



## Pneumothorax in a patient with pneumonia caused by SARS-CoV-2: A case report

### Pneumotoraks kod bolesnice sa pneumonijom izazvanom SARS-CoV-2

Ljiljana Novković\*†, Ivan Čekerevac\*†

University of Kragujevac, Faculty of Medical Sciences, \*Department of Internal  
Medicine, Kragujevac, Serbia; Clinical Center of Kragujevac, †Clinic for Pulmonology,  
Kragujevac, Serbia

#### Abstract

**Introduction.** The coronavirus disease 2019 (COVID-19) is an acute infectious multisystem disease caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), manifested by acute respiratory symptoms. The novel coronavirus pneumonia (NCP) is the most common serious clinical manifestation of SARS-CoV-2 infection. In the severe NCP, the systemic manifestations of the disease were also demonstrated, and one of the rare complications, first described in Wuhan (China), is pneumothorax. **Case report.** A 65-year-old female was admitted to the Clinic for Pulmonology with a high fever, shortness of breath, sore throat, and general weakness that started five days before. Laboratory findings revealed lymphopenia, elevated values of inflammatory markers, and liver lesion. A chest X-ray (CXR) demonstrated diffusely accentuated interstitial pattern and reduced parenchymal transparency, left perihilar. Positive SARS-CoV-2 in a nasopharyngeal swab sample was detected in the real-time reverse transcription-polymerase chain reaction (RT-PCR), confirming the diagnosis of NCP. Immediately, nasal oxygen therapy with a flow rate of 8 L/min, with chloroquine phosphate, antibiotics, and symptomatic treatment, was initiated. On the 8th day, her condition suddenly deteriorated, and she developed severe hypoxemia. A repeated CXR showed complete left-sided pneumothorax. Thoracic drainage was successfully performed with complete reexpansion of the lungs the very next day. The patient was released from the hospital in good general condition with normal arterial blood gases. **Conclusion.** Pneumothorax may develop as a complication in patients with pneumonia caused by SARS-CoV-2, without previous pulmonary comorbidities, due to alveolar damage. Acute deterioration with rapid oxygen desaturation in these patients should raise the suspicion of pneumothorax. Early diagnosis and prompt treatment are necessary to reduce mortality.

#### Key words:

covid-19; pneumonia; pneumothorax; polymerase chain reaction; radiography.

#### Apstrakt

**Uvod.** Koronavirusna bolest 2019 (COVID-19) je akutna, infektivna multisistemska bolest koja se najčešće manifestuje akutnim respiratornim simptomima. Izaziva je *severe acute respiratory syndrome coronavirus 2* (SARS-CoV-2). Nova koronavirusna pneumonija (NCP) je najčešća ozbiljna klinička manifestacija SARS-CoV-2 infekcije. U teškoj NCP ispoljene su i sistemske manifestacije bolesti, a jedna od retkih komplikacija, prvi put opisana u Vuhanu (Kina), je pneumotoraks. **Prikaz bolesnika.** Bolesnica stara 65 godina primljena je u Kliniku za pulmologiju zbog febrilnosti, otežanog disanja, gušobolje i opšte malaksalosti koje je imala prethodnih 5 dana. Laboratorijskim ispitivanjem otkriveni su limfopenija, povišene vrednosti parametara zapaljenja i lezija jetre. Radiografijom (RDG) grudnog koša utvrđeno je difuzno naglašen intersticijum i smanjena transparentija parenhima levo perihilarno. Prisustvo SARS-CoV-2 u uzorku nazofaringealnog brisa otkriveno je lančanom reakcijom polimeraze (PCR), čime je potvrđena dijagnoza NCP. Odmah je započeta terapija kiseonikom preko nazalne kanile protoka 8 L/min, uz hlorokin fosfat, antibiotike i simptomatsku terapiju. Osmog dana, stanje bolesnice se naglo pogoršalo i razvila je tešku hipoksemiju. Ponovljenom RDG grudnog koša potvrđen je kompletan pneumotoraks levo. Torakalna drenaža je uspešno izvedena uz potpunu reekspanziju pluća već sledećeg dana. Bolesnica je otpuštena iz bolnice u dobrom opštem stanju, sa normalnim gasovima arterijske krvi. **Zaključak.** Usled oštećenja alveola, pneumotoraks kao komplikacija pneumonije izazvane SARS-CoV-2, može nastati bez prethodnih plućnih oboljenja. Akutno pogoršanje sa naglom desaturacijom kiseonikom kod tih bolesnika trebalo bi da pobudi sumnju na pneumotoraks. Rana dijagnoza i brzo lečenje su neophodni za smanjenje smrtnosti.

