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First case of COVID-19 infection with fulminant myocarditis complication: case report and insights

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Abstract

Background: The Coronavirus Disease 2019 (COVID-19) has been demonstrated as the cause of pneumonia. Nevertheless, it has not been reported as the cause of acute myocarditis or fulminant myocarditis.

Case presentation: A 63-year-old male was admitted with pneumonia and cardiac symptoms. He was genetically confirmed as COVID-19 by testing sputum on the first day of admission. He also had an elevated troponin-I (Trop I) level and diffuse myocardial dyskinesia along with decreased left ventricular ejection fraction (LVEF) on echocardiography. The highest level of Interleukin 6 was 272.40pg/ml. Bedside chest radiograph had typical ground-glass changes of viral pneumonia. The laboratory test results of virus that can cause myocarditis are all negative. The patient conformed to the diagnostic criteria of Chinese expert consensus statement for fulminant myocarditis. After receiving antiviral therapy and mechanical life support, the Trop I reduced to 0.10 g/L, and Interleukin 6 was 7.63 pg/ml. Meanwhile the LVEF of the patient gradually recovered to 68%.

Conclusion: COVID-19 patients may develop severe cardiac complications such as myocarditis and heart failure, and this is the first case of COVID-19 infection complicated with fulminant myocarditis. The mechanism of cardiac pathology caused by COVID-19 needs further study.

Keywords: COVID-19; coronavirus; fulminant myocarditis; infection; echocardiography.

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Background

A series of unexplained pneumonia cases have been reported in Wuhan, Hubei province, China since December 2019, which clinical manifestations very similar to viral pneumonia. A new coronavirus has been named the Coronavirus Disease 2019 (COVID-19) after sequencing analysis of samples from respiratory tract. Common symptoms are fever, cough, myalgia and/or fatigue. All patients had pneumonia and chest CT scan showed abnormalities. Complications include acute respiratory distress syndrome (ARDS), acute cardiac injury, and secondary infections[1, 2]. Here, we describe a case of COVID-19 infection complicated with fulminant myocarditis.

Case report

A 63-year-old male was admitted to the hospital due to coughing of white sticky sputum and fever up to 39.3℃, accompanied by shortness of breath and chest tightness after activity. He had no history of heart disease or hypertension. He had allergic cough for 5 years and previous smoking history of 20 years with 40 cigarettes per day and had quitted smoking for 20 years. He had recent travel history in Hubei province in China and stayed in Wuhan for half a day.

The blood gas analysis after admission showed pH 7.049, PCO2 76.4mmHg, PO2 66.2mmHg and SaO2 91.8%. Nasal and pharyngeal swabs, bronchoalveolar lavage fluid (BALF) and sputum were tested for common respiratory viruses and the result were all negative. In addition, blood samples showed elevated ALT (97U/L) and creatinine (157 mol/L), combined with hematuria, considering deranged liver and renal function. Bedside chest radiograph also had typical ground-glass changes of viral pneumonia (Figure 1). On the first day of admission, he was genetically confirmed as

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COVID-19 by testing sputum, as shown in Table 1.

Myocardial enzymes showed elevated troponin-I (Trop I) (11.37 g/L), myoglobin (Myo) (390.97 ng/mL) and n-terminal brain natriuretic peptide (NTBNP) (22600 pg/ml) (Figure 2). The electrocardiogram showed sinus tachycardia and no ST segment elevation (Figure 3). Bedside echocardiography showed an enlarged left ventricle (61mm), diffuse myocardial dyskinesia along with low left ventricular ejection fraction (LVEF) (32%), pulmonary hypertension (44mmHg), decreased IVC collapse rate, and no decrease in right cardiac function (Figure 4 and 5). No pericardial effusion was observed.

