Subaortic stenosis and mitral dysplasia in three Black Russian Terrier puppies

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ABSTRACT: A combined congenital heart defect of aortic stenosis and mitral dysplasia was diagnosed in three Black Russian Terrier puppies two months old. The aortic stenosis component included both fixed and dynamic obstructions. The fixed obstruction was subvalvularly located at the entrance to the left ventricular outflow tract. The dynamic obstruction was caused by the septal leaflet of the mitral valve protruding into the left ventricular outflow tract. Mitral dysplasia resulted in mitral insufficiency leading to regurgitation through the mitral valve closer to the septal side. The maximum pressure gradient across the aortic valve amounting to 103 mmHg measured in one puppy was consistent with the most severe grade of stenosis. The diagnosis was confirmed by autopsy in all three puppies that were males and originated in one litter, so genetic influences are supposed.

Keywords: congenital heart defects; left ventricular outflow tract; malformation of atrioventricular valves

Heart diseases in the dog are classified as acquired and congenital. The overall prevalence of cardiac diseases in the dog derived from the total number of dogs treated at a university hospital can amount to about 4.4% (Manczur et al., 2003). Disregarding the acquired heart diseases and taking only the referred cardiological patients into consideration, congenital defects occur in about 2.8% (Brambilla et al., 2003). The most commonly diagnosed congenital heart defects in the dog include aortic stenosis, patent ductus arteriosus, pulmonic stenosis, ventricular septal defects, mitral valve dysplasia, tricuspid valve dysplasia, tetralogy of Fallot and endocardial fibroelastosis (Tidholm, 1997; Ware, 2003). The aforementioned numbers can, however, be subject to great variation in accordance to national and regional differences in the abundance of individual dog breeds, prevalence of cardiac diseases and quality of veterinary care of small animals including the diagnostic possibilities. Combined congenital defects are much less common and amount only to 0.3% of the total of patients referred to the cardiology unit (Brambilla et al., 2003).

Regarding the low prevalence of combined congenital heart defects, it is the aim of this paper to analyze the clinical, diagnostic and pathological aspects in three Black Russian Terrier puppies from one litter affected by subaortic stenosis combined with mitral dysplasia.

CLINICAL CASES

A 61-day old Black Russian Terrier male was presented with a history of fatigue and exercise intolerance in comparison to its littermates. On physical examination, a systolic ejection murmur heard loudest at the left heart base was noted. The intensity of the murmur was of 3–4/6 grade. Femoral pulses were weak. It was proposed to the owner of the female having 13 puppies (7 females and 6 males) that other littermates be examined for heart murmur suggesting a congenital disease.

At that time, similar heart murmurs were found in three puppies – males from this litter. Their mother was without any symptoms of heart disease.

ECG measurements (using the ECG Seiva Praktik unit) and radiograms (using the POSKOM PXP-40HF diagnostic x-ray unit) were obtained in all three affected puppies. Electrocardiography revealed sinus tachycardia (heart rate of 150–170), mean electrical axis in individual puppies of 30, 38 and 50, and S-T segment depression. Thoracic radiographs resulted in finding left atrial and ventricular enlargement, aortic bulge indicating aortic arch enlargement and mild pulmonary oedema due to vascular congestion.

One puppy only (age 148 days, body mass 22 kg) was examined using the Aloka Pro Sound SSD-5000 ultrasonography unit and the right parasternal position. Echocardiographic measurements yielded following results: LA (left atrium) 36 mm, Ao (aorta) 27.4 mm, LVIDd (left ventricular internal dimension – diastolic) 45.7 mm, LVIDs (left ventricular internal dimension – systolic) 32.1 mm, FS (fractional shortening) 29.8%, LVPWd (left ventricular parietal wall – diastolic) 14.1 mm, LVPWs (left ventricular parietal wall – systolic) 18.9 mm, IVSs (interventricular septum – systolic) 19.1 mm, EPSS (E-point septal separation) 1.5 mm, E-F slope (mitral valve E-F slope) 8.16 cm/s, LVOT (left ventricular outflow tract) 6.9 mm, EDV (end diastolic volume) 95.7 ml, ESV (end systolic volume) 41.3 ml, SV (stroke volume) 54.6 ml, EF (ejection fraction) 0.57. Blood flow across the aortic valve: V2 (velocity distal to the obstruction) maximum 517 cm/s, V1 (velocity proximal to the obstruction) maximum 98 cm/s, maximum pressure gradient (V2) 107 mm Hg, maximum pressure gradient (V1V2) 103 mm Hg. ET (ejection time of the left ventricle) 0.217 s. Pulmonary artery: V2 maximum 98 cm/s, maximum pressure gradient 3.82 mm Hg, PA (pulmonary artery) diameter 22.8 mm, ET of the right ventricle 0.266 s. SV at the pulmonary artery 64.5 ml. The Teichholz method and formulas based on M-mode measurements were used to calculate the systolic and diastolic ventricular volumes ($EDV = 7\ EDD^3/(2.4 + EDD)$, $ESV = 7\ ESD^3/(2.4 + ESD)$, where EDD = end diastolic dimension and ESD = end systolic dimension).

