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Bullous changes in the lungs in a patient after severe COVID-19 pneumonia (Case report and literature review)

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The global outbreak of COVID-19 has been associated with various complications, including respiratory issues. This study focuses on a clinical case of bullous lung disease observed in a patient following a severe SARS-CoV-2 infection. The rarity of such complications necessitates a detailed investigation to understand the potential cause-and-effect relationships.
The case under study involves a 60-year-old woman who contracted COVID-19 in February 2021. She underwent prolonged hospitalization with systemic corticosteroids, antibacterial drugs, anticoagulants, oxygen therapy, and non-invasive ventilation. Multiple diagnostic tools, including X-rays, computed tomography scans, and fibrobronchoscopies, were employed to monitor her condition and identify the development of bullous cavities in her lungs.
Initial X-ray examination revealed bilateral polysegmental pneumonia and pneumofibrosis, accompanied by large bullous cavities in the upper lobes of both lungs. Microbiological analyses identified resistant strains of *Klebsiella pneumoniae* and *Pseudomonas aeruginosa*. Over the observation period from 2021 to 2023, the patient frequently experienced suppuration and haemoptysis, with no successful eradication of the pathogens. The progressive nature of the disease led to significant deterioration in the patient's respiratory function and overall health, including the development of pulmonary hypertension and right ventricular heart failure.
The formation of bullous cavities in the lungs after COVID-19 may be linked to prolonged inflammatory processes, fibrotic changes, and diffuse alveolar damage. These findings align with other documented cases of bullous lung disease associated with SARS and MERS infections. The study highlights the potential for severe, long-term pulmonary complications following COVID-19, emphasizing the need for continued research into the underlying mechanisms and risk factors.
Bullous lung disease presenting after severe SARS-CoV-2 pneumonia is rare and challenging to interpret, particularly due to confounding factors such as secondary bacterial infections and prolonged mechanical ventilation. Although our clinical case does not provide sufficient evidence to establish a direct causative relationship between SARS-CoV-2 infection and bullous pulmonary lesions, it highlights a clinically relevant association warranting further investigation. Clinicians should remain aware of potential pulmonary complications, including bullous changes, in patients recovering from severe COVID-19 pneumonia.
Keywords: *bullous lung cavities, COVID-19, complications.*

Бульозні зміни в легенях після тяжкої пневмонії, спричиненої COVID-19 (Клінічний випадок та огляд літератури)

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Глобальна пандемія COVID-19 спричинила значне зростання кількості випадків респіраторних захворювань. У статті наведено клінічний випадок бульозної хвороби легень, що розвинулася в пацієнтки після перенесеної тяжкої пневмонії, спричиненої інфекцією SARS-CoV-2. Рідкісність подібних ускладнень зумовлює необхідність поглибленого аналізу для кращого розуміння потенційних причинно-наслідкових зв'язків.
У статті розглянуто випадок 60-річної жінки, яка захворіла на COVID-19 у лютому 2021 року. Лікування включало тривалу госпіталізацію з призначенням системних кортикостероїдів, антибактеріальних препаратів, антикоагулянтів, оксигенотерапії та неінвазивної вентиляції легень. Для моніторингу стану пацієнтки та виявлення бульозних порожнин у легенях використовували низку діагностичних інструментів, зокрема рентгенографію, комп'ютерну томографію та фібробронхоскопію.
Рентгенологічне обстеження легень виявило двосторонню полісегментарну пневмонію та пневмофіброз, що супроводжувалися формуванням великих бульозних порожнин у верхніх частках обох легень. Мікробіологічне дослідження виявило резистентні штами *Klebsiella pneumoniae* та *Pseudomonas aeruginosa*. Упродовж періоду спостереження (2021–2023 рр.) у пацієнтки часто виникали епізоди нагноєння та кровохаркання без успішної ерадикації збудників. Захворювання мало прогресуючий характер зі значним погіршенням дихальної функції та загального стану пацієнтки, включно з розвитком легеневої гіпертензії та правошлуночкової серцевої недостатності.
Формування бульозних порожнин у легенях після COVID-19 імовірно пов'язане з тривалими запальними процесами, фіброзними змінами та дифузним ураженням альвеол. Отримані результати узгоджуються з іншими задокументованими випадками бульозних захворювань легень, асоційованих з інфекціями SARS та MERS. Наведений клінічний випадок ілюструє можливість розвитку тяжких і довготривалих легеневих ускладнень після COVID-19, що підкреслює необхідність подальших досліджень основних механізмів і факторів ризику.

