Journal of Medical Imaging & Case Reports

https://doi.org/10.17756/micr.2021-065

Case Report

Open Access

Isolated Spontaneous Pneumomediastinum in COVID-19 Patients: Case Series and Review of the Literature

Iris E. Chen*, Antoinette Roth, Mariam Thomas and Anokh Pahwa

Department of Radiological Sciences, Olive View - UCLA Medical Center, Sylmar, CA, USA

***Correspondence to:**
Dr. Iris E. Chen, MD
Department of Radiological Sciences
Olive View - UCLA Medical Center
Sylmar, CA, USA.
Tel: (310) 267-8797
E-mail: iechen@mednet.ucla.edu

Received: February 17, 2021
Accepted: March 15, 2021
Published: March 17, 2021

Citation: Chen IE, Roth A, Thomas M, Pahwa A. 2021. Isolated Spontaneous Pneumomediastinum in COVID-19 Patients: Case Series and Review of the Literature. *J Med Imaging Case Rep* 5(1): 15-21.

Copyright: © 2021 Chen et al. This is an Open Access article distributed under the terms of the Creative Commons Attribution 4.0 International License (CC-BY) (http://creativecommons.org/licenses/by/4.0/) which permits commercial use, including reproduction, adaptation, and distribution of the article provided the original author and source are credited.

Published by United Scientific Group

Abstract

While isolated spontaneous pneumomediastinum (SPM) is not commonly associated with viral respiratory infections, several cases of isolated SPM in the context of coronavirus disease 2019 (COVID-19) have emerged. Isolated SPM remains seldom presented in the current literature. We will present the clinical presentation and hospital course of isolated SPM in four patients hospitalized with COVID-19 who were not on mechanical ventilation. We will also review all cases from the current literature and compare these cases for similarities and possible patterns that may help elucidate risk factors for developing SPM. Increased use of high-flow oxygen in COVID-19 management may be a potential contributing factor to the SPM development. Isolated SPM can be an indicator of disease severity and worse prognosis.

Keywords

Coronavirus, ARDS, Spontaneous pneumomediastinum, COVID-19 complication

List of abbreviations

SPM: Spontaneous Pneumomediastinum; **COVID-19:** Coronavirus Disease 2019; **SARS-CoV-2:** Severe Acute Respiratory Syndrome Coronavirus 2; **CXR:** Chest Radiograph; **CT:** Computed Tomography; **NRB:** Non-Rebreather; **HFNC:** High Flow Nasal Cannula; **PEA:** Pulseless Electrical Activity

Introduction

Isolated spontaneous pneumomediastinum (SPM) is defined as air within the mediastinal space and is typically seen in the context of trauma, esophageal perforation, smoking, lung disease, and positive pressure from mechanical ventilation. Isolated SPM is not commonly associated with viral respiratory infections, and while many pulmonary and extra pulmonary manifestations of been described for coronavirus disease 2019 (COVID-19), cases of isolated SPM in the context of COVID-19 have rarely been presented in current literature. We present four cases of SPM in patients who were not on mechanical ventilation from April 2020 to February 2021 and review the current literature.

Patients who received previous mechanical ventilation or developed concurrent pneumothorax were excluded. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) diagnosis was defined by a positive test on reverse-transcriptase polymerase chain reaction assay. A subsequent literature review was performed

for SPM in patients with COVID-19. Data for each patient was collected – including age, sex, risk factors, presenting symptoms, treatment received, imaging findings, and ultimate outcome – and analyzed for similarities and patterns.

A total of 41 cases including four patients from our institution were included in our data analysis (Table 1). There were 28 males, 9 females, and 4 not specified. The patient age range was 17 to 82 years, with a mean of 55.2 years and median of 58 years. Comorbidities reported included hypertension (n = 7, 17.1%), hyperlipidemia (n = 3, 7.3%), diabetes mellitus (n = 7, 17.1%), and obesity (n = 2, 4.9%). Three out of 41 (7.3%) of the patients were reported to have preexisting lung disease, which included emphysema and asthma. The presenting symptoms of patients included cough (n = 33), fever (n = 23), dyspnea (n = 29), myalgia (n = 11), and diarrhea (n = 3). Management during the hospital course was reported in 16 cases and included corticosteroids (n = 19), antibiotics (n = 23), and tocilizumab (n = 6). Eight out of 40 (20%) of the patients were not treated with any supplemental oxygen prior to developing SPM. Eight out of 41 (19.5%) of the patients were found to have concurrent pneumopericardium, and 15 out of the 41 (36.6%) of the patients had concurrent subcutaneous emphysema. The mean number of inpatient days prior to the discovery of SPM was 9.7 days. The outcome included death (n = 8), improved (n = 21), worsened (n = 1), or not specified (n = 11).

Case Report

Case 1

A 67-year-old male without prior lung disease presented to our institution's emergency department with myalgia and fatigue for 3 days. His medical history was significant for hypertension and hyperlipidemia. He has a history of alcohol and tobacco use, but had quit both about 5 years ago.

