CLINICAL VIGNETTE

When an Echocardiogram is Not Enough: Mixed Aortic Valve Disease Diagnosed in Cath Lab

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Case

An 83-year-old man with a medical history significant for hypertension, type 2 diabetes mellitus, chronic kidney disease and an aortic valve repair for an unknown indication 12 years prior presented to the hospital from his skilled nursing facility for evaluation of dyspnea. The patient reported that he felt short of breath with ambulation, which resolved with rest. This was associated with a dry cough and was subjectively more severe over the last 6 weeks. Because of this, he had multiple recent hospital presentations, during which his symptoms had been attributed to deconditioning. An echocardiogram three weeks prior was limited in quality due to poor sonographic windows and prior cardiac interventions but showed a left ventricular ejection fraction of 55 to 60%, normal ventricular dimensions and a mildly calcified aortic valve with aortic regurgitation (AR) and aortic stenosis (AS), both of which were difficult to assess, but likely moderate in severity.

The patient's vital signs included normal temperature, blood pressure of 131/52 mmHg, pulse rate of 66 beats per minute, respiratory rate of 14 breaths per minute and an oxygen saturation of 100%. His physical examination was significant for a frail appearance, a normal pulmonary exam, a holosystolic murmur, no jugular venous distention and no peripheral edema. Albuterol nebulizer treatments were given without effect. An electrocardiogram, chest x-ray and CT pulmonary artery angiogram were performed. Aside from evidence of prior sternotomy and aortic valve repair, these were unremarkable. A repeat echocardiogram was concerning for AS and AR but, again, was not of sufficient quality to determine the severity.

The patient was taken to the cardiac catheterization laboratory for further evaluation. A right heart catheterization showed normal pulmonary artery and bilateral cardiac filling pressures. The cardiac index was low (2.0 L/min/m^2) by the thermodilution method. Coronary angiography reveled normal coronary anatomy without obstructive disease. A dual-lumen catheter was used to transduce simultaneous left ventricular and aortic pressures. The aortic pressure was 151/46 mmHg, notable for a widened pulse pressure. The left ventricular systolic pressure was 166 mmHg with an end-diastolic pressure of 4 mmHg. The mean systolic pressure gradient was 26 mmHg. Contrast injection into the aortic root demonstrated grade 4 (severe) AR. On fluoroscopy, the patient's aortic valve was noted to be heavily calcified and to have hardware present in its annulus.

Discussion

Dyspnea is a frequent complaint and is associated with a broad spectrum of diagnoses. The majority of these patients are diagnosed with at least one cardiopulmonary disorder and valvular heart disease is the etiology in approximately 3% of cases.[1] When there is concern for significant AR or AS, transthoracic echocardiography (TTE) is the preferred initial test. Along with cardiac magnetic resonant imaging (CMR), TTE not only has the advantages of being well-validated and noninvasive but may also provide additional information about cardiac function and the etiology of valve failure.[2,3] However, as in this case, TTE may be limited by image quality and patient anatomy while CMR may be contraindicated in patients with unknown implanted hardware or may be unhelpful if sufficient breath holding is not possible.[2]

Invasive assessment of valve lesions allows direct measurement of pressures. It is appropriate when noninvasive imaging is inconclusive or conflicts with clinical impression of severity and may be necessary in the setting of mixed valve disease.[4] Left heart catheterization has the ability to provide simultaneous left ventricular and aortic pressures. These values, along with the cardiac output obtained from right heart catheterization, may be used to assess AS by determining the mean systolic pressure gradient and calculating an estimated aortic valve area using the Gorlin equation. The Gorlin equation, which was first described in 1951, estimates valve area from the flow and pressure gradients across a valve and is derived from versions of the Bernoulli and continuity equations with an empiric constant.[5] Flow is, in turn, determined by cardiac output, heart rate and systolic ejection period with the assumption that all flow is in a single direction across the valve. The diagnosis of aortic stenosis may also be supported by the presence of calcium on the valve, which is seen on fluoroscopy. Left ventricular and aortic pressures from left heart catheterization may also be used to quantify attributes of AR such as the pulse pressure and aortic regurgitation index. Additionally, angiography of the aortic root also allows for semiquantitative assessment of AR using a grading scale from 0 (none) to 4 (severe) based on the visualization of refluxed contrast into the left ventricle.

Concomitant AS and AR, termed mixed aortic valve disease (MAVD), is associated with a high-risk of all-cause mortality and poses diagnostic challenges beyond simple aortic valve lesions, complicating clinical decision making.[6] The echocardi-

ographic criteria to assess AS are affected by left ventricular stroke volume, which is increased in the setting of significant AR to maintain cardiac output. Although this does not alter the assessment of aortic valve area as obtained from the continuity equation on TTE, it results in higher mean pressure gradients and peak jet velocities than the degree of aortic stenosis alone would normally create. AR may be assessed noninvasively using the standard criteria. Peak aortic jet velocity on TTE has been identified as a prognostic indicator in MAVD, independent of the severity of stenotic and regurgitant lesions.[7]

When invasive assessment of MAVD is needed, the degree of aortic stenosis can be very challenging to assess. As with noninvasive assessment, due to increased stroke volumes, aortic valve gradients may be higher than the degree of AS alone would cause. Additionally, the Gorlin equation, which assumes that only antegrade flow is present when deriving this value from cardiac output, underestimates valve area in the setting of MAVD.[8] In this patient, the Gorlin equation would have yielded a valve area of less than 0.9 cm^2, consistent with severe AS, while having a mean gradient consistent with only moderate AS. In-vitro study has verified that the Gorlin equation may not be reliable when even a mild AR is present and a modified version of the formula has been created to calculate valve area in the setting of MAVD.[9] However, the resultant formula has not been validated in-vivo and has limited application because it requires knowledge of the regurgitant fraction, which is not easily obtained in the catheterization laboratory. In the setting of MAVD, the severity of AR may be assessed using the usual invasive parameters described above.

Despite the nuanced physiology of MAVD, a validated management strategy is to closely follow such patients, usually with serial TTE, and to pursue aortic valve replacement (AVR) once established standard surgical criteria for either AS or AR are met.[6,7] AVR is also recommended for symptomatic MAVD patients if the valve's mean pressure gradient reaches 40 mmHg or peak jet velocity reaches 4 m/s even if valve area or regurgitation criteria for severity are not reached.[8] As frequent invasive assessment is not be feasible, a high degree of clinical discretion must be employed to manage MAVD patients appropriately if noninvasive data is unavailable or unreliable.

Case Course

The patient's invasive study verified the presence of MAVD with severe AR and excluded pulmonary hypertension and obstructive coronary artery disease. The patient was referred for aortic valve replacement. Using the "Heart Team" approach, a decision was made to proceed with transcatheter aortic valve replacement, which was completed successfully.

Conclusion

MAVD is the combination of significant stenotic and regurgitant lesions of the aortic valve. This combination provides a challenge in assessing the severity of valve disease, especially when assessing a patient with nonspecific symptoms such as dyspnea. Serial echocardiography is the preferred modality to assess MAVD patients. Valve replacement confers good long term outcomes and is typically indicated in a symptomatic patient if criteria for severe AS or severe AR are met or if either an elevated mean gradient or peak jet velocity is present. In the setting of MVAD, when noninvasive studies are not available or unreliable, invasive aortic valve assessment with hemodynamics and angiography may be helpful. However, it is challenging due to the inaccuracy of the Gorlin equation and the unique hemodynamics in this condition.

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