CLINICAL VIGNETTE

Aortic Valve Stenosis in a Middle-Age Athlete

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Case Report

A 58-year-old asymptomatic male athlete with hypertension and dyslipidemia was found to have a systolic murmur on his routine evaluation with his primary care physician in 2003. At the time, the patient underwent echocardiographic examination for further evaluation. It revealed bicuspid aortic valve, mild aortic valve stenosis, and mild aortic root dilation (41 mm in caliber). The patient was treated with aspirin, statin, and ACE-i. He deferred beta blockers due to fatigue and decreased exercise tolerance. The patient engaged in routine aerobic exercises; he was discouraged from participating in isometric exercises and weight lifting. Over the years, the patient underwent serial echocardiographic studies, revealing progression of his valvular dysfunction. In 2010, the patient became symptomatic with anginal symptoms. He underwent a repeat echocardiogram, which showed severe aortic valve stenosis. MRI/MRA showed enlarging thoracic aortic aneurysm with fusiform dilation of the ascending aorta measuring 5.0 cm in caliber. The patient underwent open-heart surgery with aortic valve replacement and repair of the ascending aortic aneurysm. The patient recuperated well from his surgical intervention, and now is asymptomatic, able to exercise vigorously without any cardiopulmonary symptoms.

Background

Bicuspid aortic valve (BAV) is the most common congenital cardiac anomaly and is seen in approximately 1-2% of the population, with a 3:1 male to female predominance[1-2]. It originates from abnormal cusp formation during valvulogenesis, resulting in the formation of a larger and a smaller cusp[1]. Because of this anomaly, the leaflets of BAV are subject to increased hemodynamic stress, predisposing to degeneration, calcification, stenosis, and incompetence. BAV is the most common etiology for severe aortic stenosis and aortic regurgitation in middle age adults[3].

Evaluation

A large majority of affected individuals are asymptomatic, and often an audible systolic ejection click or murmur during the physical examination leads to the diagnosis. Younger patients often have an early ejection click followed by a systolic ejection murmur. Aortic regurgitation (AR) is often present, and it may be the predominant functional abnormality in the adolescent and young adults[2]. In adults, auscultation findings may vary, depending on the degree of stenosis and regurgitation. The ejection click may diminish as valve calcification restricts mobility and when significant AR is present[2].

When physical examination reveals abnormal findings, echocardiography can confirm the diagnosis. The sensitivity of 2D transthoracic echocardiography for detection of BAV is 78%, with a specificity of 98%[2]. When clinically indicated, transesophageal echocardiography may be considered for further evaluation in uncertain cases.

Familial Disease

A higher prevalence of bicuspid aortic valve among first-degree relatives suggests familial clustering and heritability of bicuspid aortic valve. Determining the genetics of BAV is complex, and although several mutations in different genes have been implicated in patients with BAV, further investigation is needed to better understand the various genetic pathways. Inheritance analysis suggests an autosomal dominant pattern with variable penetrance. The 2008 ACC/AHA (American College of Cardiology/ American Heart Association) guidelines recommend echocardiographic screening for the presence of BAV in first-degree relatives of patients with BAV. Prospective parents with BAV should undergo counseling about the increased incidence (6-7%) of congenital cardiac defects in the offsprings.

Associated Cardiac Deformities

Non-valvular findings occur in about half of the adults with BAV, with dilation of the thoracic aorta as the most common abnormality. In patients with BAV and dilated aortic root, the aortic root tissue is invariably abnormal, independent of whether the valve is functionally normal, stenotic, or incompetent[1,4]. There is aortic medial disease with varying degrees of abnormality in the smooth muscle, extracellular matrix, elastin, and collagen. This alteration of the aortic media is known to predispose to dilation of the aorta, aneurysm formation, and

subsequent dissection. It is estimated that dissection occurs 5-10 times more frequently in patients with BAV than the general population[1,5]. Due to intrinsic abnormalities in the aortic wall, the aortic root may continue to dilate despite aortic valve repair or replacement. Thus, serial imaging of aortic root anatomy is recommended for all patients with BAV, regardless of severity. The frequency of the imaging depends on the caliber of aorta upon initial evaluation, change in clinical symptoms, and progression of aortic root dilation.

Coarctation of the aorta is also associated with BAV, complicating about 6% of cases[6]. Conversely, about 40% of individuals with coarctation of the aorta have concomitant bicuspid aortic valve[2]. When seen together, these anomalies are associated with an increased risk of complications, such as aortic aneurysm and dissection. Other abnormalities seen in patients with BAV include intracardiac septal defects, subvalvular aortic stenosis, parachute mitral valve, patent ductus arteriosus (PDA), bicuspid pulmonic valve, and hypoplastic left heart [7]. In addition, Turner syndrome may be associated with aortic stenosis and aortic coarctation[7]. Shone's syndrome is a constellation of multiple left-sided abnormalities such as subvalvular stenosis, bicuspid aortic valve, aortic stenosis, aortic coarctation, parachute mitral valve, or supramitral ring[7].

