Presumptive partial atrial standstill secondary to atrial cardiomyopathy in a Greyhound

Case Report

Presumptive partial atrial standstill secondary to atrial cardiomyopathy in a Greyhound☆,☆☆

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Abstract Persistent atrial standstill is a rare arrhythmia in both human and veter- inary patients. In recent decades, cases of partial atrial standstill have been recog- nized in humans. We describe a case of presumptive partial atrial standstill in a Greyhound, in which there was disparate left and right atrial electromechanical function and rapid progression to congestive heart failure over the span of fourteen weeks. An atrial cardiomyopathy characterized by severe, diffuse, fibrofatty repla- cement of the atrial myocardium was identified histologically.

KEYWORDS: Dog; Fibrofatty; Unilateral

A 4.5-year-old, 26.4-kg, female spayed Grey- hound was presented to the Veterinary Teaching Hospital of the VirginiaeMaryland College of Vet- erinary Medicine for evaluation of a newly identi- fied heart murmur and arrhythmia. Enalapril had been prescribed by her primary care veterinarian at a dose of 10mg every 12 h; the patient was also receiving monthly heartworm, flea, and tick pre- ventatives. Thoracic radiographs taken before presentation provided equivocal evidence of left atrial enlargement but the pulmonary parenchyma and vessels had a normal appearance. The verte- bral heart score was 11.2. A point-of-care test for vector-borne disease[c] had been negative two months prior. Systolic blood pressure was reported to be 140 mmHg.

On presentation, the dog was bright, alert, and panting. Her heart rate was 80 beats per minute and her body temperature was 100.7° F. A grade III/VI systolic heart murmur was heard best over the left cardiac apex and a grade II/VI systolic murmur was heard over the left heart base. The remainder of the physical examination was unremarkable.

A 6-lead electrocardiogram did not reveal evi- dence of atrial activity but a narrow QRS, pre- sumed junctional rhythm, with rates between 50 and 95 beats per minute, was evident. Evaluation of precordial leads demonstrated low amplitude P waves and atrioventricular dissociation (Fig. 1). The PeP intervals were not consistent. Intravenous administration of atropine sulfate at a dose of 0.04mg/kg did not result in an appreciable increase in the ventricular rate and the previously identified low amplitude P waves became more difficult to identify due to a further decrease in amplitude.

Transthoracic echocardiography revealed severe left atrial enlargement. Left atrial-to-aortic root ratio was 2.0 (normal: 0.9e1.6) [1]. Left atrial volume indexed to body weight was 3.7 ml/kg (normal 1.1 ml/kg) [2]. The left ventricle, right ventricle, and right atrium were deemed normal in size. Mild thickening of the mitral valve with mild mitral regurgitation was appreciated. Trace aortic regurgitation was also identified. Left ventricular outflow tract velocity was elevated at 2.8 m/sec (normal: 0.95e1.9 m/sec) [3]. The aortic valve and left ventricular outflow tract were structurally normal, and pulsed-wave Doppler interrogation failed to disclose a discrete velocity step-up sug- gesting that the left ventricular outflow velocity was attributable to breed-related characteristics [4] and increased stroke volume as a result of bradycardia. Pulsed-wave Doppler interrogation of mitral valve inflow did not reveal A waves. Aa waves were not identified during tissue Doppler interrogation of the lateral mitral valve annulus, though Aa waves were evident during lateral tri- cuspid annulus interrogation.

The patient was suspected to have an atrial cardiomyopathy that was progressing to complete atrial standstill. As there were no clinical signs, the owner declined additional diagnostic evalua- tion. Additional treatments were not recom- mended, but treatment with enalapril was continued as previously prescribed.

Fourteen weeks later, the patient was pre- sented to the Veterinary Teaching Hospital with a 1e2 week history of increased breathing rates and recent onset of several syncopal episodes. During evaluation earlier in the day at an emergency facility, the dog was bradycardic and was diag- nosed with pleural and peritoneal effusion. All electrolytes were normal. Evaluation of thoracic radiographs revealed cardiomegaly, (vertebral heart score 11.6) with evidence of left atrial enlargement, a small volume of pleural effusion and a mild to moderate interstitial pulmonary pattern suggestive of early pulmonary edema.

Physical examination revealed a heart rate of 35 beats per minute, hyperkinetic femoral arterial pulse, and unchanged heart murmurs. The patient was panting throughout the examination and had mild abdominal distention.

