Pediatric Viral Myocarditis —
Pathophysiology and Treatment

Myocarditis is an inflammatory condition of the heart that is usually a consequence of a viral illness. Enteroviruses and adenoviruses are the most commonly identified etiologies for the condition. Inflammatory cellular infiltrates of the myocardium and myocyte necrosis is usually evident in the acute phase of the illness. Diagnostic workup includes polymerase chain reaction testing to identify the viral cause, echocardiography to assess the left ventricular function and advanced imaging techniques that confirm inflammation of the myocardium. Treatment is mainly supportive.

Overview

Myocarditis is defined as the inflammation of the myocardium due to a viral etiology. The result of this inflammatory process is the necrosis of myocytes and the infiltration of the myocardium by inflammatory cells. The most common viral etiologies of myocarditis are adenovirus and enterovirus, but non-infectious causes due to drug toxicity have also been described.
Acute myocarditis is defined as the **acute and abundant presence of inflammatory cells and myocardial necrosis**. Borderline myocarditis is a condition that is also characterized by the death of myocytes, but with very little inflammatory cellular infiltrates.

**Epidemiology of Myocarditis**

Myocarditis is a **very rare condition**. The estimated incidence of myocarditis as a complication of enterovirus infection is around 1 to 4%. Myocarditis has been described with an equal incidence in both sexes, but the disease’s aggressiveness is thought to be higher in males.

**Newborns and infants are the most likely patients to develop myocarditis**, presumably due to the incomplete development of their immune system. The mortality rate of viral myocarditis is very high in neonates, 75%. Older children with myocarditis have a considerably lower mortality rate, 25%, but the condition is still considered as very serious.

Complete recovery of the left ventricular function after myocarditis has been described in up to 50% of the cases. The most common complications of myocarditis are ventricular arrhythmias, congestive heart failure, thromboembolism, dilated cardiomyopathy and recurrent ongoing chronic myocarditis.

**Pathophysiology of Myocarditis**

The most common causes of myocarditis are viral in origin. The **enteroviruses “coxsackieviruses type A and B”** are implicated in the majority of the cases. Adenovirus types 2 and 5 also account for a significant number of the cases.

**Parvovirus B19 and herpesvirus 6** have been identified as the most common etiologies of acute myocarditis when a polymerase chain reaction test is used for diagnosis. Other viruses, such as the cytomegalovirus, can also cause myocarditis, especially in immunocompromised children.

**Mumps, rubella, measles and varicella** have all been implicated with viral myocarditis. Finally, the human immunodeficiency virus can cause myocarditis in the acute stage of the disease.

Once the child acquires one of the previously mentioned viruses, the virus undergoes an **initial phase of replication within the myocytes**. The **natural killer cells are activated** and they help to lyse infected myocytes to contain the infection.

The second late phase is characterized by the **activation of T lymphocytes** which causes inflammation of the myocardium. Additionally, **apoptosis is activated** and is believed to be responsible for dilated cardiomyopathy which is commonly seen in patients with myocarditis.

**Auto-antibodies** are also synthesized and are present in up to 60% of the cases of myocarditis. The exact role of these auto-antibodies in the pathophysiology of myocarditis is not yet known, but they are helpful in establishing the diagnosis. Anti-myosin heavy chain antibodies, anti-alpha myosin antibodies, and anti-myolemma antibodies have been all seen in the sera of patients with myocarditis.
Clinical Presentation of Myocarditis

Patients who develop myocarditis can have **no symptoms**, **be mildly symptomatic** or **have a life-threatening illness**. A prodromal phase of a flu-like illness usually precedes the development of cardiac specific symptoms in most patients.

The most common presentation of myocarditis is **acute heart failure**. Younger children usually present with signs and symptoms suggestive of impaired peripheral perfusion due to acute cardiac decompensation, while older adults might complain of chest pain before the development of overt heart failure.
The most common cardiac arrhythmia seen in myocarditis is sinus tachycardia due to cardiac dysfunction. More severe ventricular arrhythmias can also happen, and they are usually associated with a worse outcome.

Fever, when present, is usually low-grade. Patients can be also lethargic, can develop shortness of breath, and be anorexic. Excessive sweating is also commonly seen in patients with myocarditis.

Signs of decreased cardiac output can be seen on physical examination and include weak peripheral pulses, delayed capillary refill time and cool extremities. Pericarditis and pericardial effusion can complicate the picture. Patients with pericarditis usually have muffled heart sounds.

Diagnostic Workup for Myocarditis

Laboratory investigations are helpful in excluding other causes of acute heart failure in children, such as anemia and sepsis. Lymphocytosis might be seen in viral infections, and can be noticed in patients with myocarditis due to viral etiologies.

The erythrocyte sedimentation rate and c-reactive protein serum levels are usually elevated. These are non-specific inflammatory markers. Nasopharyngeal swabs are helpful in the isolation and identification of the viral etiology of myocarditis.

Antibody-viral specific titers that show a 4-fold increase confirm the diagnosis of an acute viral infection and are helpful. Polymerase chain reaction testing is helpful in the identification of the viral DNA or RNA despite a low viral load.

Patients with myocarditis are expected to have myocardial cell necrosis; therefore, elevated levels of creatinine kinase MB isoenzymes are commonly seen. Troponin I levels are usually elevated due to myocardial damage.

Imaging studies are very helpful in the evaluation of the patient suspected to have myocarditis. A chest x-ray might reveal cardiomegaly due to dilated cardiomyopathy.

Magnetic resonance imaging with gadolinium contrast administration is helpful in the evaluation of myocarditis. Due to the inflammatory nature of the condition, enhanced gadolinium contrast detection can be observed in the myocardium.

Echocardiography is the most commonly used diagnostic test in the evaluation of myocarditis. The most common finding is decreased ventricular wall motion, global hypokinesis. Increased left ventricular end diastolic and systolic volumes, suggestive of dilated cardiomyopathy, are commonly seen. Impaired left ventricular systolic function is another common finding with myocarditis.

When a biopsy is performed, the classification of the disease’s stage becomes feasible. Microscopic examination of the tissue obtained in acute myocarditis is characterized by the presence of interstitial inflammatory cellular infiltrates. Possible inflammatory cells that one can see on histology examination include mononuclear cells, lymphocytes, plasma cells and eosinophils. Polymerase chain reaction testing can be used on tissue samples to help amplify the viral genome and identify the etiology.

Treatment of Myocarditis

The mainstay treatment for myocarditis is supportive in nature. All patients with suspected myocarditis should be admitted to the hospital, regardless of the severity of the condition.
Patients with myocarditis might develop hypoxemia. Supplemental oxygen therapy has been associated with an improved outcome and is therefore recommended. Inotropic agents and anticoagulation therapy should be reserved for more severe cases.

Patients who develop severe left ventricular dysfunction might benefit from a temporary left ventricular assist device. This approach is usually used as a bridge to transplantation.

Those who develop congestive heart failure as a complication to myocarditis should be put on a low-salt diet. Bed rest is very important, especially in the acute phase of myocarditis. Decreasing left ventricular function is commonly seen in patients who developed myocarditis; therefore, serial echocardiography is indicated. Chronic use of inotropes is not recommended.

References


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