

Quadricuspid Aortic Valve, Single Coronary Artery, Solitary Kidney and Oblique Facial Cleft. A Unique Constellation of Congenital Abnormalities: Case Report and Review of the Literature

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Abstract

Quadricuspid aortic valve (QAV) is a rare congenital anomaly which is associated with coronary artery anomalies in 10% of the patients. The association of QAV with single coronary artery (SCA) is very rare has been reported only in one case previously. We report the case of a 30-year-old male patient with a unique constellation of congenital anomalies including QAV, SCA, solitary kidney and Tessier type 3 oblique facial cleft with cleft palate. To our knowledge, this unique combination has never been described previously. We describe his case and review the topic of QAV and its reported cardiac and systemic associations.

Keywords: Congenital abnormalities; Aortic valve; Quinticuspid; Coronary artery

Case Report

A 30-year-old male patient was admitted to the hospital for correction of right nostril deformity. He had been in good health apart from a history of solitary kidney, Tessier type 3 oblique facial cleft with a cleft palate that has been surgically corrected 11 years previously and right eye blindness. During preoperative evaluation, a murmur was detected, and he was referred for cardiac assessment. He denied having chest pain, shortness of breath or lower limb swelling. He was never diagnosed to have a cardiac illness, and there was no history suggestive of rheumatic fever. There was no known family history of congenital heart disease. He was not on medications.

Physical examination revealed a blood pressure of 130/70 mmHg. The pulse rate was regular at 78 beats per minute. Peripheral signs of severe aortic regurgitation were present. The jugular venous pressure was normal. An early diastolic murmur was heard along the left sternal border. The chest was clear, and there was no peripheral edema.

Transthoracic echocardiography (TTE) detected severe aortic regurgitation, severely dilated left ventricle and preserved ejection

fraction. A transesophageal echocardiography (TEE) revealed that the aortic valve was quadricuspid with thickened non-coapting cusps; a single coronary artery (SCA) was noted originating from the "right coronary cusp" and assuming a retroaortic course (Figure 1). There was mild dilatation of the ascending aorta.

A coronary computed tomography angiography was requested for further assessment of the coronary artery course. This confirmed the TEE findings. The left main coronary artery arose originating from the SCA just after its takeoff and coursed retroaortic to give the left anterior descending artery, diagonals as well as the circumflex artery. The ascending aorta was mildly dilated and the left ventricle was severely dilated (Figure 2). At the time of assessment, the patient was asymptomatic and had no echocardiographic criteria for surgical correction. The surgery for the nostril deformity was deferred. He was discharged and was given a follow-up appointment with cardiology.

The ascending aorta was mildly dilated and the left ventricle was severely dilated (Figure 2). At the time of assessment, the patient was asymptomatic and had no echocardiographic criteria for surgical correction. The surgery for the nostril deformity was deferred. He was discharged and was given a follow-up appointment with cardiology.

