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Ascending Aortic Aneurysm and Dissection in Young Adults with Bicuspid Aortic Valve: Implications for Echocardiographic Surveillance

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Summary: Bicuspid aortic valve (BAV) is an independent risk factor for aneurysm and dissection of the ascending aorta. Despite this association, routine imaging of the aorta has not been recommended for patients with BAV. We describe two young men who developed life-threatening aneurysm or dissection of the ascending aorta; one had a normally functioning BAV and the other was 10 years after valve replacement. The pathology of this condition is very similar to that found in the Marfan syndrome. We recommend echocardiographic surveillance of the ascending aorta at regular intervals, and consideration of beta-adrenergic blockade among patients with significant dilation.

Key words: bicuspid aortic valve, aortic aneurysm, aortic dissection, echocardiography

Introduction

Aortic dissection is characteristically a medical emergency of sudden onset, occurring primarily in patients aged ≥40, most commonly with a history of hypertension.[1] A well-recognized exception to this is the Marfan syndrome, characterized by dilation of the ascending aorta (often at an early age) which may be complicated by aortic regurgitation or ascending aortic aneurysm and dissection.[2] Bicuspid aortic valve (BAV) is also a major risk factor for ascending aortic dissection.[1,3] In a review of 21,417 necropsies, which included 161 cases of aortic dissection, BAV was tenfold more frequent among patients with ascending aortic dissections than in the total population, and the patients with a bicuspid valve were nine times as likely to suffer a fatal dissection (18 of 293, 6.14%) as those with tricuspid aortic valves (141 of 21,105, 0.67%).

Bicuspid aortic valve occurs in about 1% of births,[4] and is accurately detected by echocardiography, especially among young persons.[5] Although these valves may become stenotic or regurgitant, many function normally for decades and thus escape detection by routine clinical examination.[4,6] The true incidence of aortic aneurysm or dissection in persons with BAV is therefore uncertain, although the association has been recognized for decades.[7,8] Modern imaging modalities may allow the detection of patients at risk for aortic rupture before it occurs.[9]

Regular echocardiographic surveillance of the ascending aorta is a standard recommendation for patients with the Marfan syndrome.[2] However, despite the finding of BAV as often as the Marfan syndrome among patients with dissection,[10] standard cardiology[11] and echocardiography[12] textbooks make no recommendation for periodic echocardiographic examination of the aortic root among patients with BAV.

We report here two cases of severe, life-threatening aortic disease in young men with BAV. Based upon a review of the literature, we suggest that regular echocardiographic surveillance of the ascending aorta is indicated for patients with BAV.

Case Reports

Case No. 1

An 18-year-old male complained of chest discomfort and collapsed. In the emergency room, he related that he had repair of aortic coarctation at age 9. Physical examination revealed a slender youth with a dusky, somewhat violaceous discoloration of his face. Blood pressure was 103/59, the pulse 108. Carotid pulses were of normal volume and jugular pulses were distended. The lungs were clear to auscultation. Cardiac examination revealed sinus tachycardia, normal first and second heart sounds, and no murmur or pericardial rub. Peripheral pulses were intact.

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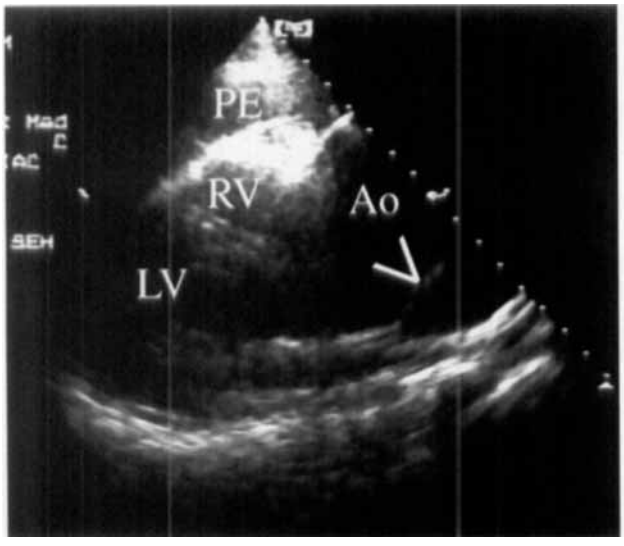

FIG. 1 Transthoracic echocardiogram in Case No. 1: Parasternal long-axis view showing markedly dilated aortic root (Ao) at right with dissection flap (arrowhead). Pericardial effusion (PE) is seen at top, adjacent to right ventricular (RV) free wall. LV = left ventricle.