Conventional echocardiography and Doppler examination findings were consistent with concentric

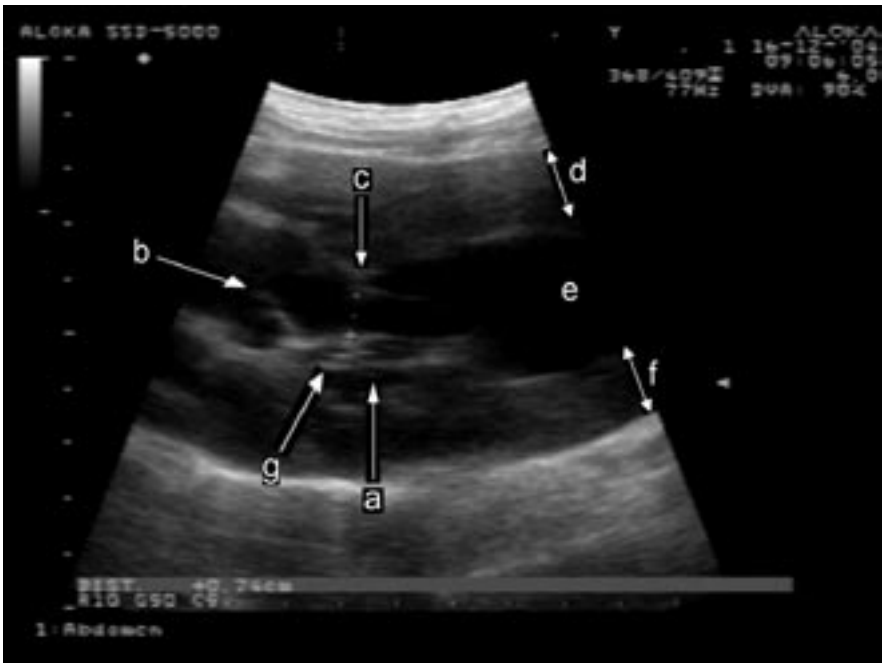

Figure 1. B-mode echocardiographic right parasternal long-axis view of the left ventricular outflow tract in systole showing the subaortic stenosis. Structures shown are (a) thickened *chordae tendinae*, (b) opened aortic valve, (c) a thick fibrous band at the entrance to the left ventricular outflow tract representing the fixed part of the subaortic stenosis (see a in Figure 3), (d) interventricular septum, (e) left ventricle, (f) left ventricular wall, and (g) septal leaflet of the mitral valve. It can be seen that the septal leaflet of the mitral valve protrudes into the long axis of the left ventricular outflow tract in systole participating thus, together with the thick fibrous band on the opposite side, in the subaortic stenosis

