Using Contrast-Enhanced Cardiac Magnetic Resonance Imaging to Diagnose Acute Myocarditis

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**ABSTRACT**

This case describes a 19-year-old white man without a significant past medical history who presented with substernal chest pain, inferolateral ST segment elevation, and elevated cardiac enzymes. Coronary angiography showed normal coronary arteries. Magnetic resonance imaging (MRI) following gadolinium infusion showed focally delayed hyperenhancement of the subepicardium and intramyocardium of the posterior and lateral regions, sparing the subendocardium, a pattern typical of myocarditis. Myocarditis is an inflammatory process of the heart muscle and symptoms can often mimic those of acute coronary syndrome. Available diagnostic tools are unsatisfactory, thus there is a need to develop noninvasive techniques that can aid diagnosis, prognosis, and follow-up. Contrast-enhanced MRI is a valuable tool for the evaluation of inflammatory heart disease, such as myocarditis.

A 19-year-old white man with no significant past medical history presented 3 hours after awakening from sleep with substernal chest pressure associated with dyspnea, diaphoresis, and nausea. The pain was not positional and he had no associated orthopnea, edema, or syncope. Four days earlier, he had had an upper respiratory tract infection with associated diarrhea and fever. He denied use of any drugs and has never smoked or abused alcohol. On admission, he was afebrile, and his physical examination was unremarkable. An electrocardiogram (EKG; Figure 1) showed ST segment elevation in the inferior and lateral leads. Complete blood count, chemistry panel, urinalysis, and urine drug screen were within normal limits. Initially, his creatine kinase (CK) was 400 U/L (normal, 20–230 U/L), CK-MB 60 ng/mL (normal, 1–8 ng/mL), and troponin I 4.0 ng/mL (normal, 0–2.0 ng/mL). This increased to CK 660 U/L, CK-MB 94 ng/mL, and troponin I 11 ng/mL 6 hours later.

The patient was admitted to the cardiac intensive care unit with suspected acute pericarditis versus myocarditis. However, the elevated cardiac enzymes along with focal EKG findings made it difficult to exclude an acute myocardial infarction (MI). Aspirin, β-blocker, heparin, and antiplatelet aggregation therapy were given. An echocardiogram showed a mildly decreased left ventricular ejection fraction without other abnormalities. Coronary angiography showed normal coronary arteries.

A diagnosis of probable myocarditis was made; anticoagulation was discontinued, and the patient remained on telemetry monitoring. He had intermittent runs of short nonsustained ventricular tachycardia, but remained hemodynamically stable. His cardiac enzymes gradually trended to normal. He was started on an angiotensin-converting enzyme (ACE) inhibitor, a nonsteroidal anti-inflammatory agent, and a β-blocker. Serologic tests for enterovirus, herpesvirus, cytomegalovirus, hepatitis panel, and HIV all were negative. Rheumatologic workup, including rheumatoid factor and antinuclear antibody, also was negative. Cardiac magnetic resonance imaging (MRI) was done in follow-up to clarify the diagnosis. Gadolinium-enhanced cardiac MRI showed delayed uptake of contrast with a subepicardial and intramyocardial patchy pattern that spared the subendocardium and was localized to the posterior and lateral regions—highly suggestive of myocarditis (Figure 2). The patient was discharged 4 days after admission in stable condition.

**DISCUSSION**

Myocarditis is inflammation of the myocardium caused by infection, systemic disease, drugs, or toxins. It is sometimes divided into primary myocarditis, which is presumed to be caused by an acute viral infection or an autoimmune response to a virus and secondary myocarditis, which is inflammation caused by a specific pathogen. Pathogens can include infectious agents, drugs, chemicals, physical agents, and inflammatory diseases.

The epidemiology of myocarditis is difficult to characterize because of the wide range of causes. Much of what we know of the epidemiology of myocarditis comes from postmortem studies. Myocardial inflammation is identified in 1% to 9% of routine postmortem examinations. The incidence is even higher in young persons who experience sudden death, accounting for 20% of cases. Primary viral myocarditis is usually suspected when arrhythmias or heart
failure develops in the setting of a systemic febrile illness or after an upper respiratory tract illness. In most cases, no definite cause is ever established.

In patients with primary or viral myocarditis, the illness begins with viral symptoms related to the portal of entry, most commonly the upper respiratory or gastrointestinal tract. The initial infection may be mild and pass unnoticed, with a delay of days to weeks before cardiac symptoms appear. Cardiac manifestations can range from asymptomatic electrocardiographic abnormalities to fulminant heart failure or sudden cardiac death.

**Diagnostic Testing**

The diagnosis of acute myocarditis often can be clinically difficult as a result of symptoms that are highly suggestive of myocardial ischemia and the rise in enzymes, which follow a typical curve. Usually, myocarditis is associated with a degree of pericarditis and the major EKG manifestation is widespread ST segment elevation without the reciprocal changes seen in acute infarction. Other common EKG findings include tachycardia, heart blocks, and atrial and ventricular extrasystoles.3 Angiographically normal coronary vessels make the diagnosis of myocarditis probable.