In the emergency department, he was found to be hypoxic to 77% on room air. He was also tachypneic at 33 respirations per minute and tachycardic at 109 beats per minute. Physical exam demonstrated clear breath sounds bilaterally. A point-of-care ultrasound demonstrated diffuse B lines, normal ejection fraction, a hyperdynamic heart, and no pericardial effusion. He was confirmed to be positive for SARS-CoV-2 and admitted to our in-patient floor.

He was treated with antibiotics, corticosteroids, prophylactic anticoagulation, and remdesivir. He was placed on supplemental oxygen, initially on 15 L non-rebreather (NRB). During his hospitalization, he continued to have an increased need for oxygen and required 15 L NRB and 60 L high flow nasal cannula (HFNC). On day 10 of his hospitalization, he developed worsening dyspnea despite maximum non-invasive oxygen support, and new leukocytosis and fever. A CXR was ordered and demonstrated SPM and subcutaneous emphysema without pneumopericardium or pneumothorax. He continued to receive supplemental oxygen with NRB and HFNC. Two days later, he had an episode of bradycardia with pulseless electrical activity (PEA) with hypoxia. Code blue was called and he received 4 rounds of cardiopulmonary resuscitation and epinephrine with return of spontaneous circulation. He was intubated at that time and escalated to the intensive care unit. He died on day 13 of hospitalization.

Case 2

A 52-year-old male without prior lung disease presented to our institution's emergency department with cough, dyspnea, myalgia, and diarrhea for 10 days. His medical history was significant for diabetes mellitus. He denied tobacco, alcohol, or recreational drug use. He works as a frontline healthcare worker and had multiple high-risk exposures to SARS-CoV-2. Of note, he had presented to the emergency department five days prior with cough, fever, chills, chest pain, and fatigue. At that time, he was found to be negative for SARS-CoV-2 and had a negative CXR (Figure 1). Because he was stable on room air, he was discharged home.

He was found to be mildly hypoxic at 93% on room air. He was also tachypneic at 30 respirations per minute, afebrile, normotensive, and with normal heart rate. Physical exam demonstrated decreased air movement, coarse breath sounds, rhonchi bilaterally, and crackles at the left lung base without wheezing. He was confirmed to be positive for SARS-CoV-2 and admitted to our in-patient floor.

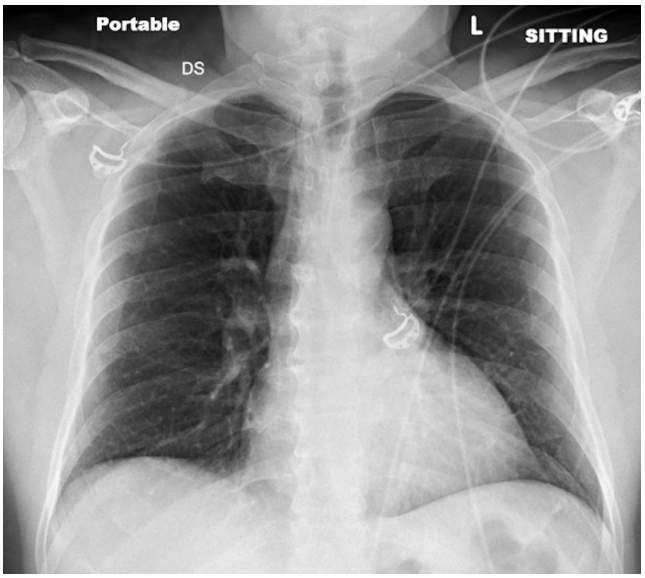

Figure 1: CXR of a 52-year-old male with a negative SARS-CoV-2 test demonstrated clear lungs. There was no SPM or pneumothorax.

During his hospitalization, he was treated with antibiotics, corticosteroids, prophylactic anticoagulation, and remdesivir. Initially, he was placed on 10 L simple face mask but had desaturations in high 80s and was transitioned to HFNC. Because he continued to require increased oxygen, he was admitted to the ICU on the day 2 of hospitalization, at which time he was placed on 60 L HFNC with NRB. On day 3 of hospitalization, he developed worsening dyspnea. A CXR was ordered which showed SPM and subcutaneous emphysema without pneumopericardium or pneumothorax (Figure

1). He continued to receive consistent respiratory therapy and was gradually weaned off supplemental oxygen. When he was able to ambulate without dyspnea, he was discharged on day 16 of hospitalization.

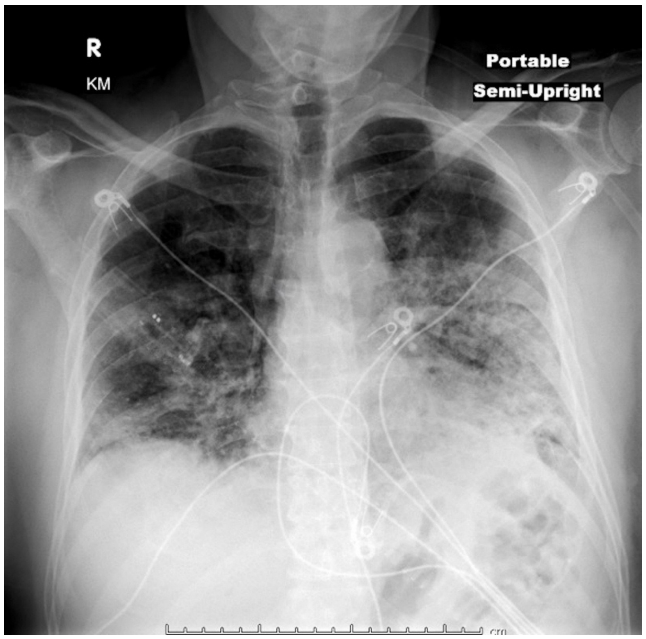

Figure 2: CXR of the same patient that was subsequently admitted with COVID-19 five days later demonstrated lucency along the left heart border and along the right paratracheal stripe, consistent with SPM. Also note diffuse peripheral-predominant interstitial and airspace disease throughout both lungs, consistent with known history of COVID-19.

