

SARS-CoV-2 and *Mycobacterium Fortuitum* Coinfection: A Case Report

SARS-CoV-2 ve *Mycobacterium Fortuitum* Koenfeksiyonu: Olgu Sunumu

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Abstract

Coronavirus disease-2019 (COVID-19) pandemic caused millions of people to become infected and had resulted several deaths. After initial resolution, in cases of clinical deterioration, it is essential to consider the possibility of coinfections. Non-tuberculous mycobacteria infections are rare and often overlooked. In this report, we present a severe acute respiratory syndrome-Coronavirus-2 and *Mycobacterium fortuitum* coinfecting patient. Our intention is to bring attention to the possibility of such coinfection without a known history of any lung diseases or immunosuppression other than COVID-19 and thus, broadening the clinical thinking process of physicians.

Keywords: SARS-CoV-2, non-tuberculous mycobacteria, COVID-19

Öz

Koronavirüs hastalığı-2019 (COVID-19) pandemisi milyonlarca insanın enfekte olmasına ve çok sayıda ölüme neden olmuştur. Başlangıçtaki iyileşme döneminin ardından klinik kötüleşme olması halinde koenfeksiyon olasılığını düşünmek gerekmektedir. Tüberküloz dışı mikobakteri enfeksiyonları nadir olup sıklıkla gözden kaçırılmaktadır. Bu yazıda şiddetli akut solunum sendromu-Koronavirüs-2 ve *Mycobacterium fortuitum* koenfeksiyonu olan bir hasta sunmaktayız. Amacımız, eşlik eden akciğer hastalığı ve COVID-19 dışında immünoşüpresyon öyküsü bulunmadığında da bu koenfeksiyonun gelişebileceğine dikkat çekmek ve hekimlerin klinik yaklaşımına katkı sağlamaktır.

Anahtar Kelimeler: SARS-CoV-2, tüberküloz dışı mikobakteri, COVID-19

Introduction

There are nearly 200 species of non-tuberculous mycobacteria (NTM), most of which live in soil and water in rural and urban areas (1). Almost half have been associated with opportunistic infections in animals and humans, causing sporadic outbreaks (1). NTM is acquired through exposure to water, aerosols, soil and dust via inhalation, ingestion, cracks

due to skin injuries, surgical procedures, or catheterization (1). Almost all patients with NTM pulmonary disease have chronic or recurring cough. Other symptoms include sputum, fatigue, malaise, dyspnea, fever, hemoptysis, chest pain, and weight loss (1). Both 2020 "Treatment of Non-tuberculous Mycobacteria/Pulmonary Disease" clinical practice guideline and expert panel group for management recommendations in NTM pulmonary diseases recommend using clinical (pulmonary symptoms, and

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exclusion of other diagnoses), radiographical (nodular or cavitary opacities on chest radiograph, or an high resolution computed tomography (CT) scan that shows multifocal bronchiectasis with multiple small nodules), and microbiological (positive cultures from at least two separate expectorated sputum samples, or one positive culture from bronchial lavage or biopsy) criteria for diagnosis (2,3).

A recent review assessing the prevalence of bacterial coinfection in Coronavirus disease-2019 (COVID-19) patients showed that the coinfection rate was between 2.5-5.1% (4). Although there are only a few studies dedicated to NTM coinfections, one case report stated a *Mycobacterium abscessus* and severe acute respiratory syndrome-Coronavirus-2 (SARS-CoV-2) coinfection in a patient with underlying multiple myeloma (5).

In this report, we present a SARS-CoV-2 and *Mycobacterium fortuitum* coinfecting patient without a known history of any lung diseases or immunosuppression other than COVID-19.

Case Presentation

A 44-year-old male patient with hypertension presented with fever, cough, and shortness of breath. The patient's SARS-CoV-2 reverse transcriptase polymerase chain reaction (PCR) test was positive and he was on fifth day of treatment with favipiravir and acetylsalicylic acid. The physical examination showed body temperature of 36.3 °C, heart rate of 92/min, arterial blood pressure of 120/70 mmHg, oxygen saturation of 95% in room air by pulse oximeter and bilateral diffuse rales. The initial laboratory findings were as follows: leukocytes $5150 \times 10^6/L$, neutrophil $4070 \times 10^6/L$, lymphocyte $720 \times 10^6/L$, platelet $153 \times 10^9/L$, lactate dehydrogenase 344 U/L, D-dimer 1375 ng/mL, fibrinogen 3.27 g/L, ferritin 1585 ng/mL, C-reactive protein 71mg/L, procalcitonin 0.218 ng/mL. CT pulmonary angiogram showed diffuse multilobed, multifocal, predominantly peripherally located, ground glass consolidations with approximately 25-50% of lung parenchyma being affected (Figure 1).

