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Case Series

Radiology Section

Pulmonary Cystic Lesions in Patients with COVID-19 Infection: A Case Series

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ABSTRACT

Computed Tomography has played a vital role in Coronavirus Disease 2019 (COVID-19) infection, caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) over the last two years. The typical features of COVID-19 on High Resolution Computed Tomography (HRCT) of chest including ground glass opacities and consolidation with a peripheral and lower lobar predilection have been very well documented in literature worldwide. However, thin-walled lucencies in the lung parenchyma called cysts is not very well documented. Authors, thus, present a case series comprising six SARS-CoV-2 Reverse Transcription-Polymerase Chain Reaction (RT-PCR) positive patients admitted to the hospital during the period 1st April 2021 to 31st May 2021 with lung cysts on HRCT. In this case series, the cysts were found to be thin-walled, varying in size from 5-20 mm in diameter and subpleural in distribution with no obvious lobar predilection. The immediately surrounding lung parenchyma showed features of maximal involvement by the atypical pneumonitis. All six cases had moderate to severe lung involvement entailing oxygen therapy. The high flow oxygen therapy and its duration along with degree of lung involvement, are important determinants of cystic degeneration. In the present case series, cystic changes were observed somewhere between day 15 to day 40 of the disease and thus, a part of postacute fibrosis in COVID-19 infection.

Keywords: Computed tomography, Coronavirus disease 2019, Cystic lesions of the lungs, Severe acute respiratory syndrome coronavirus 2

INTRODUCTION

The second wave of Coronavirus Disease 2019 (COVID-19) infection in India was massive and took the nation by storm. The complications that came up with this infection were hazardous and unfamiliar. Computed Tomography (CT) images keeping up with COVID-19 pneumonitis include peripheral distribution of patches of ground glass opacities and consolidation, more so in the lower lobes. Subsequent findings with advanced stages of the disease include fibrosis, septal thickening, and architectural distortion [1,2]. To date, no substantial study delineating the underlying aerodynamics has been published in India and very few worldwide [3,4]. The present case series comprises six Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) Reverse Transcription-Polymerase Chain Reaction (RT-PCR) positive patients admitted to the hospital during the period 1st April 2021 to 31st May 2021 with lung cysts on High Resolution Computed Tomography (HRCT) of chest. The present case series aimed to study the cause, timing, and significance of these lung cysts.

To begin with, authors came across such lung cysts in nine patients. The patients with a history of smoking, Chronic Obstructive Pulmonary Disease (COPD), pulmonary Koch's, and any other chronic respiratory illness were excluded from the series, only six cases were studied [Table/Fig-1].

CASE SERIES

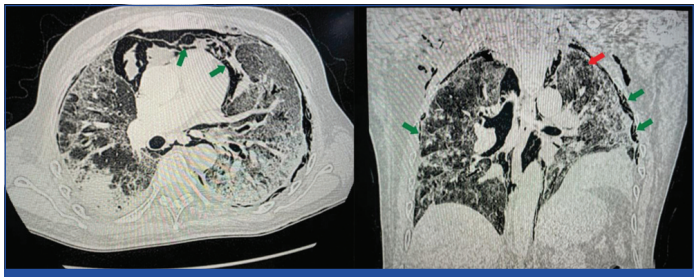
Case 1

A 62-year-old male, a known diabetic, with SARS-CoV-2, RT-PCR confirmed COVID-19 infection, presented to emergency with peripheral capillary oxygen saturation (SpO_2) of 68%. The patient was admitted to a level 1 facility for initial 13 days of illness but due to worsening of his clinical condition, he was transferred to our hospital and was admitted to the Intensive Care Unit (ICU). Patient was a non smoker, normotensive with no history of pre-existing chronic respiratory illness. The patient's HRCT chest done on day 14 from symptom onset showed extensive, diffuse bilateral

