Severe COVID-19 pneumonia complicated by cardiomyopathy and a small anterior pneumothorax

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SUMMARY

Although, cardiac injury, pneumothorax and pneumomediastinum are associated with COVID-19, differentiation of their symptoms and signs from those of COVID-19 itself is challenging. Without a high index of suspicion, cardiomyopathy and anterior pneumothorax are easily missed. These complications may be underdiagnosed in patients with COVID-19. Cardiomyopathy and pneumothorax may cause or exacerbate respiratory failure. If their management is delayed, cardiac arrest can occur. To increase the awareness of these issues, we describe the course and imaging of a 39-year-old woman with severe COVID-19 who developed cardiomyopathy and a small anterior pneumothorax with pneumomediastinum. Transthoracic echocardiography is technically challenging in the presence of anterior pneumothorax. Furthermore, although CT is the gold standard for the diagnosis of pneumothorax, this is not always feasible in critically ill patients. Lateral decubitus chest X-rays and lung ultrasound may facilitate the diagnosis of pneumothorax at the bedside of patients with COVID-19.

BACKGROUND

Cardiomyopathy, pneumothorax and pneumomediastinum are associated with COVID-19.[1] However, the incidence of pneumothorax is thought to be low,[2–4] unless mechanical ventilation is initiated and barotrauma occurs.[5] Yet, without a high index of suspicion, an anterior pneumothorax can easily be missed.

Although cardiac disease is readily assessed by echocardiography, the risk of exposing sonographers to COVID-19 has reduced the availability of this essential investigation.[6] Thus, the diagnosis of these complications is often reliant on electrocardiographs and biomarkers (eg, brain natriuretic peptide and troponin) instead. Yet, these tests cannot exclude cardiac involvement in patients with COVID-19.[6]

Therefore, cardiomyopathy and pneumothorax may be underdiagnosed in patients with COVID-19. To increase the awareness of these complications, this case report describes the course and imaging of a patient with severe COVID-19 who developed both cardiomyopathy and an anterior pneumothorax.

CASE PRESENTATION

A 39-year-old woman who was obese (body mass index 32.4 kg/m^2) but had no other comorbidities presented to hospital with persistent and worsening fever, breathlessness and cough 9 days after diagnosis of COVID-19. Her oxygen saturations were initially 87% on room air but deteriorated rapidly despite supportive therapy and treatment with oxygen and dexamethasone 6 mg daily. Awake prone positioning and continuous positive airway pressure (10 cm H$_2$O) were not beneficial as the patient began to fatigue. Therefore, non-invasive ventilation with bilevel positive airway pressure (BiPAP) was started 2 days after admission and tocilizumab 400 mg was administered on day 3. Although the patient improved and the BiPAP was weaned off by day 10, the patient remained oxygen dependent with persistent tachycardia.

INVESTIGATIONS

Table 1 correlates the patients' vital signs, investigations and treatment over the course of her illness. On admission, the chest radiograph (figure 1) demonstrated bilateral ground glass opacification and the COVID-19 PCR test was positive. The 12-lead electrocardiograph demonstrated only sinus tachycardia, the thyroid stimulating hormone level was within the reference range (1.02 mIU/L) and the levels of serum brain natriuretic peptide (12 pmol/L) and troponin (<10 pg/mL) were low. On day 2, the D-dimer was raised (3.77 mg/L) and CT pulmonary angiography (CTPA) demonstrated extensive bilateral ground glass opacification (figure 2) but excluded pulmonary embolism. Sputum cultures were negative.

The series of chest X-rays performed on admission, days 2 and 4 (figure 1A–C) revealed worsening bilateral patchy interstitial oedema. No further X-rays were performed until day 12. However, on day 12, the chest X-ray (figure 1D) was initially thought to show some improvement.

