Two rare cases of congenital aortic stenosis showing a discrepancy between preoperative imaging diagnosis, intraoperative findings, and histopathological diagnosis

Shiro Miura (MD MSc), Katsumi Inoue (MD PhD), Satoshi Yamada (MD PhD FJCC), Takehiro Yamashita (MD PhD), Kenji Ando (MD)

論文紹介

- 当院では心臓弁膜症に対する外科的治療においても道内有数の症例数を誇ります。
- 外科的弁置換術を行う症例では、弁劣化や弁不全の原因を術前の画像診断や術後の病理診断にて確認を行い、術後の管理や臨床的追跡に役立てています。
- 本論文は、臨床的に異なる経過を多と辿ることがある先天性二尖弁と一尖弁の大動脈弁狭窄症の患者様の術前診断が非常に難しく、術後の病理診断にて最終確定し、それを今後の治療方針に反映したという２症例報告です。当院循環器内科　三浦史郎医師、　山下武廣医師、北海道大学病院循環器内科　山田聡医師らとの共著で出版されました。

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Case Report

Two rare cases of congenital aortic stenosis showing a discrepancy between preoperative imaging diagnosis, intraoperative findings, and histopathological diagnosis

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ABSTRACT

Unicuspid aortic valve (UAV) is an extremely rare congenital heart valve abnormality while bicuspid valve (BAV) has been reported as one of the most common cardiac anomalies. With a UAV usually showing similar presentations to a BAV, such as aortic regurgitation or aortic stenosis (AS), it is challenging to differentiate them from each other in clinical settings. Despite some features shared between both valve disorders, there can be a clinical significance in distinguishing UAV from BAV for the management of patients with these heart anomalies. Herein, we describe two cases where patients with hemodynamically severe AS were diagnosed with BAV and UAV, respectively based on preoperative examinations and intraoperative findings, but subsequent pathological examinations confirmed the opposite diagnosis in both cases.

<Learning objective: Preoperative diagnosis of congenital aortic valve diseases can often be challenging. There remains a remarkable number of misleading cases. Thus, it is strongly recommended that an accurate diagnosis should be attempted at the earliest stages of congenital aortic valve disease. Additionally, both careful follow-ups using multiple imaging modalities and confirmations via pathological diagnosis for patients undergoing surgery, if they are first found to be at an advanced stage or remain undiagnosed preoperatively are important.>

Introduction

Unicuspid aortic valve (UAV) is a rare congenital heart anomaly with an estimated frequency of 0.02% among the adult population [1] and often can present as a form of significant aortic stenosis (AS) or aortic regurgitation (AR) in symptomatic relatively young subjects who sometimes require cardiac surgery. Bicuspid aortic valve (BAV), on the other hand, is one of the most common cardiac malformations with an estimated incidence of 0.9–2% [2], which shows similar clinical manifestations to UAVs, as related to valve dysfunction, and is often accompanied with abnormalities of the aorta (aneurysm, dilatation, and dissection) and other cardiac malformations [3].

Despite some features shared between both valve disorders, there can be a clinical importance in distinguishing UAV from BAV for the management of patients with these heart anomalies. Serial assessments using transthoracic echocardiography (TTE) have disclosed that valve dysfunctions progress more rapidly in patients with UAV than those with BAV [4] and that UAV patients are more likely to develop symptoms at an early age [1]. Regarding the anatomical aspects, Noly et al. [5] demonstrated that there are several distinct characteristics between them. The rate of aortic dilatation was significantly lower in UAV than in BAV cases, leading to a relatively low incidence of acute aortic events in UAV. In contrast, the aortic annulus was dilated (>25 mm) in most patients with UAV requiring surgery in 71%. Consequently, preoperative discrimination of the two is of significant importance in determining an appropriate surgical approach, whether it be

