A Case of Myocardial Infarction with No Obstructive Coronary Atherosclerosis

Ajay R. Marwaha, MD, FACC
Cardiologist
The Heart Group of Lancaster General Health

Krisha M. Patel
Biological Sciences Student
University of Pittsburgh


Marwaha


Patel

CLINICAL PRESENTATION

A 56-year-old male with a past medical history of hypertension, hyperlipidemia, and benign prostatic hyperplasia presents to the emergency department (ED) for severe mid-sternal chest pain with exertion, without associated dyspnea. He describes a pressure/burning-like sensation that radiates to the left arm and is associated with a numbness/tingling sensation. He notes similar episodes for the previous two weeks, but pain has subsequently become worse. The patient has taken three to four ibuprofen pills daily but denies acid reflux symptoms. He also has been under a great deal of stress as a caregiver for a family member.

In the ED, the chest discomfort decreases to 3/10 after receiving three sublingual nitroglycerin tablets and intravenous morphine. The pain is reproducible and worsens with movement of his arm; he has musculoskeletal arthralgias but no other complaints on a review of systems.

His past medical history includes benign prostatic hypertrophy, hypercholesterolemia, and hypertension. He had a normal cardiac catheterization in 2008. The patient's family history includes diabetes and hypertension but not heart disease, and he has never smoked and says that he only drinks small amounts on social occasions.

His medications include albuterol inhaler as needed, atorvastatin 20 mg daily, ibuprofen 600 mg as needed, lisinopril 10 mg daily, tamsulosin 0.4 mg twice daily, and triamterene-hydrochlorothiazide (Dyazide®) 37.5 mg/25 mg daily.

On physical examination, he is afebrile with normal vital signs. He appears uncomfortable, moaning and groaning, with no other focal findings. Labs reveal an elevated fifth-generation troponin test of 121.80 ng/L; repeated two hours later, that number rises to 154 ng/L. The comprehensive metabolic panel and complete blood count are unremarkable, and an electrocardiogram is normal.

Computed tomography (CT) scan of the head without contrast reveals no intracranial hemorrhage, mass effect, or midline shift. A chest X-ray series demonstrates a normal cardiomediastinal silhouette, clear lungs, and bones that appear grossly unremarkable; however, there is mild hilar lymphadenopathy. CT angiogram of the chest reveals no evidence of pulmonary embolism, but again there is hilar and mediastinal lymphadenopathy.

The working diagnosis is non-ST-elevation myocardial infarction, thus a cardiology consult is obtained to consider cardiac catheterization. In the meantime, an echocardiogram is essentially normal with a left ventricular ejection fraction of 55% to 60% with normal diastolic function, and there is no evidence of left ventricular regional wall motion abnormality and no significant valvular pathology.

Cardiac catheterization reveals mild coronary artery disease with a 20% ostial left circumflex artery stenosis. There is no evidence of a recanalized lesion, distal cutoff, or spontaneous coronary artery dissection. Since the echocardiogram did not reveal any regional wall motion abnormalities, the acute myocardial injury is felt to be of unclear mechanism.

A cardiac MRI is performed and reveals normal biventricular function with no segmental wall motion abnormalities, with normal left and right ventricular ejection fractions. There is focal myocardial delayed enhancement at the basal inferolateral wall extending from the mid-myocardium to epicardial region (see Fig. 1 on page 100). This is suspicious for cardiac