Case	Age/Gender	Day of CT from the onset of symptoms	CT severity score	Number and size of lung cysts	Distribution of cysts	Accompanying pneumothorax and pneumomediastinum	Oxygen requirement	Duration of oxygen therapy
1	62 year/Male	14, 28	21/25, 24/25	Multiple,14-19 mm	Bilateral, Subpleural	Bilateral present	NIV, HFNC, Mask	18
2	64 year/Male	21	15/25	3 cyst, 5-6 mm	Subpleural, right middle and left lower lobes	Absent	High flow mask, nasal prongs	8
3	81 year/Male	18	16/25	5-6 cyst, 10-13 mm	Subpleural, right lower and left upper lobes	Left pneumothorax present	High flow mask, nasal prongs	8
4	26 year/Male	27	20/25	3-4 cyst, 10-20 mm	Subpleural, bilateral upper and lower lobes	Absent	Venturi mask	7
5	68 year/Female	22	20/25	7-8 cyst, 14-16 mm	Subpleural	Absent	High flow mask, HFNC	21
6	38 year/Female	39	25/25	8-9 cyst, 13-18 mm	Subpleural	Absent	High flow mask	33

[Table/Fig-1]: Details of High Resolution Computed Tomography (HRCT) of chest findings and oxygen therapy of the six cases.
HFNC: High flow nasal cannula; NIV: Non invasive ventilation

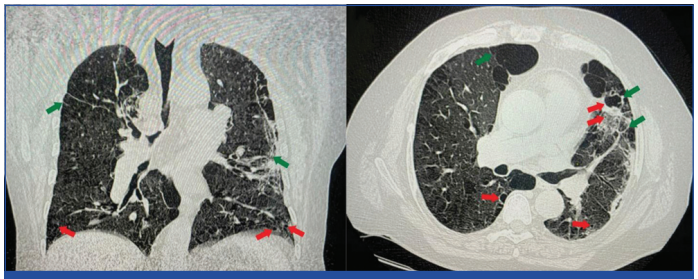
lung involvement with features of COVID-19 pneumonitis and Computed Tomography Severity Score (CTSS) of 21/25 [5]. He was initially managed with Non Invasive Ventilation (NIV) for seven days followed by High Flow Nasal Cannula oxygen (HFNC) for the next seven days. A repeat CT chest done on day 28 of symptom onset showed an increase in CTSS to 24/25 with multiple small subpleural and intraparenchymal thin-walled cysts ranging from 14-19 mm in diameter, more so in the upper lobes [Table/Fig-2]. Also, there were mild bilateral pneumothorax and minimal pneumomediastinum which were managed conservatively. In the following week, patient oxygen demand decreased, and he was given 3-4 liters of oxygen/minute through a nasal cannula. The patient was then shifted to a general ward and discharged a week later.



[Table/Fig-2]: HRCT Chest (Axial and Coronal) images of a 62-year old male who presented with advanced symptoms of COVID pneumonitis. HRCT thorax done on day 14 of disease showed extensive lung involvement with CT severity score of 21/25. There were small subpleural and intraparenchymal cysts (red arrows) predominantly in the upper lobes along with bilateral thin pneumothoraces and pneumomediastinum (green arrows).

Case 2

A 64-year-old male with COVID-19 infection confirmed 20 days ago, was brought from home isolation with worsening cough and dyspnoea. The patient was a non smoker with no history of chronic respiratory illness but was a known hypertensive and diabetic. On admission, his Random Blood Sugar (RBS) was 221 mg/dL and SpO_2 was 87% on room air. The patient's HRCT was done on the day of admission (Day 21 from the symptom onset) and showed moderate lung involvement with a CTSS of 15/25. There were three peripheral thin-walled cysts, varying in size from 5-6 mm in diameter, one in the right middle and two in the left lower lobe, which were seen amidst the areas of ground glass attenuation [Table/Fig-3]. The cysts were clear with no fluid within, and the surrounding parenchyma seemed no different from the parenchyma affected in other areas. During his hospital stay, he was on 7 L/min oxygen support for the first five days, and then the oxygen support was tapered over the next three days before discharge.



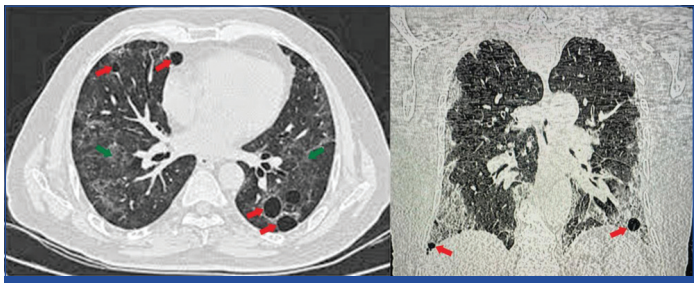
[Table/Fig-3]: HRCT Chest (Axial and Coronal) images of a 64-year old male with RTPCR confirmed COVID-19 infection. HRCT done on day 21 from symptom onset showed subpleural fibrotic bands (green arrows) with adjacent traction bronchiectasis and septal thickening are seen bilaterally. There are thin-walled smooth margined intraparenchymal cystic lesions, predominantly subpleural in distribution (red arrows).

