DOI: https://doi.org/10.2298/SARH200818045S
UDC: 616.24-002.17; 616.98:578.834

CASE REPORT / ПРИКАЗ БОЛЕСНИКА

Rapidly progressive pulmonary fibrosis in COVID-19 pneumonia

Mihailo Stjepanović[1,2], Slobodan Belić[1], Ivana Buha[1], Nikola Marić[1], Marko Baralić[3], Violeta Mihailović-Vučinić[1,2]

[1]University Clinical Center of Serbia, Clinic of Pulmonology, Belgrade, Serbia;
[2]University of Belgrade, Faculty of Medicine, Belgrade, Serbia;
[3]University Clinical Center of Serbia, Clinic of Nephrology, Belgrade, Serbia

SUMMARY

Introduction COVID-19 pneumonia does not have a characteristic course and prognosis. Many facts still remain hidden, mainly why certain patients develop complications with serious tissue damage and whether it causes a permanent organ impairment. If and when will fibrosis develop in COVID-19 pneumonia requires further research, but a link between the amount of tissue afflicted and the development of fibrosis exists.

Case outline A previously healthy, non-smoker, woman with minor symptoms on admission had suddenly developed a serious respiratory insufficiency and whose radiographic finding on computed tomography scan had shown a serious progression with the development of fibrosis in a matter of days. The exact mechanism and correlation of this clinical course remains unknown; however, it is clear that the pulmonary fibrosis is caused by COVID-19 pneumonia. Follow-up computed tomography scan, performed 50 days after initial symptoms, had shown a partial regression of consolidations and post-inflammatory fibrosis.

Conclusion Pulmonary fibrosis is the most severe complication of COVID-19 infection on the respiratory system. Who, when or if a patient will develop any complication is still unclear, as well as whether these changes are reversible? Also, the number of recovered patients who later develop some chronic complications remains to be seen.

Keywords: COVID-19; pneumonia; pulmonary fibrosis

INTRODUCTION

Near the end of 2019, in Wuhan, China there was a significant number of patients with viral pneumonia with uncharacteristic clinical manifestation and unpredictable clinical course. Shortly thereafter the cause was identified as coronavirus, and the World Health Organization had classified it as COVID-19 infection, more specifically as SARS-CoV-2 [1].

Previously, coronavirus had caused gastrointestinal symptoms in humans, and was predominantly pathogen that infects animal species [2]. In previous seven months, as of time of writing this report, this virus is one of the most common infectious agents in humans, and can lead to respiratory, cardiovascular, gastrointestinal and other difficulties. Currently, clinical manifestation of this infection is of a relatively severe course, with frequent development of complications and (one or more) organ failures, with a possibility of a lethal outcome [3]. Many clinical studies have shown that organ damage caused by COVID-19 can be irreversible [4]. Considering that coronavirus still shows new characteristics, many facts are still unknown, such as the path of transmission, period of incubation, clinical presentation, typical radiographic and laboratory findings and specific treatment.

CASE REPORT

Female patient, non-smoker, aged 45, with no previous history of any pulmonary or other medical diseases, has been hospitalized at our Clinic due to suspicion of COVID-19 infection. She presented with fever (up to 38°C), fatigue, muscle and joint pain which began a day prior to hospitalization. Initially, she was examined in the regional medical center, chest X-ray had shown a discrete reticular pattern paracardial to the right and biochemical results have shown a slightly elevated C- reactive protein (10 mg/l). Considering the positive epidemiological exposition, she was highly suspected of COVID-19 infection and was administered to our Clinic. On admission the patient was conscious, with a fever (37.8°C), eupneic, acyanotic, anicteric, with normal coloration of the skin and visible mucosa, with no signs of peripheral lymphadenopathy and fresh hemorrhagic syndrome. Auscultation of lungs had shown normal respiratory sound, O_2 saturation of blood measured on room air was 98%. Heart rate was tachycardic, rhythmic, with no murmurs, heart rate was 95 bpm, arterial tension was 120/80 mmHg. ECG had shown sinus rhythm, with no ST and T abnormalities. Laboratory findings were within referential values, except slightly elevated C-reactive protein (CRP) 9.1mg/l and interleukin 6 (IL-6) 13.1 pg/ml. Chest X ray had

