CASE REPORT

It is Myocardial Infarction with Non-Obstructive Coronary Arteries: A Myth or Reality?

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ABSTRACT

Acute myocardial infarction (AMI) is often associated with obstructed coronary arteries. However, recently, the occurrence of non-obstructive coronary arteries on angiogram in a patient with AMI has puzzled many physicians. To put forward the myth into reality, such cases have been coined into the term myocardial infarction with non-obstructive coronary arteries. It is not uncommon, is more frequent in younger women, is associated with fewer traditional risk factors, and usually presents with non-ST elevation myocardial infarction. However, due to its variable prognosis and diverse etiology, the condition continues to be a conundrum for many across the world. We report a case where a 63-year-old male presented with non-ST elevation myocardial infarction based on the Universal Definition of Myocardial Infarction. However, a subsequent coronary angiogram did not reveal obstructive coronary artery disease. We present the diagnostic and management dilemma for such cases and review the literature.

Key words: Myocardial infarction with non-obstructive coronary arteries, coronary angiogram, non-ST elevation myocardial infarction, plaque rupture

INTRODUCTION

The occurrence of acute myocardial infarction (AMI) without significant coronary artery disease (CAD) has been reported almost 80 years ago.[1] Many have since then considered it a myth with unexplained occurrence. Since the profoundly common use of coronary angiography in AMI over the past few decades, the condition has been reported on a regular basis where patients fulfilling the criteria for AMI turn up having non-obstructive coronary arteries. This eventually prompted the elders of the field to recognize it as a unique entity. Hence, the name myocardial infarction with non-obstructive coronary arteries (MINOCA) came into being. The reason behind ignoring the entity primarily relates to the inability to understand the underlying pathophysiology, to develop the diagnostic criteria, and to formulate a management algorithm. It is definitely not uncommon and found in about 6% of AMI patients; however, there is a large variability in its reported prevalence that ranges between 3.5% and 15%.[2] It is more frequent in younger women, is associated with fewer traditional risk factors, and usually presents with non-ST elevation myocardial infarction. The variable prognosis, at times comparable to AMI with CAD, and paucity of data to guide appropriate treatment may lead physicians to either falsely reassure patients or avoid digging into the etiology. Hence, we considered it prudent to report such a case as it happened to us and explore the related evidence.

CASE REPORT

A 63-year-old diabetic male presented to our center with the complaints of typical anginal chest pains for few days. The pain was substernal, brought on by exertion, and relieved by the rest. He denied any shortness of breath, palpitations, presyncope, or syncope. He was diabetic and controlled on insulin therapy. He was a non-smoker and had no history of hypertension, hyperlipidemia, or family history of premature coronary heart disease. He had documented a history of allergy to aspirin. His blood pressure was 130/70 mmHg and pulse 64/min, regular. Cardiovascular and chest examination was unremarkable.

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Electrocardiography (ECG) showed sinus rhythm, normal axis, mild ST-segment elevation V1-3, inferolateral T-wave inversions with mild ST-segment depression, and bifid p wave in V1 [Figure 1]. Laboratory tests revealed raised serial troponin-I levels, 0.08/0.1 ng/ml (abnormal >0.05 ng/ml as per our laboratory criteria). Creatinine was 88 umol/L, hemoglobin 14.6 g/dL, glycated hemoglobin 7.1%, and low-density lipoprotein 1.8 mmol/L. 2-D transthoracic echocardiography showed left ventricular (LV) hypertrophy, normal wall motion, LV ejection fraction 72%, impaired relaxation, normal valves in structure and function, no pericardial effusion, no masses, and normal pulmonary pressures.

He was diagnosed as non-ST elevation myocardial infarction, based on the Universal Definition of Myocardial Infarction.[3] Global Registry Of Acute Coronary Events risk score[4] predicted in-hospital mortality of 2.2% and 3.5% risk of death at 1 year. He was treated with clopidogrel (no aspirin as he had allergy to aspirin), atorvastatin, bisoprolol, perindopril, and subcutaneous enoxaparin. He was also commenced on intravenous tirofiban (glycoprotein 2b3a inhibitor) due to high risk. He was then transferred to a tertiary center for coronary angiogram. He was not found to have any significant CAD [Figure 2]. Cardiac magnetic resonance imaging (CMRI) was performed to exclude other causes of myocardial injury that was normal. He became pain fee and was subsequently discharged on clopidogrel, atorvastatin, bisoprolol, and perindopril. The patient will be followed in the outpatient cardiology clinic.