Case 3

An 81-year-old diabetic male, diagnosed with COVID-19-related pneumonia was admitted in our hospital with shortness of breath with SpO_2 of 85 percent and a respiratory rate of 28 breaths per minute on 18th day of illness. He was earlier admitted in a private hospital for last 7 days where he was kept on high flow oxygen therapy. His RT-PCR for SARS CoV-2 was found to be negative on admission in our hospital. The HRCT chest done on the day of admission revealed moderate lung involvement with CTSS of 16/25 and 5-6 peripheral imperceptible thin-walled cysts measuring around 10-13 mm in diameter in subpleural location in right lower lobe and left upper lobe. No bacterial superinfections were found. Also, the CT showed minimal left pneumothorax, but the patient was hemodynamically stable. During his 12 days of hospital stay, he was on oxygen support initially on a high flow mask and later tapered to nasal prongs. The pneumothorax was managed conservatively, followed with chest radiographs, and did not require chest tube insertion.

Case 4

A 26-year-old male, driver by profession, with no documented co-morbidities, reported to the hospital with severe dyspnoea, cough, and fever. Patient was in home isolation for the first two weeks of illness, was admitted to a hospital with worsened symptoms in the third week. His SpO_2 on ambient room air was 80% at the time of admission. He underwent HRCT chest on admission which showed severe bilateral pneumonitis with septal thickening, more so in the lower lobes. His CTSS was reported to be 20/25. Few (3-4) thin-walled cysts were found in bilateral upper and lower lobes [Table/Fig-4]. The average size of the cysts was less than 10-20 mm. He was put on oxygen support with a venturi mask of 8 L/min on admission and transferred to ICU. His oxygen requirement reduced over the next week and he was discharged on the 14th day from the day of admission.

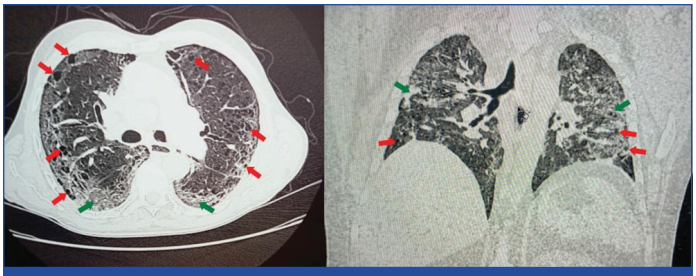


[Table/Fig-4]: Axial and Coronal images of HRCT Chest done on the 27th day of symptom onset in a 26-year-old male with Covid-19 infection. Extensive ground-glass opacities with septal thickening, fibrotic bands and patchy consolidation are seen in bilateral lungs (green arrows). The CT severity score was 20/25. Thin-walled cystic lesions are seen in bilateral upper and lower lobes (red arrows). Average size of lung cysts was <2 cm.

Case 5

A 68-year-old female patient, a known hypertensive, who came with dyspnoea and chest pain on the 22nd day of illness. She was on HFNC oxygen therapy of 30 liters/min for past 10 days in a private hospital. Her nucleic acid test by RT-PCR was initially positive on a nasopharyngeal swab on the 5th day of illness but was negative, when repeated in the hospital. With an oxygen saturation of 78% on room air, the patient was admitted to ICU and was given 10 L/min oxygen support.