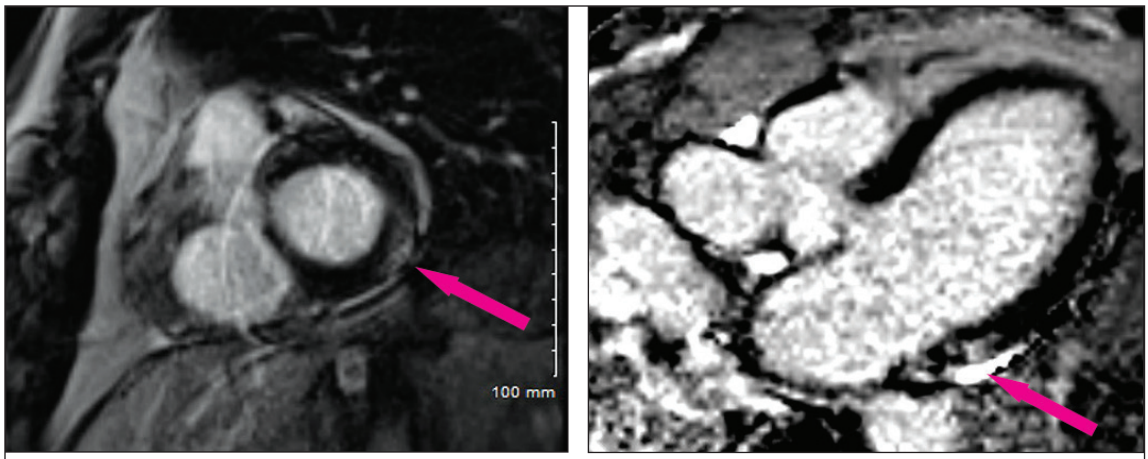


Fig. 1. Cardiac MRI images demonstrating a subepicardial inferolateral delayed enhancement pattern in short-axis imaging (left) and three-chamber long-axis imaging (right).

sarcoidosis (CS), particularly given the abnormal findings on the chest radiography.

Prior myocarditis could also be included in the differential diagnosis. There is no evidence of edema on short tau inversion recovery (STIR) imaging, a finding that may have suggested acute myocarditis. No significant valvular dysfunction is noted; trace pericardial effusion is reported, yet no abnormal pericardial thickening or enhancement is found.

DISCUSSION

The initial diagnosis was non-ST-elevation myocardial infarction. This was modified after cardiac catheterization to myocardial infarction with no obstructive coronary atherosclerosis (MINOCA) versus non-ST-elevation myocardial infarction type 2 (NSTEMI type 2).[1] MINOCA is a clinical syndrome defined by evidence of a myocardial infarction with no significant coronary artery disease (<50% stenosis severity).

The Fourth Universal Definition of Myocardial Infarction, published by the European Society of Cardiology in 2018, added MINOCA as a subset of myocardial infarction, requiring three criteria for diagnosis[2,3]:

1. The diagnosis of myocardial infarction must be established.
2. Coronary arteriography should reveal non-obstructive (<50% stenosis) coronary arteries.
3. No other diagnosis, such as pulmonary embolism or renal failure, can explain the clinical presentation.

Patients with MINOCA are more likely to be female and younger, in comparison with NSTEMI type 1.[4] MINOCA represents 6% (range 1% to 14%) of all myocardial infarctions and can be subcategorized into coronary, cardiac, and non-cardiac causes (see Table 1). In a meta-analysis, in-hospital mortality of MINOCA is 0.9%, and one-year mortality is 4.7%.[5,6]

Table 1. **Differential Diagnosis of MINOCA**[7]

Coronary	
Coronary artery spasm	
Transient coronary artery thrombosis with autolysis	
Coronary artery dissection	
Coronary artery embolism	
Cardiac	
Takotsubo cardiomyopathy	Tachycardia
Microvascular dysfunction	Cardiac sarcoidosis
Viral myocarditis	
Non-Cardiac	
Pulmonary embolism	Shock
Aortic dissection	Hypoxia
Renal impairment	Other cardiomyopathies

DIAGNOSTIC TECHNIQUE

Cardiac MRI is helpful in elucidating the etiology of MINOCA. It is the preferred next test after both echocardiography and cardiac catheterization do not reveal a clear etiology of the myocardial infarction.[8] Early use of cardiac MRI enables identification of potentially reversible causes and assists in treatment/prognosis. Failure to identify causes can lead to undertreatment.

Late gadolinium enhancement (LGE) on cardiac MRI is believed to reflect myocardial fibrosis. Additional imaging techniques, such as T1 mapping, extracellular volume (ECV), T2 mapping, and STIR