A recheck electrocardiogram revealed both narrow QRS and wide QRS escape rhythms that had average rates of approximately 30 beats per minute. Distinct, multiform atrial activity was appreciated only in the V4 lead (Fig. 1), with low voltage atrial depolarizations evident in the other chest leads. Evaluation of standard limb lead recordings did not reveal P waves. Given the changing morphology, these deflections were sus- pected to be P^0 waves arising from ectopic atrial foci. During echocardiography, a run of accel- erated idioventricular rhythm followed by a

period of asystole, presumed to reflect post-tachycardia inhibition of normal automaticity related to over- drive suppression was appreciated.

Echocardiography at this time revealed more marked dilation of the left atrium with a left atrial-to-aortic root ratio of 2.3 and a nearly dou- bled left atrial volume indexed to body weight of ml/kg. Left ventricular end-diastolic dimen- sions had increased by 1.5 cm since the previous study, whereas end-systolic dimensions were unchanged. Based on subjective evaluation, the right ventricle remained normal in size, whereas the right atrium had become moderately dilated. Left ventricular outflow tract velocities had increased to 3.6 m/sec, likely attributable to more marked, or more consistent, bradycardia and resulting increase in stroke volume. Moderate mitral regurgitation, mild aortic regurgitation, and mild tricuspid regurgitation were identified. The velocity of the tricuspid regurgitant jet was 3.12 m/sec, reflecting an estimated systolic pul- monary artery pressure of 39 mmHg. This mild pulmonary hypertension was presumptively attributed to left atrial hypertension. Mild peri- cardial effusion and mild to moderate pleural effusion were appreciated. Mitral valve motion was abnormal and mitral inflow profiles continued to lack A waves (Fig. 2). Tissue Doppler of the lateral mitral annulus failed to demonstrate Aa waves (Fig. 2). In contrast, normal tricuspid valve motion was identified, pulsed-wave Doppler eval- uation of tricuspid valve inflow revealed A waves, and Aa waves were recorded during pulsed-wave Doppler interrogation of the lateral tricuspid valve annulus (Fig. 2). The contrast in motion of the mitral and tricuspid valves as well as the dis- parate mechanical activities of the left and right atrial myocardium is depicted in Videos 1 and 2.

The patient was diagnosed with partial atrial standstill affecting the left atrium and secondary congestive heart failure. The owner elected not to pursue further treatment including permanent pacemaker placement and the dog was euthan- ized. Without additional electrophysiologic study, differentiation between partial atrial standstill with third-degree atrioventricular block and par- tial atrial standstill in which there was a segment of electrically isolated, excitable right atrial tissue was not possible. The heart was explanted for post-mortem examination.

Gross pathologic findings included severe dila- tion of the left atrium, and moderate dilation of the left atrial appendage, right atrium, right atrial appendage, left ventricle, and pulmonary veins. The left atrium and left atrial appendage had a diffuse, white to yellow discoloration, with the left atrial wall appearing grossly thinner and more translucent than surrounding tissue. There was also moderate, diffuse thickening of both the mitral and tricuspid valves.

Samples of the left and right atria, left and right ventricles, and mitral valve leaflets were collected and fixed in 10% buffered formalin solution. Sam- ples were processed by routine methods,

embedded in paraffin wax blocks, sectioned at 5- mm thickness, and stained with hematoxylin and eosin. Selected serial sections were also stained with elastic picrosirius red and Masson's trichrome to investigate collagen, elastic fibers, fibrin, and connective tissue components. Tissue sections were examined by light microscopy.

Multiple histologic sections of the left atrium and left atrial appendage showed diffuse, trans- mural, fibrofatty replacement (Fig. 3) with multi- focal areas of severe, chronic lymphoplasmacytic infiltrates associated with neoangiogenesis and myocardial atrophy. Intimal hyperplasia and fib- rosis of the adventitial layer of intramural coro- nary arteries was also observed in the left atrium and the left atrial appendage. Multiple, small chronic endocardial thrombi were identified within the left atrial appendage. Histologic sections of the right atrium, sampled near the sulcus termi- nalis, were found to have similar transmural fibrofatty replacement of the myocardium and coronary artery lesions as were found in the left atrium (Fig. 3). The myocardium of the left and right ventricles had moderate, diffuse, myocardial hypertrophy and moderate, multifocal hyperplasia of the tunica intima of small caliber intramural coronary arteries. Specialized conduction tissue was not assessed. The mitral valve was diffusely affected by myxomatous degeneration.

