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Case report

Spontaneous pneumomediastinum and COVID-19 pneumonia: Report of three cases with emphasis on CT imaging ☆

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ABSTRACT

Spontaneous pneumomediastinum is a rare complication of coronavirus disease 2019. The published literature consists mainly of case reports and small case series. There are still many questions regarding the pathogenesis, the prognostic significance and the implications on patient management. In our hospital, 3 coronavirus disease 2019 patients developed spontaneous pneumomediastinum: 1 on admission at the emergency department and the other 2 during hospitalization. In this study we describe their clinical course and computed tomography (CT) findings. All of them had severe disease according to the total severity score on admission CT. The management of pneumomediastinum was conservative and follow-up CT showed resolution in all patients. As the correlation between extension of parenchymal lung lesions and development of pneumomediastinum is still under investigation, we highlight the importance of reporting the severity score on chest CT in order to obtain more comparable results between different studies. Furthermore, in this tragic circumstance we also had the opportunity to familiarize ourselves with the otherwise uncommon occurrence of air along the bronchovascular sheaths (Macklin effect) and evaluate the ability of CT to detect it.

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Introduction

Since the onset of the worldwide coronavirus pandemic new data that enrich our knowledge and comprehension of the disease appear daily in international literature. Radiological imaging plays a crucial role in evaluating the course of coronavirus disease 2019 (COVID-19) infection and in choosing proper management of infected patients. The imaging characteristics of COVID-19 pneumonia depend on the stage of the disease. The most frequent and early presentation consists of bilateral multilobar ground glass opacities (GGO) with a peripheral and posterior distribution [1]. Septal thickening, consolidation superimposed on GGO, bronchiectasis and fibrotic-like lesions are some of the imaging findings that occur over time. A comparatively unusual complication that has been noted in recent reports [2–4] is the development of pneumomediastinum in non-intubated COVID-19 patients.

Spontaneous pneumomediastinum (SPM) is defined as the presence of free air in the mediastinal cavity that is not associated to trauma or iatrogenic causes, such as intubation, endoscopic procedures or central line placement [5]. Predisposing risk factors of SPM are a positive history of smoking, asthma, interstitial lung disease and a recent history of respiratory infection.

SPM in COVID-19 patients is isolated in some cases, while in others it is combined with pneumothorax, pneumopericardium or subcutaneous emphysema. Given the infrequent occurrence of the complication, the published literature consists mainly of case reports and case series.

The pathophysiological mechanism, which was first described by Macklin et al. [6] and is, therefore known as Macklin effect, refers to the presence of a pressure gradient between the alveoli and the lung interstitium resulting in alveolar rupture, followed by air dissection centripetally through the pulmonary interstitium along the bronchovascular sheaths toward the pulmonary hila and the mediastinum. Although the exact mechanism of alveolar rupture in COVID-19 pneumonia is unknown, it has been suggested that it may be linked to a combination of inflammation and diffuse alveolar damage caused by the SARS-COV2 virus and increased alveolar pressure due to pronounced cough [7].

The clinical significance of the radiologic finding in terms of prognosis and patient management is still under investigation. There are many questions yet to be answered; thereby it is important that every institution reports back all experiences of this rare complication and in as much detail as possible.

Material and methods

Since the outbreak of COVID-19, 3 cases of SPM have been diagnosed in our radiology department. We subsequently followed up these patients and collected all clinical and imaging data relevant to the condition.

Patient 1

A 49-year-old man with a medical history of obesity was referred to the emergency department complaining of fever associated with chest pain and dry cough. The patient was diagnosed with COVID-19 on the basis of RT-PCR analysis performed 3 days before. No medical history of smoking, emphysema or chronic lung disease was reported. His vital signs were as follows: temperature of 37.8°C, blood pressure of 123/85 mm Hg and oxygen saturation of 79% on room air. The patient was immediately placed on supplemental oxygen via Venturi mask (maximum oxygen concentration). Laboratory studies were remarkable for normal white blood cells count of 6.900/μL with a neutrophil count of 85.7%, elevated C-reactive protein at 255 mg/L and elevated soluble urokinase plasminogen activator receptor biomarker (suPAR) at 16 ng/mL. His D-dimer was 1,51 mg/L. Chest computed tomography (CT) (Figs. 1A and B) revealed extensive bilateral ground glass lesions. According to the method proposed by Li et al. [8], the total severity score (TSS) was 19 per 20. Unexpectedly, extraluminal gas was observed in the mediastinum anterior to the pulmonary artery and aortic arch and in the left hila (perihilar Macklin effect).

