

The Role of Bronchoalveolar Lavage in the Diagnosis of Suspected COVID-19 Pneumonia After Multiple Negative Nasopharyngeal Swabs

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ABSTRACT

The coronavirus disease 2019 (COVID-19) pandemic, which is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), became a huge risk to public health. The gold standard to diagnose COVID-19 is by real-time reverse transcription polymerase chain reaction (RT-PCR). Nevertheless, false-negative RT-PCR results have been reported in many studies.

Here we present a case of suspected COVID-19 pneumonia in a patient who received three negative RT-PCR results from nasopharyngeal swabs result who was subsequently diagnosed with COVID-19 pneumonia by RT-PCR from bronchoalveolar lavage (BAL) collected by performing a bronchoscopy procedure.

Our findings remind healthcare providers that having negative nasopharyngeal swab RT-PCR tests should not exclude the diagnosis of COVID-19 pneumonia. The clinical suspicion, history, laboratory results and radiological imaging play an important role in diagnosing COVID-19 pneumonia. Performing bronchoscopy to collect lower respiratory tract sample (BAL) for suspected COVID-19 pneumonia can be considered in specific situations.

INTRODUCTION

Coronavirus disease 2019 (COVID-19) was first discovered in Wuhan, China, in December 2019 and was found to be caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)¹. SARS-CoV-2 infection has various clinical presentations, including no symptoms, mild respiratory infection and viral pneumonia, which can result in respiratory failure and even death². COVID-19 is highly contagious, and person-to-person transmission is the leading cause of SARS-CoV-2 transmission³. The gold standard diagnostic method for SARS-CoV-2 infection is viral nucleic acid detection by reverse transcription polymerase chain reaction (RT-PCR) in samples collected by nasopharyngeal swab⁴. However, several studies have demonstrated false negative PCR results, which is a serious issue⁵. Therefore, a bronchoalveolar lavage (BAL) specimen can be taken and tested when clinically required⁶.

The purpose of this case presentation is to report a clinical case of a patient with suspected COVID-19 pneumonia who underwent bronchoscopy for the diagnosis of COVID-19 pneumonia after three negative nasopharyngeal swabs. To our knowledge, this is the first such case reported in Kingdom of Bahrain.

CASE PRESENTATION

A 68-year-old male patient with a medical history of diabetes mellitus and dyslipidemia presented with a history of fever for one day (39°C) associated with rigors, chills and fatigue. He denied experiencing shortness of breath, chest pain, cough or any gastrointestinal symptoms (no nausea, vomiting or diarrhea). He denied traveling but confirmed having contact with a patient who tested positive for SARS-CoV-2 7 days prior to his symptom onset.

At presentation, physical examination revealed normal vital signs. In addition, he was afebrile, and his oxygen saturation was 94% in ambient

air. Reduced air entry and crackles on the left side of the chest were observed. Chest X-ray demonstrated left middle zone consolidation with right side infiltration. Initial blood work revealed that his white blood cell count was 7.95×10^9 cell/L, lymphocyte count was 21.9×10^9 cell/L and C-reactive protein level was 115 mg/L (normal range below 5 mg/L). Liver function, renal function, myocardial enzymes and electrolytes were normal. Initial nasopharyngeal swab for SARS-CoV-2 by RT-PCR (day 2 of symptoms), respiratory panel and anti-SARS-CoV-2 test were negative. Due to his clinical findings, history of contact with a positive COVID-19 case, laboratory findings and imaging, he was admitted to the airborne-isolation ward for observation and further management and was started initially on ceftriaxone and azithromycin.

On day 3 of symptoms, another nasopharyngeal swab for SARS-CoV-2 by RT-PCR was performed, and the result was again negative. On day 5 of symptoms, high-resolution computed tomography (HRCT) of the chest was performed and images revealed patchy airspace opacities and ground glass over the left lower lobe (Figure 1).

Nasopharyngeal swab RT-PCR for SARS-CoV-2 was repeated on day 8 of symptoms, and the result was negative. Given the patient's contact history with a COVID-19 case, clinical manifestation with persistent fever, HRCT imaging finding, laboratory test and worsening chest X-ray, it was decided to perform a bronchoscopy to investigate causative organisms.

On day 9 of symptoms, a bronchoscopy was performed, and BAL was collected and tested by RT-PCR for SARS-CoV-2. The result was positive, with a CT value of 27.3, and a pneumonia panel revealed *Candida krusei* and *Candida parapsilosis*. On day 14 of symptoms, the patient was tested for anti-SARS-CoV-2, which revealed anti-SARS-CoV-2(N) 58.2 and anti-SARS-CoV-2(S) 259. The patient was treated with an antiviral (remdesivir), as well as anidulafungin and dexamethasone.

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Figure 1: Chest computed tomography showing patchy airspace opacities and ground glass over the left lower lobe.

Fifteen days after admission, the patient's symptoms improved, and he was discharged after one negative nasopharyngeal swab test was obtained.

DISCUSSION

We report the case of a patient with highly suspected COVID-19-associated pneumonia who had had three consecutive negative RT-PCR tests for SARS-CoV-2 from nasopharyngeal swabs and received a positive RT-PCR test from BAL. In patients with fever and symptoms of a respiratory tract infection who report that they have been in contact with a COVID-19 case (within the last 14 days) or who is living in or recently traveled to an area with a high incidence of COVID-19 (within the last 14 days), diagnosis of COVID-19 should be a top consideration³. Collecting a nasopharyngeal swab for RT-PCR to detect SARS-CoV-2 is the gold standard technique to diagnose COVID-19⁴. The World Health Organization (WHO) has revealed that PCR assays for SARS-CoV-2 have a high specificity (100%) for COVID-19 and a sensitivity of 61%–68%, which can be increased to 71%–79% with repeated PCR testing⁷. Due to the low sensitivity of diagnosing COVID-19 by PCR, some studies have suggested that solely using PCR assays is not reliable⁸.