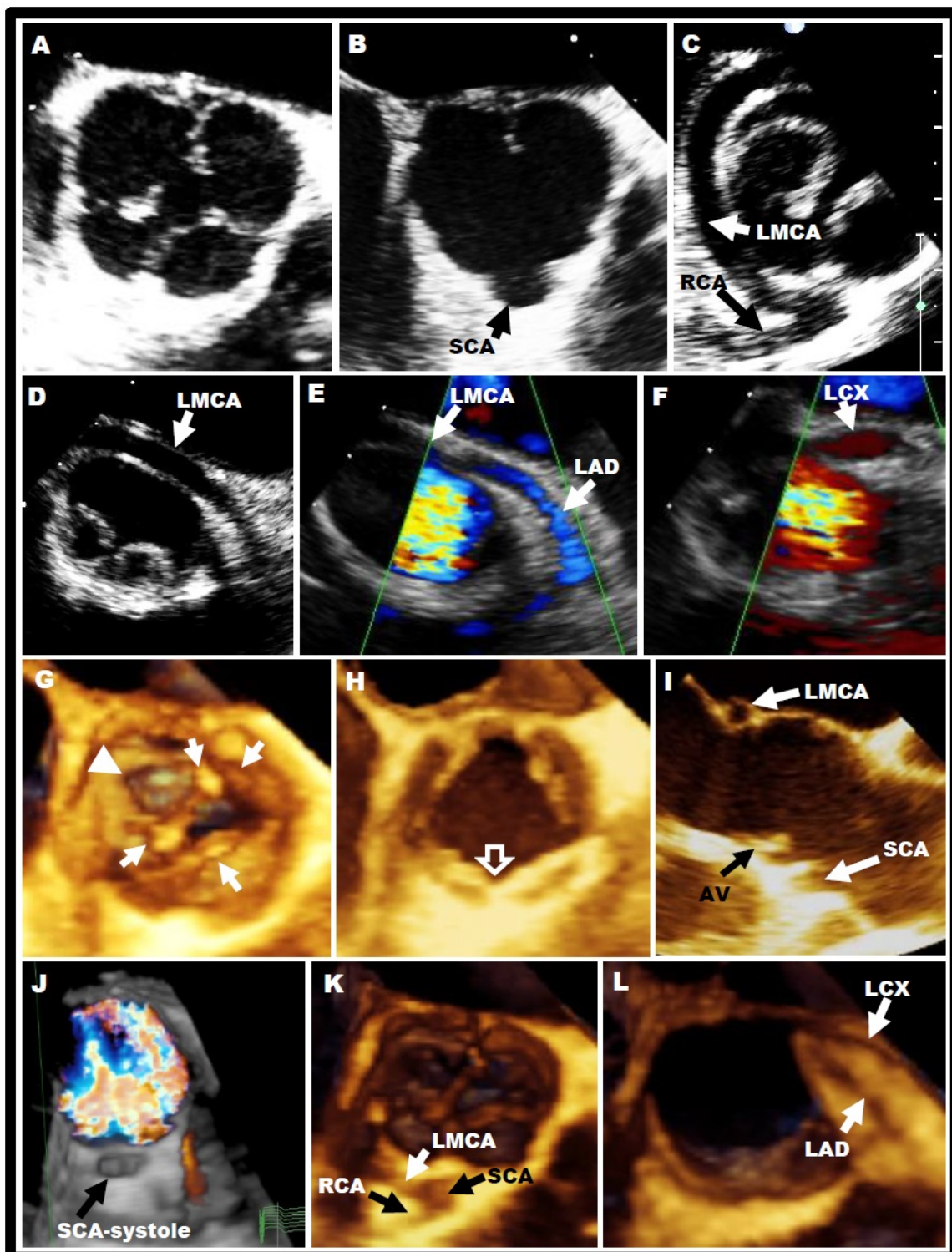


Figure 1: Echocardiographic findings. 2D-TEE. (A) Short axis of the QAV. (B) The SCA is seen originating from the “right coronary sinus” giving rise to the RCA and LMCA (C) before dividing into LAD and LCX arteries (E and F respectively). 3D-TEE. (G) corpus arantii (arrows) on the 4 valve leaflets, a leaflet fenestration (arrow head) and (H) short raphe (open arrow) are noted. (I) 3D reformat image demonstrating the high takeoff of the SCA (just above the sinutubular junction). A cross section of the LMCA is also noted. (J) 3D color image, showing the ostium of the SCA during systole. (K) Branching of the LMCA into LAD and LCX (L). 2D-2-dimensional; 3D-3 dimensional; SCA- single coronary artery; TEE-transesophageal echocardiography; LAD-left anterior descending; LCX-circumflex artery; LMCA-left main coronary artery; QAV-quadricuspid aortic valve; RCA-right coronary artery.