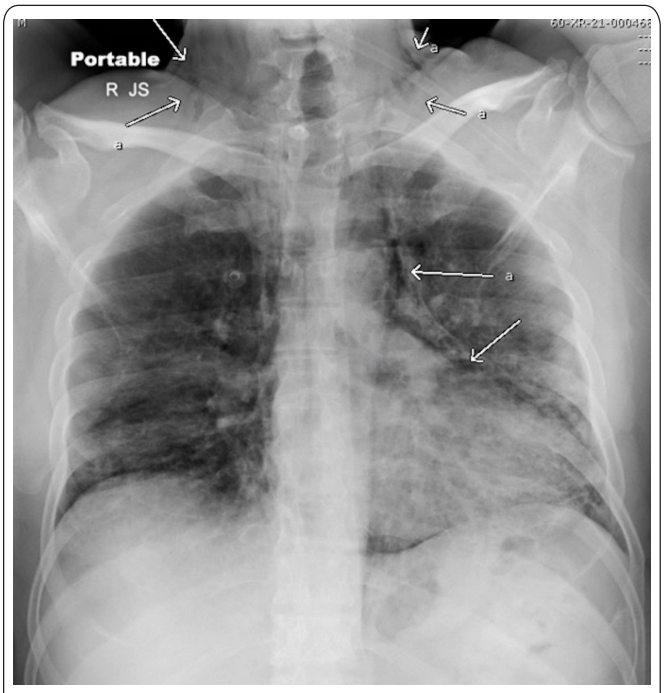

Figure 3: CXR of the same patient four days later demonstrates increased conspicuity of the SPM, along with development of extensive air within the subcutaneous soft tissues of the right neck, consistent with subcutaneous emphysema. No pneumothorax is visualized.

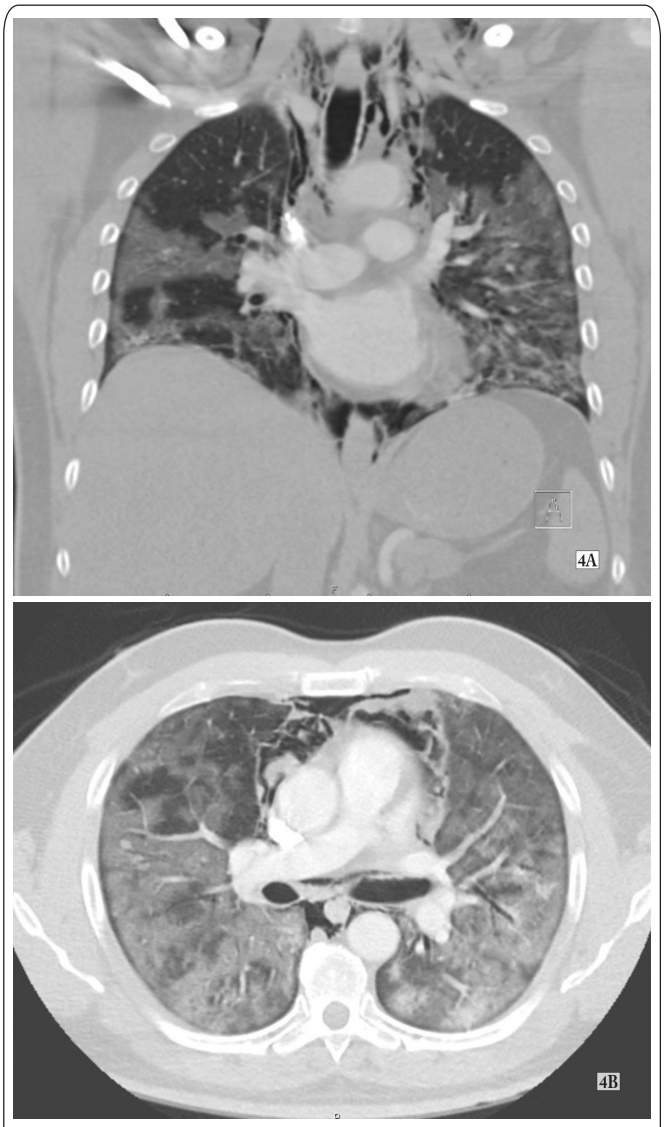

Figure 4: A: Coronal and **B:** Axial CT images of the same patient demonstrate extensive SPM with gas tracking into the neck base. There are also extensive peripheral and basilar predominant geographic pulmonary ground-glass opacities and multifocal consolidations.