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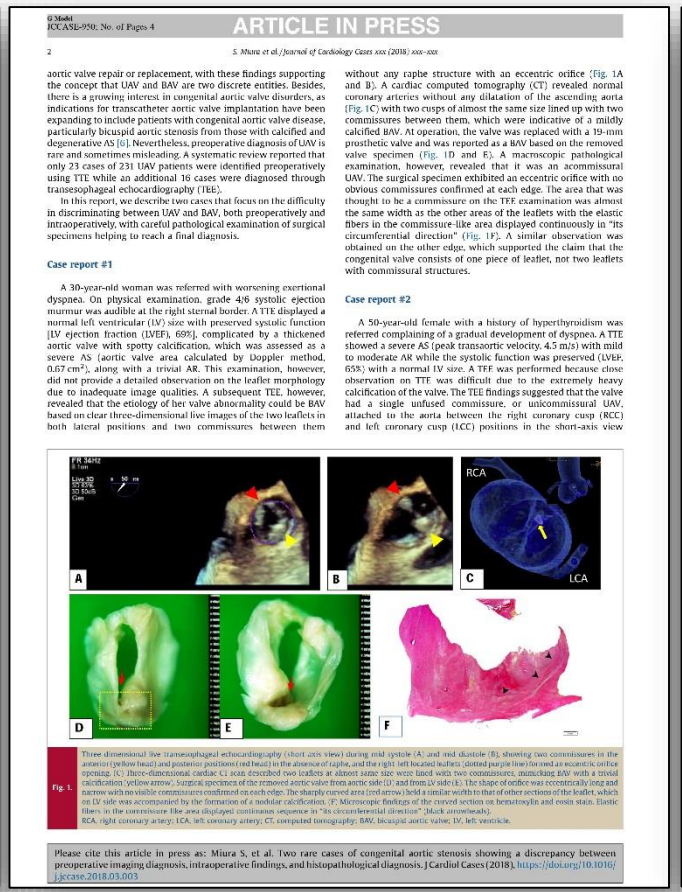

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aortic valve repair or replacement, with these findings supporting the concept that UAV and BAV are two discrete entities. Besides, there is a growing interest in congenital aortic valve disorders, as indications for transcatheter aortic valve implantation have been expanding to include patients with congenital aortic valve disease, particularly bicuspid aortic stenosis from those with calcified and degenerative AS [6]. Nevertheless, preoperative diagnosis of UAV is rare and sometimes misleading. A systematic review reported that only 23 cases of 231 UAV patients were identified preoperatively using TTE while an additional 16 cases were diagnosed through transesophageal echocardiography (TEE).

In this report, we describe two cases that focus on the difficulty in discriminating between UAV and BAV, both preoperatively and intraoperatively, with careful pathological examination of surgical specimens helping to reach a final diagnosis.

Case report #1

A 30-year-old woman was referred with worsening exertional dyspnea. On physical examination, grade 4/6 systolic ejection murmur was audible at the right sternal border. A TTE displayed a normal left ventricular (LV) size with preserved systolic function [LV ejection fraction (LVEF), 69%], complicated by a thickened aortic valve with sporty calcification, which was assessed as a severe AS (aortic valve area calculated by Doppler method, 0.67 cm^2), along with a trivial AR. This examination, however, did not provide a detailed observation on the leaflet morphology due to inadequate image qualities. A subsequent TEE, however, revealed that the etiology of her valve abnormality could be BAV based on clear three-dimensional live images of the two leaflets in both lateral positions and two commissures between them without any raphe structure with an eccentric orifice (Fig. 1A and B). A cardiac computed tomography (CT) revealed normal coronary arteries without any dilatation of the ascending aorta (Fig. 1C) with two cusps of almost the same size lined up with two commissures between them, which were indicative of a mildly calcified BAV. At operation, the valve was replaced with a 19-mm prosthetic valve and was reported as a BAV based on the removed valve specimen (Fig. 1D and E). A macroscopic pathological examination, however, revealed that it was an acommissural UAV. The surgical specimen exhibited an eccentric orifice with no obvious commissures confirmed at each edge. The area that was thought to be a commissure on the TEE examination was almost the same width as the other areas of the leaflets with the elastic fibers in the commissure-like area displayed continuously in "its circumferential direction" (Fig. 1F). A similar observation was obtained on the other edge, which supported the claim that the congenital valve consists of one piece of leaflet, not two leaflets with commissural structures.

