The Suspicion of COVID-19 Infection at the Expense of Diagnosing Infective Endocarditis; the Effect of the Pandemic in Diagnosing Other Infections

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ABSTRACT

Infective endocarditis is a relatively common cardiac infection with variable clinical presentations. The main symptoms of fever, dyspnea and cough can be easily confused with COVID-19 infection. Cardiac murmurs are present in 85% of patients with infective endocarditis, and a thorough physical examination is essential to aid in the diagnosis.

This case report describes the clinical history of a 65-year-old male presented with flu like symptoms and admitted to the quarantine ward due to a suspected COVID-19 infection. Prior to his hospital discharge he had a sudden deterioration and turned out to have infective endocarditis, with severe mitral regurgitation requiring an emergency mitral valve replacement surgery.

This case demonstrates the importance of considering other life-threatening infections during a global pandemic like COVID-19. A comprehensive physical examination should be thoroughly performed to avoid missing alternative serious diagnoses.

INTRODUCTION

Infective endocarditis is defined as an infection of the heart endocardial surface and affects one or more cardiac valves[1]. It is a relatively common serious cardiac infection with a variable clinical presentation, and some of the symptoms are nonspecific and can overlap with many other diagnoses. Fever is the most common symptom (90% of patients); other symptoms include abdominal pain, dyspnea, and headache. This highlights the importance of the physical examination in the diagnosis of infective endocarditis. Cardiac murmurs are found in 85% of patients; skin and/or mucosal petechiae are seen in 20-40% of patients. Less common signs are splinter hemorrhages, roth spots and Osler nodes. Patients can present with cardiac complications such as heart failure, valvular insufficiency, or other systemic complications like peripheral or CNS emboli[2,3]. Risk factors include a previous history of infective endocarditis, pre-existing congenital heart disease, intravenous drug use, and recent dental or surgical procedures. The modified Duke criteria are used for confirming the diagnosis of infective endocarditis[4]. In the setting of a global pandemic, fever associated with dyspnea is often attributed to a suspected infection with the severe acute respiratory syndrome-related coronavirus 2 (SARS-CoV-2) even if the swab results are negative. A case was published in Belgian of a 51-year-old man who had a delayed diagnosis of infective endocarditis because he had symptoms similar to Corona Virus disease - 19 (COVID-19), and he developed heart failure and extensive endocarditis of the mitral valve[5].

In this case report, the suspicion of COVID-19 delayed the diagnosis of infective endocarditis and caused the patient to undergo an emergency, lifesaving mitral valve replacement surgery, with the anticipated higher surgical risk both at the perioperative and post-operative periods.
This case confirms the importance of a proper physical examination in aiding the diagnosis. Even during the global pandemic, when a patient has new symptoms, these new symptoms should always be addressed. It highlights the importance of considering infections other than COVID-19 as these diseases can be more life threatening than COVID-19, and this case emphasizes the importance of an early recognition of infective endocarditis to prevent rapid progression and deadly complications.

CASE PRESENTATION

A 65-year-old Asian gentleman, not known to have any medical

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illnesses, presented to the hospital with a one-week history of fever, weakness, and abdominal pain, along with 3 days history of shortness of breath. He initially had no chest pain, loss of consciousness, nausea, vomiting, or any history of contacting COVID-19 positive case. Apart from his gender and age above 60 years, he had no risk factors for acquiring infective endocarditis, and he had no prior history of sharing needles for substance abuse, no previous history of valvular heart disease, and no history of recent dental or surgical procedures prior to his presentation.

On chest examination, he had fine bilateral crepitations with bilateral equal air entry. S1 and S2 heart sounds were present, but there was no documentation of any murmurs auscultated. In addition, the initial clinical impression was COVID-19 pneumonia.

Table 1 illustrates the results of the laboratory investigations done for the patient. The trend of white cell counts (WBC), and inflammatory markers are shown in [Figure 1]. His chest X-rays revealed a bilateral reticulonodular infiltration with increased broncho vascular markings suggestive of either pulmonary edema or pneumonia [Figure 2]. Repeated COVID-19 nasopharyngeal PCR assays were negative, and SARS-CoV-2 IgM and IgG antibodies were 0 and 0.15 Au/Mi, respectively. An ECG showed a sinus tachycardia [Figure 3], and the high sensitivity troponin value was normal. Based on the clinical picture along with the chest radiography findings, COVID-19 was the provisional diagnosis. The patient was admitted into the quarantine ward. He was started on azithromycin and ceftriaxone.