Бульозні захворювання легень, що виникають після тяжкої пневмонії, спричиненої SARS-CoV-2, є рідкісними та складними для інтерпретації, особливо за наявності супутніх ускладнень, як-от вторинні бактеріальні інфекції та тривала механічна вентиляція легень. Хоча наведений клінічний випадок не дозволяє встановити прямий причинно-наслідковий зв'язок між інфекцією SARS-CoV-2 та розвитком бульозних уражень легень, він демонструє клінічно значущу асоціацію, що потребує подальшого вивчення. Клініцисти мають враховувати ймовірність розвитку легеневих ускладнень, зокрема бульозних змін, у пацієнтів, які одужують після тяжкої пневмонії, спричиненої COVID-19.
Ключові слова: *бульозні ураження легень, COVID-19, ускладнення.*

The World Health Organization (WHO) has designated the novel coronavirus infection as a public health emergency of international concern, recognizing it as a global threat on 30 January 2020. On 11 March of the same year, the Director-General of the WHO declared the outbreak of the novel coronavirus disease (COVID-19) a pandemic.

The global introduction of vaccines since 2021 has significantly reduced the burden of COVID-19, despite the emergence of new, more transmissible variants of the pathogen. In light of these considerations, on 5 May 2023, the Director-General of the WHO formally declared the pandemic to be over. However, despite the observed increase in public immunity and a concomitant reduction in hospitalizations and deaths, the Director-General also indicated that there remained significant uncertainties regarding the future evolution of SARS-CoV-2. As of 26 May 2024, a total of 77,555,220 people have been infected with the virus worldwide, with 7,050,201 deaths directly or indirectly associated with the disease [1, 2]. The clinical presentation of the disease caused by the coronavirus is highly variable, ranging from asymptomatic infection to rapid deterioration and death [3].

Over 87% of individuals recovering from Coronavirus Disease 2019 (COVID-19) report at least one lingering symptom, with dyspnea among the most frequent following infection with severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) [4]. Pulmonary function tests often reveal physiological impairments such as reduced diffusion capacity and restrictive ventilatory defects [2]. Although studies of post-infectious pulmonary phenomena are ongoing, interstitial lung disease is the most commonly documented abnormality, presenting with features such as organizing pneumonia and fibrotic-like alterations – reticulations, honeycombing, and traction bronchiectasis [5–7]. Furthermore, small airways disease, characterized by air-trapping and mosaic attenuation, has also been noted on chest imaging [8, 9]. In contrast, bullous lung disease has been infrequently reported. This publication is a case report and is not intended to establish a direct cause-and-effect relationship, but only to draw attention to the possible association between severe COVID-19 and bullous changes in the lungs.

The occurrence of bullous lung disease as a consequence of SARS-CoV-2 infection has been documented on only a limited number of occasions [10].

The study was conducted according to the WMA Declaration of Helsinki – Ethical Principles for Medical Research Involving Human Subjects. The patient gave written informed consent.

