A Cold Taken to Heart

Kanika P. Mody, MD; James J. Lyons, MD; Ulrich P. Jorde, MD; Nir Uriel, MD

Foreword

Information about a real patient is presented in stages (boldface type) to expert clinicians (Dr Uriel and Dr Jorde), who respond to the information, sharing their reasoning with the reader (regular type). A discussion by the authors follows.

A 35-year-old woman with no past medical history presented to her local emergency room with 2 days of fevers, chills, and myalgias. She was febrile with a temperature of 102°F, blood pressure of 95/60 (72) mm Hg, heart rate of 110 bpm, respiratory rate of 20 breaths per minute, and an oxygen saturation of 100% on 2 L oxygen. The physical examination was notable for cool extremities, clear lungs, and tachycardic heart sounds with no s3, s4, or friction rub. The patient decompensated quickly and developed hypotension, requiring rapid up titration of norepinephrine to 12 μg·kg⁻¹·min⁻¹. The ECG (Figure 1) showed sinus tachycardia with ST-segment elevation in the inferolateral leads. Laboratory results were notable for cardiac troponin of 3.89 ng/mL (normal range, 0–0.08 ng/mL), venous lactate of 3.5 mmol/L (normal range, 0.50–2.20 mmol/L), white blood cell count of 17.0×10⁹ per 1 L (normal range, 3.5–9.1×10⁹ per 1 L), and hemoglobin of 12.4 g/dL (normal range, 13.3–16.2 g/dL) with preserved hepatic and renal function.

Dr Uriel: Interpretation of the clinical course so far: A young woman with no medical history presents with an infectious syndrome and rapidly deteriorates. At this point, one must consider the different processes that would result in such a dramatic clinical picture. It is important to begin to rapidly rule out life-threatening processes and to perform the appropriate clinical testing in a manner that will not delay treatment. Given the increasing hypoxia, an assessment of the lung parenchyma would be beneficial at this point. A computed tomographic angiogram may be considered to simultaneously examine for an infectious process, pulmonary edema, and pulmonary embolism. In addition, cardiac assessment would also be important at this point, particularly in the setting of hypotension and hypoxia. Hypotension can be divided into different types: secondary to systolic dysfunction, vasodilation, or hypovolemia. A transthoracic echocardiogram would help further elucidate the cardiac process, particularly with the assessment of ventricular function and size. Left ventricular (LV) dysfunction would be expected if there was direct cardiac involvement such as coronary disease or myocardial inflammation, whereas a hyperdynamic ventricle would be expected in a state of vasodilation or hypovolemia. Given the abnormal cardiac troponin, it is important to rule out epicardial coronary ischemia. A coronary angiogram should be performed to rule out an acute coronary syndrome, which, in this age group, would most likely be related to spontaneous coronary artery dissection or thrombosis resulting from a hypercoagulable state. Myocarditis should also be considered, particularly in the setting of a prodrome of fevers and myalgias.

Patient presentation (continued): A computed tomographic angiogram was performed that was negative for pulmonary embolism and showed small bilateral pleural effusions. A bedside transthoracic echocardiogram showed a large pericardial effusion, a dilated inferior vena cava, and right atrial and right ventricular (RV) diastolic collapse. The LV ejection fraction was visually estimated to be 45% to 50%.

Simultaneous right and left heart catheterization showed elevated filling pressures and is summarized in Table 1. The coronary angiogram was normal.

Dr Uriel: With a negative coronary angiogram and negative computed tomographic angiogram, the catheterization of the right side of the heart and echocardiogram should be further evaluated. With a large pericardial effusion seen on echocardiography, it is important to determine whether the effusion is hemodynamically significant. The first clue that the effusion is significant is the presence of RV and right atrial collapse on the echocardiogram. This is further suggested by the equalization of the diastolic pressures on catheterization of the right and left sides of the heart.1 Diastolic equalization of pressures signifies the impairment of diastolic filling and can be attributable to either decreased compliance such as in the setting of constrictive pericarditis or extrinsic compression such as in the setting of a large pericardial effusion or tamponade. Other clinical signs of tamponade are nonspecific and are typically signs of cardiogenic shock such as tachycardia, hypotension, and cool extremities on clinical examination. Jugular venous congestion is common, and jugular venous pressure waveforms usually demonstrate steep x and y descents. The hallmark sign of tamponade is pulsus paradoxus, defined as a drop in systolic pressure by at least 10 mm Hg during the inspiratory phase of normal breathing, which corresponds to interventricular interdependence and decreased inspiratory LV inflow.
Patient presentation (continued): With worsening acidosis (pH 7.2), persistent hypotension, and tachycardia despite rapidly rising pressors and the equalization of diastolic pressures with a large pericardial effusion, the patient was taken to the operating room for pericardial window placement to treat tamponade. Despite successful placement of the pericardial window, the patient developed worsening shock, requiring the emergent placement of an intra-aortic balloon pump while still in the operating room. The patient was then transferred to our institution for further management.

