

Delayed Spontaneous Pneumothorax Presentation in Covid-19: Case Series and Review

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ABSTRACT

Background: Since the presentation of the 2019 novel coronavirus (2019-nCoV), there have been several published papers outlining the clinical and radiological course of the disease. However there is minimal data regarding delayed complications.

Methods: In this retrospective, single-centre study, we identify patients who have presented with spontaneous pneumothorax, several weeks after their initial symptoms. All these cases are without history of recent invasive ventilation.

Findings: To date, we have four cases of spontaneous pneumothorax, presenting several weeks after initial symptoms of Covid-19. All these cases are male, with ages ranging from 40 to 90 years old. Only one had known interstitial lung disease, the others had normal previous lung imaging.

Interpretation: Current literature appears to be centred on the acute features of Covid-19. There is little data available regarding the sub-acute presentation of this disease. To our knowledge, there have only been a handful of reported cases of spontaneous pneumothorax, with the majority of papers reporting no cases. Our small case series highlights that the risk of spontaneous pneumothorax may be under-reported. We discuss the current known pathophysiological mechanisms of Covid-19 and discuss the potential delayed complications of this disease.

Keywords: *Pneumothorax, Covid-19, SARS CoV-2, Thoracic Computed Tomography*

Introduction

Since the reported cases from Wuhan on December 31, 2019, severe acute respiratory syndrome coronavirus 2 (SARS CoV-2) has fast become a pandemic, with over 4 million global cases and the first reported case in the UK on January 31, 2020.2 During this outbreak, thoracic computed tomography (CT) has played a pivotal role in disease management (Li Y *et al*., 2020) as well as evaluation of patients with suspected COVID-19 infection (with or without a positive RT-PCR result) (Bernheim *et al*., 2020; Huang *et al*., 2020). The clinical features (Chen *et al*., 2020) and radiological appearances on CT have been widely reported (Xu *et al*., 2020; Pan *et al*., 2020; Ding *et al*., 2020) with the most consistently reported CT feature of COVID-19 being ground glass opacification (often bilateral, peripheral or posterior) and predominantly located in lower lobes (Salehi *et al*., 2020). Approximately two weeks after onset (Pan *et al*., 2020), patients may develop confluent consolidations. It is about two to three weeks into the disease process, that CT may show bronchial wall and interlobular septal thickening. These features are found to be consistent with the archetypal response to acute lung injury (Xu XW *et al*., 2020). There are, however several less commonly reported findings, such as pleural effusion, pericardial effusion, lymphadenopathy and cavitation (Bernheim *et al*., 2020; Salehi *et al*., 2020). Another rare finding is pneumothorax which is believed to have a prevalence of 1% in patients with COVID-19 (Chen *et al*., 2020).

Development of a pneumothorax and/or pneumomediastinum, are recognised sequelae of mechanical ventilation in patients with underlying lung diseases (Hsu and Sun, 2014) and acute respiratory distress syndrome (Weg *et al*., 1998). It follows that patients with COVID-19 receiving non-invasive or invasive ventilation are at risk for these complications. However, there have been recently reported cases of secondary spontaneous pneumothorax in non-ventilated COVID-19 positive patients (Sun *et al*., 2020; Liu *et al*., 2020; Wang W *et al*., 2020; Rohailla *et al*., 2020; Kolani *et al*., 2020). It is vital that this rare complication is recognised and managed, both in ambulatory patients and in those destined for intensive treatment. In this retrospective case series we discuss four, non-ventilated, male patients with confirmed COVID-19, who developed pneumothoraces during the mid-late course of their active infection.

Cases

Case 1 is a 90 year old man recently returned from India woke suddenly at home at 4 am with sharp, left sided chest pain. On admission to hospital he did not require any oxygen therapy; COVID-19 RT-PCR was positive. Past medical history included poorly controlled type II diabetes, hypertension, chronic kidney disease, peripheral vascular disease, coronary artery disease, prostate cancer and mild, asymptomatic lung fibrosis (usual interstitial pneumonia (UIP) pattern was evident on a CT chest from 2015).