Clinical case. A 60-year-old woman had been experiencing symptoms of illness since February 2021, when she contracted the coronavirus disease (PCR for SARS-CoV-2 positive). The initial course of the disease was severe, as she required intensive oxygen supplementation due to respiratory distress. Chest X-ray examination reveled the presence of bilateral polysegmental pneumonia. Patient was hospitalized from 19.02.2021 to 31.05.2021 in the intensive care unit. The treatment involved the prolonged use of systemic corticosteroids, antibacterial drugs (amoxicillin-clavulanic acid, azithromycin, cefepime, imipenem, moxifloxacin, linezolid), anticoagulants (subcutaneous enoxaparin), oxygen therapy and non-invasive lung ventilation methods (CPAP therapy) in order to alleviate the disease. X-ray on 05.06.2021 (before discharge) revealed signs of pneumofibrosis and bullous changes. The patient was discharged in the care of her family doctor, her complaints on discharge were shortness of breath and mild cough. She received only mucolytics after the discharge. Additionally, the patient's electrocardiogram (ECG) exhibited indications of right heart overload. The clinical blood test demonstrated leukocytosis with a left shift in the formula, and elevated procalcitonin and C-reactive protein levels, which constituted the rationale for antibiotic therapy, which she received (linezolid).

The patient contracted SARS-CoV-2 again in December 2021, received outpatient car, and in January 2022 was admitted to the Ivano-Frankivsk Regional Phthisiology and Pulmonology Centre with cough and signs lung failure. The chest X-rays (Fig. 1a, b) demonstrated an increased and deformed lung pattern, as well as infiltration of the lung tissue in the lower lobes of both lungs, which were absent on 06.05.2021. In the upper lobes, thin-walled bullous cavities with areas of fibrosis, fibrosis-altered lung roots, and unchanged heart borders were observed. The sinuses were free of any abnormalities. She received appropriate treatment that helped with her respiratory function, but did not fully alleviate her from the symptoms. All subsequent hospitalizations to the Department of Thoracic Surgery and Pulmonology of the Ivano-Frankivsk Regional Clinical Hospital and the Regional Phthisiology and Pulmonology Centre were attributed to complaints of intense cough with purulent sputum and haemoptysis, shortness of breath, and fever. A series of X-rays and computed tomography scans revealed the presence of multiple thin-walled cavities in the upper lobes of both lungs. The largest cavity in the right upper lobe measured 8.1 × 9.8 × 8.4 cm, while the largest in the left upper lobe was 6. The dimensions of the lesion were 5 × 4.6 × 8.7 cm, with a horizontal fluid level, multiple small nodules in the adjacent lung tissue, and fibrosis foci subpleural and mediastinal lymphadenopathy (up to 17–18 mm) (Fig. 2).

From 2022 to 2023, there were negative radiographic dynamics (Fig. 3a, b), namely thickening of the cavity walls in both lungs, the presence of horizontal contents, increased pulmonary pattern with fibrous changes, and decreased pneumatisation of the lung tissue in the lower lobes.

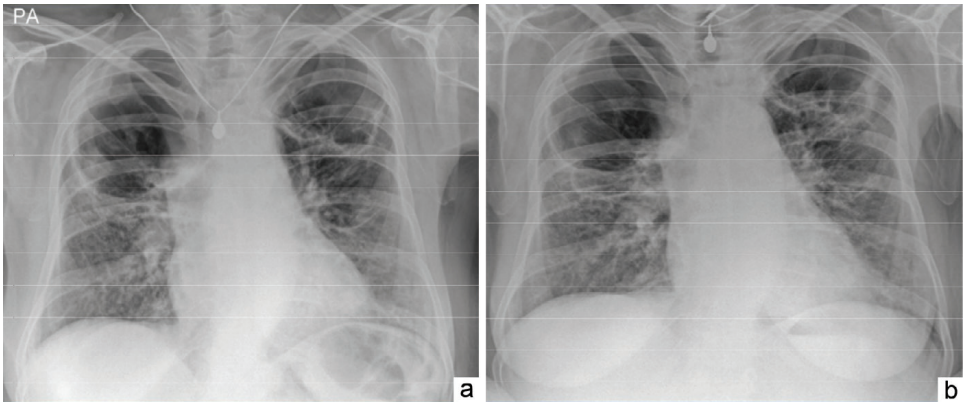

Fig 1. X-rays of the patient's chest organs dated 03.12.2021 (a) and 25.01.2022 (b)