Case report #2

A 50-year-old female with a history of hyperthyroidism was referred complaining of a gradual development of dyspnea. A TTE showed a severe AS (peak transaortic velocity, 4.5 m/s) with mild to moderate AR while the systolic function was preserved (LVEF, 65%) with a normal LV size. A TEE was performed because close observation on TTE was difficult due to the extremely heavy calcification of the valve. The TEE findings suggested that the valve had a single unfused commissure, or unicommissural UAV, attached to the aorta between the right coronary cusp (RCC) and left coronary cusp (LCC) positions in the short-axis view

Fig. 1. Three-dimensional live transesophageal echocardiography (short axis view) during mid-systole (A) and mid-diastole (B), showing two commissures in the anterior (yellow head) and posterior positions (red head) in the absence of raphe, and the right–left located leaflets (dotted purple line) formed an eccentric orifice opening. (C) Three-dimensional cardiac CT scan described two leaflets at almost same size were lined with two commissures, mimicking BAV with a trivial calcification (yellow arrow). Surgical specimen of the removed aortic valve from aortic side (D) and from LV side (E). The shape of orifice was eccentrically long and narrow with no visible commissures confirmed on each edge. The sharply curved area (red arrow) held a similar width to that of other sections of the leaflet, which on LV side was accompanied by the formation of a nodular calcification. (F) Microscopic findings of the curved section on hematoxylin and eosin stain. Elastic fibers in the commissure like area displayed continuous sequence in "its circumferential direction" (black arrowheads).
RCA, right coronary artery; LCA, left coronary artery; CT, computed tomography; BAV, bicuspid aortic valve; LV, left ventricle.

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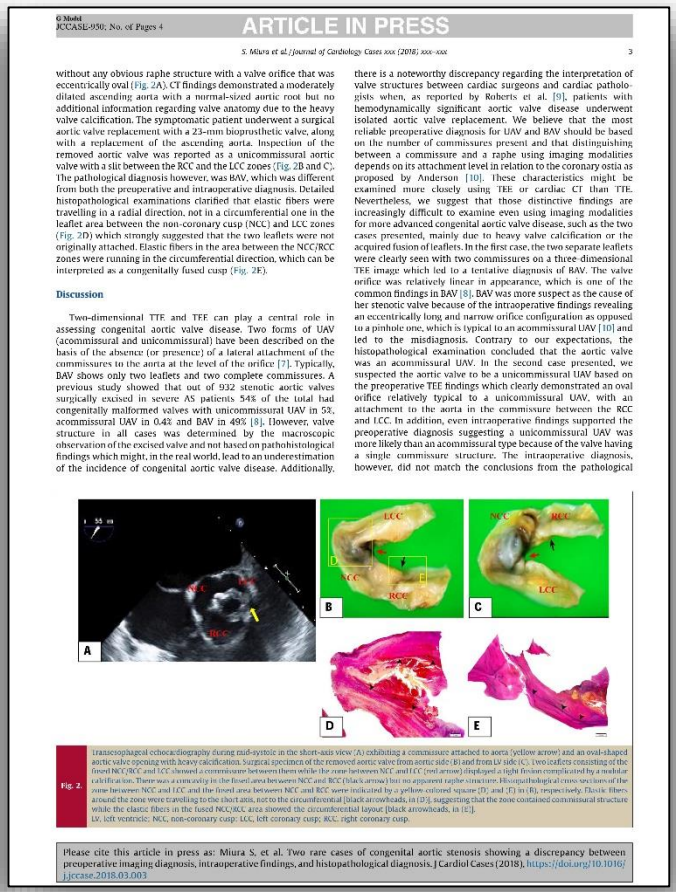

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without any obvious raphe structure with a valve orifice that was eccentrically oval (Fig. 2A). CT findings demonstrated a moderately dilated ascending aorta with a normal-sized aortic root but no additional information regarding valve anatomy due to the heavy valve calcification. The symptomatic patient underwent a surgical aortic valve replacement with a 23-mm bioprosthetic valve, along with a replacement of the ascending aorta. Inspection of the removed aortic valve was reported as a unicommissural aortic valve with a slit between the RCC and the LCC zones (Fig. 2B and C). The pathological diagnosis however, was BAV, which was different from both the preoperative and intraoperative diagnosis. Detailed histopathological examinations clarified that elastic fibers were travelling in a radial direction, not in a circumferential one in the leaflet area between the non-coronary cusp (NCC) and LCC zones (Fig. 2D) which strongly suggested that the two leaflets were not originally attached. Elastic fibers in the area between the NCC/RCC zones were running in the circumferential direction, which can be interpreted as a congenitally fused cusp (Fig. 2E).

