CLINICAL VIGNETTE

Is It Thrombus or Embolism? Etiologies of Myocardial Infarction with No Obstructive Coronary Atherosclerosis (MINOCA)

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Introduction

Myocardial Infarction with no Obstructive Coronary Atherosclerosis (MINOCA), defined as a rise and fall of cardiac troponin in the setting of nonobstructive coronary artery disease (CAD) without appropriate alternative diagnosis, comprises approximately 5% of patients with acute myocardial infarction (MI).[1] The potential etiology of MINOCA for each case is broad, however, the most common underlying etiology is disruption of a small, nonobstructive plaque within the affected coronary artery. Mortality following MINOCA is shockingly high. Multiple studies report long-term mortality roughly equivalent to that of patients with obstructive CAD following primary acute coronary syndrome (ACS).[1-5] This highlights the need for providers to be aware of MINOCA and the evaluation and management of potential etiologies.

Clinical Case

A 37-year-old man was admitted following cardiac arrest with return of spontaneous circulation in the field. The patient was using an exercise machine in a community gym when he collapsed. Chest compressions were initiated, and an automatic external defibrillator was applied, delivering one shock with subsequent return of spontaneous circulation. Emergency medical personnel noted the patient was diaphoretic and speaking incoherently, and he was transported to the nearest hospital capable of percutaneous coronary intervention.

In the emergency department, electrocardiogram demonstrated 1 mm ST-elevation in aVL, with ST depressions inferiorly. Examination was notable for head laceration. Laboratory data was significant for elevated serum troponin of 2.2 ng/mL (reference < 0.1 ng/mL), creatinine 1.4 mg/dL, and lactate 57 mg/dL (reference 5-25 mg/dL). Head computerized tomography and chest radiograph were unremarkable, and urine toxicology was negative.

The patient received aspirin 324mg and ticagrelor 180mg orally prior to undergoing coronary angiogram, which demonstrated a large thrombus in the mid left anterior descending (LAD) coronary artery without calcification or epicardial disease (Figure 1). Intravascular ultrasound (IVUS) to the LAD noted reference vessel diameter of 5 mm with heavy thrombus burden in the mid LAD without ultrasonic evidence of atheromatous disease. Optical Coherence Tomography (OCT) was inadequate secondary to large thrombus burden. Aspiration thrombectomy was performed, and intra-coronary eptifibatide bolus was administered for residual thrombus. No arterial dissection or perforation was noted. The patient was diagnosed with MINOCA and transferred to the intensive care unit.

In the intensive care unit, the patient was initiated on heparin and eptifibatide intravenous infusions. Serum troponin peaked at 15.0 ng/mL, and repeat lactate was normal. Transthoracic echocardiogram showed normal biventricular size and function. However, injection of agitated normal saline suggested Patient Foramen Ovale (PFO).

After extubation, he provided additional history of a 12-hour airplane trip the previous week, and a sensation of chest tightness and left arm discomfort three days prior to presentation during an exercise class. He confirmed absence of significant risk factors for coronary artery disease (CAD) denying history of smoking, thromboembolic disease, or family history of premature coronary artery disease. Laboratory values for low-density lipoprotein and lipoprotein (a) were within normal limits. Family history was notable for prior pulmonary embolism in his father.

Hematology/oncology was consulted. Full hypercoagulable workup returned negative (cardiolipin immunoglobulins, beta-2 glycoproteins, protein C, protein S, antithrombin III, homocysteine, Factor V-Leiden, prothrombin gene mutation) except for positive dilute Russell viper venom time which was attributed to heparin infusion. Duplex ultrasonography of all extremities was negative for deep vein thrombi. The patient was initiated on aspirin, ticagrelor, metoprolol, and atorvastatin. Eptifibatide infusion was discontinued.

On hospital day four, the patient underwent repeat coronary angiogram with IVUS and OCT, which showed atherosclerotic

plaque measuring 0.5-0.7 mm in thickness with mild residual thrombus in the mid LAD (Figure 2**)**. Transesophageal echocardiogram with color doppler and agitated saline also suggested PFO. The patient was discharged on triple therapy (aspirin, ticagrelor, apixaban).

