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Case Report

Biopsy detection and clinical management of acute lymphocytic myocarditis in pregnancy



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ABSTRACT

Acute lymphocytic myocarditis in pregnancy is rare, with no established management guidelines to date. A 40-year-old woman at 34 weeks of gestation complained of shortness of breath upon exertion. An electrocardiogram revealed broad ST elevation, and echocardiography showed diffuse impairment of left ventricular contractility. The patient was immediately transferred to our hospital for suspected takotsubo cardiomyopathy. We considered myocarditis based on the patient's prior cold-like symptoms and additional examination. Myocardial biopsy revealed lymphocyte infiltration, which confirmed acute lymphocytic myocarditis. Although there were no signs of heart failure or conduction disturbance under catecholamine, her hemodynamics were weak. Emergency cesarean section was performed because of possible hemodynamic failure during the remaining course of pregnancy. Both the mother and baby were discharged without any subsequent events. If acute myocarditis is suspected during pregnancy, prompt myocardial biopsy is crucial for timely pathological diagnosis and treatment decisions. Clinicians should consider premature delivery prior to a possible failure in maternal hemodynamics.

<Learning objective: Acute lymphocytic myocarditis in pregnancy is rare; the condition is difficult to diagnose, and management protocols have not been established. If acute myocarditis is suspected during pregnancy, early myocardial biopsy is vital for prompt diagnosis and treatment decisions. Premature delivery should be considered if maternal hemodynamics is expected to destabilize.>

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Introduction

Acute lymphocytic myocarditis is of the viral origin and can manifest in various severities, ranging from a slight increase in the myocardial enzyme levels to cardiogenic shock due to a rapid decline in cardiac function. However, the onset of lymphocytic myocarditis is not well understood; even young individuals may experience the condition because of a common cold. Acute lymphocytic myocarditis during pregnancy is rare, and no relevant criteria for delivery method or timing have been established. We herein describe a case of acute lymphocytic myocarditis in

pregnancy and successful management of the mother and child by cesarean section.

Case report

A 40-year-old woman (gravida 3, para 2) experienced cold-like symptoms at 32 weeks and 4 days of gestation and reported palpitations and shortness of breath upon exertion from 33 weeks of gestation. During a regular visit to the hospital at 34 weeks and 0 days of gestation, an electrocardiogram revealed broad ST elevation and echocardiography showed diffuse impairment of left ventricular contractility. The patient was immediately transferred to our hospital for suspected takotsubo cardiomyopathy. Upon admission, the blood pressure was 92/72 mmHg, pulse was 92 bpm, body temperature was 36.2 °C, and peripheral oxygen saturation was 98% (in room air). The patient's respiratory and circulatory conditions were relatively stable. No physical signs of

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heart failure, such as edema, and abnormal heart or chest sounds on auscultation were noted. Significant findings were as follows: aspartate transaminase level: 32 IU/L, white blood cell count 5280 cells/ μ L, C-reactive protein level: 1.53 mg/dL, creatine kinase (CK) level: 726U/L, creatine kinase muscle/brain (CK-MB) level: 107 ng/mL, troponin T level: 3.320 ng/mL, and N-terminal pro-brain natriuretic peptide level: 10581.0 pg/mL. Moreover, the electrocardiogram revealed low potential in the limb leads and broad ST elevation without obvious conduction disturbance (Fig. 1A). Echocardiography showed diffuse impairment of left ventricular contractility especially around the apical area (Fig. 1B) (Supplementary data 1, 2). A myocardial biopsy on admission day 2 showed a high lymphocytic infiltration in the myocardial stroma, cardiomyocytes were found to be degenerating, suggestive of necrosis (Fig. 1C). A final diagnosis of acute lymphocytic myocarditis was made on the basis of abundant lymphocytic infiltration in the myocardium. Right heart catheter examination revealed a pulmonary artery wedge pressure of 17 mmHg and cardiac index of 1.78 L/min/m², which were high and low, respectively, for a young pregnant woman.

