CASE REPORT

Congenital quadricuspid aortic valve anomaly associated with hypertrophic non-obstructive cardiomyopathy: a case report and review of the literature

Uwe Janssens, Heinrich G Klues, Peter Hanrath

Abstract

A case is reported of a 38 year old woman without known cardiac congenital abnormality but a history of well controlled arterial hypertension who was admitted to hospital after successful resuscitation at home following cardiac arrest. There was no evidence of myocardial infarction on 12-lead electrocardiogram but there were signs of left ventricular hypertrophy. Transoesophageal echocardiography revealed a rare quadricuspid aortic valve (QAV) malformation with concomitant mild aortic regurgitation. The left ventricle showed a massive concentric hypertrophy without obstruction. The patient was eventually transferred in a persistent vegetative state to a home care facility. A review of the literature revealed 70 cases of QAV diagnosed by transthoracic or transoesophageal echocardiography (26 cases), at necropsy (25), during surgery (15), and during angiography (4). The present case is the first report of QAV associated with non-obstructive hypertrophic cardiomyopathy.

(*Heart* 1997;78:83–87)

Keywords: heart defects; congenital anomaly; echocardiography; cardiomyopathy; aortic valve abnormalities

Congenital abnormalities affecting the quadricuspid aortic valve (QAV) are very rare, far less common than unicuspid or bicuspid valve congenital abnormalities which have received considerable attention in recent years.[1] Most cases of QAV have been discovered as an incidental finding at necropsy, during aortic valve replacement or aortic angiography.[2–4] Cross sectional transthoracic or transoesophageal echocardiography are the preferred methods to detect this malformation.[2 5–16]

Medical Clinic I, University of Aachen, Aachen, Germany
U Janssens
H G Klues
P Hanrath

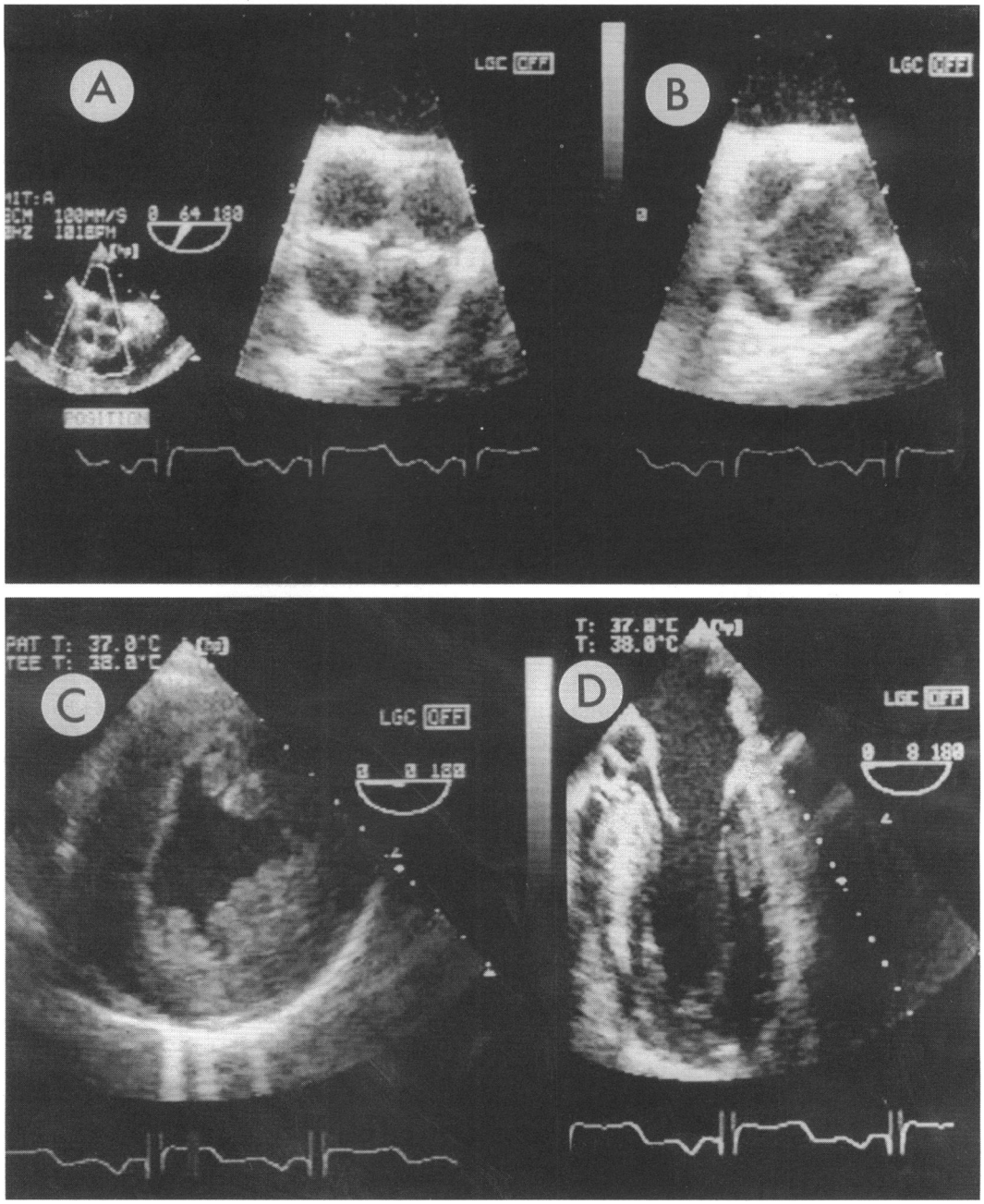
Correspondence to:
Dr.med. U Janssens, Medical Clinic I, University of Aachen, Pauwelsstraße 30, D-52057 Aachen, Germany.