Urine routine analysis was done, and it was negative for microscopic hematuria. Urea and creatinine were also in the normal range, 5.1 mmol/L and 69 umol/L respectively.

At day 4 of his admission, he suddenly developed chest pain, with a progressive shortness of breath and a decrease in his level of consciousness. An arterial blood gas analysis showed a respiratory acidosis with type II respiratory failure. He was intubated and artificially ventilated due to the severe respiratory distress. Cardiac auscultation revealed a grade 4/6 pan-systolic murmur at the cardiac apex. Transthoracic echocardiography (TTE) was performed and showed left ventricle is normal in size with hyper dynamic contractility. Left ventricular function was 67%. Left atrium size was normal with normal right ventricular function. It also showed a highly oscillating mass attached on the anterior mitral leaflet (AML) distorting the mitral valvular structure, which was complicated by a severe mitral regurgitation. The aortic valve leaflet noted to be thickened. Transesophageal echocardiography (TOE) confirmed the mitral valve pathology, along with another oscillating mass on the aortic valve, which is consistent with one of the major criteria for a diagnosis of infective endocarditis. Blood cultures were collected; vancomycin was added empirically to the antibiotic regimen after consulting with the infectious disease specialist. The patient underwent emergency mitral and aortic valve replacements.

The patient underwent an emergency surgery for mitral valve and aortic valve replacements with tissue valves. His blood cultures and tissue cultures were negative. His post-operative course was uneventful. He was kept for 6 weeks for intravenous antibiotic therapy as per infectious disease recommendations.

Warfarin therapy: Warfarin was continued for total of three months post-operatively. The patient's inflammatory makers normalized, and repeated blood cultures were all negative. Transthoracic echocardiography post-surgery showed normal functioning bioprosthetic mitral and aortic valves with a paradoxical septum due to the post-operative state. His left ventricular function was normal.
The patient was seen in the outpatient department three weeks post discharge, and he was doing well. He was instructed to have prophylactic therapy for infective endocarditis prior to dental procedures. An echocardiography was repeated six months post discharge and showed a normal left ventricular systolic function with normal functioning bioprosthetic mitral and aortic valves.

Table 1: Laboratory investigations that were done to our patient

Investigation	Result
Hematology	
WBC	11.44 x10^9/L
Hb	11.2 g/dL
Platelets	200 x10^9/L
Neutrophils%	81.1 %
Cardiac biomarkers	
Troponin-I	0.007 ng/mL
Creatine kinase	34 U/L
Lactic dehydrogenase	294 U/L
Biochemistry	
Urea	5.1 mmol/L
Creatinine	69.00 µmol/L
Electrolytes panel	
Na+	135 mmol/L
K+	4.0 mmol/L
Cl-	100 mmol/L
HCO3-	24 mmol/L
Microbiology	
SARS-COV-2 NPS	Negative
Respiratory profile antibodies in blood	Seronegative for all tested respiratory pathogens*
Urine C+S	Culture sterile
Central blood C+S	Culture sterile
Peripheral blood C+S	Culture sterile
Vascular catheter tip C+S	Culture sterile
Valvular tissue C+S	Culture sterile

*Tested antibodies include both IgG and IgM for the following pathogens: Legionella pnuemophilia, Mycoplasma pneumonia, Coxiella burnettii, Chlamydia pneumonia, Adenovirus, Respiratory Sync virus, Influenza A, Influenza B, Parainfluenza

DISCUSSION

The infective symptoms this patient presented with of fever, loose motion, and shortness of breath, were pointing towards COVID-19 pneumonia as the top diagnosis to exclude, although repeated nasopharyngeal PCR assays were negative for SARS-CoV-2.

In the treating institute, the implemented protocol to treat COVID-19 suspected patients is to isolate cases with fever and shortness of breath. All cases should be admitted to specific ward for repeated COVID-19 testing and further investigation. This explains the decision to suspect COVID-19 pneumonia in this patient. However, with the worsening of his clinical condition and the repeated negative samples for COVID-19 infection other differential diagnosis were suspected.