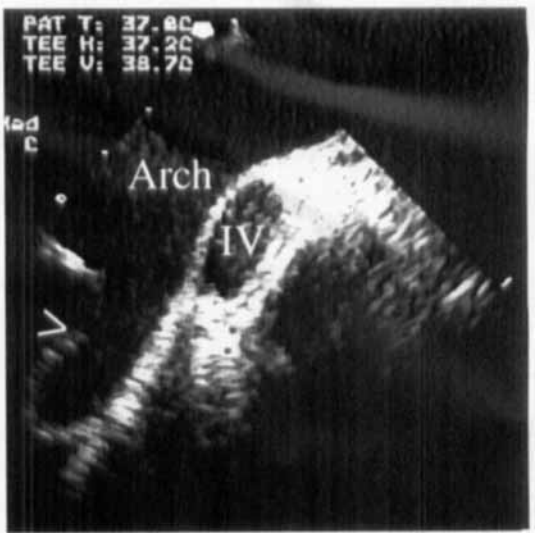

FIG. 2 Transesophageal echocardiogram in Case No. 1: Horizontal plane, showing dissection flap (arrowhead) terminating in proximal aortic arch. Oval cavity in center is innominate vein (IV) which was compressed and showed spontaneous echo contrast.

Chest x-ray showed a widened mediastinum. A transthoracic echocardiogram (Fig. 1) showed marked dilation of the ascending aorta and a dissection flap beginning just above the aortic valve along the posterior wall of the aorta. There was a large pericardial effusion with obvious compression of the right ventricle. A transesophageal echocardiogram confirmed dissection of the ascending aorta, with a tear beginning just above the aortic valve and ending in the ascending aorta before the transverse arch (Fig. 2). The diameter of the ascending aorta was 6.7 cm. The aortic valve was bicuspid, not stenotic, and showed only mild central regurgitation (Fig. 3). Successful repair of the aorta was performed with a 34 mm Hemashield graft placed above the level of the aortic valve. The ascending aorta showed histologic evidence of cystic medial degeneration.

Historical data revealed that the coarct had been detected at age 9 during an examination for a blood pressure of 120/90. Blood pressure was normal after coarct repair. Bicuspid aortic valve was noted by echocardiography at the time of surgery; the ascending aorta was noted to be slightly dilated by fluoroscopy but normal by echocardiography. Interval physical examinations indicated normal function of the BAV; echocardiography was not performed.

Case No. 2

A 36-year-old man had undergone aortic valve replacement at age 25 because of symptomatic congenital aortic stenosis. The valve was severely deformed, calcified, and bicuspid. Serial chest x-rays showed progressive prominence of the ascending aorta (Fig. 4).

Prosthetic valve function was normal. A focused echocardiographic examination was performed, including left and right parasternal views. This revealed severe dilation of the mid-ascending aorta to a diameter of 5.9 cm. Transesophageal echocardiography confirmed these findings and showed further that the pathologic dilation began at the sinotubular junction and ended before the transverse arch. There was no evidence for dissection (Fig. 5). Surgical replacement of the ascending aorta was performed. Pathologic examination showed evidence for cystic medial degeneration, focally severe (Fig. 6).

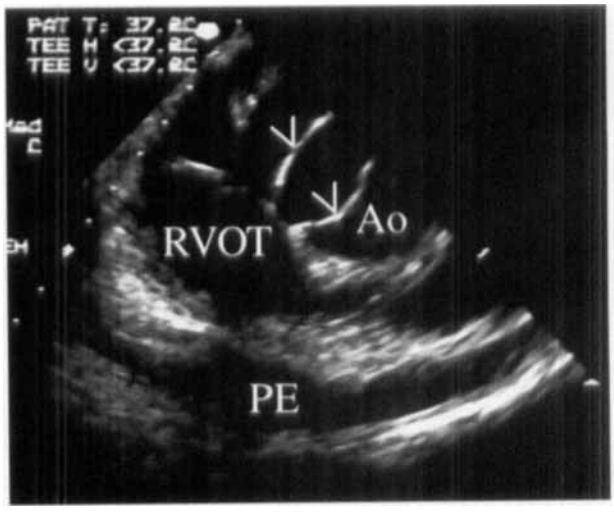

FIG. 3 Transesophageal echocardiogram in Case No. 1: Longitudinal plane, showing bicuspid aortic valve (arrowheads), with right ventricular outflow tract (RVOT) and pericardial effusion (PE) beneath.

