



# Cystic Lung Disease as a Sequela of Severe COVID-19: Case Series

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## Abstract

Coronavirus disease 2019 (COVID-19) presented in December 2019 and has persisted since. The global pandemic has given rise to a novel acute disease process with a continually rapidly increasing prevalence of chronic disease and associated complications. There is minimal information on the long-term pulmonary complications of this disease. We present a series of 9 patient case reports and their respective imaging admitted with COVID-19 acute respiratory distress syndrome (ARDS) to highlight the cystic lung disease complications which may arise due to severity and disease progression. Our aim is to raise awareness of the sequela of COVID-19 ARDS, including its potentially catastrophic long-term consequences to the respiratory tract involving cystic lung disease.

## Keywords

pulmonary critical care, radiology/imaging, infectious disease, COVID, cystic lung disease, acute respiratory distress syndrome, ARDS

## Background

As the novel coronavirus disease 2019 (COVID-19) pandemic continues, understanding of its mechanism becomes further elucidated. However, there is no clear information on natural history, progression, and recovery from this illness. The long-term complications also remain unclear.<sup>1–3</sup>

Lung cysts are air-filled lesions that can be present in a vast spectrum of diseases or conditions. Their association with COVID-19 has been reported as a potential sequela, although cases are still rare.<sup>4</sup> Cysts can prolong hospitalization and oxygen requirements, and increase morbidity and mortality.<sup>5</sup>

When considering the large-scale infectious rate, persistent damages in even a relatively small proportion can likely represent a significant burden to the health care system. Therefore, it is imperative to recognize any resultant damage that may impact overall outcomes.<sup>1,6</sup>

We present a case series of 9 patients who developed lung cysts as late complications of COVID-19, to report under-recognized complications and increase literature on the progression of this disease.

## Case Presentations

### Case 1

A 68-year-old male with history of hypertension and asthma presented with 6 days of symptoms associated with positive

COVID-19 polymerase chain reaction (PCR) testing. His initial chest radiograph (CXR) showed extensive bilateral pulmonary parenchymal disease (Figure 1). He was initiated on dexamethasone and remdesivir. Due to worsening hypoxia he was titrated up on oxygen, and 3 days into admission required mechanical ventilation support, and further prone per acute respiratory distress syndrome (ARDS) protocol. After a week of mechanical ventilation, he was successfully extubated.

Computed tomography (CT) of the chest performed showed patchy, confluent, extensive bilateral consolidative, and interstitial ground-glass opacities, increased from the prior CXR. Also noted were bilateral peripheral bronchiectasis and diffuse distortion of the pulmonary architecture with newly formed predominantly air-filled cysts mainly in the left anterior upper lobe and in the left lateral lower lobe (Figure 2).

Systemic steroids were restarted, which assisted in titration of oxygen requirements. A repeat chest CT showed improvement of the diffuse bilateral ground-glass opacities;