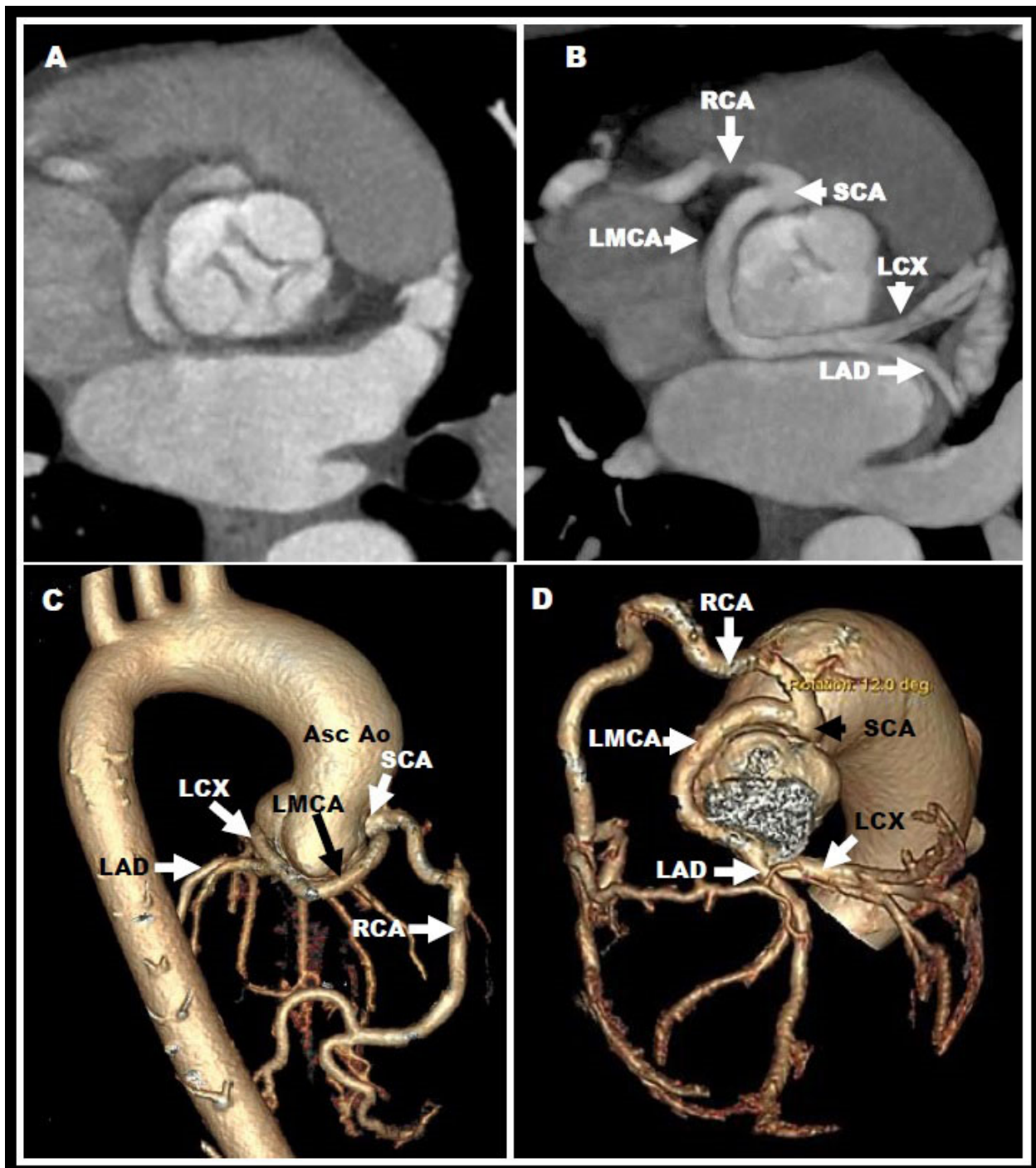


Figure 2: Computed tomographic angiography (CTA) images of the aortic valve and SCA. (A) Short axis view of the quadricuspid aortic valve. (B) Multi-planner reconstruction of coronary CTA with contrast showing the single coronary artery (SCA) arising from the right coronary cusp and its main branches. The left main coronary artery (LMCA) arises from the single coronary just after its takeoff from the right coronary cusp and taking a retro-aortic course. (C) and (D) rendered 3D formatted images showing the dilated ascending aorta (Asc Ao) and the origin and course of the SCA. LAD= left anterior descending artery; LCX= left circumflex artery; RCA= right coronary artery.