Accepted for publication 29 January 1997

Case report

A 38 year old woman (155 cm, 80 kg) with a 10 year history of arterial hypertension well controlled with β blockers and clonidine suffered sudden syncope, apnoea and documented bradycardia followed by cardiac arrest. She was successfully resuscitated at home after a latency period of 10 minutes. On admission the patient was deeply comatose. She was mechanically ventilated but intravenous analgesics and sedatives were not administered. The patient had a sinus tachycardia (120 beats/min) and blood pressure was 200/120 mm Hg. A 12-lead electrocardiogram showed no signs of acute myocardial infarction, however, there were signs of left ventricular hypertrophy—a positive Sokolow-Lyon index (S in V1 and R in V5 4·4 mV) and negative T waves in leads V4–V6. There was no significant elevation of aspartate aminotransferase, lactic dehydrogenase, or creatinine kinase on admission or during later serial measurements. Cardiac output measured by thermodilution was within the normal range (5·6 l/min) as were pulmonary artery wedge pressure (10 mm Hg) and pulmonary-systemic vascular resistance (72 dyn.sec.cm^{-5}/1296 dyn.sec.cm^{-5}). Cranial computed tomography excluded cerebral haemorrhage, masses, and cerebral oedema. Fundoscopic examination showed grade 1 vascular changes according to the Keith-Wagener classification. Transthoracic and transoesophageal cross sectional echocardiography revealed massive concentric hypertrophy (figure) of a nondilated left ventricle without regional wall motion abnormalities. There was no systolic anterior motion (SAM) of the mitral valve. Septal thickness was 24 mm and free wall thickness 18 mm (septal to free wall ratio 1·3:1). Continuous wave and pulsed Doppler ultrasound excluded flow acceleration within the left ventricular outflow tract. Short axis view of the aortic valve demonstrated four thin cusps all of equal size with an "x-shaped" commissural pattern of the closed valve and normal full excursion of the leaflets to the margins of the aortic annulus (figure). The accessory cusp was situated between the right and left coronary cusp, the left coronary ostium was located in the middle of the left coronary cusp, and the right coronary ostium in the middle of the right coronary cusp. There was only mild central aortic insufficiency detected by colour flow mapping resulting from incomplete diastolic coaptation of the cusps.

Clinical course was determined by the development of a persistent vegetative state owing to the delayed resuscitation. The



Magnification of the transoesophageal short axis view of the aortic valve during diastole (A) and systole (B) demonstrating four equally sized aortic valve cusps. Transgastric short axis view (C) and slightly modified transoesophageal two chamber view (D) of a patient with hypertrophic non-obstructive cardiomyopathy and a septal thickness of 24 mm.

patient was transferred to a home care facility.