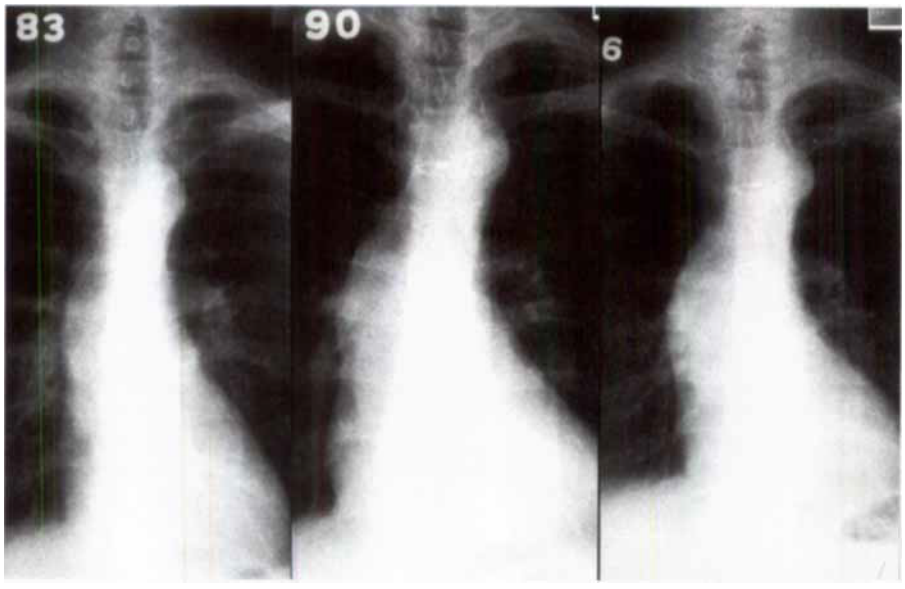

FIG. 4 Serial chest x-rays in Case No. 2: 2 years prior to aortic valve replacement, 4 years after and 10 years after (left to right). Note increasing prominence of ascending aorta.

There was no pathologic evidence in either case for extensive scar or chronic dissection to suggest that the prior aortic surgery played a role in the subsequent course.

Discussion

Aortic dissection contributes significantly to cases of sudden cardiac death in young persons. In a series of 182 autopsies, Basso *et al.* found that aortic dissection was the cause of death in 7 (3.8%) whose ages ranged from 27 to 31 years.[13] Of these, two patients had the Marfan syndrome and five had BAV (three with associated coarctation and two with an isolated, normally pliable valve). Sudden death, defined as occurring within 6 h of onset of symptoms, was the presenting manifestation of disease in all.

Ascending aortic dissection is a recognized late complication of coarctation,[14] and BAV occurs commonly among these patients.[7, 14] However, risk of aortic dissection for patients with BAV does not depend on the presence of a coarct. In the combined autopsy series of Edwards *et al.*,[15] Roberts and Roberts,[16] and Larson and Edwards,[1] 466 aortic dissections were studied. Of these, BAV was found in 43 (9.2%), none of whom had features of the Marfan syndrome, and coexistent coarctation in only 6. The combination of BAV with coarctation may present particularly high risk, however. Among 200 fatal cases of aortic coarctation studied by Abbott in the presurgical era,[7] 46 were identified with BAV and dissection occurred in 17 (37%) of these.

The frequency with which BAV contributes to dissection in the young was studied by Gore[8] in an autopsy series taken from deaths in the military population. Thirty-two fatal dissections were encountered among persons < 40 years of age. Bicuspid aortic valve was present in nine (28%) and coarctation in four; one patient had both. Arachnodactyly was noted in three, none with BAV.