The patient was placed on antibacterial, antiviral, corticosteroid treatment and thromboprophylaxis with low molecular weight heparin (LMWH). During the hospital course his hypoxia worsened requiring transition to increasing levels of supplemental oxygen to reach the level of 60L/min by high flow nasal cannula (HFNC) to maintain his oxygenation.

Two more chest CT examinations were requested on hospital days 6 and 13, due to episodes of fever and raised inflammatory markers. They showed resolution of previous pneumomediastinum (Figs. 1C and D) and gradual progression of GGO into denser consolidations and more fibrotic lesions.

His antibiotic treatment was adjusted and a gradual clinical improvement with reducing oxygen requirements was observed. Eventually, 22 days after admission, in stable condition, he was discharged home.

Patient 2

A 66-year- old man with a history of hypertension, dyslipidemia and obesity presented to the emergency department with a 3-day history of fever, dyspnea, dry cough and a positive rapid test for COVID-19. Smoking history was also reported. Vital signs were temperature of 36.8°C, blood pressure of 110/60 mm Hg and oxygen saturation of 90% on room air. Laboratory tests revealed normal white blood cells count (4.900/μL) with an elevated neutrophilic count (85,4%), elevated C-reactive protein (144 mg/L) and suPAR biomarker (6,20 ng/mL). The patient was placed on supplemental oxygen via Venturi mask (oxygen concentration 50%). Chest CT on admission revealed extensive GGO involving all lobes, with a TSS of 9.

The patient was placed on antibacterial, antiviral, corticosteroid treatment and thromboprophylaxis with LMWH. During hospitalization the patient started to decline clinically, presenting increasing oxygen requirements. He was eventually placed on a high flow nasal cannula (HFNC, FiO2: 91%, 60L/min). A modification of his antibiotic treatment was also necessary due to raised inflammatory markers.

On hospital day 10, he had a CT pulmonary angiography because of clinical deterioration and suspicion of pulmonary