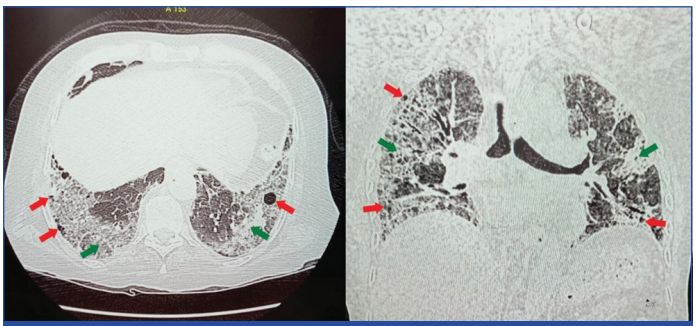
HRCT chest shows, ground glass attenuation with fibrotic bands and traction bronchiectasis in the lower lobes with a CT severity score of 20/25. Multiple (7-8) subpleural cysts (14-16 mm in diameter) were seen more so in the right lung [Table/Fig-5]. She was significantly hypoxaemic, with falling of saturation even on 15 L/min oxygen via a non rebreather mask, a high respiratory rate of 42 breaths per minute, and tachycardia. Patient was required to put on 40 liters/min of oxygen therapy with HFNC for 14 days. During the subsequent week, her oxygen requirements gradually reduced to 5 liters/min by nasal prongs. She was discharged on domiciliary therapy of around 2 liters/min of oxygen. She was maintaining normal oxygen saturation on ambient room air on her next follow-up visit in Medicine OPD after 2 weeks of discharge.



[Table/Fig-5]: HRCT thorax Images (Axial and Coronal) of a 68-year-old female patient who was RTPCR positive for Covid-19 infection. This CT was done on day 22 from symptom onset. There is presence of subpleural ground-glass opacities, fibrosis, septal thickening (green arrows) and subpleural cysts (red arrows).

Case 6

A 38-year-old female who was diagnosed with COVID-19 pneumonitis and was earlier admitted in ICU of a private setup for 2 weeks, where she was on oxygen therapy with poor maintenance of saturation. She was admitted on the 39th day of illness in our hospital on clinical deterioration. She had no known comorbidities and her SpO_2 on admission was 64 percent. She had leucocytosis and elevated inflammatory biomarkers in her blood reports initially. Her previous CT Chest done elsewhere, showed a CTSS of 18/25. Repeat CT done in our hospital on the day of admission showed worsened pneumonitis with CTSS of 25/25. There was fibrosis, more so subpleural and multiple (8-9) intraparenchymal cysts, varying between 13-18 mm in diameter [Table/Fig-6]. She initially required NIV support in ICU for 8 days followed by 35 liters/min support by HFNC for the next 15 days. Thereafter, the oxygen requirement reduced to 10 liters/min over the next week and further to 5-6 liters/min in the next three days when she was discharged on domiciliary oxygen therapy. She needed oxygen support at home for a week after discharge, as per the follow-up received from her family and thereafter the oxygen was completely weaned off.



[Table/Fig-6]: HRCT Chest images of a 38-year-old female patient done on day 39 of the disease. Extensive resolving pattern of pneumonitis with fibrosis (green arrows) is seen along with multiple subpleural cysts (red arrows).

DISCUSSION

The COVID-19 infection, caused by SARS-CoV-2, though may present as a multiorgan disease, has a predilection for the lungs. The CT, which has a sensitivity of 89-97%, has played a vital role in the pandemic, for patient triage even before the RT-PCR results, to predict the disease course, and to diagnose and confirm complications [6].

Now, it has been clear that initially ground glass opacities and consolidation predominate having peripheral and lower lobar predilection. These findings peak at around 10-14 days. Thereafter, they either resolve or progress in week 3 where consolidation may be admixed with reticular opacities. Post acute fibrosis, now called Post Acute Sequelae COVID-19 (PASC) can thereafter develop, wherein CT the multifocal ground glass and reticular opacities may persist, along with interlobular septal thickening; however, signs of fibrosis emerge including subpleural parenchymal bands with or without architectural distortion, traction bronchiectasis, areas of mosaic attenuation with emphysema and cysts [1,2,7,8].

Acute Respiratory Distress Syndrome (ARDS), direct virus injury, and barotrauma due to mechanical ventilation have been attributed to the aetiology of PASC lung. Radiologically, the extent of initial lung involvement may be a predictor for PASC [7].

There are few case reports on the association of COVID-19 with cystic diseases so far.

