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# Giant lung bulla as a late-onset complication of mild SARS-CoV-2 pneumonia

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## Author contributions statement

|                                                |                     |
|------------------------------------------------|---------------------|
| <b>Study concepts:</b>                         | <b>PB, MP, PS</b>   |
| <b>Study design:</b>                           | <b>PB, MP, PS</b>   |
| <b>Data acquisition:</b>                       | <b>All authors</b>  |
| <b>Quality control of data and algorithms:</b> | <b>All authors</b>  |
| <b>Data analysis and interpretation:</b>       | <b>All authors.</b> |
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**Informed consent:** Written consent was obtained by the patient.

## **Abstract**

A 49-year-old Caucasian man was admitted to the Emergency Department for shortness of breath and cough. CT imaging showed bilateral a mild COVID-19 related pneumonia. He was hospitalized in the low-intensity COVID-19 unit where he received O<sub>2</sub> therapy and oral corticosteroids (CS). Three weeks after discharge a high-resolution computed tomography (HRCT) find a giant bulla of the inferior lobe. The bulla was resected by video-assisted thoracoscopic surgery (VATS) and the patient recovered completely. In our patient, it is reasonable to suspect that the development of the bulla is a result of SARS-CoV-2 infection, since no bulla was observed in the first HRCT two months before. SARS-CoV-2 related pneumonia may be responsible for lung remodeling due to diffuse alveolar damage and later interstitial myofibroblastic proliferation. Corticosteroids might have played a role in increasing SARS-CoV-2 dystrophic action. COVID-19 leads to pulmonary damages, which are still partially unknown and might result in development of bullae. In fit patient surgical treatment can be carried out safely.

**Key words:** Emphysema, bullae, minimally invasive surgery, COVID-19

## **Introduction**

COVID-19 pandemic spread in the last two years throughout the world with a significant number of deaths. According to the Centers for Disease Control and Prevention, common symptoms of COVID-19 include fever, cough, shortness of breath, muscle aches and in some cases loss of taste or smell. Gastrointestinal manifestations may include nausea, vomiting, diarrhea and abnormal liver function. Other less common manifestations encompass headaches, dizziness, conjunctivitis, ocular irritation and erythematous rash [1].

In this report, we present the case of a patient who developed a massive lung bulla two months after COVID-19 pneumonia and he was successfully treated with a surgical resection.

## Case Report

Written consent was obtained by the patient.

On 8<sup>th</sup> November 2021, a 49-year-old Caucasian man was admitted to the Emergency Department for shortness of breath and cough. He tested positive for SARS-CoV-2 PCR nasal swab, and he was not vaccinated. His past medical history was negative for significant comorbidities, including smoking history. CT imaging showed bilateral diffuse ground-glass areas compatible with a mild COVID-19 related pneumonia (Figure 1 A-D).

Due to mild symptoms, the patient was discharged home with empiric antibiotic therapy (azithromycin), antithrombotic prophylaxis with low-molecular-weight heparin (LMWH) and anti-inflammatory treatment. The day after, his family doctor implemented the therapy with oral corticosteroids (prednisone 25 mg per day).

On 12<sup>th</sup> November the patient returned to the Emergency Department for worsening of dyspnea and cough. Six-minute walking test was positive for desaturation, but the radiological evaluation did not reveal significant changes; the patient was then transferred to the low-intensity COVID-19 unit where he received O<sub>2</sub> therapy with nasal cannula and oral corticosteroids (CS), with a notable improvement of respiratory function. On 18<sup>th</sup> November he was discharged again with prescription of home isolation and corticosteroid.

Three weeks after discharge, he tested negative for SARS-CoV-2 PCR nasal swab and a follow-up chest X-ray was performed showing a large pneumothorax; the patient only referred a slight worsening of his dyspnea and he was hospitalized again. A pleural drainage was inserted with no benefit on symptoms and no resolution of pneumothorax. A high-resolution computed tomography (HRCT) showed a large amount of air in left hemithorax with a differential diagnosis of either a pneumothorax or a giant bulla developing in the fissure between left upper and lower lobes (Figure 2 A-D).

The patient was therefore transferred to our hospital and on 27<sup>th</sup> December he underwent a biportal thoracoscopy (timeline summarized in Figure 3). During surgery, a giant bulla with a diameter of roughly 10 cm arising from the fissure face of the left lower lobe was discovered. Dense adhesions attached the bulla to the upper lobe and to the chest wall. A diffuse parietal pleural thickening and inflammation was visible, while the remaining lung was macroscopically normal. After gentle dissection, the bulla was resected from the lung parenchyma using a reinforced endoscopic stapler. A TachoSil® strip was applied to prevent airleaks. The postoperative course was uneventful; the chest drain was removed on 5<sup>th</sup>

postoperative day and the patient was discharged the following day. Histopathological examination showed evidence of bullous emphysema and squamous metaplasia with the presence of macrophages and lymphocytes in the specimen.