On closer inspection, and careful comparison to the previous imaging (figure 1A–C); the improved definition of the left hemidiaphragm and medial lucencies (figure 3) raised the suspicion of anterior pneumothorax with pneumomediastinum. Although lateral decubitus X-ray chest was considered, this would not have excluded pulmonary embolism. Thus, CTPA was repeated. This confirmed the presence of the pneumothorax and pneumomediastinum (figure 4). The pneumothorax developed at some point between days 4 and 12.

On day 26, CT chest demonstrated resolution of the pneumothorax but persistent reticulation and traction bronchiectasis were consistent with interstitial lung disease due to COVID-19 (figure 5). Point-of-care lung ultrasound could have facilitated the investigation and monitoring of this patient's respiratory disease. However, the clinicians managing

Table 1 Timeline correlating arterial blood gases and respiratory support with select investigations and treatment

Day	0	0	1	1	2	3	4	6	8	9	11	12	13	26	32	33
Time**	00:00	08:30	15:35	18:40	08:40	08:10	06:50	08:50	09:20	10:30	11:30	06:40	06:40	07:30	15:30	16:25
Intervention	None	Steroid started			CTPA no PTX	Tocilizumab 400 mg					Steroid stopped	CXR PTX	CTPA PTX	CT no PTX	TTE LVEF 45%	
Hb (g/L)	113	102			106	117	113	118	118	119	132	138	145	130	143	143
WBC (×10^9/L)	4.72	6.81			6.38	5.58	4.35	4.36	4.94	6.47	5.22	3.78	4.02	4.03	5.92	5.2
CRP (mg/L)					89	91										
Troponin I (pg/mL)	<10											<10		10	6	7
BNP (pmol/L)	12				29.2										<2.9	
D-dimer (mg/L)	0.43	0.44			3.77							2.36				
HR (beats/min)	110	110	104	104	73	92	85	77	99	96	118	105	119	107	111	104
BP (mm Hg)	124/64	119/54	127/73	127/73	133/68	149/70	134/76	103/50	119/57	146/86	132/90	117/72	128/86	117/66	133/78	132/71
SpO$_2$ (%)	94	95	93	86	94	97	89	91	93	92	91	90	93	94	94	94
RR (breaths/min)	23	45	35	32	35	24	28	25	25	21	24	25	25	25	25	21
Respiratory support††	None	FM	FM	FM and CPAP 10 cm H20	NRB and BiPAP EPAP 10 cm H20, IPAP 15 cm H20	NRB and BiPAP EPAP 8 cm H20, IPAP 22 cm H20	NRB and BiPAP EPAP 8 cm H20, IPAP 14 cm H20	FM and BiPAP EPAP 8 cm H20, IPAP 14 cm H20	FM and BiPAP EPAP 8 cm H20, IPAP 14 cm H20	NC and BiPAP EPAP 8 cm H20, IPAP 14 cm H20	NC	NC	NC	NC	NC	NC
O$_2$ flow (L/min)	RA	6	6	6	15	12	15	5	4	2	2	2	2	1	4	1
pH		7.408	7.409	7.442	7.502	7.512	7.447	7.43	7.437	7.418		‡			7.4	
PaCO$_2$ (mm Hg)		40.8	40	42.5	45.2	43.7	50.1	50.1	47.3	51.2					52.3	
Bicarbonate		25.1	24.8	28.3	34.6	34.2	33.8	32.5	31.2	32.3					31.7	
BE (mmol/L)		0.4	0.1	3.8	10	10.2	8.5	7.1	6.1	6.5					5.5	
PaO$_2$ (mm Hg)		57.5	77.6	62.9	53.7	51	48.6	65.7	52.8	54.5					55.2	
PaO$_2$/FiO$_2$		274	369.5	157.3	90	243	231	313	147	259.6					263	

*The stated time refers to the sampling of arterial blood gases or laboratory blood tests and the measurement of the vital signs.

†All arterial blood gases were taken while the patient was receiving oxygen but not non-invasive ventilatory support.

‡The patient refused to allow samples of arterial blood to be taken between day 12 and day 31 because of severe wrist and arm pain.

