Clinical Variability in Presentation and Management of Quadricuspid Aortic Valve: A Case Series

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INTRODUCTION

Quadricuspid aortic valve (QAV) is a rare congenital cardiac condition in which the aortic valve (AV) comprises four cusps of varying sizes as opposed to three equal-sized cusps.[1,2] The embryologic origins of QAV are still debated, with possible etiologies including abnormal septation of normal valve tissue, anomalous septation of the conotruncus, excavation of a valve cushion, or division of a mesenchymal ridge, which normally gives rise to the aortic cushion.[3-6] Regardless of its underlying etiology, identifying a QAV is of clinical importance because of the risks for complications and associated hemodynamic changes. The clinical presentation of QAV varies with underlying functional status. The aim of this case series is to share high-quality echocardiographic images of this rare condition, add to the literature of reported QAV cases, and highlight the variability of patient demographics, presentations, diagnostic modalities, and treatment options for this unique cardiac malformation.

CASE PRESENTATIONS

Case 1

An 81-year-old Caucasian man with a history of hypertension and coronary artery disease presented with dyspnea on exertion and occasional chest pain. Physical examination was notable for a 2/6 systolic ejection murmur at the right upper sternal border. Transthoracic echocardiography (TTE) was performed and revealed concentric left ventricular (LV) hypertrophy, moderate aortic regurgitation (AR), and mild mitral regurgitation. Transesophageal echocardiography (TEE) was ordered for further characterization. TEE revealed a severely calcified QAV, moderate aortic stenosis (AS), and severe AR (Figure 1, Video 1), leading to subsequent surgical evaluation. Further workup included right and left heart catheterization, which revealed severe multivessel disease. The patient underwent quadruple coronary artery bypass graft surgery and AV replacement with a bioprosthetic valve. The procedure was tolerated well, and the patient was asymptomatic postoperatively.

Case 2

A 34-year-old Caucasian woman presented for preoperative risk stratification due to a history of known QAV. The patient had not received any further cardiac evaluation for the QAV since the initial diagnosis. At this time, the patient reported excellent exercise tolerance with no symptoms. Cardiac examination was significant for a 2/6 systolic murmur and a 1/6 grade diastolic murmur. TEE was recommended to further evaluate the extent of AR and characterize AV anatomy. TEE confirmed the presence of a QAV, which was noted to be focally thickened, with mild to moderate AR (Figure 2, Video 2). Additional echocardiographic characteristics are shown in Table 1. The patient was deemed to be at low cardiac risk for procedure by cardiology, who recommended follow-up with an adult congenital heart disease clinic.

Case 3

A 54-year-old Caucasian woman with a history of hyperlipidemia was referred to cardiology for evaluation after a left central retinal artery occlusion. The patient reported no other cardiac symptoms. Physical examination revealed normal heart sounds with no murmur. A loop recorder was placed, which showed no evidence of atrial fibrillation. TEE revealed a QAV with mild to moderate AR, a small area of tissue redundancy concerning a small fibroelastoma, healed vegetation, or redundant tissue, and a patent foramen ovale with a long tunnel (Figure 3, Video 3). There was no gross evidence of atrial septal aneurysm, but right-to-left shunting was observed on a bubble study. Dual-antiplatelet therapy with aspirin and clopidogrel was initiated for stroke risk reduction. Yearly echocardiography to monitor the degree of AR and evaluate for LV dilation or decreased LV function were performed. The patient continued dual-antiplatelet therapy for the patent foramen ovale and underwent TTE intermittently for evaluation of AR associated with the QAV.

DISCUSSION

The estimated incidence of QAV is 0.013% to 0.043%, though the expanded availability of cardiac imaging has led to increased detection in recent years. Commonly reported symptoms of QAV include chest pain, palpitations, syncope, shortness of breath, fatigue, and pedal edema.[7-9] A regurgitant murmur is a common finding, with the classic

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VIDEO HIGHLIGHTS

Video 1: Case 1. Two-dimensional TEE, midesophageal simultaneous biplane short-axis (50°) and long-axis (140°) views, demonstrates four distinct cusps characteristic of QAV with leaflet thickening, calcification, and mild stenosis.