The difficulty in diagnosing myocarditis lies in the poor specificity and sensitivity of the various diagnostic techniques used. Systematic biochemical measurements are not diagnostic and an increase in cardiotropic virus antibodies only reflects the response to a recent viral infection, but does not indicate active myocarditis. Radioactive isotope studies, such as gallium scanning and antimony scans, have been used for the diagnosis of myocarditis but are limited by their low specificity, exposure to radiation, and their cost.4 Endomyocardial biopsy is considered the diagnostic gold standard. However, it is associated with a considerable risk of morbidity, including ventricular perforation (1 in 250 are at risk of perforation and 1 in 1000 are at risk of death in experienced hands), and may be best reserved for when there is clinical suspicion of a treatable specific form of myocarditis, such as giant-cell myocarditis or cardiac sarcoidosis.5 The diagnostic sensitivity of endomyocardial biopsy is limited by possible sampling errors due to the focal involvement of the myocardium.6 Biopsy specimens are small and often are taken from the right ventricular portion of the septum without information about the location of inflammatory foci.7

Delayed contrast-enhanced MRI (CMR) has emerged over recent years as a promising diagnostic technique in patients with a high clinical suspicion of myocarditis. Cardiac MRI shows the accumulation of contrast in the myocardium as a consequence of myocyte membrane breakdown resulting from the inflammatory process. Using a combination of T2-weighted imaging, global relative (early) hyperenhancement following gadolinium infusion, and delayed hyperenhancement (DHE), Abdel-Aty et al obtained 76% sensitivity, 95.5% specificity, and 85% diagnostic accuracy, respectively.8 The uptake of contrast usually has a characteristic patchy pattern for approximately 2 weeks after the acute event, later becoming more disseminated.9 The pattern of DHE may be particularly helpful in differentiating between MI and myocarditis. In MI, the DHE pattern typically involves the subendocardial border and is in a coronary artery distribution, whereas in myocarditis, DHE is seen in the epicardium or mid-myocardium wall but never within the subendocardium.9

Mahrholdt et al found a clear association between the focal uptake of contrast and histopathologically determined foci of active myocarditis.10 Myocarditic infiltrations occur in a peculiar pattern, predominantly in the subepicardial region of the lateral free wall, which has been shown previously in...
postmortem studies. In contrast, a relatively low density of inflammatory cells was found on the right ventricular half of the septum, which is the usual location of endomyocardial biopsy. Interestingly, in our case, the DHE was localized to the epicardial portion of the inferolateral wall, correlating to the distribution of the most severe ST segment elevations seen on the EKG.

It is unclear whether the amount of delayed hyperenhancement seen in myocarditis is of prognostic significance. The patient described here had myocardial necrosis manifested as frequent episodes of nonsustained ventricular tachycardia and a depressed ejection fraction (EF). Mahrholdt et al found no close correlation between the initial extent of contrast enhancement and the initial EF, end diastolic volume, end systolic volume, or the improvement in EF during follow-up.15

**TREATMENT AND PROGNOSIS**

Treatment of myocarditis consists of both specific therapy aimed at the cause of myocarditis and nonspecific therapy aimed at the clinical manifestations, such as arrhythmias and heart failure. Antiviral therapy with ribavirin or α interferon reduces the severity of myocardial lesions and mortality in experimental murine myocarditis due to coxsackievirus B3. The applicability of these findings to humans is uncertain, as patients with viral myocarditis usually are not seen in the earlier stages. Immunosuppressive therapy (corticosteroids, azathioprine, and cyclosporine) has shown potential clinical benefit in a number of initial therapeutic studies in humans, mostly uncontrolled. However, evaluation of true effectiveness is difficult in myocarditis because of the high rate of spontaneous recovery.17

Nonspecific measures may be important in the treatment of myocarditis, regardless of etiology, and include avoidance of exercise (to reduce the work of the heart during the acute phase of myocarditis), EKG monitoring, antiarrhythmic drugs in selected patients, treatment of heart failure, and anticoagulation (when heart failure is symptomatic with a left ventricular EF below 20, or if the patient is in atrial fibrillation). Most patients with acute viral myocarditis make a full clinical recovery with supportive management, including EKG monitoring, initial avoidance of exercise, and β-blocker. Review of current literature suggests that the long-term prognosis of myocarditis is dependent upon both the cause and severity of disease and can be difficult to assess because the manifestations of this acute disease are variable, diagnosis is difficult, and the current “gold standard” diagnostic tool—endomyocardial biopsy—tends to apply only to patients with major clinical manifestations, such as life-threatening arrhythmias and heart failure.18

**CONCLUSIONS**

Our case demonstrates how acute myocarditis may mimic MI, with many common features, including characteristic substernal chest pain, ST segment elevations on EKG, elevation of cardiac enzymes, and short runs of ventricular tachycardia. Ultimately, the diagnosis was made based on a combination of diagnostic tests, including cardiac MRI. Once the diagnosis was made, the patient was treated with initial avoidance of exercise, an ACE inhibitor, and β-blocker. He was discharged in stable condition and made full clinical recovery at follow-up. Contrast CMR can be used to identify patients with active myocarditis in the setting of suspected MI or new-onset heart failure. Myocarditic infiltrations tend to occur in a peculiar pattern, predominantly in the lateral wall, originating from the epicardial surface of the ventricular wall. Contrast CMR is a valuable tool for the evaluation and monitoring of progression or regression of inflammatory heart disease. Whether the extent of myocardial damage as measured by contrast CMR correlates with long-term outcome measures remains to be investigated.

**References**