Pulmonary oedema was another differential diagnosis to consider, especially considering the presence of the increase broncho vascular markings in the chest X-ray, but the patient had no past medical history or risk factors for this condition.

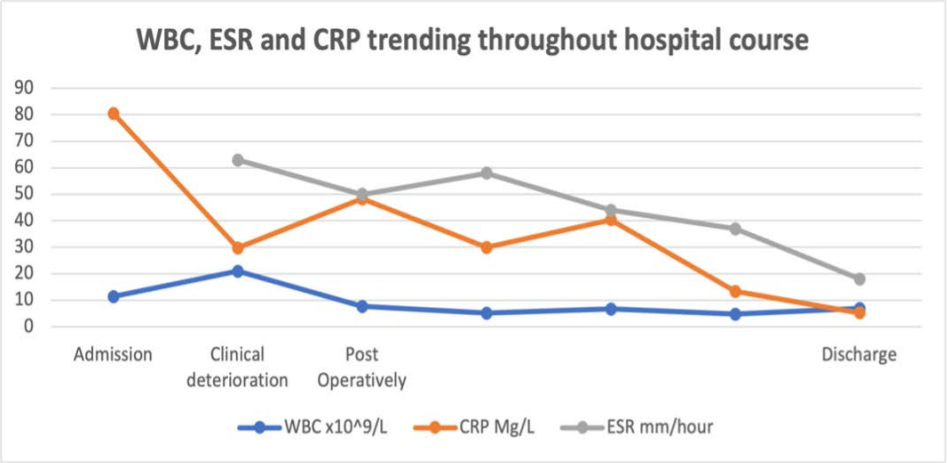

Figure 1: The trends of white cell count, C reactive protein and erythrocytes sedimentation rate from the time of admission till discharge

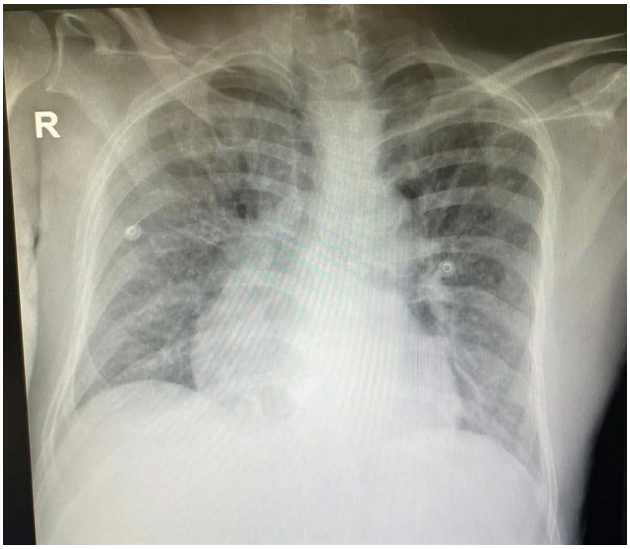

Figure 2: AP view of chest x- ray showing increase hilar shadow with prominent broncho vascular markings especially upper lobe indicative of pulmonary venous hypertension