Discussion

We thus describe a rare case of multiple congenital abnormalities including a quadricuspid aortic valve (QAV), single coronary artery, solitary kidney and Tessier type 3 oblique facial cleft with cleft palate. To our knowledge, this constellation has never been described before. The combination of quadricuspid aortic valve and single coronary artery has been described before only in one case [1].

The quadricuspid aortic valve

In congenital aortic anomalies, variable numbers of the aortic valve leaflets have been reported including the two leaflet bicuspid aortic valve (BAV) which is identified in 0.9%- 1.36% of the population [2], the unicuspid aortic valve which has a prevalence of 0.02% [3], the rare QAV (discussed below), and the very rare quinticuspid (pentacuspid) valve of which only 8 cases have been reported to date [4-6].

QAV has an estimated incidence of 0.008% to 0.033% in autopsy and 0.043% in echocardiography studies [7]. A recent review identified 271 cases reported in the medical literature and showed a slight male predominance, with a male to female ratio of 1.55:1[8]. The prevalence of QAVs is less than that of quadricuspid pulmonic valves which are 5 times more common [9].

Two major theories are proposed to explain the etiology of the QAV; abnormal septation of one of the three endocardial cushions that give rise to the normal aortic cusps or abnormal septation of the truncus arteriosus (cardiac outflow tract)[10]. The first mechanism has been demonstrated in an animal model where the process starts at a very early stage of valvulogenesis, namely, when the conotruncal ridges begin to fuse at the distal portion of the embryonic cardiac outflow tract [11]. The other theory implicates aberrant fusion of the aortopulmonary septum or abnormal mesenchymal proliferation in the common trunk leading to abnormal cusp formation. Since the development of the aortic valve leaflets occurs just after the development of the coronary artery origins from the sinuses of Valsalva, it has been suggested that a single developmental abnormality might affect them both [12].

Reported cardiac and systemic associations with QAVs

Cardiac associations: QAVs commonly occur in isolation, although concomitant cardiac lesions coexist in 18% of the cases [13]. As the aortic valve normally forms from the embryonic truncus arteriosus, abnormalities in this area may lead to the development of a quadricuspid aortic valve as well as other congenital cardiac defects involving the coronary arteries, the left ventricular outflow tract, the pulmonary valve or the inter-atrial septum [14]. A host of congenital cardiac anomalies has been reported in association with QAV which include, ventricular or atrial septal defect (VSD, ASD) [15,16], pulmonary valve stenosis, sub-aortic fibromuscular stenosis [17], supra-valvular stenosis with left coronary atresia [12], dilatation of the ascending aorta (rarely in contrast to BAV) [8], patent ductus arteriosus [18], tetralogy of Fallot [19,20] with pulmonary atresia [20], hypertrophic obstructive cardiomyopathy [21], aneurysm of Valsalva sinus [22,23] descending aorta-to-pulmonary artery fistula [24] mitral valve prolapse [25], persistent left superior vena cava, right ventricular non-compaction [26] and partial pulmonary venous return anomaly (with ASD) [26].

Coronary artery anomalies, as a group, are reported in 10% of QAV cases [13]. While in the majority of patients with QAV, the ostia of the

coronary arteries are in the normal anatomical positions relative to the aortic root, the position of the coronary artery ostia relative to the aortic sinuses of Valsalva will naturally vary from that in the trileaflet valve [8]. Reported coronary artery anomalies include anomalous position of one of the coronary ostia, single coronary ostium [27], coronary-pulmonary artery fistula [24,28] and giant coronary artery aneurysm [28]. The association of QAV and single coronary ostium is very rare and has only been reported in one case before [1]. This association is of importance as there has been a report of sudden cardiac death due to a dome-like occlusion of the left main coronary ostium by the accessory cusp [29] and acute myocardial infarction in another patient from partially adhered small aortic cusp to the orifice of the left main coronary artery [30].