The treatment course of the patient is shown in Fig. 2. We started dobutamine (2 γ) and large amounts of gamma globulin (2 g/kg for 2 days). Although hemodynamics could be managed, the risk of conduction disturbance and ventricular arrhythmia prompted an emergency cesarean section on admission day 3 (34 weeks and 2 days of gestation). The procedure was successfully completed under general anesthesia, with 550 mL of blood loss and no dynamic circulation collapse. A female infant weighing 2142 g was delivered, with Apgar scores at 1 and 5 min of 8 and 9, respectively. Before surgery, we had observed ameliorations in the cardiac muscle enzymes and ST elevation on electrocardiography. Therefore, dobutamine was gradually reduced after confirming an improvement in the cardiac function and subsequently switched to an angiotensin-converting-enzyme inhibitor and β -blocker for myocardial protection. The electrocardiogram at the time of discharge showed QRS width shortening and improved ST change (Fig. 3A). A follow-up myocardial biopsy on day 21 after admission revealed diminished lymphocytic infiltration, although with moderate interstitial fibrosis (Fig. 3B, C). Right heart catheter examination on the same day showed improved cardiac index (1.99 L/min/m²). The patient was discharged 24 days after admission. The baby was discharged at the age of 38 days, although transient hyperventilation and prolonged periodic breathing were noted.

In general, the antibody titer of the causal virus in acute viral myocarditis increases by a factor of 4. In our patient, Influenza type A antibodies increased four-fold at discharge (at admission: 4 times, at discharge: 16 times), and the patient, therefore, considered to have had influenza A virus infection. At 10 months after discharge, the patient's cardiac function improved to the lower limit of normal (ejection fraction 58%) and there were no signs of heart failure.

Discussion

There were two important points in this case: first, myocardial biopsy plays an important role in the diagnosis of acute myocarditis, and second, termination of pregnancy should be considered in patients with acute lymphocytic myocarditis when appropriate.

Myocardial biopsy is the gold standard for a definitive pathologic diagnosis of acute myocarditis. Identification of acute myocarditis is often based on the Dallas criteria, which is described as the infiltration of myocardial inflammatory cells (with necrosis or degeneration of the adjacent cardiomyocytes) that are not typical of ischemic heart disease associated with coronary artery disease [1]. In the present case, myocardial biopsy revealed inflammatory cell infiltration in the myocardium. Although biopsies are highly invasive, they should be considered for diagnostic decisions, especially in cases of suspected acute myocarditis. During histological classification, lymphocytes mostly result from viral infections, whereas giant cell, eosinophilic, and granulomatous myocarditis result from cardiotoxic substances, drugs, and autoimmune influences. The lymphocytic infiltration indicated viral myocarditis in the present case. Approximately 20 viruses are known to cause acute myocarditis; however, myocarditis due to the influenza virus is reportedly rare. The condition also presents a wide range of clinical symptoms depending on the spread and activity of inflammation; therefore, the prediction of clinical outcomes is often difficult. Young individuals, especially females, are highly susceptible to severe forms of myocarditis due to the influenza virus [2]. As the present case was a pregnant woman, we treated her in consideration of a severe outcome. An earlier report implicated influenza A as the causative virus in 2% of myocarditis cases [3], and approximately 10% of patients suffering from influenza A virus infection have been suggested to experience myocarditis [4]. Most cases of viral cardiomyopathy exhibit only minor cold symptoms, with no