There was no history of hypertrophic cardiomyopathy or sudden cardiac death in the patient's family. Her father and one brother died from complications associated with myocardial infarction. A sister with two sons had no echocardiographic abnormalities.

Discussion

Normally, after septation of the embryological arterial trunk, three mesenchymal swellings develop into semilunar leaflets of the aortic and pulmonary trunk. However, in the setting of a QAV, the entire formation of the aortic root must deviate from normal with formation of sinuses, leaflets, and interleaflet triangles. The mechanism involved in this formation is not fully understood.[8] This congenital malformation has to be distinguished from pseudoquadricuspid aortic valves that results from bacterial endocarditis and other pathological processes such as rheumatic valve disease eroding through a cusp, thus leading to the appearance of a QAV. Pathologists and clinicians pay attention to semilunar valves with an abnormal number of cusps, especially bicuspid (2% of the general population)[17] and unicuspid valves because these malformations are frequently stenotic or incompetent and may require surgical treatment. Quadricuspid semilunar valves seem to be far less common and are reported to occur nine times more frequently in pulmonic valves than aortic valves.[18]

In 1923 Simonds reported five cases of native QAVs in 25 666 necropsies collected from the world literature—an incidence of 0·003%.[19] In another series of 6000 necropsies, two QAVs were found (0·008%).[1] A retrospective analysis of 60 446 echocardiograms revealed eight QAVs (0·013%).[6]

Our review of the international literature found 70 QAVs (table). Most of these were diagnosed most recently by transthoracic

Quadricuspid aortic valve: review of the literature

Reference, year of publication	*n*	*Diagnostic method*	*Functional status of QAV*	*Associated cardiac malformations*	*Age (years)*	*Sex*
Simonds,[19] 1923	5	Necropsy	Unknown Unknown	None (4) PDA (1)	Unknown	Unknown
Wyatt *et al*[27] 1948	1	Necropsy	AI	Displacement of left coronary orifice above the aortic ring	Unknown	Unknown
McRonald *et al*[33] 1966	1	Necropsy	AI	None	67	M
Robicsek *et al*[20] 1969	1	Surgery	AI	Displacement of left coronary orifice	35	F
Peretz *et al*[26] 1969	1	Aortography/ Surgery	AI	None	61	M
Hurwitz *et al*[1] 1973	2	Necropsy	AI (1) Normal (1)	None VSD	51 11	F F
Nalbantgil *et al*[34] 1975	1	Aortography/ Surgery	AI		44	F
Davia *et al*[18] 1977	7	Necropsy	AI (2) AI (1) Normal (4)	CAD None CAD	35–78 mean 59	7 M
Iglesias *et al*[30] 1981	1	Surgery	AI	Fibromuscular subaortic stenosis	42	M
Lanzillo *et al*[22] 1981	1	Surgery	AI	Displacement of right coronary orifice	44	M
Kurosawa *et al*[25] 1981	1	Necropsy	Normal	Isolation of origin of left coronary artery	16	F
Sievers *et al*[23] 1982	1	Surgery	AI	Unknown	44	M
Stassano *et al*[35] 1982	1	Surgery	AI	Unknown	Unknown	Unknown
Kosach *et al*[36] 1982	1	Surgery	AI	Unknown	Unknown	Unknown
Luisi *et al*[37] 1984	1	Surgery	AI	None	70	F
Chandrasekaran *et al*[9] 1984	2	Echo/ Aortography/ Surgery Echo/Necropsy	AI AI Normal	Fistula arising from sinus of accessory cusp communicating with right ventricle None	30 35	M F
Matsumoto *et al*[38] 1985	1	Surgery	AI	Unknown	57	M
Subramanian *et al*[39] 1985	1	Surgery	Unknown	Unknown	65	M
Coeurderoy *et al*[11] 1986	1	Echo	Normal	None	6	F
Amioka *et al*[14] 1986	1	Echo/ Aortography/ Surgery	AI	None	62	F
Chamsi-Pasha *et al*[5] 1988	2	Echo	Normal (1) Normal (1)	None CAD	59 40	M M
Matsukawa *et al*[2] 1988	1	Echo/ Aortography/ Surgery	AI (Endocarditis)	None	40	M
Kim *et al*[28] 1988	1	Necropsy	Unknown	Single coronary ostium	59	F
Fernicola *et al*[31] 1989	6	Necropsy	Normal (1) Normal (1) AI (1) Normal (3)	VSD Deficient posterior half of the anterior mitral leaflet; CAD CAD CAD	11–76 mean 47	3 M, 3 F
Matsui *et al*[3] 1989	1	Aortography/ Surgery	AI	None	59	F
Waller *et al*[40] 1990	1	Surgery	AI	Unknown	Unknown	Unknown
Feldman *et al*[6] 1990	8	Echo	AI (2) AI/AS (1) Unknown (5)	None None None	28–71 mean 46	3 M, 5 F
Koizumi *et al*[41] 1990	1	Surgery	AI	None	67	M
Mathison *et al*[21] 1990	2	Surgery (1) Echo/ Aortography/ Surgery	AI AI	None Displacement of right coronary orifice	66 46	F M
Fischler *et al*[42] 1990	1	Necropsy	Normal	PFO	Unknown	Unknown
Shioi *et al*[43] 1991	1	Surgery	AI	CAD	54	M
Barbosa *et al*[13] 1991	2	Echo	AI (2)	None	14 28	M F
Chah-Po *et al*[7] 1991	1	Echo/Surgery	AI	None	40	M
Lai *et al*[15] 1991	1	Echo	AI	None	40	M
Costa Martorell *et al*[16] 1992	1	Echo	Normal	None	Unknown	Unknown
Aoyagi *et al*[44] 1992	1	Surgery	AI	Unknown	62	M
Lim *et al*[10] 1992	1	Echo	Normal	Unknown	Unknown	Unknown
Cruz *et al*[12] 1993	1	Echo/Surgery	AI	None	45	M
Brouwer *et al*[8] 1993	2	Echo (1) Surgery (1)	Normal AI	None Left coronary artery rising right sinus coronarius	36 44	M F
Irisawa *et al*[45] 1993	1	Echo/Surgery	AI/MI	None	60	M
Suda *et al*[24] 1993	1	Echo/ Aortography/ Surgery	AI	Displacement of right coronary orifice	70	M
Shinkai *et al*[4] 1994	1	Aortography	AI	None	43	M