BE, base excess; BiPAP, bilevel positive airway pressure; BNP, brain natriuretic peptide; CPAP, continuous positive airway pressure; CRP, C reactive protein; CTPA, CT pulmonary angiography; CXR, chest X-ray; EPAP, expiratory positive airway pressure; FM, face mask; Hb, haemoglobin; ILD, interstitial lung disease; IPAP, inspiratory positive airway pressure; LDH, lactate dehydrogenase; LVEF, left ventricular ejection fraction; NC, nasal canula; NRB, non-rebreathe; PTX, pneumothorax; PTX, pneumothorax with pneumomediastinum; RR, respiratory rate; TTE, transthoracic echocardiography.
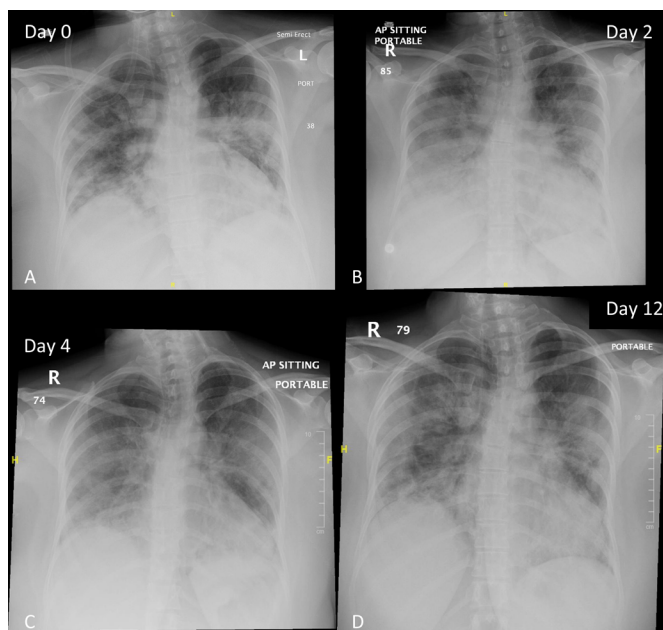
Figure 1 Series of chest X-rays demonstrating the progression of COVID-19 pneumonia with worsening bilateral patchy alveolar infiltrate and consolidation. (A) Chest X-ray on admission. (B) Chest X-ray performed 2 days after admission. (C) Chest X-ray performed 4 days after admission. (D) Chest X-ray performed 12 days after admission.

Figure 3 Chest X-ray performed 12 days after admission labelled to show radiographic findings suggestive of anterior pneumothorax and pneumomediastinum.

this case prior to the resolution of the pneumothorax were not credentialed to perform point-of-care ultrasound (PoCUS).

While echocardiography was considered on day 13, it was postponed after the left-sided anterior pneumothorax was diagnosed. The pneumothorax may have impaired the echocardiographic windows and, in addition to the COVID-19 pneumonia, was thought to account for the patient's oxygen dependence and tachycardia. However, despite low brain natriuretic peptide (<2.9 pmol/L) and troponin (<10 pg/mL), when performed after the pneumothorax resolved; echocardiography demonstrated mild cardiomyopathy (left ventricular ejection fraction 45%; figures 6 and 7 and videos 1 and 2).

DIFFERENTIAL DIAGNOSIS
Although the patient was diagnosed with COVID-19 pneumonia, she remained oxygen-dependent and persistently tachycardic. So,

additional causes for respiratory failure were sought. Although the patient was initially treated for superimposed bacterial infection empirically, respiratory cultures were subsequently negative. Although the incidence of pulmonary embolism is high in COVID-19, this was excluded by CTPA on day 2 (figure 2B) and day 13 (figure 3B). Detailed review of chest X-ray performed on day 12 (figures 1D and 3A) suggested the presence of anterior pneumothorax with pneumomediastinum. This was confirmed by the CTPA performed on day 13.

