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CLINICAL VIGNETTE

Hidden Inflammation: Severe Post-Inflammatory Aortic Regurgitation Due to Leaflet Prolapse

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Introduction

Aortic valve cusp prolapse is a rare entity that is much less common in trileaflet valves without aortic root pathology. It is more commonly seen with bicuspid aortic valves, but has also been implicated in a variety of inflammatory and connective tissue disease states. It is an important clinical finding because it can lead to progressive aortic insufficiency and eventual left ventricular failure if undiagnosed.

Case Presentation

A 40-year-old male presented to the emergency department (ED) with symptoms of palpitations and chest discomfort. He had a past medical history of atrial fibrillation and alcoholic cirrhosis, and was status post orthotopic liver transplant 8-months prior to presentation. Before his transplant he underwent cardiac evaluation with a transthoracic echocardiogram which revealed mildly elevated pulmonary artery systolic pressure of 42 mmHg, mildly thickened aortic valve leaflets consistent with aortic sclerosis, no aortic regurgitation, moderate left atrial enlargement, and severe right atrial enlargement. There was trace tricuspid regurgitation and a structurally normal tricuspid valve. Right heart catheterization results were as follows: right atrium 11 mmHg, right ventricle 28/8 mmHg, pulmonary artery 25/15 mmHg (mean 20 mmHg), pulmonary capillary wedge pressure 15 mmHg, cardiac output 10.85 L/min, cardiac index 5.3 L/min/m².

In the ED his physical exam was notable for an irregular rhythm, a 2/6 diastolic murmur appreciated best at the apex, clear lungs, and no peripheral edema. He had multiple premature atrial contractions (PACs) on monitor and was hemodynamically stable. A stress echocardiogram was negative for wall motion abnormalities but did show at least moderate aortic regurgitation. He was started on metoprolol for control of his PACs and was discharged to follow up with the cardiology service. An outpatient transthoracic echocardiogram, showed severely increased left ventricular size with a left ventricular internal diameter in diastole (LVIDd) of 7.68 cm. The estimated left ventricular ejection fraction was approximately 55 to 60%. There was mild mitral and tricuspid valve regurgitation. The left atrium was severely dilated. Most notably there was severe aortic regurgitation from what appeared to be a redundant valve with suggestion of possible prolapse of the right coronary cusp (Figure 1). The pressure half time of the regurgitant jet was 227 msec and there was diastolic flow reversal seen in the descend-

ing aorta (Figures 2 and 3). Given the abnormalities seen on the transthoracic echocardiogram, the patient underwent transesophageal echocardiography for further investigation of the etiology of his severe aortic insufficiency.

This confirmed significant prolapse of the right coronary cusp of the aortic valve causing a severe eccentric aortic regurgitant jet (Figure 4). The pressure half time of the regurgitation was 212 msec. The aortic root was normal in size and structure. There was also very mild tricuspid valve prolapse, most prominently seen in the anterior leaflet, with trace tricuspid regurgitation. It is important to note that if used in isolation, the pressure half time of 212 msec would underestimate the severity of the aortic regurgitation. In cases of more chronic aortic regurgitation, LV function and aortic compliance change to accommodate the larger regurgitant volumes. This process prolongs the equalization of trans-aortic pressures and leads to misleadingly longer pressure half-time values as in our case.

Given the severity of the regurgitation and the degree of dilation of the left ventricle, the patient was sent for consultation with cardiothoracic surgery for consideration of surgical aortic valve replacement. As part of this workup he underwent coronary angiography, which showed no coronary artery disease but revealed an elevated left ventricular end diastolic pressure of 22 mmHg and severe aortic regurgitation during an aortogram. The patient underwent surgical aortic valve replacement with a bioprosthetic valve and tolerated the procedure well. Tissue pathology surprisingly showed that the aortic valve leaflets had myxoid degeneration, neovascularization, chronic inflammation, and plasma cell accumulation, consistent with post-inflammatory valve disease (Figure 5). There was no evidence of valve destruction or perforation to suggest prior infective endocarditis. The differential diagnosis for these histopathologic findings includes rheumatic valve disease and other collagenous vascular diseases, in particular HLA-B27 associated diseases. As such he was referred to rheumatology and is undergoing further investigation into the presence of a chronic inflammatory disease process which may have contributed to his cardiac disease. At this time the workup has been non-diagnostic, but is ongoing.

Discussion

The prevalence of aortic valve prolapse in patients with trileaflet valves without aortic root pathology is very low. In a prospective observational trial, the incidence of aortic valve prolapse in 2,000 consecutive patients being screened with transthoracic echocardiography was 1.2%. Of those 24 patients, only 3 had the combination of normal aortic root sizes, trileaflet valves, no evidence of destructive endocarditis, and lacked corresponding mitral valve prolapse as in our patient's case.¹ This makes his case a very atypical presentation of the disorder.