AI, aortic insufficiency; AS, aortic stenosis; CAD, coronary artery disease; F, female; M, male; PDA, patent ductus arteriosus; PFO, patent foramen ovale; QAV, quadricuspid aortic valve; VSD, ventricle septum defect.

or transoesophageal echocardiography (26 cases), followed by necropsy (25), surgery (15), and angiography (4).

The mean age when QAV was first diagnosed was 49 years (range 6–78). Thirty six (62%) of the patients were male and 28 (38%) were female. Hurwitz and Roberts also found quadricuspid pulmonic valves to be more common in men.[1]

A recent report described different anatomical variations according to the size of the individual aortic valve cusps: four unequal cusps, three equal cusps and one smaller cusp, and up to four equal cusps.[1] The cusps in our patient were all of equal size representing the less common distribution. In this case the accessory cusp was located between the right and left cusp. Transoesophageal echocardiography allowed imaging of the proximal portions of the left and right coronary artery. There was no displacement or obstruction of the right or left coronary ostium by accessory

cusp tissue as has been reported in some patients with QAV proved at surgery or necropsy.[8 20-24] One sudden cardiac death occurred in a 16 year old boy with QAV and complete isolation of the orifice of the left coronary artery by an adherent aortic valve cusp.[25]

Aortic regurgitation appears to be the most prevalent haemodynamic abnormality associated with QAV and occurred in 39 of 70 (56%) cases, whereas valvular stenosis was very rare. In 26 of the cases, aortic valve replacement was necessary because of severe valve incompetence. Only 18 QAVs had a normal functional status without significant regurgitation or stenosis. Aortic regurgitation seems to be more common in patients with an additional smaller cusp leading to unequal distribution of stress and abnormal leaflet coaptation that possibly results in progression of aortic regurgitation.[6] Therefore, these patients may require prophylaxis against subacute bacterial endocarditis, although in general the equally sized QAVs have no increased risk for infection. Infective fenestration of a valve cusp or fibrous valve thickening may also result in incomplete coaptation of the cusps thus leading to regurgitation.[26]