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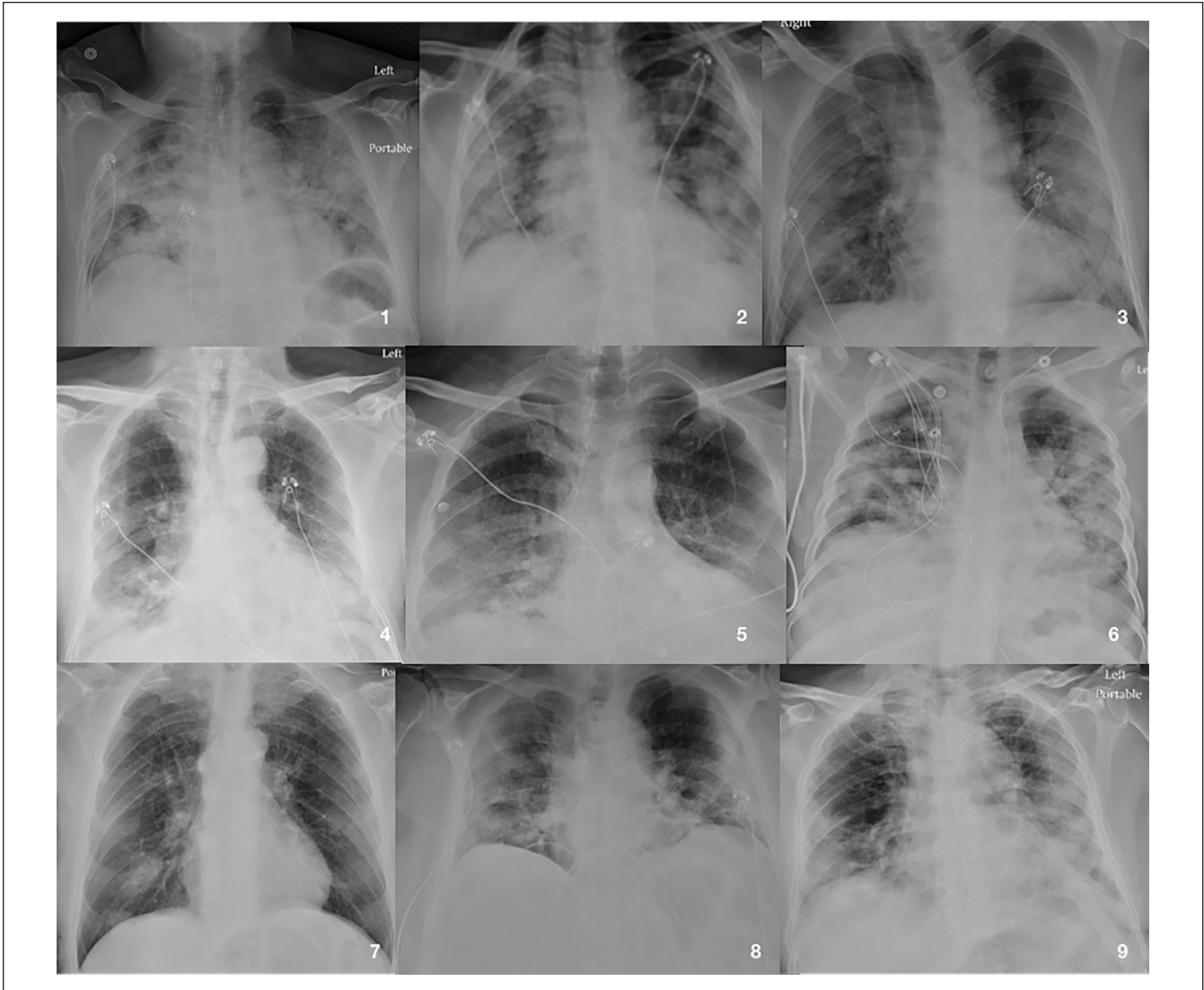
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**Figure 1.** Initial presentation chest radiographs portraying diffuse bilateral opacities, compatible with COVID-19.

Number on image corresponds, respectively, to patient case.

Abbreviation: COVID-19, coronavirus disease 2019.

however, air-filled cystic foci within the left anterior lower lobe remained unchanged (Figure 2).

The patient was eventually discharged home on oxygen via nasal cannula.