The diagnosis was considered as severe pneumonia, ARDS, fulminant myocarditis and multiple organ dysfunction syndrome (MODS). The treatment regimen was ventilatory support, high-flow oxygen, lopinavir-ritonavir antiviral therapy, Interferon α-1b, Methylprednisolone, immunoglobulin, piperacillin-tazobactam and continuous renal replacement therapy (CRRT). Noted that 11 days after admission, however, the patient's clinical symptoms and blood oxygen status were still poor, the ventricular septum thickened to 14mm, and Interleukin 6 increased by 272.40 pg/ml. Therefore, extracorporeal membrane oxygenation (ECMO) was used to reduce the cardiopulmonary burden. The rotating speed is 3000 revolutions per minute, the flow rate is 3.65L/min, the air flow rate is 3.5L/min, and FiO2 is 80%. Blood test three days later revealed the Trop I reduced to 0.10 g/L, NTBNP 750 pg/ml and Interleukin 6 was 7.63 pg/ml. After treatment, the LVEF of the patient gradually recovered to 68%, and the left ventricle and wall thickness to the normal range.

Discussion

The clinical manifestations of COVID-19 has great resemblance with SARS-CoV. Severe patients

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can develop ARDS, requiring ICU hospitalization and oxygen therapy. Patients with COVID-19 may developed cardiac symptoms, whereas fewer patients with MERS-CoV or SARS-CoV infection had cardiac symptoms[3, 4]. Fulminant myocarditis is mainly caused by a variety of virus infection, which can lead to severe heart failure. It is characterized by rapid occurrence of cardiogenic shock and hypotension, with a mortality rate of up to 50%-70%[5]. In this case, the patient had the following features: sudden attacks, obvious symptoms of viral infection, rapid emergence of severe hemodynamic disorders, severe myocardial injury, diffuse decreased ventricular wall movement. The above features all accord with the diagnostic criteria of fulminant myocarditis[5].

After clinical observation of 334 cases with COVID-19, including 20 cases of severe pneumonia, 12 cases of critical pneumonia, only one patient was found to have reduced LVEF and was diagnosed with fulminant myocarditis. Thus, we suspect that fulminant myocarditis either appears early or does not appear. Cardiac damage is not uncommon in patients with coronavirus infection, but progression to such severe myocarditis is rare. There were studies that confirmed coronavirus infection can cause myocarditis and even congestive heart failure[6]. It has been reported that some patients with SARS have temporary abnormal myocardial enzyme[7]. In a report from Saudi Arabia, 28% of MERS cases have underlying cardiac disease[4]. Moreover, a case demonstrated that MERS-CoV may cause acute myocarditis and acute-onset heart failure[8]. In this case, the patient had no history of heart disease, therefore the decreased cardiac function is likely to be caused by COVID-19 infection.

Pathological changes in heart tissue may be due directly to the virus replication in the myocardium or indirectly to systemic responses to respiratory failure or to harmful immune responses caused by

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viral infection, which can vary from different virus. For instance, SARS-CoV can result in myocardial inflammation and injury related to the down regulation of the ACE2 system, and this may cause the myocardial dysfunction and adverse cardiac outcome[9]. An animal model study clearly stated that MERS-CoV RNA could be seen in cardiac tissue, implying direct cardiac pathology.

Chinese expert consensus statement indicated that direct damage is more common in neonates, whereas immunogenic damage is a major factor in adults[5]. The rapid recovery of cardiac structure and function without significant decrease or even slight increase in viral load suggests that apart from viral replication in the myocardium, it is possible that immune response/cytokine storms may also play a significant role. Cytokine storm refers to the phenomenon of rapid and massive production of various cytokines in body fluid after the organism is infected with microorganisms, which is an important cause of acute respiratory distress syndrome and multiple organ failure[10]. A study showed that after SARS-CoV infection, interferon-related cytokine storms may be involved in the immunopathology of SARS patients[11]. The patient in this case had significantly elevated interleukin, suggesting the presence of cytokine storms. Cytokine storms may lead to increased vascular wall permeability and myocardial edema, this may explain the thickening of the interventricular septum in this patient. In view of the patient's rapid recovery, the myocarditis was considered to be transient damage from viral infection. The use of CRRT removes part of the cytokines from the blood, reducing the excessive immune response of cytokines in the body and further reducing the damage of myocardium. Furthermore, a study shows complete atrioventricular block, ventricular tachycardia or fibrillation are risk factors for in-hospital death in fulminant myocarditis patients. Extensive QRS waves also predict poor outcomes in such cases[12]. The