One month following hospitalization, computerized tomography coronary angiogram showed no residual thrombus or evidence of coronary atherosclerosis/calcification. However, the study was significant for an outpouching of the anterior right ventricular (RV) wall with areas of subtle fatty infiltration and reduced RV ejection fraction to 42% (Figure 3). Follow-up cardiac magnetic resonance imaging (MRI) and magnetic resonance angiography chest confirmed focal anterior bulge of RV free wall with mild regional dyskinesia and abnormal mid/apical anterior RV wall transmural enhancement (Figure 4). Additionally, transmural delayed myocardial enhancement was noted in the mid anterior wall of the left ventricle consistent with ischemic scar (Figure 5).

In subsequent follow up, the patient was referred for consideration of PFO closure, as well as electrophysiological study and implantable cardioverter-defibrillator implantation. His case was discussed in an academic committee of interventional cardiologists, which resulted in inconclusive recommendation regarding PFO closure. After discussion with the patient, given his age, inconclusive evidence of paradoxical embolization, and no prior history of antiplatelet failure, PFO closure was not pursued. After he completed 3 months of apixaban and one year of ticagrelor, he was continued on aspirin and atorvastatin.

Discussion

MINOCA is a clinical syndrome with variable etiologies which increasingly recognized in a small but significant proportion of acute MI cases.[1,2] Our patient met criteria with the rise and fall of cardiac troponin in the setting of nonobstructive CAD ($\leq$ 50%) and no appropriate alternative diagnosis.[1] Considering the descriptive nature of this diagnosis, its utility lies in prompting additional investigation to discern the etiology and to initiate multiple therapies in parallel, depending on pretest clinical suspicion.[1,3] Uncovering the etiology and addressing it are of utmost importance, as risk of secondary major adverse cardiac events and mortality is high.[4] Long-term mortality may be similar to patients with obstructive CAD following primary ACS.[2,5-7]

Known clinical etiologies for MINOCA include coronary plaque disruption, coronary emboli, coronary thrombus, spontaneous coronary artery dissection, coronary artery vasospasm, microvascular disease, Takotsubo or other cardiomyopathies, myocarditis, or an obstructive CAD not diagnosed on initial catheterization.[1,8] Although a listing of all causes is long, epidemiologic data and clinical history gathered in real time can facilitate a prioritized differential diagnosis quickly.[1]

Roughly 40% of patients with MINOCA demonstrate plaque disruption when studied by IVUS and/or OCT.[1,9] Although hypercoagulable assays are a less invasive workup, thrombophilia disorders have been detected in up to 14% of various MINOCA cohorts.[2] Coronary embolism-related MI is relatively rare. One study estimated prevalence of MINOCA due to coronary embolism at 2.9%, with 15% of cases demonstrating emboli to multiple coronary arteries.[10] Most are caused by atrial fibrillation (73%), while coronary embolism due to paradoxical emboli (4%) or endocarditis (4%) is rare.[10]

Our patient's finding of thrombus within the LAD quickly narrowed the differential for etiologies of MINOCA, yet his abnormal follow-up imaging stimulates multiple considerations as to the cause of his disease. The evidence of a probable coronary plaque by OCT within the LAD accompanied by thrombus is highly suggestive of a coronary plaque disruption event, leading to infarction as evidenced by myocardial scar noted on cardiac MRI within this vascular territory. However, the additional finding of RV free wall dyskinesia could suggest that a second ischemic event occurred. A cardiac arrest during exercise, in the setting of prior plane flight, could also be explained by a paradoxical embolism passing through a PFO following Valsalva, subsequently embedding within two separate arterial distributions.

Although it is not possible to state definitively the precise etiology for this patient's cardiac arrest, it is an excellent reminder of the AHA guidelines to carefully review angiography findings and perform cardiac MRI in patients with MINOCA.[1] In our case, it stimulated a discussion regarding the possibility of embolism or thrombus, but in other cases a subtle coronary artery dissection or evidence of myocarditis might be noted.