Case 3

A 59-year-old female with history of asthma presented to our institution's emergency department with dyspnea, productive cough, chest pain, fever, and diarrhea. Her medical history was significant for hypertension and multiple myeloma currently on chemotherapy. She had a history of smoking (1 pack-year) and quit 30 years ago. She also had a history of alcohol (6-pack on special occasions) and quit 25 years ago. She denied any recreational drug use. Of note, she had recently presented to our institution five days ago with dyspnea requiring NC oxygen supplementation due to COVID-19 and was discharged to home on dexamethasone. At that time, her CXR did not show pneumomediastinum.

In the emergency department, she was found to be hypoxic at 50% on room air, which improved to 96% on 50 L

HFNC. She had a fever of 38.7 degrees Celsius that corrected with acetaminophen. She was also tachypneic at 24 respirations per minute, normotensive, and with normal heart rate. Physical exam demonstrated crackles at the right greater than left lung bases. She was confirmed to be positive for SARS-CoV-2 and admitted to our in-patient floor.

She was treated with corticosteroids, prophylactic anticoagulation, and remdesivir. A CXR was ordered which showed SPM without pneumopericardium, pneumothorax, or subcutaneous emphysema. Initially, she was placed on HFNC but had desaturations and was subsequently transitioned to BIPAP. On day 7 of hospitalization, she had acutely increased work of breathing and was tachycardic. A rapid response was called, and she was intubated and admitted to the ICU. She died on day 16 of hospitalization.

Case 4

A 50-year-old female without history of prior lung disease presented to our institution's emergency department with worsening dyspnea, productive cough, fever, and nausea. She states that she tested positive 3 days prior at an outside hospital and was discharged to home without oxygen after receiving steroids. Her medical history was significant for hypertension, hyperlipidemia, obesity, diabetes, and chronic kidney disease. She denied history of smoking, alcohol, or recreational drug use.

In the emergency department, her oxygen status was 96% on 15L of NRB. She was also found to be breathing at 19 respirations per minute, afebrile, normotensive, and with normal heart rate. Physical exam demonstrated clear breath sounds. She was confirmed to be positive for SARS-CoV-2 and admitted to our in-patient floor.

During her hospitalization, she was treated with corticosteroids, prophylactic anticoagulation, and antibiotics. She did not receive remdesivir or plasma therapy since she was outside the therapeutic window. Her respiratory status declined, and she required 60 L HFNC and 15 L NRB non-invasive oxygen supplementation, including. On day seven of hospitalization, she endorsed chest pain and a CXR was ordered, which showed SPM without pneumopericardium, pneumothorax, or subcutaneous emphysema. Later that same day, she had acutely increased work of breathing and had desaturations on HFNC and NRB. A rapid response was called, and she was intubated and admitted to the ICU. She died on day 31 of hospitalization.

Discussion

The mechanism for SPM is thought to be related to alveolar rupture and interstitial emphysema from diffuse alveolar damage, causing extrapulmonary air to dissect along the perivascular and peribronchial connective tissue sheaths into the mediastinum, described as the Macklin effect [1, 2]. Increased alveolar pressure and subsequent alveolar rupture can be attributed to coughing, which was present in most of the cases of SPM from the literature. Age-associated diminished lung function resulting in decreased lung elastic recoil may also increase risk of alveolar rupture [3]. The higher mean age we found in the literature may reflect the increased incidence of SPM in an older population associated with decreased lung elastic recoil. However, the patients with isolated SPM in the setting of COVID-19 were as young as 17 years old.

Additionally, all four of the patients in our institution were receiving significant flows of oxygen at 50-60 L of HFNC with some amount of NRB prior to being diagnosed with SPM. The significant level of high flow oxygen supplementation is now more prevalent in COVID-19 treatment to reduce the need for invasive ventilation and escalation of treatment [4, 5]. This is particularly useful in patients for whom tracheal intubation is not yet necessary but low-flow nasal oxygen or facemask oxygen is inadequate [4, 5]. The use of high-flow oxygen may be a potential contributing factor to development of SPM.

Previous studies have shown that isolated SPM can often occur in patients without a smoking history, without previous history of lung disease, and in the absence of positive pressure ventilation [6]. This was congruent with our findings, as the majority of the patients from the literature did not have any comorbidities, and only 7.3% of the patients were reported to have preexisting lung disease. Only one of the patients at our institution had preexisting lung disease. There were more male patients who developed isolated SPM than female patients.

Clinical manifestations of SPM can include retrosternal chest pain exacerbated by deep breathing and coughing, progressive dyspnea, dysphagia, or neck pain, although the patient may also be asymptomatic [7, 8]. All of the patients at our institution were in respiratory distress with an increased need for oxygen supplementation, which prompted the need for additional chest imaging. Physical examination may demonstrate crepitations in the cervical region on auscultation (Hamman's sign) and palpation [9], particularly when there is concurrent subcutaneous emphysema. Vital signs may indicate tachycardia, tachypnea, or hypotension. SPM can be best visualized on imaging on chest computed tomography (CT), although can be seen on chest radiograph (CXR) with lower sensitivity as well [10]. All of the patients at our institution were initially diagnosed with SPM on radiograph.

