Pneumomediastinum Associated with COVID-19: A Case Series

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Coronavirus disease 2019 (COVID-19), caused by the new coronavirus SARS-CoV-2, is an infectious disease that has caused an increase in hospitalizations for pneumonia; the spectrum of clinical presentation is variable. One such presentation, pneumomediastinum (PM), is defined as the presence of air or some other gas in the mediastinum. It is a rare condition, usually benign and self-limited; it has been seen in patients with COVID-19. Although most cases are, as explained above, self-limited and in addition, can be managed conservatively, close monitoring is recommended, as PM can cause life-threatening hemodynamic and respiratory disturbances. We present a case series of 4 patients with SARS-CoV-2 infection, in whom PM was found, and who were admitted to the Regional Hospital of High Specialty of the Yucatan Peninsula during the period of May 2020 through August 2020.

Key words: Pneumomediastinum, COVID-19, Macklin effect

Coronavirus disease 2019 (COVID-19), caused by the new coronavirus SARS-CoV-2, is an infectious disease that has led to an increase in hospitalizations due to pneumonia and multiple organ failure. The clinical presentation can vary from an asymptomatic phase to the development of acute respiratory distress syndrome (ARDS) requiring management with invasive mechanical ventilation (IMV) (1,2).

Pneumomediastinum (PM) is defined as the presence of air or some other gas in the mediastinum. It is a rare condition, though usually benign; it can be spontaneous, traumatic, iatrogenic, or barotraumatic (3). PM has been seen in patients with COVID-19 (2,4). Even though most cases might be self-limiting and managed conservatively, it is advisable that patients be closely monitored because PM can cause potentially fatal hemodynamic and respiratory disorders (4–6).

So far, the real-life impact of PM on the outcomes of COVID-19 patients has not been determined to the degree necessary to definitively consider COVID-19–related PM to be a risk factor for death. Nonetheless, once PM is present, patients should be under constant observation to prevent respiratory deterioration. Therefore, the objective of the current article is to describe a case series of COVID-19 patients who developed PM during hospitalization.

Presentation of clinical cases

We retrospectively analyzed clinical data from all the cases with a diagnosis of COVID-19 and who developed PM at the Hospital Regional de Alta Especialidad de la Peninsula de Yucatán from May 2020 through August 2020. The relevant clinical, laboratory, and imaging data were retrieved from medical records and included the following variables: age, morbidities, laboratory tests (complete blood count, C-reactive protein, D-dimer, ferritin, and lactate dehydrogenase), radiological findings (chest radiography and computed tomography [CT]), clinical management, and each patient's evolution and outcome (alive or dead).

Of 335 hospital admissions for COVID-19, 4 cases (1.19%) were patients who developed PM and were from 58 to 75 years old; 3 of these were men and 1 was a woman. None of the cases had a previous history of lung disease. All the patients tested positive (reverse transcriptase–polymerase chain reaction) for SARS-CoV-2. On admission, all the patients required supplemental oxygen, 2 through a face mask (flow 10 L/min), and the other 2 via IMV. Three developed subcutaneous emphysema and therefore underwent imaging studies that resulted in their being diagnosed with PM. Table 1 summarizes the most relevant clinical characteristics of the patients.

The baseline laboratory analyses, radiological abnormalities, and baseline ventilation parameters are described in Table 2. Two patients developed what was considered to be spontaneous PM, while the other 2 cases also developed PM, but related to the use of ventilation. None of them required surgical treatment. Three patients died during their hospital stay due to multiple organ failure derived from COVID-19, and 1 was discharged and is still alive. We are not aware of long-term complications since the patient has not adhered properly to medical follow-up.

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Table 1. Clinical characteristics of patients

Cases	Age/Gender	Comorbidity(ies)	Symptoms	Time of evolution prior to the development of pneumomediastinum	Mechanical ventilation	Pneumomediastinum treatment	Outcome
Case 1	75/Male	smoking	cough, dysphagia, fever, dyspnea	14 days	no	conservative	alive
Case 2	58/Male	dyslipidemia, obesity I, arrhythmia	cough, myalgia, fever, malaise	13 days	yes	conservative	dead
Case 3	64/Female	obesity I, DM2, RA hypothyroidism	cough, fever, headache, dyspnea	12 days	yes	conservative	dead
Case 4	61/Male	SAH	fever, cough, chest and abdominal pain, dyspnea	10 days	yes	conservative	dead

DM2: type 2 diabetes mellitus; RA: rheumatoid arthritis; SAH: systemic arterial hypertension

Discussion

Spontaneous PM is rarely diagnosed in the general population (prevalence of 1 out of 44,500 accidents and emergencies) (3). It has been related to several medical conditions, such as asthma, chronic lung disease, and several infectious diseases, and has been found in patients requiring IMV. The precise mechanism underlying the development of PM during respiratory infections is unknown (4). However, it has been described in patients with COVID-19 associated with the severe acute respiratory syndrome (SARS) (7).

