JACC: CASE REPORTS VOL. 4, NO. 13, 2022

CASE REPORT

ADVANCED

HEART CARE TEAM/MULTIDISCIPLINARY TEAM LIVE

Peripartum Cardiomyopathy Presenting With Incessant Ventricular Arrhythmias

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ABSTRACT

Sudden cardiac death is hypothesized to be one of the leading causes of mortality in peripartum cardiomyopathy. This case illustrates a patient who presented with cardiac arrest, and it discusses the importance of considering multiple causes of fulminant ventricular arrhythmias in the setting of decreased left ventricular function during the peripartum period. (**Level of Difficulty: Advanced.**) (J Am Coll Cardiol Case Rep 2022;4:759–763) © 2022 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

HISTORY OF PRESENTATION

A 33-year-old postpartum woman presented to the cardiac intensive care unit after an out-of-hospital cardiac arrest. Prior to presentation, her husband found her pulseless with agonal breathing. Cardiopulmonary resuscitation was initiated by the husband and then taken over by emergency medical services. The initial rhythm was ventricular fibrillation (**Figure 1**). After return of spontaneous circulation, the subsequent rhythm was noted to be sinus tachycardia with a rate of 126 beats/min (**Figure 2**), and blood pressure was 114/85 mm Hg. She was admitted to the cardiac intensive care unit, intubated, sedated, and initiated on a targeted temperature management protocol. She was tested for COVID-19 on admission via polymerase chain reaction, and test results were negative. Day 2 of the hospitalization was complicated by worsening cardiogenic shock and recurrent polymorphic ventricular tachycardia. Despite being treated with sedation, amiodarone, and lidocaine, the ventricular arrhythmias remained incessant.

LEARNING OBJECTIVES

- To make a differential diagnosis in a patient who presents with fulminant ventricular tachycardia/fibrillation in the peripartum period.
- To understand the role of genetic testing in patients with a dilated cardiomyopathy or who experience sudden cardiac arrest.

PAST MEDICAL HISTORY

The patient was gravida 3 para 3, 4 months postpartum, with a medical history of gestational diabetes, pre-eclampsia, and gastroesophageal reflux disease. She developed gestational diabetes with her third pregnancy, and she developed mild pre-eclampsia with all 3 of her pregnancies.

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The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the Author Center.

Manuscript received June 30, 2021; revised manuscript received January 21, 2022, accepted March 1, 2022.

ISSN 2666-0849 https://doi.org/10.1016/j.jaccas.2022.03.006

JACC: CASE REPORTS, VOL. 4, NO. 13, 2022
JULY 6, 2022:759–763

ABBREVIATIONS AND ACRONYMS

EMB = endomyocardial biopsy

QUESTION 1: WHAT IS THE DIFFERENTIAL DIAGNOSIS OF A POSTPARTUM WOMAN WHO PRESENTS WITH VENTRICULAR ARRHYTHMIAS?

Answer 1: The patient's clinical presentation was suspicious for peripartum cardiomyopathy. Other possible etiologies included acute coronary syndrome, myocarditis, and other genetic causes of ventricular tachycardia.

QUESTION 2: HOW WOULD YOU WORK UP THE DIFFERENTIAL DIAGNOSIS?