A chest radiograph showed bilateral patchy airspace opacification with reticulation at the bases (Fig. 1). Typical features of COVID-19 infection were evident on a CT pulmonary angiogram (CTPA) with bilateral, posterior, subpleural ground-glass opacification and scattered foci of interlobular septal thickening (Fig 2). In addition, there was a shallow left sided pneumothorax. No pulmonary embolus was detected. The patient was managed conservatively and discharged on day two with a plan for follow-up chest radiograph in two weeks.

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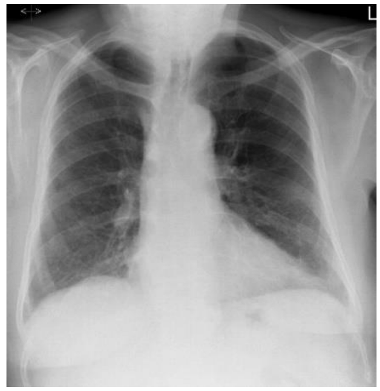

Figure 1: Chest radiograph of a 90 year old man with confirmed COVID-19 infection demonstrating bilateral, airspace opacification and stable basal reticulation

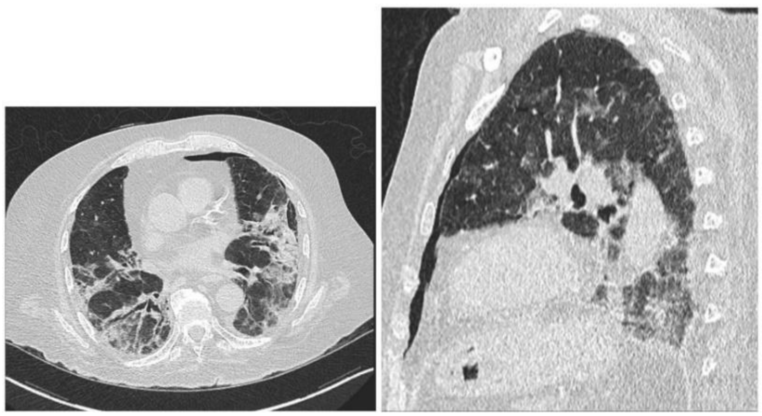

Figure 2: Axial (a) and sagittal (b) CT images of a 90 year old man with confirmed COVID-19 infection demonstrating bilateral, posterior, subpleural ground-glass opacification and scattered foci of interlobular septal thickening as well as a shallow left sided pneumothorax

Case 2 is a 40 year old man with confirmed COVID-19 infection was admitted in the early hours with acute, sharp, right sided chest pain. He had a three week history of cough, fever and chest pain and had just been discharged from hospital on the previous evening. He was saturating at 96% on room air on admission. The patient had a medical history of bicuspid aortic valve with severe aortic regurgitation and was also obese. He had no underlying lung condition.

A chest radiograph on admission demonstrated bilateral airspace infiltrates (improved from previous chest radiograph) plus a new right midzone density suggestive for an encysted effusion (Fig. 3). A CTPA confirmed improved bilateral, patchy, peripheral ground glass opacification (Fig. 4). In addition there was a new encysted gas/fluid collection adjacent to the right oblique fissure consistent with a hydropneumothorax. A further, small right-sided hydropneumothorax had also developed. No pulmonary embolus was detected. The patient was treated conservatively and discharged on day three. The patient re-presented three times over the following month with ongoing shortness of breath. The hydropneumothoraces remained stable in appearance.

