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Case Report

Quadricuspid Aortic Valve with Ascending Aortic Aneurysm: A Case Report and Histopathological Investigation

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We describe the case of a 69 year-old woman with a dilated ascending aorta, who presented with aortic valve regurgitation due to a quadricuspid aortic valve (QAV). There are only a few reports in the literature describing aortic replacement and subsequent aortic valve replacement for a malfunctioning QAV. We discuss the pathogenesis of the dilated ascending aorta in this patient and the indication for ascending aorta replacement in such cases.

Key words: aneurysm, ascending aorta, matrix metalloproteinase quadricuspid valve

Introduction

Among abnormal congenital aortic valve malformations, quadricuspid aortic valve (QAV) is very rarely encountered. Its reported incidence varies from 0.008%[1)] to 0.033%,[1, 2)] while, among patients undergoing aortic valve replacement, its incidence ranges from 0.55% to 1.46%.[3)] In those reports, the QAV associated with aortic regurgitation and the coexisting dilated ascending aorta were replaced. There are many reports that hypothesize that the aortic dilatation seen in congenital aortic valve malformation, especially in bicuspidal aortic valve (BAV), could have a different pathogenesis from that of tricuspidal aortic valve (TAV).[4–6)] We discuss the pathogenesis of the dilated ascending aorta, and the indication for ascending aorta replacement in such patients.

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Case

A 69-year old woman was referred to our hospital due to exertional shortness of breath and palpitation. She had a hypertension that was well controlled with candesartan, carvedilol and nifedipine. Her height, weight and calculated body surface area (BSA) were 148 cm, 54.7 kg and 1.47 m^2, respectively. She had a regular rhythm and a grade II/VI diastolic murmur best heard in the aortic area. A chest X ray showed an auxocardia with cardiothoracic ratio of 59%. Transthoracic echocardiography revealed severe aortic regurgitation with an 83% left ventricular ejection fraction and the characteristic X shaped commissural pattern of a QAV in short axis view of the aortic root (**Fig. 1**). Neither significant stenosis of coronary arteries nor displacement of the coronary ostia was detected by coronary angiography. Aortography showed an aortic valve with four cusps and Sellers grade III aortic regurgitation (**Fig. 2**). Dilatation of the ascending aorta, but not of the aortic root, was also noted. The maximal diameter of the ascending aorta measured in a thorax computer tomograph was 4.4 cm, which was indexed to BSA with a value of 3.0 cm/m^2. Extracorporeal circulation was established using the left common femoral artery. The aortic valve was consisted of two equal-sized larger cusps and two equal-sized smaller cusps, which is referred to as "type c" by Hurwitz et al. (**Fig. 3**).[1)] None of the leaflets was calcified, though

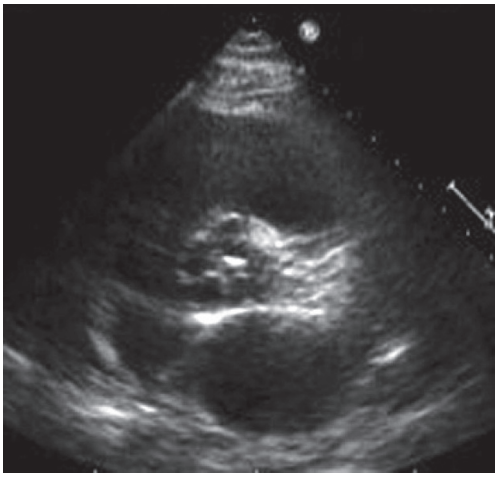

Fig. 1 X shaped commissural pattern in short axis view of the aortic root.

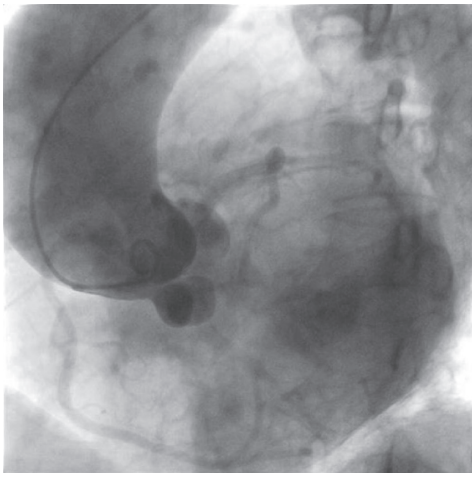

Fig. 3 Operative view of aortic valve consisted of two equal-sized larger cusps and two equal-sized smaller cusps.

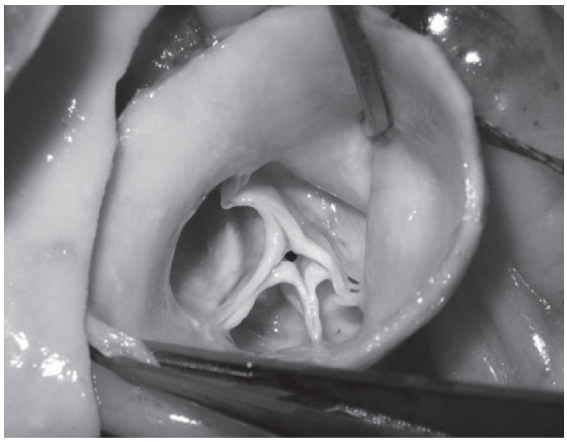

Fig. 2 Aortic valve with four cusps with a severe aortic regurgitation.