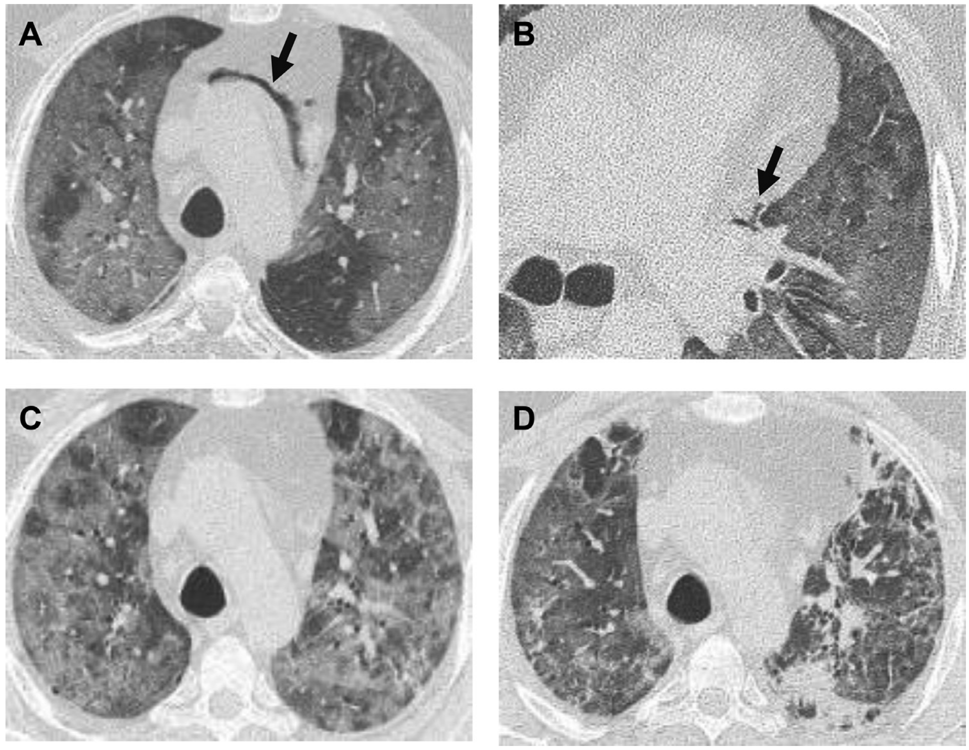

Fig. 1 – (Patient 1): (A) Chest computed tomography (CT) on admission demonstrating a gas collection anterior to the aortic arch and extensive parenchymal ground glass lesions. (B) CT on admission showing left perihilar Macklin effect. (C) Chest CT on hospital day 6 showing resolution of the pneumomediastinum. More extensive and denser parenchymal lesions are evident in comparison to A. (D) CT on hospital day 13 showing the appearance of fibrotic lesions.

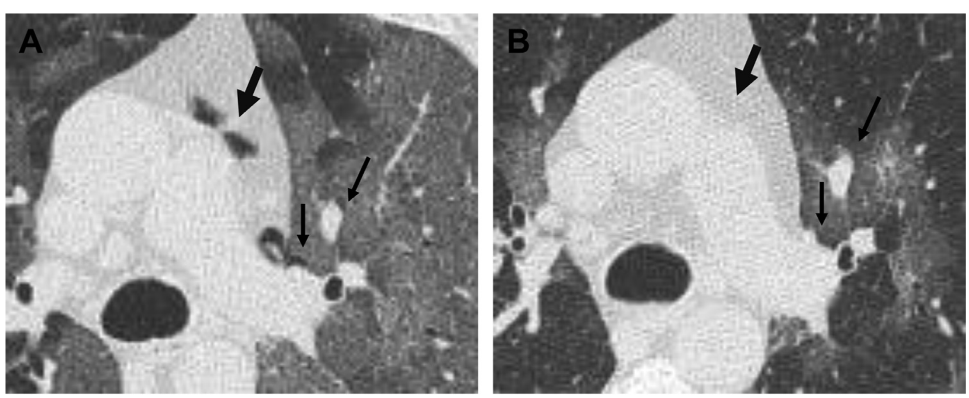

Fig. 2 – (Patient 2): (A) Chest computed tomography (CT), lung window, performed on hospital day 10 showing pneumomediastinum (thick black arrow), perihilar and peripheral Macklin effect (thin black arrows). Extensive ground glass lesions with thickened interlobular septa are also evident. (B) Chest CT, lung window, on admission. No sign of pneumomediastinum (thick black arrow) or Macklin effect (thin black arrows) at that time.

embolism (Fig. 2). Small filling defects in right upper lobe subsegmental arteries were noted. Surprisingly, gas bubbles were revealed in the anterior compartment of the mediastinum and in the left hila (perihilar Macklin effect). A more careful examination of the left lung parenchyma permitted the identification of linear air collections along branches of the left upper pulmonary vein (peripheral Macklin effect). Previous ground glass lesions were accompanied by thickened interlobular septa and were more extensive in comparison to the admission CT.

The patient received Fondaparinoux for the treatment of pulmonary embolism. Conservative treatment was advised for pneumomediastinum. His respiratory status continued to worsen with increasing oxygen requirements and ultimately

