



## CASE REPORT / ПРИКАЗ БОЛЕСНИКА

# Unrecognized tuberculosis in a patient with COVID-19

Mihailo Stjepanović<sup>1,2</sup>, Slobodan Belić<sup>1</sup>, Ivana Buha<sup>1</sup>, Nikola Marić<sup>1</sup>, Marko Baralić<sup>3</sup>, Violeta Mihailović-Vučinić<sup>1,2</sup>

<sup>1</sup>Clinical Center of Serbia, Clinic of pulmonology, Belgrade, Serbia;

<sup>2</sup>University of Belgrade, Faculty of Medicine, Belgrade, Serbia;

<sup>3</sup>Clinical Center of Serbia, Clinic of nephrology, Belgrade, Serbia

## SUMMARY

**Introduction** COVID-19 is responsible for the current global pandemic. Globally, over 15 million people are currently infected, and just over 600,000 have died due to being infected. It is known that people with chronic illnesses and compromised immune systems can develop more severe clinical presentation. Tuberculosis (TB) is still one of the biggest epidemiological problems worldwide. Both of these diseases can be misdiagnosed and can manifest in a similar way. We will present a case study of a patient who was initially treated as a COVID-19 infection, with TB being diagnosed later on. The recovery began only after being treated for both diseases simultaneously.

**Case report** The patient is a 27-year-old male, non-smoker, with no history of any significant diseases. He presented with fever, fatigue and hemoptysis. Computed tomography pulmoangiography had shown massive consolidations and excavations, which could be caused by COVID-19. Despite being treated for COVID-19, there was no clinical improvement. On the follow-up chest X-ray, beside signs of COVID-19, there were also changes that could indicate TB. TB was detected in sputum, using PCR and Mycobacteria Growth Indicator Tube, and only after being treated for both diseases did his condition improve.

**Conclusion** There are a few reported cases of COVID-19 and TB coinfections, and we believe that there are many more patients with this coinfection being unrecognized.

**Keywords:** COVID-19; tuberculosis; infection; diagnosis

## INTRODUCTION

Corona virus has, until recently, caused only animal infection (feline and bat infections), however, currently it is the most common cause of pneumonia in humans, and can lead to death. Many facts are still unknown regarding this virus, such as transmission, period of incubation, full clinical presentation, radiography, laboratory findings, immune response and specific treatment. Most studies have shown that the respiratory pathway is the most common way of transmission and infection (through coughing, sneezing, talking...). The incubation period varies greatly, between two and 14 days, and can go up to 28 days, but most commonly the incubation lasts for five days [1]. The clinical presentation also varies, and is not specific. The infection can be anything between asymptomatic or mild, which is present in the majority of patients, and severe, with a lethal outcome. The most common symptoms are: fever, cough, difficulty of breathing, fatigue, muscle pain, diarrhea, nausea and headache [2]. Severe forms of the infection manifest with a massive pneumonia followed by acute respiratory failure or sepsis, which in turn demands mechanical ventilation [3]. In the laboratory findings there are leucopenia, thrombocytopenia, increased values of liver enzymes,

fibrinogen, D-dimer, LDH, interleukin 6 and presepsin. Inflammation markers (fibrinogen, C reactive protein) can be within reference values; however, they are elevated most of the time [4]. Chest radiography shows interstitial thickening with peripheral consolidation, as well as ground glass changes. Uncommonly, one can find segmental and lobar consolidation and pleural effusion [5]. Specific vaccine has not yet been discovered, and the treatment protocols differ between centers, and is still in early stages of development. Depending on the illness stage, different therapy treatments have shown success: antibiotics, hydroxychloroquine, vitamin, antiviral and systemic corticosteroids. Drugs with immunomodulation have shown promising results in severe forms of the disease [6].

