



Spontaneous pneumomediastinum secondary to COVID-19 in Iran: A case series study

Shahla Afrasiabian¹, Hero Yazdanpanah², Naseh Sigari³, Susan Mohamaddi⁴,
Karo Servatyari²

1 Department of Infectious Diseases, Faculty of Medicine, Kurdistan University of Medical Sciences, Sanandaj, Iran

2 Student Research Committee, Kurdistan University of Medical Sciences, Sanandaj, Iran

3 Department of Internal Medicine, Faculty of Medicine, Kurdistan University of Medical Sciences, Sanandaj, Iran

4 Department of Radiology, Faculty of Medicine, Kurdistan University of Medical Sciences, Sanandaj, Iran

Case Report

Abstract

BACKGROUND: Pneumomediastinum is defined as open-air in the mediastinum. Spontaneous pneumomediastinum (SPM) occurs when air leaks into the surrounding vascular sheath through small alveolar ruptures.

CASE REPORT: We want to introduce 4 different cases with different outcomes. The first case was a 60-year-old man with a history of psychological disorders, the second case was a 41-year-old man with a history of hypertension (HTN) and asthma, the third case was a 50-year-old heavy smoker with no history of an underlying disease, and the fourth case was a 60-year-old man with a history of schizophrenia. They suddenly developed an exacerbation of cough, dyspnea, chest pain, and a severe decrease in oxygen saturation during hospitalization. Antibiotic therapy, corticosteroids, and high-dose oxygen therapy were administered to the patients. One of these patients died.

CONCLUSION: All patients can potentially be at risk for this complication and have a good prognosis if diagnosed early and treated properly overall.

KEYWORDS: Mediastinal Emphysema; COVID-19; Iran

Date of submission: 16 Oct. 2021, **Date of acceptance:** 26 Jan. 2022

Citation: Afrasiabian S, Yazdanpanah H, Sigari N, Mohamaddi S, Servatyari K. **Spontaneous pneumomediastinum secondary to COVID-19 in Iran: A case series study.** Chron Dis J 2023; 11(1): 63-7.

Introduction

Coronavirus disease 2019 (COVID-19) is an emerging disease caused by the coronavirus, first reported in Wuhan, China. It was identified and spread rapidly around the world, leading to a global pandemic.¹ Due to the ways the virus is transmitted, the rate of spread around the world has been very high, and on the other hand, the lack of therapeutic drugs has led to high mortality rates in these patients.² COVID-19 has many clinical signs and symptoms (such as

cough, fever and chills, lethargy, myalgia, fatigue, headache, dyspnea, etc.) and also has many complications.³ Pneumomediastinum is defined as a condition in which air is present in the mediastinum and is generally classified into two types, spontaneous pneumomediastinum (SPM) and secondary pneumomediastinum. SPM is usually benign and idiopathic, while secondary pneumomediastinum is due to trauma, intrathoracic infections, rupture of the esophagus, or rupture of the bronchi and alveoli.³ Major early complaints in these patients included chest pain, shortness of breath, and subcutaneous emphysema. Flaming and asthma attacks can be a trigger for this disease.⁴ SPM

Corresponding Author:

Karo Servatyari; Student Research Committee, Kurdistan University of Medical Sciences, Sanandaj, Iran

Email: servatyarikaro@yahoo.com

occurs when air leaks into the surrounding vascular sheath through small alveolar ruptures.⁵ These complications are likely to be caused by a sudden increase in mediastinal pressure. Most severe pneumomediastinum has been associated with or without thoracic trauma.⁶ Computed tomography (CT) scan is a useful test to diagnose these patients.⁷ Because of COVID-19, patients are at high risk for respiratory failure; it is recommended that even seemingly benign cases of pneumomediastinum be closely monitored.⁷

Case Report

Case 1: The patient was a 60-year-old man with a history of anxiety disorders and panic attacks and was under psychological treatment but with no history of smoking. He had not taken any psychological medication since he was diagnosed with COVID-19. He was treated for 12 days with a diagnosis of COVID-19 which was confirmed based on radiological findings and a positive polymerase chain reaction (PCR) test. On the fourth day of treatment in the hospital, despite receiving interferon beta-1a (IFN- β -1a) (subcutaneous injection of ReciGen every other day for 5 doses) and corticosteroid [intravenous (IV) injection of dexamethasone 8 mg every day] without a history of trauma, the patient suddenly developed an exacerbation of cough, dyspnea, chest pain, and a severe decrease in oxygen saturation. Therefore, a high-resolution chest CT scan was immediately requested again for the patient and he was transferred to the intensive care unit (ICU) with a definite diagnosis of pneumomediastinum. On follow-up imaging of the patient, thoracic wall emphysema was seen extending into the deeper layers. The patient was admitted to the ICU for 7 days. During this period, appropriate antibiotics (ampicillam 2 g every 8 hours and vancomycin 1 g every 8 hours) and high-dose oxygen therapy were performed. The patient was transferred from

the ICU to the general ward without the need for a ventilator and was finally discharged after 11 days in good general condition and complete recovery.

