Journal of Cardiothoracic Surgery

CASE REPORT

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Heart transplantation under mechanical circulatory support for fulminant myocarditis: a Case Report

Zhaohua Yang[1], Shuyang Lu[1], Gao Liu[1], Hongqiang Zhang[1] and Chunsheng Wang[1*]

Abstract

Fulminant myocarditis has been defined as the clinical manifestation of cardiac inflammation with rapid-onset heart failure and cardiogenic shock. We report on the case of a 17-year-old boy with hemodynamic derangement and cardiac arrest due to fulminant myocarditis. After about 2 h of intensive cardiopulmonary resuscitation, with 13 days of extracorporeal membrane oxygenation support, the patient finally bridged to orthotopic heart transplantation. The patient recovered uneventfully and was discharged 37 days after transplantation. The explanted heart revealed diffuse lymphocytic infiltration and myocyte necrosis in all four cardiac chamber walls confirming the diagnosis and identifying the underlying cause of fulminant myocarditis.

Keywords Fulminant myocarditis, Heart transplantation, Extracorporeal cardiopulmonary resuscitation, Cardiac arrest

Introduction

Fulminant myocarditis (FM) is an uncommon syndrome characterized by sudden and severe diffuse cardiac inflammation. It often leads to death resulting from cardiogenic shock, ventricular arrhythmias, or multi-organ system failure [1]. Patients with FM usually need immediate and aggressive mechanical-device support to bridge to recovery, or even to transplantation [2]. Here, we describe the clinical presentation and management of a young fulminant myocarditis patient with acute heart failure and severe hemodynamic compromise support with extracorporeal membrane oxygenation (ECMO), which ultimately bridging to a successful orthotopic heart transplantation.

*Correspondence:
Chunsheng Wang
wangchunsheng_md@163.com
[1]Department of Cardiac Surgery, Zhongshan Hospital, Fudan University, No. 180 Fenglin Rd, Shanghai 200032, China

Case presentation

A 17-year-old boy without a previous history of cardiovascular disease or any other medical history had a feeling of having a common cold, general malaise, and epigastric discomfort. Two days later, he came to the local emergency department for high temperature (39.1℃), tachycardia, increasing shortness of breath, cough, nausea, vomiting, and diarrhea. At the time of presentation, his vital signs included a heart rate of 107 bpm, blood pressure of 98/54 mmHg, pulse oximetry of 94% SpO_2, respiratory rate of 20 breaths per minute, and body temperature of 38.6℃. Laboratory results were significant for elevated cardiac troponin I>100 ng/mL, creatine kinase MB isozyme at 33 ng/mL, creatinine at 244 umol/L, serum myoglobin at 13,400 ng/mL, C-reactive protein at 16.59 mg/L and pro-B-type natriuretic peptide at 8459 pg/mL. The initial electrocardiogram noted sinus tachycardia and a diffuse elevation of the ST-segment. The portable transthoracic echocardiogram demonstrated a left ventricle with global hypokinesia, severely reduced systolic function, an ejection fraction of

20% (LV end-diastolic dimension of 56 mm, end-systolic dimension of 50 mm, and wall thickness of 9 mm), without valvular heart disease and pericardial effusion. The initial workup revealed a negative result of SARS CoV-2 polymerase chain reaction testing and an elevated Coxsackie B virus titer.