Video 2: Case 2. Three-dimensional TEE, midesophageal simultaneous biplane short-axis (40°) and long-axis (130°) views with volume-rendered reconstruction en face display of the AV from the perspective of the aorta with *(top left)* and without *(right)* color flow Doppler, and three-dimensional TEE en face photo-realistic display of the AV from the perspective of the aorta *(bottom left)*, demonstrate four distinct, focally thickened cusps characteristic of QAV, and mild to moderate central AR *(bottom right)*.

Video 3: Case 3. Three-dimensional TEE, midesophageal simultaneous biplane short- and long-axis views with *(left)* and without *(right)* color-flow Doppler and volume-rendered display from the perspective of the aorta, demonstrates four distinct cusps characteristic of QAV, with mild leaflet thickening and mild AR.

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description of a decrescendo diastolic murmur at the left sternal border.[10] However, the characterization of the murmur depends on the degree of regurgitation or stenosis present. When present, AR (75% of reported cases) may progress to moderate to severe during adulthood, requiring intervention. Normal AV function can be seen (16%); however, AS is uncommon.[11] Additionally, QAV can predispose to infective endocarditis, which is reported in 1.4% of cases. There is debate among experts about antibiotic prophylaxis, with some suggesting that it should be used in QAV with AR and cusps of different sizes.[3,12-14] However, the American College of Cardiology/American Heart Association guidelines do not recommend the routine use of antibiotics in QAV cases unless there is an active infection.[15] In <10% of cases, QAV is associated with abnormally placed coronary ostia, which is important to note for further interventional and surgical correction.[16] The preferred diagnostic tool for QAV is TEE, which reveals the four-cusp QAV, which is best viewed in the short-axis view of the AV during diastole.[17,18]

The current reference standard for visualizing AV morphology and diagnosing QAV is echocardiography. Both two-dimensional TTE and real-time three-dimensional TEE are used for QAV diagnosis and evaluation, with TEE being the more sensitive method because of higher image quality and the ability to visualize the coronary ostia.[1,11] Color-flow and pulsed-wave Doppler are used to evaluate hemodynamics, including the severity of AR. The case series presented here highlights the higher sensitivity of TEE compared with TTE in case 1, as the QAV went undiagnosed over 12 years and eight transthoracic echocardiographic examinations before finally being identified on TEE. Cases with suboptimal imaging windows can prove challenging for accurate visualization and delineation of the four cusps with TTE.[2] In addition to TEE, alternative advanced imaging modalities for QAV evaluation include cardiovascular magnetic resonance imaging and cardiac computed tomography. Cardiovascular magnetic resonance is useful in identifying QAV morphology, AR volume, AS, cardiac function, and the presence of associated cardiac disorders.[18] Cardiac computed tomography additionally can reliably identify coronary ostia location and aorta dimensions.[19] The most popular diagnostic modality continues to be TEE, given its widespread availability. Although imaging is vital to identify and assess QAV, the utility of the physical examination cannot be forgotten, as a majority of the cases in this report were sent for further evaluation after the identification of a murmur on cardiac auscultation.

QAV is frequently associated with progressive AR and rarely with AS.[20] The time of presentation varies and depends on how rapidly the regurgitation progresses and becomes clinically symptomatic. In this series, all three patients had AR on initial echocardiographic evaluation. Of note, the prevalence of AS increases significantly with age, reaching nearly 10% in those >80 years of age.[21] In case 1, the combination of both severe calcification and regurgitation suggests a compound effect of the congenital QAV anomaly and age-related degenerative changes. Eventual surgical management for QAV is required in nearly 50% of patients, usually occurring at 50 to 60 years of age.[11] Indications for AV surgery in QAV include symptomatic

