A 35-year-old female with history of endometriosis and recent upper respiratory infection (URI) presented to the emergency department with syncope and hypotension. Ten days prior to admission, she developed URI symptoms, including rhinorrhea, cough and subjective fever. Despite developing progressive fatigue and weakness, she traveled to Utah to attend Sundance Film Festival in January, where she did moderate amount of hiking. When she returned home, she visited an urgent care clinic for persistent symptoms. She was prescribed amoxicillin-clavulanic acid for suspected otitis media and sinusitis. Over the next 24 hours, she developed nausea, vomiting, and diarrhea. She fainted while being driven to see her primary care doctor the next day. In clinic, she was hypotensive with systolic blood pressure of 70mmHg and had another syncopal event waiting for EMS transport to the Emergency Department (ED) for further evaluation. In the ED, of the local community hospital her systolic blood pressure 90mmHg. She received intravenous normal saline bolus before having another witnessed syncope. She developed significant shortness of breath and cyanosis prompting urgent intubation. She was started on norepinephrine for hypotension as well as broad-spectrum antibiotics.

Physical exam was notable for cyanosis, cold, clammy extremities. Her cardiac exam revealed distant heart sounds but no murmur. Laboratory values notable for WBC 7, procalcitonin < 0.10, elevated lactate, troponin 1.6, BNP of 1000. Rapid influenza antigen test was negative. Chest x-ray was unremarkable. Electrocardiogram demonstrated sinus tachycardia with low voltage, rightward axis, and non-specific T-wave changes in inferior leads. Transthoracic echocardiogram (TTE) demonstrated severe global hypokinesis with a left ventricular ejection fraction of 20-25% and small to moderate pericardial effusion with tamponade requiring pericardial window. She was consulted given high suspicion for cardiogenic shock due to myocarditis given recent upper respiratory infection.

Over the next 12 hours, the patient became progressively hypotensive and tachycardic with increasing vasopressor and inotropic requirements. Interventional cardiology was consulted for implantation of percutaneous mechanical circulatory support due to progressive cardiogenic shock despite maximum doses of norepinephrine, dopamine, phenylephrine and dobutamine. The UCLA Cardiomyopathy team was consulted for life-threatening transfer of extracorporeal membrane oxygenation (ECMO).

While awaiting transfer, the patient was taken to the cardiac catheterization laboratory for coronary angiography, and Impella percutaneous mechanical circulatory support placement. No evidence of coronary artery disease was seen on coronary angiography. Right heart catheterization confirmed severe cardiogenic shock with elevated left and right-sided filling pressures (mean wedge pressure of 18 mmHg with mean right atrial pressure of 17 mmHg) and severely low cardiac output of 1.88 L/min (cardiac index of 0.96 L/min/m2) by thermodilution and Fick calculation. The patient developed worsening hypotension and was transferred Ronald Reagan/UCLA for ECMO.

Repeat transthoracic echocardiogram demonstrated LVEF of 10%. She was placed on veno-arterial extracorporeal membrane oxygenation (VA-ECMO). The Impella device was kept in place to offload the left ventricle as isolated VA-ECMO would increase the afterload resulting in worsening pulmonary edema/respiratory failure given the acutely failing left ventricle. Extensive infectious workup was positive for influenza B by PCR of nasopharyngeal sampling. She was treated with oseltamivir, intravenous immunoglobulin and high-dose methylprednisolone.

Vasopressor support was weaned, and she remained critically ill on ECMO and Impella. She was extubated on day 2 of her hospitalization and remained stable on high-flow nasal cannula. Repeat TTE on day 4 of ECMO showed improved LVEF 50%. ECMO was decannulated and Impella removed on hospital day 5. Her hospital course was complicated by acute blood loss anemia requiring multiple blood transfusions and a large pericardial effusion with tamponade requiring pericardial window. Fortunately, she recovered and was discharged home on hospital day 12 with complete recovery of left ventricular systolic function.

At 6-month follow-up, BNP had normalized and TTE demonstrated LVEF 65-70% with normal stress echocardiogram.

