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Case Report

A case report, bilateral spontaneous pneumothorax as a late complication for SARS CoV-2 infection✩

Miguel Angel Plata-Corona, MDa,b,✩, Mayra Alejandra López-Aguilar, MDc, Juan Manuel Ibarra-Hernández, PhDd, Jorge Tello-Cavazos, MDe, Luis Fernando Marcial-Cuevas, MDa,b

a General Surgery Department, Specialty Hospital National Medical Center "La Raza" Instituto Mexicano del Seguro Social, Azcapotzalco s/n, La Raza, Azcapotzalco, Ciudad de México, C.P. 02990, México
b General Surgery Department, General Regional Hospital No. 196 “Fidel Velázquez Sánchez” Instituto Mexicano del Seguro Social. Avenida Central esquina la Piedad s/n, San Agustín Tercera Sección, Ecatepec, Estado de México, C.P. 55130, México
c Medicine School, Universidad Popular Autónoma de Puebla, Av 21 Sur 1103, Barrio de Santiago, Puebla, C.P. 72410, Puebla, México
d Institute of Physiology, Benemérita Universidad Autónoma de Puebla, 14 Sur. 6301, Ciudad Universitaria, Jardines de San Manuel, Puebla, Puebla, C. P. 72570, México
e Clinical Neurophysiology Service, Specialty Hospital "Dr. Bernardo Sepúlveda Gutiérrez" del Centro Médico Nacional Siglo XXI, Instituto Mexicano del Seguro Social, Av Cuauhtémoc 330, Doctores, Cuauhtémoc, Ciudad de México, C.P. 06720, México

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A B S T R A C T

The beta-coronavirus discovered in Wuhan in 2019 (COVID-19) provokes a series of affections from mild symptoms to life-threatening complications. There is evidence that associates the disease to spontaneous pneumothorax, however, the mechanism is unknown. The patient was a 45-year-old male with previous pneumonia due to COVID-19 who was attended the emergency department, where chest radiography was taken, confirming the diagnosis of right pneumothorax. However, the patient developed a new episode of pleuritic pain three days later, and a new radiograph showed left pneumothorax requiring a new chest tube. The simple tomography shows intraparenchymal bullae in the apical region of both lungs. The patient was kept under observation, and when improving, both endopleural chest drains were removed, and the patient was discharged. Spontaneous bilateral pneumothorax is a rare and potentially life-threatening complication. Identifying pulmonary bullae in patients with COVID-19 could be an early sign for these patients to develop spontaneous pneumothorax.

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* Corresponding author.
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Introduction

Coronavirus disease-19 (COVID-19) is an infection caused by the Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2), a new virus identified in Wuhan in 2019 and spread all over the world. Its clinical presentation varies from an asymptomatic state to a severe disease that causes sepsis, multiorgan failure, acute respiratory distress syndrome (ARDS), among others [1,2]. It has been reported that the presence of spontaneous pneumothorax, caused by bacteria Mycobacterium and viruses like the human immunodeficiency virus, is related to the formation of subpleural bullae [3].

Pneumothorax related to SARS CoV-2 infection is rare, reporting from 0.66% to 1% among the cases [4,5]. So far, spontaneous pneumothorax’s formation mechanism remains unknown in patients with active infection or as a sequel of COVID-19, but it has been linked to pulmonary bullae formation. Within this article, we described a case of spontaneous bilateral pneumothorax development in a patient with previous mild symptoms due to SARS-CoV2 infection with the posterior development of pulmonary bullae and treated satisfactorily in a second-level hospital in Mexico City.

Case

This study reports a 45-year-old male with a clinical history of arterial hypertension treated with losartan and no immunizations history against SARS-CoV-2. The patient counts on previous pneumonia symptoms starting on April 26, 2021, handled with ceftriaxone and azithromycin under suspect of bacterial pneumonia, then no improvement occurred, thereby a polymerase chain reaction test for COVID-19 was done, confirming the infection on May 2, 2021. The patient showed mild symptoms controlled with paracetamol and had a clinical recovery 2 weeks later.

On May 30, 2021, the patient had a wet cough moderate pleuritic chest pain, mainly on the right hemithorax, and 24 hours later, the patient had sudden dyspnea, decreasing oxygen saturation to 88%. The patient went to a private doctor, who prescribed intramuscular betamethasone and salbutamol with no signs of improvement. On June 2, the patient presented dyspnea at rest, tachycardia (115 beats/minute), and an increasing thoracic pain of severe intensity on the right hemithorax, so the patient came to the Emergency Department in our hospital.