The pathophysiological explanation would seem to have something to do with the Macklin effect, which consists of the sudden generation of a driving pressure between the alveoli and the interstitium leading to interstitial emphysema resulting from alveolar rupture that may further progress to the mediastinal space and induce subcutaneous emphysema (4,8). The presentation of PM in COVID-19 has been associated with a severe clinical course involving a cytokine storm and the sudden development of ARDS (9). It should be noted that all our cases had extensive bilateral pneumonia and 2 required initial management with IMV.

PM associated with IMV is considered traumatic or iatrogenic and occurs within the first 24 hours of orotracheal intubation. Related mechanisms include disruptions of the trachea, excessive inflation of the endotracheal tube cuff, and difficult airways (3,10). Referring to the latter, none of our cases requiring IMV developed PM within the first 24 hours of intubation; therefore, we ruled out traumatic and iatrogenic causes.

Once a patient is under IMV, close monitoring is mandatory because of the several risk factors for airway injury that are associated with ventilation, among which are the endotracheal tube cuff pressure, the levels of inspiratory and positive end-expiratory pressures, patient–ventilator asynchronies (PVA), and sedation level (11). Regarding the risk factors associated with IMV, our data allowed us to establish that none of our cases were at levels of pressures higher than what is considered to be a risk factor for the development of barotrauma. Nonetheless, 2 patients consistently had variations in their levels of sedation, increasing the risk that the performance of a Valsalva maneuver would raise intrathoracic pressure and potentially lead to PVA. PVA is associated with such adverse effects as barotrauma (a pressure-related lung injury), volutrauma (hyperinflation), and atelectrauma (the cyclic collapse of poorly ventilated regions); any or all of these might be related to the development of PM (12–14).

Even though, PM is considered a benign condition, its presence in SARS has been associated with poor outcomes (7). In 2 previous reports, 1 from Suwanwongse et al. and 1 from Eperjesiova et al., 100% of the COVID-19 patients in the respective studies who were under IMV and who developed PM died (9,15). In our study, 3 of the 4 patients died; they were also the ones who required IMV due to severe COVID-19 pneumonia.

Table 2. Laboratory characteristics, imaging, and initial programming of invasive mechanical ventilation.

Variable	Patient 1	Patient 2	Patient 3	Patient 4
Laboratory studies				
Leukocytes (x10^3/µL)	31.05	21.59	20.80	11.9
Neutrophils (x10^3/µL)	29.04	20.12	18.87	10.63
Lymphocytes (x10^3/µL)	0.81	0.54	0.55	0.70
CRP (mg/L)	186	239	84	284
LDH (U/L)	1030	1211	527	1176
Ferritin (ng/ml)	1190	2408	445	748
D-dimer (ng/ml)	420	32766	3350	107758
Tomographic pattern				
CO-RADS	5	5	5	5
Programming of initial invasive mechanical ventilation	NR	FiO2: 100% PEEP: 10 mmHg VT: 320 ml RR: 20, inspT: 1.1 sec	FiO2: 80% PEEP: 12 mmHg, VT: 320ml RR: 18 inspT: 1 sec	FiO2: 90% PEEP: 12 mmHg VT: 420ml RR: 20 inspT: 0.8 sec

CO-RADS: COVID-19 reporting and data system; CRP: C-reactive protein; LDH: lactic dehydrogenase; FiO2: fraction of inspired oxygen; PEEP: positive end-expiratory pressure; PIP: peak inspiratory pressure; VT: tidal volume; RR: respiratory rate; inspT: inspiratory time; sec: seconds; NR: not required