#### Ključne reči:

covid-19; pneumonija; pneumotoraks; polimeraza, reakcija stvaranja lanaca; radiografija.

## Introduction

The coronavirus disease 2019 (COVID-19) is an acute infectious multisystem disease caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), primarily affecting the respiratory tract. The disease was first detected in December 2019 in Wuhan, China. It spread rapidly throughout the world, and hence the World Health Organization (WHO) declared a pandemic on the 11th of March 2020<sup>1</sup>.

Clinical presentations of SARS-CoV-2 infection have a broad spectrum that can range from asymptomatic forms to critical manifestations of the disease. Asymptomatic persons seem to account for approximately 40% to 45% of the SARS-CoV-2 infection<sup>2</sup>. Even though the majority of cases result in mild symptoms of a typical viral infection, up to 5% of the cases can develop critical illness and multiorgan failure<sup>3</sup>. Pneumonia is the most common serious clinical manifestation of the SARS-CoV-2 infection. It has been identified as novel coronavirus pneumonia (NCP).

As the COVID-19 pandemic progresses, over the past few months, awareness and knowledge of unusual disease presentations, such as pneumothorax, have increased. Pneumothorax is a known and well-described complication of mechanical ventilation (MV) when it supports the COVID-19 treatment and is attributed to barotrauma<sup>4</sup>. Additionally, patients with COVID-19 are often treated with noninvasive ventilation (NIV) or oxygen *via* high-flow nasal cannula (HFNC) for respiratory support. The applied positive pressure can facilitate the development of pneumothorax.

However, recent reports suggest that pneumothorax can be present in the context of COVID-19, even in the absence of MV-related and NIV-related barotrauma<sup>5–10</sup>.

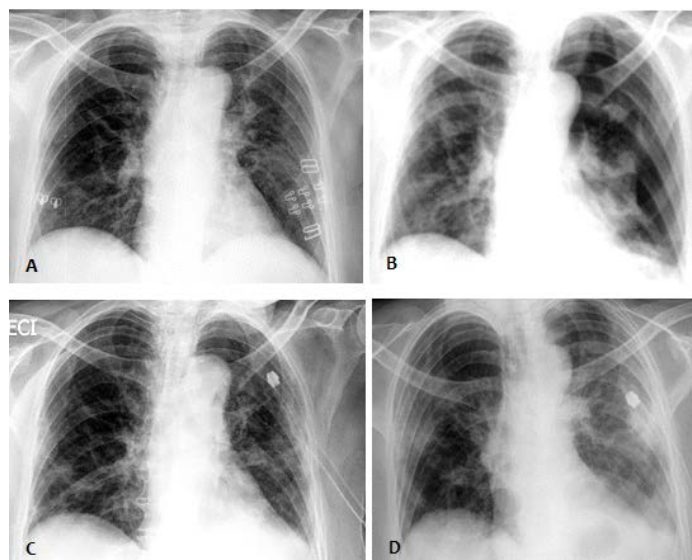
We presented a case of a patient with pneumonia

caused by SARS-CoV-2 who developed spontaneous pneumothorax as a rare complication.

## Case report

A 65-year-old female with a past medical history of hypertension and regulated hyperthyroidism was admitted to the Clinic for Pulmonology, Clinical Center of Kragujevac, Kragujevac, Serbia with a high fever, shortness of breath, sore throat, and general weakness that started five days before. The patient had never smoked, and she denied previous pulmonary diseases. Upon admission, her general condition was poor - she was dyspnoic, adynamic, and dehydrated. Her vital signs showed tachypnea (31 breaths/min), with high temperature (38.5°C), increased heart rate (123 beats/min), and arterial blood pressure reading of 110/70 mmHg. The initial oxygen saturation (SpO<sub>2</sub>) was 89%, normal values > 95% on room air and 95% with a binasal cannula, 8 lit/min of O<sub>2</sub>. Chest examination revealed basal crackles on the left side. Other systemic examinations were orderly.