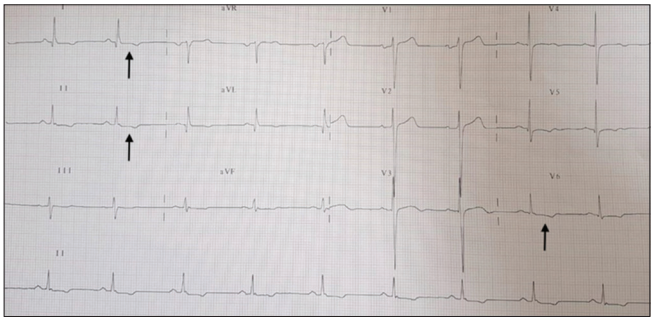

Figure 1: Electrocardiography showed sinus rhythm, normal axis, mild ST-segment elevation V1-3, inferolateral T-wave inversions with mild ST-segment depression, and bifid p wave in V1

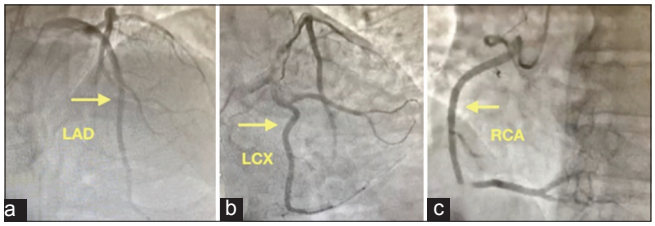

Figure 2: Coronary angiogram showing the left and right coronary systems a)Left Anterior Descending Artery b)Left Circumflex Artery c)Right Coronary Artery

DISCUSSION

We believe that our case with MINOCA is just a drop in the ocean of natural occurrences that puzzle science and therefore inspire researchers. DeWood *et al*. demonstrated, in his early AMI coronary angiography studies, that ST-segment elevation myocardial infarction was more frequently associated with occluded coronary artery compared to non-ST elevation myocardial infarction.[5,6] Overall, >90% had angiographic evidence of obstructive CAD, underscoring the importance of the atherosclerotic process in the pathogenesis of AMI. Still, it is fascinating that about 10% had no significant CAD on coronary angiography.

Several large AMI registries have confirmed the incidence of 1–13% of AMIs that occurred in the absence of obstructive CAD.[7,8] This sparked an array of questions including the mechanism of myocardial damage, patient characteristics, and management strategies for such cases. This led the clinical researchers to design the diagnosis of MINOCA.

Only recently, the European Society of Cardiology (ESC) working group position paper[9] has provided the diagnostic criteria for MINOCA that comprises of (a) AMI criteria as per the Third Universal Definition of Myocardial Infarction, (b) non-obstructive CAD on angiography, and, (c) no clinically overt specific cause for the acute presentation. On dissecting the definition, we found out that it has very wisely mentioned the steps to follow. The initial clinical diagnosis of AMI takes precedence and involves considering the symptoms, rise/fall of troponin values, ECG, and echocardiography features, as per the definition of myocardial infarction.[3] Once the diagnosis has been made, almost everyone undergoes coronary angiography. The skill of radial approach has alleviated major bleeding concerns that have made angiography popular. The ESC diagnostic criteria[9] have clearly defined obstructive CAD as coronary artery stenosis ≥50% in any potential infarct-related artery. This includes both patients with normal coronary arteries (no stenosis <30%) and mild coronary stenosis (stenosis >30% but <50%). The third segment of the diagnostic criteria means that, at the time of angiography, the cause and thus a specific diagnosis for the clinical presentation are not apparent. Accordingly, there is a need for further evaluation. Importantly, MINOCA is a "working diagnosis" and should prompt the physician to investigate underlying causes, analogous to heart failure.

MINOCA has many possible etiologies and pathogenic mechanisms. Therefore, the key principle in the management of this syndrome is to clarify the underlying mechanism to achieve patient-specific treatment. Scalone *et al*.[10] provided a framework to diagnose the underlying mechanism of myocardial injury. Clinical history, ECG, cardiac enzymes, echocardiography, coronary angiography, and LV angiography represent the first-level diagnostic investigations. In particular,

the findings of regional wall motion abnormalities at LV angiography limited to a single epicardial coronary artery territory identify an "epicardial pattern," whereas wall motion abnormalities extending beyond a single coronary artery territory identify a "microvascular pattern." The most common causes include coronary artery plaque disease, coronary dissection and coronary artery spasm "epicardial causes," and coronary microvascular spasm, Takotsubo cardiomyopathy, myocarditis, and coronary thromboembolism "microvascular causes." In our case, normal echocardiography excluded causes such as Takotsubo disease, coronary angiogram excluded coronary dissection, and normal cardiac MRI excluded myocarditis. Therefore, the most likely cause could be either coronary spasm or microvascular disease.

