Severe Asymptomatic Unicuspid Aortic Stenosis, Myocardial Fibrosis, and Sudden Death: Relevance of Multimodality Imaging

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INTRODUCTION

We report the case of an asymptomatic patient with a unicuspid aortic valve and severe aortic stenosis (AS) who presented with sudden arrhythmic death, in which myocardial fibrosis was detected on cardiac magnetic resonance (CMR). We then briefly review the predictors of arrhythmic death in patients with AS.

CASE PRESENTATION

A 39-year-old man collapsed while participating in a running event. Advanced life support was administered along with two electrical cardioversions for ventricular fibrillation. Medical history was relevant for severe asymptomatic bicuspid aortic valve stenosis. Results of a treadmill test 1 year prior were normal (13.4 metabolic equivalents), and the patient had remained free of symptoms until the acute presentation. Following his sudden death episode, coronary angiography showed normal arteries. On a transesophageal long-axis view of the aortic valve, the coaptation line appeared eccentric, with a hypermobile leaflet posteriorly and heavy calcification and restriction anteriorly (Figure 1A, Video 1). Prolapse of the belly of the cusp in the left ventricular (LV) outflow tract was also apparent. Color Doppler showed a turbulent aortic jet with trivial aortic regurgitation (Video 2). On a short-axis view, there was a single commissure between the left and noncoronary cusps, a posteriorly located orifice, two visible anterior raphes, and heavy leaflet calcification (Figure 1B, Video 3). These findings were diagnostic for unicuspid aortic valve.[1] Aortic valve area by two-dimensional planimetry was 1.2 cm^2, but it was suspected to be overestimated because of the funnel shape of the valve orifice.

On transthoracic echocardiography, there was isolated AS with a mean gradient of 38 mm Hg, an aortic valve area of 1.2 cm^2 using the continuity equation, and a Doppler velocity index of 0.25 (Figure 1C). The aortic annulus (25 mm) and the ascending aorta (48 mm) were moderately dilated. Despite supranormal LV ejection fraction, speckle-tracking strain analysis demonstrated reduced longitudinal function in the basal and midanterolateral segments associated with a reduced global longitudinal strain (GLS) of −17.6% (Figure 1D).

CMR examination showed a high-normal LV ejection fraction (74%) and mild concentric LV hypertrophy (indexed mass 93 g/m^2 [normal range, 59–92 g/m^2]). Late inversion-recovery sequences after gadolinium injection displayed two focal areas of predominantly midwall enhancement, the largest one extending over 22 mm in the midanterolateral wall and a smaller one at the basal level, suggesting myocardial replacement fibrosis (Figures 1E and 1F).

The patient underwent a Ross procedure with extra-aortic annuloplasty and replacement of the ascending aorta and hemiarch. On intraoperative inspection, the aortic valve was unicommissural, and its opening was critically reduced. The decision was made to implant a cardioverter-defibrillator before discharge on the basis of the presence of fibrosis on CMR and the history of sudden death.

DISCUSSION

This case highlights the presence and impact of myocardial fibrosis using noninvasive imaging in a patient with severe asymptomatic AS. This presumably acted as a substrate for ventricular fibrillation when exposed to intense physical exertion.

Malignant ventricular arrhythmias and sudden death can occur with an estimated risk of approximately 1% to 1.5% per year in patients with severe asymptomatic AS.[2] Although many parameters (echocardiographic severity indices, treadmill testing, stress echocardiography, biomarkers, multi-imaging modalities) are validated for the stratification of asymptomatic AS (mostly for the prediction of symptoms or aortic valve replacement), scarce data exist on their ability to predict sudden cardiac death.[3] In a meta-analysis by Rafique *et al.*,[4] which included seven studies of patients with severe asymptomatic AS, none of the 179 patients with normal treadmill test results had cardiac death, while nine of 183 (4.9%) with abnormal stress test results had sudden cardiac death (hazard ratio, 0.18; 95% confidence interval, 0.03–1.01; $P = .05$).

A potentially useful marker of arrhythmic risk in patients with AS is the detection of myocardial fibrosis.[5] Two types of fibrosis can occur in patients with AS: interstitial fibrosis, which occurs at an earlier stage and can be reversible, and replacement fibrosis, which occurs later as a result of myocyte loss and is irreversible.[5] Replacement fibrosis can be suspected with reduced GLS and confirmed with CMR late gadolinium enhancement (LGE) imaging.

CMR LGE imaging is considered the gold standard for the noninvasive detection of myocardial replacement fibrosis. It is a well-established marker and is a strong predictor of sudden death for nonischemic dilated and hypertrophic cardiomyopathy.[6,7] Fewer data are available for AS. Dweck *et al.*[8] performed CMR imaging in 143 patients with moderate to severe AS. LGE was found in 66%