Laboratory analysis showed white blood cell (WBC) count  $13.63 \times 10^9/L$  [normal range (nr)  $3.7 \times 10^9/L$ ]. The WBC differential count showed 82.84% neutrophils (nr 44%–72%) and lymphopenia of 8.43% (nr 20%–46%). Initial laboratory tests were significant for elevated C-reactive protein (CRP) of 57.6 mg/L (nr 0–5 mg/L), aspartate aminotransferase (AST) of 62 IU/L (nr 0–40 U/L), alanine aminotransferase (ALT) of 51 IU/L (nr 0–40 U/L), lactate dehydrogenase (LDH) of 855 U/L (nr 220–450 U/L), D-dimer of 1.84 µg/mL (nr < 0.50 µg/mL), and ferritin of 609 µg/L (nr 20–300 µg/mL). A chest X-ray (CXR) on admission demonstrated accentuated interstitial pattern bilaterally, linear-banded perihilar shadows, and reduced left perihilar transparency (Figure 1A).



**Fig. 1 – Chest X-ray: A) Chest X-ray on admission showing a diffusely accentuated interstitial pattern, linear-banded shadows perihilar and reduced parenchymal transparency left perihilar; B) Chest X-ray on the 8th day of hospitalization showing complete left-sided pneumothorax; C) Chest X-ray showing complete reexpansion of the lung parenchyma on the left side; D) Chest X-ray showing diffusely reduced parenchymal transparency left and consolidation right infraclavicular.**

The nasopharynx swab, real-time reverse transcription-polymerase chain reaction (RT-PCR) test for SARS-CoV-2, was positive two days after admission.

The patient was labeled as moderate NCP. She started with the treatment for the SARS-CoV-2 caused pneumonia, guided by the valid local protocol in our country at the moment: chloroquine phosphate, parenteral antibiotics (ceftriaxone and azithromycin), supplemental oxygen with a nasal cannula, vitamins and symptomatic therapy, with a prophylactic dose of low molecular weight heparins (LMWH) in order to prevent venous thromboembolism.

The patient felt subjectively better and hemodynamically stable. For a week, she remained on the 4 L/min oxygen *via* nasal cannula, maintaining an oxygen saturation of 96%. No significant changes in AST and ALT values were observed in control laboratory tests (AST: 55 IU/L, ALT: 68 IU/L). In the electrocardiographic finding, sinus rhythm persisted without extrasystoles and changes in the final oscillation. The value of the QTC interval was 423 ms, normal values < 470 ms.

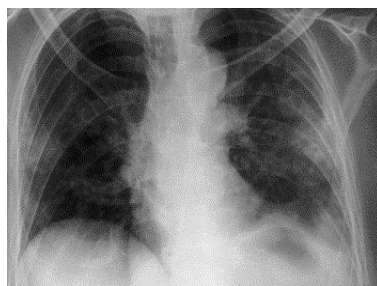
On day 8, her condition suddenly deteriorated. The patient complained of intense shortness of breath, accompanied by an irritating dry cough and developed O<sub>2</sub> desaturation of 78%. Gas analysis showed recorded severe hypoxemia [arterial pressure oxygen – pO<sub>2</sub> = 6.0 kPa, normal values > 10.6 kPa] and mild hypocapnia [pCO<sub>2</sub> = 4.4 kPa]. The patient required 15 L/min of oxygen *via* a face mask and was transferred to the Intensive Care Unit. A repeated CXR showed complete left-sided pneumothorax (Figure 1B). The emergency intervention by a thoracic surgeon was undertaken, a chest drain was inserted, and the patient's oxygen saturation improved. The next day, control CXR showed complete reexpansion of the lung parenchyma on

the left side (Figure 1C). At no point during her stay, did she require the use of NIV or oxygen *via* HFNC. Her oxygen requirements decreased over the next 2 days, and she was transferred to the medical ward with a binasal cannula, 3 L/min of O<sub>2</sub>.

