Rheumatic Heart Disease: A Rare Cause of Very Severe Valvular Aortic Stenosis

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INTRODUCTION

There are 3 major forms of valvular aortic stenosis (AS): degenerative calcific stenosis of a 3- leaflet aortic valve (AV), bicuspid AV stenosis, and rheumatic AS.[1] The nonrheumatic pathologies that comprise most cases of AS result from an inflammatory process triggered by endothelial damage associated with mechanical stress, which in turn leads to leaflet thickening, fibrosis, and calcification. In contrast, rheumatic AS is the chronic sequela of an immunologically mediated valvulopathy that may follow acute rheumatic fever.[2]

Severe rheumatic AS is an infrequent finding even in the regions of the world where rheumatic heart disease (RHD) remains prevalent, and it is exceedingly uncommon in high-income countries.[3]

We present 2 cases of rheumatic AS—one severe and one moderate—that illustrate the use of transesophageal echocardiography (TEE) and cardiac computed tomography (CCT) in distinguishing rheumatic disease from the more common nonrheumatic etiologies of AS.

CASE PRESENTATION 1

A 53-year-old woman with a history of RHD in sinus rhythm who presented with an acute stroke was referred for TEE to evaluate for a cardiac source of emboli.

The AV was trileaflet with fusion of the 3 commissures and severe calcification along the free edges of the leaflets (that spared the cusps themselves) consistent with rheumatic disease. (Figure 1, Video 1 and 2) This resulted in the combination of severe high-gradient valvular AS and moderate aortic regurgitation (AR). The AV peak velocity of 4.8 m/sec and peak and mean gradients of 92 and 55 mm Hg, respectively, were recorded. By continuity equation, the calculated AV area (AVA) was 0.51 cm^2 (0.28 cm^2/m^2). The aortic regurgitant jet area/left ventricular outflow tract (LVOT) area was 0.20, and the AR jet pressure half-time (PHT) was 366 msec, consistent with moderate AR (Figure 2, Video 1).

VIDEO HIGHLIGHTS

Video 1: Two-dimensional TEE, midesophageal long-axis, short-axis, and transgastric views, demonstrates severe calcified and thickened aortic leaflets. The restricted opening and closing of the 3 AV leaflets lead to severe AS and moderate AR recorded by color-flow Doppler. Data recording and basic measurements of AS severity are illustrated at the end of the video. *Asc Ao*, Ascending aorta; *LV*, left ventricle; *RA*, right atrium; *RV*, right ventricle; *RVOT*, right ventricular outflow tract.

Video 2: Two-dimensional and 3D TEE, midesophageal short-axis views, demonstrate thickening and calcification of the 3 AV leaflets, more dominant at the edges of the leaflets. The typical commissural fusion leads to a triangular opening of the valve in systole. The acoustic shadow of the calcified commissure leads to the dropout in aortic leaflets continuity in 2D and 3D (*yellow asterisk*). This should be differentiated from real dropout due to leaflet perforation. *LCC*, Left coronary cusp; *NCC*, noncoronary cusp; *RCC*, right coronary cusp.

Video 3: Three-dimensional TEE, midesophageal zoomed short-axis view of MV, and CCT imaging of AV amd MV illustrate the morphology of a severe rheumatic MS and moderate AS. The anterolateral and posteromedial commissural fusion of the MV leads to restricted opening in diastole. *ALC*, Anterolateral commissure; *AML*, anterior mitral leaflet; *PMC*, posteromedial commissure; *PML*, posterior mitral leaflet.

Video 4: Three-dimensional TEE, midesophageal zoomed short-axis view, and CCT imaging of the AV reveal morphologic changes of moderate rheumatic stenosis. Commissural fusion of the 3 AV leaflets leads to restricted motion and triangle-shape opening of the valve in systole.

View the video content online at www.cvcasejournal.com.

