Caseous Mitral Annular Calcification Presenting as a Stroke: A Cracking of the Shell

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Abstract

Caseous mitral anulus calcification is a rare form of mitral valve annular calcification that can be associated with cerebral vascular accidents. Described mechanisms involve complete rupture of the shell surrounding the pasty core material with presumed embolization of a portion of the pasty core. Our case only demonstrates a dehiscence of a portion of the calcify shell resulting in a stroke. The patient has been successfully treated with dual antiplatelet agents for over two years without recurrence.

Keywords: Mitral valve disorders; Cardio embolic stroke; Caseous mitral annular calcification; Mitral annular calcification

Introduction

Mitral annulus calcification (MAC) is a relatively common condition in the elderly occurring in about 10% of the population. In the Framingham study MAC was associated with a higher incidence of cardiovascular disease (1.5 times) cardiovascular death (1.6 times) and all-cause mortality (1.3 times) [1]. The risk of stroke is higher in patients with mitral annular calcification, and a higher incidence of Cerebrovascular Accident (CVA) is associated with more extensive MAC [2-3]. The higher incidence of stroke is due to an increased incidence of atrial fibrillation [4] and an increased incidence of aortic calcification, independently associated with a higher incidence of CVA [5]. Caseous Mitral Annular Calcification (C-MAC) is a special type of MAC in which a pasty inflammatory viscous liquid forms inside an external shell of calcium. It is much less common, occurring in only 0.63% of patients with MAC [6]. This distinctive form of MAC is sometimes confused with a cardiac tumor or with endocarditis. When large, it can interfere with mitral valve function resulting in stenosis and insufficiency, requiring surgical intervention. Our case report involves a patient presenting with an acute CVA. Using multiple imaging techniques, C-MAC was identified as the likely mechanism of stroke related to the anatomy of her mitral annular disease.

Case Presentation

We present the case of a 72-year-old female with a past medical history of hypertension and hyperlipidemia who presented with right eye visual disturbances and confusion. Head CT and bilateral carotid ultrasound were negative for acute changes. Ophthalmology evaluated the patient discovering she had a central retinal artery occlusion in her right eye. An echocardiogram revealed mild to moderate Mitral Regurgitation (MR), a normal ejection fraction of 65-70%, and a subaortic echogenic mobile density but no significant aortic insufficiency. Initial differential diagnosis of the mobile mass included a papillary fibroelastoma, a metastatic tumor, or a primary cardiac tumor. Transesophageal echocardiogram showed a cystic-like structure measuring 2.1 x 2.1 cm externally, compressing the posterior, and postermedial mitral annulus. The structure had a small highly mobile echo density noted on the ventricular side of the posterior mitral annulus that appeared to be sequela of a ruptured calcify shell of cystic annular calcification (Figure 1). Cardiac Magnetic Resonance imaging (CMR) was performed shortly thereafter showing a basal inferior wall non-enhancing 5.8 x 2.8 x 3.3 cm mass without internal matrix fluid (Figure 2). The mass abutted the posterior leaflet of the mitral valve consistent with caseous mitral annular calcification versus thrombus. A Cardiac Computed Tomography (CCT) complemented the MRI and identified the calcified shell (Figure 3) making CMAC the most likely diagnosis. This was confirmed on transesophageal echocardiogram (Figure 4). Because of her recurrent bouts of global amnesia and subsequent right retinal artery embolus, the patient and treating physician elected to pursue cardiac surgery with evaluation for perioperative risks. A perioperative coronary angiogram revealed normal coronary arteries and confirmed the mitral annular calcification without tumor blush to that area. After clinical review at

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a cardiology-cardiac surgery disposition conference, the responsible cardiologist elected to treat the patient with antiplatelet agents without surgery. Since initiation therapy, the patient has not had any new symptoms or signs of CVA. A subsequent transthoracic echo at 4 months also showed the C-MAC to be unchanged and the mobile mass still present. After 2 years, the patient is experiencing slow recovery of her vision and no recurrent stroke symptoms on dual anti platelet therapy. Follow up surface echoes at 6 months and 18 months showed continued minimal resolution of the caseous center and denser calcification.