Received • Примљено: August 18, 2020
Accepted • Прихваћено: May 22, 2021
Online first: May 26, 2021

Correspondence to:
Mihailo STJEPANOVIĆ
University Clinical Center of Serbia
Clinic for Pulmonology
Koste Todorovića 26/20
11000 Belgrade, Serbia
mihailostjepanovic@gmail.com

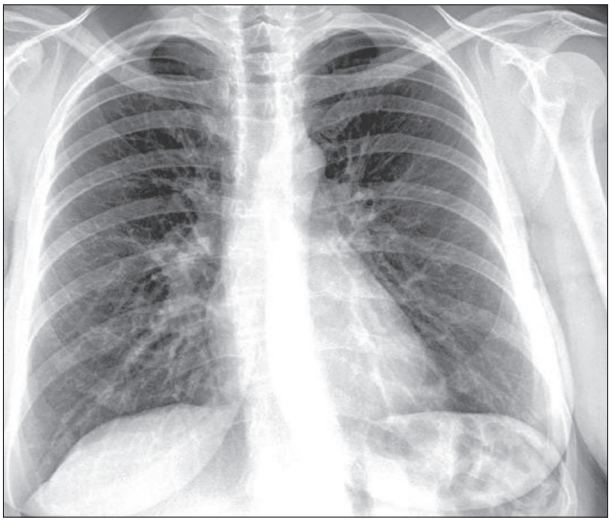

Figure 1. Chest X-ray on admission, with signs of diffuse bronchovascular markings

shown emphasized bronchovascular markings (Figure 1). Serological analysis for COVID-19 were initially negative, as well as the first two nasopharyngeal swabs. However, the third swab came back positive, and the patient was started with COVID-19 treatment suggested by the National protocol for COVID-19 infection, provided by the Ministry of Health of Serbia (third generation cephalosporins, chloroquine, anticoagulant and poli-vitamin treatment). After the beginning of treatment, clinically the patient felt well, with the exception of daily elevations of body temperature (up to 39°C). On the fifth day of hospitalization, there was an elevation of CRP (23.7 mg/l) and IL-6 (35.7 pg/ml); serum iron was decreased (4.3 umol/ml) with newly discovered mild thrombocytopenia (142×10^9) and leucocytes count of 3.6×10^9. Follow-up chest X-ray did not show any significant changes compared to the one on admission. Fluoroquinolone was added to the treatment. On the seventh day of hospitalization, as a part of reevaluation of the disease, a CT scan was performed which had shown multiple bilateral and subpleural oval areas of ground glass opacification with a minimal reaction of interlobular interstitium, with the exception of X segment, in which was an area 6 × 3.2 cm, with evident interlobar septal thickening with fibrosis and bronchiectasis. The location of the areas with ground glass opacification were as follows: the left lung 2.5 × 1.5 cm in the upper lobe, 2.8 × 2.4 cm in the lingula, 5.4 × 2 cm in the VI segment, roughly 4.5 cm in the IX, and 1.5 cm in the X segment; the right lung in the posterior part of the upper lobe 5.7 × 2 cm, 7 × 3 cm in the VI segment, and up to 1.5 cm in the VIII segment. There were several lymph nodes up to 1 cm in the 4R and 5L group (Figure 2).

On the tenth day of hospitalization, there was an acute worsening of the general state of the patient with a sudden development of hypoxia (O_2 sat 92%). There was a further increase of the inflammatory factors (CRP 138.6 mg/l, fibrinogen 4.9 g/l, ferritin 544 ug/l, IL-6 63 pg/ml), with a significant increase of presepsin 1340 pg/ml. There was also a pathological finding of the liver enzymes (AST 54 U/l, ALT 49 U/l). Chest X ray had shown further progression of the finding, with diffuse consolidation, especially peripherally in the basal regions (Figure 3). The patient was put on a triple antibiotic treatment (third antibiotic was a derivate of imidazole), and was placed on a continuous controlled oxigenotherapy. Considering the presence of both clinical and radiological worsening, as well as the further increase of the inflammatory factors, it was decided to administer tocilizumab in the dose of 40 mg parenterally, followed by systemic corticosteroid therapy (methylprednisolone, 2 mg/kg with successive decrease of the dose). After the change of the treatment, the respiratory insufficiency is further worsened (arterial blood gas test had shown pH 7.46, pO_2 7.78 kPa, pCO_2 5.07 kPa, lactates 2.2 mmol/l, O_2 sat 91%), which lead to the administration of the high flow oxygenator. The treatment proved successful, there was an improvement of the arterial blood gas test pH 7.49, pO_2 11.5 kPa, pCO_2 4.44 kPa, O_2 sat 95.5%, starting from the 13th day of the hospitalization the patient did not have any fever, and felt significantly better, however, she was still dependent on high flow oxygenator. New lab results have shown a normalization of the bloodwork as well as CRP (2.5 mg/l), and a relatively higher value of IL-6 (195 pg/ml), which was expected after the initiation of the immunosuppressive therapy. The control chest X-ray has started to show initial signs of the regression; however, it did show a certain degree of the newly developed pulmonary fibrosis (Figure 4). The further administration of

