Calcified Amorphous Tumor-Induced Acute Cerebral Infarction A Case Report and Histopathologic Comparison of Calcified Amorphous Tumor and Mitral Annular Calcification

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Summary

We report the case of a 38-year-old woman who was admitted for acute cerebral infarction linked to a cardiac calcified amorphous tumor (CAT) and related mitral annular calcification (MAC). The cardiac mass was removed, and mitral valve replacement surgery was performed. Pathological examination revealed an amorphous accumulation of degenerating material within both lesions, indicating that build-up of calcium along the mitral annulus and subsequent rupture of the fibrotic tissue may be involved in the initiation and progression of CAT.

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Key words: Cardiogenic cerebral embolism, Echocardiography, Cardiac tumor

Calcified amorphous tumor (CAT), first described by Reynolds, *et al*⁽¹⁾ in 1997, is a non-neoplastic cardiac tumor, and reports of some cases have suggested that CAT can cause cerebral infarction. The etiology of CAT remains unknown. CAT can arise from any of the four chambers of the heart or any of the four annuli. Most CATs originating from the mitral valve are related to extensive mitral annular calcification (MAC).²⁻⁵⁾ Regardless of the features of the CAT, including its site of origin, surgical excision is usually necessary.⁶⁾

Although CAT and MAC are related, there has been no reported histologic comparison of these two clinical entities. We encountered a MAC-related CAT that was responsible for a patient's cerebral infarction and also informative in terms of the tumor etiology.

Case Report

A 38-year-old woman was referred to our hospital with acute right hemiplegia. She had been undergoing hemodialysis for 31 years because of chronic kidney failure resulting from systemic lupus erythematosus and secondary nephrotic syndrome and had been treated at various times with prednisolone, precipitated calcium carbonate, bixalomer, and/or cinacalcet hydrochloride. Her medical history also included rupture of a colonic diverticulum. Upon admission to our hospital, a systolic murmur was heard at the cardiac apex, and right hemiplegia with motor aphasia was observed. Brain magnetic resonance imaging

showed acute cerebral infarction in the middle cerebral artery territory. Electrocardiography showed sinus tachycardia at 110 bpm.

Both transthoracic echocardiography and transesophageal echocardiography revealed enlargement of the left atrium (50 × 42 mm), concentric left ventricular (LV) hypertrophy (LV mass index, 130 g/m²; relative wall thickness, 0.50), mild mitral regurgitation, and a mobile cord-like structure and MAC at the middle part of the anterior leaflet (Figure 1A, B). LV systolic function was normal with an LV ejection fraction of 67%, and LV wall motion was within normal range. No other potential source of cerebral embolism, such as a thrombus in the left atrial appendage, a patent foramen ovale, or an atrial septal aneurysm, was seen, there was no spontaneous echo contrast, and there were no physiologic or laboratory findings suggestive of infective endocarditis. No coronary artery stenosis was seen upon coronary angiography. The mobile cord-like structure was thought to be related to the cerebral infarction, which was now considered cardioembolic, and resection of the structure, diagnosed preoperatively as a CAT, was indicated to prevent relapse.

Surgery was begun with a midline sternotomy and sagittal incision of the left atrium. We proceeded with visual intracardiac inspection, but we could not find the tumor in our approach from the left. However, we found heavy MACs, portions of which were fragile and/or disintegrating. We found the cord-like structure adhered to the middle part of the anterior mitral leaflet very close to, but

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Figure 1. Transthoracic (A) and transesophageal (B) echocardiograms obtained shortly after the patient's admission show a mobile pedunculated tumor (arrow) originating from the calcified mitral valve leaflet (arrowhead). LV indicates left ventricle; Ao, ascending aorta; and LA, left atrium.

Figure 2. Operative view. Once the LA was opened, we observed both a yellowish, mobile tumor (arrow) that adhered to the middle part of the anterior mitral valve leaflet and mitral annular calcification (arrowhead). LA indicates left atrium; LV, left ventricle; and MV, mitral valve.

not adjoining, the fragile portion of the MAC (Figure 2). Because we considered the disintegrating mitral valve annulus tissue a potential embolic source, we undertook mi-

Figure 3. Histological examination of hematoxylin and eosin-stained sections of tumor tissue revealed widely dispersed degenerated blood elements (*) intermixed with fibrin (arrows) and calcium deposits (arrowheads). A: $\times 2$ magnification, B: $\times 20$ magnification of the area outlined in A.

tral valve replacement. Histologic examination of the resected tissue revealed that it consisted of fibrin, calcium deposits and an amorphous accumulation of degenerating blood elements (Figure 3A, B). No myxomatous degeneration or inflammatory cell infiltration was seen. The calcific deposits were covered with fibrotic tissue, and overall the lesion consisted of microcalcifications suspended in degenerated blood materials and fibrin (Figure 4A, B), but no myxomatous tissue or inflammatory cell infiltration was seen. On the basis of the histologic features, cardiac CAT was diagnosed. The immediate postoperative course was good, and the patient has suffered no further embolic event since the surgery, which was performed 10 months before the writing of this report.

Discussion

The case we describe is that of a cardiogenic cerebral embolism resulting from a CAT in a fairly young patient. Upon histologic examination of the resected tissue, we observed degenerated blood elements and surrounding fibrin within the mitral annulus lesion, and this amorphous material resembled the originally described CAT constituents.¹⁾ No myxomatous degeneration or inflammatory cell infiltration was seen within either the CAT or MAC. These findings are consistent with previously reported features of cardiac CAT.^{3-6,8)} Although the MAC and CAT were not contiguous, the adherent CAT was very close to the heavy MACs. This particular feature suggests that the degenerative material proliferating within the calcific le-

Figure 4. Histologic examination of hematoxylin and eosin-stained sections of the calcified mitral annulus tissue revealed an amorphous mixture of degenerative materials, fibrin (arrows), and calcium deposits (arrowheads) underneath the fibrin cap (*). **A:** $\times 1$ magnification; red arrow indicates the mitral valve. **B:** $\times 20$ magnification of the area outlined in A.

sion ruptured the fibrin cap and continued to develop as a CAT with embolic potential.

In an analysis of a Framingham Study cohort, MAC was found, after adjustment for multiple conventional risk factors, to double the risk of stroke.⁷⁾ However, it is unclear whether MAC is a direct cause of stroke or merely a marker of increased risk in association with other predictors. Masuda, *et al* reported a CAT localized to the mitral valve leaflet without MAC⁸⁾; however, most CATs originating from the mitral valve are related to extensive MAC and renal dysfunction,^{3,4)} as in our case. Therefore, it is likely that MAC and CAT act in concert as an embolic source. Although MAC-related CAT is considered a CAT

subtype, there have been no reports comparing the pathologic features of MAC with those of CAT. To the best of our knowledge, ours is the first report showing that the materials surrounding the MACs resemble CAT constituents. Abnormal calcium metabolism due to renal dysfunction and inflammation associated with hemodialysis may contribute to the genesis and further development of both MAC and CAT; most patients, including ours, with CAT originating from a heart chamber have renal dysfunction.⁵⁾

A definitive diagnosis of cardiac CAT is based on histologic examination that also rules out infective vegetation, myxoma,⁹⁾ and papillary fibroelastoma. It is difficult to differentiate a mobile cardiac tumor by means of diagnostic imaging, including transthoracic and transesophageal echocardiography, before surgical resection. Because all such cardiac tumors can be a source of emboli, careful follow-up is necessary, and surgical resection should be regarded as a necessity.

Disclosures

Conflicts of interest: None.

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