Congenital bicuspid aortic valve in an English bulldog

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Abstract
A bicuspid aortic valve (BAV) demonstrating moderate valvular stenosis and mild insufficiency was identified in an asymptomatic 1-year-old male cryptorchid English bulldog by transthoracic and transesophageal echocardiography. The BAV was most consistent with type 3 morphology, based upon human classification. Pulmonary valve dysplasia with mild pulmonary stenosis and a suspected persistent left cranial vena cava were also identified. Although BAV is the most common congenital cardiac malformation in humans, it is rare in the dog.

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A 1-year-old, intact, male English bulldog weighing 20.4 kg was referred to The Ohio State University Veterinary Medical Center for evaluation of a heart murmur prior to undergoing general anesthesia for elective castration. The heart murmur was first ausculted when the dog was 7 months of age. The dog was asymptomatic for heart disease at the time of presentation and was not receiving any medications. Physical examination revealed a grade II/VI left basilar systolic murmur, stertorous inspiratory sounds, malodorous facial fold dermatitis and only one descended testicle.
A transthoracic two-dimensional (2D) and Doppler echocardiographic study\(^a\) was performed using a 4 MHz phased-array transducer\(^b\) (Video 1). Sedation with acepromazine (0.025 mg/kg IM) and butorphanol (0.2 mg/kg IM) was administered 1 h prior to the echocardiographic study. Two-dimensional images obtained from the right parasternal short axis basilar view revealed a bicuspid aortic valve (BAV) with both aortic cusps of approximately equal size (Fig. 1A). When evaluated using a human classification scheme,\(^1\) the BAV of this dog was most consistent with a type 3 BAV (fusion of left and non-coronary cusps) with absent raphe (Fig. 2), though it was difficult to be certain by echocardiographic evaluation alone. Right parasternal long axis views of the left ventricular outflow tract demonstrated eccentric closure of the aortic valve (Fig. 1B), while color flow Doppler illustrated turbulent blood flow in the ascending aorta and subjectively mild eccentric aortic valve insufficiency (Fig. 1C) typical of BAV in humans.\(^2\) Spectral Doppler analysis from the subcostal view demonstrated moderate valvular aortic stenosis with a peak systolic velocity of 4 m/s, corresponding to an instantaneous transaortic pressure gradient of 64 mmHg (Fig. 1D). Left heart chamber size and wall thickness were normal when compared to published allometric weight-based normal reference ranges.\(^3\) Although common in humans with BAV,\(^2,^4\) there was no apparent dilation of the ascending aorta in this dog. Coronary artery anatomy was presumed normal as a distinct coronary ostium was visualized leaving each aortic cusp. A dysplastic pulmonary valve was also noted, exhibiting mild valvular stenosis with a peak systolic velocity of approximately 3 m/s, corresponding to an instantaneous transpulmonary pressure gradient of 36 mmHg, and subjectively mild pulmonary insufficiency. A modified left cranial view of the pulmonary valve in short axis revealed 3 leaflets. Incidentally, a persistent left cranial vena cava was suspected due to dilation of the coronary sinus and great cardiac vein. The remainder of the echocardiographic study was unremarkable and the dog was discharged to the client.

Approximately 5 months following initial evaluation, the dog returned to our hospital and underwent a successful castration procedure. Just prior to surgery, while under general anesthesia, transesophageal echocardiography (TEE)\(^c\) was performed using a pediatric transducer.\(^c\) Transesophageal echocardiographic imaging of the aortic valve confirmed the findings of the earlier transthoracic study (Video 1). Better 2D imaging of the pulmonary valve was obtained with TEE. The pulmonary valve appeared mildly thickened and exhibited systolic doming with commissural fusion of the leaflets. Serial recheck echocardiographic studies were advised on an annual basis to monitor for progressive cardiac changes. At the time of writing, the dog is apparently healthy.