Considering a worsening cardiovascular status and with positive viral titers, there was a high suspicion of acute fulminant myocarditis and he was transferred to the intensive care unit (ICU). Shortly after admittance, the patient became hypotensive and hypoxemic with clinical signs of pulmonary edema. His blood pressure dropped to 85/40 mmHg and SaO_2 level dropped below 80% on the pulse oximetry (nasal cannula, oxygen 8 L/min), which led to intubation and invasive mechanical ventilation. There were signs and symptoms of shock and end-organ hypoperfusion. Bedside chest X-ray showed ground glass opacities in the periphery of both lungs (Fig. 1A). Despite the use of high-dose inotropic agents (dobutamine plus norepinephrine), his hemodynamics remained unstable. Hypotension progressed accompanied by ventricular tachycardia and ventricular fibrillation, then in-hospital cardiac arrest developed. Standard cardiopulmonary resuscitation (CPR) was commenced. Despite 120 min of cardiopulmonary resuscitation, the cardiac arrest persisted, and normal cardiac rhythm was not recovered. The patient received a veno-arterial extracorporeal membrane oxygenator (VA-ECMO) via the femoral artery and vein. Subsequent emergency coronary angiography revealed no evidence of coronary artery lesions or vasospasm.

On the 4th day of ECMO support, the patient was alert enough to recognize his family members and obey simple commands with full recovery of consciousness, but the arterial pulsation curve completely disappeared. Follow-up echocardiography showed global hypokinesia of the left ventricle with an ejection fraction of 16% and the patient received an intra-aortic balloon pump (IABP). However, Cardiac function did not improve and the worsening of the condition led to multiple organ failure. Continuous veno-venous hemodialysis was applied due to metabolic acidosis and oliguria.

On the 8th day of mechanical circulatory support, another echocardiogram showed an increase in LV cavity dimensions without any effective contraction, with severe spontaneous echo-contrast in the LV cavity, and borderline thickened LV walls (11 mm). The biomarkers of myocardial injury were still significantly elevated. MB isoenzyme of creatinine kinase (CK-MB) and cardiac troponin-T elevated to 29 ng/mL and >10.0 ng/mL, respectively. C-reactive protein was 68.8 mg/L and procalcitonin was 2.69 ng/ml. NT-proBNP was 6419 pg/mL. On hospital day 10, after a preliminary evaluation revealed without any previous sign of cardiac improvement and no major contraindications to heart transplantation, he was urgently listed for heart transplantation. On hospital day 13, the patient successfully received an orthotopic heart transplantation. The donor was a young girl (age 14 years) who had been fatally brain injury in an accident. The donor heart was flushed with the University of Wisconsin (UW) solution at 0–4 °C, then immersing it into preservation solution at the same temperature until transplantation. Allograft cold ischemic time was 150 min, cardiopulmonary bypass (CPB) duration of 95 min and cross clamp time of 32 min. His immediate postoperative support included dobutamine 10 ug/kg/