There are only a few reports concerning the association of QAV with other cardiac defects. Of these, anomalies of the coronary ostium and coronary arteries are the most frequent.[6 8 20-22 25 27 28] Apart from ventricular septal defects, patent ductus arteriosus, subaortic fibromuscular stenosis, and a malformation of the mitral valve can be associated with a QAV.[1 19 29-31]

To the best of our knowledge this is the first report of a QAV associated with non-obstructive hypertrophic cardiomyopathy. The patient had a history of arterial hypertension, used elsewhere as an exclusion criterion when making the diagnosis of idiopathic hypertrophic cardiomyopathy. Duration of hypertension was only 10 years and well controlled with β blockers and clonidine according to her family and her physician. These facts and the results of fundoscopy (grade 1) showed that there was no accelerated malignant form of hypertension. Our echocardiographic findings of massive left ventricular hypertrophy with asymmetric septal hypertrophy (septal to free wall ratio 1·3:1) cannot be explained solely by the patient's mild hypertension and has therefore to be regarded as a genuine disorder of the heart in terms of hypertrophic non-obstructive cardiomyopathy.

Karam *et al* investigated 39 patients with hypertrophic cardiomyopathy and hypertension and compared them with age and sex matched patients with cardiomyopathy alone. Their results indicate that hypertrophic cardiomyopathy with associated hypertension might be a disease of the elderly. The echocardiographic features of the patients with hypertension were indistinguishable from those with cardiomyopathy without hypertension. These findings suggest that hypertension may make hypertrophy worse, but that it is not the primary cause of the cardiomyopathy. Thus this condition should be better termed "hypertrophic cardiomyopathy with hypertension".[32]

This case report and the review of the literature demonstrate that the QAV is a very rare, congenital anomaly of the aortic valve with an incidence between 0·003% and 0·013%. It may be found incidentally in an asymptomatic patient but is most often found in patients with aortic regurgitation. In the past, QAV was recognised at surgery or necropsy but now transthoracic and transoesophageal echocardiography play a pivotal role in diagnosing this rare valve malformation. Cross sectional echocardiography, colour flow Doppler and particularly the transoesophageal approach can easily assess the morphological and functional status of such a valve.