Tuberculosis is an infectious disease caused by *Mycobacterium tuberculosis* spp. The disease most commonly affects the lungs, although other organs can also be afflicted (nervous, gastrointestinal system, bones, kidneys). The infection does not mean the disease, since only 10% of infected manifest as an active form of the disease. Whether or not the disease will manifest, depends of the infective agent, as well as the immune status of the infected. Risk factors are well known, and almost all of them are related to immunodeficiency (HIV infection, alcoholism, drug abuse...) [7]. The

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**Correspondence to:**

Mihailo STJEPANOVIĆ  
Clinical Center of Serbia  
Clinic for Pulmonology  
Koste Todorovića 26/20  
11000 Belgrade

[mihailostjepanovic@gmail.com](mailto:mihailostjepanovic@gmail.com)

symptoms include fever, fatigue, night sweats, loss of body mass, coughing of sputum, pus or fresh blood. In advanced form of the disease, acute respiratory failure is not uncommon, and chest pain is present if the pleura is afflicted. If the extrapulmonary form of the disease is present, the symptoms are organ specific [8]. The clinical presentation varies greatly, from asymptomatic to severe. Radiological findings are specific, and pleural effusion is frequently present. Definitive diagnosis is given when the bacteria is identified, directly, by PCR method or with a pathohistological finding in different tissues, urine, stool or sputum sample. Treatment consists of antituberculous drugs in standardized protocols [9, 10, 11].

We will present a patient initially treated for COVID-19 infection, as well as tuberculosis, which was discovered later on as a coinfection. The recovery began only after being treated for both diseases simultaneously.

## CASE REPORT

The patient we present is male, aged 27, with no history of medical illnesses and history. He was first admitted in the Emergency room because of fever (38°C), fatigue and hemoptysis; the symptoms were present for three days prior to admission. Computed tomography angiography was performed, there were no signs of embolism, however it did show massive consolidations of pulmonary parenchyma with excavation which could be caused by COVID-19. Initially, he was hospitalized in regional medical center where COVID-19 was confirmed using PCR method, and was treated using chloroquine (1000 mg/daily) and dual antibiotic therapy (fluoroquinolone and the third generation cephalosporine) with symptomatic support. Despite treatment, no clinical and radiological improvement was achieved, and the patient was transferred to the Clinical Center of Serbia.

On admission patient had fever (37.7°C), was hypotensive (90/60 mmHg), however he maintained oxygen saturation ( $O_2$ sat 98%). Hemoptysis was still present. Blood analysis had shown neutrophilia (77.6%), elevated sedimentation rate (20 mm/h), C reactive protein (20.2 mg/l) and presepsin (726 pg/ml). Initially, he was treated with azithromycin.

Chest X ray had findings highly indicative for COVID-19 infection. However, changes in both upper lobes were suspicious for tuberculosis (Figure 1).

Further anamnestic data had shown that six months prior to current infection, the patient's father was diagnosed and treated for active tuberculosis. Our experience so far had shown that hemoptysis is not a sign for COVID-19 pneumonia. Considering that the patient had been in contact with tuberculosis, we have collected patient's sputum. In sputum, using PCR method, *M. tuberculosis* was discovered, and was further confirmed using cultivation on Mycobacteria Growth Indicator Tube. The patient was started on antituberculous treatment (Isoniazid 300 mg/daily, Rifampicin 600 mg/daily, Pyrazinamide 1200 mg/daily, Ethambutol 1200 mg/daily).



**Figure 1.** First follow-up chest X-radiography showing both signs of COVID-19 and Tuberculosis infection

Five days after the beginning of the treatment, the patient was afebrile, with subjective and clinical improvement. Since coughing had stopped, the control sputum was not taken. After receiving two negative PCR tests for COVID-19, the patient was discharged.

## DISCUSSION

COVID-19 is responsible for the current global pandemic. As of writing this case report, over 15 million people are infected globally, and over 600,000 people have died due to its complications [12]. It is known that patients with chronic illnesses and compromised immune system are more susceptible to infection as well as development of more severe forms of the disease. It should be noted that symptoms of pneumonia caused by this virus do not differ from symptoms caused by other pathogens.

Tuberculosis (TB) is still one of the most important epidemiological problems. According to World Health Organization, between eight and ten million people annually get infected, and roughly three million people of tuberculosis. Vaccine and modern therapeutic methods have virtually eradicated TB in developed countries, although the presence of HIV and other causes of immunodeficiency have challenged this claim [13].