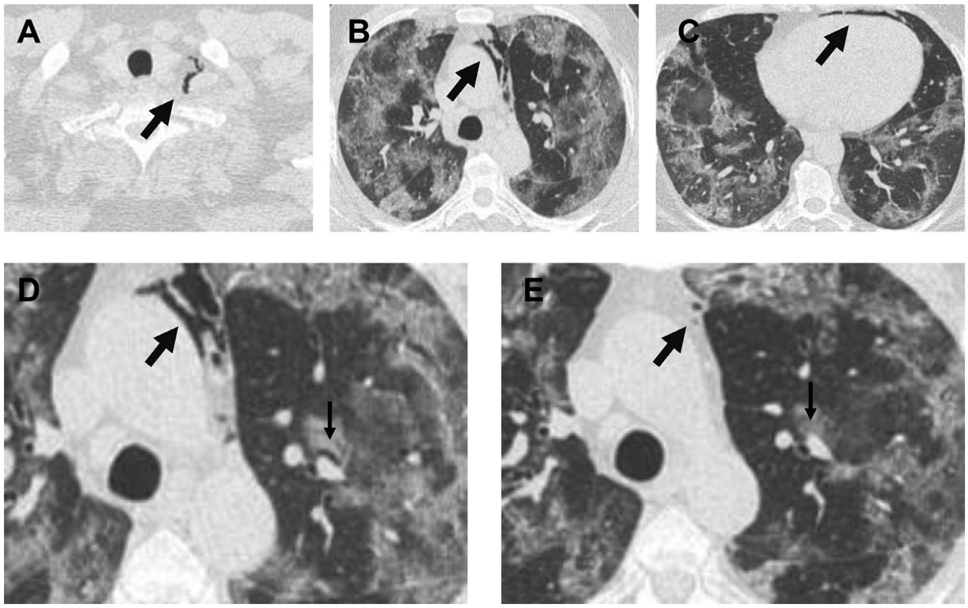

Fig. 3 – (Patient 3): (A-C) Chest computed tomography (CT) on day 8 showing emphysema mainly extending into the left cervical region (A), pneumomediastinum (B), and pneumopericardium (C). (D) Chest CT on day 8 demonstrating pneumomediastinum (thick arrow) and peripheral Macklin effect. (E) Chest CT on day 13 showing resolution of the Macklin effect (thin arrow) and persistence of small gas bubbles in the anterior mediastinum (thick arrow).

necessitating endotracheal intubation. Transfer to the intensive care unit (ICU) was decided. We would like to highlight the fact that his complicated clinical course was mainly due to extensive lung disease, septic episodes and bleeding diathesis and was unrelated to the pneumomediastinum. In fact, on hospital day 30 a chest CT was obtained that showed its resolution. At the moment of writing the patient remains in the ICU.

Patient 3

A 44-year-old man was admitted to the emergency department complaining of a 5-day history of fever, dyspnea and dry cough. He had tested positive for COVID-19 eight days before presentation via a rapid test. No medical history was reported. His vital signs were temperature of 36.2°C, blood pressure of 163/102 mm Hg, and oxygen saturation of 84% on room air. The patient was initially placed on supplemental oxygen via nasal cannula (3 L/min) and then on a Venturi mask (40%). His laboratoty tests were remarkable for slightly elevated white blood cell count of 11.900/μL with a neutrophil count of 90.6%, elevated C-reactive protein at 181 mg/L and elevated suPAR at 7.6 ng/mL His D-dimer was 0.86 mg/L.

Admission chest CT showed extensive ground glass lesions (TSS 12).

The patient was placed on antibacterial, antiviral, corticosteroid treatment and thromboprophylaxis with LMWH. During hospitalization his oxygen requirements increased and he was placed on high flow nasal cannula (HFNC, FiO2: 89%, 60 L/min) to maintain his oxygenation. A modification of his antibiotic treatment was also decided.

On hospital day 8, a CT pulmonary angiography was performed because of a clinical suspicion of pulmonary embolism. In fact, CT confirmed the presence of small bilateral contrast filling defects of segmental and subsegmental arteries. Additionally, it revealed the presence of pneumomediastinum, pneumopericardium and subcutaneous emphysema. Perihilar and peripheral Macklin effect was evident (Fig. 3D).

The patient received Fondaparinoux for the treatment of pulmonary embolism. In the following days there was an improvement in the respiratory condition and general status of the patient. Chest CT on hospital day 13 showed minimal gas persistence in the anterior mediastinum. Peripheral Macklin effect was not evident anymore (Fig. 3E).

The patient was successfully discharged home 18 days after admission, in good general condition.