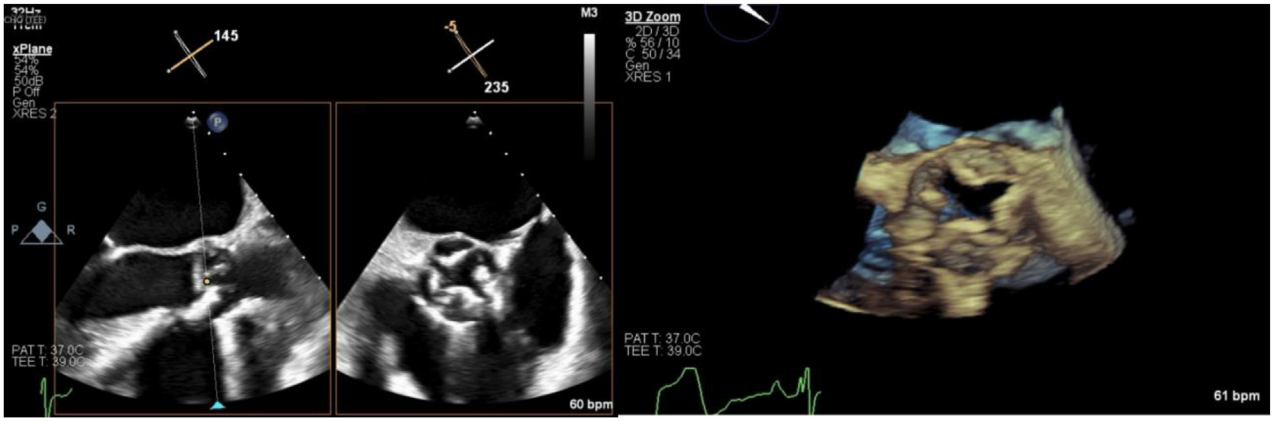

Figure 1 Case 1. Two-dimensional TEE, midesophageal simultaneous biplane long axis (145°) and short-axis (55°) systolic views *(left)* and three-dimensional TEE, volume-rendered reconstruction en face systolic display of the AV from the perspective of the aorta *(right)*, demonstrate four distinct cusps characteristic of QAV with leaflet thickening, calcification, and mild stenosis.