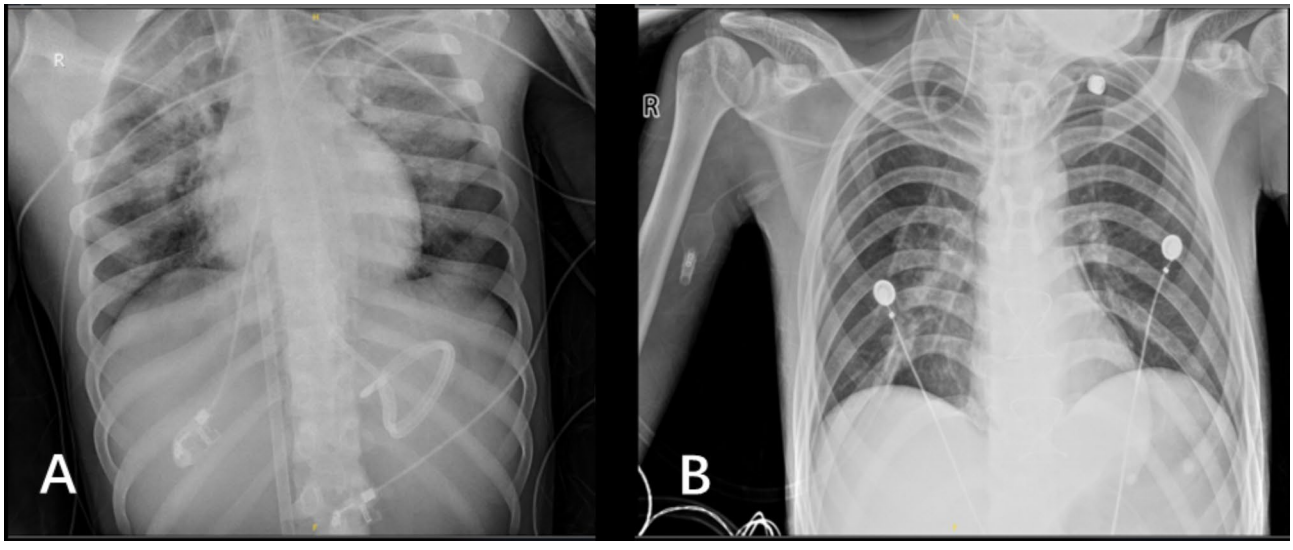

Fig. 1 (**A**) Chest X-ray shows an enlarged heart, pulmonary congestion, and edema that appears as cloudy white areas extending to the outer portions of the lungs before transplantation. (**B**) chest X-ray shows that the heart shadow is of regular size and shape, and the lung fields appear clear after heart transplantation

min, norepinephrine 0.2 ug/kg/min, inhaled nitric oxide 20 ppm, but no mechanical circulatory support. ECMO and IABP were successfully weaned off during the operation. He was extubated by postoperative day 6, and the acute renal failure was completely resolved after two weeks. chest X-ray didn't show any abnormalities of lung, heart, or chest wall diseases (Fig. 1B).

Pathologic examination of the explanted heart showed diffuse infiltration of inflammatory cells, mostly in myocardium areas but focally extended to endocardium and pericardium, and cardiomyocyte damage and necrosis accompanied (Fig. 2A). The infiltrating inflammatory cells were dominated by lymphocytes. Most of lymphocytes were T phenotype ($CD3^+$), with only a few associated B lymphocytes ($CD20^+$) and Natural killer cells ($CD56^+$). (Fig. 2B, C, D). Histologic findings were compatible with fulminant myocarditis of the Dallas criteria.

The patient fully recovered and was discharged from the hospital for cardiovascular rehabilitation without any neurological sequela or cardiac symptoms by postoperative day 37.

Discussion

Fulminant myocarditis is a rare and severe form of myocarditis that develops rapidly and can lead to acute heart failure and death [2]. It is a challenging clinical condition to diagnose and treat. In this case report, we described a 17-yr-old fulminant myocarditis patient presenting shock mimicking acute coronary syndrome, about 2 h of intensive cardiopulmonary resuscitation, with 13 days of extracorporeal membrane oxygenation support, finally successful bridging to orthotopic heart transplantation; the pathological substratum revealed diffuse lymphocytic infiltration and myocyte necrosis in the all four cardiac chambers. The postoperative pathology further confirmed the diagnosis of FM. We speculated that the following factors might have contributed to his successful recovery from FM.

First, in this case, the patient experienced respiratory and circulatory failure during the hospital visit, coupled with a significant decrease in cardiac function indicated by cardiac ultrasound examination, resulting in high suspicion of FM. He was immediately transferred to the ICU ward, creating conditions for subsequent cardiac arrest rescue. The literature shows that early effective cardiopulmonary resuscitation is closely related to the prognosis of cardiac arrest [3]. Times to initiation of CPR greater than 2 min were associated with a survival of 14.7% as compared with 17.1% if CPR was begun in 2 min or less [4]. The survival rate was only 4% after 6 min resuscitation, and it was almost impossible to succeed after 10 min resuscitation [5]. For this patient, CPR started as soon as