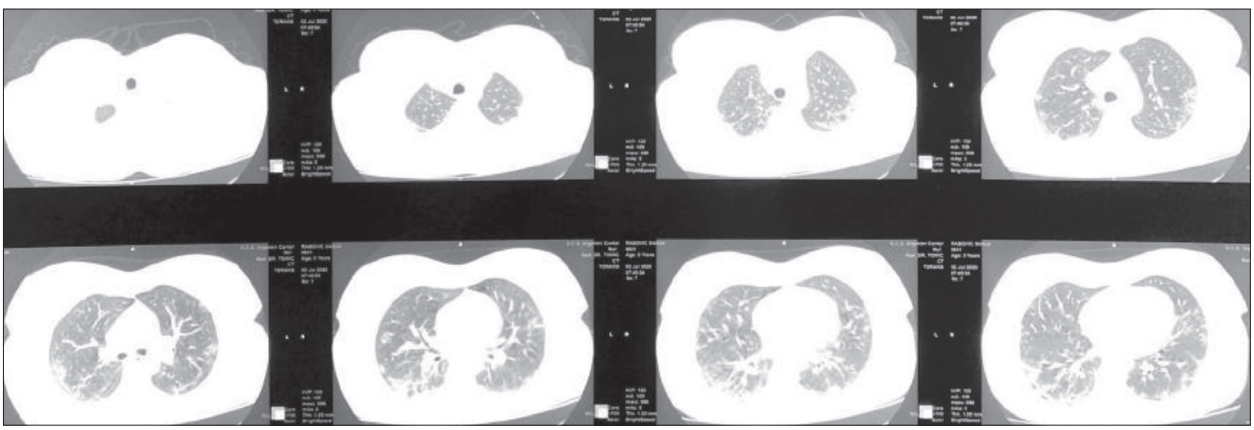

Figure 2. First computed tomography scan showing multiple subpleural ground glass opacifications

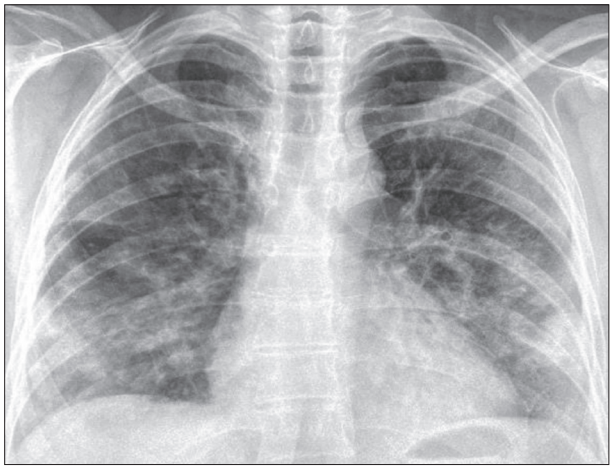

Figure 3. Follow-up chest X-ray now showing the changes initially seen only on the computed tomography scan

