Myocarditis

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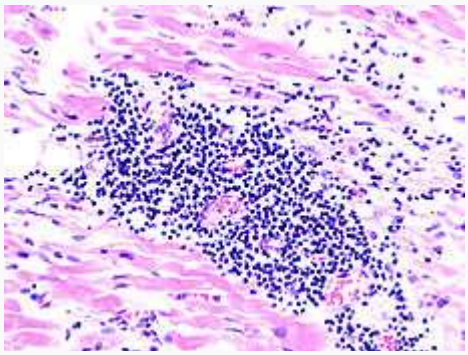
Myocarditis
Classification and external resources

Histopathological image of myocarditis at autopsy in a patient with acute onset of congestive heart failure.

In medicine (cardiology), **myocarditis** is inflammation of heart muscle (myocardium). It resembles a heart attack but coronary arteries are not blocked.

Myocarditis is most often due to infection by common viruses, such as parvovirus B19, less commonly non-viral pathogens such as Borrelia burgdorferi (Lyme disease) or Trypanosoma cruzi, or as a hypersensitivity response to drugs.[1]

The definition of myocarditis varies, but the central feature is an infection of the heart, with an inflammatory infiltrate, and damage to the heart muscle, *without* the blockage of coronary arteries that define a heart attack (myocardial infarction) or other common non-infectious causes. [2] Myocarditis may or may not include death (necrosis) of heart tissue. It may include dilated cardiomyopathy.[1]

Myocarditis is often an autoimmune reaction. Streptococcal M protein and coxsackievirus B have regions (epitopes) that are immunologically similar to cardiac myosin. After the virus is gone, the immune system may attack cardiac myosin.[1]

Because a definitive diagnosis requires a heart biopsy, which doctors are reluctant to do because they are invasive, statistics on the incidence of myocarditis vary widely.[1]

The consequences of myocarditis vary widely. It can cause a mild disease without any symptoms that resolves itself, or it may cause chest pain, heart failure, or sudden death. An acute myocardial infarction-like syndrome with normal coronary arteries has a good prognosis. Heart failure, even with dilated left ventricle, may have a good prognosis. Ventricular arrhythmias and high-degree heart block have a poor prognosis. Loss of right ventricular function is a strong predictor of death.[1]

Signs and symptoms

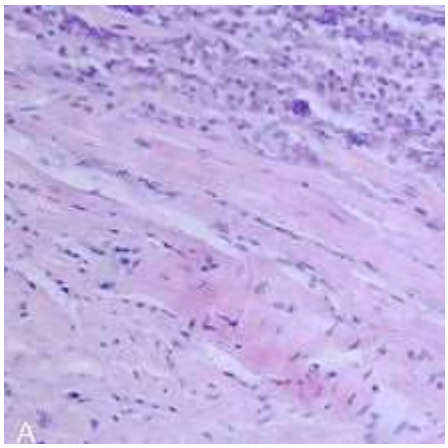
The signs and symptoms associated with myocarditis are varied, and relate either to the actual inflammation of the myocardium, or the weakness of the heart muscle that is secondary to the inflammation. Signs and symptoms of myocarditis include:[3]

- Chest pain (often described as "stabbing" in character)
- Congestive heart failure (leading to edema, breathlessness and hepatic congestion)
- Palpitations (due to arrhythmias)
- Sudden death (in young adults, myocarditis causes up to 20% of all cases of sudden death)[4]
- Fever (especially when infectious, e.g. in rheumatic fever)
- Symptoms in infants and toddlers tend to be more non-specific with generalized malaise, poor appetite, abdominal pain, chronic cough. Later stages of the illness will present with respiratory symptoms with increased work of breathing and is often mistaken for asthma.

Since myocarditis is often due to a viral illness, many patients give a history of symptoms consistent with a recent viral infection, including fever, rash, diarrhea, joint pains, and easy fatigueability.

Myocarditis is often associated with pericarditis, and many patients present with signs and symptoms that suggest concurrent myocarditis and pericarditis.

Diagnosis



Endomyocardial biopsy specimen. Extensive eosinophilic infiltrate involving the endocardium and myocardium (hematoxylin and eosin stain).