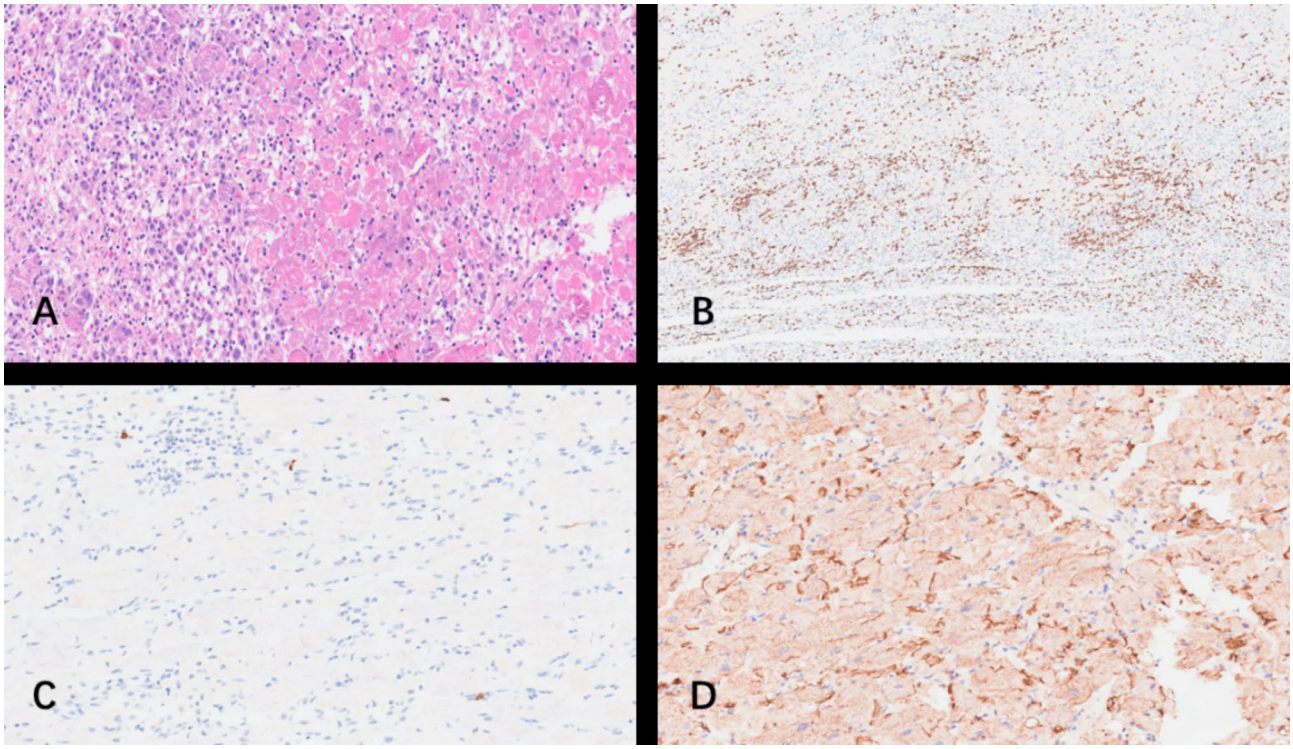

Fig. 2 Pathological analysis of the explanted heart. Histology: **A.** (H&E stains X200) Pathologic examination of the explanted heart revealed an inflammatory infiltration predominantly composed of Lymphocytes and cardiomyocyte damage and necrosis accompanied. immunohistochemical staining showed that most of lymphocytes were T phenotype $CD3^+$(**B**, X200), with only a few associated B lymphocytes $CD20^+$(**C**, X200) and Natural killer cells $CD56^+$(**D**, X200)