Dr Jorde: After drainage of the effusion, it is expected that the patient will recover some hemodynamic stability. In this case, however, the patient continues to deteriorate. At this point, further hemodynamic assessment would be beneficial, particularly because the patient is now showing signs of shock. Catheterization of the right side of the heart should be considered to determine whether this process is related primarily to a cardiogenic process or is rather a vasodilatory or septic process.

Patient presentation (continued): On arrival to our institution, which was <24 hours after initial presentation, the patient had a blood pressure of 83/63 (70) mm Hg, augmenting to 90 mm Hg with an intra-aortic balloon pump at 1:1, and was in sinus tachycardia with heart rate in the 130 beats per minute range on milrinone at 0.25 μg·kg⁻¹·min⁻¹ and norepinephrine at 15 μg·kg⁻¹·min⁻¹. The patient’s urine output had decreased to 15 cm³/h in the 4 hours before transfer despite the current support measures. A Swan-Ganz catheter was placed, which showed elevated filling pressures and a low cardiac output (Table 2).

Dr Uriel: The patient now has elevated filling pressures with a low cardiac output, consistent with cardiogenic shock. At this point, management should focus on improving cardiac output to preserve end-organ perfusion. Cardiogenic shock is defined as systolic blood pressure <80 to 90 mm Hg or mean arterial pressure 30 mm Hg less than baseline and severe reduction in cardiac index to <1.8 L·min⁻¹·m⁻² without support or <2.0 to 2.2 L·min⁻¹·m⁻² with support in the setting of elevated filling pressures, defined by an LV end-diastolic pressure >18 mm Hg or RV end-diastolic pressure >10 to 15 mm Hg.²

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**Table 1. Simultaneous Catheterization of the Right and Left Sides of the Heart**

<table>
<thead>
<tr>
<th>Hemodynamics</th>
<th>Right</th>
<th>Left</th>
</tr>
</thead>
<tbody>
<tr>
<td>RAP, mm Hg</td>
<td>18</td>
<td>16</td>
</tr>
<tr>
<td>RVP, mm Hg</td>
<td>31/18</td>
<td>41/10</td>
</tr>
<tr>
<td>PAP, mm Hg</td>
<td>33/20 (24)</td>
<td>34/20 (25)</td>
</tr>
<tr>
<td>PCWP, mm Hg</td>
<td>20</td>
<td>24</td>
</tr>
<tr>
<td>TPG, mm Hg</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>LVEDP, mm Hg</td>
<td>21</td>
<td>60</td>
</tr>
<tr>
<td>PA sat, %</td>
<td>60</td>
<td>60</td>
</tr>
<tr>
<td>SVR, dynes·cm⁻¹·m⁻²</td>
<td>944</td>
<td>1350</td>
</tr>
<tr>
<td>Fick cardiac output, L/min</td>
<td>3.81</td>
<td>3.20</td>
</tr>
<tr>
<td>Fick cardiac index, L·min⁻¹·m⁻²</td>
<td>2.06</td>
<td>1.73</td>
</tr>
<tr>
<td>BP, mm Hg</td>
<td>90/50 (63)</td>
<td>83/63 (70)</td>
</tr>
<tr>
<td>HR, bpm</td>
<td>130</td>
<td>130</td>
</tr>
<tr>
<td>RVSWI, mm Hg·L·m⁻²</td>
<td>0.03</td>
<td>0.12</td>
</tr>
</tbody>
</table>

BP indicates blood pressure; HR, heart rate; LVEDP, left ventricular end-diastolic pressure; PA sat, pulmonary artery saturation; PAP, pulmonary artery pressure; PCWP, pulmonary capillary wedge pressure; RAP, right atrial pressure; RVP, right ventricular pressure; RVSWI, right ventricular stroke work index; SVR, systemic vascular resistance; and TPG, transpulmonary gradient.