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absence of such electrocardiogram anomaly in this case may have contributed to the rapid improvement in the patient's heart condition.

Conclusion

COVID-19 patients may develop severe cardiac complications such as myocarditis and heart failure, and this is the first case of COVID-19 that is complicated with fulminant myocarditis. The lessons learn from this case: First, the heart is the second target organ besides the lung. It can not only show abnormal myocardial enzymes, but also show structural and functional damage. Second, immune injury may be the main cause of myocardial injury caused by virus infection. The outbreak of myocarditis may occur either early or never. Third, the prognosis of such patients may be better if no malignant arrhythmia is present. The important question as to whether COVID-19 can cause direct cardiac pathology needed further study.

Ethics approval and consent to participate

The study was approved by the Ethics Committee of Shenzhen Third People's Hospital on 11th Feb, 2020 (No. 2020-006). Written informed consent was obtained from the patient.

Consent for publication

Written informed consent was obtained from the patient for publication of this case and any accompanying images. A copy of the written consent is available for review by the Editor of this journal.

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Conflict of interest

On behalf of all authors, the corresponding author states that there is no conflict of interest.

Availability of data and material

All available information is contained within the present manuscript.

Author Contributions

Jia-hui Zeng and Cheng Feng had full access to all of the data in the case and take responsibility for the integrity and the accuracy of the data.

Concept and design: Lei Liu, Cheng Feng, Yao Wang, Chang-Feng Dong.

Acquisition, analysis, or interpretation of data: All authors.

Drafting of the manuscript: Jia-hui Zeng.

Critical revision of the manuscript for important intellectual content: Jing Yuan, Fu-Xiang Wang, Wei-Bo Wu, Hong Gao, Ying-Xia Liu.

Supervision: Lei Liu, Ying-Xia Liu, Cheng Feng.

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Day after admission	Pharyngeal swab	Sputum	BALF
1	-	22	/
2	-	/	/
3	/	/	24
4	30	22	/
5	20	/	/
6	-	/	/
7	/	29	/
8	-	-	/
9	33	/	/
10	31	/	/
11	/	/	27
12	27	/	24
13	/	/	27

Table 1. The cycle threshold of respiratory specimens. "-": negative; "/": untested; BALF: bronchoalveolar lavage fluid.

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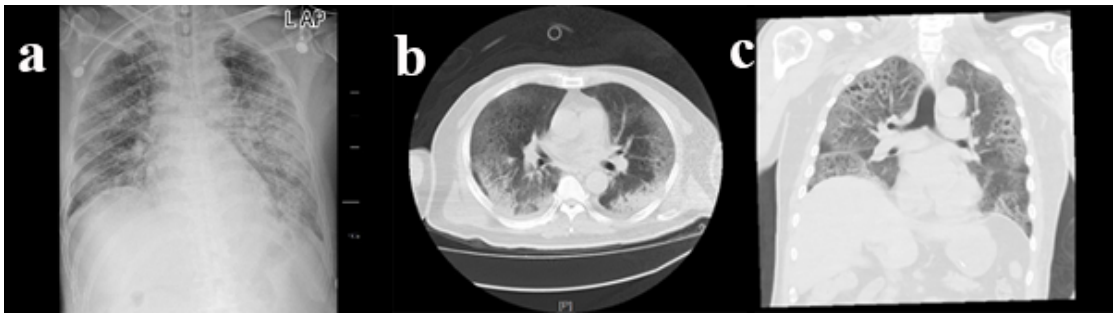

Figure 1. a: bedside chest radiograph on first day of admission; b and c: computerized tomography on the 9th day showed typical ground-glass changes of viral pneumonia.

