Delayed Diagnosis and Treatment of a Critically Ill Patient with Infective Endocarditis Due to a False-Positive Molecular Diagnostic Test for SARS-CoV-2

Authors' Contribution:
Study Design A
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Patient:	**Male, 53-year-old**
Final Diagnosis:	**Infective endocarditis**
Symptoms:	**Dynpnea • fever**
Medication:	**—**
Clinical Procedure:	**Surgical aortic valve replacement**
Specialty:	**Cardiac surgery**

Objective: **Challenging differential diagnosis**

Background: The worldwide spread of the severe acute respiratory syndrome-coronavirus-2 (SARS-COV-2) has created unprecedented situations for healthcare professionals and healthcare systems. Although infection with this virus is considered the main health problem currently, other diseases are still prevalent.

Case Report: This report describes a 59-year-old man who presented with symptoms of dyspnea and fever that were attributed to Covid-19 infection. His clinical condition deteriorated and further examinations revealed a subjacent severe aortic regurgitation due to acute infective endocarditis. Surgical treatment was successful.

Conclusions: The results of diagnostic tests for Covid-19 should be re-evaluated whenever there are clinical mismatches or doubts, as false-positive Covid-19 test results can occur. Clinical interpretation should not be determined exclusively by the Covid-19 pandemic**.** This case report highlights the importance of using validated and approved serological and molecular testing to detect infection with SARS-CoV-2, and to repeat tests when there is doubt about presenting symptoms.

MeSH Keywords: **Aortic Valve Insufficiency • Coronavirus • COVID-19 • Endocarditis, Bacterial**

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Background

The SARS-COV-2 pandemic has spread over almost all countries throughout the world, with millions of people being infected and the number of deaths constantly increasing. This viral infection is characterized by its rapid transmission, although its symptoms can range from asymptomatic to severe pneumonia and acute respiratory distress syndrome [1]. Enhanced clinical suspicion of this infection is associated with the justified fear of uncontrolled transmission, especially during this pandemic period, but it can undermine the diagnosis of alternative clinical entities.

Tests currently available in Greece for the diagnosis of SARS-COV-2 are all based on real-time reverse transcription-polymerase chain reaction (RT-PCR) assays of nasopharyngeal swab or mouthwash samples. The sensitivity, specificity, and accuracy of these tests remain unclear, and test results must be carefully interpreted following the onset of symptoms. Although the sensitivity of real-time RT-PCR assays of nasopharyngeal swab samples can be as high as 72%, sensitivity is highly dependent on both the method of specimen collection and the stage of the disease due its long incubation period [2]. The percentages of false-negative test results remain unclear, and physicians are instructed to perform repeated tests in patients with high clinical suspicion. Because the specificity of real-time RT-PCR has not been determined, the likelihood of false-positive tests is uncertain [3].

This case report describes a 59-year-old man with symptoms of dyspnea and fever who was diagnosed with Covid-19 infection. His clinical condition deteriorated and further examinations revealed a subjacent severe aortic regurgitation. Aortic valve replacement was performed due to rapidly evolving infective endocarditis, while re-examination demonstrated that the initial test for SARS-COV-2 was a false-positive.

Case Report

A 59-year-old man presented at a local hospital near Athens with dyspnea and fever reaching 38.5°C. His medical history included hypertension and he mentioned that he had experienced mild symptoms for 1 week. Because of the SARS-COV-2 pandemic, he was suspected of being infected with this virus and he was transferred to our hospital. The Z-Path COVID-19-CE IVD PCR test yielded positive results. Because he showed respiratory instability, the patient was hospitalized in the Covid-19 unit of our hospital. His breathing rapidly deteriorated, and he was placed on non-invasive mechanical ventilation.

Chest X-ray findings were compatible with pulmonary edema, which was confirmed by thoracic computed tomography (CT),

which also revealed findings indicating acute pulmonary edema. There were no signs of pulmonary infiltrations, ground glass opacities or acute respiratory distress syndrome (ARDS). Echocardiography, performed due to a suspicion of acute heart failure, revealed severe acute aortic valve regurgitation, with left ventricular end-diastolic and end-systolic diameters of 72 mm and 55 mm, respectively, and an ejection fraction below 30%. Blood samples were cultured due to a suspicion of infective endocarditis. Thoracic CT confirmed the presence of acute pulmonary edema, but signs indicating ARDS due to lower respiratory infection compatible with Covid-19 were not present. After 4 days on non-invasive mechanical ventilation, he was diagnosed with acute heart failure and intubated.