Valvular Complications

Aortic stenosis: Aortic valve sclerosis begins in the second decade of life, and aortic valve calcification is often noted by the 4th decade[1]. In the setting of aortic valve stenosis (AS), the presence of factors associated with atherosclerosis tends to be predictive of valve structure. These include age >65, total cholesterol >200, BMI >30, and CAD[8]. Even in the absence of clinical risk factors, however, many patients will require eventual aortic valve replacement (AVR).

Aortic regurgitation: Studies suggest that 15-20% of individuals with BAV have incomplete valve closure, and may present at age 20-40 with asymptomatic diastolic murmur, cardiomegaly, or AR symptoms[9]. Once significant AR is present, natural history is determined by LV response to chronic volume overload, and many patients will eventually require AVR[9]. Progression of AR is, in most cases, directly correlated with the degree of aortic root dilation[1].

Infective Endocarditis (IE): Individuals with BAV are at higher risk of developing infective endocarditis. Endocarditis is the most common cause of severe AR in patients with BAV, accounting for about 50% of cases of severe AR[2]. In patients with BAV and IE, there is a greater risk for IE-associated morbidities, including heart failure, valvular or myocardial abscess, and death within 6 months[9].

Management

Once BAV is recognized, the patient should be educated about the natural progression of valvular dysfunction, risk of IE, and the possibility of aortic aneurysm formation and aortic dissection[2]. Two important risk factors associated with accelerated calcific stenosis in BAV are elevated total cholesterol and systemic hypertension[8]. While clear evidence supporting the use of medical therapy to alter the natural history of BAV is lacking[1], the ACC/AHA suggest using beta blockers in patients with BAV and aortic root dilation[2]. Benefit of beta blockers has been previously shown in patients with Marfan syndrome and acute aortic dissection. In patients with BAV and concomitant systemic hypertension, afterload reduction can be done carefully to lower left-ventricular wall tension. However, diastolic parameters need to be monitored to avoid reduction of diastolic coronary perfusion. The current ACC/AHA guidelines also suggest treating patients with BAV and risk factors for atherosclerosis with statins, although no clinical trials have confirmed benefit[7].

Individuals with known BAV are advised routine echocardiogram every 2 years to monitor the progression of aortic valve disease. Annual studies are recommended when patients develop a mean gradient > 30 mmHg, or when greater than mild regurgitation is detected. Symptoms and the degree of dysfunction should indicate the timing of surgical intervention[5]. Concomitant aortic root repair or replacement may also be indicated for patients with dilated aortic root. Even after surgical replacement, however, patients are at risk for future aortic root dilatation, aneurysm formation, and dissection due to intrinsic abnormality in the aortic wall[2].

IE Prophylaxis: Recent guidelines no longer recommend IE prophylaxis in patients with BAV prior to dental procedures that involve manipulation of gingival tissue[10]. Prophylaxis is reserved for high-risk patients, classified as those who have undergone AVR, valve repair with prosthetic material, or those with a prior history of IE.

Pregnancy: Prepregnancy counseling is recommended for women contemplating pregnancy. Women with BAV and ascending aorta diameter greater than 4.5 cm should be counseled about the high risks of

pregnancy. In women with mild to moderate AS or class I/II symptoms with AR, pregnancy is typically well tolerated. In general, women at high risk (class III/IV symptoms, severe left ventricular outflow obstruction, mean gradient > 50 mmHg) should avoid pregnancy until underlying valvular abnormalities are corrected[5]. Patient referral to a pediatric cardiologist experienced in fetal echocardiography should be considered in the second trimester of pregnancy to search for cardiac defects in the fetus.

Exercise Recommendations: The impact of athletic training and its natural course on patients with BAV is not entirely clear. In theory, the adaptive changes seen in the dynamic athlete's heart, eccentric hypertrophy and ventricular dilation, may project unfavorably in the setting of pre-existing pathological adaptation to AS or AR[11]. Athletes involved in static exercise, pressure loads may accelerate aortic dilatation and regurgitation secondary to increased aortic wall tension[11]. Current consensus guidelines suggest that individuals with BAV and no aortic root dilatation and no significant AS or AR may participate in all competitive sports without restriction[12]. Those with moderately dilated aortic root (40-45 mm) may compete in moderate static or low/moderate dynamic sports (i.e. golf, baseball, volleyball, sprinting), but should avoid any sports in these categories that involve the potential for bodily collision or trauma, such as American football and rugby. Finally, those with aortic roots > 45 mm should participate in only low-intensity competitive sports (i.e. golf, cricket, curling), and any athletes with severe AS or AR with LV dilation > 65mm are advised not to participate in any competitive athletics.

Conclusion

In summary, BAV is a common congenital anomaly that benefits from early diagnosis, continuing patient education, and close monitoring of symptoms and progression of valvular abnormality. The natural history is characterized by progression towards valvular dysfunction which may require aortic valve replacement. Prophylaxis against infective endo-carditis is not routinely recommended for isolated BAV, and the decision to become pregnant or participate in competitive sports should be guided by the severity of symptoms and aortic valve dysfunction and comorbidities.

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