Fig. 4 (**A**) HE staining revealed a mild atherosclerotic change with localized intimal thickenings accompanied by foam cell infiltration. Smooth muscle cells (SMCs) in the media were well preserved.
(**B**) Elastin in the media was well preserved in EvG staining. (Original magnification × 100)

fibrous sclerosis was found in each Arantius body. A Carpentier-Edwards Perimount valve of 19 mm in diameter was implanted after excision of the native valve. The ascending aorta was excised and replaced with a 24mm J Graft Shield Neo. Her postoperative course was uneventful, and she was discharged on the 10th postoperative day.

Histological study of the aortic wall in hematoxylin and eosin (HE) staining revealed a mild atherosclerotic change with localized intimal thickening accompanied by foam cell infiltration. Smooth muscle cells (SMCs) in the media were well preserved, and there was no cystic medial degeneration. Elastin in the media was well preserved as revealed by Elastica van Gieson (EvG) staining (**Fig. 4**).

Discussion

QAV is a very rare aortic valve malformation whose incidence of QAV ranges from 0.55% to 1.46% among patients undergoing aortic replacement.[3)] Whereas aortic regurgitation in QAV is common and seen in 75% of the patients,[7)] the concurrent presence of an ascending aortic aneurysm has been only rarely reported. In fact, there

had been only two previous QAV cases before this report, in which the coexisting ascending aneurysm was replaced.[8, 9] An additional aortic surgery for the sole purpose of valve replacement elevates the operative risk and, in the case of our patient, the operative risk calculated in Euroscore increased from 3.50% (AVR without surgery of the thoracic aorta) to 10.36% (AVR with surgery of the thoracic aorta). In patients found to have a BAV due to abnormal valvulogenesis, dilatation of the ascending aorta was a common consequence.[10] However, it is recommended that the ascending aorta with a BAV be replaced at the time of aortic valve intervention due to a late aortic event, if the diameter of the aorta exceeds 4.5cm.[11] On the other hand, aortic replacement is recommended when the aortic valve without congenital malformation must be replaced, and the diameter of the ascending aorta is 4.8cm or more.[11] Thus, which criterion should we have followed for the ascending aorta replacement not to increase the operative risk of our patient?

It was reported that the dilatation of the ascending aorta in patients with a BAV was progressive, even if the BAVs were replaced, and hemodynamic wall stress were attenuated.[12] Nataatmadja et al. suggested that, in BAV thoracic aorta, there might be a fundamental cellular abnormality, as often seen in Marfan syndrome (MS), characterized by intracellular accumulation of fibrillin which induced activation of MMP-2 and apoptosis of cultured SMCs derived from the ascending aorta of patients with MS and those with a BAV.[13] Actually, Bonderman et al. revealed that apoptosis of vascular SMCs played an important role in the degradation of the aortic wall, which led to the dilatation of the thoracic aorta.[6] Their interesting hypothesis was that a genetic developmental defect of the neural crest cells, which are the origin of aortic valvular cusps and the arterial media, could result in the premature apoptosis of vascular SMCs. In a previous investigation on the occurrence of a QAV in developing embryos of Syrian hamster, it was concluded that the supernumerary cusp resulted from abnormal invagination of the endocardial layer of one of the three normally positioned mesenchymal swellings.[14] In regard to the study by Bonderman et al., it is questioned whether the aortic dilatation seen in this QAV had derived from embryological defect of medial SMCs, as it has been seen in the case of BAV.

Lemaitre et al. investigated the mechanisms underlying the development of ascending aortic aneurysm in patients with a BAV by comparing the histopathological characteristics and expression of MMPs, which are involved in the remodeling of the aortic wall, to those of patients with a TAV.[4] In their investigation, the BAV ascending aorta showed less inflammatory cell infiltration and more elastic content. Furthermore, an increased expression of MMP-2 and a normal level of MMP-9 were observed in the BAV ascending aorta, whereas, an elevated MMP-9 and normal level of MMP-2 were seen in the TAV ascending aorta.

In our patients, whose ascending aortic diameter was 4.4 cm, the aortic wall showed mild inflammation and well preserved elastin content. Unfortunately, we could not identify the characteristic patterns of MMPs expressions in this single case of the QAV ascending aorta. Thus, we could not conclude whether dilatation of the QAV ascending aorta derived from a genetic abnormality of the ascending aortic wall. However, Niwa et al. reported that structural abnormalities of the thoracic aorta were widespread in congenital heart diseases, including BAV, and would predispose to aortic events such as dissection or rupture.[15] Therefore, it might be that dilatation of the ascending aorta accompanying QAV with a diameter of 4.4 cm might predispose to a risk for aortic events as high as that of BAV.

On the other hand, McDonald et al. reported that women undergoing aortic valve replacement had a worse prognosis compared to men because of late aortic events.[16] They recommended considering aortic replacement for women who were indicated to aortic replacement, if the diameter of the ascending aorta exceeds 4.0cm or the indexed diameter is 2.4 cm/m^2. The diameter of the ascending aorta of our patient was 4.4 cm, and the indexed diameter was 3.0 cm/m^2. From this point of view, it was reasonable to subject this patient to an aortic replacement, even if the biological abnormalities of the QAV ascending aorta are not as well established as in the case of BAV ascending aortas.

For the reasons described above, we considered that it was adequate to replace the QAV ascending aorta of this patient.

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