One of the earliest cases of lung cysts in COVID-19 pneumonia was reported in Europe in 2020 where several thin-walled cysts were found in a 67-year-old male patient in CT on day 20 of the illness. This patient had a history of acute thromboembolism and was mechanically ventilated for 10 days [9]. In another case report, a large bulla in the left lung apex was reported in an 82-year-old woman, who had features of COVID-19 pneumonia on HRCT after 6 months of treatment. Chest CT showed a large bulla (47 mm×29 mm) in the left lung apex, although pneumonia had partially resolved. No radiological findings on further follow-up have been however mentioned [10]. Liu K et al., also reported chest CT findings of cystic lesions in 2 patients confirmed to have COVID-19 pneumonia. The pulmonary cysts occurred more than 30 days after symptom onset and one patient had been on mechanical ventilation [11]. An Indian case report of a 51-year-old COVID-19 infection patient, who initially presented with ground-glass opacities and consolidation but eventually developed a large pulmonary cyst was reported in Gujarat, India in October 2020 [12]. As far as cysts are concerned, they must be differentiated from cavities as their aetiologies differ. Cyst is defined as a well-defined, thin-walled (usually epithelial or fibrous, less than 3 mm in thickness), air or fluid containing lesion, 1 cm or more in diameter [13].

Commonly, cysts are found in subpleural areas of the lung and represent emphysema, bullae of honey-combing. Cystic disease related to COVID-19 has not been commonly reported with the prevalence cited in literature so far between 9% and 25% [8]. Such cysts are usually well-defined, thin-walled (2-4 mm), variable in size, usually less than 2.5 cm; though larger cysts have also been described in a few case reports [3,14].

None of the patients showing pulmonary cystic lesions was diagnosed with superadded infection during their hospital stay.

In the present case series, the cysts were found to be thin-walled and subpleural in distribution. The immediately surrounding lung parenchyma showed features of maximal involvement by the atypical pneumonitis. Similar findings were reported in a previous study wherein, the cysts were located in the region of peak disease activity [3]. Also, all six of the presented cases had moderate to severe lung involvement as per CTSS. Authors assume that extensive lung involvement is suggestive of higher inflammatory activity in the region. Also, there is more likelihood of assisted ventilation requirements in such patients. The combination of these underlying factors probably results in predisposing patients with more severe diseases to have higher chances of developing cystic complications. In current case series, two patients received NIV, two required HFNC and the rest were on high flow or venturi mask. Thus, authors found that though, the mode of oxygen delivery was varying, yet the high flow oxygen therapy and its duration along with degree of lung involvement, are important determinants of cystic degeneration.

The aetiology of these cysts is still unclear. Two schools of thought prevail, one believes that these cysts are secondary to parenchymal damage, fibrosis, and low compliance which may be associated with mechanical ventilation in some cases, but can also arise in advanced ARDS. Others believe that they arise due to architectural distortion when consolidation resolves [9,10].

Interestingly such cysts have not been reported in other viral pneumonia unless there was pre-existing interstitial lung disease or emphysema [3,13]. This may be since the infection with COVID-19 and other coronaviruses cause persistent airflow obstruction which

is not the case with other viral pneumonia [15]. It is postulated that such airway obstruction by mucus plugs or fibromyxoid exudates may have a valve effect on the bronchus and persistent coughing or assisted ventilation may result in a sudden increase in intra-alveolar pressure and alveolar rupture resulting in subpleural cysts or even pneumothorax [11]. Two out of six patients in the present case series developed pneumothorax.

In the presented cases, HRCT Chest was performed after the administration of high flow oxygen therapy had begun and cystic changes were observed somewhere between day 15 to day 40 of the disease. The authors contemplate it to be the time taken by inflammatory storm to bring about the evolution of pulmonary lesions and the effect of prolonged oxygen therapy administered to the patients. This time lag was also reported in other case reports [4,11].

Authors followed-up with the presented patients in post COVID-19 clinic in the hospital after their discharge. As per the protocol, regular follow-up was done with clinical assessment, chest radiography and pulmonary rehabilitation. These patients improved clinically over time and did not develop obvious pneumothorax on chest radiography. Considering the radiation exposure, HRCT was not part of the follow-up protocol and so the progression or resolution of the cysts cannot be commented upon.

CONCLUSION(S)

Authors conclude that, prolonged oxygen therapy particularly high flow oxygen therapy like NIV or HFNC, in the backdrop of extensive parenchymal involvement by COVID-19 pneumonitis resulted in mechanical injury to the alveoli, resulting in cyst formation, predominantly in the subpleural distribution.

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