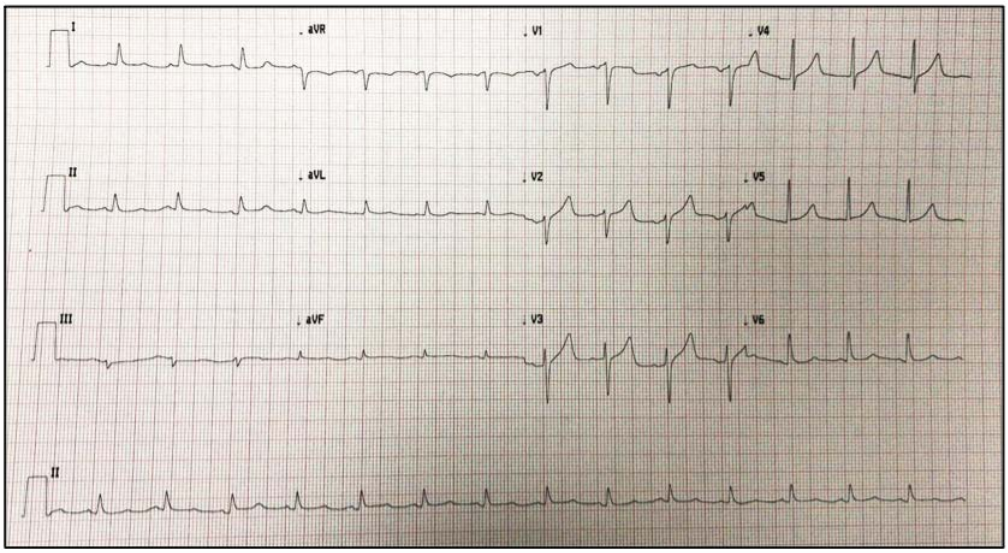

Figure 3: 12 lead electrocardiograms at time of admission showing normal sinus rhythm with heart rate of 99/min and non-specific ST/T changes at the inferior leads

Infective endocarditis, although the definitive diagnosis in this case, was not considered until the patient had rapidly deteriorated and developed acute cardiogenic shock secondary to severe mitral regurgitation.

Focusing on the exclusion of COVID-19 or any pandemic infection can hinder the diagnosis and treatment of other infectious diseases; a well reported example is when thousands of people died from other preventable diseases during Liberia's 2014-2016 Ebola virus crisis, as they were not getting enough care[6].

Moreover, during pandemics many patients have a delay in treatment, either because their access to the treatment is difficult or their diagnosis is missed or delayed. Physicians can be pre-occupied by COVID-19 infection and consider it as the provisional diagnosis if they have a patient presenting with fever and other systemic symptoms.

In the United States, there is another example of how this pandemic affected other life-threatening diseases. There was a 38% reduction in laboratory evaluations and cardiac catheterizations of ST-segment elevation Myocardial infarction (STEMI) when comparing the monthly total and average number of STEMI activations in three hospitals before and during the pandemic. These results could not only be attributed to misdiagnoses or an increase the use of pharmacological reperfusion due to COVID-19 but also to patients' factors including fear of catching SARS-CoV-2 from hospitals[7].

Here, the patient's symptoms of fever, dyspnea, and weakness of one-week duration raised the suspicion of COVID-19 as a possible diagnosis, despite the four nasopharyngeal SARS-CoV-2 RT-PCR tests that were negative. Since there are still well documented false negative results of this test, he was admitted to the quarantine ward[8]. Has was diagnosed with COVID-19 and did not receive a comprehensive clinical examination. His alarming pan systolic murmur was missed and the severe mitral regurgitation that was detected by a transthoracic echo.

In Belgian, a similar case of a 51-year-old man with a delayed infective endocarditis diagnosis was reported, where the patient presented twice with fever and systemic symptoms and was sent home for home quarantine on both occasions. He then developed blurry vision and was diagnosed with heart failure and a cardiac murmur. Computerized Tomography of the lungs revealed changes similar to the ones seen in COVID-19. The nasopharyngeal swab was negative for COVID-19, and blood cultures were positive for Streptococcus species. The patient was diagnosed with an extensive endocarditis of the mitral valve with vegetation on both the anterior and posterior leaflets on TTE and TOE[5].

In the last 25 years, mortality rates for infective endocarditis reached 40% at one year after diagnosis[1]. It is vital to diagnose infective endocarditis as early as possible to prevent life threatening complications, such as heart failure and embolic events, and to prevent severe complications.

During pandemics, the suspicion of COVID-19 should not overlook other life-threatening infections. Obtaining a comprehensive history and a physical examination is mandatory for a proper assessment and to guide the medical therapy.

CONCLUSION

In conclusion, during the COVID-19 pandemic, it is important to consider COVID-19 as the primary diagnosis for patients presenting with fever and shortness of breath, but this should not overshadow the consideration of other infectious diseases especially life-threatening ones like infective endocarditis. The clinical diagnosis of infective endocarditis is guided by a proper history and physical examination, and early suspicion and treatment can help to prevent complications.

Although medicine is evolving rapidly, a thorough history and physical examination remain the best tools to guide clinicians towards an accurate diagnosis and help them to wisely use available resources.

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