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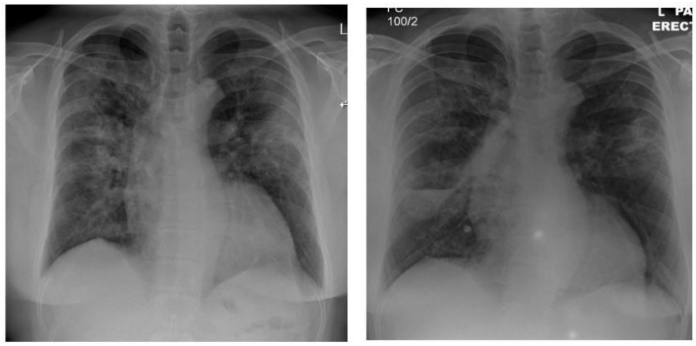

Figure 3: Chest radiographs of a 40 year old man with confirmed COVID-19 infection showing bilateral airspace infiltrates (a) which have improved on subsequent imaging (b). A new, encysted right pleural effusion is evident on the second radiograph (b)

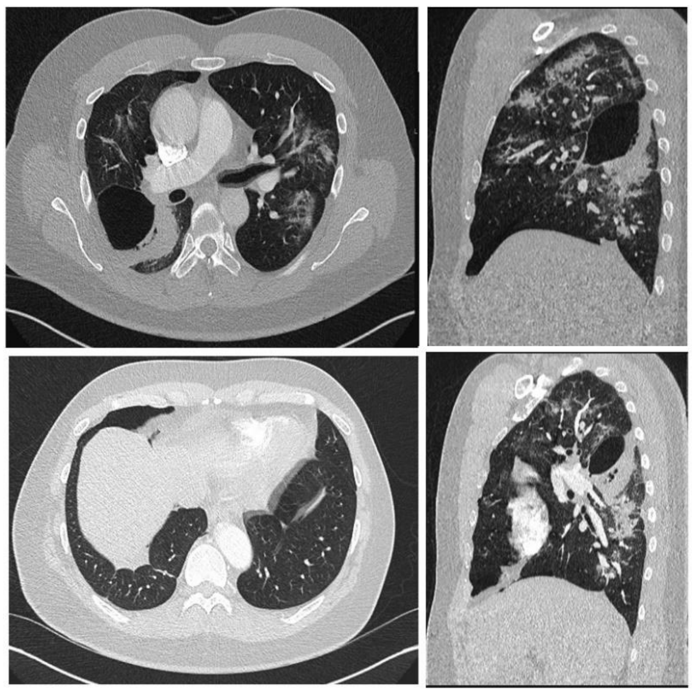

Figure 4: CTPA of a 40 year old man with confirmed COVID-19 infection. Axial (a) and sagittal (b) images show a right hydropneumothorax abutting the right oblique fissure on the background of bilateral multi-focal, groundglass opacification. Axial (c) and sagittal (d) images taken at a different level show a further, smaller right basal hydropneumothorax (*)

Case 3 is a 75 year old man with confirmed COVID-19 infection presented with chest pain and haemoptysis. He had recently been in hospital for 11 days for persistent shortness of breath (no NIV or intubation during the admission). He had a background medical history of COPD (GOLD stage 3; FEV1 39 %) requiring home oxygen and mild obstructive sleep apnoea.

Chest radiograph on admission showed bilateral atelectasis plus an air-fluid level at the left costophrenic angle (Fig. 5). A CTPA demonstrated interval improvement of bilateral ground glass opacification from imaging 18 days previously but the development of several areas of more confluent consolidation (Fig. 6). In addition, a new small-moderate left hydropneumothorax had developed. No pulmonary embolus was detected. The patient was treated conservatively and discharged on the same day.