Discussion

Atrial standstill is an arrhythmia characterized by the absence of P waves and an escape rhythm of junctional or ventricular origin. It is defined not only by the lack of atrial activity on the surface electrocardiogram and intracavity electrogram but also by a lack of mechanical activity and the inability to electrically stimulate the atrial myo- cardium [5,6]. The classification of atrial standstill has long been divided into temporary and persis- tent forms, with temporary forms most often associated with drug toxicities, hyperkalemia, and hypoxia [7]. Persistent atrial standstill, on the other hand, is typically associated with extensive underlying atrial disease. As electrophysiologic studies have increased in frequency, a partial form of atrial standstill has also been described in humans [8e11]. Vacillation between partial and total atrial standstill has been documented as well and suggests that in many cases, partial atrial standstill may precede complete loss of atrial function [11]. Interestingly, partial atrial standstill in humans appears to preferentially affect the upper right atrial tissue first, with right atrial tis- sue just above the tricuspid valve apparatus and left atrial tissue adjacent to the coronary sinus more commonly having a preserved pacing response [10,11].

In veterinary medicine, persistent atrial stand- still has been described in both dogs and cats, though it is considered rare [12e18]. In dogs, the disease has been associated with chronic cardiac disease [19], myocarditis [14,17,18], and muscular dystrophy [12]. The case presented here depicts the first documented veterinary case of partial atrial standstill with strong supportive echo- cardiographic imaging. Two previously reported cases of persistent atrial standstill [15,20] descri- bed small, low voltage P waves similar to those appreciated in this reported case and in human patients with partial atrial standstill [9]. These cases may have also represented a partial form of atrial standstill had electrophysiologic atrial map- ping been performed. In addition, in one series of briefly described atrial standstill cases, there is mention of one Old English Sheepdog with atrial standstill affecting only the left atrium; however, full case details were not provided [12,19].

The dominant pathologic findings in this case involved both the left atrium and the right atrium, though serial echocardiographic changes and residual atrial electromechanical activity in the right atrium point to a process that began in the left atrium and progressed over time to involve the right atrium as well. Previously reported patho- logic findings associated with persistent atrial standstill in the dog describe markedly enlarged and paper-thin atria with fibrous connective tissue replacing the majority of the normal right and left atrial myocardial tissue [12]. In a more recent publication, similar characteristic pathologic find- ings were reported, with fatty degeneration also noted [16]. The severity of fatty degeneration was not quantified within the text, however figures within that

report suggest the fatty degeneration was relatively mild [16]. In the present case, prominent fibrofatty replacement similar to that reported in Boxer dogs with arrhythmogenic right ventricular cardiomyopathy (ARVC) predominated [21]. Similar fibrofatty infiltration was also appre- ciated in a single human case report of persistent atrial standstill of unknown etiology, with fibroe- lastosis and vacuolization of the remaining atrial musculature also noted [8].

Multifocal lymphoplasmacytic infiltrates con- sistent with areas of chronic myocarditis were appreciated within the myocardium of the left atrium and the left atrial appendage in the present case. A distinction between primary myocarditis and a secondary reaction to spontaneous cell death is unclear, however primary myocarditis was considered less likely given the lack of active necrosis and the absence of concurrent inflam- mation throughout other cardiac chambers. Atrial-specific myocarditis has been reported in man [22,23], however, and was also reported once in the dog, though an area of ventricular necrosis was identified in that case as well [18]. In this case report, the areas of lymphoplasmacytic infiltrates found in combination with significant fibrofatty replacement again mimics findings typical of Boxer dogs with ARVC, where a cycle of myocarditis and fibrofatty myocardial injury and repair is reported [21]. Affected Boxers ultimately develop electrical instability and ectopic ventricular arrhythmias as a result of their ventricular lesions [21]. Whether or not a period of increased arrhythmogenicity arising from electrically unstable left atrial tissue pre- ceded the period of left atrial inexcitability in this patient is unknown. In humans, severe atrial electrical disturbances including atrial fibrillation and ectropic atrial rhythms such as focal and multifocal atrial tachycardia have been shown to precede permanent, bilateral atrial standstill [9e11].