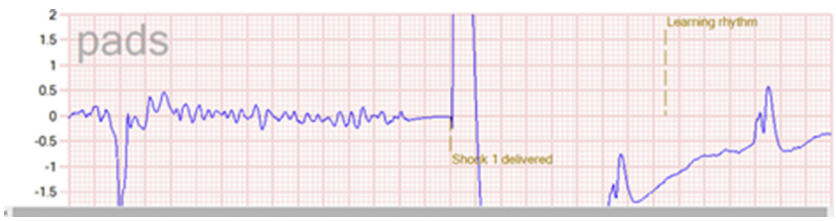
Answer 2: Troponin I on admission was 3.04 ng/mL and trended down to 2.37 ng/mL. B-natriuretic peptide levels on admission were 88 pg/mL. A transthoracic echocardiogram revealed a left ventricular ejection fraction of 15% with severe global hypokinesis, a left ventricular internal diameter end-diastole measurement of 5.1 cm, and no significant valvular abnormalities (Videos 1 to 4). Coronary angiogram showed normal coronaries. Results of endomyocardial biopsy (EMB) did not show evidence of giant cell myocarditis or sarcoidosis (**Figures 3 to 6**). Given the incessant nature of the ventricular arrhythmias and absence of underlying myocardial inflammation in the setting of unrevealing biopsy results, a primary genetic arrhythmia was suspected. Genetic testing was performed and revealed monoallelic variants in genes implicated in long QT syndrome type 8, Brugada syndrome, short QT syndrome, and dilated cardiomyopathy. All these genetic variants were of undetermined significance.

QUESTION 3: WHAT IS THE RATIONALE FOR YOUR DIFFERENTIAL DIAGNOSIS?

ANSWER 3A: PERIPARTUM CARDIOMYOPATHY. Peripartum cardiomyopathy is a rare disorder that occurs in the last month of pregnancy or in the 5 months after pregnancy. It occurs in ~1 in 3000 pregnancies in the United States. It is hypothesized to be secondary to inflammatory, immune, and environmental causes. Women with this diagnosis may present with fatal unstable arrhythmias. Data on arrhythmias are limited to case reports and case series, and the prevalence has not been well described. However, a study by Honigberg et al reported that the rate of sudden cardiac death in these women is approximately 2.1%.[1] Another study by Mallikethi-Reddy et al[2] hypothesized that ~18.7% of patients who present with a diagnosis of peripartum cardiomyopathy present with arrhythmias, and 4.2% of those have ventricular arrhythmias. Alternatively, there are hypotheses that peripartum cardiomyopathy is, in part, caused by a genetic component. There is evidence showing that similar genes found in patients with dilated cardiomyopathy are also found in those with peripartum cardiomyopathy.[3] Genetic testing was performed in our patient and revealed a heterozygous *CTF1* gene. The *CTF1* gene has no well-established disease association; however, some preliminary evidence supports correlation with autosomal dominant dilated cardiomyopathy. Furthermore, not all variants of this gene cause disease. All in all, research has suggested that the development of peripartum cardiomyopathy can point toward a 2-hit hypothesis involving multiple genetic factors and hormonal factors in the later gestational period. The patient's known history of pre-eclampsia and the presence of the autosomal dominant *CTF1* gene could have contributed to the development of this diagnosis.

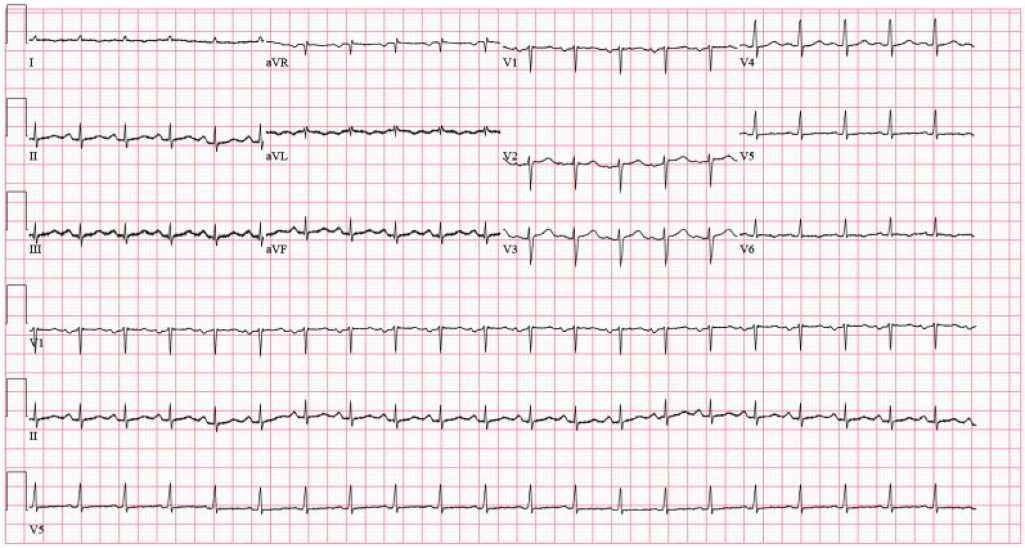
ANSWER 3B: VIRAL MYOCARDITIS. Viral myocarditis refers to inflammation of the myocardium that results from exposure to viruses.[4] Since 2020, the COVID-19 virus has been described as a cause of viral myocarditis, although rare. Specifically, it has been