Management for isolated SPM is nonspecific and generally involves symptomatic treatment [6]. Oxygen therapy has been described to increase the resorption of free air in the mediastinum secondary to a higher nitrogen concentration. Continued treatment for COVID-19 is also essential as the virus may continue to damage type II pneumocytes in the lungs and subsequently damage alveolar membranes [11]. All of the patients in our institution received oxygen supplementation for their increased respiratory distress, including intubation in three out of four of our patients after having developed SPM.

While SPM is often benign and self-limiting, fatal complications such as tension pneumothorax and cardiac tamponade can occur [12]. These complications may result in cardiopulmonary compromise and subsequently require invasive interventions. Typically, in isolated SPM without secondary

Table 1: Comprehensive summary of patients with SARS-CoV-2 and isolated SPM (3, 6-8, 10, 11, 13-15, 20-30).

Study	Age (years)	Sex	Comorbidities	Cough	Fever	Dyspnea	Myalgia	Diarrhea	Steroids	Antibiotics	Tocilizumab	Oxygen	PM	PP	PTX	SE	Inpatient days before event	Outcome
Current Study	67	M	HTN, HLD	N	N	N	Y	N	Y	Y	N	NRB	Y	N	N	Y	10	Died
Current Study	52	M	DM	Y	N	Y	Y	Y	Y	Y	N	NC	Y	N	N	Y	3	Discharged
Current Study	59	F	HTN, asthma	Y	Y	Y	N	Y	Y	N	N	NC	Y	N	N	N	0	Died
Current Study	50	F	HTN, HLD, DM, obesity, CKD	Y	Y	Y	N	N	Y	Y	N	NRB, NC	Y	N	N	Y	7	Died
Advances in Respiratory Medicine 2020	80	M	U	Y	Y	Y	U	U	Y	Y	U	Noninvasive	Y	N	N	Y	U	Discharged
American Journal of Emergency Medicine 2020	52	M	None	Y	Y	Y	U	U	U	Y	U	U	Y	N	N	N	0	Discharged
Archivos de Bronconeumologia 2020 [20]	65	F	No smoking	Y	Y	Y	N	U	N	Y	N	NRB, NC	Y	N	N	N	20	Improved
Archivos de Bronconeumologia 2020 [20]	60	F	No smoking	Y	N	Y	N	U	Y	N	Y	NRB, NC	Y	N	N	N	12	Worsening
Archivos de Bronconeumologia 2020 [20]	62	M	No smoking	Y	Y	N	Y	U	N	Y	Y	NRB, NC	Y	N	N	N	19	Improved
Archivos de Bronconeumologia 2020 [20]	58	M	No smoking	Y	Y	Y	N	U	Y	Y	N	NRB, NC	Y	N	N	N	18	Improved
Archivos de Bronconeumologia 2020 [21]	48	M	No lung disease	Y	Y	Y	Y	N	Y	Y	Y	U	Y	Y	N	N	11	Discharged
Archivos de Bronconeumologia 2020 [21]	36	M	No lung disease	U	U	U	U	U	U	U	U	U	Y	Y	N	N	18	Discharged
Archivos de Bronconeumologia 2020 [21]	46	M	No lung disease	U	U	U	U	U	U	U	U	U	Y	Y	N	Y	1	Died
Archivos de Bronconeumologia 2020 [21]	75	F	No lung disease	Y	Y	Y	Y	N	Y	Y	N	U	Y	Y	N	Y	5	Died
Archivos de Bronconeumologia 2020 [21]	62	M	No lung disease	Y	Y	Y	Y	N	Y	Y	N	U	Y	Y	N	N	11	Discharged
Archivos de Bronconeumologia 2020 [21]	58	M	No lung disease	Y	Y	Y	Y	N	Y	Y	N	U	Y	Y	N	N	4	Discharged
Archivos de Bronconeumologia 2020 [21]	57	F	No lung disease	Y	Y	Y	Y	N	Y	Y	N	U	Y	Y	N	N	17	Died
British Journal of Radiology Case Reports 2020	17	M	None	Y	N	Y	U	U	U	U	U	U	Y	N	N	N	0	U
British Medical Journal Case Reports 2020	49	M	HTN, DM	Y	N	Y	U	U	Y	Y	U	NC	Y	N	N	Y	5	Discharged
Case Reports in Medicine 2020	65	M	None	Y	Y	Y	Y	U	U	Y	Y	NRB	Y	N	N	N	16	Discharged
Chest 2020	63	M	HTN, HLD, DM	U	Y	Y	U	U	U	Y	U	N	Y	U	N	Y	0	Died
Clinical Imaging 2020	82	M	U	Y	Y	Y	U	U	U	U	U	NC	Y	U	N	N	18	U
Clinical Imaging 2020	38	M	U	N	N	U	U	U	U	U	U	N	Y	U	N	Y	3	U
Clinical Imaging 2020	72	M	U	Y	N	Y	U	U	U	U	U	NC	Y	U	N	Y	14	U
Clinical Imaging 2020	60	M	U	Y	N	Y	U	U	U	U	U	CPAP	Y	U	N	N	16	U
Clinical Imaging 2020	38	M	U	Y	Y	Y	U	U	U	U	U	NRB	Y	U	N	N	15	U
Clinical Imaging 2020	57	F	U	Y	N	Y	U	U	U	U	U	BPAP	Y	U	N	N	14	U
Clinical Medicine Journal 2020	64	M	DM, OSA	U	U	U	U	U	U	U	U	NC	Y	N	N	N	0	Discharged
Cureus 2020 [24]	U	U	Emphysema	N	U	U	U	U	U	U	U	N	Y	N	N	Y	0	U
Cureus 2020 [24]	U	U	No lung disease	Y	U	U	U	U	U	U	U	N	Y	N	N	Y	10	U
Cureus 2020 [24]	U	U	Asthma	Y	U	U	U	U	U	U	U	N	Y	N	N	Y	15	U
Cureus 2020 [24]	U	U	No lung disease	Y	U	U	U	U	U	U	U	N	Y	N	N	N	0	U
Cureus 2020 [26]	44	M	No lung disease	Y	Y	Y	Y	U	U	Y	U	Noninvasive	Y	N	N	N	U	Discharged
Heart and Lung 2020 [10]	78	F	HTN, DM	Y	Y	Y	U	U	Y	Y	U	Noninvasive	Y	N	N	N	0	Improved
Heart and Lung 2020 [6]	37	M	Obesity	Y	Y	Y	U	U	Y	Y	Y	NRB	Y	Y	N	N	14	Discharged
Heart and Lung 2020 [6]	34	M	No lung disease	Y	Y	U	U	Y	Y	Y	Y	NRB	Y	N	N	N	36	Discharged
ID cases 2020	23	F	None	N	N	N	N	U	Y	U	U	N	Y	N	N	N	0	Discharged
Lancet 2020	38	M	U	Y	Y	Y	U	U	Y	Y	N	N	Y	N	N	Y	11	Discharged
Medicina Clinica 2020	80	M	U	Y	Y	Y	U	U	Y	Y	U	Noninvasive	Y	N	N	N	19	Discharged
Radiology Case Reports 2020	54	M	HTN, DM	Y	U	Y	U	U	U	U	U	U	Y	U	N	Y	0	Died
World Journal of Clinical Cases 2020	62	M	None	Y	Y	Y	Y	U	U	Y	U	NC	Y	N	N	N	12	Discharged

