

Title:

A Viral Illness, Congestive Heart Failure and a Road Show: Anesthetic Considerations for a Child with Constrictive Pericarditis

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Objectives:

1. To recognize potential complications of viral illness, such as myocarditis, cardiomyopathy, pericardial effusion, restrictive pericarditis, thyroiditis and their anesthetic implications.
2. To discuss the advantages and limitations of transthoracic vs. transesophageal echocardiogram, MRI and cardiac catheterization in evaluating the cardiac structure and function.
3. To organize age appropriate anesthetic plan for a critically ill pediatric patient undergoing diagnostic procedures in various non-OR locations
4. To formulate anesthetic plan for a major procedure, such as pericardial stripping, in a critically ill child with constrictive pericarditis.

Case presentation:

A 5 year-old girl is admitted to the hospital with dyspnea, tachypnea and tachycardia. She was healthy until a week ago when she had symptoms of clear rhinorrhea and 101°F fever for 3 days, now afebrile. She appears sick, physical examination reveals neck vein distension and liver enlargement. Complete blood count, basic metabolic set, sedimentation rate (ESR) and coagulation studies show elevation of white blood cell count to 12,000 cells/mcL and ESR of 25 mm/hr. Chest radiography shows clear lungs, increased vascular markings and cardiomegaly. A transthoracic echocardiogram reveals moderate myocardial thickening, minimal pericardial thickening and possible effusion, poor systolic function and diastolic relaxation. Patient is scheduled for cardiac catheterization and transesophageal echocardiogram for further evaluation.

Does this child need any additional evaluation prior to cardiac catheterization?
What are procedure and patient dependent anesthetic considerations?
Cardiac catheterization confirmed elevated bilateral atrial and ventricular end-diastolic pressure; endomyocardial biopsy showed mild myocarditis.
What is the differential diagnosis at this point?

Patient is now scheduled for cardiac MRI for further evaluation. What are advantages of CMRI over previous studies? What are specific anesthetic considerations for CMRI?

CMRI shows pericardial thickening and severe constrictive pericarditis. The child is now scheduled for pericardial stripping procedure.

Model Discussion:

Viral infection is a well-established cause of respiratory illness, generally characterized by acute onset of fever, myalgia and various respiratory symptoms. In an otherwise healthy person, viral infection usually resolves without residual problems. In some patients, respiratory and cardiovascular complications may follow.

Subacute thyroiditis is a well-known complication of acute illness caused by certain viruses, such as mumps, influenza or common cold. The resulting fluctuations of thyroid hormone levels can cause symptoms of decreased cardiac output and may mimic myocardial damage. Therefore it is imperative to exclude subacute thyroiditis and hypothyroidism as a cause of low cardiac output. In addition, co-existence of subacute thyroiditis may exacerbate symptoms of cardiac complications.

Cardiovascular complications associated with viral infection are myocarditis and/or pericarditis. Although viral infections are responsible for most cases, there are many other causes of both. Between 1950 and 1990, Coxsackie virus-B was most frequently detected. At the end of last century, adenovirus was added to the list and parvovirus B19 has been frequently detected in patients suffering from pericarditis and myocarditis. The initial clinical presentation of both can be similar. However, it is important to differentiate between these entities early in the disease, as treatment is different and can prevent or diminish complications of each.

In cases of myocardial infection there is direct invasion by cardiotropic virus causing immunologic activation. It is characterized by inflammatory cellular infiltration by natural killer cells and macrophages with subsequent expression of pro-inflammatory cytokines such as IL-1, IL-2, TNF and interferon. As a result, activation of cell-mediated immunity prompts clonal expansion of B cells, resulting in further myocytolysis, additional local inflammation and production of circulating anti-myocardial antibodies. In patients with normal immune system there are several processes that facilitate viral clearing and allow healing to occur, whereas abnormal immunoresponsiveness can alter the delicate balance by either promoting ineffective viral clearing or favoring persistent T-cell or antibody mediated myocyte destruction. Acute dilated cardiomyopathy (DCM) and less frequently restrictive cardiomyopathy are serious potential complications of viral myocarditis. ECG changes in the area of distribution of more than 1 coronary vessel, lack of risk factors for coronary disease and global ventricular dysfunction support the diagnosis of DCM, which can be confirmed by endomyocardial biopsy.¹

Coxsackie virus B is the most common cause of pericarditis following acute viral illness. However, influenza A, HIV and arbovirus are often implicated as well. The other common causes of pericarditis include tuberculosis, uremia, mediastinal irradiation and previous cardiac surgical procedures.²

Acute pericarditis often presents with chest pain, fever, weakness, shortness of breath, palpitations and coughing. Most cases of pericarditis are mild and self-limited.

