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TITLE: Calcified Nodule as a Cause of Myocardial Infarction with Non-Obstructive Coronary Artery Disease

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**ABSTRACT**

**Introduction**

In patients presenting with myocardial infarction (MI), angiography most often reveals obstructive coronary artery disease (CAD) but 5-20% of patients with MI have non-obstructive CAD (MINOCA) at angiography. Calcified nodule has been identified as a cause of MI with obstructive CAD but to date has not been reported as a cause of MINOCA. Intravascular ultrasound (IVUS) may find an underlying cause of MINOCA but has limited sensitivity for calcified nodule. We report a case of calcified nodule in a patient with MINOCA diagnosed by optical coherence tomography (OCT).

**Case Report**

The patient was a 60 year old male former smoker with CAD risk factors who presented with one hour of mid-sternal chest pain. Troponin peaked at 1.28 ng/ml. EKG was normal. Coronary angiography showed minimal luminal irregularities. The patient underwent intracoronary OCT. On OCT, thrombus was identified overlying a calcified plaque with protrusion into the right coronary artery lumen. The appearance was characteristic of calcified nodule. Cardiac MRI showed hypokinesis in the basal inferoseptal and basal anterior walls without late gadolinium enhancement. The patient was treated with dual antiplatelet therapy (aspirin and clopidogrel) and a high intensity statin.

**Conclusion**

These combined clinical, OCT and CMR findings confirm that calcified nodule is a cause of MINOCA and underscore the utility of intracoronary imaging to determine the pathophysiology of MINOCA. Even without intracoronary imaging, plaque
disruption (e.g. plaque rupture, erosion, or calcified nodule) should be considered in cases of MINOCA based on prevalence of at least 35-40% in prior studies.

Keywords: Myocardial infarction non-obstructive CAD, MI with non-obstructive CAD, MINOCA, calcified nodule, OCT
INTRODUCTION

In patients presenting with acute coronary syndrome (ACS) and elevated cardiac biomarkers, angiography most often reveals obstructive coronary artery disease (CAD) (defined as angiographic stenosis ≥50% in any major epicardial vessel). However, 5-20% of patients presenting with myocardial infarction (MI) have no obstructive CAD at angiography. [1] MI with non-obstructive CAD (MINOCA) is a common problem, with estimated incidence of 54,000-187,000 people annually in the US. [1-2] Angiography alone does not identify the underlying etiology of MINOCA. Prior studies using intravascular ultrasound (IVUS) have identified plaque disruption (rupture or ulceration) in 35-40% of these patients. [3-4] However, IVUS has limited sensitivity for other types of plaque disruption such as plaque erosion and calcified nodule. A newer imaging technology, optical coherence tomography (OCT), has emerged to better characterize plaque morphology. OCT uses near-infrared light to acquire images. OCT has the advantage of far improved surface resolution and enhanced detail of the luminal surface of the coronary artery, though the depth of the vessel imaged may be less than with IVUS. [5-6] As such OCT can provide insight into the mechanism of MI, particularly when angiography reveals non-obstructive CAD.

The calcified nodule has been identified as a potentially vulnerable plaque. It is defined based on OCT imaging criteria as a signal-poor region with poorly delineated borders which protrudes into the arterial lumen. [7] It is typically associated with thrombus. Thrombus on OCT is recognized based on protruding and often irregular surfaces associated with backscatter. The nodular calcification distinguishes it from other forms of plaque. The underlying pathophysiology of MI with calcified nodule is thought to be related to an abnormal endothelial interface which induces thrombus formation. A recent OCT analysis of patients presenting with ACS and obstructive CAD found that patients with calcified nodules tended to present with non-ST elevation myocardial infarction, were older, and had higher rates of hypertension and
chronic renal disease. [7] To date, calcified nodule has not been reported as a cause of MINOCA. Herein we report a case of a calcified nodule in a patient with MINOCA.