PM = pneumomediastinum; PP = pneumopericardium; PTX = pneumothorax; SE = subcutaneous emphysema; N/A = not applicable (from our institution);
M = male; F = female; Y = yes; N = no; U = unknown; HTN = hypertension, HLD = hyperlipidemia; DM = diabetes mellitus; OSA = obstructive sleep apnea;
NRB = non-rebreather; NC = nasal cannula; CPAP = continuous positive airway pressure; BPAP = bilevel positive airway pressure.

Table 2: Comprehensive summary of patients with SARS-CoV-2 and isolated SPM who was deceased.

Study	Age (years)	Sex	Comorbidities	Cough	Fever	Dyspnea	Myalgia	Diarrhea	Steroids	Antibiotics	Tocilizumab	Oxygen	PM	PP	PTX	SE	Inpatient days before event
Current Study	67	M	HTN, HLD	N	N	N	Y	N	Y	Y	N	NRB	Y	N	N	Y	10
Current Study	59	F	HTN, asthma	Y	Y	Y	N	Y	Y	N	N	NC	Y	N	N	N	0
Current Study	50	F	HTN, HLD, DM, obesity, CKD	Y	Y	Y	N	N	Y	Y	N	NRB, NC	Y	N	N	Y	7
Archivos de Bronconeumo-logia 2020 [21]	46	M	No lung disease	U	U	U	U	U	U	U	U	U	Y	Y	N	Y	1
Archivos de Bronconeumo-logia 2020 [21]	75	F	No lung disease	Y	Y	Y	Y	N	Y	Y	N	U	Y	Y	N	Y	5
Archivos de Bronconeumo-logia 2020 [21]	57	F	No lung disease	Y	Y	Y	Y	N	Y	Y	N	U	Y	Y	N	N	17
Chest 2020	63	M	HTN, HLD, DM	U	Y	Y	U	U	U	Y	U	N	Y	U	N	Y	0
Radiology Case Reports 2020	54	M	HTN, DM	Y	U	Y	U	U	U	U	U	U	Y	U	N	Y	0

PM = pneumomediastinum; PP = pneumopericardium; PTX = pneumothorax; SE = subcutaneous emphysema; N/A = not applicable (from our institution);
M = male; F = female; Y = yes; N = no; U = unknown; HTN = hypertension, HLD = hyperlipidemia; DM = diabetes mellitus; NRB = non-rebreather.

causes, mortality is low to none. However, this appears to be different in the setting of COVID-19. Three of the patients at our institution required intubation and ultimately died after developing SPM.

Isolated SPM may portend a worse prognosis in patients hospitalized with COVID-19 [13-15]. From the combination of our cases and the patients with COVID-19 who developed isolated SPM in the literature, eight out of 31 (25.8%) patients with available data on outcome expired. This mortality rate from our case review was higher compared to the overall mortality rate of hospitalized patients with COVID-19, which ranged from 9.06% to 20.3% [16-18]. This difference in mortality rate may even be greater as mortality rates were demonstrated to have declined over the first few months of the pandemic [17]. Among the eight patients in our case review who died, the mean age was 58.9 years, with range 46-75 years, which was higher compared to the mean age of all patients with isolated SPM (Table 2). This mean age was similar to the mean age of all COVID-19 patients who died with or without SPM [16].