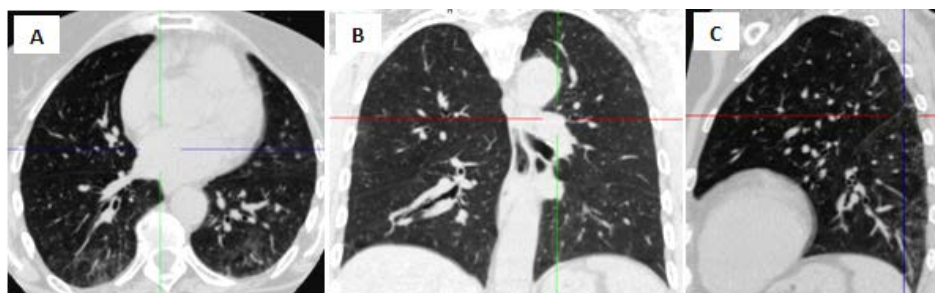
However, her condition continued to deteriorate. The patient became febrile and dyspnoic with O<sub>2</sub> desaturation. Laboratory results showed an increased value of D-dimer (3.47 µg/mL) and raised inflammatory markers, CRP: 185 mg/L, procalcitonin: 2.35 ng/mL (normal values < 0.05 ng/mL) and ferritin: 998 µg/L, whereas CXR registered diffusely reduced left parenchymal transparency and consolidation right infraclavicular (Figure 1D).

There was clinical suspicion of bacterial superinfection but also a dilemma about the possible severe SARS-CoV-2 pneumonia. At that time, chest computed tomography (CT) was not available. The patient responded well to parenteral antibiotics (meropenem and vancomycin), a therapeutic dose of LMWH, glucocorticoid (methylprednisolone 40 mg *iv*) with O<sub>2</sub> supplementation for seven days. The drain was removed a week after administration. The patient was discharged from the hospital in a good general condition on day 21. CXR showed marked radiological regression of the described changes (Figure 2). Arterial blood gas analysis without oxygen therapy showed normal values at discharge.

The patient felt well in the following period. She was monitored by a thoracic surgeon, who described a normal CXR. Four months later, when the epidemiological situation allowed, a chest CT scan was performed, which described ground-glass opacity bilaterally in the lower lobes with elements of interstitial fibrosis and thickening of the parietal pleura in the left upper lobe (Figure 3).



**Fig. 2 – Chest X-ray on discharge from the hospital showing radiological regression of the previous described changes (in Figure 1).**



**Fig. 3 – Chest computed tomography (CT) scans: A) axial, B) coronal, and C) sagittal plane showing ground-glass opacity with elements of interstitial fibrosis bilaterally in the lower lobes and thickening of the parietal pleura in the left upper lobe.**

For our patient, pulmonary function testing (spirometry, diffusion capacity for CO), control chest CT, and further monitoring are planned. There are currently no recommendations for the use of glucocorticoids in such patients.

## Discussion

The severity of COVID-19 is variable, from mild to critical disease. The most common symptoms of SARS-CoV-2 infection, widely characterized in large-scale studies, include fever, cough, and shortness of breath. NCP is the most common serious clinical manifestation of SARS-CoV-2 infection<sup>11</sup>. Patients with severe NCP usually present with dyspnea (respiratory rate > 30 breaths/min) and/or hypoxemia (SpO<sub>2</sub> < 90% on room air) with bilateral infiltrates present on chest imaging. In very severe cases, the disease can progress rapidly and become complicated by acute respiratory distress syndrome (ARDS) and coagulopathies<sup>11</sup>. To date, it is recommended that the definitive diagnosis of SARS-CoV-2 infection be confirmed by a positive RT-PCR test or genetic sequencing<sup>12</sup>.

Pneumothorax is an uncommon and rare finding in patients with NCP, with a frequency of 1% according to the current literature<sup>13</sup>.

Pneumothorax is a clinical entity defined as the presence of air in the pleural space<sup>14</sup>. It can occur spontaneously or following a trauma. Spontaneous pneumothorax, being the most common type, can be primary or secondary, depending on the absence or presence of an underlying lung disease<sup>14</sup>.

The well-known risk factors for the development of spontaneous pneumothorax include the following: male gender, tobacco use, tall stature, age-group from 10–30 years, and strenuous exercise. Additionally, the most frequent underlying disorders responsible for secondary spontaneous pneumothorax include chronic obstructive pulmonary disease (COPD) with emphysema, interstitial lung disease, tuberculosis, and lung cancer or *Pneumocystis carinii* pneumonia<sup>14</sup>.

Pneumothorax is a potential complication usually associated with cystic lung formation due to rupture of the lung tissue.

Liu et al.<sup>15</sup> reported that COVID-19 may independently result in pulmonary cyst formations and the development of pneumothorax. SARS-CoV-2 infected alveolar units tend to be peripheral and subpleural, which is confirmed by radiological findings of COVID-19 in the peripheral lung parenchyma. This tropism of SARS-CoV-2 may increase the risk of peripheral cystic formation facilitating its rupture into the pleural cavity and the development of pneumothorax.