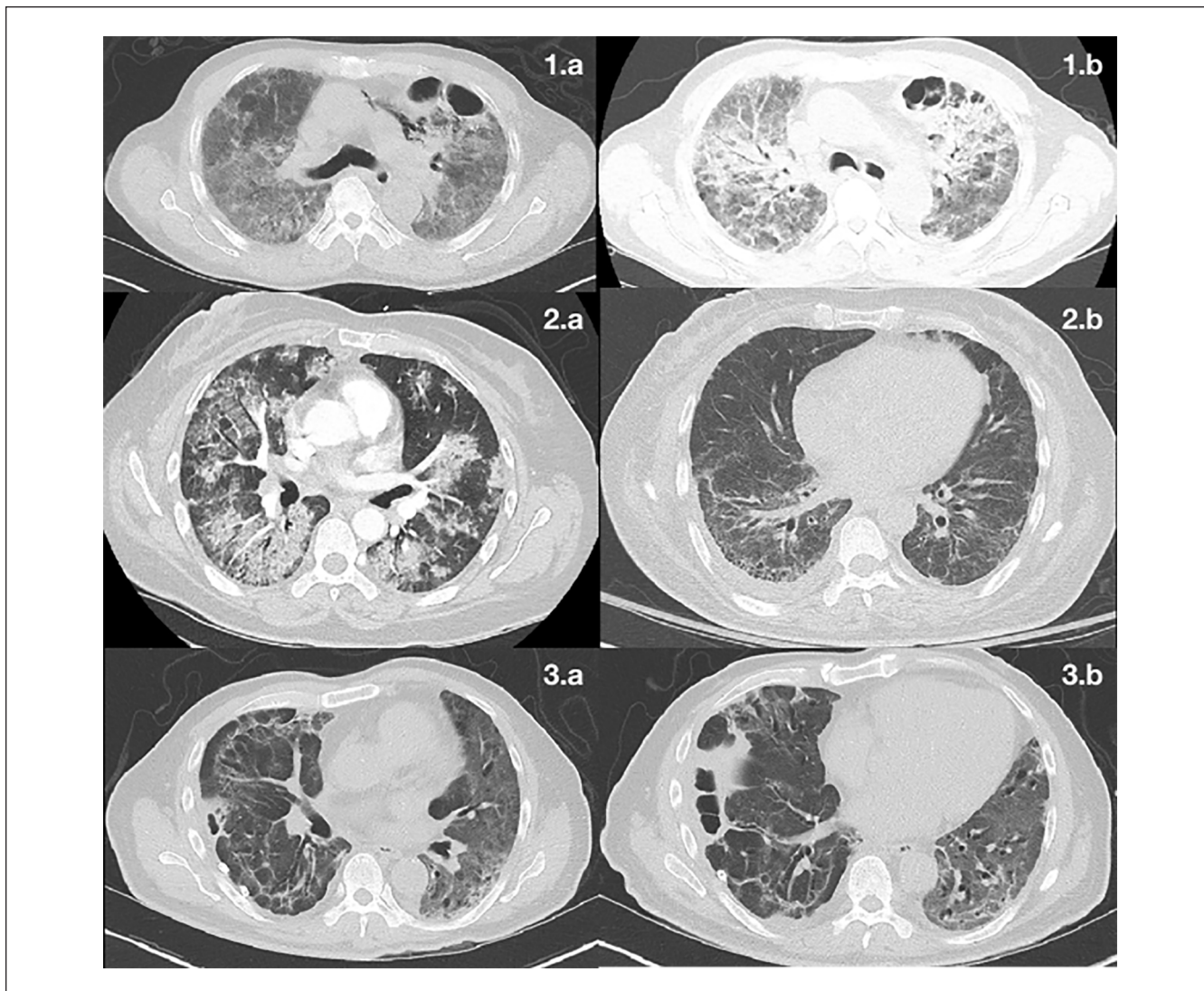
## Case 2

A 53-year-old female with history of diabetes mellitus and hypertension presented with symptoms associated to positive COVID-19 PCR, initially requiring nasal cannula oxygen therapy. Her initial CXR demonstrated patchy, bilateral airspace disease (Figure 1). A CT chest demonstrated patchy, confluent ground-glass and consolidative opacities (Figure 2).

Due to worsening hypoxia, she was titrated up on oxygen, and on day of admission required mechanical ventilation and

further prone per ARDS protocol. With minimal improvement after 48 hours of mechanical ventilation, she was placed on extracorporeal membranous oxygenation (ECMO). She improved, underwent tracheostomy, and was explanted from ECMO 1 week after implantation. She was discharged to a nursing home where she was subsequently decannulated from tracheostomy. Further, she returned with severe respiratory distress. Computed tomography of the chest showed near resolution of the initial patchy airspace disease, and honeycombing of bilateral lung bases (Figure 2). She was treated symptomatically and discharged home.