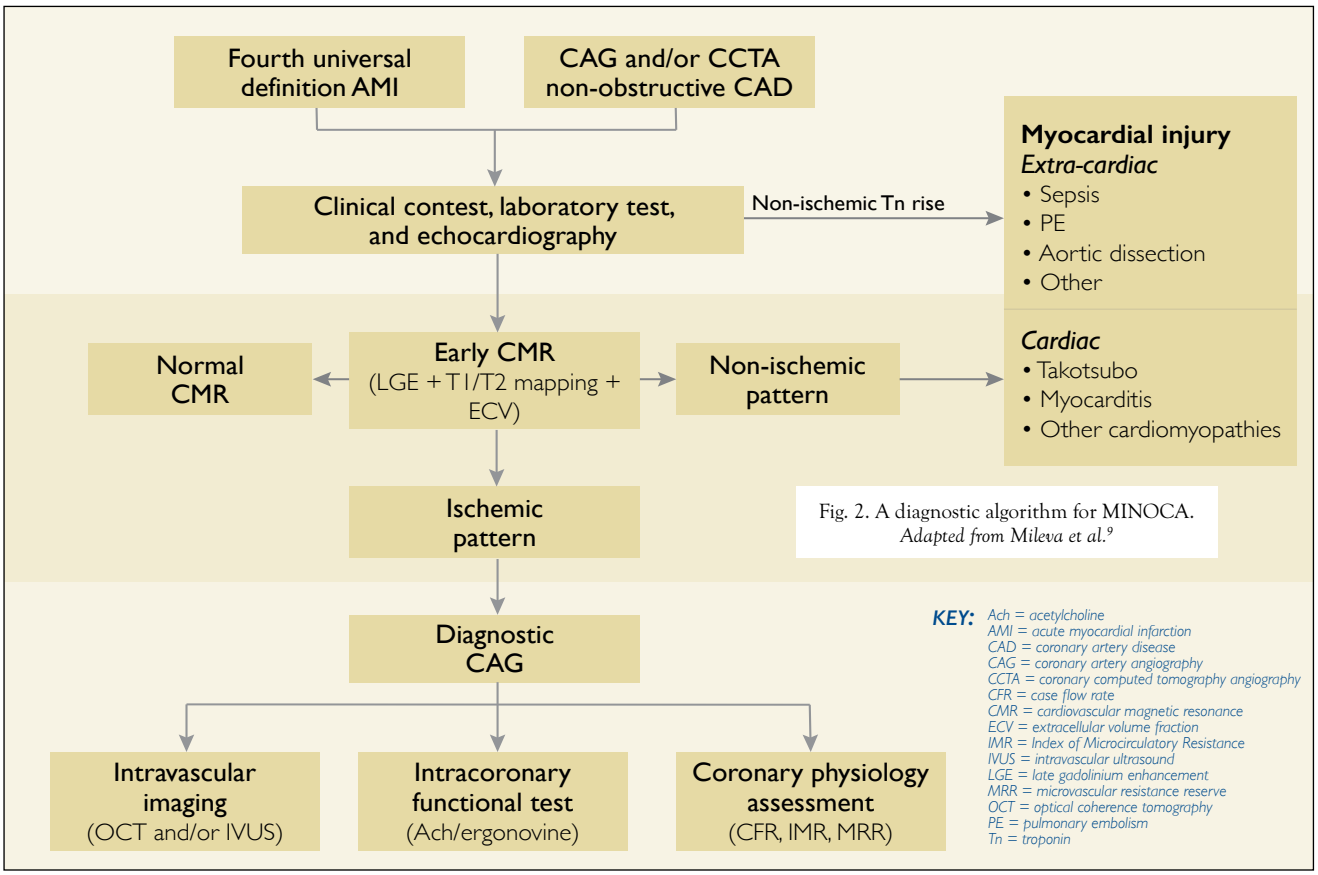


Fig. 2. A diagnostic algorithm for MINOCA. *Adapted from Mileva et al.*[9]

weighted imaging, can reveal evidence of acute myocarditis. Varying patterns of LGE correlate with and suggest specific cardiac pathologies without necessitating myocardial biopsy for tissue characterization. These include infarction, myocarditis, and cardiomyopathies.

Quantification of the extent of myocardial LGE helps stratify the prognosis. Approximately 25% of patients with MINOCA are found to have a normal myocardium after cardiac MRI, and a clear etiology of the presentation is not elucidated. Cardiac MRI reclassifies 68% of patients with MINOCA and confirms myocardial infarction in 22%, providing valuable diagnostic and prognostic information (see Fig. 2).[9] Transesophageal echocardiography can be considered in cases of suspected coronary artery embolism.

