Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Case Report

Myocardial injury in a patient with severe coronavirus disease: A case report☆

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ABSTRACT

Introduction: Coronavirus disease (COVID-19) can lead to severe disease or death and is characterized by a wide range of mild to severe symptoms. In addition to the lungs, studies have reported the involvement of the stomach, intestine, and angiotensin-converting enzyme 2 receptors in the heart.

Case report: We present a case of a patient with COVID-19 who died soon after developing multi-organ failure and myocardial injury due to COVID-19-associated pneumonia. A 71-year-old man who contracted COVID-19 was admitted to the hospital after presenting with fever for 7 days and developed dyspnea. Following treatment, his respiratory status worsened. Thus, he was transferred to our hospital for intensive care on day 11. Physical examination revealed fever, dyspnea, respiratory distress, and no chest pain. Invasive positive pressure ventilation was initiated for acute respiratory distress syndrome on day 14. On day 15, we observed renal, liver, and coagulation dysfunction, indicating multi-organ failure. Chest radiography did not show clear signs of an increased cardiothoracic ratio or pulmonary congestion. An electrocardiogram (ECG) showed signs of myocardial infarction, which was confirmed by elevated troponin I and creatine kinase levels. The patient's circulatory dynamics did not improve on medication, and he died on day 16.

Conclusions: We report the case of a patient with severe COVID-19 who died from an exacerbation of myocardial injury. Clinicians should not only evaluate respiration but also assess the heart by performing a 12-lead ECG, echocardiogram, and myocardial injury marker examination. Together, these tools can help predict which patients will develop severe COVID-19.

1. Introduction

The number of patients with coronavirus disease (COVID-19) is rapidly increasing worldwide, creating a critical situation. Patients with COVID-19 can develop severe disease and die from various causes. Patients with severe COVID-19 require intensive care, invasive positive pressure ventilation, continuous renal replacement therapy, and extracorporeal membrane oxygenation. COVID-19 primarily involves the respiratory organs. However, unlike severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome, COVID-19 is characterized by a wide range of mild to severe symptoms [1,2]. In addition to the lungs, a study has reported the involvement of the stomach, intestines, and heart with angiotensin-converting enzyme 2 (ACE2) receptors [3]. Previous

Abbreviations: ACE2, angiotensin-converting enzyme 2; COVID-19, coronavirus disease; CRP, C-reactive protein; ECG, electrocardiogram; PCI, percutaneous coronary intervention; SARS, severe acute respiratory syndrome; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; SpO_2, peripheral oxygen saturation; STEMI, ST-segment elevation myocardial infarction.

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studies also reported the occurrence of cardiac complications in patients with COVID-19, including myocardial injury and ventricular arrhythmia [4–6].

Here, we present the case of a patient with COVID-19 who died soon after developing multi-organ failure and myocardial injury due to COVID-19-associated pneumonia.

2. Case report

The patient was a 71-year-old man who had contracted COVID-19. He had a fever for 7 days. When the patient developed dyspnea, he was transferred to another hospital by ambulance. His medical history included hypertension, with no family history of aortic disease, sudden death, or structural cardiac abnormalities of any kind. He had a 5-pack per year smoking history and was not on any regular medication. The patient's human immunodeficiency virus antigen and antibodies, hepatitis B antigen, and C antibodies were negative. A polymerase chain reaction test for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) from a nasopharyngeal swab was performed after admission, which returned positive results. Upon admission, his peripheral oxygen saturation (SpO_2) was 92%–95% with room air. A 12-lead electrocardiogram (ECG) showed tachycardia (143 beats/min) (Fig. 1B); however, the patient complained of no chest pain. Chest radiography and chest computed tomography showed ground-glass opacities throughout the periphery of both lungs (Fig. 1A). Ceftriaxone and azithromycin were administered along with ciclesonide inhalation and oral favipiravir to prevent secondary infections. However, as his oxygen saturation gradually deteriorated further, he was transferred to our hospital for intensive care on day 11.