Because of the frequent absence of a pathologic murmur, data regarding the occurrence of dissection among persons with BAV are currently available only from autopsy studies. Roberts found 13 functionally normal but bicuspid valves among 1,440 necropsies, an incidence of 0.9%.[4] These subjects ranged in age from 23 to 59 years; 2 of the 13 died of aortic dissection. Fenoglio *et al.* studied records

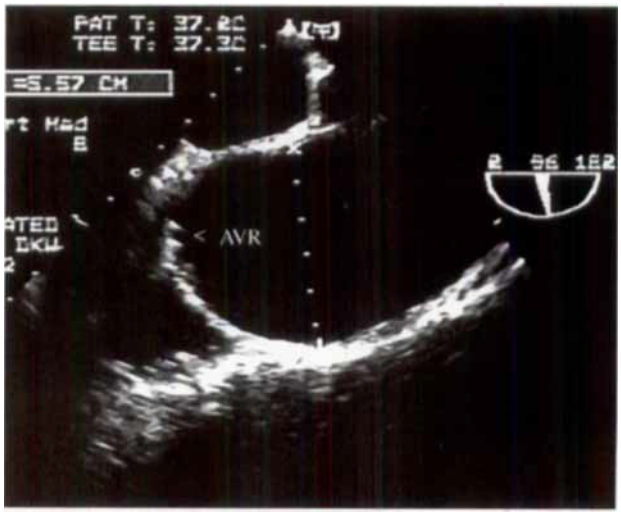

FIG. 5 Transesophageal echocardiogram in Case No. 2: Longitudinal plan, showing marked dilation of ascending aorta. Prosthetic aortic valve (AVR) is at left.

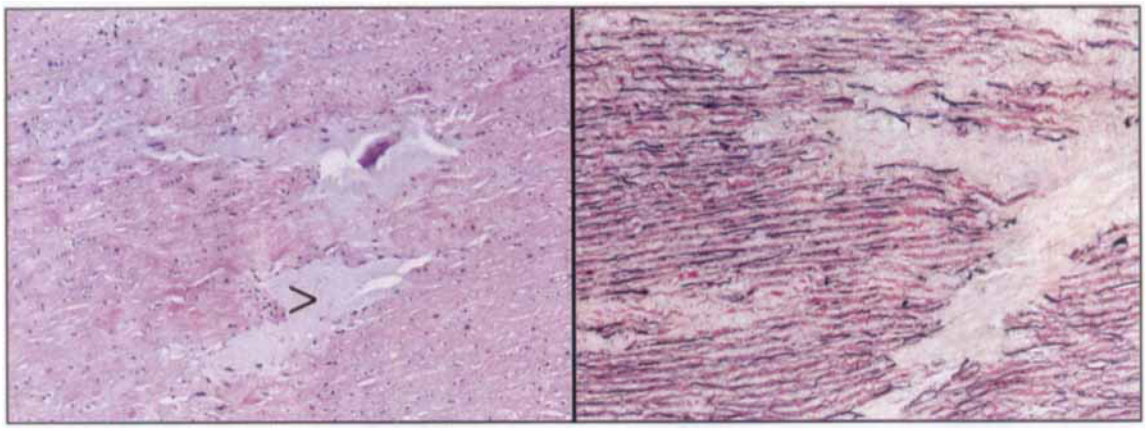

FIG. 6 Microscopic sections of aorta from Case No. 2. Hematoxylin and eosin stain at left shows cystic medial degeneration containing mucoid material (arrow). Elastic stain at right shows loss of black-staining elastic fibers in cystic area and adjacent media.

of 152 patients with BAV at autopsy.[6] Aortic dissection, without coarctation, was the cause of death in 8 (5.2%). Larson and Edwards noted that fatal dissection occurred in 6.1% of their 293 patients with BAV, and that the risk for dissection was not eliminated by repair of coarctation or control of hypertension.[1]

Given that BAV is an important independent risk factor for ascending aortic dissection[1,3] and that this is independent of coarctation[1,16] hypertension,[3] or the hemodynamic status of the valve,[1] two important questions arise. What is the pathophysiologic substrate for this, and could it be identified and treated prophylactically?

In 1928, Abbott noted an association between BAV and spontaneous rupture of the ascending aorta in patients with coarctation, and speculated that thinning of the aortic wall was part of the same congenital abnormality that led to BAV.[7] Gore recognized that dissection in persons younger than age 40 was associated with a degenerative process involving elastic lamellae of the media. He considered this the sine qua non of the disease.[8] In 1972, McKusick discussed a father and son, each of whom had BAV and died of aortic dissection.[17] Neither had a Marfanoid habitus or coarctation. Both had cystic degeneration of the aortic media, and McKusick suspected a developmental defect of the arterial tree, expressed variably as coarctation, BAV, cystic medial degeneration, or combinations of these.