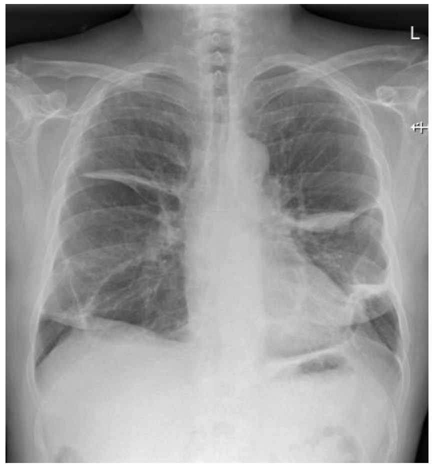

Figure 5: Chest radiograph of a 75 year old man with confirmed COVID-19 infection demonstrating multiple, bilateral foci of atelectasis plus an air-fluid level at the left base

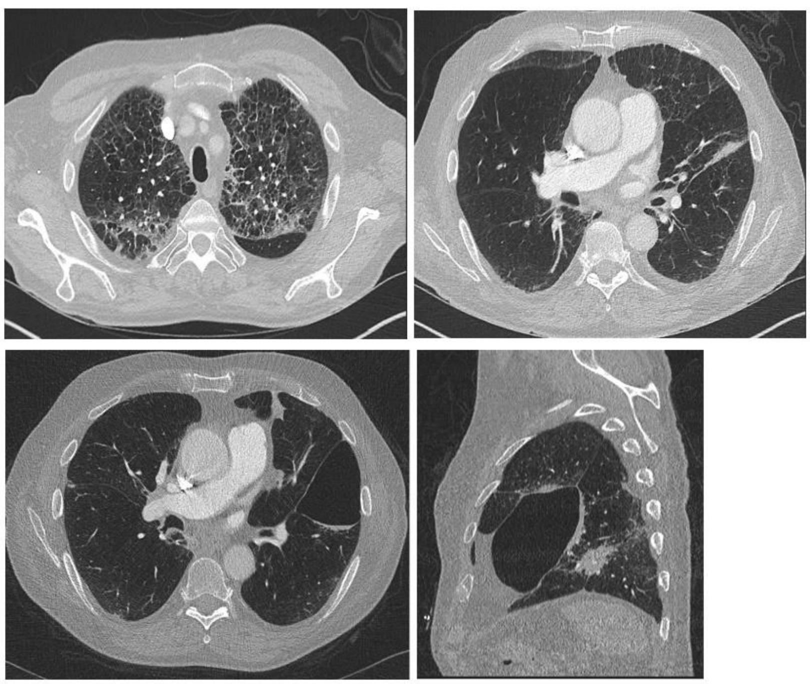

Figure 6: CTPA of a 75 year old man with confirmed COVID-19 infection on initial presentation (a, b) and 18 days later (c, d). Bilateral ground glass opacification is present on a background of moderate-severe upper lobe predominant centrilobular emphysema (a, b). On the follow up images, the ground glass component has reduced with evidence of confluent consolidation/organising pneumonia. A new small-moderate left hydro pneumothorax has now developed

Case 4 is an 80-year-old man with confirmed COVID-19 infection presented with a two day history of sudden onset left-sided chest pain and shortness of breath following an intense bout of coughing, 40 days following initial symptoms. Past medical history included ischaemic heart disease, hypertension, chronic renal failure (stage 3) and recently diagnosed COPD. On initial medical assessment he was short of breath with oxygen saturations in the low 90s, improving to 95% on 2-3L via nasal cannula.

Chest radiograph on admission demonstrated a new left-sided pneumothorax (Fig. 7). CT chest confirmed a large left-sided pneumothorax with mild mediastinal shift to the right plus classic COVID-19 lung changes with superimposed bilateral lower lobe consolidation (Fig. 8).