In the terms of comorbidity, the majority of the patients who died (6/8 or 75%) had concurrent subcutaneous emphysema. There was a higher percentage of patients who had other comorbidities, as three (37.5%) of the patients had diabetes, and four (50%) of the patients had hypertension. The association with comorbidities in patients with SPM who died was also stronger compared to all COVID-19 patients who died with comorbidities [16, 19]. Oxygen supplementation during hospitalization may have played role in mortality as only three out of eight (37.5%) of the patients received oxygen supplementation prior to developing SPM. The mean number of days hospitalized prior to developing SPM for patients who died was 3.6 days, which was fewer compared to the mean of 9.8 days for all patients with isolated SPM, possibly representing a more acute and aggressive onset of disease.

Isolated SPM is an infrequent but possibly fatal complication and may be a sign of worse prognosis in patients with COVID-19 without history of mechanical ventilation or positive airway pressure support. Three out of four patients in this case study died after a (prolonged) hospital stay. Recognition of isolated SPM involves close clinical and imaging monitoring of patients.

Conflict of Interest

The authors declare no conflict of Interest

Funding

Research was conducted in the absence of any interests including financial, commercial or other relationships that might be perceived by the academic community as representing a potential conflict of interest.

Acknowledgements

None

References

1. Murayama S, Gibo S. 2014. Spontaneous pneumomediastinum and macklin effect: overview and appearance on computed tomography. *World J Radiol* 6(11): 850-854. https://doi.org/10.4329/wjr.v6.i11.850
2. Marsico S, Del Carpio Bellido LA, Zuccarino F. 2021. Spontaneous pneumomediastinum and macklin effect in COVID-19 patients. *Arch Bronconeumol* 57(Suppl 1): 67. https://doi.org/10.1016/j.arbres.2020.07.030
3. Kong N, Gao C, Xu MS, Xie YL, Zhou CY. 2020. Spontaneous pneumomediastinum in an elderly COVID-19 patient: A case report. *World J Clin Cases* 8(16): 3573-3577. https://doi.org/10.12998/wjcc.v8.i16.3573
4. Agarwal A, Basmaji J, Muttalib F, Granton D, Chaudhuri D, et al. 2020. High-flow nasal cannula for acute hypoxemic respiratory failure in patients with COVID-19: systematic reviews of effectiveness and its risks of aerosolization, dispersion, and infection transmission. *Can J Anaesth* 67(9): 1217-1248. https://doi.org/10.1007/s12630-020-01740-2
5. Guy T, Créac'hcadec A, Ricordel C, Salé A, Arnouat B, et al. 2020. High-flow nasal oxygen: a safe, efficient treatment for COVID-19 patients not in an ICU. *Eur Respir J* 56(5): 2001154. https://doi.org/10.1183/13993003.01154-2020