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**Table 2. Catheterization of the Right Side of the Heart**

<table>
<thead>
<tr>
<th>Hemodynamics</th>
<th>Right</th>
</tr>
</thead>
<tbody>
<tr>
<td>RAP, mm Hg</td>
<td>16</td>
</tr>
<tr>
<td>RVP, mm Hg</td>
<td>41/10</td>
</tr>
<tr>
<td>PAP, mm Hg</td>
<td>34/20 (25)</td>
</tr>
<tr>
<td>PCWP, mm Hg</td>
<td>24</td>
</tr>
<tr>
<td>TPG, mm Hg</td>
<td>1</td>
</tr>
<tr>
<td>PA sat, %</td>
<td>60</td>
</tr>
<tr>
<td>SVR, dynes·cm⁻¹·m⁻²</td>
<td>1350</td>
</tr>
<tr>
<td>Fick cardiac output, L/min</td>
<td>3.20</td>
</tr>
<tr>
<td>Fick cardiac index, L·min⁻¹·m⁻²</td>
<td>1.73</td>
</tr>
<tr>
<td>BP, mm Hg</td>
<td>83/63 (70)</td>
</tr>
<tr>
<td>HR, bpm</td>
<td>130</td>
</tr>
<tr>
<td>RVSWI, mm Hg·L·m⁻²</td>
<td>0.12</td>
</tr>
</tbody>
</table>

BP indicates blood pressure; HR, heart rate; LVEDP, left ventricular end-diastolic pressure; PA sat, pulmonary artery saturation; PAP, pulmonary artery pressure; PCWP, pulmonary capillary wedge pressure; RAP, right atrial pressure; RVP, right ventricular pressure; RVSWI, right ventricular stroke work index; SVR, systemic vascular resistance; and TPG, transpulmonary gradient.
Clinical signs of cardiogenic shock include signs of hypoperfusion and end-organ dysfunction such as cool extremities, decreased urine output, renal failure, liver dysfunction, and altered mental status. Given this low-flow state, mechanical circulatory support (MCS) would be indicated at this time. In our case, biventricular support should be considered, given the signs of biventricular failure demonstrated by the hemodynamics. Venoarterial extracorporeal membrane oxygenation or a CentriMag biventricular assist device (BIV AD; Thoratec, Pleasanton, CA) would be the more appropriate options to provide optimal cardiac output in this case (Table 3).

Patient presentation (continued): The patient was taken to the operating room for CentriMag BIV AD implantation, and a core heart biopsy was sent to pathology. The intraoperative transesophageal echocardiogram revealed small cardiac chambers and an LV ejection fraction of <20%.

Dr Jorde: It is important to consider the possible differential diagnoses because the shock is progressing quite rapidly. Among the most likely causes are a myocardial process and a myopericardial process, given the elevated troponin and LV dysfunction. Because of the acute presentation, an autoimmune process such as giant-cell myocarditis or a viral myocarditis should also be considered in this case. Although giant-cell myocarditis typically presents with ventricular arrhythmia and is rarely associated with pericardial effusion, its natural history may be altered by early immunosuppressive therapy, so early diagnosis should be considered.

Dr Uriel: Although the data are limited, treatment with immunosuppressive therapy has been controversial and is highly dependent on the pathogenesis of the myocarditis.

Viral myocarditis: Several reports using steroids for the treatment of viral myocarditis show some benefit; however, there are also reports showing no benefit.3–6 Interferon-β has been shown to reduce myocardial viral load in patients infected with enterovirus or adenovirus,7 but larger randomized trials are lacking and are needed to clarify the role of immunosuppression in myocarditis.

