32 Myocarditis and Cardiomyopathy

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Myocarditis

Myocarditis is an inflammatory disease of the myocardium most commonly caused by cardiotropic viruses, most of which have no specific antiviral therapies. Therapies are largely supportive to try to allow the myocardium to recover while supported either pharmacologically or with mechanical circulatory support. Making the diagnosis of myocarditis is difficult because viral syndromes are very common in children and it can be difficult to determine whether a child presenting with a viral prodrome or ongoing viral illness and heart failure actually has an acute process or has had a subclinical longer-standing cardiomyopathy (typically dilated cardiomyopathy [DCM]) that has been "tipped over the edge" by the increased stress and metabolic demands of an intercurrent infectious illness.

Diagnosis

Laboratory studies that are typically ordered include sedimentation rate (ESR), C-reactive protein (CRP), CBC with differential, troponins and cardiotropic viral PCRs of the blood, nasal washing and/or tracheal aspirate, if intubated. Viral PCRs are preferred over viral serologies. Electrolytes, BUN, creatinine, lactate, LFTs, amylase, and lipase are checked to estimate the degree of end-organ compromise. Brain natiuretic peptide is also measured. Significantly elevated ESR, CRP, troponins, and a positive PCR favor a diagnosis of myocarditis over DCM.

In myocarditis, the ECG often demonstrates ST- and T-wave changes that mimic ischemia (Figure 32-1). Very low voltages may be seen. DCM more typically demonstrates LVH with nonspecific ST changes, T-wave inversion, or a strain pattern.

The echocardiogram demonstrates varying degrees of dysfunction, but often the LV function is severely depressed. A more normal LV end-diastolic dimension with severe dysfunction favors myocarditis while a severely dilated thin-walled LV favors DCM.

Cardiac MRI (CMR) has become a frequently used tool to assess for evidence of cardiac inflammation; scarring would suggest a more long-standing process. However, CMR often requires anesthesia, the risk of which often outweighs the benefit in a critically ill child with severe cardiac dysfunction. Findings often do not change therapy, further reducing the risk-benefit ratio.

Endomyocardial biopsy is the gold standard for the diagnosis of myocarditis, however it also carries significant risks, including anesthesia in a critically ill child. Sampling error reduces the reliability of this test since the histopathologic changes of myocarditis can be patchy and absent in the samples taken. Similar to CMR, findings often do not change therapy.

Treatment

Therapy is largely supportive. If a virus is found that has specific antiviral therapy, the antiviral agent should be used. Diuretics, inotropes, and vasopressor support are titrated per cardiorespiratory status. While milrinone (if BP is adequate) and/or epinephrine

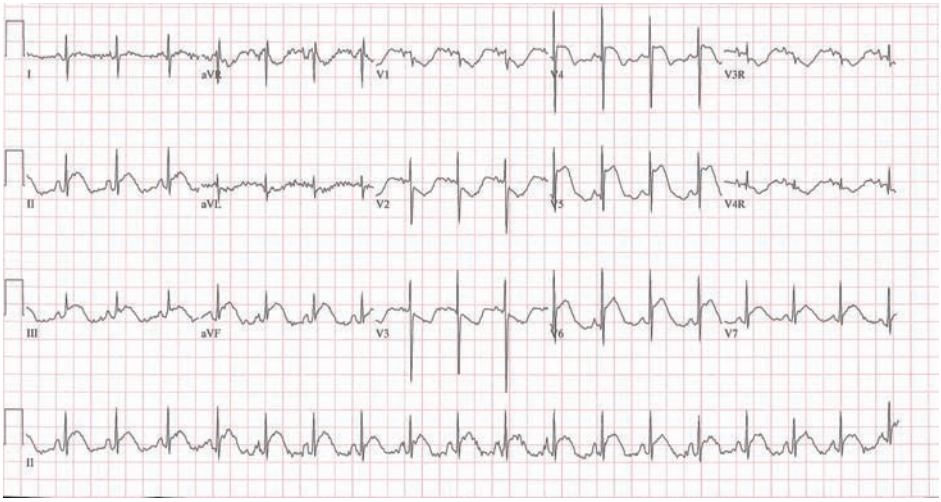

Figure 32-1. ECG from a patient with myocarditis demonstrating marked ST-segment elevation in the inferior leads and V4 to V7 with "tombstoning", most classically shown in leads V5 and V6. ST-segment depression is seen in aVR, aVL, and V1 to V3.