FIGURE 1 Electrocardiogram on Emergency Medical Services Presentation



Ventricular fibrillation.

FIGURE 2 Electrocardiogram After Return of Spontaneous Circulation

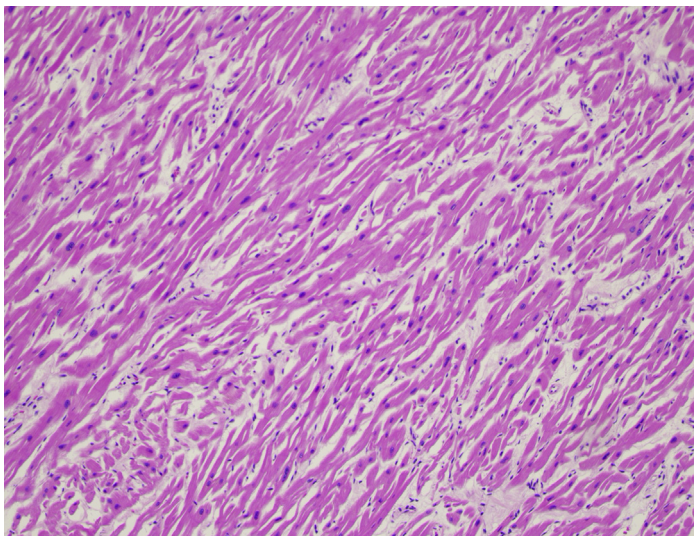


Sinus tachycardia with a rate of 126 beats/min, nonspecific ST-T changes.

shown in preliminary reports that the localization of severe acute respiratory syndrome coronavirus 2 was not found to be in the cardiomyocytes but rather an invasion of interstitial cells or macrophages in the myocardial tissue. Research is ongoing in this area, however. In addition, it is hypothesized that myocardial injury is the result of profound inflammatory activation and the release of cytokines.[5] Myocarditis is a cause of ventricular arrhythmias, and they occur commonly in viral myocarditis. This was considered as another etiology for the cause of the patient's incessant ventricular tachycardia/ventricular fibrillation; however, this patient did not have COVID-19 or a recent history of viral illness to support viral myocarditis.

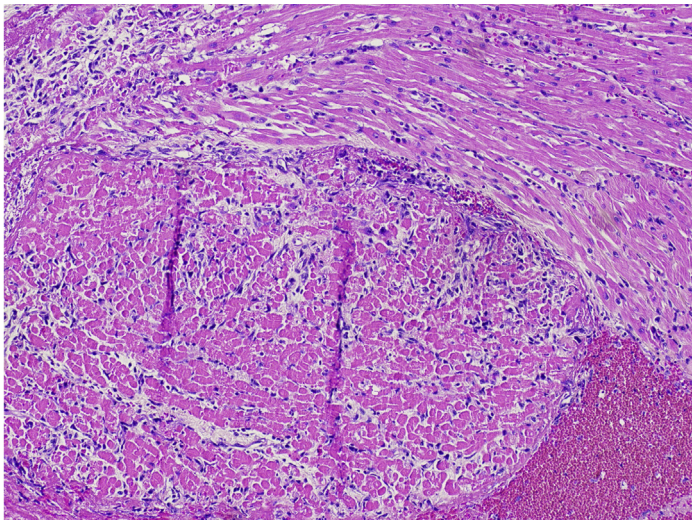
ANSWER 3C: FULMINANT OR GIANT CELL MYOCARDITIS. Fulminant myocarditis is an uncommon condition that results in sudden and widespread myocardial inflammation that often leads to death as a result of cardiogenic shock, ventricular arrhythmias, and multiorgan failure. In the setting of cardiogenic shock, pulmonary artery catheter-guided management and coronary angiography are pivotal in directing management strategies. According to a joint statement from the American Heart Association, the American College of Cardiology, and the European Society of Cardiology, there are 2 Class I indications for EMB. The first indication is presentation with acute and new-onset heart failure with hemodynamic compromise, and the second indication is presentation with unexplained new heart failure between 2 weeks and 3 months in the setting of dilated left ventricle and new arrhythmias. Our patient met the