The biventricular hypertrophy noted in this patient was attributed to chronic bradycardia. This adaptive mechanism is well documented in research dogs with induced chronic, complete atrioventricular block [24,25]. Biventricular hypertrophy in this setting has also been shown to prolong the action potential duration and predis- pose to early afterdepolarizations and triggered activity [24,25]. Similar electrical remodeling in this case could have provided a stimulus for the ventricular arrhythmias appreciated during the second examination.

This case report does have limitations, with the first being the lack of invasive electrophysiologic evaluation and atrial mapping to corroborate the echocardiographic evidence of disparate atrial mechanical function and the electrocardiographic findings of focal atrial activity. In addition, without histopathology of the specialized conduction tis- sue, further definition of how this unusual disease process affected the sinoatrial and atrioven- tricular nodes in this case is lacking. Finally, the underlying etiology of this atrial cardiomyopathy remains unknown.

In conclusion, a case of presumptive partial atrial standstill in a veterinary patient is pre- sented. Clinical progression from the time of initial examination was rapid and resulted in the devel- opment of syncopal episodes and congestive heart failure. Pathologic findings revealed an atrial car- diomyopathy characterized by fibrofatty replace- ment of the atrial myocardium with striking similarities to the classic right ventricular lesions described in Boxers with ARVC.

Conflicts of Interest

The authors do not have any conflicts of interest to disclose.

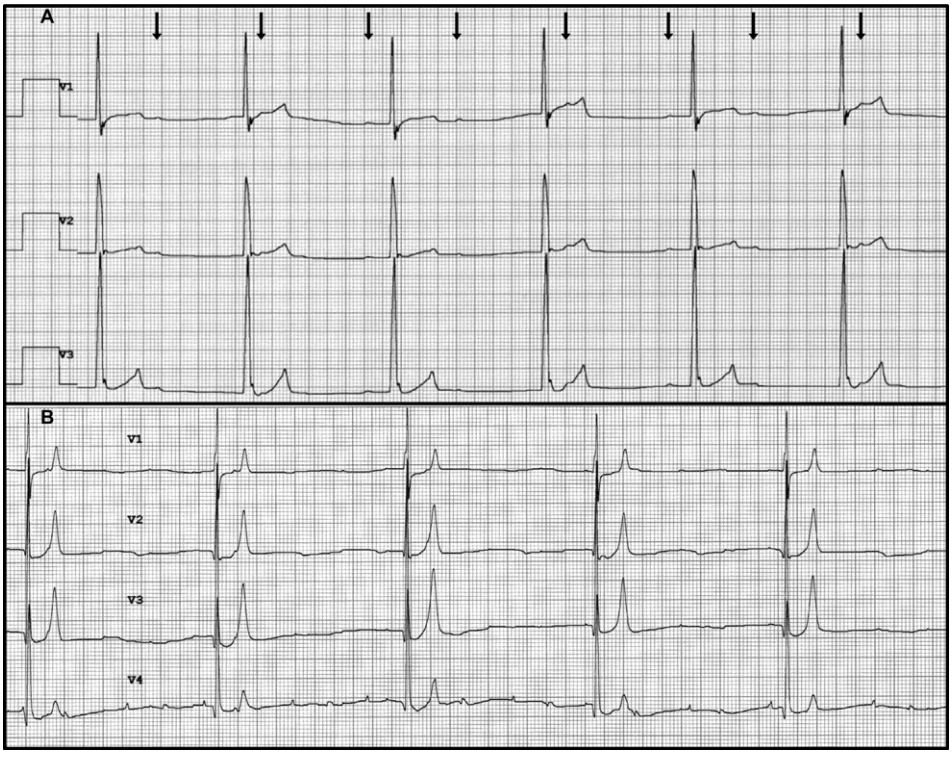

Figure 1 (A) ECG from visit one revealing a presumed junctional rhythm with low voltage atrial activity denoted by arrows. Paper speed: 50 mm/s; amplitude: 10 mm/mV (B) ECG from visit two revealing an escape rhythm with multiform P^0 waves in lead V4. Paper speed: 25 mm/s; amplitude: 10 mm/mV.