The rheumatic etiology of AS was bolstered by the presence of concomitant rheumatic mitral valve (MV) disease. The MV exhibited marked leaflet thickening, focal calcification, and pathognomonic hockey stick appearance of the anterior mitral leaflet. There was bicommissural fusion that created the diastolic fish mouth appearance of the valve characteristic of rheumatic mitral stenosis (MS). Three-dimensional (3D) TEE planimetry, using multiplane reconstruction, revealed an MV area (MVA) of 2.8 cm^2, consistent with mild MS. Doppler evaluation of the MV confirmed nonsevere MS. The MV mean diastolic gradient was 2 mm Hg at a heart rate (HR) of 64 bpm, and the PHT

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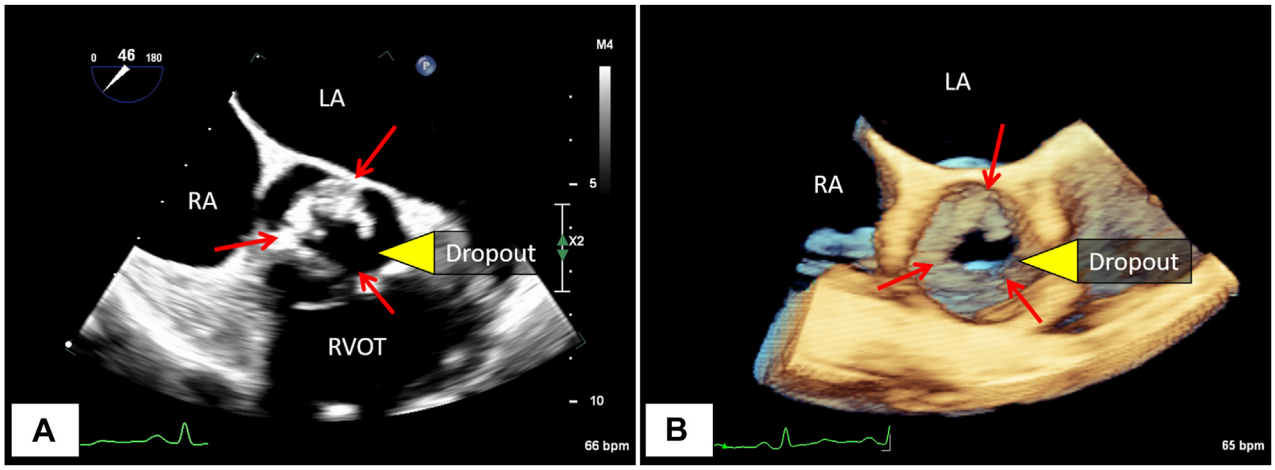
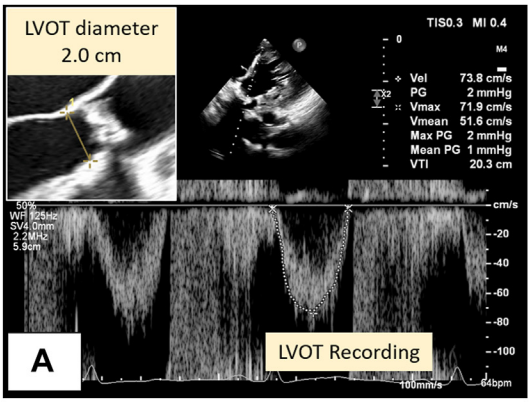
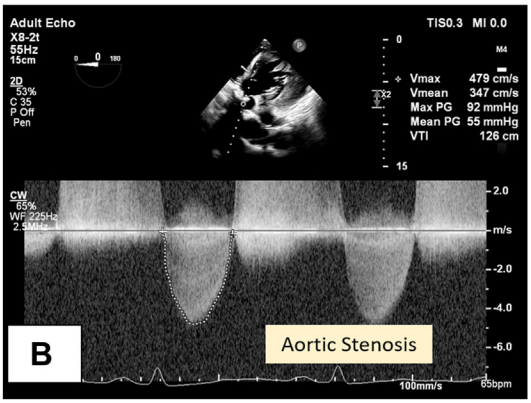


Figure 1 Morphologic changes in rheumatic valvular AS in case 1. Two-dimensional **(A)** and 3D **(B)** TEE, midesophageal short-axis views of the AV in midsystole, illustrates morphologic findings of a severe rheumatic AS. There are 3 leaflets with thickening and fusion of the 3 commissures (*red arrows*) and severe calcification along the free edges, sparing the mid and base of leaflets. The commissural fusion results in a triangular systolic orifice. The acoustic shadow of the calcified commissure leads to the dropout in aortic leaflets continuity in 2D and 3D TEE (*yellow arrowhead*). This should be differentiated from real dropout due to leaflet perforation. *RA*, Right atrium; *RVOT*, right ventricular outflow tract.