FIGURE 3 Endomyocardial Biopsy Pathology Slide 1



Myocardium with mild inflammatory cell infiltrate without evidence of multinucleated giant cells.

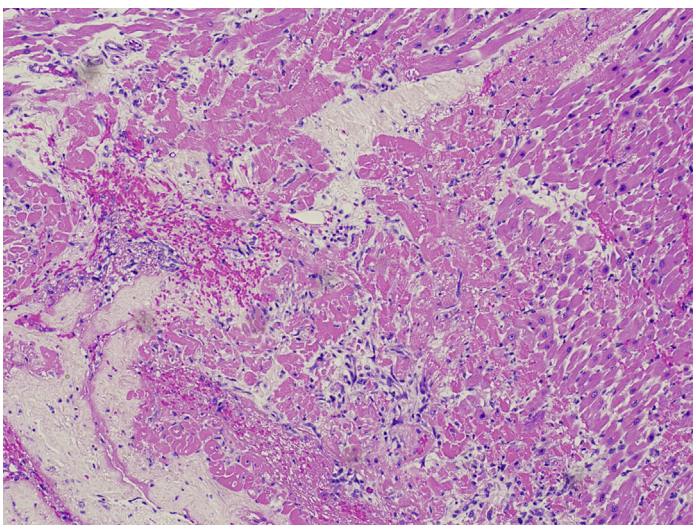
FIGURE 4 Endomyocardial Biopsy Pathology Slide 2



Myocardium with mild inflammatory cell infiltrate without evidence of multinucleated giant cells.

first criteria, and a decision was made to proceed with tissue evaluation, as there was concern for giant cell myocarditis. Results of EMB of giant cell myocarditis classically reveal giant cells with active inflammation and scar tissue. The giant cells are typically at the end of the inflamed tissue and exhibit evidence of myocyte damage.[6] On the contrary, our patient's pathologic investigation merely showed mild inflammatory cell infiltrate with no multinucleated giant cells. Fulminant myocarditis was therefore deemed not to be the cause of her presentation. There were also no histologic findings consistent with peripartum cardiomyopathy.

FIGURE 5 Endomyocardial Biopsy Pathology Slide 3



Myocardium with mild inflammatory cell infiltrate without evidence of multinucleated giant cells.

ANSWER 3D: OTHER GENETIC CASES OF VENTRICULAR TACHYCARDIA. The occurrence of sudden cardiac death in individuals aged <40 years is rare in the United States. It is estimated to occur in 3 per 100,000 persons. It typically occurs in those with structurally normal hearts, is secondary to genetic causes, and is typically autosomal dominant.[7] The most common genetic arrhythmias that lead to sudden cardiac death include long QT syndrome, Brugada syndromes, catecholaminergic polymorphic ventricular tachycardia, short QT syndrome, idiopathic ventricular fibrillation, and progressive cardiac conduction system disease.[8]

Genetic testing was performed on our patient, and there were several heterozygous variants of genes; however, they were all determined to be variants of undetermined significance. As a result of her complex presentation, a combined panel that evaluates genes associated with cardiomyopathy and arrhythmias was evaluated. Most of the genetic information that is available in the genetic databases are from patients of European ancestry and have little information about patients of other ancestral groups. Our patient was of Middle Eastern descent. This may be a reason why there were several genes of uncertain significance.

