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Mitral Annular Calcification in Marfan Syndrome: A 38-Year Follow-Up Observation

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Abstract

Background Mitral annular calcification (MAC) associated with Marfan syndrome is rare in comparison with that frequently found in elderlies with valvular disease.

Case Presentation A 17-year-old woman with Marfan syndrome underwent mitral valve replacement for severe mitral regurgitation. Preoperative examination showed mitral valve prolapse and a dense C-shaped MAC. We evaluated MAC and adjacent area, respectively, in postoperative 18 and 38 years, and neither progression nor expansion of calcification was observed.

Conclusion MAC associated with Marfan syndrome is more likely to be caused by stresses due to valve prolapse than by connective tissue disorder.

Keywords
- mitral annular calcification
- Marfan syndrome
- mitral valve prolapse

Background

Elderly women and patients with renal failure are predisposed to mitral annular calcification (MAC). In them, age-related atherosclerosis, chronic renal disease, and hypertension are considered to be contributing factors.[1] About 10% of patients with Marfan syndrome have been reported as having MAC as uncommon cases, and massive calcification of the mitral annulus has been found in young patients with mitral valve prolapse.[2–5]

The pathogenesis of MAC in Marfan syndrome has been unknown. This article reports a 38-year follow-up observation on a surgical case of mitral valve replacement for Marfan syndrome in whom MAC was revealed by the preoperative examination.

Case Description

A 17-year-old woman with Marfan syndrome in whom the typical features such as arachnodactyly, tall stature, and long extremities were recognized. Her father who had the same physical characteristics had died suddenly in his 30s and no autopsy was performed. She underwent mitral valve replacement in 1981. Preoperative cardiac catheterization demonstrated a severe degree of mitral valve regurgitation due to valve prolapse with C-shaped MAC (►**Fig. 1**).[5] She had no history of previous inflammatory process. Intraoperative findings revealed calcified changes expanded from the anterolateral commissure to the posteromedial commissure along the posterior annulus, and farther distributed in places into the left atrial wall. However, the valve leaflet, chordae tendineae, and left ventricle wall seemed to be free from calcification. During the valve replacement using a 29-mm Medtronic-Hall valve (Medtronic Inc., Minneapolis, Minnesota, United States), almost all the calcified areas in the posterior annulus were removed, and the pliable posterior leaflet was incorporated into pledgeted sutures. Calcified areas projected and scattered in the left atrial wall were left untouched. Histological examinations of resected valve showed myxomatous degeneration. Postoperative course was uneventful. During follow-up for postoperative mitral valve replacement, aortic regurgitant murmur had been audible. We suspected the aortic root involvement peculiar to Marfan syndrome. After then, annual computed tomography

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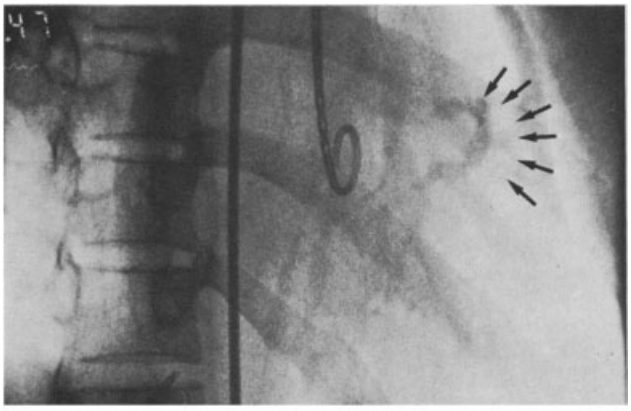

Fig. 1 Cardiac fluoroscopy recorded in 1981: a dense C-shaped calcification about the posterior mitral annulus is noted. (Reproduced with permission of Nankoh-Doh, Tokyo, Japan.)

(CT) and echocardiography had been evaluated. Eighteen years after the mitral valve operation, aortic root replacement was performed for *a 50-mm aortic root dilation and severe aortic valve regurgitation*, which frequently occurs in patients with Marfan syndrome. Preoperative evaluation for aortic root replacement showed no progression of calcification in the mitral valve apparatus including the left atrium (►**Fig. 2**). Twenty years after successfully performed aortic root replacement, no progression of other aortic dilatation had been recognized on CT. In regard to the anticoagulant treatment, she had received warfarin and had the blood examination including international prothrombin time and international normalized ratio once every 2 months. No complication of anticoagulation had occurred. She has worked well as a clerk from the first operation to now, consistently. Further reexaminations were conducted on MAC by CT and fluoroscopic analyses, and neither extension nor development of calcification was found in the mitral annulus (►**Fig. 3**).