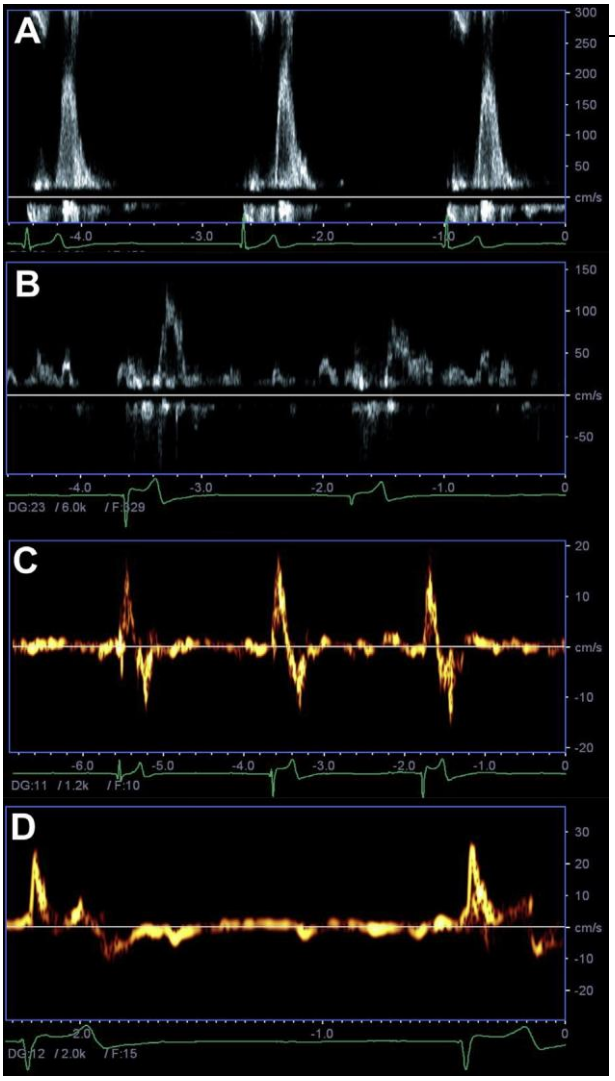

Figure 2 Mitral (A) and tricuspid (B) inflow from visit two. Only E waves are appreciable on the mitral inflow trace, whereas both E and A waves are appreciable on the tricuspid inflow trace. Mitral (C) and tricuspid (D) tissue Doppler of the respective lateral annulus from visit two that depicts Ea waves on both images, whereas Aa waves suggestive of atrial contraction are only appreciated in (D).

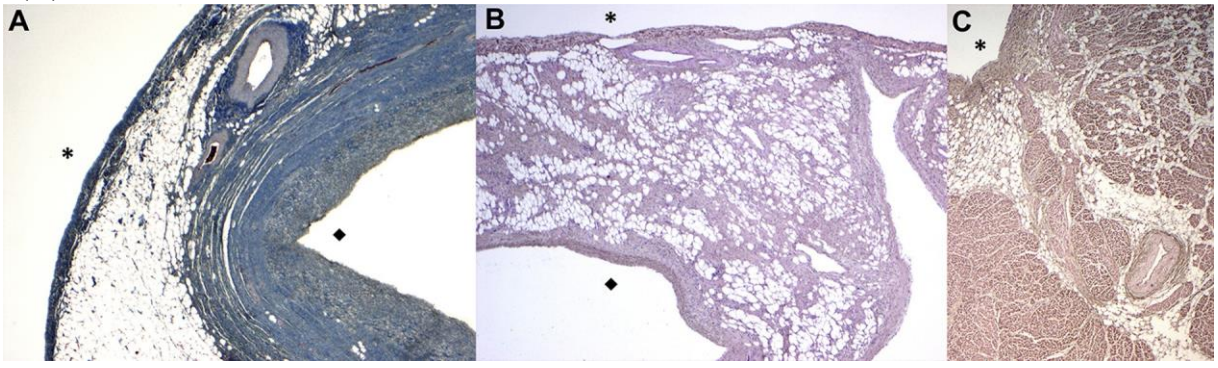

Figure 3 Histologic sections from the (A) left atrium, (B) left atrial appendage, and (C) right atrium demonstrating severe, fibrofatty replacement of the myocardium. Epicardial surface (*), endocardial surface (A). Stains: Masson's Trichrome (A), hematoxylin and eosin (B and C), 2.5× magnification.

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