Echocardiographic identification of aortic cusp prolapse can be difficult with transthoracic echocardiography and it is important to screen for this in the presence of aortic regurgitation, especially when the aortic root is of normal size. In individuals with trileaflet valves, aortic cusp coaptation occurs at the mid-height of the sinuses of Valsalva. Cusp prolapse is therefore defined as the visualization of an aortic cusp below this physiologic height of coaptation and prolapsing into the left ventricle during diastole.² It is important to note an association between aortic cusp prolapse and juxta-arterial ventricular septal defects with an incidence between 36% to 79%.³ Our patient lacked this congenital abnormality. Aortic cusp prolapse can be as result of valve degeneration from long-standing hypertension, however, the finding can also be seen with connective tissue disease like Marfan's syndrome and Ehler's Danlos, or from prior endocarditis.^{1,4} It can also occur as a result of post-inflammatory degeneration of valvular tissue seen with rheumatic heart disease as well as HLA-B27 related diseases such as ankylosing spondylitis (AKS). When the aortic valve is implicated in rheumatic heart disease, there is very commonly mitral valve involvement as well. In addition, the hallmark of rheumatic etiology of aortic regurgitation is commissural fusion of the leaflets. Furthermore the jet is predominantly central. In our patient, despite some previously noted aortic sclerosis, there was no commissural fusion, and the jet was eccentric. There were also no classic findings on the mitral valve, making rheumatic heart disease very unlikely.⁵

Ankylosing spondylitis (AKS) is a chronic inflammatory disease which primarily involves the sacroiliac joint and spine, most commonly in young adult males. Extraarticular manifestations can include ophthalmologic, pulmonary, neurological and cardiac manifestations. Cardiac pathology most commonly includes aortic insufficiency, aortitis of the ascending aorta, and atrioventricular block. Cardiac involvement in AKS patients has been reported as high as 2-10%.^{6,7} It has been observed that the inflammatory cellular process that leads to aortic insufficiency in AKS leads to valve tissue thickening and fibroblast hyperactivity.^{6,8} Our patient exhibited findings of aortic valve thickening and aortic sclerosis a year prior to his presentation. He also had evidence of fibrosis and diffuse inflammatory cell accumulation raising the concern that AKS was a possible underlying etiology of his aortic insufficiency. Due to his hepatic failure prior to his liver transplant he was in a chronic state of high cardiac output, evidenced by his pre-

operative cardiac output of 10.85 L/min (index 5.3 L/min/m²). It is possible this high-flow state put increased demand on his already inflamed sclerotic aortic valve leading to the morphologic changes that created a prolapsed leaflet. From our literature review there were no cases describing similar findings on patients post liver transplant.

Tricuspid valve prolapse is also an uncommon finding, but when identified, is commonly associated with mitral valve prolapse.⁹ This combination is seen in patients with myxomatous valvular degeneration and with connective tissue diseases.¹⁰ However, the combination of isolated aortic and tricuspid valve prolapse is very uncommon. The identification of mild tricuspid prolapse in our patient may be of minimal clinical significance at present as the valve was competent without significant regurgitation, but if he does have a chronic inflammatory disorder this finding may progress and become problematic. This investigation is ongoing. The finding of severe right atrial enlargement draws concern that we underestimated the degree of tricuspid regurgitation. At the time of our studies it did not seem to be significant, but we cannot exclude that during higher volume states prior to his liver transplant, that the degree of regurgitation was more significant.

Conclusion

It is important to screen for aortic cusp prolapse in the setting of aortic insufficiency in a patient with a trileaflet valve and a normal aortic root. Identification of this process can allow for surgical correction, whether aortic valve repair or replacement, which can limit continued damage to the left ventricle.¹¹ This case is also unique in that a diagnosis of an inflammatory disease process may have been made through aortic valve tissue histopathologic analysis. It is a testament to the importance of case reports and thorough clinical investigation, as without the push to closely examine the valve for the purposes of this article, this diagnosis may not have been made.

Acknowledgments

We appreciate and thank the patient for providing permission for us to present his case.

Figures

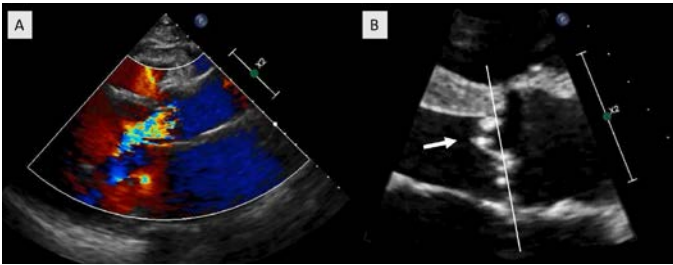


Figure 1. (A) Transthoracic parasternal long axis view showing a large regurgitant jet with color Doppler nearly filling the entire left ventricular outflow tract consistent with severe aortic regurgitation. (B) Zoomed in parasternal long axis view of the aortic valve showing prolapse of the right coronary cusp (arrow) in diastole beyond the superimposed line of coaptation.