On day 26, chest CT demonstrated resolution of the pneumothorax and pneumomediastinum but demonstrated persistent interstitial changes secondary to COVID-19 (figure 4). The probability of cardiac disease was thought to be low in the

Figure 2 CT chest angiography performed 2 days after admission demonstrating extensive bilateral ground glass opacities with patchy consolidation. (A) Sagittal image and (B) transverse image at the level of the midpoint of the seventh thoracic vertebra.
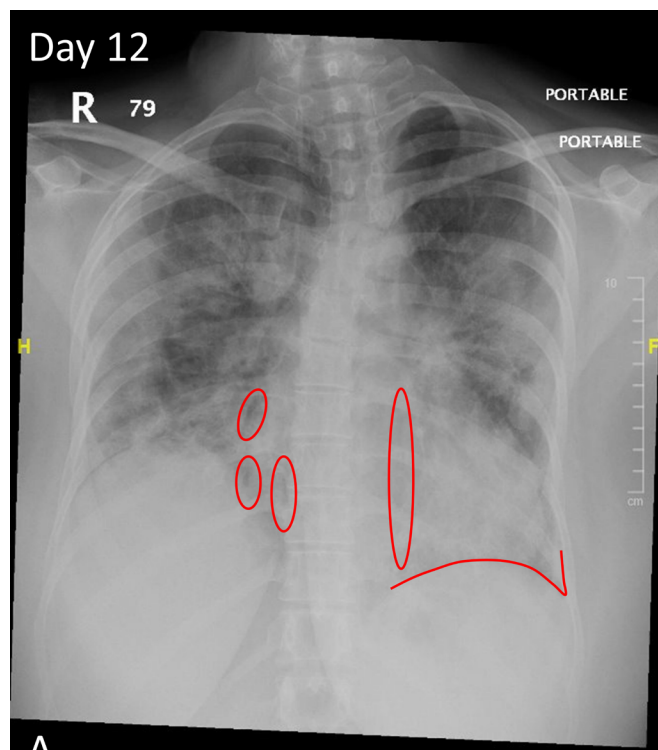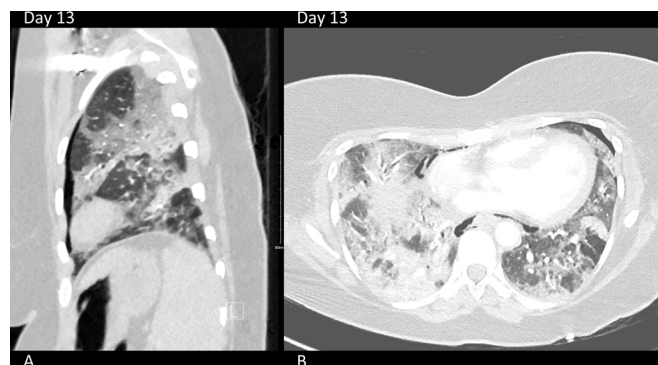

Figure 4 CT chest angiography performed 13 days after admission demonstrating a small, left-sided, anterior pneumothorax with pneumomediastinum in addition to the extensive bilateral ground glass opacities and patchy consolidation that were previously seen (figure 2). (A) Sagittal image and (B) transverse image at the level of the midpoint of the seventh thoracic vertebra.
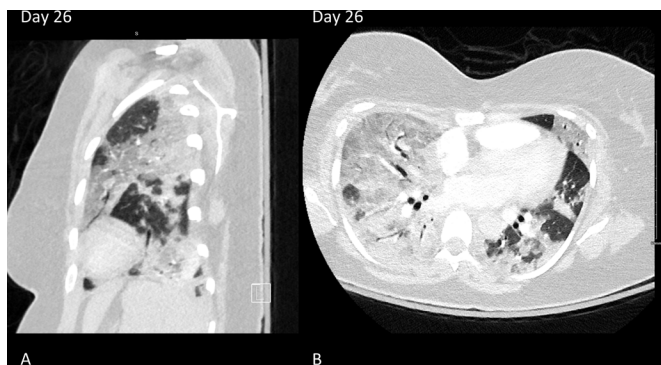
Figure 5 CT performed 26 days after admission demonstrating complete resolution of the left-sided, anterior pneumothorax with pneumomediastinum but persistent, bilateral ground glass opacities and patchy consolidation. (A) Sagittal image and (B) transverse image at the level of the midpoint of the seventh thoracic vertebra.

context of the low serum concentration of brain natriuretic peptide on admission, day 2 and day 32. Furthermore, the serum troponin concentration was also low (<10 pg/mL) on admission, day 12 and day 32. However, on day 32, echocardiography, performed after resolution of the pneumothorax, demonstrated cardiomyopathy.