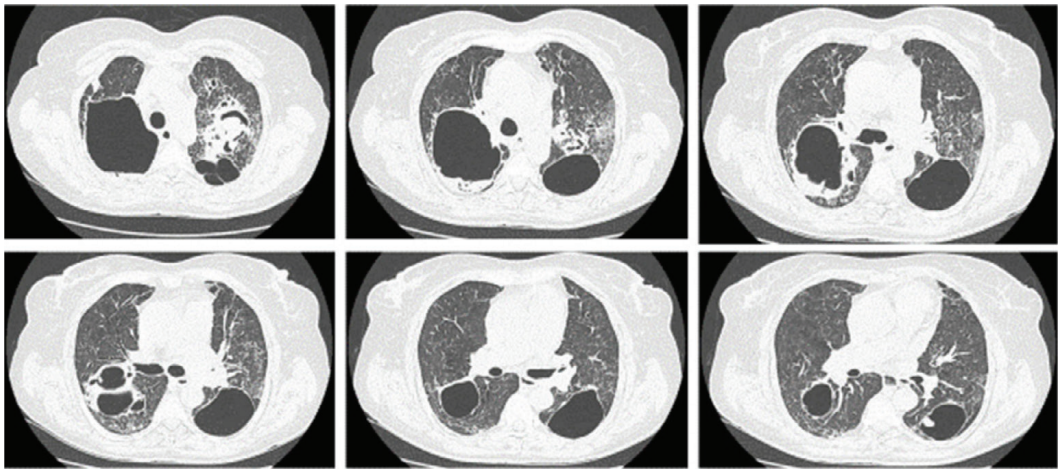

Fig 2. Results of computed tomography of the patient's chest 19.05.2022

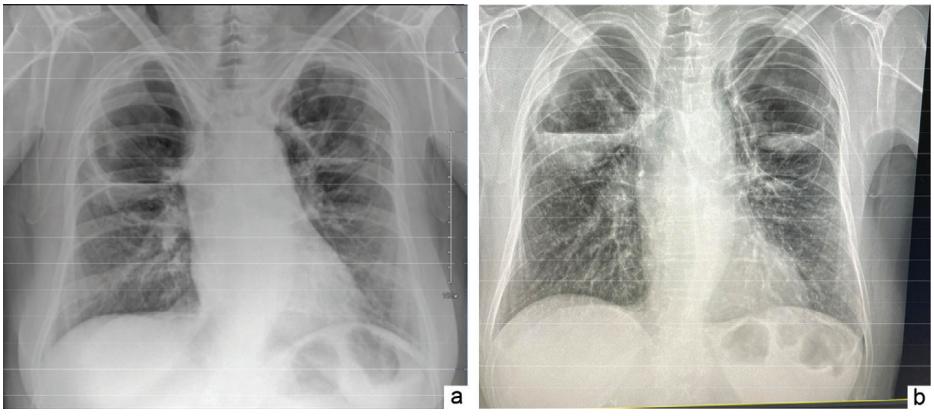

Fig. 3. Chest X-rays of the patient on 13.07.2022 (a) and 14.03.2023 (b)

Considering the persistence of the symptoms, fibrobronchoscopy was performed for diagnostic and therapeutic purposes. Hyperaemia, oedema, increased vulnerability of the bronchial tree mucosa, narrowing of the upper lobe bronchi due to oedema, and thick purulent secretion were detected. Antiseptic solutions were used for sanitation. Microbiological studies of sputum and bronchial lavage water after fibrobronchoscopies revealed *Klebsiella pneumoniae* and *Pseudomonas aeruginosa* cultures with resistance to most antibacterial drugs, except polymyxin and amikacin. During the observation period, the lung cavities were often accompanied by suppuration and haemoptysis, and eradication of the pathogens was not achieved. The decision of the team of pulmonologists, thoracic surgeons, and radiologists was that the volume of the affected lung tissue was large and did not allow for radical surgical treatment.