AV Vmax	4.79 m/s
Peak/mean AV gradient	92/55 mm Hg
LVOT Diameter	2. 0 cm
LVOT Area	3.14 cm^2
LVOT Vmax	0.74 m/s
LV Stroke Volume (Indexed)	20 cm x 3.14 = 63 mL (35 mL/m^2)
Aortic Valve Area (Indexed)	0.51 cm^2 (0.28 cm^2/m^2)
Dimensionless Velocity index	0.74 / 4.79 = 0.15



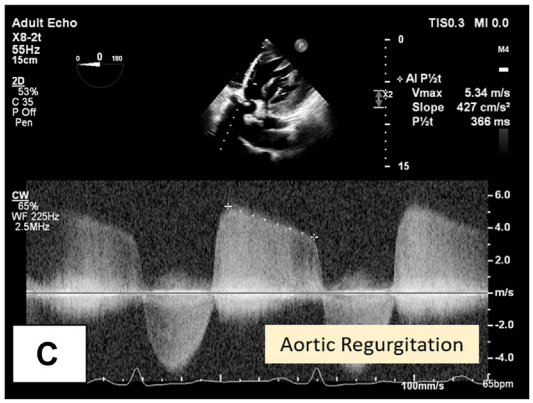


Figure 2 Hemodynamic parameters for evaluation of valvular AS severity in case 1. Spectral Doppler tracings by TEE were obtained from the 5-chamber transgastric view **(A, B**, and **C)**, and the LVOT diameter (*inset to panel A*) was obtained from the midesophageal long-axis view. Panel A represents LVOT and panels B and C represent AV recordings of AS and regurgitation, respectively. Data analysis is summarized in the table located in the *top right panel*. *LV*, Left ventricle, *Vmax*, maximum velocity.

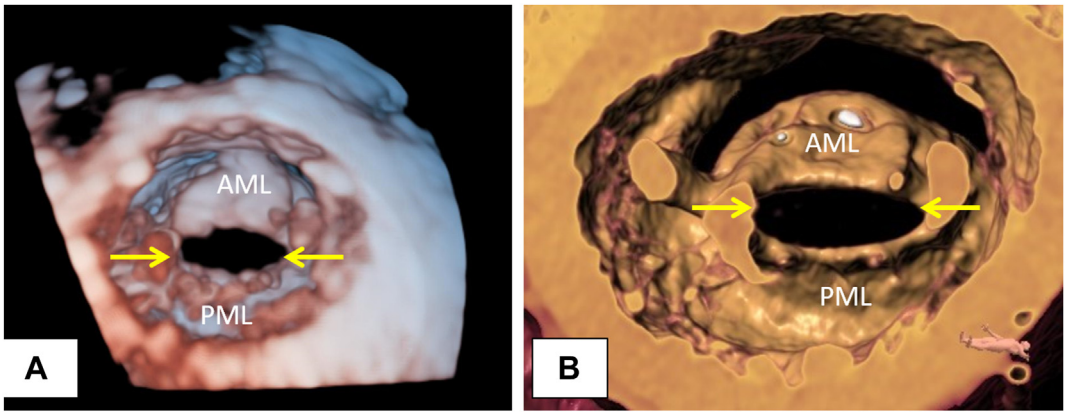


Figure 3 Morphology of MV in case 2. Three-dimensional TEE zoomed image of a rheumatic MV in diastole is shown in panel A from the ventricular perspective. Corresponding CCT image of the MV in diastole of the same patient is shown in panel B. *Yellow arrows* point to commissural fusions, the hallmark of rheumatic MS. Also, note leaflet thickening in both TEE and CCT imaging. *AML*, Anterior mitral leaflet; *PML*, posterior mitral leaflet.