Because of his deteriorating condition, delay was regarded as detrimental. Appropriate measures were taken to protect the staff and other patients from possible COVID-19 infection. A median sternotomy was performed, showing that the aortic valve was almost destroyed, with vegetations present in the right and non-coronary cusps. A mechanical aortic valve was inserted and the surgery was completed uneventfully.

Although we expected that the symptoms caused by the viral infection would be more intense after surgery, the patient's respiratory function and chest X-ray findings gradually improved, with no episodes of fever. Echocardiography showed that his heart function was satisfactory, with left ventricular end-diastolic and end-systolic diameters of 58 mm and 43 mm, respectively, and an ejection fraction of 55%.

Blood culture results on the second post-operative day confirmed bacterial infective endocarditis due to infection with *Staphylococcus lugdunensis*. He was treated with antibiotics according to the antibiogram and switched to vancomycin, gentamycin and ceftriaxone. Two additional RT-PCR tests for SARS-CoV-2 infection were performed within 72 h after his admission to our hospital. Both the Cepheid/GenXpert and Abbott ID now SARS-CoV-2 RT-PCR tests yielded negative results.

The patient's in-hospital course was uncomplicated and he was discharged after 4 weeks, although he continued intravenous antibiotic treatment as an out-patient. He was also quarantined for 14 days, but he never developed symptoms of Covid-19 infection. Two weeks after the first positive PCR test, the patient was tested for anti- SARS-CoV-2 antibodies using the GenBody Covid-19 IgM/IgG Immunoasssay. This test yielded negative results, suggesting that this patient had not been infected with SARS-COV-2 or that he had a low copy number detectable by the Z-Path COVID-19-CE IVD PCR test.

Discussion

In clinical practice, it is difficult to distinguish between cardiogenic and non-cardiogenic pulmonary edema especially when the initial symptoms mimic ARDS due to low respiratory infection [4]. Based on RT-PCR testing, our patient was initially diagnosed as being positive for SARS-COV-2 infection and was treated accordingly. Because his condition deteriorated, a chest CT was performed to estimate the severity of the infection. The sensitivity of the RT-PCR test for Covid-19 has been reported to range from 50% to 79% and may be as high as 97.2% when combined with specific thoracic CT findings [5].

Although several studies have reported rates of false-negative results of RT-PCR tests for COVID-19, none to our knowledge has reported the percentages of false-positive results. Although RT-PCR tests are highly unlikely to yield false-positive results, this possibility is dependent on the threshold of the test and the severity of the disease. To date, no studies have estimated the specificity of RT-PCR tests used globally [6]. Rapid tests used globally for the diagnosis of influenza yield results within 15–30 minutes, despite their relatively lower sensitivity and specificity when compared with RT-PCR [7].

Diagnosis of SARS-COV-2 infection is of absolute importance during the pandemic period. The techniques used for viral detection are improving rapidly, with very satisfactory results in symptomatic patients. Nevertheless, the sensitivity and specificity of these tests remain uncertain during the incubation phase of the virus and the recovery period [8]. The method of sample collection is also important, as nasopharyngeal swabs are considered more reliable than oropharyngeal swabs, with their combination being even more accurate [9]. False-positive results may be due to sample contamination, which interferes with the process of nucleic acid extraction and PCR amplification [10]. False-positive results can be prevented by using only approved diagnostic tests. The U.S. Centers for Disease Control and Prevention have designed a SARS-CoV-2 Real-Time RT-PCR Diagnostic Panel [10]. Also, diagnostic tests should be repeated a few days later.

The life-saving intervention for this man was delayed due to the false diagnosis, resulting in the need for emergency surgery. RT-PCR tests can only indicate the presence of viral material, not whether an individual had been infected and subsequently recovered. Consequently, there is a need for more accurate tests as well as better interpretation of their results. False-negative results can increase the spread of disease [11], whereas the effects of false-positive results remain less clear, although these results can also be lethal, as in our patient. Awareness of the possibility of SARS-CoV-2 infection has affected the necessary treatment of individuals with chronic and acute diseases [12].

Conclusions

This case report indicates that the results of diagnostic tests for SARS-COV-2 should be re-evaluated whenever there are clinical mismatches or doubts, due to the possibility of false-positive test results. Proper treatment may be delayed or omitted in patients misdiagnosed with COVID-19. The clinical interpretation of a patient's condition should not be determined exclusively by the SARS-COV-2 pandemic. This case report highlights the importance of using validated and approved serological and molecular testing to detect infection with SARS-CoV-2, and to repeat testing when there is doubt about presenting symptoms.

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