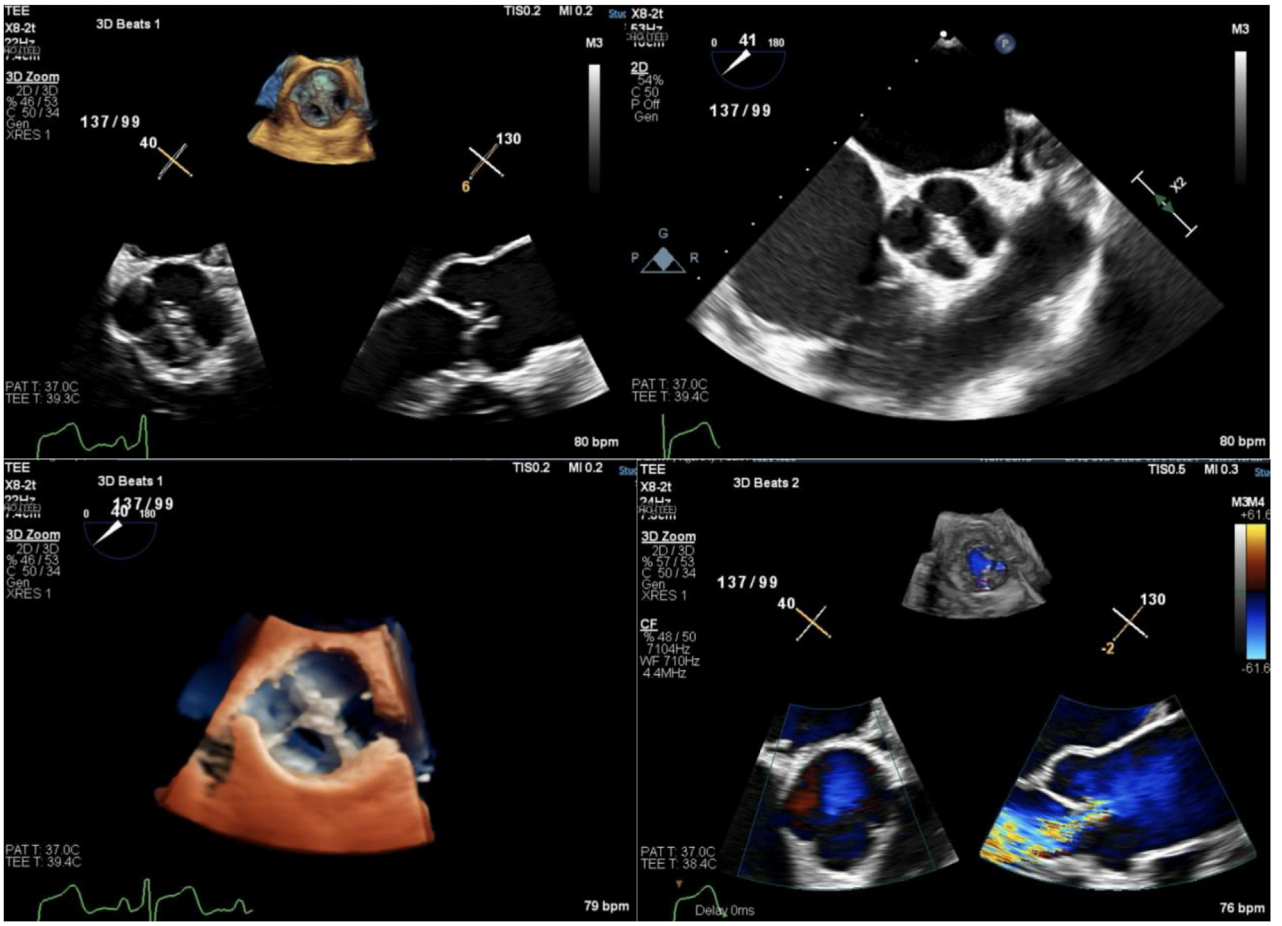

Figure 2 Case 2. Three-dimensional (3D) TEE, midesophageal simultaneous biplane short-axis (40°) and long-axis (130°) diastolic views with volume-rendered reconstruction en face diastolic display of the AV from the perspective of the aorta without *(top left)* and with *(bottom right)* color flow Doppler, two-dimensional TEE, short-axis (41°) diastolic view *(top right)*, and 3D TEE en face diastolic photorealistic display of the AV from the perspective of the aorta *(bottom left)*, demonstrate four distinct, focally thickened cusps characteristic of QAV and mild to moderate central AR *(bottom right)*.

Table 1 Echocardiographic parameters

	Case 1	Case 2	Case 3
Type	TEE	TEE	TEE
Functional status	Mild AS and moderate AR	Mild to moderate AR, no AS	Mild AR, no AS
AV thickening	Severely thickened AV leaflets	Focally thickened AV leaflets	Mildly thickened AV
AV calcification	Severely calcified AV leaflets	None	None
Jet width (% of LVOT)	68	25	27
AR pressure half-time, ms	267	824	557
AR vena contracta width, cm	0.6	0.3	0.4
AR 3D vena contracta area, cm^2	0.36	0.2	0.15
AR effective regurgitant orifice area, cm^2	0.36	0.19	0.17
AV area (3D planimetry), cm^2	1.7	2.8	3.8
AV area index, cm^2/m^2	0.83	1.58	1.85
AR maximum velocity, cm/s	503	507	390

3D, Three-dimensional; *LVOT*, left ventricular outflow tract.