Symptoms of both of these diseases are relatively similar: fever, cough and fatigue. Initial computed tomography scan in this patient did show changes indicative for bilateral COVID-19 pneumonia. The diagnosis cannot be based solely on radiographic finding, as both infections can have atypical findings, and can be completely normal. Despite having positive PCR test for COVID-19, which could explain almost all clinical, radiological and biochemical findings, the presence of hemoptysis demanded further testing. Detailed medical, especially socio-epidemiological, history, and the presence of bilateral apical findings on follow-up X-ray were crucial in narrowing of possible diagnosis. After positive PCR and cultivation on Mycobacteria Growth Indicator Tube, it was clear that the patient had COVID-19

and TB coinfection. Only after simultaneously treating both diseases did the patient show signs of improvement, he was no longer febrile and hemoptysis stopped. Follow-up chest X ray, after initiating both treatments, was almost unchanged, which is expected in TB infections after such a short period of treatment. The control of TB infections is still a vital medical problem. The emergence of COVID-19 pandemic has caused that other pulmonary diseases are being taken into consideration significantly less frequent. Tuberculosis is curable in majority of cases, but if left undiscovered and untreated, can lead to serious problems, primarily health related, especially in the wake of the new pandemic. Preventive methods of COVID-19 do not differ significantly, when compared to TB. Mandatory face masks, with special regards to particular masks, which is present in many countries globally, as a tool of combating COVID-19, also reduces the transmission of TB. It is understandable that COVID-19 is priority number one, however, one must not forget the incidence and mortality that TB causes daily [14–17].

The main purpose of this paper is to emphasize the importance of overall approach to the patient despite COVID-19 pandemic. The authors of this paper strongly

believe that the number of patients with COVID-19 and TB coinfection is much larger than currently presented, and that many cases are left unrecognized. Regarding our patient, it is still unclear whether the asymptomatic infection with *M. tuberculosis* has caused the compromise of immune system and in turn made the patient susceptible to COVID-19, or that the viral infection was the trigger for reactivation of TB. Regardless, the simultaneous treatment of both diseases has given excellent results.

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**Ethical standards:** Written consent to publish all shown material was obtained from the patient.

**Conflict of interest:** None declared

## REFERENCES

1. Zhao Y, Zhao Z, Wang Y, Zhou Y, Ma Y, Zou W. Single-cell RNA expression profiling of ACE2, The Receptor of SARS-CoV-2. *Am J Respir Crit Care Med.* 2020;202(5):756–9.
2. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet.* 2020;395(10223):497–506.
3. Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J, et al. Clinical Characteristics of 138 Hospitalized Patients with 2019 Novel Coronavirus- Infected Pneumonia in Wuhan, China. *JAMA.* 2020;323(11):1061–9.
4. Huang Y, Tu M, Wang S, Chen S, Zhou W, Chen D, et al. Clinical characteristics of laboratory confirmed positive cases of SARS-CoV-2 infection in Wuhan, China: A retrospective single center analysis. *Travel Med Infect Dis.* 2020;36:101606.
5. Cheng Z, Lu Y, Cao Q, Qin L, Pan Z, Yan F, et al. Clinical Features and Chest CT Manifestations of Coronavirus Disease 2019 (COVID-19) in a Single-Center Study in Shanghai, China. *AJR Am J Roentgenol.* 2020;215(1):121–6.
6. Sanders JM, Nonogue ML, Jodlowski TZ, Cutrell JB. Pharmacological Treatments for Coronavirus Disease 2019 (COVID-19): A Review. *JAMA.* 2020;323(18):1824–36.
7. Menzies NA, Wolf E, Connors D, Bellerose M, Sbarra AN, Cohen T, et al. Progression from latent infection to active disease in dynamic tuberculosis transmission models: a systematic review of the validity of modelling assumptions. *Lancet Infect Dis.* 2018;18(8):e228–38.
8. Stjepanovic M, Mihailovic Vucinic V, Maskovic J, Colovic N, Gvozdenovic B, Stojkovic-Lalosevic M, et al. Alcohol use and clinical manifestation of tuberculosis. *Srp Arh Celok Lek.* 2018;146(1–2):110–1.
9. World Health Organization. Global tuberculosis report 2017. World Health Organization. Dec 13. 2017.
10. Lenaerts A, Barry CE 3rd, Dartois V. Heterogeneity in tuberculosis pathology, microenvironments and therapeutic responses. *Immunol Rev.* 2015;264(1):288–307.
11. Stjepanovic M, Skodric-Trifunovic V, Radisavljevic-Pavlovic S, Roksandic-Milenkovic M, Milin-Lazovic J, Babic U, et al. Patient, Healthcare System and Total Delay in Tuberculosis Diagnosis and Treatment Among Serbian Population. *Acta Clin Croat.* 2018;57(2):257–63.
12. Worldmeters. (2020), July 23. 2020, <https://www.worldometers.info/coronavirus>
13. He G, Wu J, Shi J, Dai J, Gamber M, Jiang X, et al. COVID-19 in Tuberculosis patients: a report of three cases. *J Med Virol.* 2020;92(10):1802–6.
14. Chopra KK, Arora VK, Singh S. COVID 19 and tuberculosis. *Indian J Tuberc.* 2020;67(2):149–51.
15. Saunders MJ, Evans CA. COVID-19, tuberculosis and poverty: preventing a perfect storm. *Eur Respir J.* 2020;56(1):2001348.
16. Pijls B, Jolani S, Atherley A, Derckx R, Dijkstra J, Franssen G, et al. Demographic risk factors for COVID-19 infection, severity, ICU admission and death: a meta-analysis of 59 studies. *BMJ Open.* 2021;11(1):e044640.
17. Les Bujanda I, Loureiro-Amigo J, Capdevila Bastons F, Elejalde Guerra I, Annicchero Sanchez J, Murgadella-Sancho A, et al. Treatment of COVID-19 pneumonia with glucocorticoids (CORTIVID): a structured summary of a study protocol for a randomized controlled trial. *Trials.* 2021;22(1):43.