Case 2: The patient was a 41-year-old man with a history of hypertension (HTN) and a previous history of asthma and salbutamol spray use who was treated for 9 days with dyspnea, fever, chills, and myalgia with a definitive diagnosis of COVID-19 (based on radiological findings and positive PCR test). During the treatment with IFN- β -1a (subcutaneous injection of ReciGen every other day for 5 doses) and corticosteroid (IV injection of dexamethasone 8 mg every day), he suddenly experienced a severe cough, shortness of breath, and a decrease in oxygen saturation, and did not improve despite appropriate supportive treatments. A cardiac workup was performed immediately on the patient, but no evidence of heart involvement was found. The further chest CT scan showed evidence of pneumomediastinum, subcutaneous emphysema, and pneumothorax, and the patient was transferred to the ICU, and respiratory supportive care (high-dose oxygen therapy with venturi mask) was administered to the patient. Fortunately, with timely and sufficient therapy, the patient completely recovered.

Case 3: The patient was a 50-year-old man, heavy smoker with no history of the underlying disease who was treated for 14 days with shortness of breath, fever, chills, and myalgia and a diagnosis of COVID-19 which was confirmed based on radiological findings and a positive PCR test. During treatment of COVID-19 in the hospital, he suddenly experienced a decrease in oxygen saturation, shortness of breath, and cough. A chest CT scan was requested for the patient, and the CT scan showed evidence in favor of pneumomediastinum. The patient was immediately transferred to the ICU and received high-dose oxygen therapy with

non-invasive ventilation (NIV), antibiotic therapy (meropenem 1 g every 8 hours and vancomycin 1 g every 8 hours), and corticosteroids (IV injection of dexamethasone 8 mg every day). Fortunately, with timely and sufficient management during this time, the patient recovered completely.

Case 4: The patient was a 60-year-old man with a history of schizophrenia from the age of 18, who had been weak, lethargic, with fever and gastrointestinal symptoms (including severe nausea and vomiting and decreased sense of smell and taste) from 21 days ago and had a severe productive cough. He was taken to the hospital with a loss of consciousness. Molecular testing and CT scan were requested from the patient and the diagnosis of COVID-19 was confirmed. The patient was hospitalized and, despite receiving high doses of oxygen, an antiviral agent (IV injection of remdesivir for 5 days), and corticosteroid, suddenly developed severe respiratory distress and hypoxia. A new chest CT scan showed evidence of pneumomediastinum and emphysema of the soft tissues of the neck and upper thoracic wall. The patient was immediately transferred to the ICU and was intubated. Antibiotic therapy (meropenem 1 g every 8 hours and vancomycin 1 g every 8 hours) and corticosteroid (dexamethasone 12 mg once daily) were also started for the patient, but unfortunately after 2 days, despite proper treatment, the patient died.

The laboratory findings of the patients are observed in table 1.

According to table 1, troponin was positive in one case and negative in other cases. D-dimer, erythrocyte sedimentation rate (ESR), and C-reactive protein (CRP) were positive in 3 patients and negative in one patient. Besides, leukocytosis was observed in two cases. The rest of the evaluated laboratory indicators were normal.