Myocarditis refers to an underlying process that causes inflammation and injury of the heart. It does not refer to inflammation of the heart as a consequence of some other insult. Many secondary causes, such as a heart attack, can lead to inflammation of the myocardium and therefore the diagnosis of myocarditis can not be made by evidence of inflammation of the myocardium alone.[5]

Myocardial inflammation can be suspected on the basis of electrocardiographic results (ECG), elevated C-reactive protein (CRP) and/or Erythrocyte sedimentation rate (ESR) and increased IgM (serology) against viruses known to affect the myocardium. Markers of myocardial damage (troponin or creatine kinase cardiac isoenzymes) are elevated.[3]

The electrocardiogram (ECG) findings most commonly seen in myocarditis are diffuse T wave inversions; saddle-shaped ST-segment elevations may be present (these are also seen in pericarditis).[3]

The gold standard is still biopsy of the myocardium, generally done in the setting of angiography. A small tissue sample of the endocardium and myocardium is taken, and investigated by a pathologist by light microscopy and—if necessary—immunochemistry and special staining methods. Histopathological features are: myocardial interstitium with abundant edema and inflammatory infiltrate, rich in lymphocytes and macrophages. Focal destruction of myocytes explains the myocardial pump failure.[3]

Cardiac magnetic resonance imaging (cMRI or CMR) has been shown to be very useful in diagnosing myocarditis by visualizing markers for inflammation of the myocardium.[6] Recently, consensus criteria for the diagnosis of myocarditis by CMR have been published [7]

Causes

A large number of causes of myocarditis have been identified, but often a cause cannot be found. In Europe and North America, viruses are common culprits. Worldwide, however, the most common cause is Chagas' disease, an illness endemic to Central and South America that is due to infection by the protozoan *Trypanosoma cruzi*.[3]

Infections

- Viral (Parvovirus B19, Coxsackie virus, HIV, enterovirus, rubella virus, polio virus, cytomegalovirus, human herpesvirus 6 and possibly hepatitis C)
- Protozoan (*Trypanosoma cruzi* and *Toxoplasma gondii*)
- Bacterial (brucella, *Corynebacterium diphtheriae*, gonococcus, *Haemophilus influenzae*, *Actinomyces*, *Tropheryma whipplei*, *Vibrio cholerae*, *Borrelia burgdorferi*, leptospirosis, Rickettsia)
- Fungal (aspergillus)
- Parasitic (ascaris, *Echinococcus granulosus*, *Paragonimus westermani*, schistosoma, *Taenia solium*, *Trichinella spiralis*, visceral larva migrans, and *Wuchereria bancrofti*)

Bacterial myocarditis is rare in patients without immunodeficiency.

Toxins

- Drugs (ethanol, anthracyclines and some other forms of chemotherapy, and antipsychotics, e.g. clozapine)

Immunologic Reactions

- Allergic (acetazolamide, amitriptyline)
- Rejection after a heart transplant
- Autoantigens (scleroderma, systemic lupus erythematosis, sarcoidosis, systemic vasculitis such as Churg-Strauss syndrome, Wegener's granulomatosis)
- Toxins (arsenic, carbon monoxide, snake venom)
- Heavy metals (copper, iron)

] Physical agents

- electric shock, hyperpyrexia, and radiation

Epidemiology

The exact incidence of myocarditis is unknown. However, in series of routine autopsies, 1–9% of all patients had evidence of myocardial inflammation. In young adults, up to 20% of all cases of sudden death are due to myocarditis.[3]

Among patients with HIV, myocarditis is the most common cardiac pathological finding at autopsy, with prevalence of 50% or more. [1]

Therapy

As most viral infections cannot be treated with directed therapy, symptomatic treatment is the only form of therapy for those forms of myocarditis. In the acute phase, supportive therapy including bed rest is indicated. For symptomatic patients, digoxin and diuretics provide clinical improvement. For patients with moderate to severe dysfunction, cardiac function can be supported by use of inotropes such as Milrinone in acute phase followed by oral therapy with ACE inhibitors (Captopril, Lisinopril) when tolerated. Patients who do not respond to conventional therapy are candidates for bridge therapy with left ventricular assist devices (LVADs). Heart transplantation is reserved for patients who fail to improve with conventional therapy.

Famous deaths

- Rod Donald, 48
- Andrea Dworkin, 58.
- Alexei Cherepanov, 19.
- Andy Gibb, 30.
- Janet Munro, 38.
- Helen Chadwick, 43.
- Donald B. Gillies, 46.
- Yangji Lee, 37.
- Clair S. Tappaan, 54.
- Sandy Pearce, 47.
- Elston Howard, 51.

Myocarditis

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What is myocarditis?

Myocarditis is inflammation of heart muscle.

What causes myocarditis?