In conclusion, MINOCA is increasingly recognized as a significant etiology of MI warranting detailed, comprehensive workup. Often, treatment of multiple potential etiologies is warranted to reduce overall long-term risk, which is significant. In our patient, evaluation of potential etiologies for MINOCA led to parallel treatment directed towards risk-reduction of both embolus (anticoagulation and consideration of PFO closure) and plaque rupture/thrombus (antiplatelet and statin therapy). Coronary angiography with vascular imaging (IVUS, OCT) and cardiac MRI should be carefully reviewed and performed in all patients diagnosed with MINOCA. Ongoing education about and recognition of this disease entity is important to ensure the appropriate care of patients presenting with MINOCA.

Figures and Figure Legends

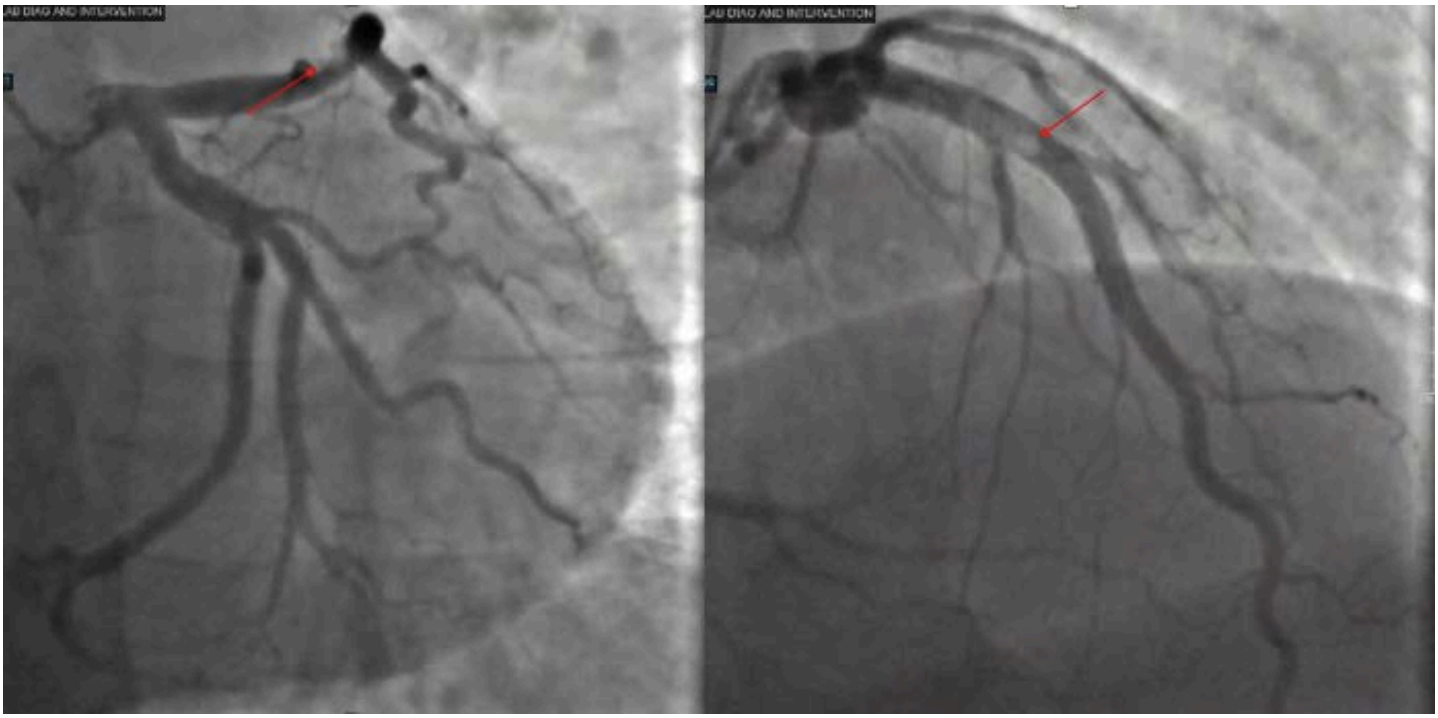

Figure 1. Initial coronary angiogram in right anterior oblique caudal (left) and cranial (right) images demonstrating large thrombus in the proximal LAD artery.