**CASE REPORT**

The patient was a 60 year old male former smoker with hyperlipidemia, hypertension, paroxysmal atrial fibrillation, heart failure with preserved ejection fraction, Factor V Leiden deficiency, and previously treated prostate cancer who presented with one hour of mid-sternal chest pain, the first such episode in his life. Troponin was 0.576 on admission and peaked at 1.280 (upper limit of normal 0.04 ng/ml). The EKG was normal. He was treated with aspirin, clopidogrel, unfractionated heparin, and a high-dose statin and was referred for cardiac catheterization.

At the time of coronary angiography, the left anterior descending (LAD) artery, left circumflex (LCx) artery, and right coronary artery (RCA) had minimal luminal irregularities (Figure 1). As part of an ongoing research study for which the patient had provided informed consent (NCT02270359), he underwent optical coherence tomography (OCT) of the left and right coronary arteries. OCT images were reviewed by an experienced observer (A.M.) who was blinded to all clinical information, including angiographic findings, at the time of review. As seen in Figure 2, thrombus was identified overlying a calcified plaque with protrusion into the lumen of the right coronary artery. Although thrombus was present in the lumen of the artery, it did not obstruct flow; nor was there evidence of a stenosis ≥50% on angiography as previously mentioned. The appearance was characteristic of calcified nodule.

Cardiac MRI was also performed per protocol and showed hypokinesis in the basal inferoseptal and basal anterior walls. Late gadolinium enhancement imaging did not show evidence of significant myocardial necrosis.

The patient was continued on dual antiplatelet therapy and a high intensity statin. Intracoronary OCT, which was high imaging resolution, made the diagnosis in this case. Based on the identification of an underlying etiology involving thrombosis on the OCT, the patient will be treated with dual antiplatelet therapy for one year followed by lifelong aspirin in addition to a high intensity statin.
DISCUSSION
These findings confirm that calcified nodule is a cause of MI with non-obstructive CAD (MINOCA) and underscore the utility of intracoronary imaging to determine the mechanism of MI when angiography shows non-obstructive CAD. Intracoronary imaging and cardiac MRI may provide complementary supporting evidence of the underlying diagnosis in patients with MINOCA. Even in the absence of intracoronary imaging, plaque disruption should be considered as a cause of MINOCA (i.e., plaque rupture, erosion, or calcified nodule) based on prevalence of at least 35-40% in prior studies. Treatment of MI due to calcified nodule and other forms of plaque disruption in MINOCA should be considered with guideline-recommended treatment of NSTEMI or STEMI, according to the clinical presentation.

CONCLUSION
Calcified nodule is a cause of myocardial infarction with non-obstructive coronary artery disease.

DISCLOSURES
Dr. Akiko Maehara has received a speaker fee from St. Jude Medical and is a Consultant for Boston Scientific and ACIST.

AUTHOR’S CONTRIBUTIONS
Kaitlyn Dugan MD
Group 2 - Drafting the article, Critical revision of the article

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REFERENCES


FIGURE LEGENDS

Figure 1: Angiogram. Panel A, right coronary artery. The arrow indicates the location of the OCT images in Figure 2 Panels B-D, Left coronary angiogram. There is no obstructive coronary artery disease (<50% stenosis).

Figure 2: Successive images of optical coherence tomography at the location indicated in figure 1A. Note the irregular, protruding nodularity showing high attenuation of light, masking the arterial wall behind it in a radial direction representing red thrombus (short red arrows) and the oval density with sharp border underlying the intima representing calcification (long white arrow).
FIGURES

Figure 1: Angiogram. Panel a, right coronary artery. The arrow indicates the location of the OCT images in Figure 2 Panels B-D, Left coronary angiogram. There is no obstructive coronary artery disease (<50% stenosis).
Figure 2: Successive images of optical coherence tomography at the location indicated in figure 1A. Note the irregular, protruding nodularity showing high attenuation of light, masking the arterial wall behind it in a radial direction representing red thrombus (short red arrows) and the oval density with sharp border underlying the intima representing calcification (long white arrow).