However, few patients develop complications such as cardiac tamponade and constrictive pericarditis that require additional treatment.

Constrictive pericarditis is a rare but severely disabling consequence of the inflammation of the pericardium. The constrictive pericarditis is characterized by thickened, fibrotic pericardium leading to impaired diastolic relaxation and filling of the ventricles with subsequently reduced ventricular function. Constrictive pericarditis is a chronic condition usually well tolerated by the patient until it is well advanced. The key feature of constrictive pericarditis is increased ventricular filling pressure and decreased stroke volume, which often resembles a restrictive cardiomyopathy and in the setting of acute viral illness presents a diagnostic dilemma. Since the treatment of these entities is very different, it is imperative to identify the type and extent of cardiac involvement as early as possible.³

Unlike restrictive cardiomyopathy, patients with constrictive pericarditis have preserved ventricular relaxation. The ventricular diastolic filling is restricted by thickened pericardium, therefore normal ventricular end-diastolic volumes are not obtained and stroke volume is decreased. Compensatory increase in endogenous catecholamine levels results in increased heart rate and contractility and is a common clinical presentation of a patient with constrictive pericarditis. If decrease in ventricular diastolic volume is prolonged and severe, it causes a decline in cardiac output and leads to decreased renal perfusion. The decreased renal perfusion leads to an increased aldosterone level, sodium and water reabsorption and increased extracellular volume. The greater extracellular volume increases RV filling pressure, which is essential for maintaining ventricular diastolic volume in the presence of severe pericardial constriction.

Patients with constrictive pericarditis and pericardial tamponade have similar presentation and hemodynamic features. Clinical presentations can be fatigue, peripheral edema, breathlessness, and abdominal swelling, which may be aggravated by a protein-losing enteropathy. Typically, there is a long delay between the initial pericardial inflammation and the onset of constriction. Venous congestion, hepatomegaly, pleural effusions and ascites signify decompensation. Hemodynamic impairment of the patient can be additionally aggravated by a systolic dysfunction due to myocardial fibrosis or atrophy. Differential diagnosis has to include acute dilatation of the heart, pulmonary embolism, right ventricular infarction, pleural effusion, chronic obstructive lung disease and restrictive cardiomyopathy.

Physical findings, ECG, chest radiography, CT and hemodynamic measurements are important initial steps in evaluating a patient with suspected constrictive pericarditis. The analysis of respiratory changes with or without changes of preload by Doppler and/or tissue Doppler echocardiography can distinguish constrictive pericarditis from restrictive cardiomyopathy. Noninvasive diagnostic myocardial imaging techniques may include echocardiography, nuclear imaging with gallium⁶⁷- or indium¹¹¹-labeled antimyosin monoclonal antibodies, and MRI. Cardiac catheterization and endomyocardial biopsy may be helpful as well. The following discussion will focus on the strengths and weaknesses of these diagnostic tests.

Transthoracic echocardiography is an important noninvasive technique for the initial evaluation of a patient with suspected peri- or myocarditis. Echocardiography is

used to identify and quantify the pericardial effusion, detect cardiac tamponade or evaluate ventricular function. Pinamonti et al retrospectively analyzed echocardiographic findings of 42 patients with biopsy-proven myocarditis. In this study 64% of the patients showed left ventricular dysfunction, even though left ventricular cavity enlargement was minimal or absent; 23% had right ventricular dysfunction, and 64% of them had segmental wall motion abnormalities with hypokinetic, akinetic and frankly dyskinetic regions. Left ventricular hypertrophy was reversible in 20% of these patients, 15% had ventricular thrombi and 7% of the patients developed restrictive ventricular filling. The anatomic echocardiographic findings can be varied and relatively nonspecific.⁴

However ultrasonic tissue characterization can detect the presence of myocardial interstitial edema. Tissue Doppler imaging and myocardial velocity measurements can detect changes in acute myocarditis and monitor these parameters over time.⁵