Nonviral inflammatory myocarditis: A significant improvement in LV ejection fraction and decrease in LV chamber size were also demonstrated in the TIMIC (Immunosuppressive Therapy in Patients With Virus Negative Inflammatory Cardiomyopathy) study after the use of prednisone and azathioprine.8

Giant-cell myocarditis: Several reports show that early immunosuppressive therapy improves survival from 3 to 12 months, although some will require mechanical support or heart transplantation within 1 year.9,10

Dr Jorde: Endomyocardial biopsy (EMB) remains the gold standard for the diagnosis of acute myocarditis of various causes. However, in many cases, EMB is not used, and the

| Table 3. Mechanical Circulatory Support for Cardiogenic Shock |
|------------------|------------------|------------------|------------------|------------------|
| Insertion        | IABP             | Impella 5.0      | Tandem Heart     | ECMO             | CentriMag        |
| CO               | Improve by 40%   | 3.5–4 L         | 8 L / 5 L        | 4 L              | 10 L             |
| Ventricular support | Left            | Left            | Left/right       | Left/right       | Left/right       |
| Pulmonary        | No effect        | No effect       | No effect        | Yes              | Optional (oxygenator chamber) |
| Support time (off-label use) | Days          | Days            | Weeks            | Days             | Weeks            |

CO indicates cardiac output; ECMO, extracorporeal membrane oxygenator; and IABP, intra-aortic balloon pump.
diagnosis is based on clinical presentation or other modalities such as ECG, transthoracic echocardiogram, and cardiac magnetic resonance imaging. In most cases, EMB is reserved for patients who present with an acute-onset cardiomyopathy of unknown origin that is refractory to routine supportive measures or those with refractory arrhythmias, as advocated by the American College of Cardiology/American Heart Association/European Society of Cardiology guidelines. EMB has also been helpful in those cases of suspected infiltrative diseases such as amyloidosis and sarcoidosis because specific staining can help identify the cause of the cardiomyopathy and can guide treatment. However, with more sophisticated imaging modalities such as tagged positron emission tomography scans, the diagnosis of these infiltrative diseases is less dependent on biopsy, particularly given the risk of sampling error and false-negative pathology. In addition, with modern techniques, isolation of the viral pathogen in the biopsy specimen may be possible, allowing tailoring of the antiviral therapy. Although sampling error has been a common argument against the use of EMB, cardiac magnetic resonance imaging may be useful in

**Table 4. Weaning Trial Hemodynamic Data for Patients With BIVAD CentriMag Support**

<table>
<thead>
<tr>
<th>RVAD Speed, rpm</th>
<th>RVAD Flow, L/min</th>
<th>LVAD Speed, rpm</th>
<th>LVAD Flow, L/min</th>
<th>BP, mm Hg</th>
<th>HR, bpm</th>
<th>CVP, mm Hg</th>
<th>PCWP, mm Hg</th>
<th>PA sat, %</th>
<th>LVEDD, cm</th>
<th>LVEF, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>2350</td>
<td>4.1</td>
<td>3200</td>
<td>4.95</td>
<td>83/73 (76)</td>
<td>101</td>
<td>6</td>
<td>25/16 (19)</td>
<td>9</td>
<td>83</td>
<td>3.5</td>
</tr>
<tr>
<td>1800</td>
<td>2.77</td>
<td>3200</td>
<td>4.68</td>
<td>82/78 (80)</td>
<td>102</td>
<td>6</td>
<td>25/15 (18)</td>
<td>7</td>
<td>81</td>
<td>3.1</td>
</tr>
<tr>
<td>1500</td>
<td>2.05</td>
<td>3200</td>
<td>4.35</td>
<td>82/78 (79)</td>
<td>101</td>
<td>7</td>
<td>25/11 (16)</td>
<td>6</td>
<td>81</td>
<td>3.1</td>
</tr>
<tr>
<td>1500</td>
<td>2.02</td>
<td>2700</td>
<td>3.8</td>
<td>86/74 (78)</td>
<td>104</td>
<td>7</td>
<td>27/13 (18)</td>
<td>8</td>
<td>3.1</td>
<td></td>
</tr>
<tr>
<td>1500</td>
<td>2.0</td>
<td>2200</td>
<td>2.57</td>
<td>89/68 (75)</td>
<td>104</td>
<td>6</td>
<td>27/15 (22)</td>
<td>10</td>
<td>83</td>
<td>3.1</td>
</tr>
<tr>
<td>1500</td>
<td>2.0</td>
<td>1700</td>
<td>1.4</td>
<td>84/64 (71)</td>
<td>104</td>
<td>9</td>
<td>28/14 (19)</td>
<td>11</td>
<td>76</td>
<td>3.4</td>
</tr>
</tbody>
</table>

