in patients with COVID-19 is secondary to barotrauma, such as the use of mechanical ventilators (15). The rate of pneumothorax in ARDS patients in need of mechanical ventilation is high, especially if it lasts more than two weeks (15).

Table 2: Imaging data and related risk factor of the presented cases.

Patient	Gender/ Age (years)	Lung involvement score based on CT scan	Risk factor for PTX	Time to onset (days)	PTX Size	Chest tube	Outcomes
Case1	M/66	17/24	None	10	Large PTX	Yes	Survived
Case2	M/49	24/24	Smoking	11	Moderate PTX, Extensive subcutaneous emphysema in the soft tissue	Yes	Survived
Case 3	M/77	17/24 Extensive fibrotic lesions in both lungs	Previous COVID-19 three weeks earlier, History of mechanical ventilator	21	Large PTX	No	Died
Case4	M/47	22/24	Heavy smoker	14	Small PTX, Pneumomediastinum	No	Died
Case 5		18/24	No		Small PTX, Subcutaneous emphysema in the thorax andn pneumopericardium	Yes	Died
Case 6		20/24	No		Moderate PTX, Extensive subcutaneous emphysema in the anterior and left side of the thorax	Yes	Died
Case 7	M/67	22/24	Cough	7	Mild PTX on both sides, Extensive pneumomediastinum, Subcutaneous emphysema in the thorax and neck	No	Survived

PTX: Pneumothorax, pulmonary involvement scores based on the amount of patchy ground glass and consolidation opacities (max score: 24).

In the present study, we identified seven COVID-19 patients who developed spontaneous pneumothorax, pneumomediastinum, as well as subcutaneous emphysema during the course of the disease. They were not ventilated mechanically before hospital admission. In some cases, pneumothorax was the first presentation of the disease in the hospital. Even mild cases of pneumothorax in these patients progressed rapidly to severe pneumothorax. It was also found that patients with spontaneous progression of pneumothorax can develop subcutaneous emphysema. Previous studies reported only six COVID-19 cases with spontaneous pneumomediastinum and pneumothorax in China and Spain (3,8,10,12).

Despite the unknown cause of pneumothorax in COVID-19 patients, it seems that in these patients, alveolar injury due to the direct and indirect effects of COVID-19 is the main cause of pneumothorax. Subcutaneous emphysema and pneumomediastinum occur as a result of air leakage through the interstitial space, particularly when intrathoracic pressure increases in conditions such as coughing (12). Although pneumothorax can occur any time during the disease, in all seven cases, pneumothorax developed at beginning of the disease and was associated with higher mortality.

Pneumothorax and pneumomediastinum are among uncommon manifestations of COVID-19 disease which seem to have been increasing due to the appearance of new variants. In the absence of a mechanical ventilator and due to severe lung involvement, we witnessed the occurrence of pneumothorax and pneumomediastinum in the reported cases. We observed that even mild cases can progress rapidly; therefore, it is necessary to consider these complications in the COVID-19 patients in terms of diagnosis and treatment. Moreover, it is recommended that the COVID-19 patients should be closely monitored for these pulmonary complications as a potential indicator of worsening disease.

Ethical Approval

The present case series has been approved by the Ethics Committee at Mashhad University of Medical Sciences (IR.MUMS.REC). Informed consent was obtained from the patients or their guardians.

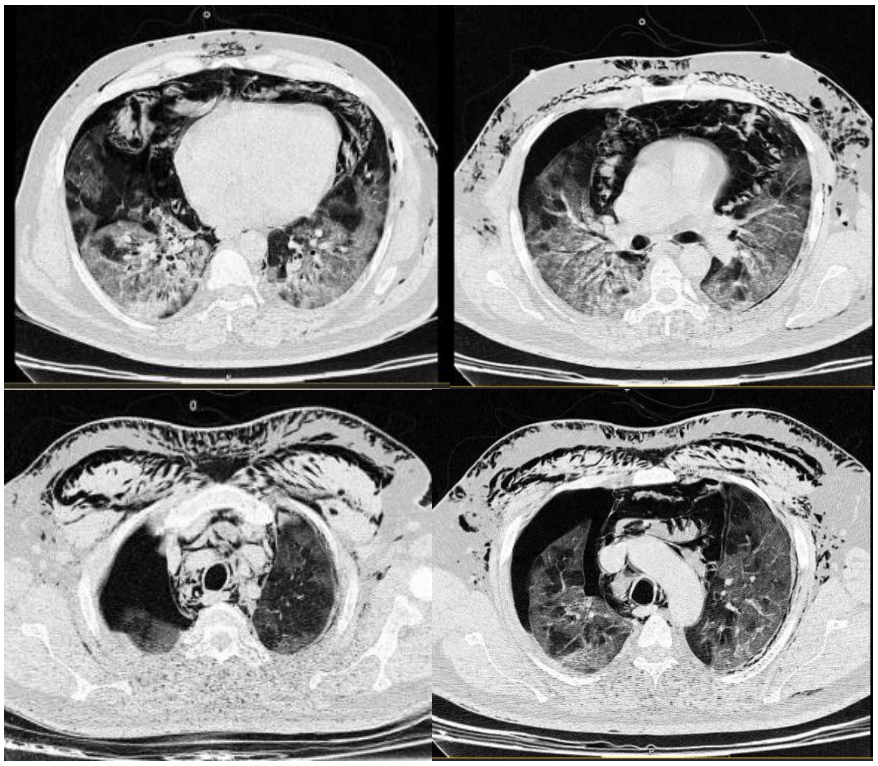

Figure 1. Baseline chest CT scan of the cases.

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