1 Hurwitz LE, Roberts WC. Quadricuspid semilunar valve. *Am J Cardiol* 1973;**31**:623–6.
2 Matsukawa T, Yoshii S, Hashimoto R, Muto S, Suzuki S, Ueno A. Quadricuspid aortic valve perforation resulting from bacterial endocarditis—2-D echo- and angiographic diagnosis and its surgical treatment. *Jpn Circ J* 1988; **52**:437–40.
3 Matsui K, Kohno H, Kurisu K, Murakami S, Fukuyama T. Quadricuspid aortic valve—report of a case associated with severe aortic regurgitation and review of the literature. *Jpn J Surg* 1989;**19**:93–7.
4 Shinkai M, Okazaki T, Fujiwara H, Nasu M, Sono J, Okada Y, *et al*. An operative case of aortic regurgitation due to quadricuspid valve. *Kyobu Geka* 1994;**47**:311–14.
5 Chamsi-Pasha H, Barnes PC, Beton DC. Echocardiographic diagnosis of quadricuspid aortic valve. *Eur Heart J* 1988;**9**:1269–70.
6 Feldman BJ, Khanderia BK, Warnes CA, Seward JB, Taylor CL, Tajik AJ. Incidence, description and functional assessment of isolated quadricuspid aortic valves. *Am J Cardiol* 1990;**65**:937–8.
7 Chah-Po L, Koyanagi S, Sadoshima J, Takeshita A. Transesophageal echocardiographic findings of quadricuspid aortic valves. *Jpn Heart J* 1991;**32**:731–4.
8 Brouwer MHJ, de Graaf JJ, Ebels T. Congenital quadricuspid aortic valve. *Int J Cardiol* 1993;**38**:196–8.
9 Chandrasekaran K, Tajik AJ, Edwards WD, Seward JB. Two-dimensional echocardiographic diagnosis of quadricuspid aortic valve. *Am J Cardiol* 1984;**53**:1732–3.
10 Lim YT, Choo MH, Ling LH. Echocardiographic diagnosis of quadricuspid aortic valve. *Ann Acad Med Singapore* 1992;**21**:841–2.
11 Coeurderoy A, Biron Y, Laurent M, Almange C. Congenital quadricuspid aortic valve. Apropos of a case. Review of the literature. *Arch Mal Coeur Vaiss* 1986;**79**: 745–8.
12 Cruz LA, Castier MB, Ferro ME, Menezes CC, Albanesi Filho FM. Aortic insufficiency due to quadricuspid aortic valve. *Arq Bras Cardiol* 1993;**60**:103–5.
13 Barbosa MM, Motta MS. Quadricuspid aortic valve and aortic regurgitation diagnosed by Doppler echocardiography: report of two cases and review of the literature. *J Am Soc Echocardiogr* 1991;**4**:69–74.
14 Amioka H, Okamoto M, Matsumoto K, Yamagata T, Yokote Y, Sakura E, *et al*. Echo and Doppler cardiographic findings of isolated quadricuspid aortic valve: a case report and a review of the literature. *J Cardiogr* 1986;**16**:1003–11.
15 Lai CP, Koyanagi S, Sadoshima J, Takeshita A, Tokunaga K. Transesophageal echocardiographic findings of quadricuspid aortic valve. *Jpn Heart J* 1991;**32**:731–4.
16 Costa Martorell J, Rivas Puy I, Peraire JJ, Bardaji A, Ridao C, Richart C. Quadricuspid aortic valve. Presentation of a new case and review of the literature. *Rev Esp Cardiol* 1992;**45**:608–10.
17 Roberts WC. The congenitally bicuspid aortic valve. A study of 85 autopsy cases. *Am J Cardiol* 1970;**26**:72–83.
18 Davia JE, Fenoglio JJ, DeCastro CM, McAllister HA, Cheitlin MD. Quadricuspid semilunar valves. *Chest* 1977;**72**:186–9.
19 Simonds JP. Congenital malformations of the aortic and pulmonary valves. *Am J Med Sci* 1923;**166**:584–95.
20 Robicsek F, Sanger PW, Daugherty HK, Montgomery CC. Congenital quadricuspid aortic valve with displacement of the left coronary orifice. *Am J Cardiol* 1969;**23**: 288–90.
21 Mathison M, Furuse A, Kotsuda H, Tanaka O, Chikada M. Quadricuspid aortic valve: case reports. *Kyobu Geka* 1990;**43**:383–8.
22 Lanzillo G, Breccia PA, Intonti F. Congenital quadricuspid aortic valve with displacement of the right coronary orifice. *Scand J Thorac Cardiovasc Surg* 1981;**15**:149–51.
23 Sievers HH, Regensburger D, Bernhard A. Quadricuspid aortic valve with significant insufficiency. *Thorac Cardiovasc Surg* 1982;**30**:44–5.
24 Suda H, Rikitake K, Furukawa K, Shiraishi R, Kurashige Y, Mori E, Itoh T. Quadricuspid aortic valve: a case