6. Diaz A, Patel D, Sayedy N, Anjum F. 2020. COVID-19 and spontaneous pneumomediastinum: A case series. *Heart Lung* 50(2): 202-205. https://doi.org/10.1016/j.hrtlng.2020.12.002
7. Bellini D, Lichtner M, Vicini S, Rengo M, Ambrogi C, et al. 2020. Spontaneous pneumomediastinum as the only CT finding in an asymptomatic adolescent positive for COVID-19. *BJR Case Rep* 6(3): 20200051. https://doi.org/10.1259/bjrcr.20200051
8. Kolani S, Houari N, Haloua M, Alaoui Lamrani Y, Boubbou M, et al. 2020. Spontaneous pneumomediastinum occurring in the SARS-COV-2 infection. *IDCases* 21: e00806. https://doi.org/10.1016/j.idcr.2020.e00806
9. Underner M, Peiffer G, Perriot J, Jaafari N. 2020. Spontaneous pneumomediastinum: A rare complication of COVID-19? *Rev Mal Respir* 37(8): 680-683. https://doi.org/10.1016/j.rmr.2020.06.013
10. Brogna B, Bignardi E, Salvatore P, Alberigo M, Brogna C, et al. 2020. Unusual presentations of COVID-19 pneumonia on CT scans with spontaneous pneumomediastinum and loculated pneumothorax: A report of two cases and a review of the literature. *Heart Lung* 49(6): 864-868. https://doi.org/10.1016/j.hrtlng.2020.06.005
11. Mimouni H, Diyas S, Ouachaou J, Laaribi I, Oujidi Y, et al. 2020. Spontaneous pneumomediastinum associated with COVID-19 pneumonia. *Case Rep Med* 2020: 4969486. https://doi.org/10.1155/2020/4969486
12. Al-Azzawi M, Douedi S, Alshami A, Al-Saoudi G, Mikhail J. 2020. Spontaneous subcutaneous emphysema and pneumomediastinum in COVID-19 patients: an indicator of poor prognosis? *Am J Case Rep* 21: e925557. https://doi.org/10.12659/ajcr.925557
13. Janssen J, Kamps MJA, Joosten TMB, Barten DG. 2021. Spontaneous pneumomediastinum in a male adult with COVID-19 pneumonia. *Am J Emerg Med* 40: 228.e3-228.e5. https://doi.org/10.1016/j.ajem.2020.07.066
14. Manna S, Maron SZ, Cedillo MA, Voutsinas N, Toussie D, et al. 2020. Spontaneous subcutaneous emphysema and pneumomediastinum in non-intubated patients with COVID-19. *Clin Imaging* 67: 207-213.
15. Urigo C, Soin S, Sahu A. 2020. Spontaneous pneumomediastinum as a complication of a COVID-19 related pneumonia: case report and review of literature. *Radiol Case Rep* 15(12): 2577-2581. https://doi.org/10.1016/j.radcr.2020.09.052
16. Zheng Z, Peng F, Xu B, Zhao J, Liu H, et al. 2020. Risk factors of critical & mortal COVID-19 cases: A systematic literature review and meta-analysis. *J Infect* 81(2): e16-e25. https://doi.org/10.1016/j.jinf.2020.04.021
17. Asch DA, Sheils NE, Islam MN, Chen Y, Werner RM, et al. 2020. Variation in US hospital mortality rates for patients admitted with COVID-19 during the first 6 months of the pandemic. *JAMA Intern* Med e208193. https://doi.org/10.1001/jamainternmed.2020.8193
18. Rosenthal N, Cao Z, Gundrum J, Sianis J, Safo S. 2020. Risk factors associated with in-hospital mortality in a US national sample of patients with COVID-19. *JAMA Netw Open* 3(12): e2029058. https://doi.org/10.1001/jamanetworkopen.2020.29058
19. Zhang JJY, Lee KS, Ang LW, Leo YS, Young BE. 2020. Risk factors for severe disease and efficacy of treatment in patients infected with COVID-19: a systematic review, meta-analysis, and meta-regression analysis. *Clin Infect Dis* 71(16): 2199-2206. https://doi.org/10.1093/cid/ciaa576
20. Gorospe L, Ayala-Carbonero A, Ureña-Vacas A, Fra Fernández S, Muñoz-Molina GM, et al. 2020. Spontaneous pneumomediastinum in patients with COVID-19: a case series of four patients. *Arch Bronconeumol* 56(11): 754-756. https://doi.org/10.1016/j.arbres.2020.06.008
21. Juárez-Lloclla JP, León-Jiménez F, Urquiaga-Calderón J, Temoche-Nizama H, Bryce-Alberti M, et al. 2021. Spontaneous Pneumopericardium and pneumomediastinum in twelve COVID-19 patients. *Arch Bronconeumol* 57(Suppl 1): 86-88. https://doi.org/10.1016/j.arbres.2020.09.013
22. Mohan V, Tauseen RA. 2020. Spontaneous pneumomediastinum in COVID-19. *BMJ Case Rep* 13(5): e236519. http://doi.org/10.1136/bcr-2020-236519
23. Marchon KA, Nunn MO, Chakera AJ. 2020. Images of the month: An incidental finding of spontaneous pneumomediastinum (Hamman's syndrome) secondary to diabetic ketoacidosis during the coronavirus pandemic. *Clin Med (Lond)* 20(6): e275-e277. https://doi.org/10.7861/clinmed.2020-0739
24. Eperjesiova B, Hart E, Shokr M, Sinha P, Ferguson GT. 2020. Spontaneous pneumomediastinum/pneumothorax in patients with COVID-19. *Cureus* 12(7): e8996. https://doi.org/10.7759/cureus.8996
25. Li S, Chau E, Ghasem W, Sohn J, Yaghmour B. 2020. Air should not be there: A case of pneumomediastinum and pneumopericardium in COVID-19. *Cureus* 12(11): e11696. https://doi.org/10.7759/cureus.11696
26. Wegner U, Jeffery G, Abrajan O, Sampablo I, Singh C. 2020. Spontaneous pneumomediastinum associated with SARS-CoV-2: infrequent complication of the novel disease. *Cureus* 12(7): e9189. https://doi.org/10.7759/cureus.9189
27. Ghani M, Rodriguez-Ortiz Y, Ahmad D, Pham J, Tamsukhin P, et al. 2020. Spontaneous pneumomediastinum in patients with SARS-COV-2 virus (COVID-19). *Chest* 158(4): A1231-A1232. https://doi.org/10.1016%2Fj.chest.2020.08.1121
28. Zhou C, Gao C, Xie Y, Xu M. 2020. COVID-19 with spontaneous pneumomediastinum. *Lancet Infect Dis* 20(4): 510. https://doi.org/10.1016/s1473-3099(20)30156-0
29. Fernández-Raga S, Fidalgo-Navarro A, Bernardo-Cofiño J. 2020. Spontaneous neumomediastin in coronavirus-associated pneumonitis. *Med Clin (Barc)* 155(9): 421. https://doi.org/10.1016/j.medcli.2020.04.055
30. Vazzana N, Ognibene S, Dipaola F. 2020. Pneumomediastinum and subcutaneous emphysema after noninvasive ventilation in a COVID-19 patient. *Adv Respir Med* 88(5): 466-467. https://doi.org/10.5603/arm.a2020.0141