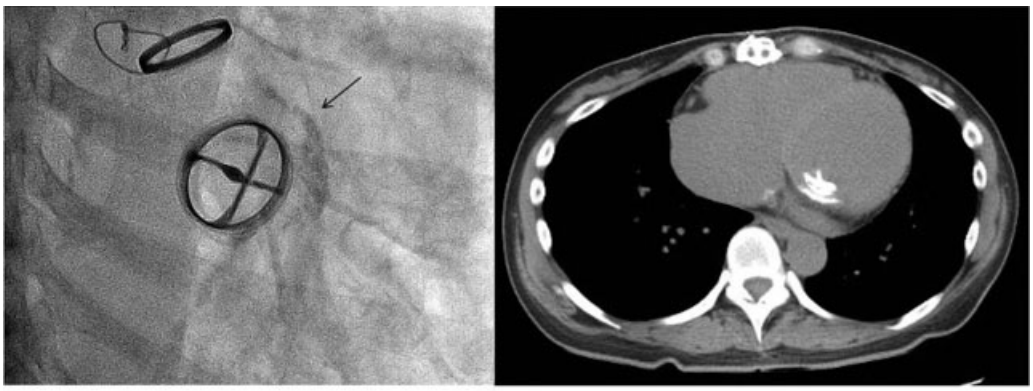

Fig. 2 Eighteen years after the first mitral valve operation, fluoroscopy (**A**) and CT scan (**B**) images were obtained for preoperative evaluations of aortic root replacement. The scattered calcification areas that remain unchanged are seen in the left atrium. CT, computed tomography.

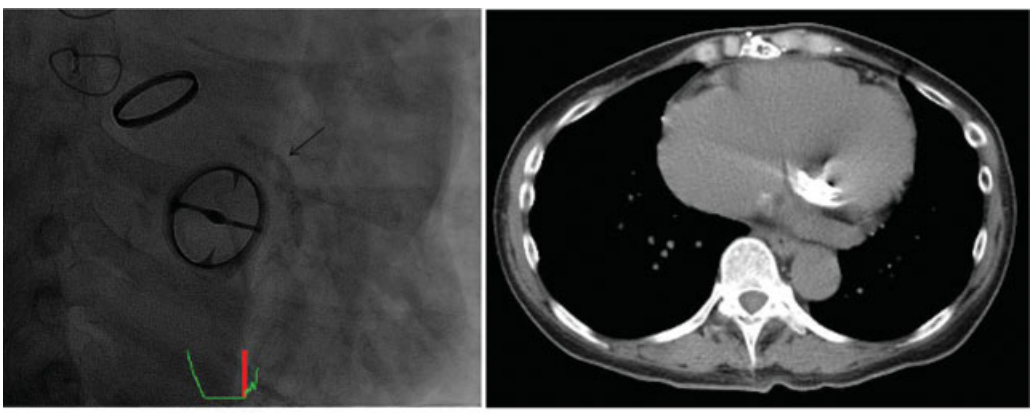

Fig. 3 Neither progression nor expansion of calcification is seen in the fluoroscopy (**A**) and CT scan (**B**) images obtained 38 years after the first surgical operation. CT, computed tomography.

Discussion

MAC has been considered as passive degeneration and/or degradation with aging. At the same time, some say it is a result derived from the process of active atherosclerosis.[1] However, Fulkerson et al emphasized that increased mitral valve stresses, such as hypertension, aortic stenosis, hypertrophic cardiomyopathy, and mitral valve prolapse, might accelerate MAC.[6] The theory of a close relationship between increase in mitral valve stresses and MAC has been demonstrated even in patients with caged-ball mitral valve replacement. A study reports that in such a situation, constant to-and-fro motion of the rigid frame may be a risk factor causing MAC.[7]

The pathophysiological mechanism contributing to the formation of MAC in Marfan syndrome remains unknown. Marfan syndrome is a connective tissue disorder inherited in an autosomal dominant fashion. Therefore, it has been reported that an intrinsic abnormality of connective tissue composing the annulus can lead to the development of MAC in young patients.[6] However, according to the theory by Fulkerson et al, early occurrence of mitral valve prolapse in young patients may have relevance to the formation of MAC.[6] As far as we know, there has been no report in the literature of a long-term observation in regard to MAC in a young patient with Marfan syndrome. Our long-term follow-up observation findings indicate that the early surgical intervention for mitral prolapse has reduced the stresses applied on the mitral annulus and gives a preventive effect on the acceleration of calcification in the mitral valve complex, which leads to no progression of calcification in the mitral apparatus including the region adjacent to the posterior ring. We consider that if mitral valve prolapse in a young patient with Marfan syndrome is surgically untreated, MAC may develop more rapidly than that in a treated case. Therefore, we think that the factor contributing to MAC in Marfan syndrome is more likely to be cardio-hemodynamic stresses applied on the mitral valve due to valve prolapse than metabolic disorder induced by hereditary disposition.

Conflict of Interest
None declared.

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