TREATMENT OF MINOCA

Dual antiplatelet therapy with aspirin and $P2Y_{12}$ inhibition have not been found to improve outcomes in MINOCA. Statin and angiotensin-converting enzyme inhibitors/angiotensin receptor blockers use resulted in a 23% and 18% reduction in major adverse cardiovascular outcomes, respectively, in the SWEDEHEART registry consisting of more than 9,000 MINOCA patients.[10] Beta-blocker therapy may have provided some benefit to patients in this registry, but there have been no major randomized clinical trials of this treatment for patients with MINOCA.

In our patient, a CT angiogram of the chest revealed mediastinal and hilar lymphadenopathy with no evidence of pulmonary embolism, and the cardiac MRI demonstrated subepicardial delayed gadolinium enhancement of the inferolateral wall, consistent with cardiac sarcoidosis. Therefore, CS was the working diagnosis.

The patient did not demonstrate ventricular arrhythmias and did not undergo an electrophysiology study. Instead, he was discharged from the hospital with a plan for outpatient telemetry monitoring and positron emission tomography (PET) scan. The latter was unremarkable, suggesting burnt-out CS without active inflammation. Immunosuppressive therapy for CS was not initiated.

CS PREVALENCE AND TREATMENT OPTIONS

Sarcoidosis is a heterogeneous multisystem disease of unknown etiology, characterized by the formation of noncaseating granulomas.[11] The etiology of CS is

unknown. Approximately 5% of patients with sarcoidosis have cardiac involvement, making CS a rare condition. Up to 25% of CS cases are isolated without involvement of extracardiac tissues.[12,13]

Countries in more northern latitudes may have higher prevalence of cardiac sarcoidosis, like sarcoidosis in general, yet registries are incomplete.[14] It can present asymptomatically, although patients may have ventricular arrhythmia or high-grade block, may experience palpitations or syncope, and may even present with congestive heart failure (CHF) or with sudden cardiac death. Atrial arrhythmias are uncommonly associated with CS.

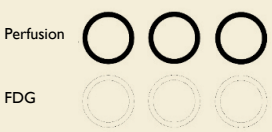
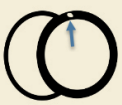
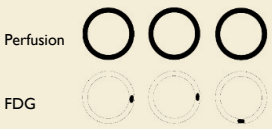
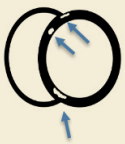
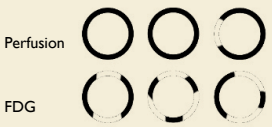
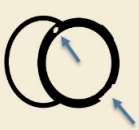
Approximately 14% of CS patients initially present with sudden death. Sudden death due to ventricular tachyarrhythmias or conduction block accounts for 25% to 65% of CS-associated mortality. CHF accounts for 20% of initial presentations. Elevated levels of cardiac troponins, serum angiotensin converting enzyme (ACE), and urinary calcium have been reported in CS.

Computed tomography, cardiac MRI, and cardiac PET scans are utilized in the diagnosis,[15-18] which can be very difficult to establish.[19] Imaging techniques, diagnostic criteria for extra-cardiac disease, and endomyocardial biopsy are utilized to confirm the diagnosis. Cardiac MRI and PET scanning (see Table 2) are often used as diagnostic gold standards for CS.[20-23] Varying patterns of myocardial delayed enhancement on cardiac MRI and fluorodeoxyglucose (FDG) uptake on PET scanning correlate with an increased likelihood of CS.[24]

Endomyocardial biopsy is generally reserved for cases of high clinical suspicion with non-diagnostic imaging.[25,26] Given the sparse location of myocardial granulomas, random septal biopsy may result in a high rate of falsely negative specimens.

