Haemoptysis in COVID-19 pneumonia

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Shareable abstract (@ERSpublications)
Pulmonary artery pseudoaneurysm is a differential diagnosis to be considered in COVID-19 patients presenting with or developing haemoptysis in order to facilitate early recognition as delayed management could be catastrophic https://bit.ly/3rQTrDT

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A 77-year-old man presented to the emergency department with symptoms of fever, cough, and myalgia for 2 days. His past medical history included type 2 diabetes mellitus, hypertension, and end-stage renal failure on regular (three times per week) haemodialysis. On physical examination, he was alert with a respiratory rate of 18 breaths per min. His blood pressure was 178/60 mmHg, pulse rate 90 beats per min, and he was afebrile. His pulse oximetry was 98% under room air. Respiratory system examination was unremarkable.

A coronavirus disease 2019 (COVID-19) nasopharyngeal reverse transcriptase PCR test on admission was positive. His chest radiograph was performed (figure 1a). He was diagnosed with COVID-19 infection and was admitted for observation in view of his comorbidities.

He saturated well until day five of illness, when he started requiring supplemental oxygen *via* nasal prongs (2 L·min^{-1}) to maintain a peripheral oxygen saturation (S_{pO_2}) of 95%. He was treated with intravenous methylprednisolone for 3 days followed by dexamethasone. On day 16 of illness, his oxygen requirement increased to 5 L·min^{-1} *via* facemask. A chest radiograph was repeated (figure 1b).

Task 1

Compare and describe the findings in the chest radiographs (figure 1).

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He remained persistently hypoxic, and his oxygen requirements continued to rise. His heart rate was 90 beats per min, blood pressure was 135/71 mmHg. His D-dimer was raised at 1.8 µg·mL^{-1}. His arterial blood gas showed pH 7.378, carbon dioxide tension 29 mmHg, oxygen tension 75.5 mmHg and HCO_3^- 22.5 mEq·L^{-1} on facemask oxygen at 8 L·min^{-1}.

A computed tomography scan of pulmonary artery (CTPA) was done on day 20 of illness (figure 2) to look for causes of the persistent hypoxia including pulmonary embolism.

Task 2

Describe and discuss the CTPA findings (figure 2).

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This was initially considered an incidental finding as patient denied having haemoptysis. However, the following day, he reported haemoptysis of about 20 cm^3 of fresh blood. His blood pressure was 159/92 mmHg, with heart rate of 125 beats per min, S_{pO_2} 100% under high-flow mask. His haemoglobin

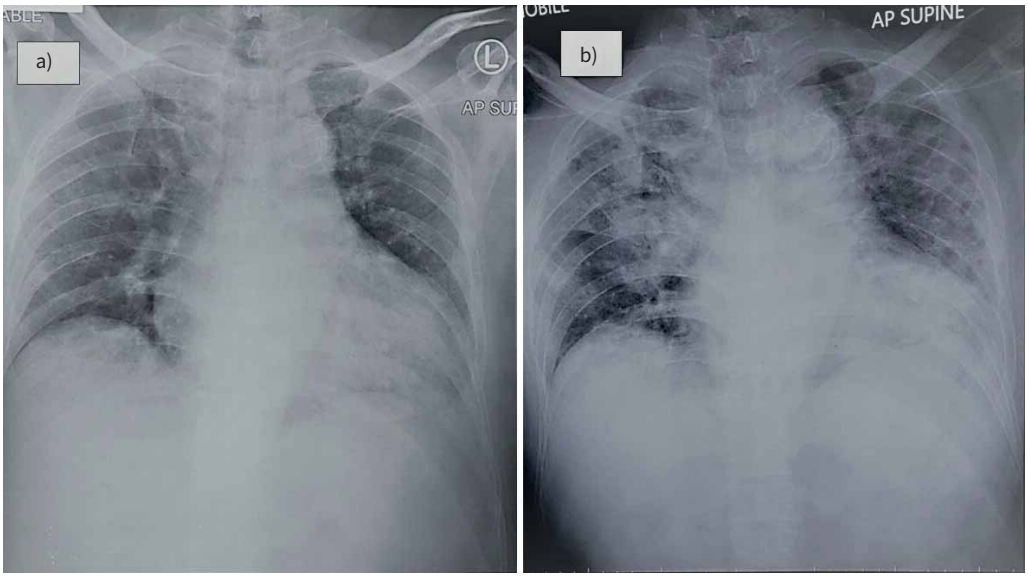

FIGURE 1 a) Chest radiograph on admission. b) Repeated chest radiograph on day 16 of illness.