The patient was admitted to COVID-19 ward and the treatment was rearranged as favipiravir 2x600 mg tb, enoxaparin 2x0.4 cc sc and acetylsalicylic acid 1x100 mg tb. During his 2nd day at the ward, methylprednisolone 1x80 mg IV was started upon the need for 2 Lt/min nasal oxygen support. Due to onset of fever (38.3 °C), increase of cough, new sputum complaints and significant rise in D-dimer levels (9767 ng/mL), CT pulmonary angiogram was repeated on 6th day of follow-up. The result revealed significant progression with approximately 50-75% of the lung parenchyma being affected (Figure 2). Accompanying laboratory results are summarized in Table 1. Antimicrobial therapy was initiated: meropenem 3x1 gr IV and

tygecycline 2x50 mg IV following 1x100 mg IV loading dose. No growth in blood and urine culture was detected. Serum cytomegalovirus PCR, Galactomannan and *Aspergillus* spp. PCR, and sputum *Pneumocystis jirovecii* PCR were negative, as well. Evaluation of the gram-stained sputum smear under $\times 100$ magnification revealed <10 epithelial cells and >25

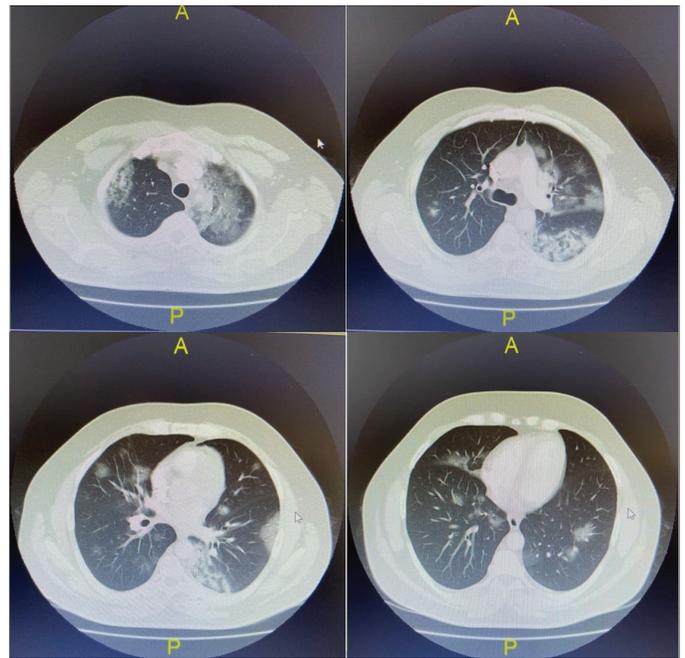


Figure 1: Initial computed tomography pulmonary angiogram: diffuse multilobed, multifocal, predominantly peripherally located, ground glass consolidations with approximately 25-50% of lung parenchyma being affected

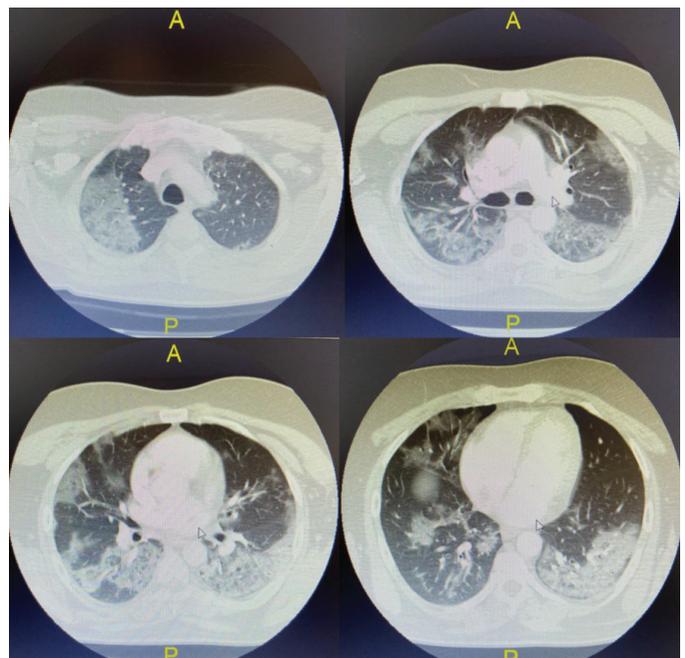


Figure 2: Repeated computed tomography pulmonary angiogram on 6th day of follow-up: Significant progression with approximately 50-75% of the lung parenchyma being affected