Support for this is found in the observations of Schievink and Mokri, who reported three families in whom there were both BAV and dissections of the aorta or the cerebral (internal carotid or vertebral) vessels.[18] They pointed out that a disorder of migration of neural crest cells might explain these associations, since the cusps of the aortic valve and the media of the aorta both derive embryonically from the neural crest.

If it is true that dissection occurs as a result of a congenital abnormality of the aortic media, early evidence for this might be found in apparently healthy patients with BAV. Such evidence has been documented in the prevalence studies of Hahn *et al.*,[19] who studied aortic root dimensions in patients with normal echocardiograms and subjects with BAV and varying severity of stenosis or regurgitation. Aortic dimensions were larger among subjects with BAV in all hemodynamic groups than among those with a trileaflet valve. Hahn *et al.* suggested that the data supported a primary abnormality of the aortic root in patients with BAV. However, longitudinal data to establish the frequency and rate of progressive aortic root dilation in patients with BAV are still not available.

Information about progressive dilation of the aortic root is available for patients with the Marfan syndrome, and this dilation is retarded by beta-adrenergic blockade.[2] Since the occurrence of dissection and aortic regurgitation among these patients is directly related to the size of the aortic root, regular echocardiographic surveillance, at least annually, is recommended.[2] Dissection occurs rarely below a diameter of 55 mm in adults, and this diameter has been proposed as an indication for elective aortic root replacement.[2] Chronic beta-adrenergic blockade is now routine treatment for patients with the Marfan syndrome.[2]

Acquisition of longitudinal data is more difficult among patients with BAV because of its variable presentation and the relatively low frequency of progression to dissection. Unless associated with a significant hemodynamic abnormality, BAV may not be detected on routine clinical examination. The Marfan syndrome, on the other hand, may be initially suspected by physical appearance alone. Occurring with a frequency of 1 per 10,000,[2] Marfan's accounts for 6 to 9% of all dissections.[10] Bicuspid aortic valve is present in a greater number, that is, 7 to 14% of dissections,[10] but is many times more common in the population than Marfan's. The reported relative risk for dissection among patients with Marfan's (17–38%) is therefore much higher than that among patients with BAV (2.4–6.1%).[1] The greater frequency of clinical end points (aneurysm and dissection) makes it easier to perform longitudinal studies of natural history and interventions in patients with Marfan's. However, tall, thin persons with aortic root enlargement may not have the Marfan syndrome when they are carefully studied; BAV may be present.[20] These pa-

tients should not be ignored. Dissection occurs, on average, a decade earlier in patients with BAV than in those with a tricuspid aortic valve.[1]

Among patients with aortic stenosis and tricuspid valve, some dilation of the ascending aorta is common and is considered to be due to mechanical effects of the high-velocity systolic jet on the aortic wall. Progressive dilation and dissection of the aortic root after valve replacement is very rare, occurring as a result of other factors such as hypertension. However, among patients with BAV, correction of hemodynamic abnormality with valve replacement does not prevent subsequent aneurysm formation and dissection.[21] "Post-stenotic dilation" is not a benign finding in patients with BAV. It results from both hemodynamic stresses and, more important, from intrinsic weakness of the aortic wall, and merits ongoing surveillance after corrective valve surgery.

Based on the evidence presented above, it seems reasonable that patients with BAV undergo periodic echocardiograms for assessment of aortic root dimension. In the absence of longitudinal data to guide the timing of elective aortic root replacement among these patients, we used the data from the patients with Marfan syndrome to aid our decision in Case No. 2. Although there is no proof that aortic rupture was imminent in this case, the cystic degeneration of the media (Fig. 6) was severe. Therefore, until longitudinal data are available, we suggest echocardiographic evaluation at about 2 to 3 year intervals if no abnormality is detected, and more frequently if dilation of the ascending aorta is present.

Conclusion

Bicuspid aortic valve is clearly an independent risk factor for aneurysm and dissection of the ascending aorta among young adults. Abnormal dilation of the ascending aorta is present in patients who have a normally functioning BAV, but data are not yet available to establish the rate of progressive dilation and the risk for dissection at different aortic dimensions. This is an important topic for investigation. Regular echocardiographic surveillance of the ascending aorta seems prudent in patients with BAV, and beta-blockade should be considered in patients with significant dilation.

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