are commonly used, other institutions commonly use other agents. Ventilatory support is often needed and can help with cardiac support to some extent.

The use of IV immunoglobulin (IVIG) and other immunomodulating drugs has had mixed results in a variety of study types. In patients with a preponderance of evidence suggesting myocarditis, as opposed to acutely decompensated DCM, IVIG is used. We reserve corticosteroids for those with "tombstoning" ST segments on ECG.

In patients who continue to decline despite maximal medical therapy with poor oxygenation, ECMO with an LA vent or atrial septostomy may be needed. If the pulmonary status is not severely compromised, a temporary left ventricular assist device (LVAD) is preferred due to better LV decompression, which is important to promote LV recovery. If there is no, or very limited myocardial recovery, the patient may need to be transitioned to long-term LVAD support to await cardiac transplantation.

Outcomes

Those with a fulminant presentation frequently are the most likely to recover with aggressive early support. Freedom from death and transplant varies widely in reports from 50 to 90%, with about 75-80% being a reasonable statistic to quote.

Dilated Cardiomyopathy (DCM)

DCM is a disease of the heart muscle characterized by an enlarged LV chamber and in most cases, impaired systolic function. It is the most common form of cardiomyopathy in children in the US. Symptoms of heart failure may progress to end-stage disease necessitating mechanical circulatory support (MCS) as a bridge to transplant.

Diagnosis

The most common time of diagnosis of DCM is infancy. Signs of heart failure are typically present, including hepatomegaly, gallop rhythm, failure to gain weight, diaphoresis while feeding, tachypnea, and retractions. In older children, symptoms may include abdominal pain, vomiting, fatigue, dyspnea with exertion, and orthopnea. CXR usually reveals cardiomegaly and less commonly, pulmonary vascular congestion and/or pleural effusions. The ECG often demonstrates LVH and nonspecific ST-segment abnormalities. Sinus tachycardia is common. A fixed tachycardia should be investigated for possible tachycardia-induced cardiomyopathy, as this is a potentially reversible cause. Conduction disturbances may occur. Echocardiography reveals a dilated LV with depressed systolic function, with or without MR.

Causes

Most cases are "idiopathic", as a cause usually is not determined. Metabolic causes/inborn errors of metabolism and malformation syndromes should be assessed for, particularly in infants. Neuromuscular diseases should be excluded. Other etiologies include familial or genetic mutations and possible infectious or inflammatory diseases. Genetic testing is recommended.

Treatment

When presenting with decompensated heart failure, the primary therapeutic goals are alleviation of symptoms and correction of hemodynamic derangements. IV diuretics are usually necessary and effective for treating congestion. Inotropic agents such as milrinone and epinephrine are useful for treating low cardiac output. Once symptoms are relieved and fluid balance restored, oral therapies are initiated. If tolerated, most outpatients should be treated with a beta-blocker (carvedilol or long-acting metoprolol), angiotensin-converting enzyme (ACE) inhibitor and an aldosterone antagonist (spironolactone). If symptoms cannot be controlled and there is evidence of progressive end-organ damage, MCS should be considered. Temporary LV support can be transitioned to a long-term LVAD for those without evidence of ventricular recovery. Long-term RV mechanical support is seldom necessary.

Outcome

Survival after diagnosis of DCM varies widely. For all causes of DCM, 5-year freedom from death or transplantation is about 50%.