TREATMENT
The patient was reviewed by a multidisciplinary team including internists, pulmonologists, intensivists and thoracic surgeons. Although the pneumothorax was small, it was decided that it should be drained. The team were concerned that if positive pressure ventilation was required, this could worsen the pneumothorax and/or induce tension pneumothorax.

The pneumothorax was initially treated with insertion of a basal chest drain on day 13. However, as the position of the drain was suboptimal, the pneumothorax persisted despite application of suction to the drain. So, a second, apical drain was inserted on day 15 and suction was applied to both drains. On day 19, the basal drain was removed. After complete resolution of the pneumomediastinum and pneumothorax, the apical drain was removed on day 25. The cardiomyopathy was treated with fluid restriction, furosemide and metoprolol.

OUTCOME AND FOLLOW-UP
The patient gradually improved and oxygen was weaned. The chest drains were removed sequentially after resolution of the pneumothorax. However, the patient remained limited by breathlessness on exertion that was accompanied by a reduction
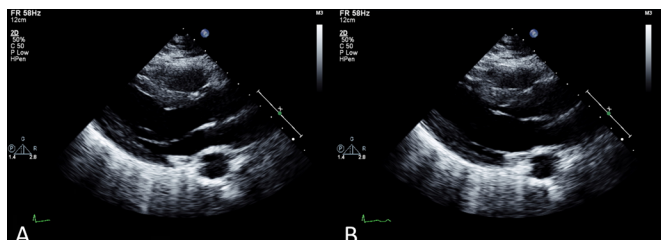

Figure 6 Parasternal long-axis transthoracic echocardiogram. Labelled 2D parasternal long-axis TTE view of the heart in (A) systole and (B) diastole. These images are taken from video 1 which shows mildly reduced left ventricular systolic function. LA, left atrium; LV, left ventricle; TTE, transthoracic echocardiograph.
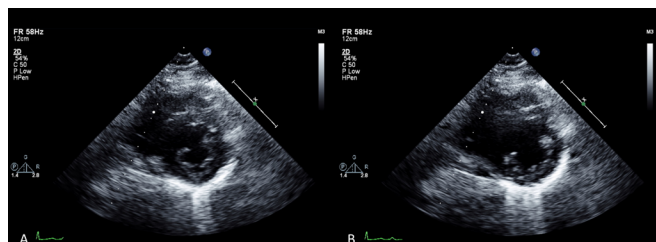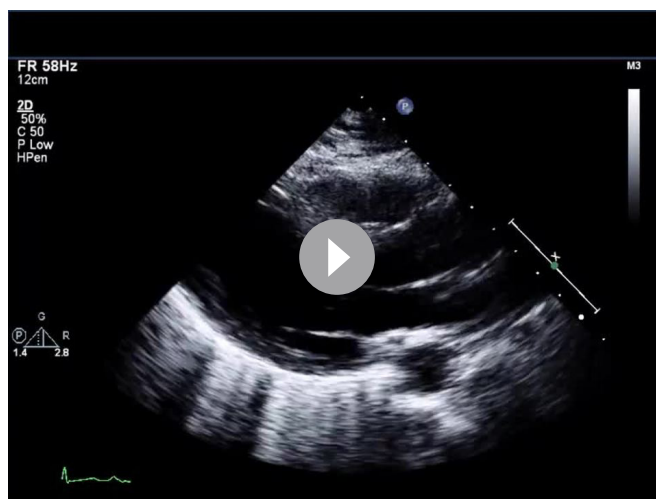