Histological confirmation of noncaseating granuloma on extracardiac biopsy can help confirm the diagnosis in the right clinical setting. Therefore, cardiac MRI may play a greater role in risk stratification of patients with systemic or suspected cardiac sarcoidosis. Further, biventricular LGE is associated with markedly increased odds of ventricular arrhythmias (OR = 43.6; 95% CI: 16.2-117.2), and the absence of delayed en-

Table 2. **Patterns of Cardiac MRI and PET Imaging in the Diagnosis of Cardiac Sarcoidosis**
Adapted from Vita et al.[23]

Likelihood Probability	MRI Likelihood	MRI Example	PET Likelihood	PET Example
No CS (<10%)	No late gadolinium enhancement (LGE).		No perfusion defect **and** no F-fluorodeoxyglucose (FDG) uptake.	
Possible CS (10%-50%)	One focal area of LGE.		No perfusion defect and nonspecific FDG uptake.	
Probable CS (50%-90%)	Multifocal LGE in a pattern consistent with CS, but cannot rule out myocarditis.		Multiple focal areas of FDG uptake +/- small perfusion defects.	
Highly Probable CS (>90%)	Multifocal LGE in a pattern strongly consistent with CS.		Multiple focal areas of FDG uptake or multiple perfusion defects.	

hancement is associated with a very low risk of adverse cardiac events and likely excludes the presence of cardiac sarcoidosis.

Treatment options for CS can include immunosuppressants to improve ejection fraction and decrease ventricular arrhythmias associated with active inflammation[24,27,28] (see Fig. 3). Prednisone in doses of 60 mg to 80 mg/day have been suggested and may be tapered if effective to a maintenance dose of 10 mg to 15 mg/day. In those patients for whom this is not effective, anti-malarial drugs, methotrexate, or azathioprine should be considered.[29]

High-grade atrioventricular block necessitates pacemaker implantation. However, when ventricular arrhythmias cannot be

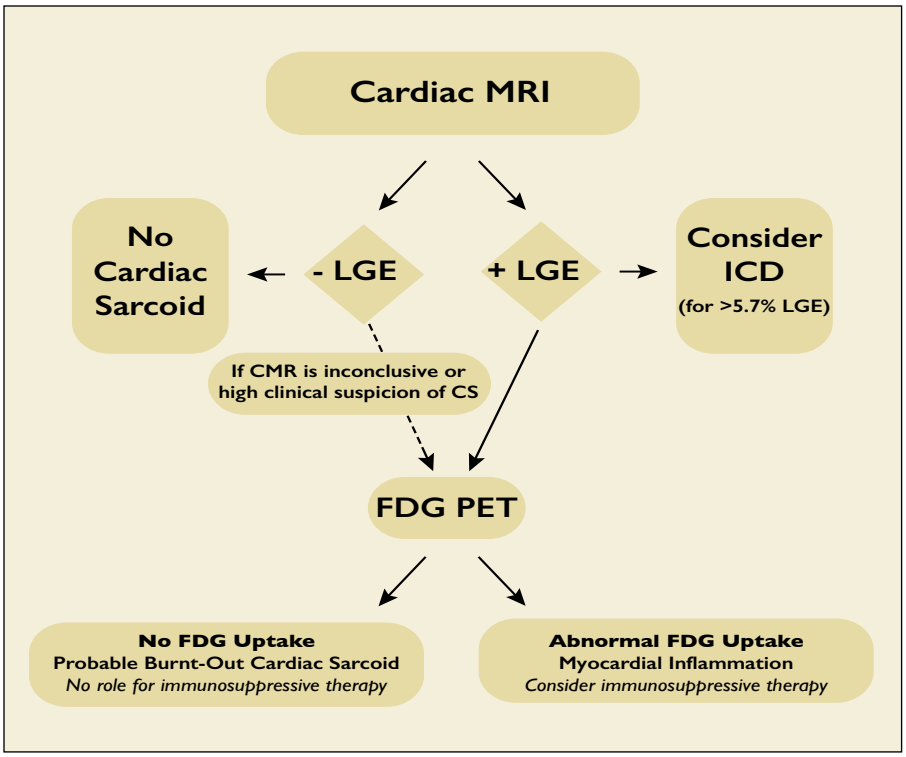


Fig. 3. A suggested algorithm for the diagnosis and immunosuppressive treatment of cardiac sarcoidosis.
Adapted from Vita et al.[23]