At follow up in outpatients clinic, chest X-ray showed a complete re-expansion of the lung; the patient reported a full resolution of symptoms (Figure 4).

## **Discussion**

Late-onset pneumothorax is a common complication of mechanical ventilation due to possible barotrauma on the airway. Thus, pneumothorax and pneumomediastinum have not been uncommon in COVID-19 patients who are treated with invasive ventilation [2]. On the other hand, the development of a bulla is a rare event in COVID-19 patients who have not undergone intubation. In literature, only a few cases have been reported so far. Similarly, to our cases, Yasukawa and Murayama reported patients with mild COVID-19 pneumonia, no relevant medical history and no SARS-CoV-2 vaccination. None of the patients underwent mechanical ventilation. In first case [3] the patient was treated with medical treatment (remdesivir), convalescent plasma and a chest drain was positioned, while in the second case [4] the authors do not describe any specific treatment and no surgical procedures were performed. To the best of our knowledge this is one of the first cases describing a bulla resection after COVID-19.

In our patient, it is reasonable to suspect that the development of the bulla is a result of SARS-CoV-2 infection, since no bulla was observed in the first HRCT two months before. Liu *et al.* linked SARS-CoV-2 infection to lung cystic dystrophy, but the physiopathology is still unknown [5]. According to Pednekar [6] SARS-CoV-2 related pneumonia may be responsible for lung remodeling due to diffuse alveolar damage and later interstitial myofibroblastic proliferation; we can speculate that this remodeling of lung parenchyma could be the base for the development of giant bullae.

We also focused our attention on the potential role of corticosteroids in developing bullous dystrophy. Although they have no direct role in damaging lung parenchyma it is well known that corticosteroids cause in a significant reduction of tissue regeneration. Moreover, Rocco *et al.* [7] state that prolonged use of corticosteroids for acute alveolar damage reduces elastic properties of lung tissue. Our patient was treated with corticosteroids to counteract the chronic inflammation produced by SARS-CoV-2, but on the other hand it might have delayed the virus

clearance [8]. We can therefore hypothesize that corticosteroids might have played a role in increasing SARS-CoV-2 dystrophic action.

Lastly, we can also speculate that vaccination could have prevented the developing of viral pneumonia and possibly the resulting long-term complications.

More studies are needed to better understand the connection between COVID-19 pneumonia and long-term pulmonary damages. However, a careful follow-up with chest imaging in these patients is mandatory.

In conclusion, the developing of lung bullae could be a late-onset complication in patients with COVID-19 pneumonia. Surgical approach can be safely proposed based on bulla features and patients' comorbidities.

Although the etiopathology is still unclear, we can hypothesize that SARS-CoV-2 and corticosteroids play a simultaneous impairing role on lung parenchyma.

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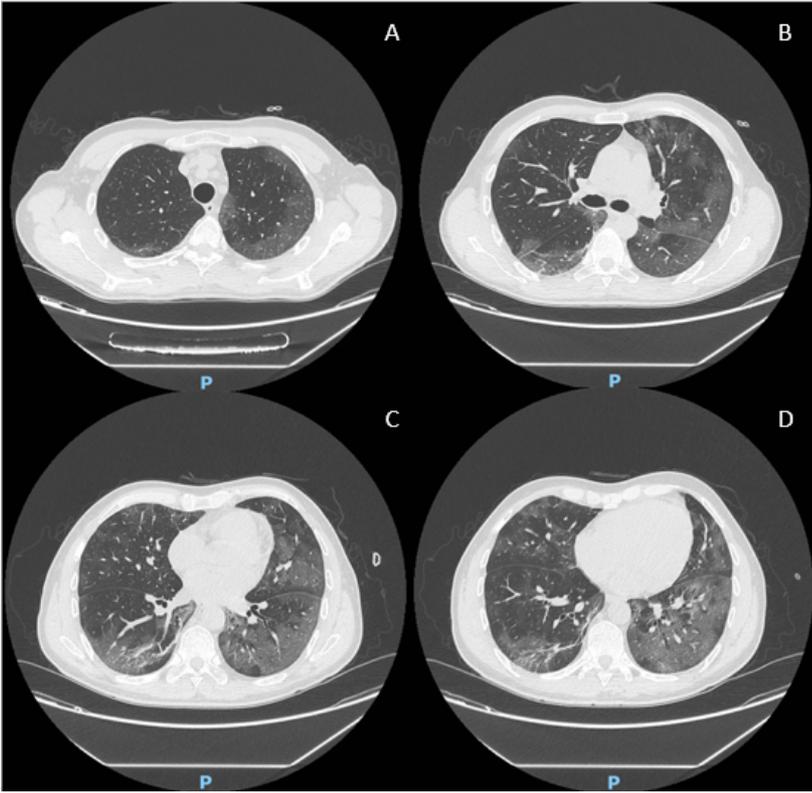


Figure 1. A-D) CT scan showing mild COVID-19 pneumonia with no bullae.