Figure 7 Parasternal short-axis transthoracic echocardiogram. Labelled 2D parasternal short-axis TTE view of the heart in (A)systole and (B) at the level of the papillary muscles in diastole. These images are taken from video 2 which shows mildly reduced left ventricular systolic function. LA, left atrium; LV, left ventricle; TTE, transthoracic echocardiograph.

in oxygen saturations and sinus tachycardia. These symptoms were improved with diuresis. The patient was diagnosed with COVID-19 pneumonia that had been complicated by pneumothorax, cardiomyopathy and persistent interstitial lung disease. The patient was discharged home 33 days after her initial presentation with metoprolol 75 mg twice daily, furosemide 40 mg daily and supplemental oxygen for use as required. On outpatient review, 3 weeks post discharge the patient remained symptomatic and so she was referred for pulmonary rehabilitation.

DISCUSSION
Cardiomyopathy, pneumothorax and pneumomediastinum are potentially life-threatening complications of COVID-19.[1–6] Yet, it is difficult to differentiate their symptoms and signs from those of COVID-19 itself. The heart is involved in approximately 25% of patients with COVID-19.[7] Yet, the pathogenesis of these complications remains unclear.[6 7] It is likely to be multifactorial and probably includes hypoxaemia, cytokine-mediated injury, microvascular damage, pericarditis, myocarditis or stress-induced cardiomyopathy.[6–8]

Pneumothorax may also cause or exacerbate acute respiratory failure. If management is delayed, tension pneumothorax can cause cardiac arrest. It has been suggested that pneumothorax occurs in 1% of those patients with COVID-19 requiring hospitalisation, 2% of those admitted to a critical care area and 1% of those who die from COVID-19.[2–4] Yet,

Video 1 Parasternal long-axis transthoracic echocardiographic view of the heart. Left ventricular function is mildly impaired.
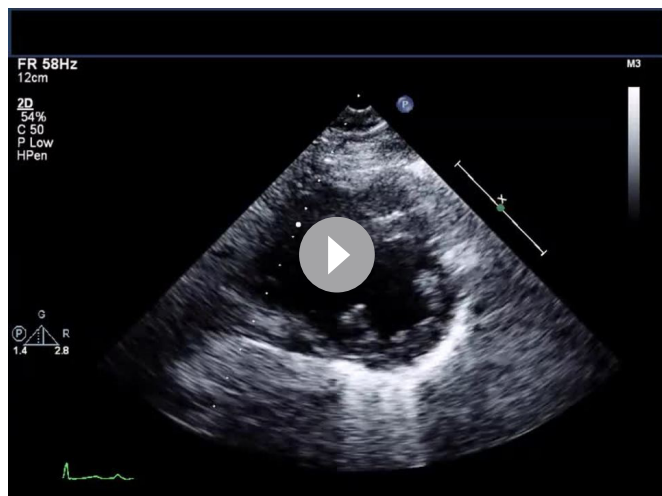
Video 2 Parasternal short-axis transthoracic echocardiographic view of the heart at the level of the papillary muscles. Left ventricular function is mildly impaired.

in mechanically ventilated patients with COVID-19, the incidence of barotrauma (ie, pneumothorax and pneumomediastinum) may be up to 15%.[5]

However, the studies from which these estimates were derived were all published early in the course of the pandemic. The factors which predispose to the development of cardiomyopathy, pneumothorax and pneumomediastinum in COVID-19 are not clearly defined. Several studies have demonstrated that the outcomes of COVID-19 pneumonia are significantly improved by steroids,[9] and interleukin-6 inhibitors (eg, tocilizumab).[10] It is therefore possible that these agents modify the incidence of complications of COVID-19 pneumonitis.

Thus, the complications of this enigmatic disease must be described in the context of the treatments which were administered. This case describes the development of cardiomyopathy and anterior pneumothorax in a patient with COVID-19 pneumonia treated with dexamethasone, tocilizumab and non-invasive ventilation.