Felker et al. distinguished fulminant myocarditis with rapid onset of illness with severe hemodynamic compromise from acute myocarditis by echocardiographic criteria of septal thickness and left ventricular dimensions. Patients with fulminant myocarditis had near normal left ventricular dimensions, but increased septal thickness at presentation, while those with acute myocarditis had increased diastolic dimensions but normal septal thickness.⁶

The advantage of transesophageal echocardiogram (TEE) over TTE was shown to be insignificant in these cases. Subjectively, the image quality was better by TEE; however, this did not have any impact on the management or outcome. In addition, TEE in children usually requires general anesthesia with endotracheal intubation and positive pressure ventilation of the patients. Therefore TEE should be reserved for those cases where adequate transthoracic study cannot be performed.

Nuclear medicine techniques include Gallium-67 and indium-111 monoclonal antimyosin antibody and other isotope imaging.

O'Connell et al evaluated Gallium-67 myocardial imaging as an adjunct to endomyocardial biopsy in the diagnosis of myocarditis in 68 patients with dilated cardiomyopathy. Histologic myocarditis was identified in only 8% of biopsy specimens. Five of 6 biopsy samples (87%) with myocarditis showed dense gallium-67 uptake, whereas only 9 of 65 negative biopsy samples (14%) were paired with equivocally positive gallium-67 scan ($P < 0.001$). Single photon emission computed tomography (SPECT) improved the differentiation between pericardial and myocardial localization, which was difficult with planar images alone. However, the use of gallium imaging has diminished over time mainly because of a lack of specificity.

Yasuda et al. were the first who reported the use of an indium-111 monoclonal antimyosin antibody imaging in the diagnosis of acute myocarditis and myocardial necrosis. As compared to the gold standard, i.e. a right ventricular biopsy, the sensitivity of antimyosin scan is 100% sensitive and 58% specific. Owing to the high sensitivity of antimyosin scans, it has been an important cornerstone in the diagnosis of myocarditis over last 30 years.

Other tracers. Technetium-99m-sestamibi (methoxyisobutylisonitrile) SPECT (99mTc-MIBI SPECT) has proven to be an important adjunct in assessing the severity of myocardial ischemia. Sun et al. compared 99mTc-MIBI SPECT with other cardiac evaluation methods in order to assess its role in the diagnosis of Coxsackie viral myocarditis in children. Their results suggest that the presence of myocardial uptake of

^{99m}Tc-MIBI may be a marker of myocardial inflammation and necrosis. Thallium-201 myocardial perfusion defects at rest are suggestive of fibrosis evoked by myocarditis, however no differences were found in athletes and volunteers. Therefore these and other tracers have not been used in clinical setting.

In summary, indium 111-antimyosin antibody imaging has been intensively used for more than two decades for diagnosis of myocarditis. However, at present the availability in the US is limited, radiation exposure, which is especially of concern in younger patients, and 48 hour lag in obtaining images after injection caused the application to fall out of favor over the last decade.

Cardiac magnetic resonance imaging (CMRI) has emerged as an important technique in the diagnosis of cardiovascular disease. This technique allows the analysis of functional parameters of the heart such as left ventricular function, regional wall motion abnormalities, dimensions and flow properties within the heart chambers and major blood vessels, as well as imaging of myocardial tissue and detection of focal or global inflammation to a greater degree than other imaging modalities. Most scans are T1-weighted images before and after gadolinium enhancement.

Addition of gadolinium diethylenetriaminepentacetate in its protonated form (usually referred to as gadopentetate dimeglumine or Gd-DTPA) enhances imaging of blood vessels and of inflamed or diseased tissue when the blood vessels' permeability is increased. Diffuse myocyte injury can increase the volume of distribution and subsequently the extraction fraction of extracellular compounds such as Gd-DTPA resulting in abnormal myocardial enhancement. In comparison to healthy volunteers, the patients with suspected acute myocarditis had an increased global relative signal enhancement of the left ventricular myocardium.⁷

A combination of different techniques including T1 spin echo before and after gadolinium enhancement was studied in 12 patients with suspected acute myocarditis. Ten of 12 patients in the myocarditis group showed focal myocardial enhancement with associated regional wall motion abnormalities.

