

## COVID-19 with positive bronchoalveolar lavage fluid (BALF) but negative nasopharyngeal and oropharyngeal swabs: case report and insights

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### Abstract

Coronavirus disease 2019 (COVID-19), caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), mainly affects the respiratory system with some patients rapidly progressing to acute respiratory distress syndrome (ARDS). The most common symptoms of the patients are fever, cough, dyspnea, myalgia, and fatigue. Nasopharyngeal and oropharyngeal swab specimens tested by *real-time* reverse transcription-polymerase chain reaction (RT-PCR) are the most commonly used methods to diagnose COVID-19. Herein, we investigate and discuss a young case of COVID-19, without any pre-existing medical conditions, whose both nasopharyngeal and oropharyngeal swab tests of SARS-CoV-2 were negative in the prodromal phase. However, after three days, with severe dyspnea and rapidly progressed acute respiratory distress syndrome (ARDS), the case was identified as infected by COVID-19 by testing bronchoalveolar lavage fluid (BALF). The patient was intubated in the intensive care unit (ICU) but expired on the fourth day. This case shows the importance of active and accurate monitoring of the patients showing COVID-19 symptoms. Although the BALF test has a higher exposure risk, it is considered more accurate and recommended if performed by an expert operator.

**Keywords:** COVID-19; SARS-CoV-2; ARDS; bronchoalveolar lavage fluid (BALF)

## Introduction

In late December of 2019, a new coronavirus, called SARS-CoV-2, was detected in Wuhan, China. The World Health Organization named the disease caused by this virus COVID-19 [1]. The disease quickly spread to Chinese cities and other parts of the world. The same as SARS-CoV, the novel coronavirus (SARS-CoV-2) uses angiotensin-converting enzyme 2 (ACE2) receptor to enter the host target cell but mainly spreads through the lower respiratory tract [2]. Previous reports show that fever (98%), cough (76%), dyspnea (55%), myalgia or fatigue (44%) are the most common complaints of patients [3-5]. Gastrointestinal involvement, acute cardiac injury, and acute kidney injury caused by COVID-19 are also reported in other studies [4, 6].

By affecting the respiratory system, COVID-19 rapidly progresses to acute respiratory distress syndrome (ARDS) in some patients, and make them likely to be admitted to the intensive care unit (ICU) or die [7, 8]. Nasopharyngeal and oropharyngeal swab specimens tested by real-time reverse transcription-polymerase chain reaction (RT-PCR) are the most commonly used methods to diagnose COVID-19. In this study, we investigate and discuss an unusual case of COVID-19 who was not identified as infected in his first visit in spite of performing the RT-PCR test using both nasopharyngeal and oropharyngeal swabs. However, the patient was again referred after three days, with a severely progressed acute respiratory distress leading to his death.

## Case study

A 33-year-old man was referred to the COVID-19 screening clinic of Abu-Ali-Sina Hospital (in Shiraz, Iran), with dry cough, sore throat, a fever of 38.2°C, chills, muscle pain, and with no other apparent symptoms on April 28, 2020. He had no specific underlying disease, and he denied any involvement with people suspected of having COVID-19. His family members did not have COVID-19 either. On arrival, he had a pulse rate of 80 beats/minute, respiratory rate of 16 breaths per minute, blood pressure of 115/75 mmHg, oxygen saturation of 97% on room air, and he did not have dyspnea. Based on his symptoms, the patient was considered a suspected case of COVID-19, according to the Iran Ministry of Health Protocol for COVID 19. Therefore, an RT-PCR test by taking both nasopharyngeal and oropharyngeal swab specimens was performed on him. The result was negative, and he was advised to stay home in quarantine to recover.

After three days of symptomatic treatment and taking antipyretic, he did not improve, and on May 1, 2020, he was seen in the emergency department of this hospital with acute respiratory distress added to his previous symptoms. On admission, physical examination revealed vital signs as follows: a pulse rate of 140 beats/minute, respiratory rate of 40 breaths per minute, blood pressure of 100/60 mmHg, and a fever of 38.5°C. Lung auscultation revealed bilateral rhonchi, and arterial blood gas analysis indicated PH 7.26, PaO<sub>2</sub> 30 mmHg, PaCO<sub>2</sub> 49 mmHg, PaHCO<sub>3</sub> 21 mEq/L, oxygen saturation of 50% (on room air). The patient did not respond to non-mechanical support and had a short and rapid breath. Therefore he was intubated, and mechanical ventilation was installed for him in the intensive care unit (ICU). He was also prescribed Propofol (50mg IV

infusion for 1 hour), midazolam (5 mg IV infusion for 1 hour), Ketamin (50 mg IV infusion for 1 hour), Hydrocortisone (200 mg stat) and Furosemide (40 mg stat).