BIVAD indicates biventricular assist device; CVP, central venous pressure; HR, heart rate; LVAD, left ventricular assist device; LVEDD, left ventricular end-diastolic dimension; LVEF, LV ejection fraction; PA sat, pulmonary artery saturation; PAP, pulmonary artery pressure; PCWP, pulmonary capillary wedge pressure; and RVAD, right ventricular assist device.
Patient presentation (continued): EMB revealed fulminant lymphocytic myocarditis (Figure 2). No steroids were given because of the lack of an autoimmune origin. Viral serologies were positive for adenovirus and parvovirus IgG, although the remaining serologies were negative. The pericardial fluid analysis was also unrevealing, with only rare white blood cells and no organisms seen on Gram stain, a negative fluid viral culture, and negative acid-fast staining for mycobacterial species. Pericardial biopsy showed slight thickening of the pericardium and was negative for significant inflammation, and no viral inclusions were identified.

The patient’s postoperative course was quite unremarkable, with quick titration off of inotropes and pressors. The patient received a heparin drip with an activated partial thromboplastin time goal of 60 to 80 seconds, which was tolerated well. Neurohormonal blockade, including β-blockers and spironolactone, was introduced the first postoperative week. After 5 days of maximal biventricular support (6 L/min on the left and 5.5 L/min on the right), support was weaned to 5 L/min on the left and 4.5 L/min on the right. On day 10, with normalized renal and liver function and adequate anticoagulation, a weaning trial was performed with a Swan-Ganz catheter and transthoracic echocardiogram guidance. The study revealed good tolerance of weaning down to 1.5-L/min flow on both sides, as was demonstrated by a low central venous pressure, low pulmonary capillary wedge pressure, preserved mean arterial pressure, and preserved LV end-diastolic dimension (indicating adequate LV filling by venous pressure, low pulmonary capillary wedge pressure, pulmonary artery pressure, pulmonary capillary wedge pressure, pulmonary artery saturation, and Fick cardiac output by the Swan-Ganz catheter). The weaning trial hemodynamic data are summarized in Table 4.

Dr Uriel: After BIVAD implantation, a weaning trial should be considered when there is reasonable end-organ recovery and hemodynamic stability off of pressors and inotropes and pressors is demonstrated (Figure 3). The patient should be on adequate anticoagulation during the weaning trial because of the risk of clot formation in the VAD equipment during low-flow settings. The study can be done at bedside in the intensive care unit or in the catheterization laboratory or operating room (depending on the center and comfort of clinicians) and should be done in conjunction with hemodynamic monitoring, including continuous blood pressure measurements by either cuff or arterial line (preferable) and, if possible, with a Swan-Ganz catheter or transesophageal echocardiogram. At baseline, the following measurements should be recorded: LV end-diastolic dimension, severity of mitral regurgitation, and severity of tricuspid regurgitation by echocardiogram; blood pressure; and central venous pressure, pulmonary artery pressure, pulmonary capillary wedge pressure, pulmonary artery saturation, and Fick cardiac output by the Swan-Ganz catheter.

The RV assist device (RVAD) should be weaned first, and flow should be decreased by 0.5 L/min and the hemodynamics should be monitored for 3 to 5 minutes before proceeding to the next stage. Signs that the patient is tolerating the weaning trial include stable LV assist device (LVAD) flows, stable mean arterial pressure, preservation of the LV end-diastolic dimension, low central venous pressure, and acceptable Fick cardiac output measurements. The RVAD and LVAD serve as 2 pumps in series, so a decrease in the RVAD flow will result in a decrease in the LVAD flow. However, if the LVAD flows remain stable, this indicates that the patient’s native RV is able to compensate for the decrease in RVAD support and provides the LV sufficient volume to maintain the LVAD flow. If the stage is tolerated, the RVAD can be weaned step-wise down by 0.5 L/min to 1 L/min. Once the patient has tolerated 1 L/min on the RVAD, the LVAD can be weaned in a similar manner. If the RVAD wean is not tolerated and the echocardiogram reveals septal shift toward the LV, the RVAD and LVAD could be weaned in alternating stages to preserve midline septal positioning during the duration of the weaning trial (Figure 4). Hemodynamics and echocardiographic parameters should be monitored, and each stage should result in a decrease in speed by 0.5 L/min on the corresponding VAD. This sequence of RVAD alternating with LVAD wean should be continued until both VADs are down to 1 L/min.