**Discussion**

Mobile masses are not infrequently associated with MAC. In 2003, Willens et al. [7] first described a mobile mass attached to calcified mitral annulus in a case report. A literature review found eighteen case reports of a mobile mass attached to a calcified mitral annulus with fifteen of these patients displaying evidence of an embolism with retinal ischemia, CVA, or embolism to an extremity. Chan and colleagues described 3 cases of a mobile thrombus arising from MAC. Two of these patients resolved with anticoagulation and one had an organized thrombus excised at the time of coronary bypass surgery [8]. One of the patients that experienced resolution of her thrombus had C-MAC. The resolution of such masses with anticoagulation along with their echo appearance and an organized thrombus on excisional biopsy demonstrates that thrombi can form on the surface of MAC or C-MAC and can presumable result in an embolic CVA (Figure 5). C-MAC occurs in a very small subset of patients with MAC with an incidence rate of 1/200 cases (0.63%) according to an echo registry study by new period. A 2016 comprehensive literature review revealed a total of 130 total patients reported with C-MAC in 86 publications. This report added 3 additional cases for a total of 133 total cases in the literature. Not surprisingly, 74 of the patients

**Figure 1:** Transthoracic apical image demonstrating a hollow structure (marked with arrow) in the mitral annulus.

**Figure 2:** Magnetic Resonance Image of the caseous lesion in the mitral valve annulus (arrow).

**Figure 3:** Arrow points to the calcified shell surround the less X-ray opaque core characteristic of caseous mitral annular calcification.

**Figure 4:** Mobile mass (arrow) attached to the calcified annulus with a lower echo density center (star) consistent with caseous calcification of the mitral annulus. See also video 1.

**Figure 5:** A) Transesophageal image of a mobile mass arising from the left ventricle side of the mitral valve and protruding into the left atrium. B) Similar view one month later after anticoagulation, demonstration resolution of the mass.
patients in this literature review had a mean age of 69.5 years and with the diagnosis especially before multi-modality testing. The 130 therapies with MAC are difficult because complete debridement adds to the length cardiopulmonary bypass and weakens the annulus such that reconstruction is needed to prevent an atriovenous groove disruption. Percutaneous therapies are increasingly being applied in part because they could eliminate the need for cardiopulmonary bypass and shorten procedures for an elderly high risk patient group. Presumably this would not apply to C-MAC where uncontrolled balloon or stent expansion could rupture the protective shell allowing for embolization of the toothpaste-like caseous material.

**Treatment of C-MAC**

Since C-MAC is a subset of MAC which can affect as many as 10% of elderly individuals, two questions are important: what can be done to lessen the incidence and progression of MAC and does the diagnosis of C-MAC imply a different clinical prognosis and therefore possibly different therapies? There are differences in incidence of MAC depending upon the diagnostic modality used. Older studies used autopsy data [19], but more recent studies have used echocardiogram. Within the last 5 years CT has become the standard with the highest sensitivity and specificity in living subjects. If MAC occurs in 8-15% of the population, then 10% of Americans or about 32,000,000 American would have MAC. Even if C-MAC is only 0.5% of all MAC cases, then there would still be 160,000 cases in the US, much more than the 133 reported in the literature. Greater awareness is needed. Dietl et al [14] have suggested that elective mitral surgery should be considered if C-MAC is detected because their review of the literature demonstrated a reported rate of embolic CVA with C-MAC at 19.2% compared to MAC at 11.8%. With such small numbers reported such a conclusions is not justified. Moreover, all C-MAC cases have severe MAC and comparing C-MAC patients to a MAC with a similar degree of calcification would be more appropriate. Most C-MAC who undergo operation do so because of valvular stenosis, mitral insufficiency, or because C-MAC was mistaken for a tumor or endocarditis. There is scant follow up data on the case reports so one could not justify any claim that elective surgery on C-MAC would reduce the incidence of recurrent stroke.

**Proposed Registry**

If there are as many as 160,000 individuals with C-MAC then many more should be identified particularly as CT is being utilized more for the evaluation of annular heart disease. Reporting these subjects. If MAC occurs in 8-15% of the population, then 10% of Americans or about 32,000,000 American would have MAC. Even if C-MAC is only 0.5% of all MAC cases, then there would still be 160,000 cases in the US, much more than the 133 reported in the literature. Greater awareness is needed. Dietl et al [14] have suggested that elective mitral surgery should be considered if C-MAC is detected because their review of the literature demonstrated a reported rate of embolic CVA with C-MAC at 19.2% compared to MAC at 11.8%. With such small numbers reported such a conclusions is not justified. Moreover, all C-MAC cases have severe MAC and comparing C-MAC patients to a MAC with a similar degree of calcification would be more appropriate. Most C-MAC who undergo operation do so because of valvular stenosis, mitral insufficiency, or because C-MAC was mistaken for a tumor or endocarditis. There is scant follow up data on the case reports so one could not justify any claim that elective surgery on C-MAC would reduce the incidence of recurrent stroke.

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Conclusions

We report another case of caseous mitral annular calcification presenting as a CVA. We propose a unique mechanism for the stroke in this particular patient. We demonstrate the value of multimodality imaging and report a favorable response (no recurrent stroke over 2 years) using dual antiplatelet therapy. If other reports in the literature are correct, C-MAC is more common than the current case reports would suggest and should be detected more frequently with more CT imaging of valvular patients. We would propose an online registry where new cases could be easily reported and then followed. Through such a registry an accurate natural history of this unusual form of atherosclerosis would be available to guide clinical decisions.

References