The findings of the lung CT scan of the patients can be seen in Figure 1

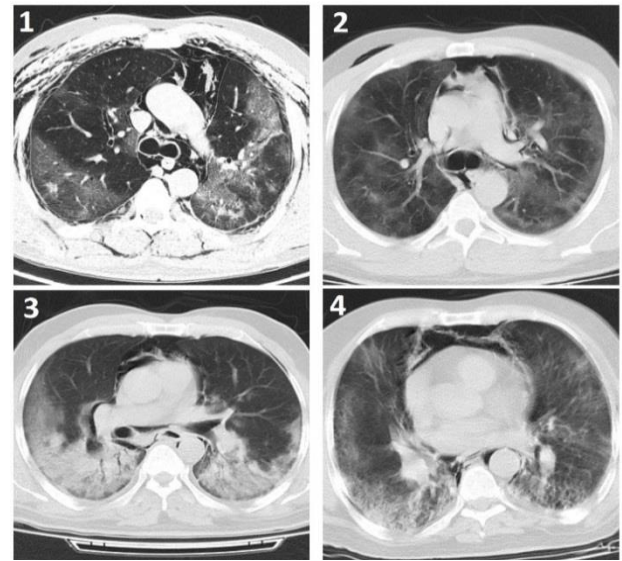


Figure 1. Axial tomographic sections of four patients with different degrees of gas present at the pericardial level and bilateral peripheral ground-glass opacities along with pneumomediastinum. 1) Subpleural ground glass opacity is seen in both lungs. Extensive pneumomediastinum and severe emphysema of soft tissue of thoracic and neck walls are seen. It extends to the deeper layers of the thoracic wall, creating a similar appearance to bilateral pneumothorax; 2) Subpleural ground glass opacity is seen in both lungs. Pneumomediastinum and emphysema are evident in the soft tissue of the thoracic wall on the right; 3) Subpleural ground glass opacity mixed with consolidation is observed in both lungs. Pneumomediastinum is also obvious; 4) Subpleural ground glass opacity and in some parts, crazy-paving is seen in the lung parenchyma. Pneumomediastinum and soft tissue emphysema at the base of the neck and upper thoracic wall are seen.

Discussion

During the treatment of COVID-19, various complications may occur which with a timely diagnosis, the occurrence of mortality and morbidity can be prevented. One of the rare but important manifestations in these patients is pneumomediastinum, which can quickly lead to risk for patients. We want to warn all colleagues and physicians in the world about the occurrence of this manifestation during the treatment of this disorder.

Table 1. Laboratory findings of the patients

Test	Reference range	Case 1	Case 2	Case 3	Case 4
WBC ($\times 1000$ per μl)	4.2-10.8	7.6	13.3	11.2	9.6
Hb (g/dl)	14.0-18.0	16.1	14.3	14.5	14.9
Platelets ($\times 10^9/\text{l}$)	130-450	208	273	332	145
LDH (U/l)	235-470	870	804	601	1083
CPK (U/l)	0-171	75	279	288	304
D-dimer (ng/ml)	< 200	288 (positive)	108 (negative)	303 (positive)	388 (positive)
ESR mm/hour	4-12	4	24	42	45
Troponin	Positive/negative	Negative	Positive	Negative	Negative

WBC: White blood cell; LDH: Lactate dehydrogenase; CPK: Creatine phosphokinase; ESR: Erythrocyte sedimentation rate; Hb: Hemoglobin

Patients with COVID-19 in the hospital all need to receive oxygen to reduce their respiratory symptoms (especially dyspnea). During oxygenation, if for any reason (including chest trauma, severe and uncontrolled cough) the alveoli of the patient's lungs rupture, it can lead to pneumothorax and pneumomediastinum.

Secondary SPM can be a long-term complication of COVID-19 due to bacterial superinfection including tuberculosis (TB), fungi infection including *Pneumocystis jirovecii* (*P. carinii*), and viruses such as human immunodeficiency virus (HIV) infection.⁸ On the other hand, because corticosteroids are one of the main treatments in hospitalized patients with COVID-19, it suppresses the immune system in these patients and predisposes the person to infection with fungi, especially *P. carinii*, which is generally delayed.⁹ It mostly occurs during long-term hospitalizations due to COVID-19.

Another mechanism of pneumomediastinum in hospitalized patients is the use of NIV with high continuous positive airway pressure (CPAP).¹⁰ This mechanism was not present in patients in our study. The exact mechanism of pneumomediastinum in COVID-19 is not yet known. In the Lee *et al.* study, increased intrathoracic pressure due to persistent coughing in combination with decreased pressure in the perialveolar space due to respiratory effort led to alveolar rupture and air leakage into the mediastinum and thorax.¹¹ On the other hand, there are different

hypotheses about the mechanism of pneumomediastinum in patients with COVID-19. In most cases, a self-contained mechanism prevents air from accumulating in the mediastinum by moving air into the subcutaneous tissue. In justifying the pathophysiology of pneumomediastinum in these patients, we can mention the Macklin effect, which includes rupture of the damaged alveoli, disruption of airflow along the bronchial vascular sheaths, and finally the expansion of interstitial pulmonary emphysema to the mediastinum.¹² On the other hand, in the study of Murayama and Gibo, various mechanisms have been proposed for pneumomediastinum, including the removal of the cutaneous or mucosal barrier (tracheobronchial tree) and the rupture of the alveoli, which causes gas to enter the mediastinum.¹³ In Caceres *et al.* study, one of the causes of SPM was severe coughing.⁴

The main triggers for SPM were emesis and asthma flare-ups that in some cases in our article were seen and sometimes, they happened without any triggers.⁴ In our study, patients developed pneumomediastinum after 1-2 weeks of hospitalization. According to the treatment protocol of Kurdistan University of Medical Sciences, Sanandaj, Iran, the treatment of these patients is supportive and includes high-dose oxygen therapy, antiviral therapy, and corticosteroid therapy, which was performed on all patients with the highest level of caution.