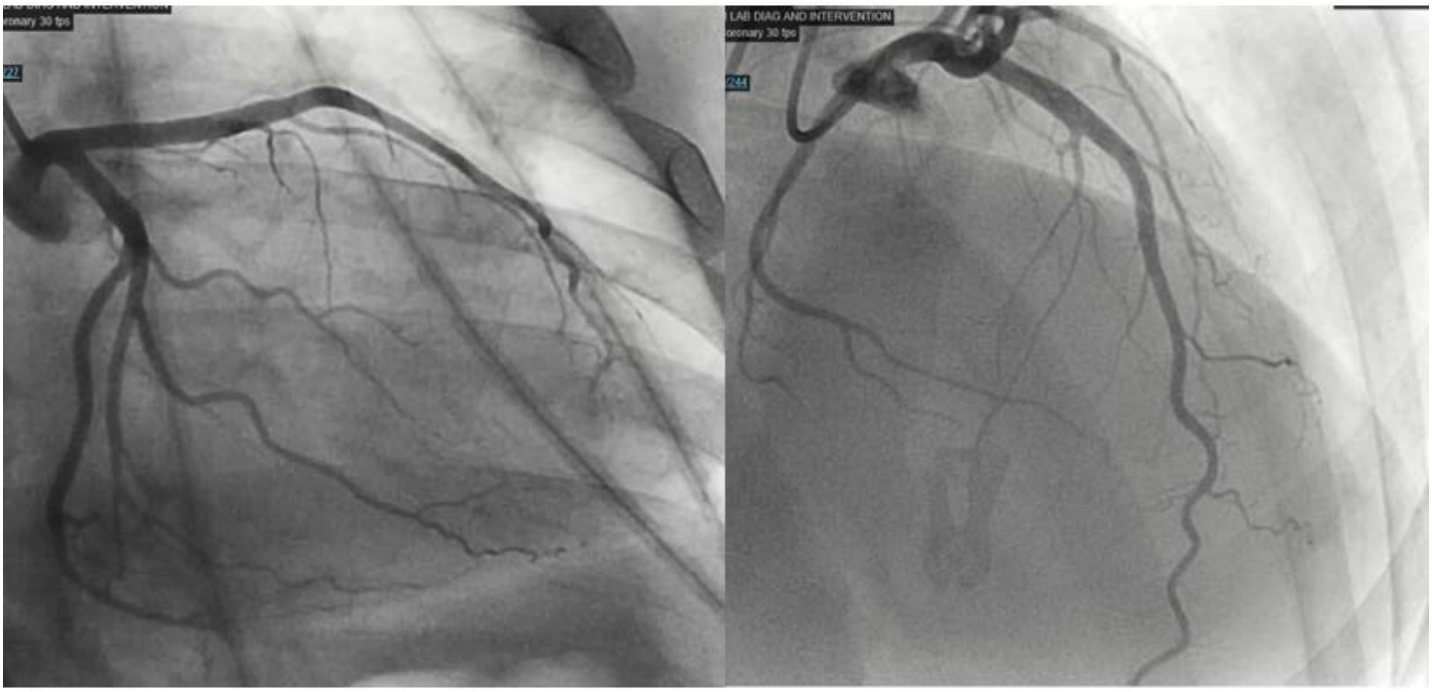

Figure 2. Second coronary angiogram in right anterior oblique caudal (left) and cranial (right) images demonstrating improvement in LAD artery thrombus burden following aspiration.