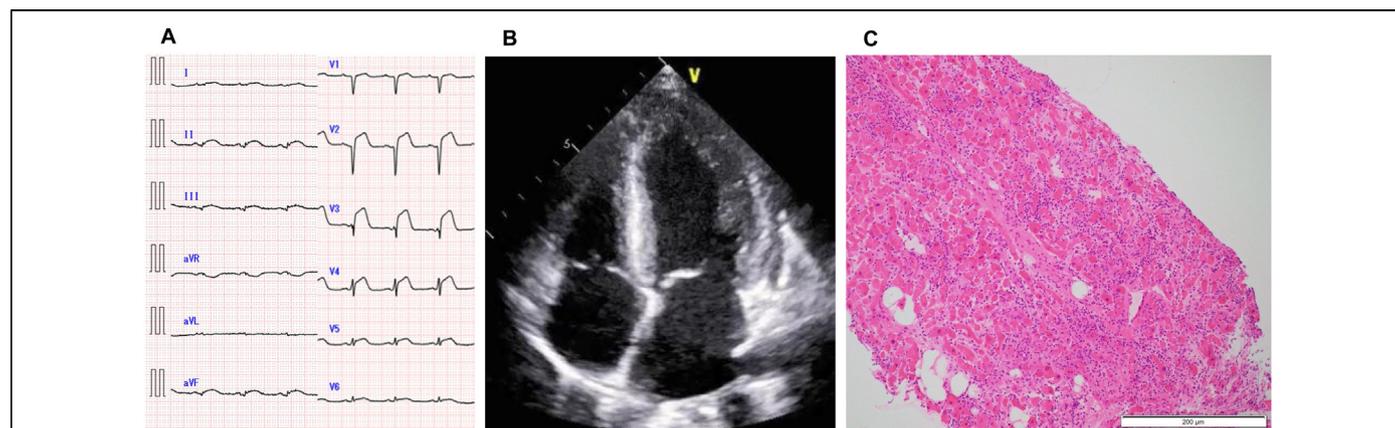


Fig. 1.

(A) Electrocardiogram at the time of admission showing normal sinus rhythm with decreased voltage in the R waves and ST elevation in all leads with especially V2–5. No obvious conduction disturbance is noted (QRS width: 84 ms, QTc: 373 ms). (B) Echocardiogram at the time of admission showing diffuse wall thickening in the left ventricle and decreased motion around the apical area not affecting the coronary artery region. Left ventricular ejection fraction was 40%, and outflow tract velocity time integral was 11 cm. (C) Microscopic image of the initial biopsy tissue on admission day 2. High degree of lymphocytic infiltration in the myocardium without deposition of eosinophils, giant cells, or amyloids, is observed, suggesting acute lymphocytic myocarditis.

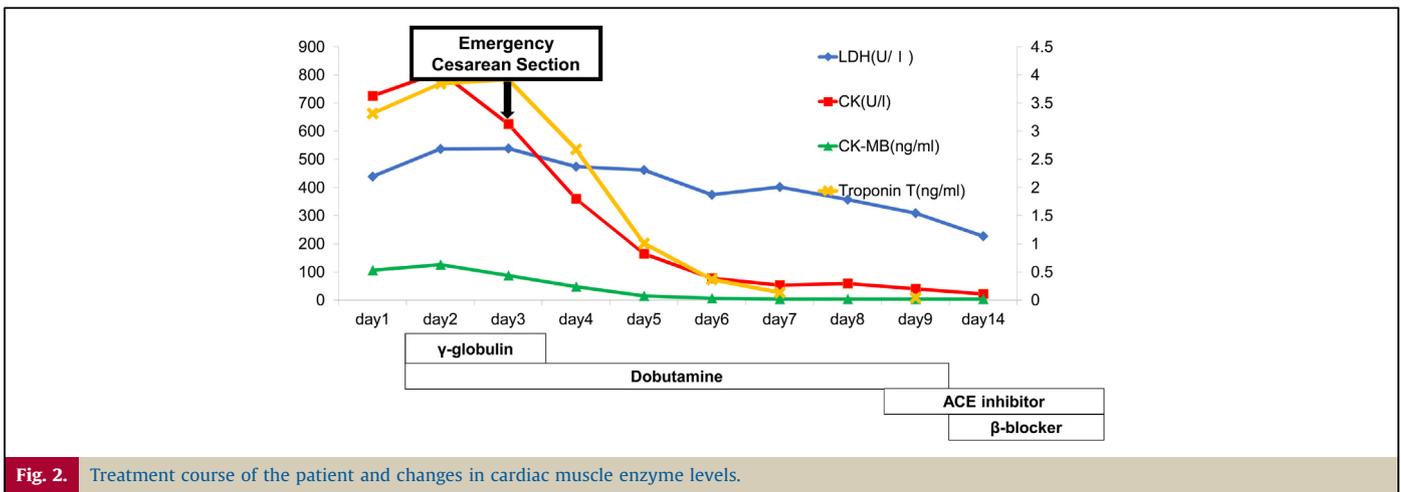


Fig. 2. Treatment course of the patient and changes in cardiac muscle enzyme levels.