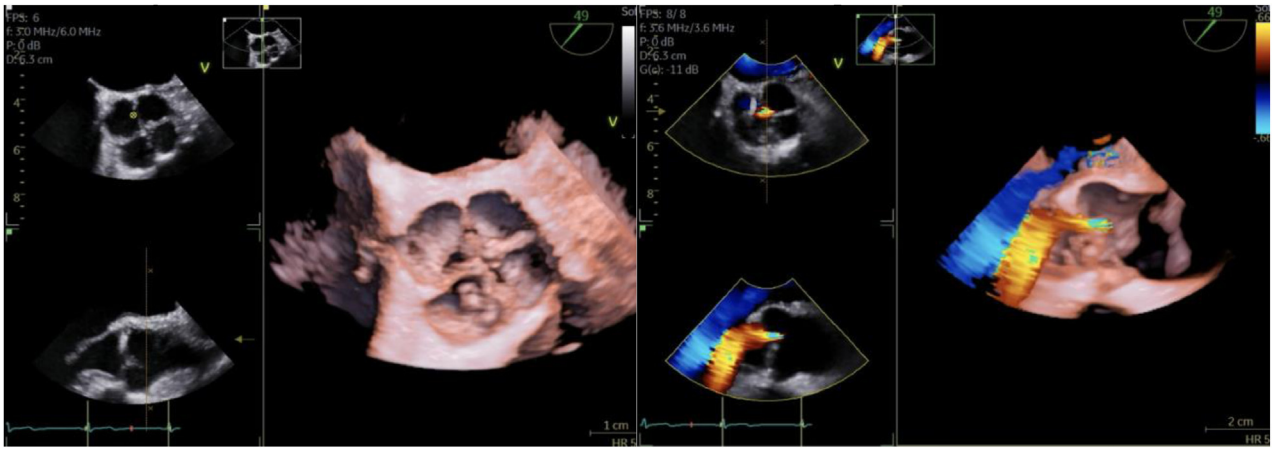

Figure 3 Case 3. Three-dimensional TEE, midesophageal simultaneous biplane short- and long-axis diastolic views with volume-rendered reconstruction en face diastolic display of the AV from the perspective of the aorta without *(left)* and with *(right)* color flow Doppler, demonstrates four distinct cusps characteristic of QAV with mild leaflet thickening and mild AR.

severe AR and symptomatic severe AS.[22] Options include AV repair and AV replacement with repair favored over replacement.[23] Successful transcatheter AV implantation has also been reported in the treatment of a severely stenosed QAV.[24] Long-term outcomes of QAV are favorable for patients without AV surgery and for those who undergo AV repair or replacement.[22] Further research on long-term clinical and surgical outcomes data are still needed to determine when to use various treatment options to maximize positive outcomes. Treatment may be unnecessary when patients remain asymptomatic and without reduced ejection fraction or LV chamber dilation, and the best course of action may be to monitor the QAV and valvular hemodynamics with TTE performed intermittently to monitor progressive valvular stenosis or regurgitation.[25] This report also highlights the variability in successful treatment options for QAV, with two-thirds of patients being monitored without valvular surgery or intervention at the time of this report. This case series also highlights the variability in presentation, with some individuals going undiagnosed into their sixth decade of life and not requiring treatment until their ninth decade of life.

CONCLUSION

QAV is a rare congenital cardiac abnormality. It often is associated with AR and can remain asymptomatic and undiagnosed until the fifth to sixth decade of life. Multimodal imaging is necessary for proper evaluation, with TEE being the current reference standard and most popular modality. QAV can affect patients from a broad range of demographics, and its clinical course varies widely. Optimal management relies on early identification for ongoing monitoring and assessment of the degree of valve regurgitation or stenosis, with many individuals requiring no treatment, while nearly half of all individuals require eventual valve intervention.

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.

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SUPPLEMENTARY DATA

Supplementary data related to this article can be found at https://doi.org/10.1016/j.case.2024.12.008.

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