**Discussion**

Influenza is associated with high morbidity and mortality worldwide but myocarditis is a rare complication of the virus. Influenza B commonly causes less severe respiratory infections in comparison to its counterpart, Influenza A, which has been documented to cause fulminant myocarditis particularly during H1N1 pandemic in 2009. Myocardial involvement
in influenza B is rare, and most cases reported are pediatric.\textsuperscript{4,5} However, this adult developed shock requiring mechanical circulatory support.\textsuperscript{4} Recovery of myocardial function has been promising when mechanical circulatory support, particularly ECMO, was initiated early in the course.\textsuperscript{4} Therefore, clinicians encountering viral symptoms associated with cardiac involvement must have a high clinical suspicion for myocarditis and appreciation for its rapidly progressive, fatal course. Early involvement of appropriate clinicians, including heart failure specialists, can reduce morbidity and mortality.

Fulminant myocarditis is an inflammatory disease of cardiac muscle that presents with heart failure symptoms and may require inotropic or mechanical circulatory support. Endomyocardial biopsy remains the gold standard for diagnosis of myocarditis, but in most cases, diagnosis is presumed based on clinical presentation.\textsuperscript{8} Cardiac MR can also aid in confirming the diagnosis of myocarditis due to characteristic findings of edema and late gadolinium enhancement in a non-ischemic pattern.\textsuperscript{8} The presentation of myocarditis is variable and ranges from fatigue and chest pain to heart failure with arrhythmias and sudden cardiac death.\textsuperscript{6,7}

Myocarditis can result from a variety of infectious and non-infectious etiologies. Among the infectious causes, viruses are the most common pathogens.\textsuperscript{8} Enteroviruses including coxsackievirus were the most frequently seen pathogens in the US until the 1990’s.\textsuperscript{8,9} In later studies, Parvovirus B-19 and human herpes virus 6 were most commonly identified.\textsuperscript{9} Other viruses seen include Influenza A/B, adenovirus, HIV, and HCV.\textsuperscript{8,9} Non-infectious etiologies include autoimmune diseases, hypersensitivity reactions, and cardiotoxins such as alcohol and cocaine.\textsuperscript{10-12}

Management of myocarditis includes disease-specific therapy, heart failure management and arrhythmia therapy. Treatment of hemodynamically stable heart failure patients includes diuresis, early initiation of ACE inhibitors, beta-blockers, and mineralocorticoid receptor antagonists. Early initiation of ACE inhibitors led to decreased myonecrosis and dystrophic calcification in a study of coxsackievirus myocarditis.\textsuperscript{13} The addition of beta-blockers led to improved outcomes.\textsuperscript{14}

VA-ECMO is a form of prolonged mechanical circulatory support that provides both hemodynamic and respiratory support to patients with refractory cardiogenic shock or cardiac arrest. During ECMO, blood is removed from the native circulation, circulated through a mechanical pump outside the body and then reintroduced into the circulation. While outside the body, blood flows through a gas exchange device, which supplies oxygen and removes carbon dioxide. Blood is removed from the venous system and then returned to the arterial system. The heart and lungs are bypassed in this process. Once on VA-ECMO, a patient must be anticoagulated. Major complications of VA-ECMO include bleeding, thromboembolism, pulmonary hemorrhage, coronary ischemia, cerebral ischemia and cardiac thrombosis.

The evidence on management of Influenza B myocarditis is limited as very few cases have been reported in the literature. Therapies of importance include antivirals, IVIG, steroids and appropriate utilization of mechanical circulatory support.\textsuperscript{4} Based on data available, influenza B myocarditis is rare but may lead to rapidly progressing, refractory cardiogenic shock and death. However, it appears to be reversible if mechanical circulatory support is initiated early in the process. A case-series and review of the literature on influenza myocarditis demonstrated that early antiviral therapy and ECMO improved mortality.\textsuperscript{4} The mean duration of mechanical circulatory support was $8.5 \pm 6$ days.\textsuperscript{5} In our patient with cardiogenic shock refractory to multiple vasopressors and Impella device, initiation of VA-ECMO allowed time for recovery of myocardial function in 5 days. The case-series included 4 similar cases who received antiviral therapy and VA-ECMO, and were successfully decannulated off ECMO and recovered.\textsuperscript{4}

The efficacy of immunomodulatory agents such as IVIG and steroids in viral myocarditis remains unclear given insufficient data. However, these agents are often used in fulminant cases due to the severity of the disease process. More studies are needed to assess their efficacy.

REFERENCES