Our patient clearly tolerated the RVAD wean with preservation of the hemodynamics and LV filling throughout the study. Because of the risk of clot formation in the cannula or tubing at low-flow settings, the BIVAD flows should be set back to 3 to 4 L/min while the next course of action is being determined.

Dr Jorde: At this point, given the risk of thromboembolism and infection, it is reasonable to consider discontinuation of support. If there is concern for LV dysfunction after the wean that may affect outcome, transition to a long-term LVAD can be considered. Some patients may require short-term bridging with inotropes and inhaled nitric oxide to provide optimal medical support to both ventricles after device explantation. The patient should also be treated with neurohormonal blockade, as recommended by the American College of Cardiology Foundation/American Heart Association heart failure guidelines,14 once pressors are no longer needed.

Figure 4. Short-axis illustration of the biventricular relationship during a weaning study. Top, Normal right ventricular–left ventricular (RV-LV) relationship. Bottom, Septal shift causing the septum to deviate or bow toward the LV, resulting in RV dyskinesis and RV distension.
Patient presentation (continued): The patient underwent device explantation on day 11. A postexplantation echocardiogram showed normal LV and RV size with an ejection fraction of 40% to 45%. The postoperative course was unremarkable. On postoperative day 2, a transthoracic echocardiogram showed normal LV and RV size and function. A repeat biopsy taken at the time of explantations showed minimal fibrosis and diffuse interstitial infiltrate of lymphocytes and monocytes with apparent interstitial edema but without myocyte necrosis, consistent with resolving myocarditis. The patient was transferred to the step-down unit and on day 5 was found to have nonsustained ventricular tachycardia. β-Blockers were uptitrated, and after much discussion with the electrophysiologist, the patient was discharged home with a Zoll Life Vest external wearable defibrillator with a plan for follow-up.

Dr Uriel: Although there is a large body of evidence supporting internal cardioverter-defibrillator placement in chronic cardiomyopathy, there are minimal data on patients with preserved ejection fraction who have undergone cardiac transplantation. Patients who have a prolonged course or poorer outcomes such as those with giant-cell or sarcoidosis-associated myocarditis or patients with viral myocarditis who require cardiac replacement therapy such as LVAD or are listed for heart transplantation. On the basis of existing data, patients who have a reversible process should be treated with optimal medical therapy with time to recover their myocardial function before internal cardioverter-defibrillator implantation. In patients with preserved ejection fraction, there are no data on the risk of death related to ventricular arrhythmias in patients with viral myocarditis. Because of the risk of infection and bleeding, as well as the cost, the overuse of internal cardioverter-defibrillator in this patient population without evidence-based decision making may not be advantageous. However, in patients who have history of ventricular cannulation and associated scar, it is unclear whether this scar can be the source of hemodynamically significant and possibly fatal ventricular arrhythmias despite full recovery of myocardial recovery. More research and experience are necessary to understand this unique subset of patients and their risk of sudden death.

Discussion
Cardiogenic shock is a life-threatening syndrome resulting in organ hypoperfusion caused by progressive depression of cardiac function. Cardiogenic shock is most commonly the result of myocardial ischemia but can also be seen after cardiomyopathy, with myocarditis, and in severe cases of decompensated heart failure. Regardless of the cause, cardiogenic shock carries a high morbidity and mortality despite advances in medical therapy. Although early identification of shock and aggressive medical management are necessary, the early use of MCS has been shown to improve the outcomes of patients. Previously, we reported improved outcomes in patients with fulminant myocarditis complicated by cardiogenic shock supported by MCS regardless of the pathogenesis and specifically in patients with giant-cell myocarditis. However, challenges remain in identifying when to consider MCS, the appropriate time to assess recovery, and the length of therapy. Here, we emphasize the step-wise approach to managing such a complicated patient presenting to the local emergency room with fulminant myopericarditis.