The radiographic signs of an anterior pneumothorax (table 2; figure 3) are easily missed on review of an anterior-posterior chest radiograph.[8] Furthermore, parenchymal disease affects lung recoil.[11] Thus, lung markings may be seen beyond the pleural line / interface in select patients with a pneumothorax.[11] A less collapsed lobe can be seen beyond the pleural surface of the portion of the lung that is more collapsed.[11]

Although there are no data in COVID-19, occult pneumothorax has been studied in the setting of trauma. In that context, the reported incidence of occult pneumothorax has varied from 4% in injured children to 64% in mechanically ventilated victims of polytrauma.[12] Regardless, the current gold standard for the diagnosis of pneumothorax is multidetector CT.[13] This imaging modality also allows accurate measurement of their volume.[13] However, the transfer of unstable critically ill patients to the CT suite is not always feasible and has been particularly challenging during the COVID-19 pandemic.

The use of PoCUS to guide the management of patients with COVID-19 is strongly recommended.[14] Focused transthoracic cardiac ultrasound can rapidly detect select cardiac complications of COVID-19.[14] However, this may be technically challenging in the presence of a pneumothorax.

Lung ultrasound, which can be performed at the bedside within minutes, has significantly better accuracy for the diagnosis of pneumothorax than chest radiography.[15] In 2013, a systematic review of investigations for pneumothorax reported that ultrasound had a pooled sensitivity of 78.6% and a specificity of 98.4%.[15] Thus, international expert consensus recommends investigation with lung ultrasound when pneumothorax is in a differential diagnosis.[16] Ultrasound can also be used to approximate the size of a pneumothorax by identification of the position of the lung point.[17]

Denitrogenating arterial blood with 100% oxygen therapy may hasten the resolution of pneumothorax.[18] However, the effect is slight and its clinical significance has been questioned.[18] Furthermore, hyperoxia can cause absorption atelectasis,[18] and delay the recognition of worsening respiratory disease. Therefore, hyperoxia was not used in this case.

Pneumothorax and pneumomediastinum may be more common in COVID-19 than previously thought. It is therefore important to have a high index of suspicion for pneumothorax in patients with COVID-19. In view of the limitations of chest radiography, the use of bedside lung ultrasound may facilitate the diagnosis of pneumothorax in patients with COVID-19. Focused cardiac ultrasound can also reduce the demand for departmental echocardiography.[11 14] Regardless, as PoCUS is not universally available or practiced[19 20]; clinicians must remain cognisant of the limitations of cardiac biomarkers and the subtle radiographic signs of anterior pnemothorax (table 2).

Table 2 Comparison of the radiographic signs of suprahilar and infrahilar anteromedial pneumothorax

Anteromedial pneumothorax	
Suprahilar	**Infrahilar**
Sharp delineation of	Sharp outline of
Superior vena cava	Cardiac border
Azygos vein	Inferior vena cava
Left subclavian artery	Deep anterior costophrenic sulcus (deep sulcus sign)
Superior pulmonary vein	Medial diaphragm visible under cardiac silhouette
Anterior junction line	Sharp delineation of pericardial fat pad

This table lists the subtle radiographic signs of anteromedial pneumothorax.[11] Indeed, while the specificity of chest radiography is nearly 100%, the sensitivity is poor (40%).[12] As the chest radiograph remains the most widely used imaging modality in patients with COVID-19, the incidence of pneumothorax is likely to be higher than previous estimates. It is therefore important to consider the use of other investigations that have greater sensitivity for pneumothorax.

Learning points

► Pneumothorax may be underdiagnosed in patients with COVID-19 as the subtle signs of anteromedial pneumothorax are easily missed on chest X-rays.
► Cardiac biomarkers cannot exclude cardiac involvement in COVID-19 which may be missed if echocardiography is not performed.
► Signs of anterior pneumothorax on X-ray include improved definition of mediastinal structures and the diaphragm.
► CT is the gold standard for the diagnosis of pneumothorax but is not always feasible in critically ill patients.
► Bedside lung ultrasound is more sensitive for pneumothorax than chest X-ray.

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