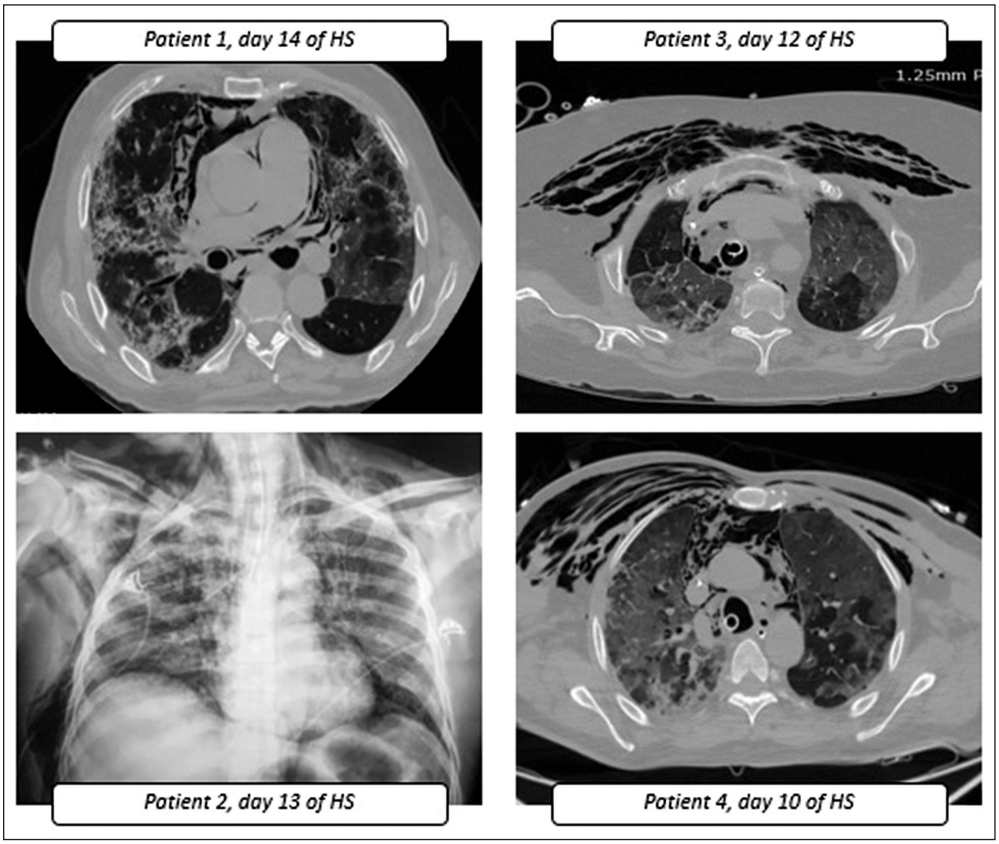

Figure 1. Chest computed tomography scans of our patients showing the presence of free air, in relation to pneumomediastinum. All had a CO-RADS 5 rating, with the presence of ground-glass opacities, areas of consolidation, and a crazy-paving pattern of peripheral subpleural distribution. Patients 2, 3, and 4 had important subcutaneous emphysema. Patient 2 had only a chest radiograph that documented the pneumomediastinum. HS: hospital stay.

Conclusion

PM might be a complication of severe COVID-19. The existence of subcutaneous emphysema is relevant to timely diagnosis. In our series, 3 of the 4 patients who developed PM had unfavorable outcomes, specifically those under IMV. Radiographic studies (x-rays and CT scans) should be performed since being on ventilation could be associated with a poor prognosis.

Resumen

La enfermedad por coronavirus-19 (COVID-19), causada por el nuevo coronavirus SARS-CoV-2, es una enfermedad infecciosa que ha ocasionado un aumento en las hospitalizaciones por neumonía; el espectro de la presentación clínica es variable. El neumomediastino (NM) se define como la presencia de aire o cualquier gas en el mediastino. Es una condición poco frecuente, usualmente benigna y autolimitada; se han descrito la presencia de NM en casos de COVID-19. Si bien la mayoría de los casos han sido autolimitados y se manejaron de manera conservadora, se recomienda la vigilancia estrecha dado que puede provocar alteraciones hemodinámicas y respiratorias potencialmente mortales. Presentamos una serie de 4 casos de pacientes ingresados en el Hospital Regional de Alta Especialidad de la Península de Yucatán durante el periodo comprendido entre mayo y agosto del 2020 con infección por SARS-CoV-2 en quienes se documentó la presencia de NM.

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