Over multiple visits due to respiratory distress she had another repeat CT chest with extensive bilateral pulmonary fibrosis and significantly worsening bilateral lower lobe honeycombing (Figure 2). She was given systemic steroids and



**Figure 2.** Axial computed tomography reconstructions of the chest: (1.a and 1.b) Case 1—Multiple large cystic lesions both in the left upper lobe and in the right lower lobe. (2.a and 2.b) Case 2—Multiple small cystic lesions distributed in a peripheral pattern. (3.a and 3.b) Case 3—Multiple cystic lesions bilateral, predominantly in right upper, middle, and lower lobes.

discharged with high-flow nasal cannula (HFNC) oxygen and was titrated down to 2 L nasal cannula oxygen with a lung transplantation referral.

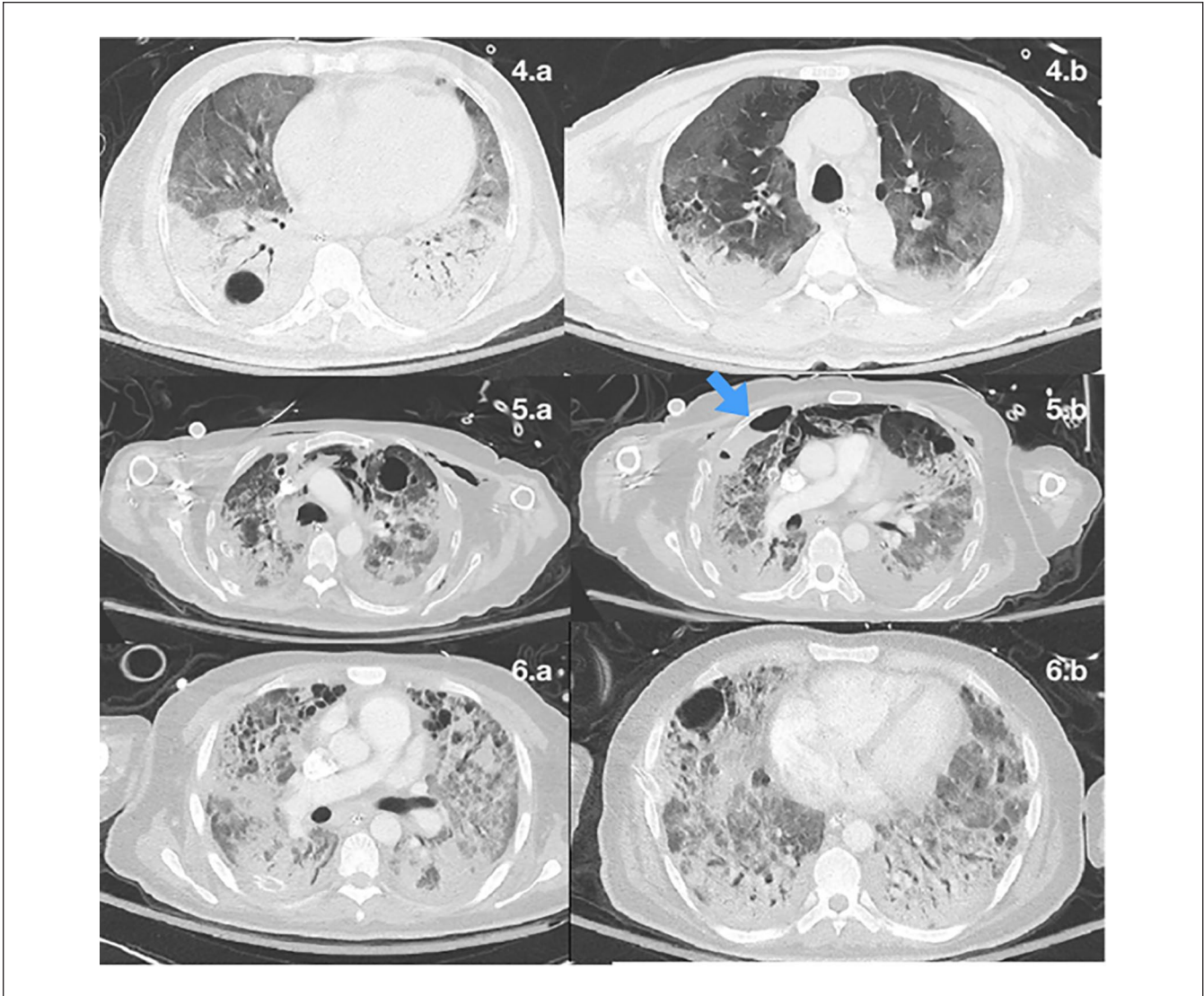
### Case 3

A 59-year-old male with history of hypertension arrived with symptoms associated with COVID-19 PCR positive. He was initially placed on nasal cannula oxygen and required HFNC for 26 days. His CXR showed patchy parenchymal airspace disease (Figure 1). He was treated with dexamethasone and remdesivir. His hospitalization was complicated by a right-sided pneumothorax, requiring chest tube placement. A CT chest revealed a diffuse fibrotic pattern with air-filled cystic areas in the bilateral periphery of the lungs (Figure 2). He

was eventually discharged to a nursing home with nasal cannula oxygen.

### Case 4

A 67-year-old male with history of hypertension presented symptoms associated with positive COVID-19 PCR. Initial CXR showed patchy airspace disease more pronounced at the bilateral periphery and bases (Figure 1). He was intubated and placed on mechanical ventilation on arrival. He was treated with dexamethasone, remdesivir, and antibiotics for superimposed bacterial infection. Computed tomography of the chest 2 weeks later revealed diffuse bilateral ground-glass opacities and dense consolidation in the lower lobes with cavitory disease in the right lower lobe (Figure 3). His



**Figure 3.** Axial computed tomography reconstructions of the chest: (4.a and 4.b) Case 4—Large cystic lesion in the right lower lobe with several other peripheral cystic lesions. (5.a and 5.b) Case 5—Multiple cystic lesions on the left upper and left middle lobes, with loculated hydropneumothorax in the right upper thorax (blue arrow) and anterior right mid-thorax. (6.a and 6.b) Case 6—Multiple bilateral cystic lesions.

health care surrogate decision-maker requested comfort measures only and he was compassionately extubated with eventual death after 25 days of mechanical ventilation.