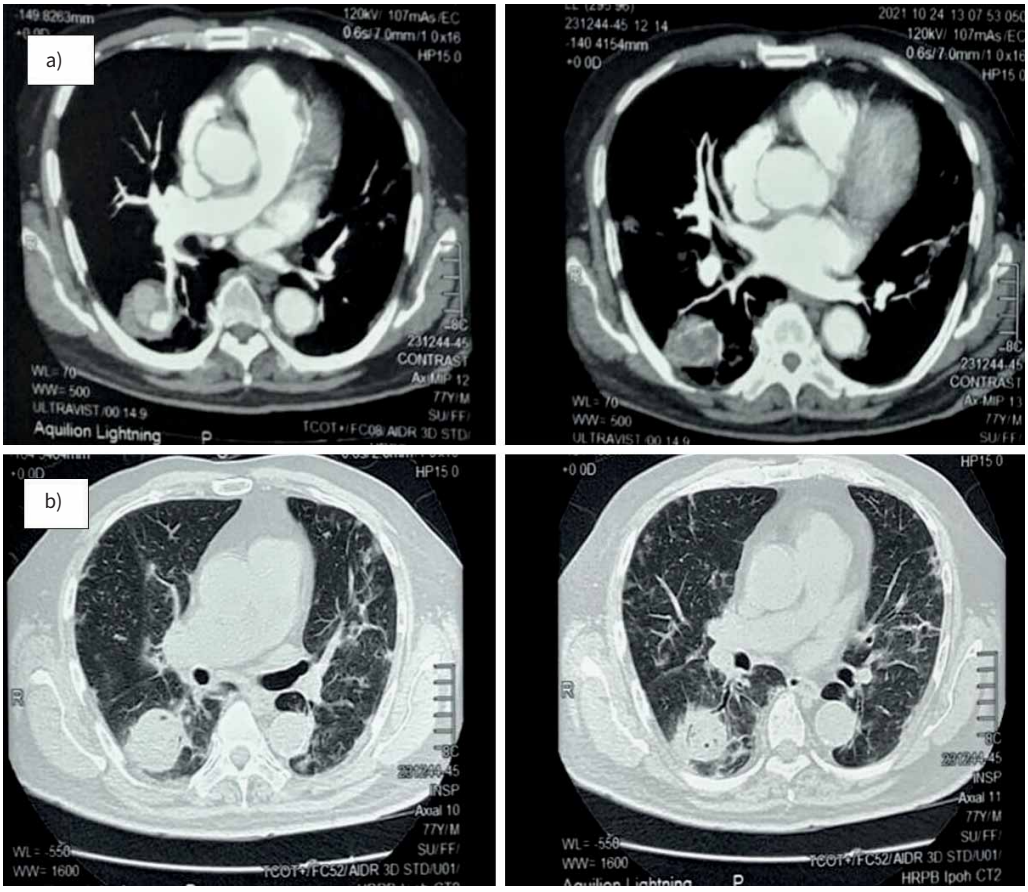

FIGURE 2 CTPA on day 20 of the illness. a) Mediastinal window, b) lung window.

dropped to 9.1 $g \cdot dL^{-1}$ from 10.4 $g \cdot dL^{-1}$, his platelet count was $274 \times 10^9 \cdot L^{-1}$, white cell count was $14.9 \times 10^9 \cdot L^{-1}$ and international normalised ratio (INR) was 0.9. A sputum sample for acid-fast bacilli direct smear and other microbiological testing (including serum galactomannan) were negative. He refused bronchoscopic examination. He was treated with intravenous tranexamic acid. Prophylaxis anticoagulation given due to the COVID-19 infection, was withheld.

Task 3

What are the causes of pulmonary artery pseudoaneurysm (PAP)? What is the most likely cause in this case?

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He was diagnosed with PAP secondary to COVID-19 pneumonia, after excluding all the other causes as mentioned above. His haemoptysis ceased after administration of tranexamic acid. However, his oxygen requirements further increased (needing a high-flow mask at 15 $L \cdot min^{-1}$ oxygen), and his haemoglobin level dropped from 9.1 $g \cdot dL^{-1}$ to 6.7 $g \cdot dL^{-1}$, suggestive of on-going pulmonary haemorrhage despite no haemoptysis. There was no source of overt bleeding found. He received one pint of packed cell transfusion. His oxygenation improved after 2 days; he was weaned to 3 $L \cdot min^{-1}$ oxygen *via* nasal prongs, with S_{pO_2} 96%.

Task 4

What should be considered as the next step of treatment?

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The patient was scheduled for urgent pulmonary artery embolisation. As the procedure was unavailable in our institution, we referred him to the nearest centre with interventional radiology services. Unfortunately, the patient transfer was delayed due to multiple logistic reasons. On arrival at the referral centre the patient no longer had haemoptysis and serial haemoglobin levels were stable. A repeat CTPA was performed at the referral centre and showed thrombosis of the pseudoaneurysm. The procedure was therefore deemed unnecessary and cancelled. He was reviewed in our outpatient respiratory clinic 1 month later, and reported no further haemoptysis, had a stable level of haemoglobin, and appeared to have recovered well from the recent infection.