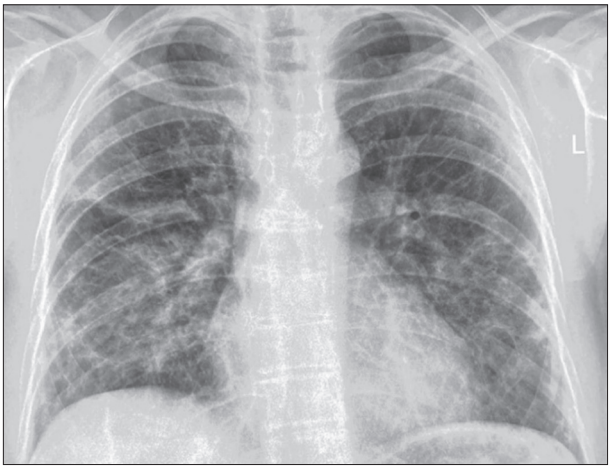

Figure 4. Follow-up chest X-ray after immunosuppressive treatment and high flow oxygenator, showing a certain degree of regression, however areas with fibrosis still remain

the corticosteroid treatment had led to the improvement of the arterial blood gases (pH 7.47, pO_2 9.5 kPa, pCO_2 4.8 kPa, O_2 sat 96%, the results were without O_2 support). With these improvements, the patient was discharged, and continued treatment from home.

The follow-up CT scan was performed 50 days after the first day of hospitalization. It had shown that subpleural, in both lungs, the previously found ground glass regions remained (right I and II segment, left I and II segment) which were interpreted as an inflammation in resolution. However, in the VI segment, in the right lung, there was a zone of consolidation with a negative areal bronchogram, and a thickening of the interstitium with a distortion of the pulmonary bronchi; bilaterally in the IX and X segment there is a thickening of the interstitial septa- all of the changes are attributed to the post inflammatory fibrosis. The follow-up pulmonary function had shown a certain degree of restriction (FVC 96%, FEV1 100%, FEV1/FVC 88.52; diffusion capacity for CO TLCOc 59%, KCOc 73%).

Written consent to publish all shown material was obtained from the patient.

DISCUSSION

We have stated that COVID-19 pneumonia has an uncharacteristic clinical presentation and an unpredictable outcome. Many characteristics still remain undiscovered, and the main enigma is why certain patients develop complications, and whether or not there is a permanent disfunction to the afflicted organs. In this case report we will discuss what is known regarding the pathophysiological mechanism of the COVID-19 infection of the respiratory system. It is known that COVID-19 enters the respiratory cells through angiotensin-converting enzyme 2 receptors (ACE2) [5]. If a certain organism causes an intensive immune response, known as "cytokine storm," it leads to the hypercoagulability and further lung damage [6]. The damaged tissue is repaired with scar tissue, which has no function, and leads to the state known as pulmonary fibrosis. Whether or not the pulmonary fibrosis will develop after COVID-19 pneumonia is still unknow, but it could be hypothesized that there is a correlation between the amount of infected tissue and the degree of fibrosis.

We have chosen to present this case in order to show how the clinical course, radiographical and laboratory findings can change in a relative short period of time, in this case in less than 48 hours. It is important to note that our patient was a relatively young woman, with no previous known diseases, no history of smoking and no professional exposition to any known respiratory agents. On admission she did not show any signs or symptoms of any organ failure. Between sixth and tenth day, the patient suffered a worsening of the symptoms and developed acute respiratory insufficiency with radiological progression. CT scan could probably show the existing pathological findings earlier than chest X-ray. The first CT scan performed on the eighth day since the start of the symptoms had shown the beginning of the lung scaring. There are two possible explanations for the development of the pulmonary fibrosis which are most probable: first is that the virus was present much longer prior to the manifestation of the first symptoms and had time to damage the lungs. The second possibility is that the virus caused the "cytokine storm" which led to the pulmonary fibrosis. The only certain causality is that COVID-19 pneumonia has led to the pulmonary fibrosis. The control CT scan had shown that there still are areas of consolidations, as well as areas with pulmonary fibrosis.

Current knowledge regarding the sequelae of COVID-19 infection is lacking. Regarding the respiratory system, pulmonary fibrosis could be considered the most severe complication of COVID-19 infection. It is still unclear who, when or if a patient will develop this complication. As of writing of this article, there are roughly 20 million infected people, with round 13 million who have recovered from COVID-19 infection [7, 8]. How many of the recovered patients will have any complications, and if those complications are reversible, only time will tell.