report and the review of the literature. *Kyobu Geka* 1993; **46**:283–6.
25 Kurosawa H, Wagenaar SS, Becker AE. Sudden death in a youth. A case of quadricuspid aortic valve with isolation of origin of left coronary artery. *Br Heart J* 1981;**46**: 211–15.
26 Peretz DI, Changfoot GH, Gourlay RH. Four-cusped aortic valve with significant hemodynamic abnormality. *Am J Cardiol* 1969;**23**:291–3.
27 Wyatt JP, Goldenberg H. Supernumeracy aortic cusps with multiple fenestrations and with displacement of the left coronary orifice. *Arch Pathol* 1948;**45**:784.
28 Kim H-S, McBride RA, Titus JL. Quadricuspid aortic valve and single coronary ostium. *Arch Pathol Lab Med* 1988;**112**:842–4.
29 Feizi ÖF, Farrer-Brown G, Emanuel R. Familial study of hypertrophic cardiomyopathy and congenital aortic valve disease. *Am J Cardiol* 1978;**41**:956–64.
30 Iglesias A, Oliver J, Munoz JE, Nunez L. Quadricuspid aortic valve associated with fibromuscular subaortic stenosis and aortic regurgitation treated by conservative surgery. *Chest* 1981;**80**:327–8.
31 Fernicola DJ, Mann JM, Roberts WC. Congenitally quadricuspid aortic valve: analysis of six necropsy patients. *Am J Cardiol* 1989;**63**:136–8.
32 Karam R, Lever HM, Healey BP. Hypertensive hypertrophic cardiomyopathy or hypertrophic cardiomyopathy with hypertension? A study of 78 patients. *J Am Coll Cardiol* 1989;**13**:580–4.
33 McRonald RE, Dean DC. Congenital quadricuspid aortic valve. *Am J Cardiol* 1966;**18**:761–3.
34 Nalbantgil I, Cagatay G. Quadricuspid aortic valve [letter]. *Chest* 1975;**67**:623–4.
35 Stassano P, Iorio D, Di Lello F, Tecchia LB, Spampinato N. Aortic insufficiency due to quadricuspid valve. *Minerva Cardioangiol* 1982;**30**:7–9.
36 Kosach GA, Evzhanov A, Serbin VI, Zubkova GA, Tadzhibaeva ZA. Quadricuspid aortic valve. *Kardiologiia* 1982;**22**:113–14.
37 Luisi VS, Pasque A, Verunelli F, Aliboni M, Urbano U, Reginato E. Quadricuspid aortic valve. *J Cardiovasc Surg Torino* 1984;**25**:252–4.
38 Matsumoto M, Miki S, Kusuhara K, Ueda Y, Ohkita Y, Tahata T, Komeda M. Quadricuspid aortic valve associated with severe aortic regurgitation. *Jpn Circ J* 1985;**49**:190–1.
39 Subramanian R, Olson LJ, Edwards WD. Surgical pathology of combined aortic stenosis and insufficiency: a study of 213 cases. *Mayo Clin Proc* 1985;**60**:247–54.
40 Waller BF, Taliercio CP, Dickos DK, Howard J, Adlam JH, Jolly W. Rare or unusual causes of chronic, isolated, pure aortic regurgitation. *Clin Cardiol* 1990;**13**:577–81.
41 Koizumi S, Arai S, Kato T. A case of quadricuspid aortic valve with aortic regurgitation. *Kyobu Geka* 1990;**43**: 505–8.
42 Fischler D, Fitzmaurice M, Ratliff NB. Quadricuspid aortic valve. *Am J Cardiovasc Pathol* 1990;**3**:91–4.
43 Shioi K, Nagata Y, Kato S, Kato R, Tsuchioka H. A case of quadricuspid aortic valve associated with coronary arterial legion. *Nippon Kyobu Geka Gakkai Zasshi* 1991;**39**: 1072–6.
44 Aoyagi S, Kawara T, Yasunaga H, Kosuga K, Oishi K. Congenital quadricuspid aortic valve associated with aortic regurgitation. *Thorac Cardiovasc Surg* 1992;**40**:225–6.
45 Irisawa T, Yoshiya K, Yokosawa T, Iwamatsu T, Arai K, Aoki T. A case of quadricuspid aortic valve associated with mitral regurgitation. *Kyobu Geka* 1993;**46**:618–21.

IMAGES IN CARDIOLOGY

Non-invasive detection of quadricuspid aortic valve

Transthoracic echocardiography of a 66 year old Japanese woman with a history of cardiac murmur from early childhood showed large regurgitant blood flow from the aortic valve into the left ventricle that continued until the end of the diastolic phase.

Cine magnetic resonance imaging (MRI) revealed unexpected results: the aortic valve was quadricuspid (normal sized right cusp, slightly smaller left cusp, and half sized two non-coronary cusps without enlargement of annulus). The images of the end diastolic phase (left panel) and the mid-systolic phase (right panel) showed that these four cusps could not close completely even at the end of the diastolic phase resulting in the formation of a "regurgitant window" (approximately 8 × 8 mm). MRI also showed that her pulmonary valve was tricuspid. This non-invasive examination clearly demonstrated both the presence of a quadricuspid aortic valve and the relation between structure and function of this rare aortic valve anomaly.

KOUJI KAJINAMI
NOBORU TAKEKOSHI
HIROSHI MABUCHI