

# Pearls & Oy-sters: Mitral Annular Calcification as a Cause of Ischemic Stroke

## A Case Report

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## Abstract

Evaluation of stroke etiology is an important aspect of stroke care affecting secondary prevention measures. Despite recent advances in diagnostic testing, determining the stroke etiology can remain a challenging task particularly for less common causes of stroke such as mitral annular calcification. This case will review the benefit of histopathologic clot evaluation after thrombectomy to identify uncommon causes of embolic stroke which may change management.

## Pearls

- Embolic mitral annular calcification (MAC) can be an infrequent and underrecognized cause of ischemic stroke.
- Histopathologic evaluation of extracted thrombus may play an important role in identifying the etiology in patients with ischemic stroke.

## Oy-sters

- Embolic MAC can clinically be difficult to distinguish from other atheroembolic or cardioembolic etiologies and may require histopathologic review.

## Case Report

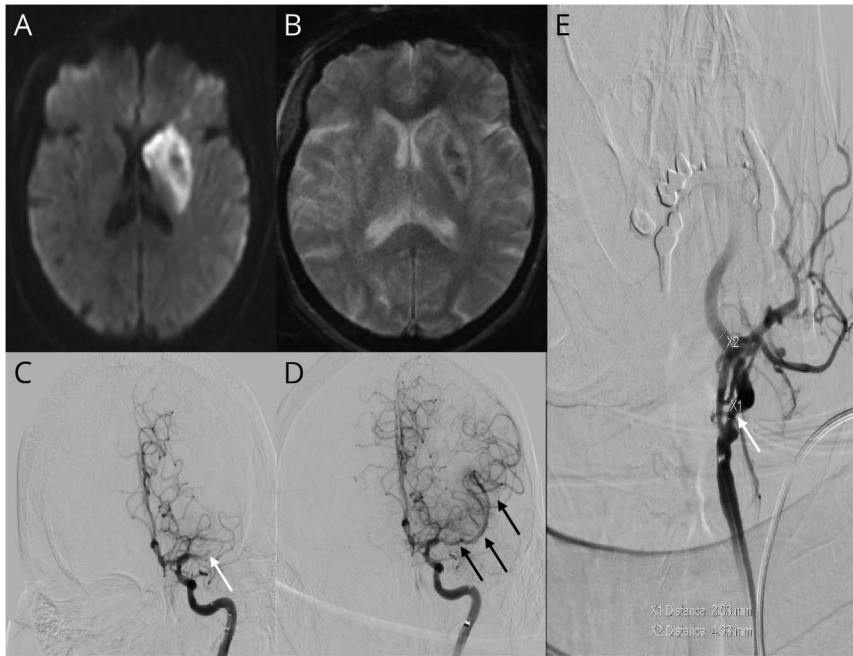
A 66-year-old woman was brought to our tertiary medical center after being found down for an unknown period of time. Her medical history was notable for hypertension, hyperlipidemia, non-insulin-dependent diabetes, and previous tobacco use. MRI of the brain showed areas of diffusion restriction involving the left caudate and lentiform nucleus with petechial hemorrhagic transformation (Figure 1, A and B). MR angiography and perfusion imaging were notable for left middle cerebral artery occlusion with associated penumbra. The patient underwent endovascular thrombectomy confirming left middle cerebral artery occlusion with thrombolysis with a cerebral infarction score of 2B (Figure 1, C and D). Angiography performed at the time of thrombectomy revealed a 60% stenosis of the left internal carotid artery at its origin by the North American Symptomatic Carotid Endarterectomy criteria (Figure 1E). Based on her embolic stroke ipsilateral to moderate left internal carotid artery stenosis, artery to artery atheroembolism was felt to be the most likely etiology, and planning for carotid endarterectomy was initiated.

Gross specimen of the thrombus was sent to pathology for routine microscopic analysis which ultimately demonstrated fibrin material with karyorrhexis of polymorphonuclear leukocytes and eosinophils (Figure 2A) overlying a core of basophilic calcified material with macrophages and foreign body type multinucleated giant cells (Figure 2B). This histologic pattern was highly suggestive of embolization from caseous mitral valve annular calcification (MAC). Transthoracic and transesophageal echocardiograms were notable for posterior mitral annular calcification. Given this finding, the stroke etiology was considered to be embolic from mitral annular calcification leading to

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**Figure 1** MRI of the Brain and Cerebral Angiogram During the Initial Presentation