Myocarditis can be caused by a variety of infections and conditions such as viruses, sarcoidosis, and immune diseases (such as systemic lupus, etc.), pregnancy, and others. The most common cause of myocarditis is infection of the heart muscle by a virus. The virus invades the heart muscle to cause local inflammation. After the initial infection subsides, the body's immune system continues to inflict inflammatory damage to the heart muscle. This immune response actually prolongs the myocarditis.

What are symptoms of myocarditis?

Myocarditis can be mild and cause virtually no noticeable symptoms. The most frequent symptom of myocarditis is pain in the chest. When myocarditis is more serious, it leads to weakening of the heart muscle. Myocarditis can then cause heart failure (with symptoms of shortness of breath, fatigue, fluid accumulation in the lungs, etc.) as well as heart rhythm irregularities from inflammation and/or scarring of the electrical system of the heart.

How is myocarditis diagnosed?

Myocarditis is diagnosed by detecting signs of irritation of heart muscle. Blood tests for heart muscle enzymes (CPK levels) can be elevated. Electrical testing (EKG) can suggest irritation of heart muscle and demonstrate irregular beating of the heart. Nuclear heart scan testing can show irregular areas of heart muscle.

What is the prognosis (outlook) for patients with myocarditis?

The prognosis for long-term damage is not predictable and only becomes evident as the patient is followed by the doctor over time. After the initial phase of myocarditis, some patients can experience complete recovery, others may develop chronic heart failure due to injured heart muscle. Infrequently, some patients develop fulminant heart failure, a fatal condition without heart transplantation.

Patients who have had myocarditis are at some risk for sudden unexpected, potentially fatal, heart rhythm abnormalities. These can often be prevented with implantable defibrillators if the heart muscle damage is severe.

In this Article

How is myocarditis treated?

Except in systemic sarcoidosis and immune inflammation (such as from systemic lupus erythematosus) where myocarditis can respond to corticosteroids, no proven effective medications are currently available for treating active myocarditis. Treatment measures mainly involves alleviating heart failure (salt restriction, water pills, ACE inhibitors, beta blockers, etc.) and treating as well as monitoring heart rhythm abnormalities.

Featured: Myocarditis Main Article
Myocarditis is an inflammation of the heart muscle and can be caused by

a variety of infections, conditions, and viruses such as sarcoidosis, immune diseases (such as lupus), pregnancy, and others. Symptoms of myocarditis include chest pain, shortness of breath, fatigue, and fluid accumulation in the lungs. Treatment mainly involves preventing heart failure with medication and diet) as well as monitoring for heart rhythm abnormalities.

Introduction

Background

Myocarditis is clinical syndrome characterized by inflammation of myocytes resulting from infectious, toxic, and autoimmune etiologies. Ongoing viral infection, myocardial destruction, and adverse remodeling can lead to persistent ventricular dysfunction and dilated cardiomyopathy.

Myocarditis is an elusive illness to study, diagnose, and treat because the clinical presentation may range from nearly asymptomatic to overt heart failure requiring transplantation; a myriad of causes exist, and it is occasionally the unrecognized culprit in cases of sudden death.

Pathophysiology

Myocarditis is defined as inflammatory changes in the heart muscle and is characterized by myocyte necrosis.

Animal models have lead to a much greater understanding of the pathophysiology of fulminant myocarditis in which susceptible patients uptake viral RNA and develop a cytotoxic necrosis and rapid (1-2 d) cell death without the appearance of any interstitial infiltrate. In both animal models and these patients, a rapid progression to severe ventricular dysfunction and cardiovascular collapse occurs.[1]

In the more typical course of the disease, 4-14 days after viral infection, cells produce an immune response including macrophage activation and cytokine expression and develop an histologically apparent infiltrate of mononuclear cells. In this subacute viral-clearing phase, natural killer cells target myocardium expressing the viral RNA and continue myocyte necrosis. Tumor necrosis factor is involved in rapidly clearing virus and signals additional proinflammatory cells, activates endothelial cells, and has direct negative inotropic effects. In the latter stages of the subacute

process, cytotoxic T lymphocytes infiltrate myocytes and trigger lysis of these cells by presenting virus fragments via the histocompatibility complex on the surface of the myocyte membrane. Neutralizing antiviral antibodies also develop to assist in the clearing of virus.[2]