Laissy et al. compared the value of different CMRI modalities in patients with acute myocarditis. Subtraction Gd-DTPA-enhanced T1 weighted CMRI accurately identified myocardial involvement. Gutberlet et al. performed retrospective analysis comparing the diagnostic accuracy of three CMRI approaches in detection of myocardial inflammation in patients clinically suspected of having chronic myocarditis. They found that the sensitivity, specificity and diagnostic accuracy of the T1-weighted imaging after contrast agent administration, compared with immunohistologic detection of inflammation were 62, 86, and 72% respectively. Wagner et al. conducted a series of CMRI and found that contrast enhancement 4 weeks after onset of symptoms was predictive for the functional and clinical long-term outcomes. T1-weighted and T1 contrast-enhanced CMRI sequence has its clinical value in differentiation of pericardial effusion, which may accompany myocarditis and pericardial inflammation in cases where constrictive pericarditis developed. T2-weighted images focus on the relaxation time, and are indicative of tissue water content, which is increased in inflammation or necrosis, i.e. early myocardial infarction or myocarditis. Gagliardi et al published two case series on the use of CMR for non-invasive diagnosis of acute myocarditis. Compared with biopsy, T2-weighted spin echo CMRI sequences were found to have a high sensitivity and specificity.⁸

However, other researchers found that these images are susceptible to motion artifacts and the image quality of the myocardium is poor. A triple inversion press hold sequence with short acquisition time (STIR) was developed and led to a much better image quality. As a result, in patients clinically suspected of having myocarditis, a STIR sequence seems to have a good sensitivity, specificity and diagnostic accuracy in detecting tissue edema, a consistent feature of the inflammatory reaction in the myocardium.

Comparison of echocardiography and cardiovascular magnetic resonance. There are several case reports with normal echocardiographic findings and a diagnosis of myocarditis made by magnetic resonance imaging. Kontongianni et al. report two male adolescents (15 and 19 years old) who were admitted to the hospital because of chest pain associated with respiratory movement even though their clinical presentation highly suggested having acute myocarditis. The echocardiogram performed in both patients failed to reveal any regional or global wall motion abnormalities or diastolic dysfunction and remained absolutely normal throughout their 3-month follow up period. CMRI within 7 days using T2-weighted and gadolinium enhanced T1-weighted images demonstrated extensive focal contrast enhancement, consistent with acute inflammatory myocardial involvement. Thus contrast CMRI is a more sensitive method than the echocardiogram for the diagnosis of acute focal myocarditis.

Computer tomography (CT) with multislice techniques is useful in the diagnosis of coronary artery disease. Brooks and Sane report two patients with clinical myocarditis who had distinctive findings at coronary CT. Both patients demonstrated delayed myocardial enhancement with iodinated contrast. The morphologic features of enhancement were similar to the myocardial enhancement with gadolinium contrast on magnetic resonance imaging recently described in patients with myocarditis and different from the enhancement patterns seen in patients with myocardial infarction.

Dambrin et al. investigated the diagnostic value of ECG-gated multidetector CT in the early phase of suspected acute myocarditis in 12 consecutive patients admitted for suspected acute myocarditis less than 10 days after onset of symptoms. All patients had clinical, electrocardiographic and laboratory findings consistent with the diagnosis. They compared the CT results to CMRI using T1-weighted delayed enhancement images after injection of gadolinium. Extent and location of hyper-enhancement at CT correlated well with that observed at MR examination.⁹

Although computed tomography can be used to diagnose myocarditis, the major limitation is the radiation exposure to the patients. Despite the dose reduction due to the use of lower tube voltage exposure, prospective ECG pulsing and utilization of new protocols, computed tomography is still limited by the radiation exposure.