When admitted, the patient had an O2 Saturation of 80% and tachycardia (112 beats/minute), we administrated supplementary oxygen with a mask to 6 liters per minute, and a chest x-ray in 2 projections was taken, showing a right pneumothorax about 30% (Fig. 1A); therefore, we placed a chest drain through getting symptomatic recovery. On June 5, three days after the patient’s admission, sudden dyspnea presents again, along with moderate pleuritic pain in the left hemithorax and a drop of O2 Sat to 82%. A new chest x-ray showed a new pneumothorax on the left side. Thus, the patient had a second chest drain implanted (see Fig. 1B). When the patient was admitted, the laboratories showed leukocytosis of 11,400/mm³ with neutrophilia of 89% and reactive protein C > 90 mg/L, and the rest of the laboratory results were within normal parameters. Neither ferritin, interleukin-6, nor other inflammation parameter was taken.

The patient continued with supplementary oxygen by nasal prongs to 3 L/minute keeping O2 Saturation >94% with a gradual reduction of both pneumothoraxes. A simple tomography was taken on June 12 (see Fig. 1C), which showed the reduction of left pneumothorax, irregular interlobar septal thickening in lungs, left basal consolidation, and 2 intraparenchymal bullae on the posterior apical region of both lungs (largest bulla was in the left lung with a size of 6 × 4 cm). According to the thorax radiograph dated June 17 (13 days after the admission), there was a re-enlargement of pulmonary parenchyma and a pneumothorax resolution (Fig. 1D). Consequently, the decision was to remove both chest drains, and the patient was discharged.

We continued monitoring the patient through outpatient services. We did a new thorax tomography a month later (Fig. 1E), which reported: fibrotic scars in the right pulmonary parenchyma and a bulla in the posterior apical segment of roughly 3 × 2 cm in the left lung.

Discussion

The presence of a bilateral spontaneous pneumothorax after a severe disease for COVID-19 in our patient coincides with the reported cases in Mexico and the world [2,6–8]. Spontaneous pneumothorax is an idiopathic pathology not related to traumas or iatrogenesis.

Additionally, other risk factors for the presentation of primary spontaneous pneumothorax have been documented in the literature, such as male sex, tall stature, a history of smoking [9], and a family history of pneumothorax about FLCN gene mutation [10] as well as related diseases including Birt-HoggDube syndrome, Marfan syndrome, vascular Ehlers-Danlos syndrome (type IV), alpha-1 antitrypsin deficiency, tuberous sclerosis complex/lymphangioleiomyomatosis, Loeys-Dietz syndrome, cystic fibrosis, homocystinuria, cutis laxa, among others [10]. The presence of lymphopenia and the elevation of inflammation markers such as C-reactive protein, lactate dehydrogenase, ferritin, D-dimer, and interleukin 6 have even been reported in patients who develop spontaneous pneumothorax with a history of COVID-19 pneumonia [4].

Records show that spontaneous pneumothoraces are often associated with a subpleural bullae breakdown [11]. A pathological piece taken from a patient who received bullectomy as a treatment for pneumothorax due to COVID-19 revealed fibrosis, vascular congestion, and data of restorative changes as deposits of hemosiderin, fibrin collections, and occasional fibromyxoid plugs with airspaces [12]. Evidence indicates that formation and subsequent bullae breakdown could be the main reason for COVID-19 related pneumothorax cases [13].

It has been suggested that the cause of pneumothorax development in patients infected with COVID-19 is a rise in the

E-mail address: apc.plata@comunidad.unam.mx (M.A. Plata-Corona).
inflammatory response with ischemic damage within the pulmonary parenchyma, jointly to the rise of respiratory effort and the resulting cough contributing to micro-injuries formation, which produces bullae formation and their breakdown influencing then a pneumothorax [2,6,12,14].

On the other hand, other risk factors for primary spontaneous pneumothorax have been registered, such as being male [9] and the elevation of inflammatory markers like the C-reactive protein and lactic dehydrogenase [4], which are some of the risk factors presented in our patient.

Most reported pneumothorax cases are treated satisfactorily by implanting a chest drain [2,12,15]. In this case and the previous case registered in Mexico, a chest drain was required, and it was removed when the patient improved, with no data showing a thoracic or pulmonary pathology through the tomography for control [7].

More evidence is necessary to establish the incidence of pneumothorax and some guidelines for its specific treatment. Efforts made through vaccination campaigns have shown positive effects, but we need time to know if the number of complications will decrease in the short and long terms, specifically for pneumothorax that, even though it presents a low incidence, it is a complication that requires urgent treatment to preserve life.