During the course of her illness, the patient's overall condition deteriorated considerably. The patient exhibited a notable loss of body weight and presented with clear indications of severe pulmonary failure. Echocardiography demonstrated the presence of pulmonary hypertension (pulmonary artery pressure 34.5 mmHg), right ventricular dilation up

to 3.3 cm, and relative insufficiency of the tricuspid valve with regurgitation 2+, indicative of the formation of a pulmonary heart and right ventricular heart failure. Additionally, she exhibited the onset of type 2 diabetes mellitus, lumbar spondyloarthrosis with L3 antilesion and laterolisthesis, and L2 compression fracture. We attribute the worsening of patients condition to the decreased lung volume due to bullous cavities and persistent infectious locus. The combination of these factors and the prolonged use of antibiotics and corticosteroids in our opinion led to the heart complications (right ventricle heart failure) and onset of type 2 diabetes. It also explains the reason for intense loss of body weight.

The formation of bullous cavities in the lungs following severe SARS-CoV-2 infection remains an infrequently described phenomenon, with only limited cases reported in medical literature thus far [11, 12]. Our patient developed significant bilateral bullous lesions after a prolonged hospitalization due to severe COVID-19 pneumonia, complicated by secondary nosocomial infections involving *Klebsiella pneumoniae* and *Pseudomonas aeruginosa*. These pathogens are known to be associated with necrotizing pneumonia, lung abscess formation, and chronic pulmonary sequelae [13]. Thus, the exact contribution of SARS-CoV-2 to the formation of the observed bullous lung disease is uncertain, and differentiation from secondary bacterial complications poses a diagnostic challenge.

Previous studies highlighted potential pathogenic mechanisms for post-viral pulmonary lesions, including prolonged inflammatory reactions, alveolar damage, and diffuse fibrosis [14, 15]. Specifically, similar radiological and histological findings, such as diffuse alveolar injury and subsequent fibrosis, have been documented after infections with SARS-CoV and MERS-CoV [16, 17]. Additionally, pulmonary barotrauma associated with non-invasive ventilation during severe respiratory distress could exacerbate lung damage and potentially facilitate bullae formation [18, 19]. However, distinguishing the direct viral-induced pathology from secondary bacterial or ventilator-associated damage remains clinically challenging.

In this clinical scenario, the patient's severe clinical deterioration, frequent haemoptysis, and persistent microbial colonization may point to a multifactorial etiology rather than a single causative factor. Therefore, asserting a direct cause-and-effect relationship between COVID-19 alone and bullous changes is scientifically premature. Rather, this case highlights the need for clinicians to maintain vigilance regarding such pulmonary complications in post-COVID-19 patients and underscores the importance of thorough microbiological and radiological follow-up.

Future research, ideally involving a larger cohort of patients, would be necessary to determine the specific pathophysiological role of SARS-CoV-2 infection in the pathogenesis of bullous lung disease and to differentiate it clearly from the effects of secondary nosocomial infections or ventilator-induced trauma.

CONCLUSIONS

Bullous lung disease presenting after severe SARS-CoV-2 pneumonia is rare and challenging to interpret, particularly due to confounding factors such as secondary bacterial infections and prolonged mechanical ventilation. Although our clinical case does not provide sufficient evidence to establish a direct causative relationship between SARS-CoV-2 infection and bullous pulmonary lesions, it highlights a clinically relevant association warranting further investigation. Clinicians should remain aware of potential pulmonary complications, including bullous changes, in patients recovering from severe COVID-19 pneumonia.

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