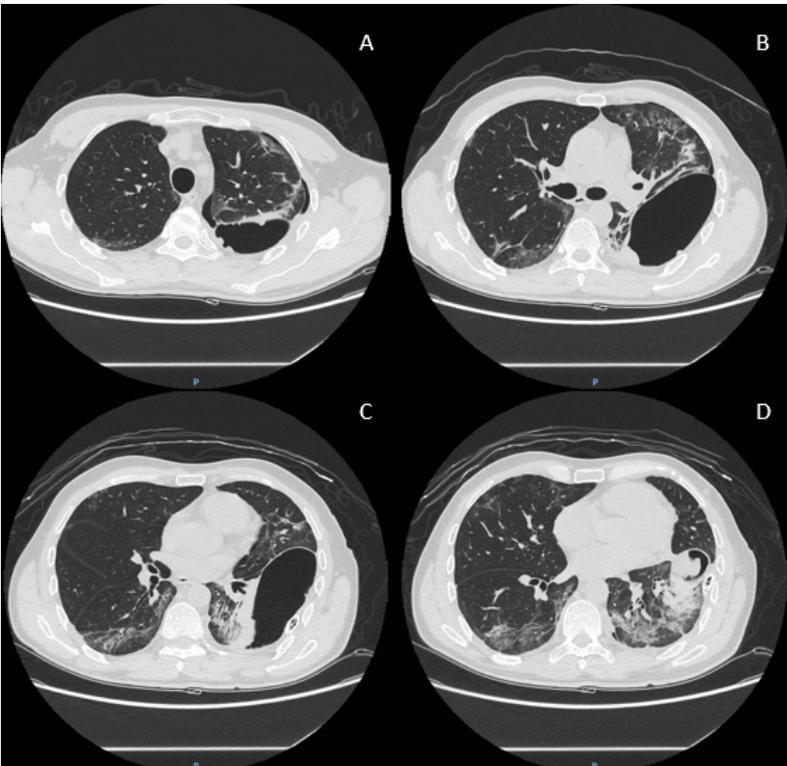


Figure 2. A-D) CT scan showing the giant bulla in the fissure between left upper and lower lobes.

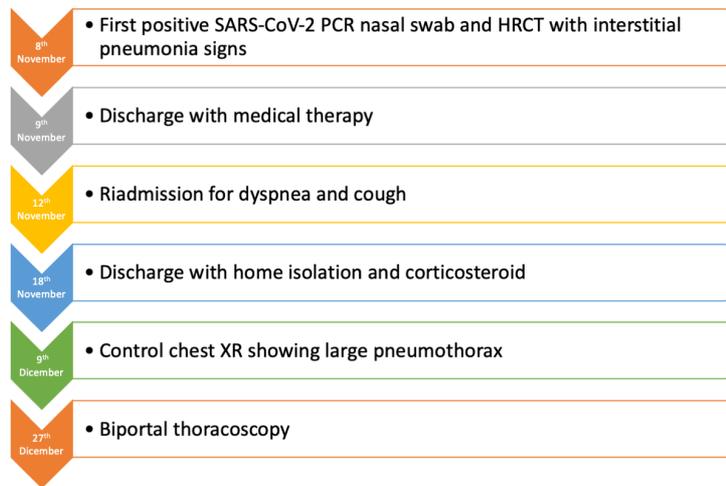


Figure 3. Our patients' timeline.

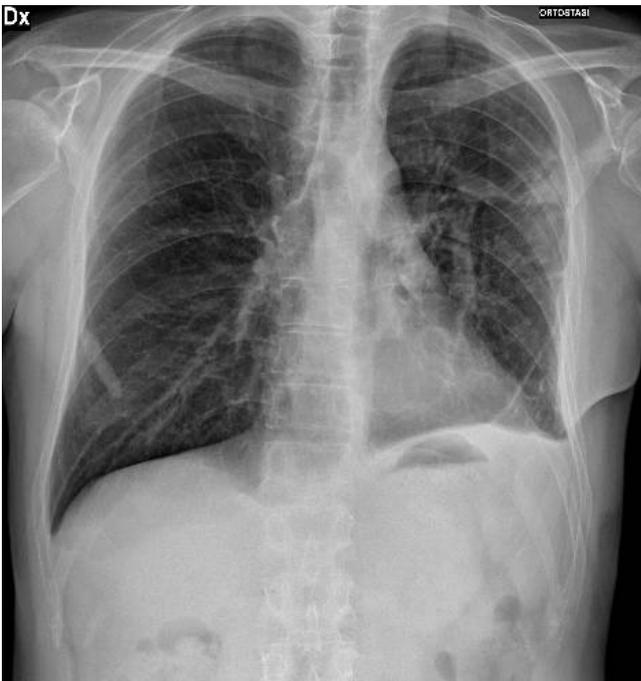


Figure 4. Postoperative chest X-ray.