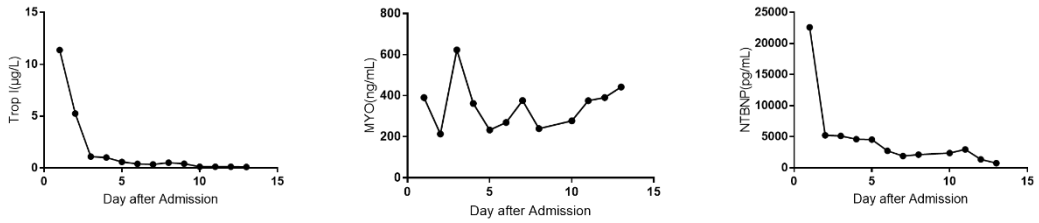

Figure 2. The line chart of the myocardial enzyme. Trop I: troponin-I; MYO: myoglobin; NTBNP: n-terminal brain natriuretic peptide. Trop I and NTBNP decreased gradually while no significant decrease in MYO was observed.

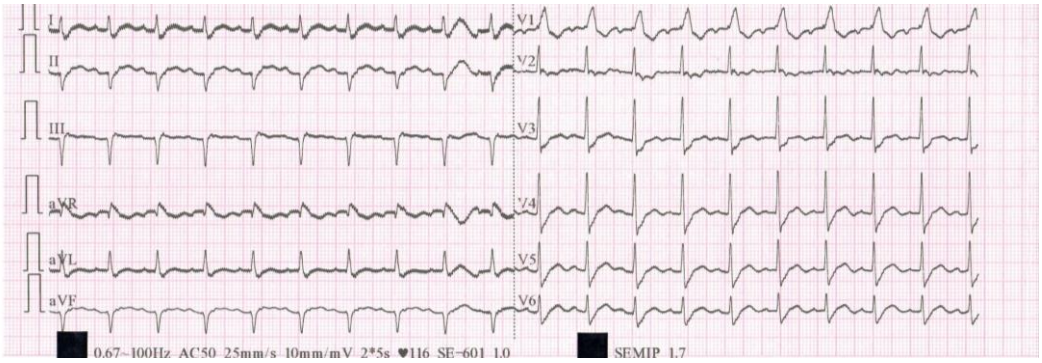

Figure 3. The electrocardiogram showed sinus tachycardia and no ST segment elevation.