### Case 5

A 54-year-old male with history of diabetes mellitus presented with symptoms associated with positive COVID-19 PCR. Initial CXR showed patchy airspace disease involving bilateral bases (Figure 1). He required HFNC and was treated with bamlanivimab, convalescent plasma, remdesivir, and dexamethasone. Due to further deterioration, he required intubation and mechanical ventilation on day of admission, with subsequent ECMO cannulation after 48 hours of

mechanical ventilation. His hospital course was complicated with right-sided pneumothorax requiring chest tube placement. He eventually had percutaneous tracheostomy after 40 days of endotracheal intubation, mechanical ventilation, and ECMO.

Computed tomography of the chest portrayed diffuse bilateral ground-glass opacification of the lungs with fibrotic changes and traction bronchiectasis in the bilateral upper lobes, along with cystic disease in the left upper lobe (Figure 3). His hospitalization was further complicated by bacteremia and left-sided tension pneumothorax requiring chest tube placement. He subsequently deceased 4 months later due to worsening septic shock while on mechanical ventilation and ECMO.

### Case 6

A 30-year-old man with no known history arrives with symptoms associated with positive COVID-19 PCR. On day of admission he was started on HFNC. His CXR revealed moderate to severe diffuse bilateral patchy pulmonary opacities, left greater than right (Figure 1). He required mechanical ventilation on day 7 of admission due to progression of respiratory failure and was started on inhaled nitric oxide therapy, remdesivir, systemic steroids, and broad-spectrum antibiotics for superimposed bacterial pneumonia. He subsequently was cannulated on ECMO 48 hours after initiation of mechanical ventilation, and received percutaneous tracheostomy 2 weeks after intubation. After 1 month of ECMO, he was explanted. His course was complicated with right pneumothorax requiring chest tube. Computed tomography of the chest revealed extensive bilateral airspace disease distributed in the mid and peripheral lung fields and evidence of numerous cystic disease predominantly in the anterior apical segments of the upper lobes (Figure 3). He later developed left pneumothorax requiring chest tube. Bilateral pneumothoraxes resolved, although the patient developed septic shock due to bacteremia and died while on mechanical ventilation 4 months from admission.