Chest CT can be used as a complementary method (with RT-PCR) for diagnosing COVID-19⁹. A previous study has determined several typical characteristics of chest CT imaging of COVID-19 pneumonia, including multifocal, bilateral ground glass opacities with peripheral distribution that commonly involves several lobes and is more frequent in inferior lobes. However, in our patient, HRCT of chest revealed patchy airspace opacities and ground glass noted over only the left lower lobe, which, according to the aforementioned study, is atypical for CT imaging in patients with COVID-19 pneumonia¹⁰.

Several cases with positive chest CT findings as reported by clinicians could present with negative RT-PCR test results. A study performed on 1014 suspected COVID-19 patients who underwent CT of the chest and RT-PCR testing concluded that 601 of the 1014 patients had positive RT-PCR and the remaining 413 patients had negative for RT-PCR tests.

Additionally, of the 413 patients with negative RT-PCR results, 308 patients had positive features of COVID-19 pneumonia on chest CT⁹.

Although our patient had atypical chest CT findings, there might be cases with positive COVID-19 pneumonia findings on their chest CT but negative RT-PCR results.

In a study conducted in London, United Kingdom, in which 4008 patients who were admitted to the medical wards were enrolled, 1792 out of 4008 patients were diagnosed with COVID-19. Of the 1792 patients who were diagnosed with COVID-19, 1391 patients had positive nasopharyngeal RT-PCR results and 283 patients received only negative nasopharyngeal RT-PCR results. Of the 283 patients who had false-negative RT-PCR results, 227 patients had a chest CT positive for RT-PCR. However, 19 of the 227 patients who were diagnosed with COVID-19 (6.7%) had negative results for both RT-PCR tests and chest CT findings (normal lung fields)¹¹. These study findings and our case who had negative results in both RT-PCR tests and chest CT findings demonstrate that depending only on chest CT as a complementary method in diagnosing COVID-19⁹, is not reliable.

There are several possible causes of negative RT-PCR results in SARS-CoV-2-positive patients. One of them is viral load, which can be affected by disease course (symptom onset) and intensity. The location from which the sample is taken can also influence the results, as the viral load can differ; for example, throat swab samples have lower viral load than samples taken from sputum, as shown in several studies¹². Other factors, such as sampling technique, kit functioning and transportation and storage of the sample, can affect the results of the RT-PCR test⁵.

As stated by the WHO, it is highly recommended to collect lower respiratory tract samples to diagnose COVID-19-associated pneumonia in a patient highly suspected of having COVID-19, even if they received negative RT-PCR results from the upper respiratory tract. Despite their recommendation, procedures to collect a lower respiratory tract specimen causes aerosols, which might increase the risk of COVID-19 transmission. Therefore, healthcare workers performing the procedure should be adequately prepared, well trained and wearing full adequate personal protective equipment. Additionally, such procedures should be performed in a room with good ventilation to reduce the risk of transmission³.

In a recent study enrolling 131 patients, the participants underwent bronchoscopy for different indications: suspected SARS-CoV-2 infection in a patient with two negative nasopharyngeal swabs, alternative diagnosis, suspected superinfection and lung atelectasis. The most frequent indication was suspected SARS-CoV-2 infection (65.5%) in a patient with double negative nasopharyngeal swabs. The SARS-CoV-2 test was positive on BAL in 43 of the 131 patients, and patients with suspected SARS-CoV-2 infection with negative nasopharyngeal swabs comprised 76% of these cases (33 out of 43). Thus, the authors concluded that 37.2% is the rate of detection of SARS-CoV-2 on BAL in patients with suspected SARS-CoV-2 infection. These findings confirm the use of BAL specially to diagnose suspected SARS-CoV-2 infection in patients with several negative nasopharyngeal swabs¹³.

Several studies have revealed that many COVID-19 cases could receive negative RT-PCR results even if they have positive findings on CT chest imaging^{9,11}; therefore, performing bronchoscopy to diagnose COVID-19 pneumonia in suspected patients could confirm the diagnosis. Bronchoscopy is an aerosolizing procedure, and it should be performed with full precautions by well-trained health workers due to the high risk of transmission during such procedures.

CONCLUSION

We report a case of suspected COVID-19 pneumonia in a patient with a history of contact with a confirmed COVID-19 case who received three negative RT-PCR tests from nasopharyngeal swabs, underwent bronchoscopy and was diagnosed with COVID-19 pneumonia by BAL. The case highlights that clinical suspicion, symptoms, history, laboratory results and radiological imaging play a vital role in diagnosing COVID-19 pneumonia. A negative nasopharyngeal RT-PCR swab should not exclude the diagnosis of COVID-19. Additionally, this case report confirms that using only nasopharyngeal RT-PCR test and CT imaging to diagnose COVID-19 pneumonia is not reliable. In addition, we emphasize that clinicians should follow the WHO recommendations to collect lower respiratory tract samples via bronchoscopy in patients with suspected COVID-19 pneumonia who received repeated negative nasopharyngeal swabs and are highly suspected of having COVID-19.

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