The patient's physical findings were as follows: lucidity, fever (38.0 °C), difficulty breathing (SpO_2: 91% at oxygen 10 L/min), respiratory distress (respiratory rate: 30/min), bloody sputum, and no chest pain. His heart rate and blood pressure were normal (83 beats/min and 111/72 mmHg, respectively). We continued the treatment recommended by another hospital. Accordingly, on day 12, we administered hydroxychloroquine. The patient's breathing and respiratory distress worsened even after oxygen concentration was increased. Therefore, invasive positive pressure ventilation was initiated on day 14. The arterial oxygen partial pressure (PaO_2) to fractional inspired oxygen (FiO_2) ratio was 95, indicating acute respiratory distress syndrome. Rocuronium was continuously administered, and the patient was placed in the prone position. The patient's blood pressure dropped and administration of low-dose norepinephrine was initiated accordingly. On day 15, we observed renal, liver, and coagulation dysfunction, indicating multi-organ failure. Furthermore, nitric oxide was administered to improve oxygenation. The patient's blood pressure dropped. A 12-lead ECG showed ST elevation in aVR, ST depression in II, III, and aVF, and negative T waves in II, III, aVF, and V1-6 (Fig. 2B). Blood tests showed high troponin I and creatine kinase levels, but creatine kinase MB was normal. Chest radiography did not show clear signs of an increased cardiothoracic ratio or pulmonary congestion (Fig. 2A). The patient's circulatory dynamics did not improve, and he died on day 16 (Fig. 3).

3. Discussion

Here, we present the case of a patient with severe COVID-19 who died from a sudden exacerbation of myocardial injury. Myocardial injury with reduced contraction and dilation of the left ventricle has been observed in patients with SARS [7]. A significant correlation between severe COVID-19 and myocardial injury has been reported [8–11]. Indeed, cardiac troponin I, high-sensitivity CRP, and cardiovascular disease are risk factors for severe COVID-19 [4,12].

In this case, no abnormality was indicated on electrocardiography prior to the observed decrease in blood pressure. However, the patient had risk factors, namely, untreated hypertension and a history of smoking, for cardiovascular disease. We found elevated ST, high CRP levels, high cardiac troponin I levels, and decreased blood pressure; thus, we suggested acute myocardial damage due to severe COVID-19 pneumonia.

The differential diagnoses of acute myocardial injury were mainly acute coronary syndrome, fulminant myocarditis, and drug-related myocarditis in this case. First, acute coronary syndrome is a

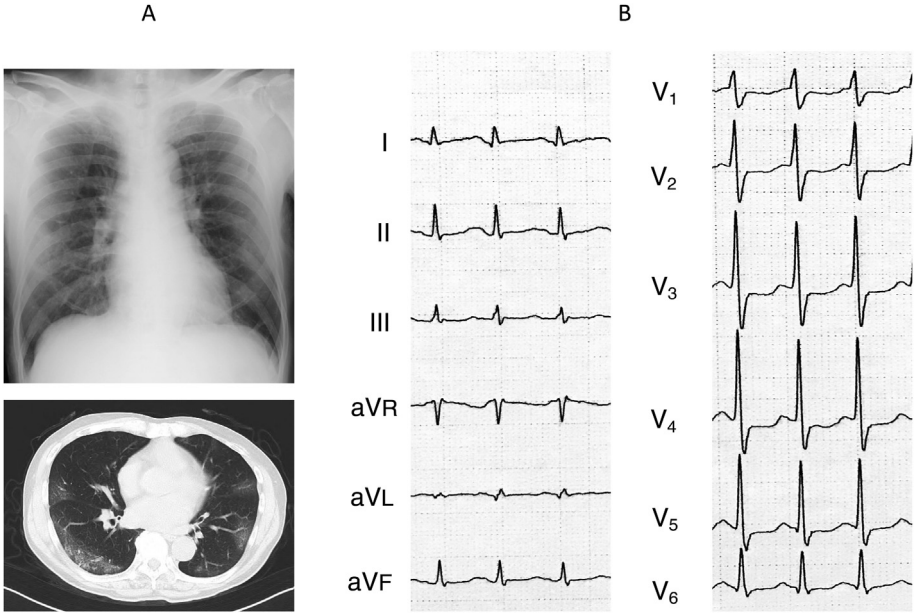

Fig. 1. A chest radiograph, computed tomography scan and a 12-lead electrocardiogram from the original hospital. A. Non-segmental ground-glass opacities were observed in both lung fields. B. A 12-lead electrocardiogram showed tachycardia.