### Case 7

A 77-year-old former smoker male with history of diabetes mellitus, hypertension, depression, and post-traumatic stress disorder arrived with hypoxemic respiratory failure and smoke inhalation after a fire in his home, and noted to be COVID-19 PCR positive. His initial CXR revealed 2 nodular opacities measuring up to 2.9 cm in the right lower lung field, without any other parenchymal changes (Figure 1). He was discharged to subacute rehabilitation without any oxygen. He subsequently returned in 2 weeks with symptoms associated with COVID-19 PCR positive. He was placed on non-rebreather oxygen and was started on remdesivir and dexamethasone. Further, he required mechanical ventilation after 24 hours. Computed tomography of the chest was performed with extensive bilateral pulmonary cystic lesions (Figure 4). He became hemodynamically unstable and died within 48 hours of intubation.

### Case 8

A 72-year-old male with history of hypertension, hyperlipidemia, and hypothyroidism presented with symptoms associated with positive COVID-19 PCR. He was initially placed on HFNC on day of admission. His initial CXR showed moderate to large regions of ground-glass opacification with increased thickening of the interlobular septa in the periphery (Figure 1). He received tocilizumab, convalescent plasma, and enrolled in a clinical trial for stem cell therapy. Due to further deterioration, he was initiated on mechanical

ventilation after 9 days of admission, prone, and started on inhaled nitric oxide. Subsequently, he received ECMO therapy after 48 hours of mechanical ventilation and percutaneous tracheostomy 45 days later. Computed tomography of the chest revealed areas of fibrosis with honeycombing and mild cylindrical bronchiectasis mainly in the lower lobes, along with diffuse bilateral cystic lesions throughout the lungs (Figure 4). His hospital course was complicated with bacteremia, superimposed bacterial pneumonia, and septic shock with eventual death 55 days into admission.