## Непрепозната туберкулоза код болесника са инфекцијом *COVID-19*

Михаило Стјепановић<sup>1,2</sup>, Слободан Белић<sup>1</sup>, Ивана Буха<sup>1</sup>, Никола Марић<sup>1</sup>, Марко Баралић<sup>3</sup>, Виолета Михаиловић-Вучинић<sup>1,2</sup>

<sup>1</sup>Клинички центар Србије, Клиника за пулмологију, Београд, Србија;

<sup>2</sup>Универзитет у Београду, Медицински факултет, Београд, Србија;

<sup>3</sup>Клинички центар Србије, Клиника за нефрологију, Београд, Србија

### САЖЕТАК

**Увод** *COVID-19* је одговоран за пандемију која је присутна широм света. Преко 15 милиона људи је заражено овим инфективним агенсом, а нешто преко 600.000 људи је преминуло због компликација изазваних инфекцијом. Добро је познато да су особе са хроничним болестима и слабијег имунитета подложније инфицирању и развоју тежих клиничких форми болести. Туберкулоза је још увек један од највећих епидемиолошких проблема. Заједничко за ове две заразне болести је то што се могу манифестовати истим симптомима и на време се не дијагностиковати. Приказујемо болесника код кога је иницијално лечена инфекција *COVID-19*, туберкулоза је откривена као коинфекција, а опоравак је започео тек после лечења и туберкулозе.

**Приказ болесника** Болесник је 27-годишњи мушкарац, непушач, без хроничних болести. Због тегоба у виду повишене телесне температуре, малаксалости, кашља са искашља-

вањем свеже крви у трајању од неколико дана учињена је компјутеризована томографија пулмоангиографија. Налаз је показао масивне консолидације плућног паренхима са знацима ексакације које би могле одговарати пнеумонији коју је изазвао *COVID-19*. Вредност телесне температуре је и даље била повишена, уз повремено искашљавање свеже крви. На радиографији грудног коша осим обостраних мрљастих промена које су вероватно последица инфекције *COVID-19*, уочавају се промене у горњим режњевима, које би могле одговарати специфичном процесу. Туберкулоза је доказана у спутуму, методом *PCR* и *MGIT*, и тек после лечења обе болести стање болесника се побољшало.

**Закључак** Досад је описано свега неколико случајева истовремене инфекције *COVID-19* и туберкулозе. Став аутора овог рада је да је инциденца много већа, али су случајеви остали непрепознати.

**Кључне речи:** *COVID-19*; туберкулоза; инфекција; дијагноза