In the chronic phases, the deleterious effects of either inadequate or inappropriately abundant immune response can lead to the long-term sequelae of dilated cardiomyopathy and heart failure. In animal models of insufficient immune response, viral replication can continue and cause chronic destruction of myocytes.[1] As a prototype of inadequate immune response, human patients with HIV are a subgroup known to do poorly, with a high rate of progression to fulminant heart failure, and polymerase chain reaction (PCR) of endomyocardial biopsy samples show a persistent expression of viral genome, both HIV and others.[3]

On the opposite extreme of immune activity, overabundant T cells may continue activity into the chronic phase, causing tissue destruction and ventricular dysfunction manifesting as chronic heart failure. Ongoing study has demonstrated the presence of antimyosin autoantibodies and other immunomodulators long after initial viral infection and has demonstrated a worsened clinical prognosis from this persistent immune response directed at myocytes.[4,5]

Frequency

United States

The true incidence of myocarditis is unknown because many cases are asymptomatic, and some symptoms related to significant morbidity may not be appropriately credited. One major urban US medical examiners office attributed 1.3% of sudden and unexpected deaths to myocarditis,[6] consistent with other autopsy studies that demonstrate evidence of myocardial inflammation in 1-1.5% of deaths. In the United States, viral and medication-related cases are the most commonly identified causes.

International

Internationally, other etiologies of myocarditis play a more important role, with Chagas disease from the parasite *Trypanosoma cruzi* infecting approximately 18 million people with 50,000 annual deaths. Worldwide

the true frequency of disease in its less severe forms is even more difficult to appreciate.[4]

Mortality/Morbidity

Because of difficulty in diagnosing myocarditis, the large number of cases that likely never come to medical attention, and its previously underappreciated role in sudden dysrhythmic death, morbidity and mortality data are difficult to construct.

- Rarely, myocarditis is fulminant and leads rapidly to cardiovascular collapse and shock sometimes requiring mechanical support. Paradoxically, if these patients survive the first 3-4 weeks of illness they have near 100% recovery and far fewer long-term complications compared with those patients with more indolent courses.[7,8]
- Mortality for clinically significant and biopsy-proven myocarditis varies widely. Patients who initially have and then subsequently clear virus as demonstrated by polymerase chain reaction of endomyocardial biopsy tissue have excellent recovery with a return to normal or near-normal left ventricular function and overall mortality less than 4%.[9]
- Patients with persistent viral genome expression and/or antimyosin autoantibodies show limited recovery of left ventricular (LV) function, decreased stroke volume index, and more stiffness of the ventricle with the resultant long-term morbidity of heart failure and a mortality of nearly 25%.[3]

Sex

The male-to-female ratio for myocarditis is 1.5:1.

Age

The average age of patients with myocarditis is 42 years. In younger patients with sudden cardiac death, as much as 20% of cases may be related to myocarditis.

Clinical

History

- Many patients with myocarditis present with a nonspecific illness characterized by fatigue, mild dyspnea, and myalgias. A few patients present acutely with fulminant congestive heart failure (CHF) secondary to widespread myocardial involvement. Small, focal inflammation in electrically sensitive areas may be the etiology of patients whose initial presentation is sudden death. Some presentations of myocarditis, especially those related to parvovirus B19, present like an acute lateral wall myocardial infarction.
- Most cases of myocarditis are subclinical; therefore, the patient rarely seeks medical attention during acute illness. These subclinical cases may have transient ECG abnormalities.
- An antecedent viral syndrome is present in more than one half of patients with myocarditis. The appearance of cardiac-specific symptoms occurs primarily in the subacute virus-clearing phase; therefore, patients commonly present 2 weeks after the acute viremia.
- Fever is present in 20% of patients.
- Other symptoms include fatigue, myalgias and arthralgias, and malaise.
- Chest pain
    - Chest discomfort is reported in 35% of patients.
    - The pain is most commonly described as a pleuritic, sharp, stabbing precordial pain. Pericarditis may be present in many cases and may cause some of the clinical presentation of pain.
    - It may be substernal and squeezing and, therefore, difficult to distinguish from that typical of ischemic pain.
- Dyspnea on exertion is common.
- Orthopnea and shortness of breath at rest may be noted if CHF is present.
- Palpitations are common. Syncope in a patient with a presentation consistent with myocarditis may signal high-grade atrioventricular (AV) block and risk for sudden death.

- Pediatric patients, particularly infants, present with nonspecific symptoms, including the following:
  - Fever
  - Respiratory distress
  - Poor feeding or, in cases with CHF, sweating while feeding
  - Cyanosis in severe cases
- In a 6-year study of pediatric ED patients, the most common presenting symptom was dyspnea and more than half of patients were initially diagnosed with asthma or pneumonia. Six percent of patients had primarily GI symptoms.[10]

Physical

Physical findings of myocarditis can range from a normal examination, through all classes of congestive heart failure (CHF) to cardiovascular collapse and shock.