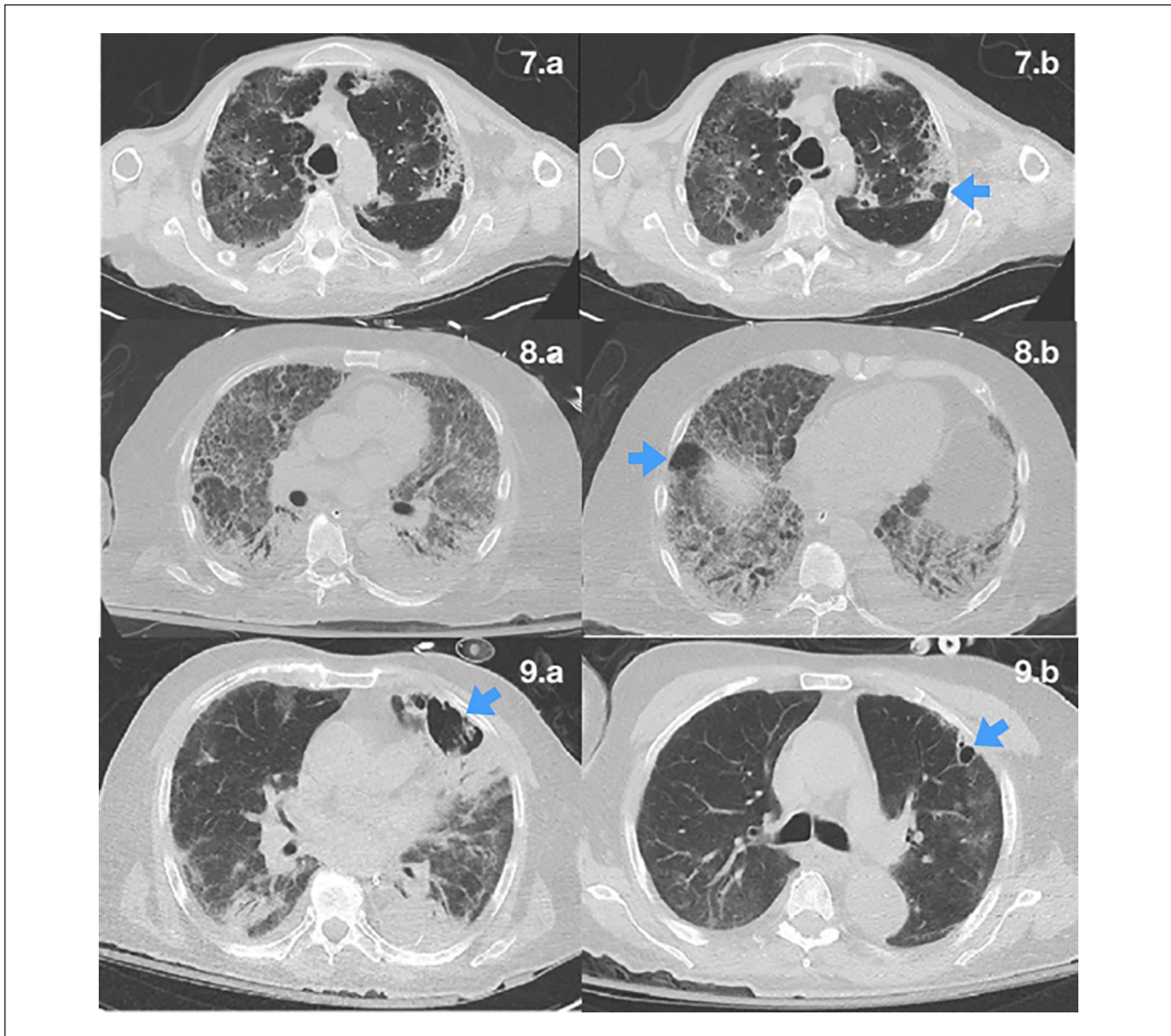
### Case 9

A 73 year-old male with a history of hypertension arrived with symptoms associated with positive COVID-19 PCR. He was started on HFNC on admission. His initial CXR showed bilateral basilar and peripheral infiltrates, without cystic disease (Figure 1). He further required mechanical ventilation 6 days into admission, and received dexamethasone and antibiotics for a superimposed bacterial infection. Computed tomography of the chest was performed after 20 days of symptom onset with extensive bilateral airspace disease and areas of ground-glass opacities; cavitory disease was noted in the left upper and right middle lobes (Figure 4). He underwent tracheostomy after 30 days of endotracheal intubation and was discharged to a nursing home 2 months after admission.

## Discussion

Pulmonary cysts consist of round, air- or fluid-filled spaces, which are usually surrounded by thin walls (<2 mm) made up of epithelial or fibrous material.<sup>7-9</sup> The most important clinical complication of pulmonary cysts includes rupture, which could lead to pneumothorax, and subsequent death.<sup>7</sup> Another complication is the development of an infected cyst, which occurred in several of our patients. The pathophysiology between COVID-19 and cystic lung disease is thought to be due to inflammatory changes leading to lung fibrosis and subsequent reduced lung compliance, ischemic damage to the lung parenchyma, and damage from inflammatory exudate.<sup>10,11</sup> Another hypothesis includes inflammation leading to mucus plug-induced obstruction of bronchioles and alveolar hyperinflation, all leading to rupture of the alveoli and the formation of cysts.<sup>10,12</sup> Lung biopsies demonstrated a diffuse inflammatory response leading to the development of fibromyxoid exudates and hyaline membranes causing alveolar destruction and fibrosis.<sup>5,13</sup>