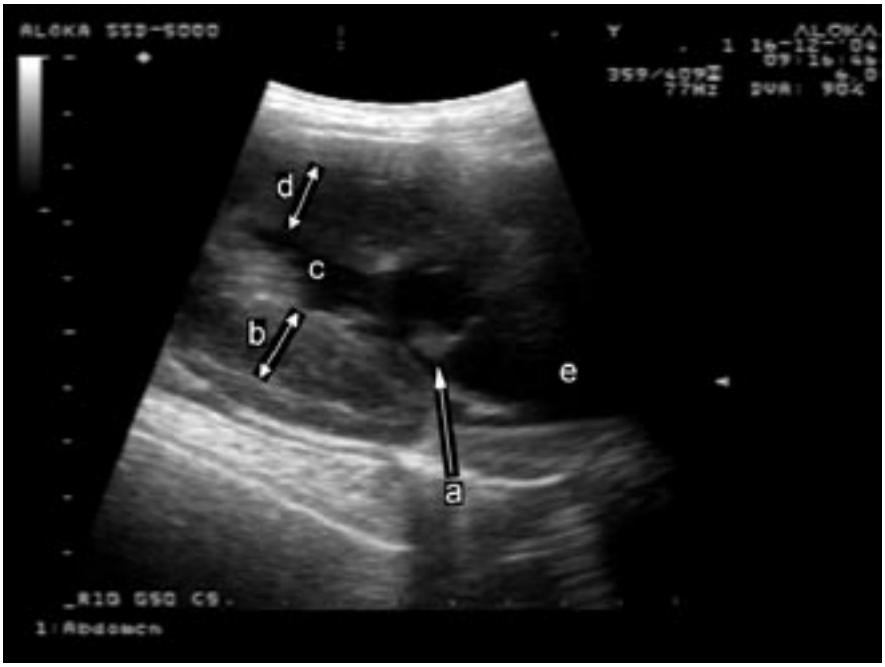

Figure 2. B-mode echocardiographic right parasternal long-axis view of the mitral valve area. Structures shown are (a) thickened mitral valve anterior leaflet, (b) left ventricular wall, (c) left ventricle, (d) interventricular septum and (e) left atrium

hypertrophy of the left ventricle including its free wall and interventricular septum, moderate left atrial dilatation, thickening and decreased mobility of the aortic (septal) leaflet of the mitral valve. The septal leaflet of the mitral valve protruded into the left ventricular outflow tract. Regurgitation through the mitral valve was closer to the septal side. Below the aortic valve there was a narrowing caused by the mitral valve on one side and a 3 mm proliferation on the side of the interventricular septum. The ventricular outflow tract was thus narrowed to nearly 7 mm. Within the aorta there was a holodiastolic regurgitation flow. The right heart was without considerable findings.

Echocardiographic conclusion was a tight subvalvular aortic stenosis of both fixed and dynamic forms, dysplasia of the mitral valve, insufficiency of the aortic valve and considerable secondary changes. B-mode echocardiographic findings demonstrating the subaortic stenosis and thickening of the mitral valve can be seen in Figures 1 and 2.

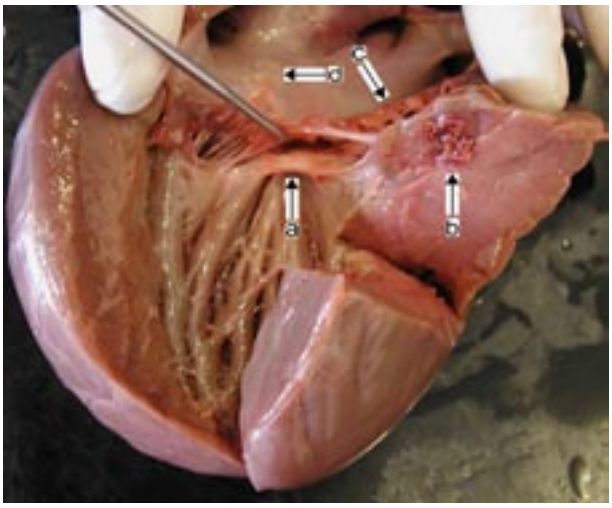

Figure 3. Gross autopsy findings in the left heart. The tip of the probe is inserted into the left ventricular outflow tract. Structures shown are (a) a thick fibrous band 2–3mm wide at the entrance to the left ventricular outflow tract, (b) an area of ischaemic necrosis in the papillary muscle, (c) a thickened and nodular leaflet of the mitral valve and (d) a scar tissue band on the wall of the left atrium probably due to the mitral valve regurgitation jet. The increased left ventricular wall thickness and short *chordae tendinae* can also be noted in this picture

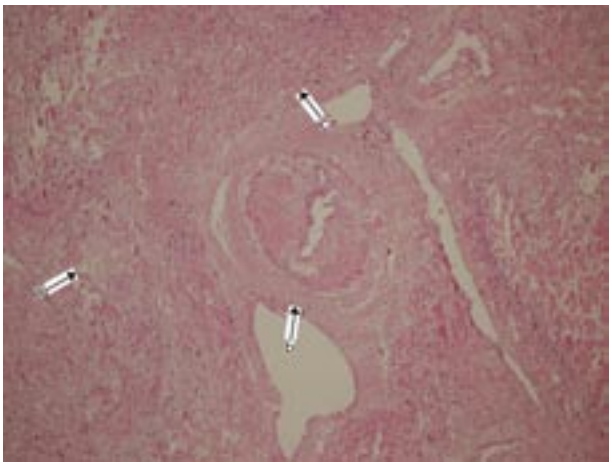

Figure 4. Histological section of the papillary muscle showing (a) necrotic tissue areas, (b) luminal narrowing and wall thickening of the coronary artery owing to hypertrophy of media and adventitia and (c) myocardial fibrosis; haematoxylin and eosin; magnification 100×

One dog was euthanatised due to poor condition and prognosis when 96 days old. Another dog died suddenly when 107 days old. The third one, medicated with atenolol, died suddenly when 215 days old. All three puppies were subjected to post-mortem examination revealing rather the same findings and confirming the diagnosis.