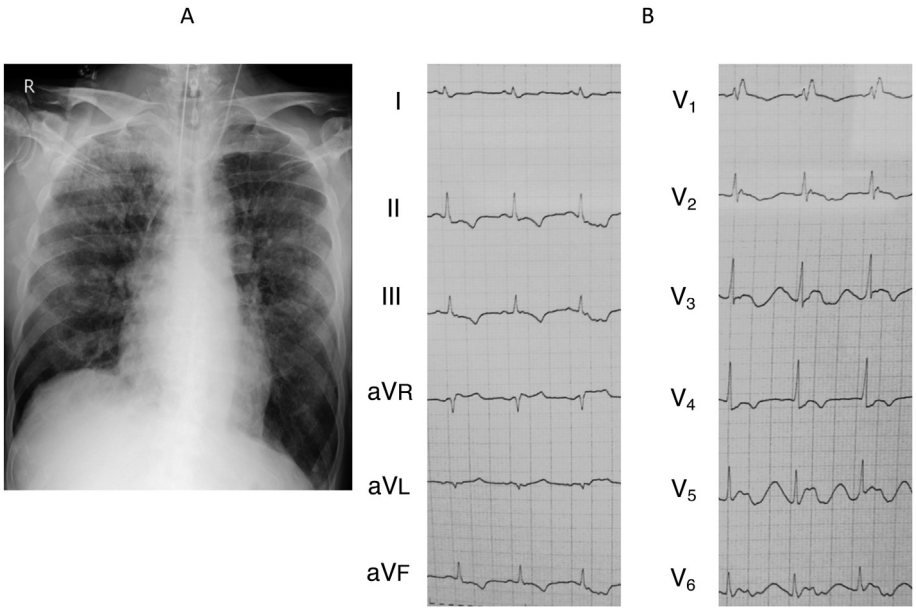

Fig. 2. A chest radiograph and a 12-lead electrocardiogram during hypotension. A. Ground-glass opacities and increased air space consolidation were observed in the entire left lung field. There were no clear signs of an increased cardiothoracic ratio or pulmonary congestion. B. A 12-lead electrocardiogram showed ST elevation in aVR, ST depression in II, III, and aVF, negative T waves in II, III, aVF, and V1-6.

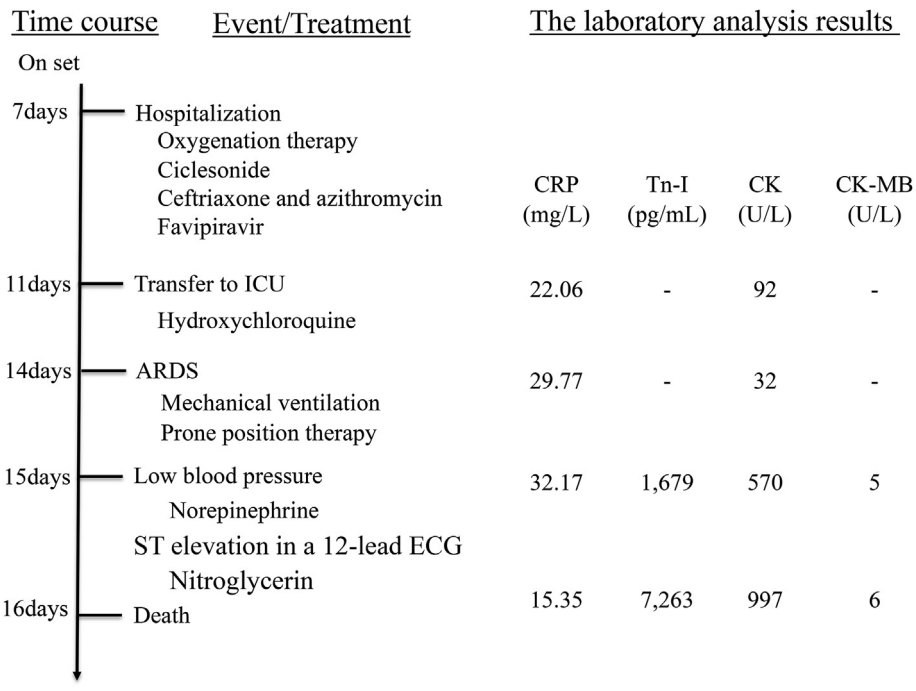

Fig. 3. Clinical course and the laboratory analysis results. A timeline of the clinical course, including relevant laboratory analysis results, is shown. ICU, intensive care unit; ARDS, acute respiratory distress syndrome; CRP, C-reactive protein; Tn-I, troponin I; CK, creatine kinase.

condition in which the lumen of the coronary artery is rapidly narrowed owing to plaque formation that results in blockage of blood flow; thus, the heart muscle becomes ischemic and necrotic; therefore, it is necessary to check for significant coronary artery stenosis accordingly [13]. In this case, ST elevation in aVR, ST depression in II, III, and aVF, and no ST elevation of V1 induction were observed, we considered ST-segment elevation myocardial infarction (STEMI) of stenosis or occlusion of the left main trunk [14]. However, the possibility of myocardial necrosis was concluded to be low owing to normal CK-MB levels, and therefore, heparin and nitroglycerin were administered without emergency cardiac catheterization. Second, fulminant myocarditis caused by common cold viruses such as Coxsackievirus is acute myocarditis with a fatal course resulting in rapid hemodynamic collapse. In this case, CK-MB levels were normal and influenza virus and hepatitis virus markers were negative; thus, the possibility of myocarditis was low. Currently, myocarditis due to coronavirus is not considered common [15], although previous studies have reported this

event [16,17]. Third, drug-related myocarditis is a possible adverse event in all patients receiving the drug and should always be monitored accordingly. Ceftriaxone and azithromycin, hydroxychloroquine, and norepinephrine used in this case have been reported to cause myocarditis [18]. The time to onset of adverse events was approximately 15 days [19]. Myocardial biopsy is essential for a definitive diagnosis and is made comprehensively based on the clinical course after discontinuation of the drug.