Table 1: Patient's laboratory results during follow-up

	Admission day	6 th day of follow-up	Discharge day	End of <i>Mycobacterium fortuitum</i> treatment
Leukocytes (nx10 ⁶ /L)	5150	11150	13070	5820
Neutrophil (nx10 ⁶ /L)	4070	8190	6390	2630
Lymphocyte (nx10 ⁶ /L)	720	1230	2820	2190
Platelet (nx10 ⁹ /L)	153	238	293	293
Lactate dehydrogenase (U/L)	344	528	350	201
D-dimer (ng/mL)	1375	9767	196	Not available
Fibrinogen (g/L)	3.27	3.87	2.79	Not available
Ferritin (ng/mL)	1585	1453	625	Not available
C-reactive protein (mg/L)	71	91.2	5.1	2.5
Procalcitonin (ng/mL)	0.22	1.20	0.10	0.08

polymorphonuclear leukocytes per field, but no microorganisms were detected. Routine sputum culture showed no microbial growth after 24 hours of incubation at 35 °C on blood agar, eosin methylene blue agar, and chocolate agar. While sputum Erlich Ziehl Neelsen stain was negative, NTM were grown in mycobacteria culture medium on the 7th day of incubation. On the 16th day of in-hospital follow-up, the patient was discharged with the treatment plan as clarithromycin, rifampicin, and ethambutol and frequent follow-up appointments. The bacteria was found to be *Mycobacterium fortuitum* which was resistant to clarithromycin, ciprofloxacin and doxycycline and sensitive to moxifloxacin, amikacin and linezolid. Clarithromycin was displaced by moxifloxacin in treatment regimen. Upon clinical improvement, triple regimen was administered for six months till two consecutive sputum samples were negative for NTM.

Discussion

Mycobacterium fortuitum has been previously identified as the causative microorganism of skin and soft tissue infections, including post-surgery or post-traumatic nosocomial infections via contaminated medical devices in immunocompetent patients (6,7). Although *Mycobacterium fortuitum* was associated with serious and life-threatening infections in immunocompromised patients before, there are also a few case reports defining pulmonary involvement in otherwise healthy patients, as well (8-10). While there are several reports indicating a rise in NTM infections in recent years, to the best of our knowledge there are no reports describing a pulmonary NTM involvement in a COVID-19 patient without any underlying pulmonary diseases (11).

Mycobacterium fortuitum is a common microorganism of environment and surfaces. Therefore, as mentioned in previous sections, it requires at least two positive cultures to conclude a patient with a diagnosis of pulmonary *Mycobacterium fortuitum* infection. In the presented case, although treatment was initiated before the growth of *Mycobacterium fortuitum*

in the second sputum sample, the improvement in clinical symptoms following therapy and the growth of *Mycobacterium fortuitum* following sputum cultures strongly suggest the definitive diagnosis.

The identification of NTM at the species level is clinically important because treatment and response rates vary depending on different subtypes (12). Anti-microbial susceptibility testing breakpoints to guide the management of rapidly growing mycobacteria infections have been recently established and updated in "CLSI M24S-ED2: 2023 Performance Standards for Susceptibility Testing of Mycobacteria, *Nocardia* spp., and Other Aerobic Actinomycetes, 2nd edition" (13). In light of the current literature, it is suggested to treat NTM infections with more than one antimicrobial for a prolonged duration (14). Therefore, growing NTM in our patient's sputum sample was sent to Republic of Türkiye, Ministry of Health, General Directorate of Public Health National Tuberculosis Reference Laboratory, and the patient was treated for more than six months with three agents.

The presence of SARS-CoV-2 infection in our case may have caused a defect in the respiratory tract epithelial tissue. We assume that SARS-CoV-2 infection and corticosteroid therapy may also be a facilitating factor for NTM infection in our patient because of generating possible immunosuppression. This assumption needs to be studied further.

Conclusion

In conclusion, with NTM being on the rise and the severity of coinfections in COVID-19, this case report was presented to shed light on this topic and to bring awareness to the possible coinfection of *Mycobacterium fortuitum* and SARS-CoV-2.

Ethics

Informed Consent: Consent was obtained from the patient and his relative.

Footnotes

Authorship Contributions

Surgical and Medical Practices: T.G., Ö.D., E.G., G.Ç., İ.A., E.M.S., M.S.B., Concept: H.M., E.G., G.Ç., İ.A., E.M.S., M.S.B., Design: Ö.D., E.G., G.Ç., İ.A., E.M.S., M.S.B., Data Collection and/or Processing: T.G., H.M., Ö.D., E.G., Analysis and/or Interpretation: E.G., H.M., Ö.D., E.G., M.S.B., Literature Search: T.G., H.M., Ö.D., E.G., G.Ç., İ.A., E.M.S., Writing: T.G., H.M., Ö.D., E.G., G.Ç., İ.A., E.M.S., M.S.B.

Conflict of Interest: There is no potential conflict of interest to declare.

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