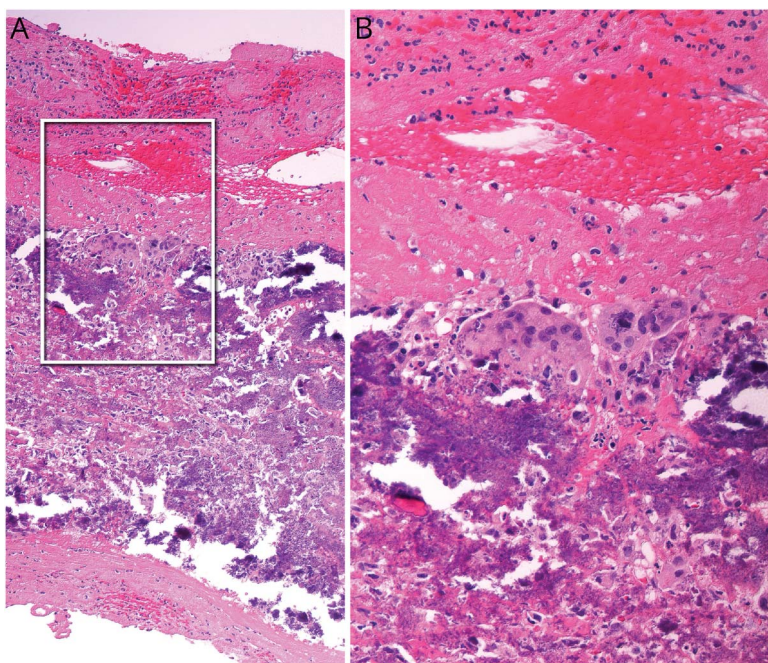
(A) Areas of increased signal on diffusion-weighted imaging highlighting the core infarct. (B) Areas of reduced signal on susceptibility-weighted imaging highlighting areas of petechial hemorrhage. (C) Middle cerebral artery occlusion (white arrow). (D) Restoration of flow post-thrombectomy (black arrows). (E) Left internal carotid stenosis (white arrow).

change in management plan from carotid revascularization to medical management of MAC. After consultation with cardiology, the patient was discharged on dual antiplatelet therapy with aspirin 81 mg and clopidogrel 75 mg daily for 6 weeks.

## Discussion

In this case report, we demonstrate evidence of embolic stroke secondary to MAC through histopathologic examination.

**Figure 2** Histopathologic Evaluation of Thrombus



Hematoxylin-eosin staining from the thrombus shown at (A)  $\times 100$  and (B)  $\times 400$  demonstrating fibrin material with karyorrhexis of polymorphonuclear leukocytes and eosinophils overlying a core of basophilic calcified material with macrophages and multinucleated giant cells.

Cardioembolic infarct is one of the major classifications of ischemic infarct according to Trial of Org 10172 in Acute Stroke Treatment classification encompassing the second largest cause of all ischemic infarcts.<sup>1</sup> The most common factors associated with cardioembolic infarcts include mechanical valve, atrial fibrillation, left atrial appendage thrombus, and infective endocarditis.<sup>1</sup> MAC is considered to be a medium risk source of embolism.<sup>1</sup> MAC is a chronic, non-inflammatory degenerative process whereby calcium deposition occurs on the fibrous annulus of the mitral valve and occurs more commonly in women than in men.<sup>2</sup> It has been associated with many common cardiovascular risk factors such as hypertension, obesity, renal dysfunction, and atrial fibrillation.<sup>2</sup> In the cardiovascular health study, MAC was found to be most prevalent in older patients and was associated with worse overall cardiovascular, renal, and metabolic profile.<sup>3</sup> MAC is usually described as an echo-dense, irregular structure associated with the mitral annulus and most commonly discovered as an incidental finding on echocardiography.<sup>4</sup> Electron-beam computed tomography and multislice computed tomography are noninvasive and effective modalities to further quantify the severity of MAC, although this is rarely necessary.<sup>3,4</sup> Although the hemodynamic impact of MAC is often minimal, conduction abnormalities appear to be more associated with the presence of MAC, including atrial fibrillation, atrioventricular blocks, and bundle branch blocks.<sup>1,4</sup> Taken together, current literature provides evidence that the presence of MAC increases risk of cardiovascular complications, and the discovery of MAC should raise awareness of patients' overall cardiovascular and metabolic health in an attempt to identify patients at elevated risk of cardiovascular diseases.

The association of MAC with ischemic stroke is not as robustly described. The LIFE study in 2013 showed that MAC was an independent predictor of stroke (hazard ratio 1.81–2.01,  $p < 0.01$ ).<sup>5</sup> In patients without known comorbid cardiovascular disease, the incidence of stroke is significantly elevated in patients with MAC (relative risk 3.12; 1.77–5.25).<sup>5</sup>

In conclusion, although MAC has been well-described in cardiovascular literature, it is a rare source of cardioembolic stroke which may be considered when more common cardioembolic stroke etiologies are ruled out. Histopathologic examination of thrombus could be useful in evaluating and diagnosing common and uncommon etiologies of stroke presenting with large vessel occlusion. In this case, although the stroke was initially attributed to large vessel atheroembolic disease, pathology proved useful in determining the etiology of stroke as MAC. There are no current evidence-based management guidelines for secondary stroke prevention in cardioembolic stroke associated with MAC which needs to be further explored in future research. An interdisciplinary management approach between neurology and cardiology is imperative for patients with stroke associated with MAC and

for further evaluation and management of possible comorbid cardiovascular and metabolic disease.

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## Disclosure

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