Pathophysiology of spontaneous pneumomediastinum in patients with SARS-CoV-2 infection: a case report

Fisiopatología del neumomediastino espontáneo en pacientes con SARS-CoV-2: reporte de caso

To the editor:

Due to the impact that the COVID-19 pandemic has had on health systems worldwide, efforts have been made to understand its pathophysiology, natural history and adverse outcomes. Spontaneous pneumomediastinum (SPM) is a rare disease entity in the population, with a reported incidence of approximately 1:44,000 patients consulting the emergency department (ED)[1]. However, it appears that the pathophysiology related to SARS-CoV-2 makes this entity more frequent. Multiple cases of SPM associated with SARS-CoV-2 have been reported[2,3]. COVID-19, mostly in patients subjected to positive pressure ventilation, a known risk factor for developing p Spontaneous pneumomediastinum neumomediastinum[4] (PnM). In this report, we present a case of SPM in a patient with COVID-19 pneumonia, which, unlike the cases reported so far, occurred in the absence of positive pressure ventilation.

A 27-year-old man with a history of active smoking and a history of close contact with a COVID-19 patient. He consulted the ED for an 8-day history of general condition, dry cough, myalgias and progressive dyspnea. In the ED his vital signs were: blood pressure 128/72 mmHg, heart rate of 105 bpm, respiratory rate (RR) of 28 vpm, oxygen saturation 90% ambient and axillary temperature of 38.6°C. Laboratory tests included 14,300 leukocytes/µL, PCR 30.4 mg/dL, interleukin 6,134 pg/mL, D-dimer 516 ng/mL, PaO_2 77 mmHg, PCO_2 33 mmHg,pH 7.46, bicarbonate 23.5 mmol/L. A portable chest X-ray was requested and showed multiple parenchymal alveolar-filled parenchymal opacities with patchy, bilateral ground-glass densities, a pattern suggestive of COVID-19 infection (Figure 1).

Initially, the patient was managed with oxygen therapy with a non-recirculation mask and alternating cycles of prono vigil, and presented clinical improvement and was hospitalized in the basic care unit. During hospitalization the patient evolved with adequate oxygenation with FiO_2 at 35%, but maintaining episodes of cough and RR of 30-40 brpm, so it was decided to add therapy with methylprednisolone 125 mg for 3 days and transfer to an intermediate care unit. During the third day of hospitalization he presented clinical deterioration with ventilatory distress, chest pain and inspiratory arrest. It was decided to perform a study with chest angiography by computed tomography (CT) to rule out pulmonary thromboembolism (PTE) and escalate therapy with high-flow nasal cannula (HFNC). The CT image showed a left PnM associated with right supraclavicular subcutaneous emphysema, images not visualized in previously requested portable radiographs, and PTE was ruled out (Figure 2). After 7 days with CNAF, the patient evolved with decreased oxygen requirements and low inflammatory parameters. He was discharged on the 14th day of hospitalization. SARS-CoV-2 virus infects cells of the respiratory system through binding to the ACE-2 membrane receptor. In most patients, it manifests with mild to moderate viral pneumonia and 60% of cases[5] present with cough. Sometimes, it manifests more severely, progressing to acute respiratory distress syndrome (ARDS) with dysfunction of one or more organs. Several published studies have shown that the main differences between mild and severe manifestations of COVID-19 are cytokine storm syndrome and altered immune cell expression in the infected host[6,7].

In conclusion, the inflammatory response plays a predominant role in the pathophysiology of COVID-19. This hyperinflammation, together with viral replication, produces damage to the lining of the pulmonary epithelium that deteriorates the alveolar barriers[6]. The latter could be a predisposing factor for the development of SPM, as postulated in the SARS-CoV infection of 2004[8].