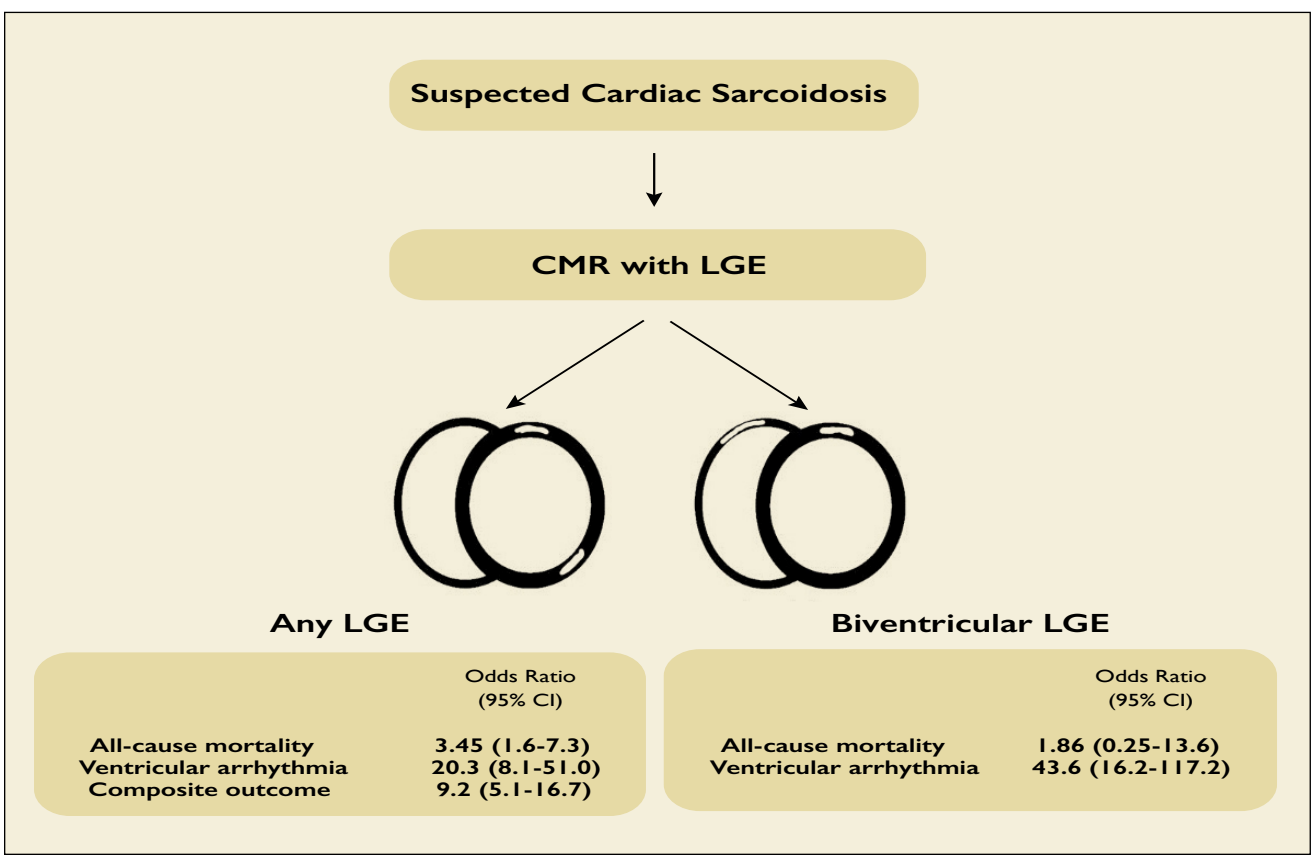


Fig. 4. Prognostic significance of late gadolinium enhancement (LGE) with known or suspected cardiac sarcoidosis.
Adapted from Stevenson et al.[28]

controlled, antiarrhythmic therapy, catheter ablation, and cardioverter defibrillator implantation may be necessary. Recent data suggest that the presence and quantity of abnormal delayed enhancement during cardiac MRI correlates significantly with an increased risk of ventricular arrhythmias and mortality (see Fig. 4 on page 103).[28] Refractory ventricular arrhythmias and heart failure may necessitate advanced heart failure therapies, such as biventricular assist device or cardiac transplantation.

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Ajay R. Marwaha, MD, FACC
The Heart Group of Lancaster General Health
217 Harrisburg Ave.
Lancaster, PA 17603
717-419-7188
drarm1@gmail.com

Krisha M. Patel
University of Pittsburgh
312 Ecker Dr.
Lititz, PA 17543
717-892-4825
kmp183@pitt.edu