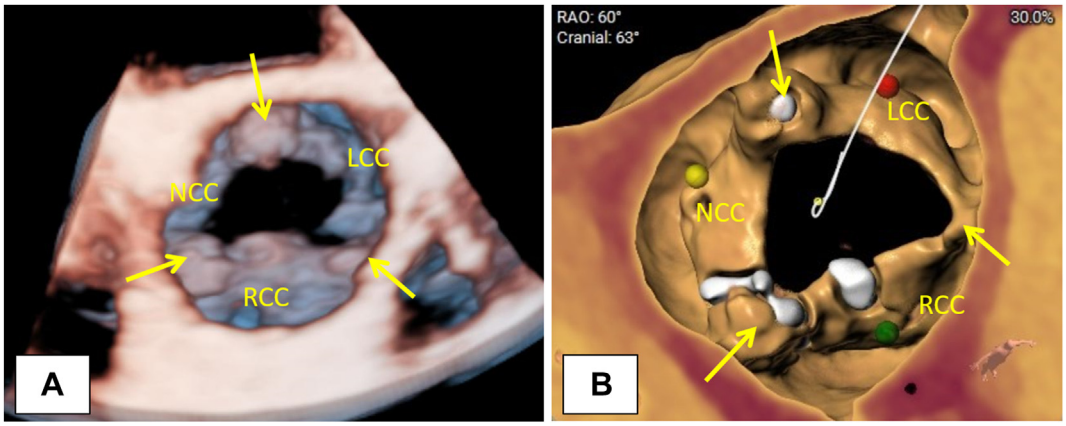


Figure 4 Morphology of AV in case 2. Three-dimensional TEE zoomed short-axis view of the AV from the ascending aorta perspective in systole at the time of large valve orifice opening **(A)**. Corresponding CCT imaging is shown in panel B. Both TEE and CCT demonstrate typical rheumatic features of the AV. Note the thickening of the 3 leaflet edges and fusion of the 3 commissures (*yellow arrows*) leading to the triangular opening of the valve. *LCC*, Left coronary cusp; *NCC*, noncoronary cusp; *RCC*, right coronary cusp.

was 92 msec, corresponding to an MVA of 2.4 cm^2. There was mild mitral regurgitation (MR).

Despite sinus rhythm, there was dense spontaneous echo contrast in the body of the markedly dilated left atrium (LA) and the left atrial appendage (LAA), but no intracardiac thrombus was seen. The LAA emptying velocity was normal (41 cm/sec; normal >40 cm/sec).

Left and right ventricular size and functions were normal, and there was no significant involvement of the tricuspid valve. No cardiac source of emboli was demonstrated. No CCT imaging of the AV was available for this case.

CASE PRESENTATION 2

A 65-year-old woman with a history of rheumatic MS and percutaneous mitral balloon valvuloplasty (PMBV) 5 years earlier was referred for repeat PMBV because of recurrent breathlessness. Cardiac computed tomography of the MV showed an MVA of 1.5 cm^2. Preprocedural TEE revealed an MV mean diastolic gradient of 4 to 5 mm Hg at an HR of 70 bpm and an MVA by 3D TEE planimetry of 1.3 cm^2 (Figure 3, Video 3). These dovetailed with the transthoracic echocardiography findings of a mean diastolic gradient of 4 mm Hg at an HR of 60 bpm and an MVA of 1.4 cm^2 by the PHT method. There was mild MR.

The trileaflet AV exhibited fusion of all 3 commissures with minimal calcification along the free edges of the cusps. The AV had a triangular shape with restricted opening of the leaflets in systole and incomplete closure in diastole. The AV peak velocity was 2.5 m/sec, and the peak and mean gradients were 26 and 16 mm Hg, respectively. Using the continuity equation, the AVA was calculated to be 1.2 cm^2, consistent with moderate AS. The AR jet width/LVOT height ratio was 0.25 and the AR PHT was 476 msec, suggesting AR of a moderate degree. Cardiac computed tomography demonstrated the presence of 3 anatomical and functional AV leaflets with thickening and fibrotic changes as well the commissural fusions characteristic of RHD (Figure 4, Video 4).