**Conclusion**

*Bilateral spontaneous pneumothorax* is a pathology that must be considered in patients with sudden dyspnea and pneumonia for COVID-19. The pulmonary inflammatory process during
pneumonia for COVID-19 could be the root of the formation of lung bullae and afterward of spontaneous pneumothorax due to its breakdown. More subsequent studies must be done to define the mechanism of bullae formation linked to SARS-CoV2 and explain predictor factors and create an effective directed therapy.

**Patient consent statement**

Written informed consent was obtained from the patient.

**REFERENCES**

[1] Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet 2020;395:497–506. doi:10.1016/S0140-6736(20)30183-5.

[2] Alhakeem A, Khan MM, Al Soub H, Yousaf Z. Case report: COVID-19–associated bilateral spontaneous pneumothorax—a literature review. Am J Trop Med Hyg 2020;103:1162–5. doi:10.4269/ajtmh.20-0680.

[3] Terzi E, Zarogoulidis K, Kougiumtzis I, Dryllis G, Kioumis I, Pitsiou G, et al. Human immunodeficiency virus infection 185 and pneumothorax. J Thorac Dis 2014;6:S377–82. doi:10.3978/j.issn.2072-1439.2014.08.03.

[4] Zantah A, Dominguez Castillo E, Townsend R, Dikengil F, Criner GJ. Pneumothorax in COVID-19 disease: incidence and clinical characteristics. Respir Res 2020;21:1–9. doi:10.1186/s12931-020-01504-y.

[5] Chen N, Zhou M, Dong X, Qu J, Gong F, Han Y, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. Lancet 2020;395:507–13. doi:10.1016/S0140-6736(20)30211-7.

[6] Dennison J, Carlson S, Faehling S, Lieb M, Mubarik A. Case report: Spontaneous pneumothorax in resolved, uncomplicated COVID-19 Pneumonia—a literature review. Respir Med Case Rep 2020;31:101291. doi:10.1016/j.rmr.2020.101291.

[7] González-Pacheco H, Gopar-nieto R, Jiménez-rodriguez G. Bilateral spontaneous pneumothorax in SARS-CoV-2 infection: a very rare, life201 threatening complication. Am J Emerg Med 2020;39:258.e1-e258.e3. doi:10.1016/j.ajem.2020.07.018.

[8] Guimarães Ferreira J, Rapparini C, Moreno Gomes C, Cabral Pinto LA, da Silva e Freire MS. Pneumothorax as a late complication of COVID-19 João. Rev Inat Med Trop Sao Paulo 2020;62:1–5. doi:10.1590/S1678-9962202062061.

[9] Gupta D, Hansell A, Nichols T, Duong T, Ayres JG, Strachan D. Epidemiology of pneumothorax in England. Thorax 2000;55:666–71. doi:10.1136/thorax.55.6.666.

[10] Boone PM, Scott RM, Marcinak SJ. Henske 210 EP, Raby BA. The genetics of pneumothorax. Am J Respir Crit Care Med 2019;199:1344–57. doi:10.1164/rccm.201811-2054CT.

[11] Vuong NL, Elshafay A, Thao LP, Abdalla AR, Mohyeldin IA, Elsabaa K, et al. Efficacy of treatments in primary spontaneous pneumothorax: a systematic review and network meta-analysis of randomized clinical trials. Respir Med 2018;137:152–66. doi:10.1016/j.rmed.2018.03.009.

[12] Martínez-Ali AW, Ingle T, Newman J, Nadeem I, Jackson K, Lane ND, et al. COVID-19 and pneumothorax: a multicentre retrospective case series. Eur Respir J 2020;56. doi:10.1183/13993003.02697-2020.

[13] Sun R, Liu H, Wang X. Mediastinal emphysema, giant bulla, and pneumothorax developed during the course of COVID-19 Pneumonia. Korean J Radiol 2020;21:541–4. doi:10.3348/kjr.2020.0180.

[14] Liu K, Zeng Y, Xie P, Ye X, Xu G, Liu J, et al. COVID-19 with cystic features on computed tomography. Medicine (Baltimore) 2020;99:e20175. doi:10.1097/md.0000000000020175.

[15] Quincho-Lopez A, Quincho-Lopez DL, Hurtado-Medina FD. Case report: Pneumothorax and pneumomediastinum as uncommon complications of COVID-19 pneumonia—literature review. Am J Trop Med Hyg 2020;103:1170–6. doi:10.4269/ajtmh.20-0815.