ACKNOWLEDGEMENTS

This study was supported by the project: Survivors of COVID-19: variety of immune responses to SARS-CoV-2 in correlation with clinical manifestation. Long term follow-up: V.I.R.U.S. (January 2021–July 2022).

Conflict of interest: None declared

REFERENCES

1. Chen Y, Klein SL, Garibaldi BT, Li H, Wu C, Osevala NM, et al. Aging in COVID-19: Vulnerability, immunity and intervention. Ageing Res Rev. 2021;65:101205.
2. Yüce M, Filiztekin E, Özkaya KG. COVID-19 diagnosis – A review of current methods. Biosens Bioelectron. 2021;172:112752.
3. Dai L, Gao GF. Viral targets for vaccines against COVID-19. Nat Rev Immunol. 2021;21(2):73–82.
4. Dao TL, Hoang VT, Gautret P. Recurrence of SARS-CoV-2 viral RNA in recovered COVID-19 patients: a narrative review. Eur J Clin Microbiol Infect Dis. 2021;40(1):13–25.
5. Luan J, Lu Y, Jin X, Zhang L. Spike protein recognition of mammalian ACE2 predicts the host range and an optimized ACE2 for SARS-CoV-2 infection. Biochem Biophys Res Commun. 2020;526(1):165–9.
6. Ojo AS, Balogun SA, Williams OT, Ojo OS. Pulmonary Fibrosis in COVID-19 Survivors: Predictive Factors and Risk Reduction Strategies. Pulm Med. 2020;2020:6175964.
7. George PM, Wells AU, Jenkins RG. Pulmonary fibrosis and COVID-19: the potential role for antifibrotic therapy. Lancet Respir Med. 2020;8(8):807–15.
8. Stjepanovic M, Belic S, Buha I, Maric N, Baralic M, Vucinic Mihailovic V. Unrecognized tuberculosis in a patient with COVID-19. Srp Arh Celok Lek. 2021;149(1–2):70–3.

Рапидно прогресивна плућна фиброза код пнеумоније изазване ковидом 19

Михаило Стјепановић[1,2], Слободан Белић[1], Ивана Буха[1], Никола Марић[1], Марко Баралић[3], Виолета Михаиловић-Вучинић[1,2]

[1]Универзитетски клинички центар Србије, Клиника за пулмологију, Београд, Србија;
[2]Универзитет у Београду, Медицински факултет, Београд, Србија;
[3]Универзитетски клинички центар Србије, Клиника за нефрологију, Београд, Србија

САЖЕТАК

Увод Пнеумонија изазвана ковидом 19 има некарактеристичну клиничку слику и непредвидив ток. Многе чињенице су остале неразјашњене, а главна енигма остаје зашто се код неких болесника развијају компликације са последичним оштећењем ткива и да ли ће те промене трајно нарушити функцију захваћених органа. Да ли ће се и када развити фиброза плућа после пнеумоније изазване ковидом 19 засад није познато, али јасно је да постоји корелација између обима захваћеног ткива вирусом и развоја ове болести.

Приказ болесника Приказујемо болесницу без хроничних болести, непушача, без професионалне изложености, која је при пријему била доброг општег стања и без знакова попуштања било ког органа. У року од неколико дана рапидно се погоршало опште стање, развила се респираторна инсуфицијенција и радиолошки су уочене масивне консолидације обострано, са појединим зонама у којима су биле ожиљне промене. Да ли је вирус био дуже присутан и да ли су прве тегобе наступиле после већ обимног нарушавања плућног ткива или су уочене фиброзне промене последица „цитокинске олује" није познато. Јасно је да су фиброзне промене последица пнеумоније изазване ковидом 19. Контролни снимак компјутеризованом томографијом грудног коша показао је да су промене у плућима присутне дифузно, обострано у свим лобулусима, делом консолидација (50 дана од почетка тегоба), а делом консолидација у резолуцији, уз присутне фиброзне промене као постинфламаторне секвеле.

Закључак Фиброза плућа је најтежа секвела коју овај вирус може проузроковати на респираторном систему. Ко, када и да ли ће развити фиброзу плућа и даље остаје неразјашњено. Колики проценат опорављених болесника има или ће развити неку од хроничних компликација показаће време, као и то да ли су присутне промене реверзибилне.

Кључне речи: ковид 19; пнеумонија; плућна фиброза