Both the echocardiographic and CCT studies revealed marked LA dilatation. The TEE revealed LA spontaneous echo contrast but no LA

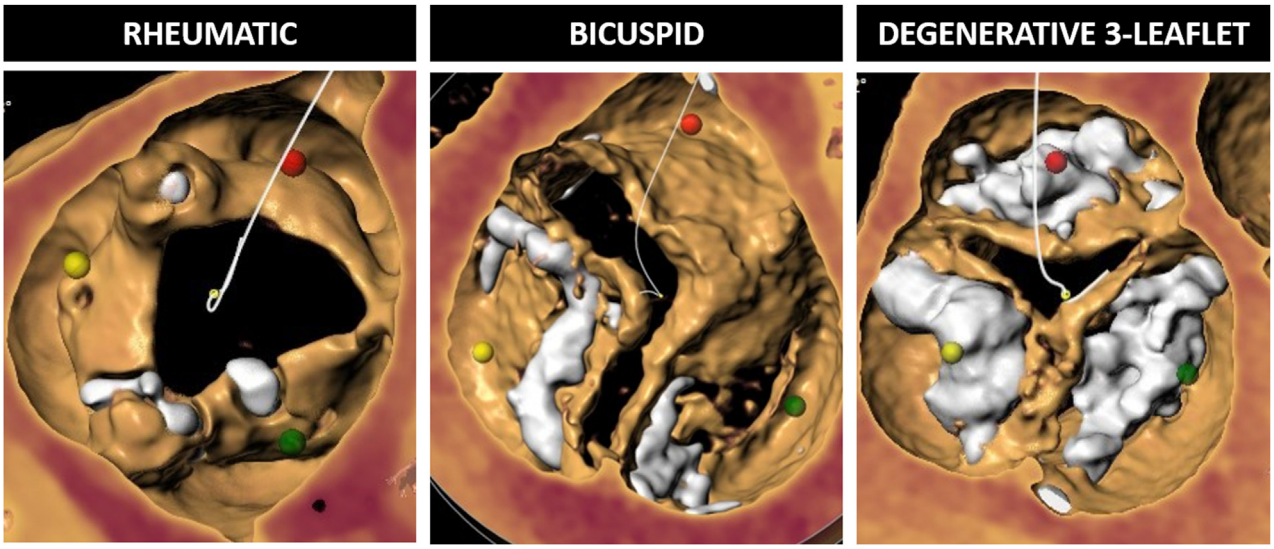


Figure 5 Predominant etiologies of AV stenosis. Cardiac computed tomography images of 3 AV morphologies commonly seen in valvular AS; the still images are taken in systole from the ascending aorta perspective at the time of the largest AV opening. *Left panel*: moderate rheumatic AS of a 3-leaflet valve characterized by fusion of the 3 commissures leading to the triangular opening of the AV; mild calcifications are noted along the free edges of the leaflets. *Middle panel*: severe AS of a bicuspid AV with a raphe between left and right coronary cusps leading to asymmetrical valve opening. Also note significant leaflet calcifications. *Right panel*: severe degenerative AS of a 3-leaflet AV. Note severe calcifications of the leaflet bodies and the absence of commissural fusion leading to a triangular shape of the AV orifice. *Red dot*, left coronary cusp; *green dot*, right coronary cusp; *yellow dot*, noncoronary cusp.

or LAA thrombus. Left ventricular outflow tract and aortic dimensions were normal. The patient underwent successful PMBV. Post-PMBV TEE revealed a decreased MV mean gradient of 2 mm Hg at an HR of 69 bpm. The MVA by 3D TEE planimetry increased to 2.0 cm^2. The patient's moderate rheumatic AV disease was managed medically.

DISCUSSION

Severe rheumatic and nonrheumatic AS differ in the average age at presentation and the anatomic basis of valvular stenosis, as well as the concomitant presence of other valvular and nonvalvular disease. Rheumatic heart disease is a very infrequent cause of severe AS in high-income countries and is rare even in regions where RHD is more prevalent.[3]

The primary anatomic basis of rheumatic AS is commissural fusion with thickening and calcification of the free edges of the leaflets, typically resulting in a triangle-shaped systolic valve orifice. In contrast, commissural fusion is typically absent from nonrheumatic AS. The pattern of valvular calcification helps differentiate rheumatic AS from degenerative AS. Whereas rheumatic AV calcification ordinarily starts at the cusp edges, degenerative senile calcification usually starts from the central parts of the leaflets. And because senile calcific valves also lack commissural fusion, this pattern of calcification often results in a 3-pointed star-shaped orifice.[1,4] The valve morphology of each of the 3 major etiologies of AS is illustrated in Figure 5.