**Discussion**

The bicuspid (or bifoliate) aortic valve is the most common congenital cardiac malformation in humans, with an estimated prevalence of 0.5%–2%.\(^5,^6\) Despite the high prevalence in humans, detailed descriptions of BAV in the dog are nearly nonexistent. In a recent survey of 976 dogs with congenital heart disease, BAV was listed twice in tabular form, once as an isolated defect causing valvular aortic stenosis and once concurrently with subaortic stenosis.\(^7\) Bicuspid aortic valve in a dog was also briefly mentioned as a rare cause of mild valvular aortic stenosis in one textbook.\(^8\) An anecdotal report in a non-peer reviewed veterinary magazine describes BAV in a 6-month old Pug dog with concurrent subaortic stenosis.\(^9\) In this publication, and in contrast to our case, the aortic valve was reported to function normally. A similar defect, bicuspid truncal valve, has been described in a dog with persistent truncus arteriosus and this valve was also reported as competent and without stenosis.\(^10\) Quadricuspid aortic valves in dogs are relatively more abundant throughout the veterinary literature and have been described as mild to moderately insufficient with minimal stenosis.\(^11–13\)

Among other veterinary species, BAV has been briefly described in a post-mortem specimen of an 8-month old Hampshire cross pig in a textbook.\(^14\) The Syrian hamster (Mesocricetus auratus) demonstrates a relatively high prevalence of BAV and coronary artery anomalies, and inbred lines have been utilized as an animal model of BAV disease in

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**Abbreviations**

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<td>2D</td>
<td>two dimensional</td>
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<td>BAV</td>
<td>bicuspid aortic valve</td>
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<td>TEE</td>
<td>transesophageal echocardiography</td>
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\(^a\) Vivid 7 Vantage with EchoPac software package, version BT09, GE Medical Systems, Milwaukee, WI.

\(^b\) M4S (4 MHz) transducer, Vivid 7 Vantage, GE Medical Systems, Milwaukee, WI.

\(^c\) 9T (4–10 MHz) transducer, Vivid 7 Vantage, GI Medical Systems, Milwaukee, WI.
The authors are not aware of other examples of BAV reported in veterinary medicine. The semilunar valves are formed early in fetal development (4th week of gestation in humans) with the formation of opposing endocardial cushions in the cephalad portion of the truncus arteriosus. Fusion of the conotruncal ridges during a spiraling decent toward the left ventricle results in the formation of the aorticopulmonary (outflow tract) septum. The septum then undergoes complex differentiation, resulting in formation of the right and left aortic valve (coronary) cusps arising from valve cushions. The third (non-coronary) cusp develops from a valve cushion on the aortic wall opposite the aorticopulmonary septum. In humans, there is thought to be a phenotypic continuum of congenital aortic valve anomalies, ranging from unicuspid to quadricuspid. A decreased number of cusps appear to be associated with increased valvular and aortic pathology, and included in this continuum is the BAV. Although the precise mechanism has yet to be elucidated, several theories propose the genesis of the BAV, including abnormal blood flow across the developing valve, genetic factors, abnormal extracellular matrix proteins, behavioral alterations of cardiac neural crest cells and the lack of endothelial nitric oxide synthase.

The earliest notation of the BAV has been credited to Leonardo da Vinci who is thought to have sketched a BAV over 400 years ago. The most common morphologic pattern of a human BAV is 2 unequally sized leaflets with the larger leaflet resulting from commissural fusion of two cusps, creating a fibrous ridge or raphe. Multiple classification schemes have been devised to characterize the valve morphology of BAV depending upon which cusps are fused and whether the leaflets are symmetrical without a raphe (“pure” bicuspid valve). Echocardiography is typically used to characterize the morphology of BAV in people and was attempted in this case. Separate coronary ostia arising from either leaflet suggested that the morphology of BAV in this dog was either type 2 (fusion between the right coronary cusp and non-coronary cusp) or type 3 (fusion between the left coronary cusp and non-coronary cusp) with absence of a
visible raphe between the fused leaflets. The position of the coaptation line (as seen in Fig. 1A) was most consistent with type 3 BAV, as the right coronary cusp was in a normal position and the opposite leaflet appeared to occupy the normal location of both the left and non-coronary cusps. Interestingly, type 3 BAV is considered the rarest form in humans, with only 1 case reported in a series of 191 adult patients with BAV.1