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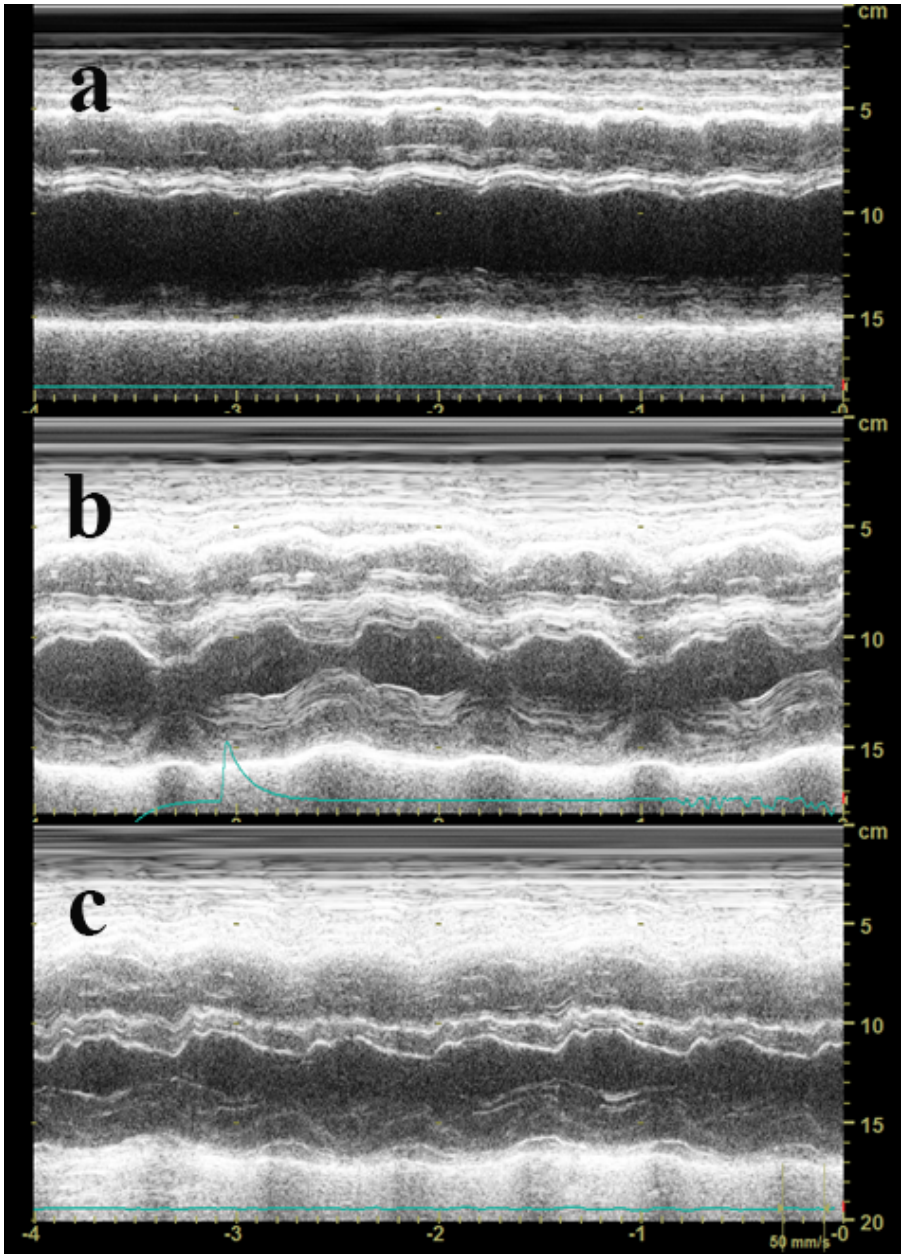

Figure 4. The echocardiographic left ventricular M-mode images of the first day, the 10th day and the 17th day after admission. a: left ventricular diameter was enlarged and ejection fraction was decreased on first day of admission; b: this figure shows edema of left ventricular wall and improvement of LVEF. c: the last examination of bedside echocardiography shows normal LVEF and wall thickness.

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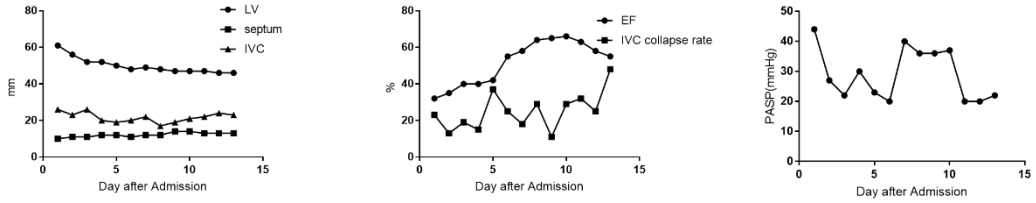

Figure 5. The line chart of the echocardiography measurements. LV: left ventricular end-diastolic diameter; IVC: inferior vena cava; EF: ejection fraction; PASP: pulmonary artery systolic pressure. LV decreased while EF and IVC collapse rate increased gradually. The interventricular septum gradually thickened to a maximum thickness of 14mm.