When non-invasive techniques cannot confirm the underlying etiology, cardiac catheterization may be the definitive test for diagnosis. Direct intracardiac pressure measurement and access to endomyocardial biopsy help establish definitive diagnosis. In euvolemic patients with constrictive pericarditis right atrial pressure is usually 15 mmHg or greater and equals left atrial pressure. Both constrictive pericarditis and cardiac tamponade demonstrate a diastolic “pressure plateau” or “equalization of pressure”, in which the right atrial pressure equals the right ventricle end-diastolic pressure, pulmonary artery diastolic pressure, and left atrial pressure. The definitive treatment should be

pericardiectomy. Pericardiectomy is the only treatment for permanent constriction. The indications are based upon clinical symptoms, echocardiography findings, CT/MRI, and heart catheterization. The approaches are subxiphoid, anterolateral thoracotomy or median sternotomy with or without cardiopulmonary bypass, with partial or complete resection of the diseased pericardium.¹⁰

Anesthetic considerations of pediatric patient with suspected/confirmed constrictive pericarditis

In pediatric patients many diagnostic tests such as transesophageal echocardiogram, cardiac MRI, CT and/or cardiac catheterization require anesthesia support prior to establishment of definitive diagnosis. Therefore complete history, physical examination and results of all noninvasive studies completed up to that point should be taken into consideration to narrow down differential diagnosis and devise anesthetic plan depending on the patient's age and the invasiveness of the procedure. Maintenance of hemodynamic stability is the most important anesthetic goal.

Monitoring should assess the compensatory mechanisms in constrictive pericarditis. The ECG should be observed for heart rate and ischemic changes, and applying proper therapeutic interventions. An indwelling arterial catheter for continuous BP monitoring should be established prior to induction of general anesthesia. A central venous pressure catheter is often indicated for venous access in patients with constrictive pericarditis undergoing more than minor procedure. The use of a pulmonary artery catheter is controversial, however, and has not been shown to improve outcomes. In patients with advanced disease, use of a pulmonary artery catheter may provide useful information about cardiac function, preload and cardiac output, particularly in the postoperative period when echocardiography is often not readily available. When these patients undergo non-cardiac surgery other than minor procedures, potential hemodynamic compromise is likely and intraoperative transesophageal echocardiogram is often indicated.

The main anesthetic goals are to minimize any effects of anesthetic techniques and drugs on the compensatory mechanisms that maintain hemodynamic stability in patients with constrictive pericarditis. Accordingly, bradycardia and myocardial depression must be avoided, and preload and afterload need to be maintained in the face of a fixed, low stroke volume and cardiac output. It is reasonable to induce general anesthesia using IV ketamine or etomidate titrated to effect. Ketamine can cause direct myocardial depression and should be used with caution. Propofol is relatively contraindicated because it may produce hypotension. Thiopental is best avoided because of venodilation and cardiac depression. A high-dose opioid anesthesia will not depress myocardial contractility, but the associated bradycardia may not be tolerated. In these patients who rely on sympathetic tone for compensation, even the use of high-dose opioids may cause sudden hemodynamic compromise during anesthetic induction and must be immediately treated, preferably with epinephrine and norepinephrine. The use of a spinal/epidural technique is not recommended in symptomatic patients with constrictive pericarditis because of the sympathectomy.

Post-pericardiectomy respiratory variations of mitral/tricuspid flow are found in 9–25%. Left ventricular ejection fraction increases due to a better ventricular filling but consistent changes of the left and right atrial sizes were not reported. Major

complications include acute perioperative cardiac insufficiency and ventricular wall rupture. Cardiac mortality and morbidity after pericardiectomy is mainly caused by the unrecognized myocardial atrophy or myocardial fibrosis. Myocardial atrophy is characterized by: (1) Thinning of the interventricular septum and posterolateral wall (<1 cm); (2) Reduction of the wall thickening during the cardiac cycle (<40%); and (3) Reduction of the left-ventricular muscle mass (LVMM)/end-diastolic volume (EDV) ratio (<1). Myocardial fibrosis should be considered whenever the thickened/calcified pericardium is not separated from the myocardium by subepicardial fat and when the myocardial wall is showing wave-like appearance with wall thinning. Simple exclusion of patients with extensive myocardial fibrosis and/or atrophy led to a reduction of the mortality rate for pericardiectomy to 5%. After pericardiectomy was performed, low cardiac output can persist and it should be treated by fluid substitution and catecholamines, high doses of digitalis, and intra-aortic balloon pump in most severe cases. If the need of pericardiectomy was established early, long-term survival after pericardiectomy corresponds to that of the general population. However, in some patients with long period of constrictive pericarditis even a complete pericardiectomy may not achieve a total restitution. Therefore it is critical to obtain early diagnosis so the proper treatment can be administered.

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