The clinical course of BAV disease in humans is variable depending on the degree of stenosis and insufficiency, but symptoms typically do not manifest until adulthood. Clinical deterioration relates to valve dysfunction (stenosis or insufficiency), aortopathy (e.g., ascending aortic aneurysm or dissection), or acquired complications such as calcific stenosis or infective endocarditis. Fortunately, fatal events related to a BAV appear to be rare.18 Approximately 25% of people with a BAV require cardiovascular surgery during the course of their lifetime.15 During childhood, aortic valve replacement is often suboptimal due to continued growth, and therefore children with a BAV and significant stenosis undergo interventional treatment with balloon aortic valvuloplasty. In adulthood, aortic valve replacement is the most common treatment for either significant aortic valve stenosis or insufficiency. Usual surgical options include valve replacement with a bioprosthetic or mechanical valve, the Ross procedure (the patient’s native pulmonary valve replaces the BAV and a pulmonary allograft replaces the pulmonary valve), or valve repair in the setting of aortic insufficiency. Replacement of the ascending aorta due to progressive dilatation is also warranted in nearly one-third of human patients.4 There appears to be

Figure 2  An adaptation of the human classification scheme for BAV morphology proposed by Shaefer et al. (2008) with orientation of the aortic valve cusps altered to reflect the typical orientation obtained from the right parasternal short axis imaging plane of a dog. The upper schematic shows the normal orientation of the aortic root in the dog with corresponding echocardiographic image from a normal dog. The lower panel details the 3 different morphologies of BAV that are appreciated in people: fusion of the right and left coronary cusps (type 1), fusion of the right and non-coronary cusps (type 2), and fusion of the left and non-coronary cusps (type 3). Each type is subdivided depending upon the absence or presence of a discernible raphe within the fused leaflets. The dog of this report is believed to have a type 3 BAV with absent raphe. LC = left coronary cusp, LCA = left coronary artery, NC = non-coronary cusp, RC = right coronary cusp, RCA = right coronary artery.
little consensus on medical therapy for BAV aside from aggressive treatment of systemic hypertension. In people, the use of beta-blockers, angiotensin-converting enzyme inhibitors, and angiotensin II receptor blockers have been advocated by some clinicians, as these drugs have been shown to slow the progression of aortic dilatation in Marfan syndrome.\textsuperscript{19} No medical therapy was initiated in the patient described in this report due to the lack of clinical signs, lack of cardiac remodeling, and the mild-to-moderate degree of valvular (aortic and pulmonary) dysfunction.

The BAV is usually an isolated defect in humans, but concurrent congenital malformations can occur, including coarctation of the aorta, patent ductus arteriosus, supravalvular aortic stenosis often associated with William’s syndrome (a complex developmental disorder affecting many body systems), ventricular septal defect, atrial septal defect, Shone’s complex (a constellation of left heart obstructive lesions), Turner’s syndrome (a syndrome of gonadal dysgenesis characterized by complete or partial absence of an X chromosome, also termed monosomy X), and coronary artery anomalies.\textsuperscript{2,15} Concurrent bicuspid semilunar valves have been reported in people\textsuperscript{20} and the Syrian hamster.\textsuperscript{21} The dog in this report also exhibited pulmonary valve dysplasia and, presumptively, a persistent left cranial vena cava in addition to his cryptorchidism.

This report represents one of the first echocardiographic descriptions of BAV in the dog. Similar to people with BAV, both stenosis and regurgitation of the aortic valve were noted, albeit of low-to-moderate severity. The dog of this report appeared to have a type 3 BAV with fusion of the left coronary cusp and non-coronary cusp, considered the rarest form of BAV in people. Serial examinations will determine if the natural history of the disease is similar to the human condition. Heightened awareness of this seemingly rare congenital lesion by those performing echocardiographic studies in dogs may identify more dogs with BAV.

Conflicts of interest
The authors declare no conflicts of interest.

Supplementary data
Supplementary data related to this article can be found online at http://dx.doi.org/10.1016/j.jvc.2012.12.001.

References

Table of Video.

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| 1            | Echocardiographic appearance of the bicuspid aortic valve Compiled images from the transthoracic and transesophageal echocardiographic studies of a 1-year-old English bulldog with a bicuspid aortic valve.


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