Figure 7: Chest radiograph of an 80 year old man with confirmed COVID-19 infection demonstrating a left sided pneumothorax plus bilateral peripheral infiltrates

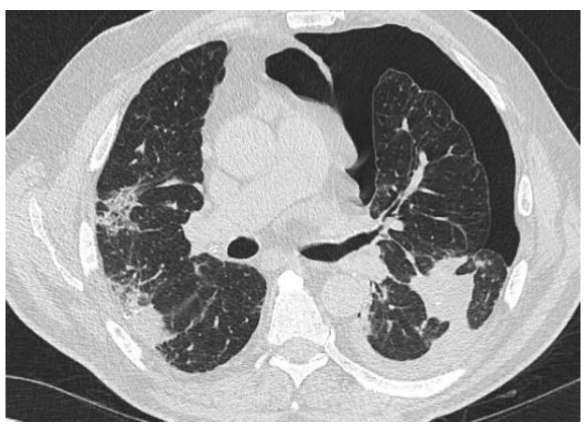

Figure 8: Axial CT image of an 80 year old man with confirmed COVID-19 infection demonstrating a moderate left pneumothorax causing rightward mediastinal shift on a background of bilateral, peripheral ground glass and confluent consolidation

The patient was managed with a left-sided percutaneous chest drain and intravenous antibiotics to cover for secondary bacterial infection. Microbiological test revealed negative blood cultures and pleural fluid and two repeat COVID-19 swabs were negative. The patient made significant clinical improvement following this management and was discharged on day three with four weeks of oral antibiotics.

Discussion

All our cases had real-time RT-PCR positive tests for SARS-CoV-2 and were male. Male prevalence in Covid-19 has previously been noted (Chen *et al*., 2020). There is, however, a published case report of spontaneous pneumomediastinum in a 23 year old female, implying that this phenomenon, although prevalent in males is not exclusive.

The age range of our cases varied from 40 to 90 years old. Some of the patients had co-morbidites, such as, diabetes mellitus, hypertension, chronic renal failure, cardiovascular disease and obesity; these have previously been reported in 'high risk' groups (Wang D *et al*., 2020; Michalakis and Ilias, 2020; Rothan and Byrareddy, 2020). Only Case 1 had a history of previous interstitial lung disease with minor existing basal fibrosis in keeping with mild usual interstitial pneumonia. The others, apart from mild chronic obstructive airways disease and obstructive sleep apnoea, had normal appearing lungs on previous imaging. It can only be presumed that the presentation of spontaneous pneumothorax is associated with the acute lung changes from SARS-CoV-2 infection.

The terms acute lung injury (ALI) and acute respiratory distress syndrome (ARDS) are not new, and have been revised over the years to include clinical and radiological features (Desai, 2002). Following on from the 2002 severe acute respiratory syndrome (SARS CoV) (Vijaynand *et al*., 2004), much work has been undertaken to understand the pathophysiological progression in Covid-19 (Kowalik *et al*., 2020), from acute lung injury (ALI) to the more severe acute respiratory distress syndrome (ARDS) (Gralinski *et al*., 2013). Both of these processes are stereotyped with the histological hallmark of DIFFUSE alveolar damage (Desai, 2002). There are three main principal phases described: the exudative, proliferative and chronic phases. In the first exudative phase, inflammatory exudates move into the interstitium, proteinaceous fluid floods the alveoli, the alveoli collapse and hyaline membranes form. This is followed by the proliferative phase where fibroblasts and type II pneumocytes proliferate and there may be persistent alveolar consolidation due to inflammation and haemorrhage. In the final chronic phase, there is proliferation of type I pneumocytes and collagen deposition (Desai, 2002). In some patients this can lead to chronic interstitial fibrosis. It is true that this fibrosis can occur rapidly and early in ALI/ARDS.

These phases are reflected in the CT imaging features of COVID-19, which can be categorised8 into four temporal stages. Stage 1 is usually less than four days from onset of symptoms, and is characterised by groundglass opacification, which likely represents pulmonary oedema/haemorrhage and hyaline membrane formation (Pan *et al*., 2020; Ye Z *et al*., 2020). As the disease progresses in stage 2 (5-8 days), crazy-paving develops reflecting alveolar oedema and the interstitial inflammation of acute lung injury.