The normal pericardium is a thin, elastic membrane that surrounds the heart and typically holds 15 to 50 mL straw-colored fluid. In the case of acute pericarditis, this membrane becomes inflamed and is associated with positional chest pain and shortness of breath. The physical examination may demonstrate tachycardia and an audible friction rub. Ninety percent of cases of acute pericarditis are viral or idiopathic, although some of the other causes include post–myocardial infarction, post–chest radiation, post–blunt chest trauma, or aortic dissection associated with hemorrhagic pericardial fluid (blood leaking into pericardial space), autoimmune disease, neoplastic invasion/metastasis to the pericardium, uremia, postcardiotomy, or medication-associated inflammation. In cases of pericarditis, the myocardium is often also involved, and this entity is called myopericarditis. In cases of myopericarditis, LV dysfunction can be seen, and this dysfunction may be transient or irreversible.

Acute pericarditis can be further complicated by pericardial tamponade, which results from the accumulation of pericardial fluid within this fixed pericardial space. With tamponade, the pericardium becomes stiff from volume expansion to the point beyond which it is able to stretch. As a result, the pericardial pressure increases, causing the cardiac chambers to become compressed and impairing cardiac inflow. Progressively, there is reduction in myocardial diastolic compliance, and ultimately, the mean diastolic pericardial pressure and cardiac chamber pressures equalize.

Intrathoracic pressure decreases during inspiration, resulting in the increase in venous return to the right heart with a transient increase in RV filling and chamber size. The normal pericardium is able to accommodate this increased RV chamber size by expanding and thus does not affect left-sided filling. In the case of tamponade, the increased RV filling with inspiration results in impairment of LV filling because the pericardium is unable to accommodate the increased chamber size. As a result, the expanding RV causes septal shift into the LV, decreasing the effective LV chamber size and thus decreasing LV filling. This process reverts in expiration, resulting in interventricular interdependence.

The treatment of cardiac tamponade consists of draining the pericardial fluid by either needle pericardiocentesis or surgical balloon pericardiotomy. A needle pericardiocentesis is preferable in most cases because of its ability to be performed at bedside and is indicated in cases of hemodynamic instability, with or without imaging guidance. In more stable cases, pericardiocentesis can be done in the catheterization laboratory with fluoroscopy guidance or at bedside with echocardiographic guidance when needed. In cases of recurrent effusions or tamponade or when the location of the effusion makes needle pericardiocentesis difficult (ie, posterior effusions), a surgical balloon pericardiotomy or window may be indicated.

Once the pericardial tamponade is treated, the hemodynamics of the patient should improve. If the patient continues to
deteriorate and all signs of tamponade are resolved, one must consider direct impairment of the myocardium such as in myocarditis or myopericarditis. Invasive hemodynamics and echocardiographic support are useful, as was demonstrated in our case, and rapid stabilization is imperative. Tissue diagnosis may also play a role, although the patient should be stable enough to undergo biopsy. In our case, tissue was taken at the time of MCS implantation, but others may opt for an EMB at the time of catheterization of the right side of the heart.

Myocarditis can be described by both the pathological evidence and the clinical features of the syndrome. The histopathological evidence for active myocarditis is traditionally described by the Dallas criteria, which require the presence of an inflammatory infiltrate of the myocardium with necrosis or degeneration of the adjacent myocytes not typical of the ischemic damage associated with coronary heart disease. In the presence of active myocyte necrosis, the myocarditis is called active, whereas infiltrate in the absence of myocyte necrosis is called borderline. This inflammatory infiltrate can be further described as lymphocytic, eosinophilic, granulomatous, or giant cell, with lymphocytic being the most common type. More cell-specific immunoperoxidase stains for human leukocyte antigens may also be used to diagnose myocarditis and may broaden the ability to diagnose myocarditis.

Clinical diagnosis of myocarditis is based on a clinical syndrome of advanced heart failure or newly diagnosed dilated cardiomyopathy with global LV dysfunction or a dilated LV end-diastolic dimension >4 cm, elevated troponin levels, and ECG with ST-segment elevations in noncoronary distribution. Typically, patients with acute myocarditis have global involvement of the myocardium and tend to have dilated ventricles, as is described in the above criteria, and present with clinical signs and symptoms of congestive heart failure. Patients with fulminant myocarditis, however, tend to have smaller, preserved chamber size, and their presentation tends to be more dramatic. Giant-cell myocarditis tends to also present with dramatic decline and is usually associated with ventricular arrhythmias.