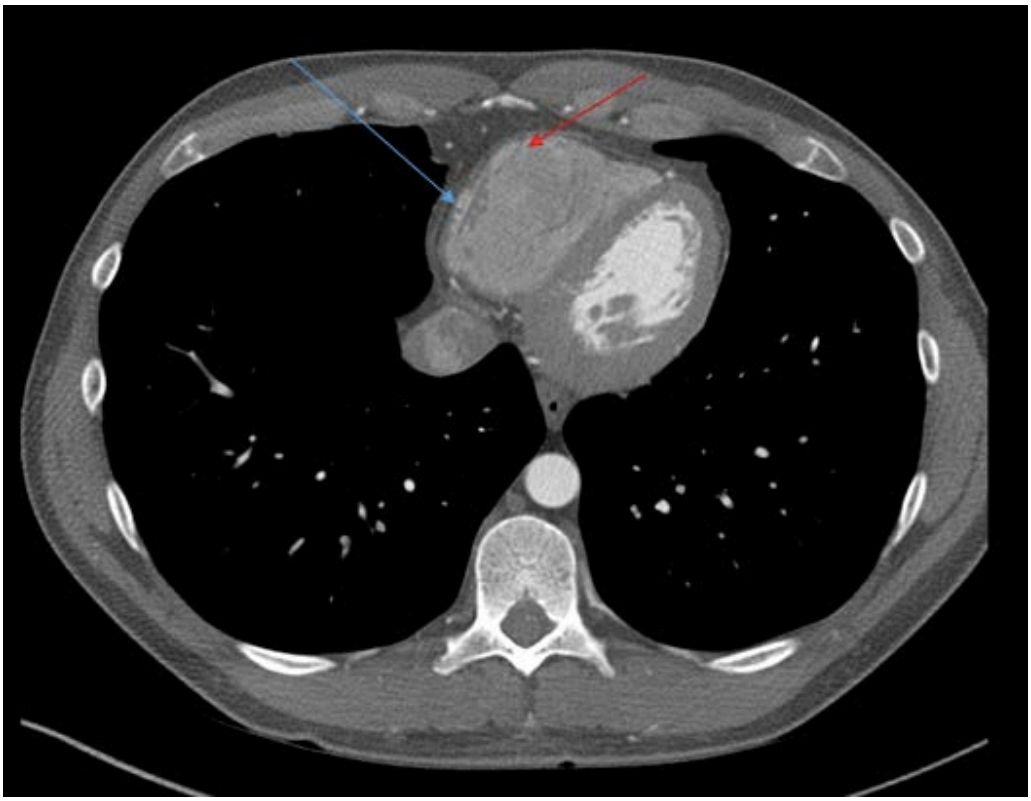

Figure 3. Computerized tomography coronary angiogram demonstrating outpouching of the anterior RV wall (red arrow) with areas of subtle fatty infiltration (blue arrow).