- Patients with mild cases of myocarditis have a nontoxic appearance and simply may appear to have a viral syndrome.
- Tachypnea and tachycardia are common. Tachycardia is often out of proportion to fever.
- More acutely ill patients have signs of circulatory impairment due to left ventricular failure.
- A widely inflamed heart shows the classic signs of ventricular dysfunction including the following:
  - Jugular venous distention
  - Bibasilar crackles
  - Ascites
  - Peripheral edema
- S_3 or a summation gallop may be noted with significant biventricular involvement.
- Intensity of S_1 may be diminished.
- Cyanosis may occur.
- Murmurs of mitral or tricuspid regurgitation may be present due to ventricular dilation.
- In cases where a dilated cardiomyopathy has developed, signs of peripheral or pulmonary thromboembolism may be found.

- Diffuse inflammation may develop leading to pericardial effusion, without tamponade, and pericardial and pleural friction rub as the inflammatory process involves surrounding structures.

Causes

The causes of myocarditis are numerous and can be roughly divided into infectious, toxic, and immunologic etiologies, with viral etiologies most common in North America.

- Amongst the infectious causes, viral acute myocarditis is by far the most common.
    - In a study of 172 patients with a biopsy sample showing myocarditis in which a viral genome was identified by polymerase chain reaction, the most common viruses were adenovirus, 8.1%; parvovirus B19, 36.6%; human herpesvirus 6 (HHV-6), 10.5%; enterovirus, 32.6%; co-infection with HHV-6 and parvovirus B19, 12.6%.[11]
    - Other viruses implicated in myocarditis include influenza virus, echovirus, herpes simplex virus, varicella-zoster virus, hepatitis, Epstein-Barr virus, and cytomegalovirus.
    - Human immunodeficiency virus (HIV) deserves special mention because it seems to function differently than other viruses. HIV-1 glycoprotein 120 can directly disrupt cardiac contractility without an inflammatory response. This may explain why HIV genomes can be amplified from patients without histologic signs of inflammation. Myocarditis is the most commonly found cardiac abnormality found on biopsy tissue, present in some degree, in more than 50% of HIV patients.[4] In addition, in patients who are infected with HIV, T-cell – mediated immune suppression increases the risk of contracting myocarditis due to other infectious causes.[3]
    - Nonviral infectious causes are numerous and varied. Worldwide, the most common bacterial cause is diphtheria, and, in South America, the protozoal Chagas disease is a common entity. Streptococcal and staphylococcal species and *Bartonella*, *Brucella*, *Leptospira*, and *Salmonella* species can spread to the myocardium as a consequence of severe cases of endocarditis. *Borrelia burgdorferi*, the

spirochete agent in Lyme disease, is also a known cause of myocarditis. Parasitic myocarditis from trypanosomiasis; trichinosis; and, in the immunocompromised host, toxoplasmosis have been identified.

- Toxic myocarditis has a number of etiologies including both medical agents and environmental agents.[12,1,4]
    - Among the most common drugs that cause hypersensitivity reactions are clozapine, penicillin, ampicillin, hydrochlorothiazide, methyldopa, and sulfonamide drugs. This syndrome is associated with peripheral eosinophilia, fever, and rash in patients who have biopsy findings of an eosinophilic infiltrate of the myocardium.
    - Numerous medications (eg, lithium, doxorubicin, cocaine, numerous catecholamines, acetaminophen) may exert a direct cytotoxic effect on the heart. Zidovudine (AZT) has been associated with myocarditis.
    - Environmental toxins include lead, arsenic, and carbon monoxide. Cases have been attributed to Chinese sumac.
    - Wasp and scorpion stings and spider bites, specifically black widows, may cause myocarditis.
    - Radiation therapy may cause a myocarditis with the development of a dilated cardiomyopathy.
- Immunologic etiologies of myocarditis encompass a number of clinical syndromes and include the following:
    - Connective tissue disorders such as systemic lupus erythematosus (SLE), rheumatoid arthritis, scleroderma, and dermatomyositis can often result in a dismal prognosis.
    - Idiopathic inflammatory and infiltrative disorders such as Kawasaki disease, sarcoidosis, and giant cell arteritis may be a cause.
- Rejection of the post transplant heart may present as inflammatory myocarditis.