QUESTION 4: HOW WOULD YOU MANAGE THIS PATIENT?

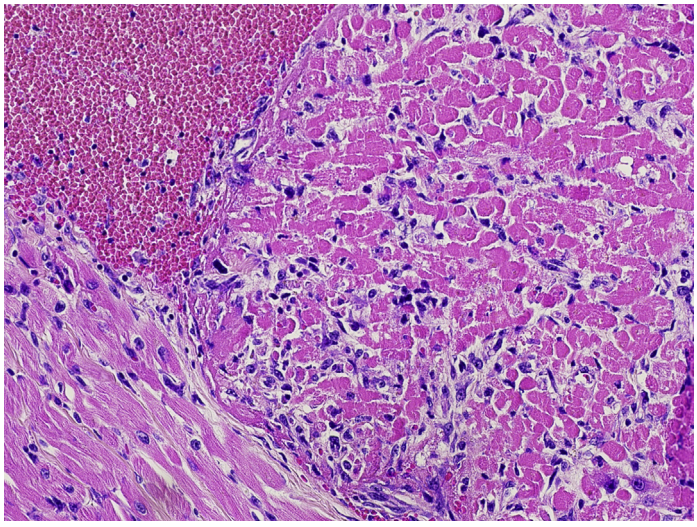
Answer 4: On presentation, the patient was started on bromocriptine given the initial suspicion for peripartum cardiomyopathy. It has been hypothesized that high levels of prolactin and the production of a cleaved terminal fragment of prolactin have contributed to the pathophysiology of peripartum cardiomyopathy. It is also hypothesized that this causes endothelial damage and cardiomyocyte dysfunction. Inhibition of prolactin release by the dopamine D_2 receptor agonist bromocriptine has been shown. In some cases, bromocriptine has also shown that it may improve left ventricular recovery and improve clinical outcomes.[9] Ventricular arrhythmias persisted despite the use of amiodarone, lidocaine, and deep sedation. The patient was pulsed with intravenous

high-dose corticosteroids in case the ventricular arrhythmias were due to giant cell myocarditis, lymphocytic myocarditis, or sarcoidosis. After a multidisciplinary heart team discussion, the patient was placed on venoarterial extracorporeal membrane oxygenation support as a bridge to heart transplant. Despite these interventions, the ventricular arrhythmias persisted. On day 7 of hospitalization, she underwent a successful emergent orthotopic heart transplant.

CONCLUSIONS/PERSPECTIVES

Although a clear diagnosis was not made for the cause of this patient's cardiac arrest and incessant ventricular arrhythmias, several mechanisms could have been involved in her presentation. The diagnosis of peripartum cardiomyopathy was ultimately made in this case as a diagnosis of exclusion. Nonetheless, it is important to consider the most common differential diagnoses in these cases, as treatment in the acute setting varies. Prompt recognition and treatment of fulminant cardiogenic shock in the postpartum period are crucial to immediate and long-term survival.

FIGURE 6 Endomyocardial Biopsy Pathology Slide 4



Myocardium with mild inflammatory cell infiltrate without evidence of multinucleated giant cells.

FUNDING SUPPORT AND AUTHOR DISCLOSURES

Dr Shah has received grant support from the National Institutes of Health (1K23HL143179). All other authors have reported that they have no relationships relevant to the contents of this paper to disclose.

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KEY WORDS peripartum cardiomyopathy, postpartum, pregnancy, venoarterial extracorporeal membrane, ventricular arrhythmia, ventricular fibrillation, ventricular tachycardia

APPENDIX For supplemental videos, please see the online version of this paper.

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