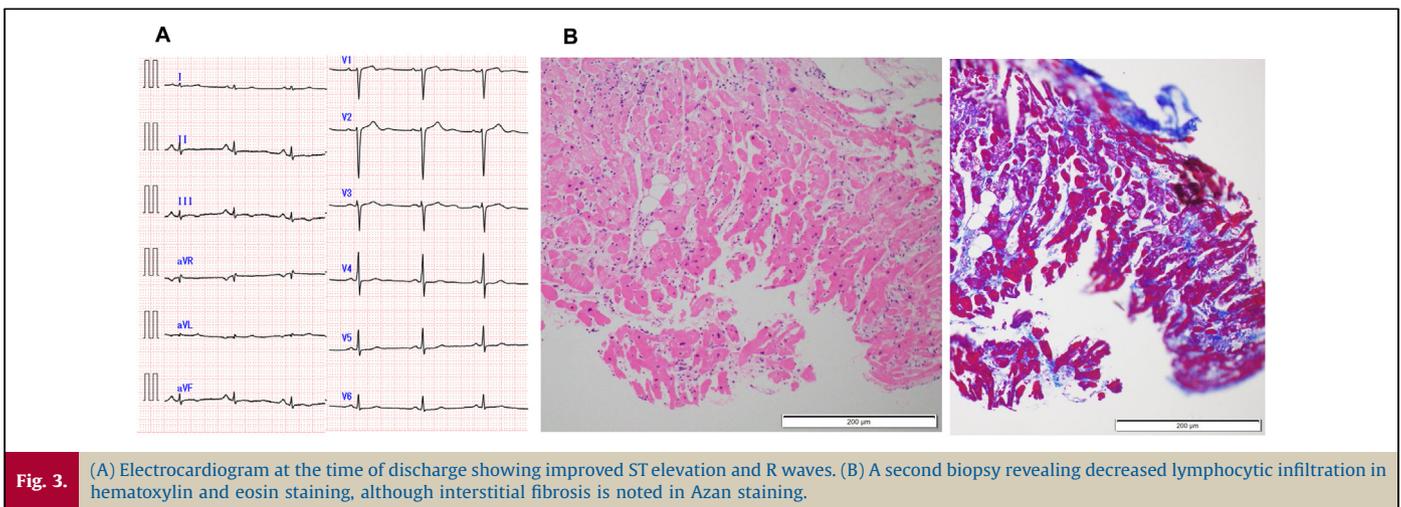


Fig. 3. (A) Electrocardiogram at the time of discharge showing improved ST elevation and R waves. (B) A second biopsy revealing decreased lymphocytic infiltration in hematoxylin and eosin staining, although interstitial fibrosis is noted in Azan staining.

changes in the electrocardiogram findings despite elevated levels of myocardial deviation enzymes, such as CK, CK-MB, and troponin I and T. However, studies have reported the progression of influenza A cardiomyopathy to fulminant myocarditis. Patient outcomes also vary, starting from fatal results regardless of the use of extra-corporeal membrane oxygenation (ECMO) and intra-aortic balloon pumping (IABP) to the complete recovery of cardiac function without intensive treatment. Several reports have attempted to predict the severity of viral myocarditis; however, the results have been inconclusive. Clinicians must, therefore, be vigilant for deteriorations in the patient condition.

There have been few reports on acute myocarditis during pregnancy, and no consensus exists on delivery strategies after 34 weeks of gestation. Some studies have described abortion [5], whereas some have also reported cases in which the mothers and their children were saved by cesarean section [6]. Both cases with abortion and successful saving of mother and child were reported.