RT-PCR test was again performed on him, but this time, by taking a specimen from the Bronchoalveolar lavage fluid (BALF), and the result was positive. A chest X-ray was also performed, as shown in Fig. 1, bilateral diffuse interstitial pulmonary edema with left-sided pleural effusion was observed. A complete blood count with the differential test was performed. Results showed leukopenia and neutropenia. However, the electrolyte level, myocardial enzymes, liver, and renal functions were all normal. Blood and sputum cultures were negative. The antigen test for influenza A and B was negative. IgM test for influenza A and B, parainfluenza, respiratory syncytial virus, adenovirus, chlamydia pneumonia, mycoplasma pneumonia, and legionella pneumophila, was negative. Blood and sputum culture were performed prior to the administration of antibiotics, and results were negative. The patient's ECG showed sinus tachycardia, and there was no evidence of cardiac ischemia. Echocardiography was performed and demonstrated an ejection fraction of 45%, moderately dilated right ventricle (RV), and mild tricuspid regurgitation, with no clot in the pulmonary artery. On the fourth day, symptoms of the patient did not improve, and he expired 28 hours after admission.

The study was approved by the ethics committee of Abu-Ali-Sina Hospital on May 6, 2020 (No. 029802), and informed consent was obtained from the patient family for publication of this case report and accompanying image.

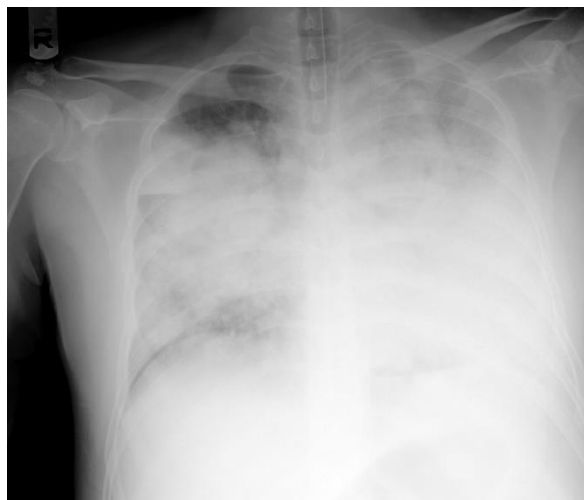


Figure 1. Chest X-ray of the patient on May 1, 2020, showing bilateral diffuse interstitial pulmonary edema with left-sided pleural effusion

## Discussion

World Health Organization (WHO) declared the outbreak of COVID-19 constitutes a Public Health Emergency of International Concern on January 30, 2020. The spectrum of this disease ranges from asymptomatic/mild to severe/life-threatening [9, 10]. SARS-CoV-2 has proven to be often deadly to the elderly and individuals with underlying disease or immunodeficiency [11],

while young patients with COVID-19 are less likely to progress to severe disease [12]. This study shows that the general population is susceptible to SARS-CoV-2, and it is essential to give serious consideration to the youth or individuals without any pre-existing medical conditions. If any symptoms of COVID-19 is observed, regardless of age, more accurate evaluation and follow-up should be performed.

The patient reported in this article was in a controversial position. The RT-PCR test of SARS-CoV-2 RNA using nasopharyngeal and oropharyngeal swabs was negative. In contrast, it was positive when a specimen was taken from the Bronchoalveolar lavage fluid (BALF). The reason is that the result of RT-PCR for identifying SARS-CoV-2 depends on the sample viral load. Angiotensin-converting enzyme-2 (ACE-2) is identified as the cell entry receptor of SARS-CoV-2. ACE-2 is expressed in the lungs more than the upper respiratory tract [13]. Therefore, influenced by the site from which the specimen is taken, the RT-PCR test result can be a false negative. This fact explains why the oropharyngeal or nasopharyngeal swab test is sometimes false-negative, while the bronchoalveolar lavage fluid (BALF) specimen test might be positive. Although the BALF test has a higher exposure risk, it is considered more accurate and recommended if performed by an expert operator.

It is still unclear why some young people show severe symptoms or die while others are asymptomatic or show only mild symptoms. Recent researches suggest that differences may lie in genes that instruct human cells to build the receptor ACE2, which SARS-CoV-2 relies on to enter airway cells [14, 15]. Variations in the ACE2 gene that alter the receptor can make it harder or easier for the virus to get into the cells.

### **Ethical approval and consent for publication**

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### **Conflict of Interest**

The authors declare that there is no conflict of interest.

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