Discussion

Two-dimensional TTE and TEE can play a central role in assessing congenital aortic valve disease. Two forms of UAV (acommissural and unicommissural) have been described on the basis of the absence (or presence) of a lateral attachment of the commissures to the aorta at the level of the orifice [7]. Typically, BAV shows only two leaflets and two complete commissures. A previous study showed that out of 932 stenotic aortic valves surgically excised in severe AS patients 54% of the total had congenitally malformed valves with unicommissural UAV in 5%, acommissural UAV in 0.4% and BAV in 49% [8]. However, valve structure in all cases was determined by the macroscopic observation of the excised valve and not based on pathohistological findings which might, in the real world, lead to an underestimation of the incidence of congenital aortic valve disease. Additionally, there is a noteworthy discrepancy regarding the interpretation of valve structures between cardiac surgeons and cardiac pathologists when, as reported by Roberts et al. [9], patients with hemodynamically significant aortic valve disease underwent isolated aortic valve replacement. We believe that the most reliable preoperative diagnosis for UAV and BAV should be based on the number of commissures present and that distinguishing between a commissure and a raphe using imaging modalities depends on its attachment level in relation to the coronary ostia as proposed by Anderson [10]. These characteristics might be examined more closely using TEE or cardiac CT than TTE. Nevertheless, we suggest that those distinctive findings are increasingly difficult to examine even using imaging modalities for more advanced congenital aortic valve disease, such as the two cases presented, mainly due to heavy valve calcification or the acquired fusion of leaflets. In the first case, the two separate leaflets were clearly seen with two commissures on a three-dimensional TEE image which led to a tentative diagnosis of BAV. The valve orifice was relatively linear in appearance, which is one of the common findings in BAV [8]. BAV was more suspect as the cause of her stenotic valve because of the intraoperative findings revealing an eccentrically long and narrow orifice configuration as opposed to a pinhole one, which is typical to an acommissural UAV [10] and led to the misdiagnosis. Contrary to our expectations, the histopathological examination concluded that the aortic valve was an acommissural UAV. In the second case presented, we suspected the aortic valve to be a unicommissural UAV based on the preoperative TEE findings which clearly demonstrated an oval orifice relatively typical to a unicommissural UAV, with an attachment to the aorta in the commissure between the RCC and LCC. In addition, even intraoperative findings supported the preoperative diagnosis suggesting a unicommissural UAV was more likely than an acommissural type because of the valve having a single commissure structure. The intraoperative diagnosis, however, did not match the conclusions from the pathological

Fig. 2. Transesophageal echocardiography during end-systole in the short-axis view (A) exhibiting a commissure attached to aorta (yellow arrow) and an oval-shaped aortic valve opening with heavy calcification. Surgical specimen of the removed aortic valve from aortic side (B) and from LV side (C), two leaflets consisting of the fused RCC/RCC and LCC showed a commissure between them while the zone between NCC and LCC (red arrow) displayed a tight fusion complicated by a nodular calcification. There was a concavity in the fused area between NCC and RCC (black arrow) but no apparent raphe structure. Histopathological cross sections of the zone between NCC and LCC and the fused area between NCC and RCC were indicated by a yellow-colored square (D) and (E) in (B), respectively. Elastic fibers around the zone were travelling to the short axis, not to the circumferential (black arrowheads, in (D)), suggesting that the zone contained commissural structure while the elastic fibers in the fused NCC/RCC area showed the circumferential layout (black arrowheads, in (E)).
LV, left ventricle; NCC, non-coronary cusp; LCC, left coronary cusp; RCC, right coronary cusp.

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