Plaque rupture and plaque erosion have been identified in over 40% of patients with MINOCA in studies using intravascular ultrasound (IVUS)[11] and optical coherence tomography (OCT). Myonecrosis in these cases is mediated by thrombosis, thromboembolism, superimposed vasospasm, or a combination of these processes. Finding of plaque rupture on OCT is associated with major adverse cardiac events.[12] Spontaneous coronary dissection typically causes an AMI by means of luminal obstruction. It is more common in women, estimated to be responsible for up to 25% of all ACS cases in women under 50 years of age. Prognosis is excellent; however, the risk of recurrence of acute events has been reported to be high (27% at 5 years).[13] Coronary artery spasm reflects vascular smooth muscle hyperreactivity to endogenous or exogenous vasospastic substances. Provocative spasm testing has demonstrated inducible spasm in 27% of patients with MINOCA.[2] Vasodilators such as nitrates and calcium antagonists provide standard treatment with the latter shown to prevent cardiac events. Coronary thrombosis may arise from hereditary or acquired thrombotic disorders such as Factor V Leiden mutation and Protein C and S deficiencies. Thrombophilia screening studies in patients with MINOCA have reported a 14% prevalence of these inherited disorders.[2] Coronary emboli may occur in the context of atrial fibrillation and valvular heart disease. They may also arise from valvular vegetations, cardiac tumors (e.g., myxoma and papillary fibroelastoma), calcified valves, and iatrogenic air emboli. Takotsubo cardiomyopathy presents as ACS with ST-segment changes, often with a stressful trigger. It is characterized by left ventricle mid-segments hypokinesis/akinesis and absence of obstructive CAD. CMRI helps to establish the diagnosis. Empiric therapeutic strategies include avoidance of sympathomimetic agents, beta-blockers, and ACE inhibitors. Myocarditis has a variable presentation and its prevalence in MINOCA patients varies based on the population studied, with a prevalence of 33% in a recent meta-analysis.[14]

CMRI is a useful tool in MINOCA of uncertain etiology. It not only provides insights into potential causes but may also confirms AMI. The present and pattern of late gadolinium enhancement (LGE) may point toward a vascular or non-vascular cause. However, 8–67% of patients with MINOCA have no evidence of LGE, myocardial edema, or wall motion abnormalities on CMRI.

The prognosis for MINOCA is quite variable. Contemporary studies evaluating the prognosis for MINOCA report a 12-month all-cause mortality of 4.7% (95% confidence interval 2.6–6.9),[2] which is better than those with AMI associated with obstructive CAD. Kang *et al*.[7] confirmed that 12-month major adverse cardiac events in patients with MINOCA were comparable to patients with AMI with single or double vessel CAD. Grodzinsky *et al*.[15] demonstrated that 25% of patients with MINOCA continued to experience angina 12 months after AMI, which is equivalent to the rate in those with AMI associated with obstructive CAD.

Considering the guarded prognosis of patients with MINOCA, no randomized trials have addressed the best treatment strategy. Lindahl *et al*.[16] examined the associations between treatment with statins, renin-angiotensin system blockers, β-blockers, dual antiplatelet therapy, and long-term cardiovascular events. He performed an observational study of MINOCA patients recorded in the SWEDEHEART registry, where 9466 consecutive unique patients with MINOCA were identified. The results indicate long-term beneficial effects of treatment with statins and angiotensin-converting enzyme inhibitors/angiotensin receptor blockers on outcome in patients with MINOCA, a trend toward a positive effect of β-blocker treatment, and a neutral effect of dual antiplatelet therapy.

CONCLUSION

MINOCA patients continue to puzzle physicians worldwide given the many possible etiologies and pathogenic mechanisms involved. Unfortunately, randomized trials are lacking to guide diagnostic and therapeutic strategies. IVUS/OCT during angiography, echocardiography (including transesophageal), and cardiac MRI helps to evaluate these patients. It is imperative to search for etiology as treatment depends on the specific cause.

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