The pathophysiology mechanism of pneumothorax formation in patients with NCP is not completely understood. However, differences between the early and late stages of the disease are indicated.

It is supposed that the complication of pneumothorax occurs secondary due to diffuse alveolar damage from the inflammation caused by a viral infection. The histology, an early phase of NCP, mainly shows the migration of neutrophils, monocytes and macrophages, vascular congestion,

mucus-like exudation in the alveoli, edema in the alveolar septum, and microthrombosis. Due to the destruction of the alveolar septa and a sudden increase of alveolar pressure, the alveoli may be prone to rupturing and forming pulmonary cystic lesions<sup>15</sup>.

At this stage, the direct cytopathogenic effect of SARS-CoV-2 on type II cells also suggests a possible pathogenetic mechanism. SARS-CoV-2 propagates within type II pneumocytes, a large number of viral particles are released, the cells undergo apoptosis and die<sup>16</sup>.

The late stages of NCP determine ischemic parenchymal damage, activation of fibroblasts, lung fibrosis, low lung compliance, and inflammatory fibromyxoid exudates into alveoli and airway. Pulmonary cystic lesions may be formed in response to fibromyxoid exudates, which form a valve in the bronchus. Moreover, due to pulmonary fibrous processes, bronchioles are narrow and distorted, and the valve mechanism could cause pulmonary cystic formation<sup>15</sup>.

Pneumothorax, associated with subcutaneous and mediastinal emphysema, is a well-described complication of mechanical ventilation in patients with critical SARS-CoV-2 pneumonia<sup>17</sup>. However, pneumothorax may also develop as a complication of NIV. The use of NIV, or the application of oxygen *via* HFNC, in conditions of continuous and excessive positive airways pressure delivery can lead to an increase of intra-alveolar pressure, rupture of the alveoli, and formation of cyst lesions<sup>15</sup>.

In addition, applied positive pressure may facilitate rupture of subpleural cysts and the development of pneumothorax.

Our patient had no predisposing risk factors, no history of previous pulmonary diseases, was a nonsmoker, and of normal body weight. Initial CXR showed no abnormalities in terms of emphysema or bullae. She did not receive NIV nor oxygenation *via* HFNC for respiratory support. She developed pneumothorax on the eighth day of hospitalization, in an early phase of NCP.

The literature describes patients who developed pneumothorax at different stages of the disease course. Al-Shokri et al.<sup>18</sup> reported three cases of SARS-CoV-2 infection complicated by pneumothorax. The first, second, and third patient developed pneumothorax on days 2, 7, and 15, respectively. Aydin et al.<sup>5</sup> and Chen et al.<sup>13</sup> reported pneumothorax as an initial manifestation in a patient with NCP.

Our case supports the opinion that pneumothorax may develop in pneumonia caused by SARS-CoV-2 due to advanced alveolar damage, rupture of the alveoli, and the formation of pulmonary cystic lesions. The increase in intrapulmonary pressure during a severe cough attack associated with viral infections can lead to cyst rupture and secondary pneumothorax.

Our case is consistent with the one in the recently published article by Sun et al.<sup>9</sup>. As detailed by the authors, pneumothorax could be a consequence of a sudden increase of the alveolar pressure into the pneumonic consolidations.

A recent review of the study by Alhakeem et al.<sup>19</sup> showed 18 case reports describing COVID-19 patients with spontaneous pneumothorax. Only three cases included fe-

males. In addition, only four cases were smokers, and three had underlying lung disease. Ten of these patients underwent chest tube insertion. Three cases were on invasive mechanical ventilation. Twelve patients had a favorable clinical course. The mortality rate was 33%.

In the literature, the diagnostic value of CXR is relatively low, 30%–60% in NCP. Despite its potential limits, some of the complications of NCP can be diagnosed with repeated CXR, as seen in the example of our patient.

## Conclusion

Pneumothorax may develop as a complication in patients with SARS-CoV-2 pneumonia, without previous pulmonary comorbidities and ventilator (MV and NIV) respiratory support, due to alveolar damage. Acute deterioration with rapid oxygen desaturation in these patients should raise the suspicion of pneumothorax. Early diagnosis and prompt treatment are necessary to reduce mortality.

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Received on June 4, 2020.

Revised on November 12, 2020.

Accepted December 22, 2020.

Online First December, 2020.