Gross pathological findings proved hyperaemia and petechiae on the surface of lungs, hydropericardium, left ventricular hypertrophy, left atrial dilatation and marked poststenotic dilatation in the ascending aorta. The mitral valve apparatus changes included thickened and short *chordae tendinae*. Both leaflets of the mitral valve were thickened and of nodular surface. There was a thick fibrous band 2–3mm wide on the septal wall at the entrance to the left ventricular outflow tract. In the left atrium just above the septal leaflet of the mitral valve there was a fibrous band resembling a scar tissue. The cut surface of the papillary muscle showed extensive signs of ischaemic necrosis. The heart weight (g) to body weight (kg) ratio averaged 14. For the gross appearance of heart changes see Figure 3.

Microscopically, the section through the area of the papillary muscle shown in Figure 3(b) could be characterised as myocardial necroses with signs of calcification, fibrosis of the myocardium and thickening of coronary arteries with luminal narrowing (cf. Figures 4 and 5). Histological section through the mitral valve leaflet (septal part) revealed connective tissue hyperplasia (Figure 6).

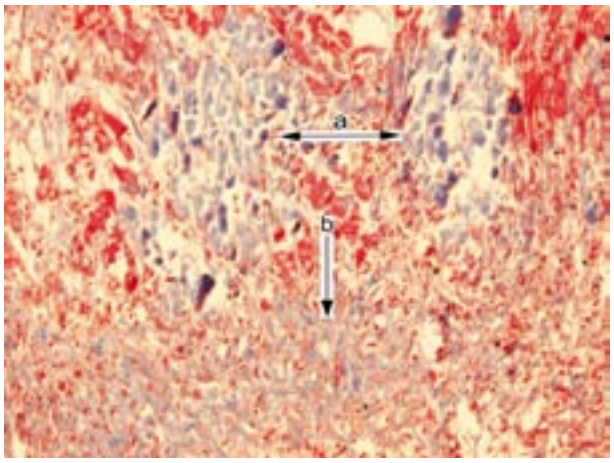

Figure 5. Histological section of the papillary muscle stained by the Masson's trichrome showing (a) two necrotic myocardial tissue areas, and (b) fibrosis within the myocardium; magnification 100×

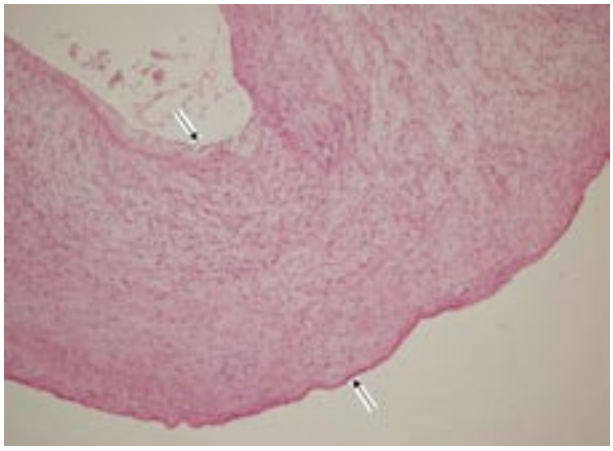

Figure 6. Histological section through the mitral valve that reveals thickening due to connective tissue hyperplasia (cf. arrows); haematoxylin and eosin; magnification 100×

DISCUSSION

Congenital heart defects are more prevalent in purebred animals. Breed predisposition for subaortic stenosis has been recognised in Newfoundland, Golden Retriever, Rottweiler, Boxer, German Shepherd Dog, English Bulldog, Great Dane, German Short-Haired Pointer, Bouvier des Flandres and Samoyed (Kienle et al., 1994; Ware, 2003). Breeds predisposed for mitral dysplasia include Bull Terrier, German Shepherd Dog, Great Dane, Golden Retriever, Newfoundland, Mastiff and Rottweiler (Kittleson, 1998; Ware, 2003). To our knowledge, there are no reports on the occurrence of subaortic stenosis and mitral dysplasia in the Black Russian Terrier. The Black Russian Terrier, however, was developed by breeding Rottweilers, Giant Schnauzers and Airedale Terriers. Regarding the origin, it is clear that it belongs to the group of dog breeds in which these two congenital heart defects have already been identified.