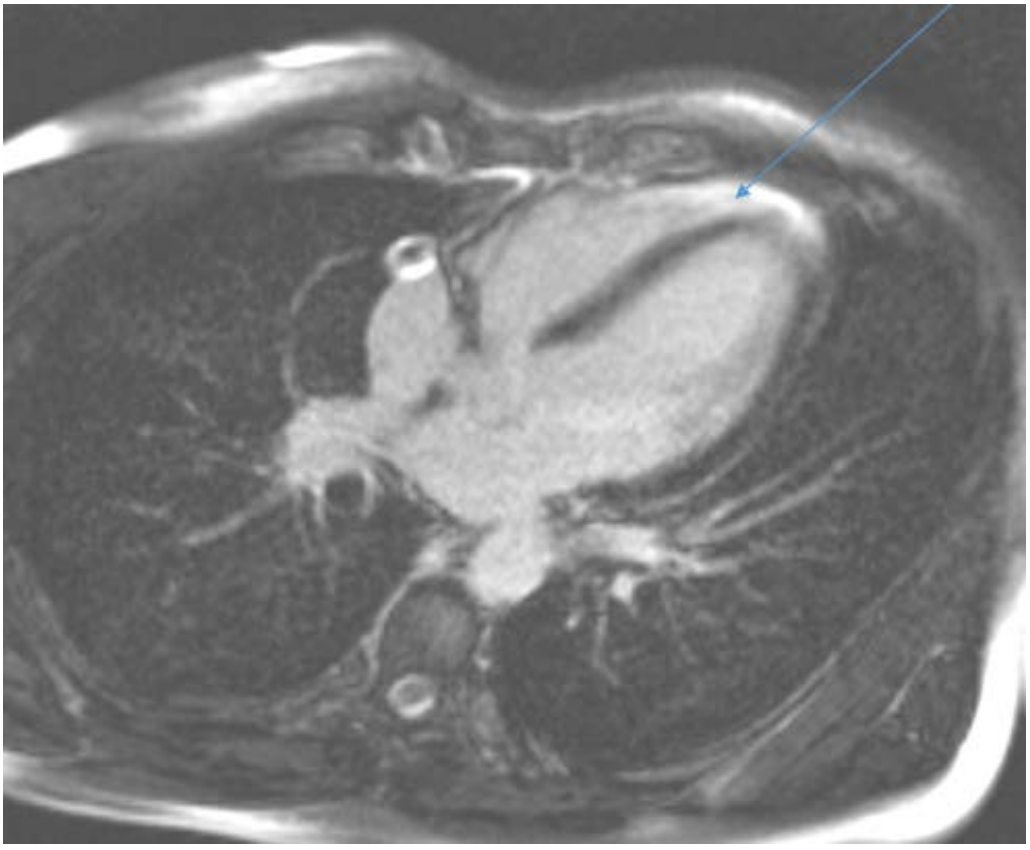

Figure 4. Cardiac MRI demonstrating abnormal transmural delayed enhancement of the mid anterior and apical anterior RV wall (blue arrow).

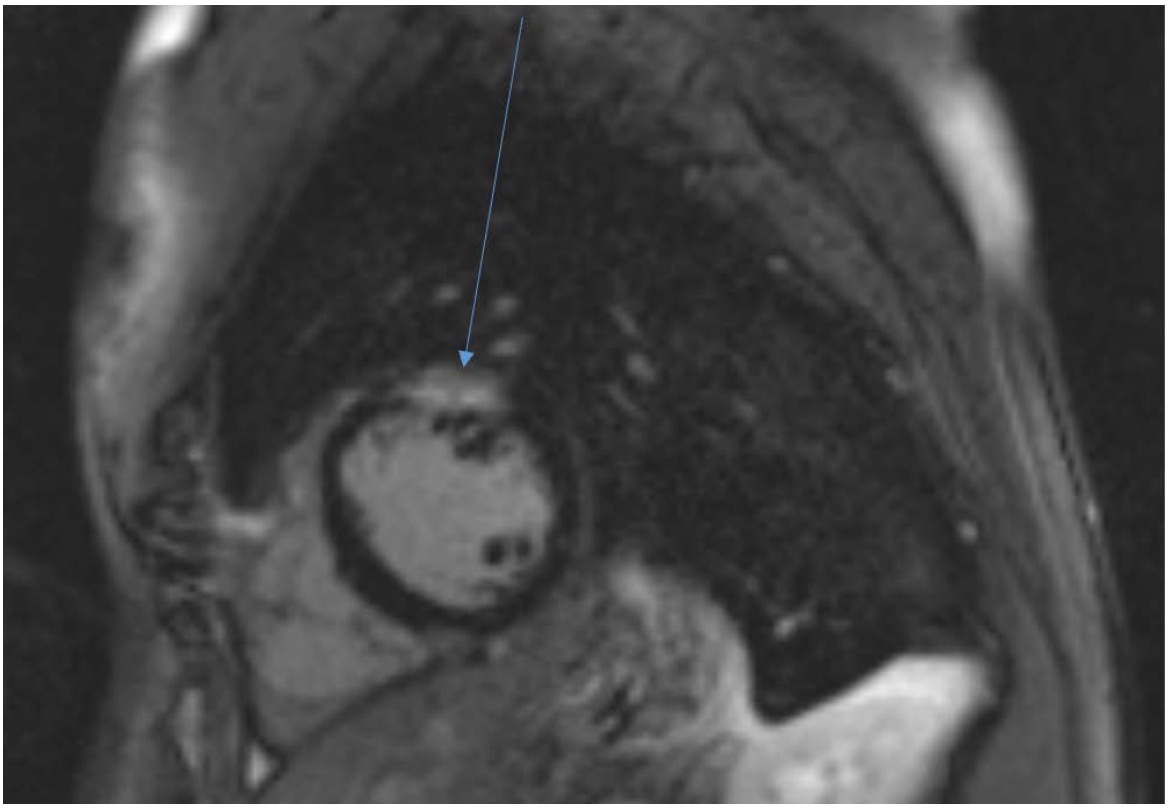

Figure 5. Cardiac MRI demonstrating transmural infarct of the mid anterior left ventricular wall (blue arrow).

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***Conflicts of interest*:** none

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