Confluent consolidation is the main CT imaging feature of stage 3 (9-13 days) and is probably caused by the accumulation of fibromyxoid exudates in alveoli. Stage 4 occurs 14 days after initial symptoms and describes resolution of consolidation (Pan *et al*., 2020). It is this close correlation between imaging features and pathological change, that has proven CT imaging to be valuable in evaluating severity and extent of disease (Bernheim *et al*., 2020). In our case series, all the patients were in the late stages of their Covid-19 infection, given their chest CTs showing a combination of residual ground glass opacification, confluent consolidation and crazy-paving.

In this case series, we have described the spontaneous presentation of the air filled intrathoracic foci as pneumothoraces. According to the Fleischner Society (Hansell *et al*., 2008), the definition of a pneumothorax is the presence of gas in the pleural space. Cases 1 and 4 are classical appearances for pneumothoraces. In the other two cases, it could be argued that these are cavities, pneumatoceles or air filled cysts. Technically in these cases, the air filled spaces are adjacent to fissures and presumably within the pleural space rather than being completely surrounded by lung, hence the description of localised pneumothorax.

Our case series highlights that the prevalence of spontaneous pneumothorax in Covid-19 may be higher than initially expected. This would follow suit, given that in the 2002 SARS epidemic, 6 in 365 patients suffered from spontaneous pneumothorax (Sihoe *et al*., 2004). The published image of the localised pneumothorax described then, is very similar to those in our cases 2 and 4. It could be that there is a similarity and that the resultant acute lung injury-associated early fibrosis in Covid-19 patients (Ye Z *et al*., 2020) may cause traction with subsequent air leak. Another theory is that pneumothorax develops secondary to subpleural bulla rupture (Light, 1993) or cyst formation (Chen *et al*., 2020). These are thought to develop due to ischaemic parenchymal damage, lung fibrosis, low lung compliance and inflammatory exudate in the airway causing bullae formation.

It is difficult to know the true prevalence of these air filled spaces in Covid-19 patients, with varying descriptions and accounts. One paper reported no pneumothorax in non ventilated Covid-19 patients (Chen *et al*., 2020), and another one case in 99 patients (Kong and Prachi, 2020). There is one report of a small cavitation (Shi *et al*., 2020) and another paper stating no cavitations (Wu J *et al*., 2020). Another paper has reported 1.5% pneumatocele presentation, with no pulmonary cavities and a 2.3% rate of pleural effusion. Of the five published case reports published (Sun *et al*., 2020; Liu *et al*., 2020; Wang W *et al*., 2020; Rohailla *et al*., 2020; Kolani *et al*., 2020), four were male and one female. Age range varied from 23 to 62 years old. The time of presentation was earliest 3 days to latest 20 days from onset of symptoms. Two patients had received non invasive ventilation. Cyst formation was noted in one of the cases prior to development of pneumothorax.

This article highlights that the development of spontaneous pneumothorax in Covid-19 patients of varying ages, with and without preceding co-morbidiities and the majority presenting later on in the disease process. This has implications for short and long term patient management. Considerations in the acute setting include the feasibility and success rate of drainage or pleurodesis, implications for assisted ventilation and the risk of life threatening tension pneumothorax development. Longer term consideration must be given to the effect on patient lung function and the need for specialist respiratory monitoring with a likely increased demand on imaging.

Learning Points

- The incidence of pneumothorax in non-ventilated patients with COVID-19 infection may be under-reported.
- Early fibrosis, traction and air-leak, cyst formation and intense coughing may result in pneumothorax development in patients with COVID-19 infection.
- Clinicians must consider pneumothorax development in ambulatory patients with COVID-19 infection especially if patients report new pleuritic chest pain or an exacerbation of their breathlessness.
- Spontaneous pneumothorax development will impact on the initial management of patients with COVID-19 infection and has implications for future pulmonary health.
- Loculated hydropneumothoraces pose particular challenges in terms of clinical management and future pulmonary health.

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