It was not possible to follow up patients after discharge from the hospital; therefore, the possibility of recurrent SPM in these patients could not be assessed.

Conclusion

Although SPM is inherently a benign phenomenon, it can sometimes cause death. Early detection by physicians can prevent a sudden decrease in oxygen saturation and reduced circulation (as a phenomenon associated with SPM) and can decrease mortality, thus improving the prognosis of these patients. Our study shows that all patients can potentially be at risk for this complication and have a good prognosis if diagnosed early and treated properly overall. Therefore, paying more attention to patients during hospitalization and prompt follow-up can increase the quality of life and longevity of these patients.

Conflict of Interests

Authors have no conflict of interests.

Acknowledgments

We would like to express our gratitude to the Research Council of the Faculty of Medicine, Kurdistan University of Medical Sciences, for approving this study. Besides, we thank the patients and their families for their cooperation. Informed consent was obtained from the patients. This project has been approved by the National Committee on Ethics in Research and Deputy of Research and Technology of Kurdistan University of Medical Sciences with code IR.MUK.REC.1399.325.

Financials support and sponsorship

This study was financially supported by Kurdistan University of Medical Sciences.

References

- Hui DS, Azhar I, Madani TA, Ntoumi F, Kock R, Dar O, et al. The continuing 2019-nCoV epidemic threat of novel coronaviruses to global health - The latest 2019 novel coronavirus outbreak in Wuhan, China. *Int J Infect Dis*. 2020; 91: 264-6.
- Goyal P, Choi JJ, Pinheiro LC, Schenck EJ, Chen R, Jabri A, et al. Clinical characteristics of COVID-19 in New York City. *N Engl J Med*. 2020; 382(24): 2372-4.
- Aiyegbusi OL, Hughes SE, Turner G, Rivera SC, McMullan C, Chandan JS, et al. Symptoms, complications and management of long COVID: A review. *J R Soc Med*. 2021; 114(9): 428-42.
- Caceres M, Ali SZ, Braud R, Weiman D, Garrett HE, Jr. Spontaneous pneumomediastinum: a comparative study and review of the literature. *Ann Thorac Surg*. 2008; 86(3): 962-6.
- Macklin CC. Transport of air along sheaths of pulmonic blood vessels from alveoli to mediastinum: Clinical implications. *Arch Intern Med (Chic)*. 1939; 64(5): 913-26.
- Banki F, Estrera AL, Harrison RG, Miller CC 3rd, Leake SS, Mitchell KG, et al. Pneumomediastinum: Etiology and a guide to diagnosis and treatment. *Am J Surg*. 2013; 206(6): 1001-6.
- Kaneki T, Kubo K, Kawashima A, Koizumi T, Sekiguchi M, Sone S. Spontaneous pneumomediastinum in 33 patients: Yield of chest computed tomography for the diagnosis of the mild type. *Respiration*. 2000; 67(4): 408-11.
- Kwas H, Zendah I, Ghedira H. Spontaneous pneumothorax secondary to tuberculosis. *Tunis Med*. 2017; 95(4): 276-9.
- Park YK, Jung HC, Kim SY, Kim MY, Jo K, Kim SY, et al. Spontaneous pneumomediastinum, pneumopericardium, and pneumothorax with respiratory failure in a patient with AIDS and *Pneumocystis jirovecii* Pneumonia. *Infect Chemother*. 2014; 46(3): 204-8.
- Gidaro A, Samartin F, Brambilla AM, Cogliati C, Ingrassia S, Banfi F, et al. Correlation between continuous Positive end-expiratory pressure (PEEP) values and occurrence of Pneumothorax and Pneumomediastinum in SARS-CoV2 patients during non-invasive ventilation with Helmet. *Sarcoidosis Vasc Diffuse Lung Dis*. 2021; 38(2): e2021017.
- Lee J, Kang BS, Kim C, Choi HJ. Tension pneumopericardium after pericardiocentesis. *J Korean Med Sci*. 2016; 31(3): 470-2.
- Wintermark M, Schnyder P. The Macklin effect: A frequent etiology for pneumomediastinum in severe blunt chest trauma. *Chest*. 2001; 120(2): 543-7.
- Murayama S, Gibo S. Spontaneous pneumomediastinum and Macklin effect: Overview and appearance on computed tomography. *World J Radiol*. 2014; 6(11): 850-4.