In order to understand the mechanism, we focused on 3 components related to the pulmonary pathophysiology involved in SARS-CoV-2 infection and how this relates to the mechanism of cough as a trigger. First, in patients with respiratory failure due to ARDS due to COVID-19 there is an increase in work of breathing determined primarily by a resistive and elastic component[9]. The increase in resistance and elastance in the airway produces an increase in work of breathing and stimulation of mechanoreceptors, which, associated with the stimulation of chemoreceptors by hypoxemia, manifests as an increase in ventilatory drive. The proinflammatory state characteristic of SARS-CoV-2 infection produces an increase in cellular metabolism and fever that also promote hyperventilation. Thus, its volume/minute increases significantly from 7.5 liters at rest to 15 to 20 liters. Secondly, patients with ARDS have a decrease in lung tissue available for gas exchange, called Baby Lung. This fact directly affects the volume of air supported by these lung tissue masses[10]. Therefore, in ARDS patients have functionally smaller lungs which, being subjected to a higher flow per minute, suffer greater stress on the alveolar wall.

Thirdly, the pathophysiological event of NM formation could be explained from the concept of the "Macklin phenomenon", where initially there is a rupture of the alveolar wall due to overdistension of the alve-

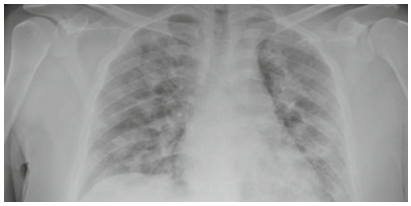

Figure 1. Portable chest X-ray. Multiple bilateral, diffuse bilateral patchy parenchymatous alveolar filling and ground-glass density parenchymal opacities are identified.

olus due to stretching and straining phenomena of the alveolar wall that cause the alveolar wall to collapse[11]. In the presence of these 3 conditions, only a stimulus that sharply increases intrathoracic pressure is needed for the alveolar walls subjected to this stress to rupture and generate NME. The cough, in an initial (inspiratory) phase, presents an increase in air inhalation that can reach up to 50% of the patient's vital capacity. In a second phase (compressive), the glottis closes and an increase in intrathoracic pressure of up to 300 mmHg is generated. In the third phase (expiratory), the glottis opens and expiratory muscles contract, generating a flow of up to 12 liters per second[12]. When the glottis is still closed, the tension of the expiratory musculature generates a transient increase in intrathoracic pressure and the alveolar walls are susceptible to rupture and generate NME. Although the amount of pneumothorax in this patient was mild, the associated chest pain and discomfort appear to have contributed significantly to his clinical deterioration. In agreement with what was reported in a large cohort study, it appears that the occurrence of an SPM in a patient with COVID-19 pneumonia is associated with a worse outcome than in those with pneumonias due to other etiologies[14]. Thus, although SPM is a rare complication of viral respiratory diseases[13,14], it should

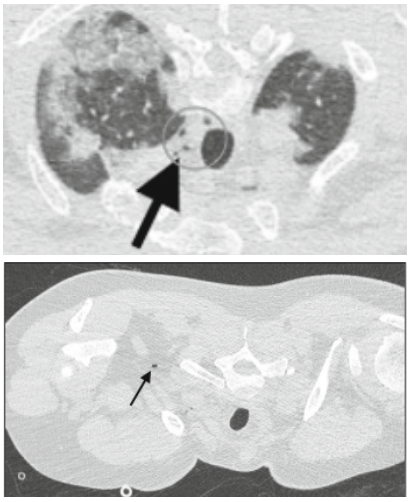

Figure 2. Above: details of the thoracic computed tomography. Mild pneumomediastinum (circle). Extensive parenchymal opacities of alveolar filling, compatible with known COVID-19 pneumopathy. Below: mild right supraclavicular emphysema (arrow).

be considered as a differential diagnosis in a COVID-19 patient with clinical worsening.

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Conflict of Interest Disclosures: None reported

Author Contributions, Funding/support, and Ethical Responsibilities: All authors have confirmed their authorship, the absence of external funding, and the maintenance of confidentiality and respect for patient rights in the document of author responsibilities, publication agreement, and assignment of rights to EMERGENCIAS. The patient has confirmed his/her consent for his/her personal information to be published.

Editor-in-charge: Òscar Miró.

Article not commissioned by the Editorial Committee and with external peer review.

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