Discussion

COVID-19 was declared a pandemic in March 2020 and to date, more that 6 million lives have been lost based on official reports. However, the majority of patients with COVID-19 infection will be asymptomatic or experience mild clinical symptoms. A minority will, however, progress to moderate-to-severe clinical disease. Some of these patients will recover over weeks, while others experience progression into a critical state [1]. Our patient demonstrated a typical course of disease progression. He was admitted on day 2 of illness with fever and myalgia not requiring oxygen supplementation, but developed hypoxia and required supplementary oxygen on day 5 of illness. His oxygenation further deteriorated on day 16 of illness prompting a CTPA and high-resolution computed tomography of the thorax to look for potential causes of deterioration.

Worsening hypoxia in COVID-19 pneumonia needs meticulous evaluation as there are a multitude of possibilities that can complicate COVID-19 pneumonia, such as acute respiratory distress syndrome, pulmonary embolism, pulmonary microangiopathy, secondary bacterial or fungal infection, pneumothorax and pneumomediastinum. In this case, his repeated chest radiograph on day 16 of illness showed progressive radiological changes. Nevertheless, the attending physician felt there was a need to exclude additional pathologies and pursued further imaging.

Imaging revealed a PAP with radiological evidence of leak. This was purely incidental as he had no haemoptysis and stable blood counts. However, as alluded above, he subsequently developed clinical evidence of bleeding. We feel the hypoxia is not solely related to this unexpected finding, but mainly contributed by the persistent interstitial changes due to COVID-19 pneumonia and the pulmonary microangiopathic changes seen on imaging. It has to be mentioned that radiologically we cannot definitively differentiate a pseudoaneurysm from a true aneurysm. This requires histological proof. But the appearance of an abnormal pulmonary artery dilatation within a cavitating lesion is reminiscent of Rasmussen's aneurysm, which was traditionally associated with cavitating pulmonary tuberculosis. The pulmonary artery wall adjacent to the diseased lung parenchyma or cavity progressively becomes

weakened as a consequence of granulation tissue replacing the adventitia and media of the pulmonary arterial wall. In turn, the granulation tissue will be replaced by fibrin resulting in thinning of the wall and formation of a pseudoaneurysm.

Classically, the term Rasmussen's aneurysm is designated for tuberculosis-related pulmonary artery aneurysm or pseudoaneurysm. Nevertheless, several reports revealed other infective causes that can lead to a similar pathological process, such as fungal and pyogenic infections [2]. Cavity formation suggests significant lung parenchymal destruction from severe infection. Hence, it is plausible for any severe infection in the lung to induce inflammation and thinning of the adjacent arterial wall and leading to pulmonary artery aneurysm or pseudoaneurysm formation. Due to its structural fragility, risk of rupture and consequent massive pulmonary haemorrhage from PAP is much higher compared to that of pulmonary artery aneurysm [3]. The mortality rate in PAP is as high as 50% in diagnosed cases [4]. Of note, cavity formation is not considered a typical radiological finding in the setting of COVID-19 pneumonia and its presence should invoke a search for other superimposed conditions such as secondary infection. However, in recent times, there have been reports of COVID-19 associated PAP; suggesting that it should not be considered a rare finding [5, 6]. We hope, with time and more registries, we will get a clearer picture of this.

Endovascular techniques are now considered the standard first-line approach for thoracic vascular aneurysms with surgical interventions reserved for cases not amenable to an endovascular approach. For PAP, pulmonary artery embolisation is the preferred technique. It can be done using gelfoam, coil, or plugs. This should not be confused with bronchial artery embolisation. In most cases with massive haemoptysis, embolisation to the bronchial artery is the treatment option as 90–95% of the haemoptysis arise from bronchial artery [5]. Importantly, in cases of persistent haemoptysis despite bronchial artery embolisation, CTPA should be performed to look for an abnormality in the pulmonary artery as the culprit of bleeding. In one study, Rasmussen's aneurysm was found in 38% of patients who re-bled after successful bronchial artery embolisations for haemoptysis [7]. The advent of multidetector computed tomography angiography has helped greatly in localising the bleeding source and preventing unnecessary embolisation of the bronchial artery [8].