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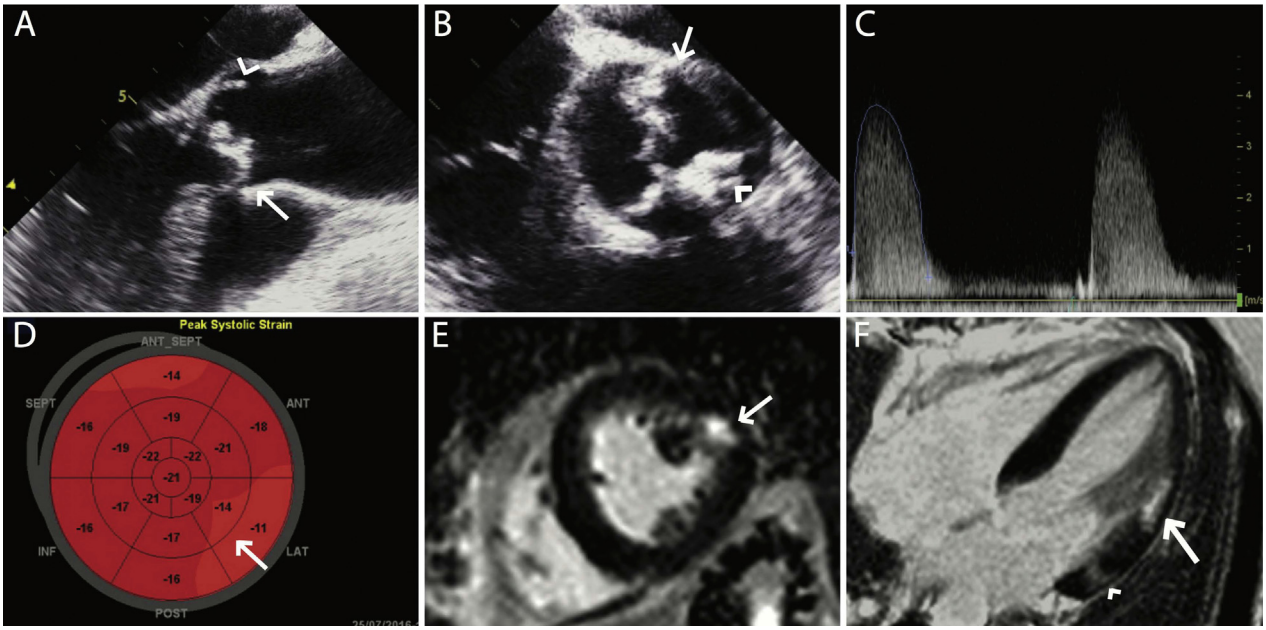

Figure 1 Echocardiographic and CMR images. **(A)** Transesophageal echocardiography (TEE). Two-dimensional midesophageal view of the aortic valve at 120° in systole showing good opening of the leaflet posteriorly (*arrowhead*) but heavy restriction and calcification anteriorly (*arrow*). **(B)** TEE. Two-dimensional midesophageal short-axis view of the aortic valve showing a posteriorly located opening orifice with a single commissure between the left and noncoronary cusps (*arrow*), two visible raphes anteriorly, and heavy calcification on the anterior aspect of the leaflet (*arrowhead*). **(C)** Transthoracic echocardiography. Continuous-wave Doppler in the right parasternal window showed a Vmax of 3.8 m/s and a mean gradient of 38 mm Hg. **(D)** Longitudinal strain analysis showing reduced deformation in the anterolateral basal (*arrow*) and midventricular wall, with GLS of −17.6%. **(E)** CMR, midventricular short-axis view. Late inversion-recovery sequences after gadolinium injection showed a focal area of enhancement (*arrow*) suggesting myocardial replacement fibrosis. **(F)** CMR, four-chamber view. Late inversion-recovery sequences after gadolinium injection showed two focal areas of predominantly midwall enhancement, the largest one extending over 22 mm in the midanterolateral wall (*arrow*) and a smaller one at the basal level (*arrowhead*), suggesting myocardial replacement fibrosis. *ANT*, Anterior; *ANT–SEPT*, antero-septal; *INF*, inferior; *LAT*, lateral; *POST*, posterior; *SEPT*, septal.

of patients with two distinct patterns: an infarct-like distribution (28% of patients) or a midwall focal distribution (38% of patients), the latter being more specific for AS. Compared with patients without any LGE, the presence of midwall LGE was associated with eight- and sixfold increases in all-cause and cardiac mortality, respectively, and was present in all three patients with sudden death.

GLS is a robust and reproducible technique for the measurement of LV longitudinal function.[9] It is a surrogate marker for myocardial fibrosis, as it has been shown to correlate with histopathologic and LGE-derived extent of fibrosis.[10,11] In the present case, segmental areas of reduced longitudinal strain were concordant with CMR-derived myocardial replacement fibrosis. Clinically, GLS is a strong marker of adverse events in patients with AS.[9,12] In a study of 395 patients with moderate to severe AS and preserved LV ejection fractions, GLS independently predicted mortality and provided incremental prognostic utility in addition to standard clinical and echocardiographic parameters.[12]

Apart from GLS, another useful strain parameter for the stratification of the arrhythmic risk is mechanical dispersion, which is the measure of the SD of the time intervals from the peak electrocardiographic R-wave to peak negative strain in a 16-segment model of the left ventricle. Mechanical dispersion has shown high predictive value for malignant arrhythmic events in studies of patients with ischemic and nonischemic cardiomyopathies, arrhythmogenic right ventricular cardiomyopathy, hypertrophic cardiomyopathy, and Chagas disease.[13-17] Unfortunately, this analysis was not available for this particular patient.

There are no available data regarding the ability of CMR LGE, GLS, or mechanical dispersion to predict sudden cardiac death in patients with severe asymptomatic AS.

CONCLUSION

We report a rare case of severe asymptomatic unicuspid AS presenting with sudden cardiac death in which multimodality imaging confirmed the presence of LV myocardial fibrosis. The detection of myocardial fibrosis in patients with severe asymptomatic AS using noninvasive imaging could be useful to stratify arrhythmic risk and guide the timing of referral to surgery.

SUPPLEMENTARY DATA

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.case.2017.02.001.

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