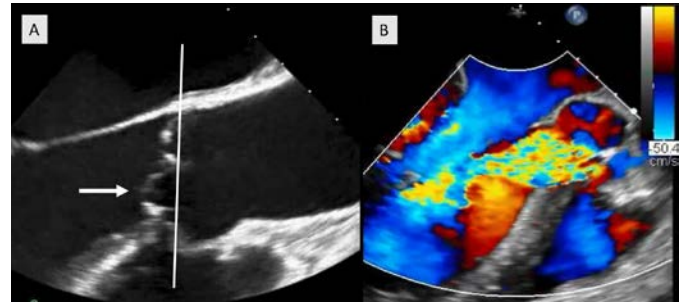


Figure 4. (A) Zoomed in transesophageal long axis view of the aortic valve showing prolapse of the right coronary cusp (arrow) in diastole beyond the superimposed line of coaptation. (B) Transesophageal long axis view showing a large regurgitant color Doppler jet filling the entire left ventricular outflow tract consistent with severe aortic regurgitation.

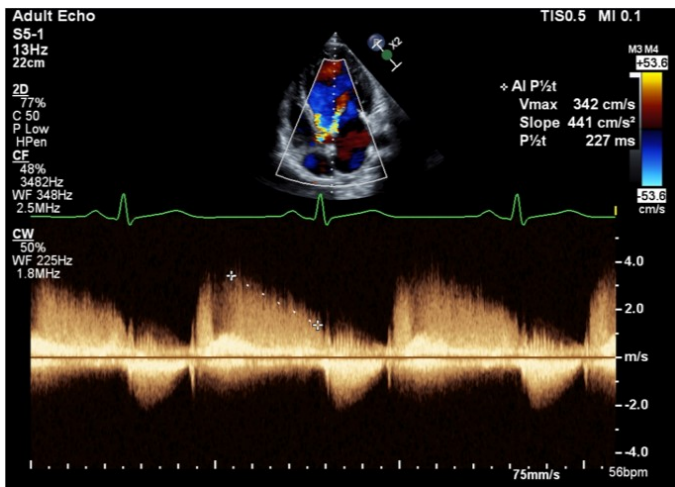


Figure 2. Continuous wave Doppler of the aortic regurgitant jet from the parasternal long axis view during transthoracic echocardiogram.

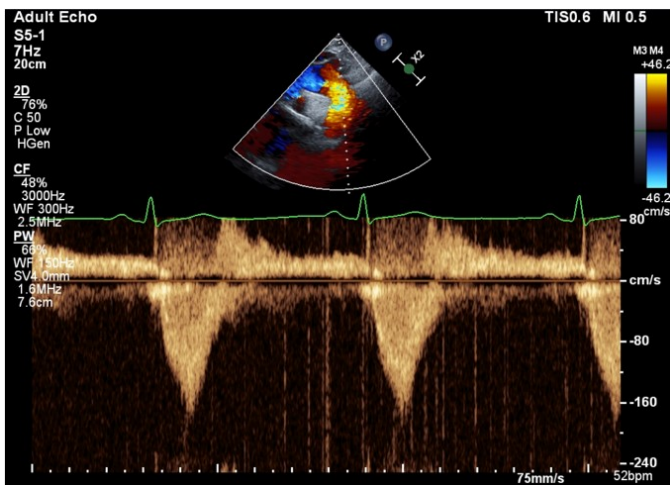


Figure 3. Continuous wave Doppler of the aortic arch and descending aorta from the suprasternal view during transthoracic echocardiogram showing diastolic flow reversal in the aorta consistent with severe aortic regurgitation.

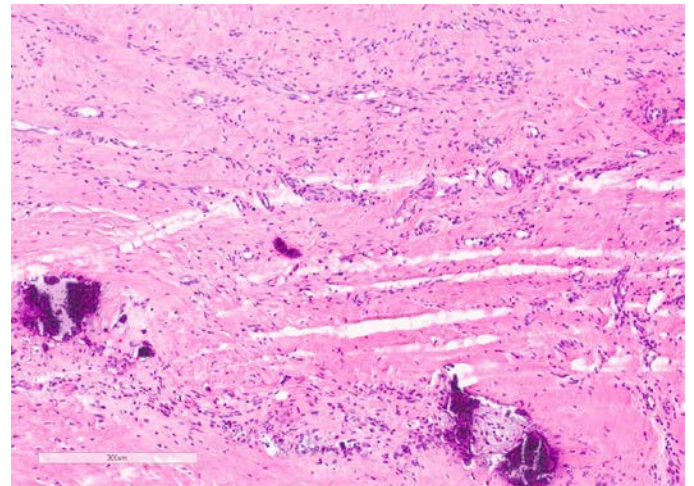


Figure 5. Histology slide of the diseased aortic valve tissue showing a high burden of inflammatory plasma cell infiltrate.

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