In our patient, a pulmonary artery embolisation was planned but the procedure was cancelled after a pre-procedure CTPA revealed that the pseudoaneurysm had undergone spontaneous thrombosis. As COVID-19 infection is known to be associated with a thrombotic state, we hypothesise that it could have aided in "closing off" the pseudoaneurysm. Nevertheless, spontaneous closure or regression of PAPs have been reported before even in non-COVID-19 infection related PAPs [9, 10]. The literature is scarce with regards to the natural history of PAP and to the best of our knowledge, there is none which report on the rates or predictive factors for spontaneous thrombosis of PAPs. This would certainly be valuable information as it would aid clinical decision-making with regards to immediate intervention *versus* a "watch-and-wait" policy. Although there are no evidence-based recommendations for patient selection to undergo embolisation in cases of PAPs, in our patient there were compelling indications for the procedure: respiratory failure (or compromised respiratory reserve) and considerable bleeding (evidenced by the significant drop in haemoglobin). There are many unknowns regarding the optimal management of PAPs, especially in COVID-19 infection, hence, we hope more research and registries will emerge to assist clinicians encountering this entity.

Our intention in sharing this case is to highlight this entity as a differential in COVID-19 patients presenting with or developing haemoptysis to facilitate early recognition as delayed management could be catastrophic, and to improve overall patient outcomes.

Answer 1

The chest radiograph in figure 1a was taken on the day of admission, *i.e.* day 2 of illness. It was carried out in AP supine position. The visualised lung fields were clear. Cardiothoracic ratio appears increased; however, this could be due to the radiograph being carried out in an AP supine position. The chest radiograph in figure 1b was taken on day 16 of illness. Patchy consolidation is appreciated bilaterally, apparent over the left peripheral lung field and right upper zone.

This progression is consistent with COVID-19 pneumonic changes on day 16, which are expected to be consolidative. Nevertheless, a focal involvement (in the right hemithorax) in the right upper zone should alert the clinician to the possibility of superimposed infection.

<< *Go to Task 1*

Answer 2

The CTPA showed a right lower lobe cavitating lesion with an intralesional pulmonary artery (superior segmental branch of right lower lobe) dilatation, most likely to be a pseudoaneurysm. The presence of contrasted material within the cavity suggested possible rupture of the pseudoaneurysm.

<< Go to Task 2

Answer 3

Causes of PAP include pulmonary infection-related PAP, such as tuberculosis, fungal infection, and bacterial infection. Other non-infective causes of PAP are trauma, neoplasm, and connective tissue diseases such as Behçet disease and Takayasu arteritis.
The most likely cause of the PAP in this case is COVID-19 pneumonia, after excluding all the other causes as mentioned above.

<< Go to Task 3

Answer 4

Pulmonary artery embolisation

<< Go to Task 4

Conflict of interest: None declared.

References

1 Cohen PA, Hall LE, John JN, *et al.* The early natural history of SARS-CoV-2 infection: clinical observations from an urban, ambulatory COVID-19 clinic. *Mayo Clin Proc* 2020; 95: 1124–1126.
2 Lee SG, Ryu DS, Park MS, *et al.* A case of pseudoaneurysm due to fungus ball within the progressive massive fibrosis in a patient with pneumoconiosis: computed tomography-pathologic correlation. *Korean J Radiol* 2016; 75: 218–221.
3 Prabhudesai V, Faughnan ME. Pulmonary vascular anomalies. *In*: Broaddus VC, Ernst JD, King Jr TE, *et al.* eds. Murray & Nadel's Textbook of Respiratory Medicine. Philadelphia, Elsevier, 2021; pp. 1212–1220.
4 Koneru H, Biswas Roy S, Islam M, *et al.* Pulmonary artery pseudoaneurysm: a rare cause of fatal massive hemoptysis. *Case Rep Pulmonol* 2018; 2018: 8251967.
5 Zoumot Z, Bonilla MF, Wahla AS, *et al.* Pulmonary cavitation: an under-recognized late complication of severe COVID-19 lung disease. *BMC Pulmonary Med* 2021; 21: 24.
6 Chen Y, Chen W, Zhou J, *et al.* Large pulmonary cavity in COVID-19 cured patient case report. *Ann Palliat Med* 2021; 10: 5786–5791.
7 Sapra R, Sharma G, Minz AK. Rasmussen's aneurysm: a rare and forgotten cause of hemoptysis. *Indian Heart J* 2015; 67: Suppl. 3, S53–S56.
8 Khalil A, Fartoukh M, Tassart M, *et al.* Role of MDCT in identification of the bleeding site and the vessels causing hemoptysis. *Am J Roentgenol* 2007; 188: W117–W125.
9 Horwitz M, Chaumoître K, Grimaldi C, *et al.* Spontaneous regression of multiple Rasmussen aneurysms in a child with Lemierre syndrome and pulmonary abscesses. *Pediatr Infect Dis J* 2013; 32: 1301–1302.
10 Generalis S, Gonçalves de Mendonça R, Marchiori E. Spontaneous regression of an infectious pulmonary artery pseudoaneurysm. *Arch Bronconeumol* 2018; 54: 402–403.