A study by McCarthy et al. looked at 147 patients who were considered to have myocarditis on the basis of EMB and the Dallas histopathological criteria. Fulminant myocarditis was diagnosed on the basis of the presence of severe hemodynamic compromise, rapid onset of symptoms, and fever and was present in 15 patients. Ninety-three percent of the patients with fulminant myocarditis were alive without heart transplantation 11 years after biopsy. Fulminant viral myocarditis and hemodynamic compromise at presentation are associated with excellent recovery if early, aggressive intervention with medications and MCS is initiated. Preserved ejection fraction and smaller LV end-diastolic and left atrial dimensions are associated with a higher likelihood of spontaneous recovery.

If the hemodynamics of the patient are too unstable for medical management, MCS is an important option to consider. The device options depend on the expertise of the center, as well as what is appropriate to address the hemodynamics of the patient. In many cases of myopericarditis, temporary LV support is sufficient, and the patient can be bridged with an intra-aortic balloon pump or Impella. In cases of biventricular failure, however, strategies that support both ventricles may result in a better outcome. Of the options, venoarterial extracorporeal membrane oxygenation and BIVADs such as the CentriMag are the most widely used.

Venoarterial extracorporeal membrane oxygenation, which consists of a pump and an oxygenator, cannulates the venous system and returns blood into the arterial system after oxygenation. The benefit of this device is its ability to peripherally cannulate with outcomes similar to those of central cannulation. Thus, when short-term or emergent support is needed, this would be an excellent option. However, an additional surgical or percutaneous strategy to “vent” or decompress the LV may be necessary, with the intra-aortic balloon pump and Impella being the more common percutaneous strategies used currently. Venoarterial extracorporeal membrane oxygenation with or without an additional venting device should be used only for several days at most or as a bridge to a longer-term device (Table 3).

The CentriMag BIVAD system drains both the right and left sides of the heart and returns blood into the pulmonic and systemic circulation. It provides up to 10 L/min flow and allows total unloading of the right and left systems. The advantage of this device is its ability to unload and to ensure optimal cardiac output while allowing the myocardium to rest in cases that require support for the short term to a few weeks or as a bridge to a more permanent device. However, it is approved for only 30 days of support and carries a risk of thromboembolism and infection that increases with time (Table 3).

In addition to providing myocardial rest and decompression, neurohormonal modulation is important in patients with myocarditis. As with any other form of myocardial dysfunction, the mainstay of treatment is renin-angiotensin blockade, β-blockade, and aldosterone antagonists.

Although early administration of renin-angiotensin blockade has been shown to reduce progression remodeling and to reduce inflammation, necrosis, and fibrosis in animal models, one should be mindful of the vasodilatory effects of the drug and the risk of postoperative vasoplegia if the patient is going to require surgical intervention in the short term. The use of β-blockers should be avoided until the acute decompensated state has resolved. Carvedilol in particular has been shown to be protective in animal models with autoimmune myocarditis by suppressing inflammatory cytokines. Propranolol has been associated with decreased myocardial necrosis and suppression of inflammatory cytokine infiltration and production. The lack of β-blocker therapy has been associated with poor outcomes in patients with suspected myocarditis.

Aldosterone antagonists are recommended in the heart failure guidelines because of their association with suppression of fibrosis. In animal models, the anti-inflammatory effects of eplerenone were shown to improve cardiac remodeling in murine viral myocarditis. Its potassium-sparing properties and its minimal action on blood pressure make it an excellent agent in these patients because it does not cause hypotension.

When a patient presents with acute hemodynamic instability attributed to myocarditis, it is imperative that early aggressive pharmacological management and early use of MCS are considered. On the basis of the pathogenesis of myocarditis,
the appropriate management strategy could result in full recovery or at least preservation of end-organ function to allow cardiac replacement therapy with destination LVAD or heart transplantation. When appropriate, early immunosuppressive and antiviral therapy should also be used to optimize the patient’s outcome. Neurohormonal blockade should be administered as recommended by the American College of Cardiology Foundation/American Heart Association heart failure guidelines to augment the progression of inflammation and remodeling and to prevent extensive fibrosis.14 Early and aggressive intervention in acute myocarditis can result in optimistic outcomes, especially in the era of MCS.

Disclosures

Drs Jorde and Uriel are consultants for Thoratec and Heartware; Drs Mody and Lyons report no conflicts.

References


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Kanika P. Mody, James J. Lyons, Ulrich P. Jorde and Nir Uriel

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