The exact pathophysiology of COVID-19-associated myocardial injury remains unknown, but four possible mechanisms have been suggested. The first of these involves the direct infiltration of myocardial cells by SARS-CoV-2. ACE2 has a strong binding affinity for the spike protein of SARS-CoV-2, the virus that causes COVID-19 [20,21]. As there are high levels of ACE2 expression in the heart, SARS-CoV-2 can invade cells through ACE2 using a specific serine protease [22]. However, histopathological findings from patients with COVID-19 showed only a small amount of inflammatory infiltration by monocytes in interstitial cardiac tissue, with no signs of substantial myocardial injury [23]. Patients infected with SARS-CoV-1, which has high genetic homology with SARS-CoV-2, exhibited a reduced left ventricular ejection fraction due to myocardial injury [7]. The presence of SARS-CoV-1 RNA in the cardiac tissue of 35% of patients infected with SARS-CoV-1 also suggests an association with ACE2 [24].

The second possible mechanism involves the release of cytokines due to systemic inflammation after COVID-19 infection. An imbalance in T1 and T2 helper cells results in a cytokine storm. This can cause coagulation abnormalities that create thrombi, causing coronary artery thrombosis and reducing coronary blood flow, which can lead to myocardial infarction [25,26]. In the present case, we thought that aVR elevation might indicate STEMI due to occlusion of the main branch of the left coronary artery. We quickly consulted a cardiologist and began treatment with nitrate and an anticoagulant. STEMI requires strict management with either thrombolytic therapy or percutaneous coronary intervention (PCI), with reperfusion being of utmost importance. PCI requires cardiac ventriculography. Ventriculography can be challenging to perform when a ventilation system is needed, as the medical staff involved must be adequately protected against infection, and a sudden change occurs [27]. Infection control protocols for COVID-19 prolong the time taken for STEMI patients to be treated [28]. Therefore, the risks and benefits of PCI for patients should be carefully considered. Furthermore, coagulation abnormalities can lead to myocardial injury in cells from fibroproliferation due to inflammation and tissue repair mediated by four protease-activated receptors [29].

The third possible mechanism involves hypoxemia caused by COVID-19-associated pneumonia. Myocardial injury can be caused by insufficient oxygen supply to the myocardium. When hypoxemia reduces the oxygen supply to the entire body, tachycardia and fever increase the demand for oxygen, and shock leads to hypotension [30].

Finally, the fourth possible mechanism involves arrhythmia. An electrolyte imbalance can induce arrhythmia, and drug-induced arrhythmia can occur when antimalarial (hydroxychloroquine) and antimicrobial (azithromycin) drugs are used as auxiliary therapies in patients with COVID-19 [31,32].

4. Conclusions

Myocardial injury caused by COVID-19 is associated with severe disease and a high mortality rate. Various underlying causes, such as acute coronary syndrome, myocarditis, and drug side effects, must be well differentiated when diagnosing myocardial damage due to COVID-19. Both direct and indirect effects may cause myocardial injury in a patient, and the mechanism of myocardial injury caused by COVID-19 is not well understood. Hence, further studies are needed to elucidate other possible mechanisms of myocardial injury in such patients. Therefore, clinicians should not only evaluate respiration but also assess the heart by performing a 12-lead ECG, echocardiogram, and blood tests to detect myocardial injury markers, which can help in predicting which patients will develop severe COVID-19.

Ethics approval and consent to participate

In this study, informed consent to publish was obtained from the patient.

Consent for publication

Informed consent was obtained from the patient's family for publication of this case report and any accompanying images.

Availability of data and materials

All data generated or analyzed during this study are included in this published article.

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Authors' contributions

YN treated the patient and was the primary author of this manuscript. TY, KK, AY, KH, and MY participated in the collection of data and supported the preparation of the manuscript. MS, SH, and BO assisted in the preparation of the manuscript by conducting a literature search and providing research advice. All authors have read and approved the final draft.

Declaration of competing interest

None.

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