Systemic associations: The association of kidney anomalies with QAV is extremely rare. Although cardiac anomalies occur in 15%-30% of patients with solitary kidney and in some patients, more than one cardiac abnormality can be found, to our knowledge, the association of solitary kidney and QAV has only been reported in one case previously. The patient had a heterozygous deletion of CYP21A2 and tenascin XB and was also reported to have congenital adrenal hyperplasia, bicornuate uterus, hyperextensible joints and bifid uvula. The coronary artery anatomy of the patient is unknown [31]. In another patient QAV was associated with right double kidney, double renal pelvis, double proximal ureter and paroxysmal supraventricular tachycardia [32].

The association of QAV and nasal deformities has been described in a Thai family with upper limb anomalies, short stature, and frontal bossing in a dominantly inherited malformation syndrome. All patients in this family had hypoplasia of the shoulder girdle resembling that observed in Holt-Oram syndrome, however, mutation of the TBX5 gene, a disease causing gene of Holt-Oram syndrome, could not be demonstrated, and a genetic association was not identified [33].

QAV has also been associated with Ehlers-Danlos syndrome in 16-year-old patient in association with neurological abnormalities (epilepsy, agenesis of the corpus callosum) The patient's family had an autosomal dominant inherited disorder of connective tissue also affecting the father and the brother, diagnosed as EDS type II [34]; and has been reported in a patient with Turner syndrome [35]. QAV has been reported in identical twins [36].

The unique features present in this case may be attributed to genetic or environmental factors or both [37]. Both renal and aortic valve development and facial cleft formation occur during the fifth-sixth week of gestation [38,39]. It is likely that a teratogenic factor genetic or environmental during this period contributes to the observed abnormalities. It is of interest that many of the cardiac anomalies reported in association with solitary kidney [40] including VSD, ASD, pulmonary valvular stenosis, patent ductus arteriosus are also reported in association with QAV [41].

Epidemiologic studies suggest that genetic factors are the predominant cause of congenital heart disease (CHD) although environmental exposures are also relevant. It is well known that chromosomal defects and single-gene disorders can cause CHD, often in the context of a multisystem disease, but known genetic causes of CHD account for less than 20% of the cases [37]. Extra-cardiac malformations including defects in intra-abdominal organs and/or associated with genetic syndromes are observed from 7 to 50% of the patients with CHD [42].

Orofacial clefts have been associated with CHD [38], but the association with QAV and coronary anomalies to our knowledge has not been reported previously. Clefts have a complex etiology and likely result from an interaction between environmental and genetic factors as well [43]. Although the etiology of oblique facial clefts is commonly attributed to failed fusion of the mesoderm during embryonic facial processes, not all clefts can be explained by this theory. After the sixth week of gestation, the human face is fully formed; it has been suggested that amniotic bands formed at this period could only result in cleft formation by tethering or disrupting the fetal tissues. Amniotic bands may be part of the amnion rupture syndrome which together with craniofacial clefts, leads to visceral or extremity defects [38].

Conclusions

We describe for the first time a unique constellation of congenital anomalies involving the aortic valve, coronary arteries, kidney and face. The unique systemic congenital malformations observed in our patient may represent a new syndrome. Physicians should be aware of such associations, particularly the cardiac anomalies. The congenital coronary artery anomaly reported in this case is of major clinical significance due to its association with myocardial ischemia and sudden death. Extra-cardiac abnormalities are common in patients with CHD and should alert physicians to search for potential cardiac involvement. Early recognition is paramount to allow for closer patient follow-up and early intervention to prevent grave complications.

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