Discussion

Before the COVID-19 outbreak SPM was an extremely rare condition, diagnosed in 1 per 44,500 of accident and emergency attendances [9]. In the context of viral infections, some sporadic cases had been published, mainly associated with influenza virus [10]. The SARS infection is a remarkable exception. Indeed, the reported frequency of SPM development in 2 different SARS studies was 12% [11,12]. In regard to COVID-19, the frequency seems to be much lower, but still notable. 3 cases of SPM out of 720 patients (frequency 0.42%) have been identified in our radiological department since November 2020, but no cases were noted earlier, during the first wave of the pandemic. These observations are in accordance with the results of larger studies [13–15]. In fact, in their study of 4081 hospitalized COVID-19 patients Brito et al. [13] report a frequency of

0.5% and in their study of 1648 patients Cut et al. [14] report a frequency of 0.66%. Moreover, Palumbo et al. [15] point out the significantly higher rate of the complication during the second wave of the pandemic.

The risk of development of SPM in COVID-19 patients has been associated with mechanical and non-invasive ventilation [16–18]. In addition, similarly to our patients 2 and 3, there are some reported cases of SPM in COVID-19 patients managed with HFNC [3,19–21,22,23,24,25], whose contribution to the occurrence of SPM is still unclear. The aforesaid observations may confound the role that COVID-19 plays in the development of SPM. Patient 1 represents one of the few cases in the published literature of SPM diagnosed on presentation at the emergency department, at the beginning of oxygen support therapy [7,26–35]. These cases are of great importance because they suggest that there must be an inherent component in the COVID-19 infection that predisposes to air leaks, which can precipitate with anything that increases the alveolar pressure [24].

Due to the vague nature of presenting symptoms [5], imaging is essential to make a diagnosis of pneumomediastinum and should be considered in all COVID-19 patients with unexplained clinical deterioration [36,37]. Chest X-ray is the first imaging modality employed and often suggests the diagnosis by showing linear or curvilinear lucencies outlining mediastinal contours. CT is more sensitive in the detection of air in the mediastinum and is very helpful in establishing or confirming the diagnosis. It may also provide extra diagnostic information regarding the exclusion of coexisting illness, such as perforated esophagus. All that certainly comes at the cost of increased radiation dose.

An additional advantage that CT offers is that it provides the mean to reveal the Macklin effect. It appears on thoracic CT as linear collections of air contiguous to the bronchovascular sheaths [38]. The main reason to communicate its occurrence is that it offers a confirmation of the proposed mechanism of SPM formation in COVID-19 patients and increases confidence that SPM is due to respiratory and not other causes of pneumomediastinum. We detected the CT Macklin effect in the perihilar area of all our patients and in the peripheral area of 2 out of 3 patients. A finding that caught our attention was that the peripheral Macklin effect was located on the left in all of our patients. The CT Macklin effect has been mentioned in few other reports on COVID-19 patients [13,29,39].

The prognostic significance of the development of SPM is still under investigation. A hypothesis is that, if indeed there is a correlation between the degree of alveolar *damage* and the presence of pneumomediastinum, then it would be more likely to occur in patients with an advanced stage of the disease with extensive pulmonary lesions and correlate with a worse outcome [28,40]. Actually, in the larger published case series [13,14,41,42] most patients with SPM had extensive lung lesions. This also applies to our study, in which all of our 3 patients that developed SPM had extensive disease with high TSS of the admission CT. However, SPM has also been described to occur in the absence of extensive lung involvement, with a favorable clinical course and recovery of the patients in the majority of these cases [28]. In addition, we would like to highlight the importance of using a CXR or CT scoring system to assess the severity of lung involvement in COVID-19 patients in order to obtain more comparable results between different studies.

Once the diagnosis of pneumomediastinum has been made, the radiologist should communicate the finding to the clinical doctor as soon as possible. Although SPM is usually a self-limiting condition, it may require some changes in the management of the respiratory support in order to maintain the balance of adequate oxygenation while preventing pneumomediastinum expansion and pneumomediastinum-related cardiovascular and respiratory complications [2,20]. Serial imaging is usually required.

Conclusion

It is important to be alert to the diagnosis of pneumomediastinum in COVID-19 patients even in the absence of mechanical ventilation. Apart from permitting early recognition, CT imaging also provides significant information, such as the severity score and the revelation of the Macklin effect. It is suggested that this information is incorporated in published studies on this topic.

Patient consent

The authors declare that written informed consent has been obtained from all the patients of this study.

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