cardiac arrest occurred, which ensured adequate blood perfusion to vital organs, particularly the heart and brain. Our patient survived without any significant neurological sequelae. Second, although the patient underwent timely cardiopulmonary resuscitation, after two hours of rescue, the autonomic cardiac rhythm could not be restored and blood pressure could not be maintained, so ECMO was implanted. Following the current AHA guidelines, mechanical circulatory support is often necessary as patients with this disease present with hemodynamic instability and are even in cardiac arrest or a pulseless arrhythmia [6]. Mechanical assist devices can lead to favorable alterations in cellular and organ geometry and reduced wall stress, with improved cardiomyocyte function and patient survival. An extracorporeal rather than an intracorporeal VAD is often chosen because of the ease by which this type of device is implanted and/or removed, and their ability to provide biventricular support. In such a situation, ECMO will enable the patient to be stabilized and allow time to assess end-organ damage and the likelihood of recovery. Afterload mismatching during veno-arterial extracorporeal membrane oxygenation (VA-ECMO) can result in left ventricular (LV) distention, which may increase patient mortality, morbidity, and extracorporeal membrane oxygenation (ECMO) duration [7]. To alleviate LV distention, an intra-aortic balloon pump (IABP) was placed. Third, although fulminant myocarditis may be more likely to lead to full recovery than other types of acute myocarditis, often within 2 weeks, if there is not sufficient myocardial functional recovery within the limited, tolerable ECMO period, permanent treatment with a ventricular assist device implanted or heart transplantation should be considered [2]. In this case, the daily echocardiograms revealed no contractile improvement of LV myocardium, and troponin I level was not decreased. Considering that there is no hope for myocardial recovery, it is necessary to implant a ventricular assist device or heart transplantation. In China, a VAD is not typically available, resulting in a default choice for heart transplantation. Approximately 2 weeks later, he successfully underwent heart transplantation. Histopathological appearance showing over 80% necrosis of the myocardial cells.

The underlying etiology of fulminant myocarditis includes viral infection, autoimmune disease, and/or exposure to various drugs and toxins [8]. Coxsackievirus and adenovirus are the most common viral causes [9]. Fulminant myocarditis is also considered a serious adverse event after COVID-19 infection [10]. In this case, the initial workup revealed an elevated Coxsackie B virus titer. Based on this, we speculated that the inflammatory response was triggered by the Coxsackie virus, which could directly infect the myocardium or cause an autoimmune reaction. Histologically, fulminant myocarditis is characterized by diffuse and severe inflammatory infiltration of the myocardium, with necrosis of myocytes and interstitial edema. There may also be evidence of fibrin deposition, thrombosis, and microvascular damage. In this case, we found that diffuse and severe inflammation of the myocardium with infiltration of immune cells such as lymphocytes, monocytes, and polymorphonuclear leukocytes. Inflammatory infiltrate is widespread and the presence of diffuse necrotic myocardial cells accounted for almost 80% of the myocardium, which also led to a loss of contractile function and the inability of the myocardium to restore normal function. Histologic findings of the explant heart confirm the diagnosis and identify the underlying cause of inflammation.

In summary, fulminant myocarditis is a severe and rapidly progressing inflammation of the myocardium, often leading to cardiac dysfunction and failure. Given the initial course can be insidious (flu-like symptoms) and followed by an abrupt circulatory collapse, there is a rapid diagnostic challenge for fulminant myocarditis. Timely diagnosis and prompt initiation of aggressive support are crucial to improve the outcomes in patients with fulminant myocarditis. In severe cases, mechanical circulatory support devices may be necessary to assist the heart in pumping blood. For some patients, a heart transplant may be needed.

Author contributions

Zhaohua Yang, Shuyang Lu and Gao Liu performed the heart transplantation and participated in postoperative management for this patient. Zhaohua yang wrote the main manuscript. Hongqiang Zhang prepared Figs. 1 and 2. Chunsheng Wang supervised this work. All authors discussed the results and contributed to the final manuscript.

Funding

Not applicable.

Data availability

No datasets were generated or analysed during the current study.

Declarations

All authors disclosed no relevant relationships.

Ethics approval and consent to participate

Written informed consent was obtained from the patient for the publication of this case report.

Competing interests

The authors declare no competing interests.

Received: 22 January 2024 / Accepted: 13 August 2024
Published online: 24 August 2024

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