The differential diagnosis of cystic lung disease over the years has become more complex. Clinical context and radiological findings are essential for diagnosis. Acute and subacute courses are suggestive of infectious or inflammatory processes while chronic courses are more suggestive of noninfectious infiltrative processes. Cystic lung disease can be classified based on the underlying pathophysiologic



**Figure 4.** Axial computed tomography reconstructions of the chest: (7.a and 7.b) Case 7—Multiple bilateral cystic lesions prevalent in the peripheral parenchyma, with larger cysts adjacent to the pleura identified by blue arrows. (8.a and 8.b) Case 8—Multiple bilateral cystic lesions prevalent in the peripheral parenchyma, with larger cysts adjacent to the pleura identified by blue arrows. (9.a and 9.b) Case 9—Multiple bilateral cystic lesions prevalent in the peripheral parenchyma, with larger cysts adjacent to the pleura identified by blue arrows.

mechanism: congenital, genetic, infectious, inflammatory, lymphoproliferative, neoplastic, or smoking related. Typically, the etiology of cystic lung disease is due to multiple mechanisms including ventilator-induced lung injury, repeated alveolar collapse and expansion, and inflammatory/bio-trauma, and can also include patient self-inflicted lung injury. As such, the true etiology remains controversial. There is lack of significant literature supporting viral or ARDS-related acquired cystic lung disease, suggesting COVID pneumonia as a unique

etiology in the development of cystic lung disease compared with other forms of ARDS.

Eight of the patients in this case series were intubated and followed strict ARDSNet criteria for ventilator management. Pulmonary cysts are a known complication of mechanical ventilation; however, COVID-19 ARDS may independently precipitate pulmonary cyst formation without the presence of mechanical ventilation.<sup>10,11,14,15</sup> For patients on prolonged mechanical ventilation, the formation of an alveolar pressure gradient may lead to cystic rupture.<sup>16,17</sup>

Cysts are more likely to form when prolonged COVID-19 ARDS progresses to the fibrotic stage, which typically occurs beyond the first several weeks of symptom onset.<sup>11,18</sup> However, literature is lacking regarding the exact temporal and radiological evolution of atypical findings, such as pulmonary cysts.<sup>5</sup> In our case series, most of the patients presented with ground-glass opacities that transitioned to fibrosis and the development of cysts after repeat chest imaging was performed several weeks after symptom onset. Treatment of COVID-19-related pulmonary cystic lung disease remains supportive.

The most common COVID-19 manifestations on chest CT are bilateral ground-glass opacities and thickening of the inter-lobar septum of the lung.<sup>10</sup> A retrospective study by Gurumurthy et al aimed to elucidate atypical findings of COVID-19 on chest CT imaging and determined that out of 298 patients, only 21.1% had atypical findings.<sup>10</sup> Out of the total number of patients, 9.0% had pulmonary cysts, which was the most common atypical finding.<sup>10</sup> The 9.0% figure of pulmonary cysts was also reported by another study from China.<sup>10,19</sup> Although they remain rare, these findings suggest that pulmonary cysts are more common than initially thought, but remain underreported.<sup>10,19</sup> Interestingly, Gurumurthy et al also report there was a positive correlation between age and the presence of atypical lung findings on chest CT, which is consistent with non-COVID-19-related cystic lung disease.<sup>7,10</sup>

## Conclusion

In summary, we present a case series of 9 patients who developed cystic lung disease as a sequelae of COVID-19 ARDS. All of our patients were intubated; however, COVID-19 ARDS may independently lead to cystic lung disease without mechanical ventilation. Clinicians should remain vigilant for the formation of cystic disease, especially in prolonged ARDS and mechanical ventilation, as they may lead to life-threatening pneumothorax. Further research is needed to determine the long-term prognosis and pathophysiology linking COVID-19 ARDS with pulmonary cystic formation.

## Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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## Ethics approval

Our institution does not require ethical approval for reporting individual cases or case series.

## Informed consent

Verbal informed consent was obtained from a legally authorized representative(s) for anonymized patient information to be published in this article.

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