It may be difficult to definitively identify a rheumatic etiology for severe AS by echocardiographic or CCT examination of the AV alone, particularly when the valve morphology is obscured by severe calcification. The recognition of a rheumatic etiology for AS therefore often relies on awareness of the company kept by this AV lesion. Although RHD typically involves multiple valves, mitral disease usually predominates. Rheumatic AV involvement almost always occurs in the presence of rheumatic MV disease.

Both of our patients exhibited classical findings of rheumatic MV disease—commissural fusion and restricted thickened leaflets—which gave further credence to RHD as the etiology of their AV disease. Because of concomitant, often profound, mitral disease, marked left atrial enlargement, a common hemodynamic sequela of MS or MR, is often seen in patients with rheumatic AS.

Bicuspid AVs are commonly associated with thoracic aortopathy, including aortic root and/or tubular ascending aortic, and sometimes arch dilation.[5] The associations of bicuspid valves with LVOT dilatation and coarctation of the aorta are also well established.[6] The LVOT and ascending aorta were normal in diameter in our patients. Associated findings of degenerative calcific AS include evidence of other disorders of aging—including atherosclerosis and degenerative MV disease. Our patients lacked evidence of any other cardiac disorders of aging.

In contrast to nonrheumatic causes of AS, patients with severe rheumatic AS tend to present at younger ages. This contrasts with an average age of severe bicuspid AS and an even higher average age for degenerative calcific AS of the 3-leaflet valve, which predominates in the elderly (>75 years).[1] Stenosis in the bicuspid AV arises about 2 decades before it does in tricuspid AVs.[6]

Our first case of very severe AS due to RHD is unusual. While AS is a valve lesion associated with RHD, severe high-grade stenosis is extremely uncommon—including in areas of the world with a relatively high prevalence of rheumatic disease. In high-income countries, even at times when acute rheumatic fever was far more common than it is now, rheumatic AS represented only a small minority of AS cases.[3]

The 2020 American College of Cardiology/American Heart Association clinical practice guidelines for the management of patients with valvular heart disease suggest a multimodality approach to the

diagnosis and assessment of valvular AS.[7] While transthoracic echocardiography is the standard diagnostic test in the initial evaluation of patients with valvular heart disease, in selected patients, additional testing such as TEE and CCT may be useful adjuncts. Cardiac computed tomography enables quantification of AV calcification as well as the measurement of the AVA.[8] Cardiac computed tomography scanning is becoming mandatory in weighing therapeutic options, especially in asymptomatic patients or those in whom there is discordance between echocardiography parameters. Cardiac computed tomography imaging is also indispensable for procedural planning for transcutaneous AV intervention.[7]

CONCLUSION

While RHD is a cause of AS, severe rheumatic AS is a very infrequent finding. Mitral valve involvement in the form of stenosis and/or regurgitation is almost always present with rheumatic AV disease. Echocardiography serves as the primary modality for AS evaluation. While the general principles of AS evaluation apply to rheumatic AS, the etiologic diagnosis usually relies on the demonstration of specific morphologic findings including the presence of commissural fusion and the pattern of leaflet calcification that typically spares the bodies of the 3 cusps. Cardiac computed tomography can contribute to the qualitative and quantitative assessment of rheumatic AS—confirming AV morphology including leaflet number, the pattern and extent of valvular calcification, and the valve area.

ETHICS STATEMENT

The authors declare that the work described has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for experiments involving humans.

CONSENT STATEMENT

The authors declare that since this was a non-interventional, retrospective, observational study utilizing de-identified data, informed consent was not required from the patient under an IRB exemption status.

FUNDING STATEMENT

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DISCLOSURE STATEMENT

The authors report no conflict of interest.

SUPPLEMENTARY DATA

Supplementary data related to this article can be found at https://doi.org/10.1016/j.case.2024.02.005.

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