Hypertrophic Cardiomyopathy (HCM)

HCM is the second most common form of cardiomyopathy in children. It is characterized by abnormally thick ventricular walls, usually with preserved or hyperdynamic systolic function. Restrictive physiology may develop in some and a "burned-out dilated" form in a small subset. HCM is the most common cause of sudden cardiac death in young athletes in the US.

Diagnosis

The signs and symptoms of HCM may be subtle or nonexistent. Symptoms may include fatigue, dyspnea with exertion, chest pain, palpitations, and lightheadedness. Sudden

death may be the first symptom, with diagnosis at autopsy. Findings on examination may include a parasternal heave, systolic ejection murmur that increases with Valsalva maneuver, and an extra heart sound. The ECG usually demonstrates LVH with or without a strain pattern. CXR may reveal a normal or minimally enlarged cardiac silhouette. On echocardiogram, asymmetric septal hypertrophy is frequently present, with or without obstruction in the LVOT. The RV is typically spared, but may be hypertrophied. Gene testing should be considered in new cases of HCM, especially when another family member is affected. Exercise testing is suggested in new cases of HCM if the resting peak instantaneous gradient is <50 mmHg for risk profile assessment for sudden death (e.g., abnormal BP response to exercise).

Causes

Most cases of HCM are likely attributable to gene mutations in sarcomeric proteins. First-degree relatives should undergo screening with echocardiography as HCM may be familial. If a gene has been identified in the proband, family members should be offered gene testing**.** Other etiologies include metabolic disorders and genetic syndromes, which are more commonly diagnosed in infancy, and neuromuscular disorders.

Treatment

There is no medical therapy for HCM that will result in remodeling of the ventricular myocardium. Treatment of HCM is focused on relief of symptoms and includes beta-blockers or calcium-channel blockers. These patients are restricted from physical education and sports. Patients who remain symptomatic with severe LVOT obstruction usually benefit from surgical myectomy. Those at increased risk of sudden death should be considered for implantation of a cardioverter-defibrillator for primary prevention. Patients considered at greater risk include those with a first-degree relative who died suddenly, documented ventricular tachycardia, syncope, and severe ventricular hypertrophy. MCS and cardiac transplantation are not usually needed in HCM, however those with refractory life-threatening arrhythmias, progressive restrictive physiology, "burned-out" forms, or other refractory symptoms may benefit from transplant.

LV Noncompaction Cardiomyopathy (LVNC)

LVNC is a less common form of cardiomyopathy and is characterized by a hypertrabeculated spongy appearance of the LV more commonly than the RV. It can manifest in dilated, hypertrophic, and restrictive forms. Treatment is based on the phenotype. These patients are also arrhythmia-, clot-, and stroke-prone, requiring vigilance for those morbidities with initiation of antithrombotic therapies, particularly in the dilated and restrictive phenotypes. Antiarrhythmic therapies, including consideration of an implantable cardioverter defibrillator, may be necessary in some at-risk patients.

Restrictive Cardiomyopathy (RCM)

RCM results in severe diastolic dysfunction with limited cardiac filling leading to low cardiac output and eventual pulmonary hypertension. There are no good medical therapies for RCM. Treatment consists of judicious use of diuretics for overt systemic or

pulmonary venous congestion and aspirin or other anticoagulant to prevent thrombosis. Prognosis is poor; within 3 years of diagnosis approximately 50% have died or undergone cardiac transplantation. Early consideration and listing for cardiac transplantation is advised as these patients are difficult to support pharmacologically and mechanically once they become critically ill.

Arrhythmogenic Right-Ventricular Cardiomyopathy (ARVC)

ARVC typically presents in late adolescents or young adults with symptoms related to ventricular arrhythmias, preceding overt cardiomyopathy. However, in early childhood, it may present as a dilated form of cardiomyopathy with a higher ventricular tachycardia burden than is typically seen in childhood DCM. Features of RCM may also be present. Treatment is directed towards arrhythmia control and the cardiac phenotype, using standard heart failure therapies.