However, the optimal mode of delivery for survival rate improvement remains unclear. While vaginal delivery is more desirable than cesarean section in pregnant women with heart disease because of lesser burden on the heart [7], women with heart failure or unstable hemodynamics may require urgent delivery by cesarean section [8]. If the use of cardiotoxic drugs or ancillary circulation devices is anticipated, the termination of pregnancy by preterm delivery, may be desirable [9]. Fulminant

acute myocarditis may cause a sudden deterioration in the hemodynamics, and ancillary circulation will place the mother at an increased risk of her life. Therefore, premature birth should be considered for maternal safety.

In the reported case, the patient survived the acute phase of acute lymphocytic myocarditis by early delivery. During pregnancy, patient hemodynamics may become unstable, and there is an uncertainty among clinicians regarding the timing and method of delivery. Further cohort study is needed including greater number of cases to establish an adequate management strategy for acute myocarditis in pregnant women.

In conclusion, we encountered a case of acute lymphocytic myocarditis in which both the mother and baby were successfully managed by emergency cesarean delivery. Prompt myocardial biopsy played a vital role in diagnosing and treating a patient's myocarditis. A biopsy should also be considered for the differentiation of myocarditis from other cardiomyopathies, such as takotsubo cardiomyopathy and peripartum cardiomyopathy. In cases with an elevated risk of maternal hemodynamic alterations and ancillary circulation, urgent delivery should be considered.

Conflict of interest

The authors declare that there is no conflict of interest.

Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:<https://doi.org/10.1016/j.jccase.2019.07.010>.

References

- [1] Aretz HT, Billingham ME, Edwards WD, Factor SM, Fallon JT, Fenoglio Jr JJ, et al. Myocarditis. A histopathologic definition and classification. *Am J Cardiovasc Pathol* 1987;1:3–14.
- [2] Kumar K, Guirgis M, Zieroth S, Lo E, Menkis AH, Arora RC, et al. Influenza myocarditis and myositis: case presentation and review of the literature. *Can J Cardiol* 2011;27:514–22.
- [3] Bowles NE, Ni J, Kearney DL, Pauschinger M, Schultheiss HP, McCarthy R, et al. Detection of viruses in myocardial tissues by polymerase chain reaction. Evidence of adenovirus as a common cause of myocarditis in children and adults. *J Am Coll Cardiol* 2003;42:466–72.
- [4] Rezkalla SH, Kloner RA. Influenza-related viral myocarditis. *WMJ* 2010;109:209–13.
- [5] Bebahmoodi F, Davoodi AR, Ghasemian R, Delavarian L. Report of two rare complications of pandemic influenza A (H1N1). *J Infect Dev Ctries* 2012;6:204–7.
- [6] Chan K, Meek D, Chakravorty I. Unusual association of ST-T abnormalities, myocarditis and cardiomyopathy with H1N1 influenza in pregnancy: two case reports and review of the literature. *J Med Case Rep* 2011;5:314.
- [7] European Society of Gynecology (ESG), Association for European Paediatric Cardiology (AEPIC), German Society for Gender Medicine (DGesGM), Regitz-Zagrosek V, Blomstrom Lundqvist C, Borghi C, et al. ESC guidelines on the management of cardiovascular diseases during pregnancy: the task force on the management of cardiovascular diseases during pregnancy of the European society of cardiology (ESC). *Eur Heart J* 2011;32:3147–97.
- [8] Sliwa K, Hilfiker-Kleiner D, Petrie MC, Mebazaa A, Pieske B, Buchmann E, et al. Current state of knowledge on aetiology, diagnosis, management, and therapy of peripartum cardiomyopathy: a position statement from the Heart Failure Association of the European Society of Cardiology Working Group on peripartum cardiomyopathy. *Eur J Heart Fail* 2010;12:767–78.
- [9] Murali S, Baldisseri MR. Peripartum cardiomyopathy. *Crit Care Med* 2005;33:S340–6.