The congenital heart defects of subaortic stenosis and mitral dysplasia can occur either isolated (White et al., 1995; Tidholm, 1997; de Majo et al., 2003; Tidholm et al., 2004) or in a combination (White et al., 1997; del Palacio et al., 1998; Brambilla et al., 2003). The pathophysiology is then due to stenosis of the left ventricular outflow tract and mitral insufficiency, the former of which has much worse effects for the animal.

According to Kienle (1998), subaortic stenosis can be fixed and dynamic. In some rare cases, as in the presented one, these two forms of subaortic stenosis can occur together. Similar congenital defects including fixed and dynamic subaortic stenosis and mitral dysplasia have been reported by Buoscio et al. (1994) in four Golden Retriever puppies and by del Palacio et al. (1998) in a Rottweiler puppy. Their patients, however, were mostly asymptomatic at the time of presentation.

The affected animals can be asymptomatic or symptomatic. It is known that most serious forms of subaortic stenosis affect dogs older than six months (Pyle et al., 1976). Dogs affected by subaortic stenosis die mostly during the first 3 years of life (Kienle et al., 1994). The median age of sudden death is 14.4 months (Kienle, 1998). Our case of a puppy dying when 107 days old is much lower and is consistent with the most severe subaortic stenosis combined with mitral dysplasia, which is prognostically very poor (Kienle et al., 1994). Another prognostic parameter that takes the severity of the obstruction into consideration is the pressure gradient in the left ventricular outflow tract. Measuring the blood flow across the aortic valve in the last living puppy (148 days old) we found pressure gradients witnessing for the most severe stenosis (the maximum pressure gradient of 103 mm Hg). We evaluated only the combined effect of both the fixed and dynamic stenosis using the modified Bernoulli equation and thus do not know which of them was the most severe. As the fixed part of the stenosis was low in the left ventricular outflow tract, at the entrance to the left ventricular outflow tract just opposite to the septal leaflet of the mitral valve acting as a partial obstruction, we considered it as one stenotic region rather than two. The severity of the stenosis, nevertheless, had to be changing during systole reaching its maximum in midsystole. The severity of the stenosis can be evidenced, for example, by the poststenotic aortic dilatation well developed in three month-old puppies and histological findings of ischaemic myocardial necrosis rather corresponding with those ones found in a Rottweiler puppy by del Palacio et al. (1998).

What is interesting is the fact that out of the litter of 13 puppies three were affected in their early age and that all were males. Congenital heart defects reportedly affect males with higher prevalence (Ware, 2003). In the study by Buoscio et al. (1994), nevertheless, evaluating four Golden Retriever puppies, three of which were littermates, the sex ratio was 2 females to 1 male.

Another point that should be addressed is the possibility of progress of clinically silent lesions with age of the animals (Kienle, 1998). It is, therefore, possible that later in their life some other puppies from this one litter will be affected.

As to the practicality of surgical treatment of combined congenital heart defects, to our knowledge, there is only one report of successful surgical treatment of combined lesions of the fixed subvalvular aortic stenosis and mitral dysplasia in the dog (White et al., 1997) with the animal still living 12 months after the surgery.

There are essentially two possibilities of factors leading to congenital defects, i.e., the genetic or teratogenic ones acting during pregnancy. As the owners exclude any intoxication, infection or drug administration to the pregnant female, genetics remains the most probable cause. In the Newfoundland Retriever, for example, selective breeding proved the subaortic stenosis to be in-

herited. It is, however, a defect that develops during the postnatal period (Pyle et al., 1976). Polygenic inheritance is, thus, responsible for the disease manifestation varying from subclinical to serious malformations.

When searching the female´s pedigree and asking for evidence of congenital heart defects, we found no reports of such a disease diagnosed. There were, however, several dogs that died suddenly when half a year, one or two years old. We might speculate that some of those unexplained deaths were due to the subaortic stenosis and mitral dysplasia. In our opinion, the Black Russian Terrier breed thus should be thoroughly checked with respect to these congenital heart diseases in the Czech Republic. This case only documents the necessity and importance of careful examination of young patients and differentiation of the so called innocent murmurs.

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