Journal of Veterinary Cardiology (2006) **8**, 63—68

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Journal of Veterinary Cardiology ESVC

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BRIEF COMMUNICATION

Syncope secondary to transient atrioventricular block in a German shepherd dog with dilated cardiomyopathy and atrial fibrillation

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Received 30 July 2005; received in revised form 25 November 2005; accepted 8 December 2005

KEYWORDS
Holter;
Dilated cardiomyopathy;
Congestive heart failure;
Asystole;
Theophylline

Abstract This case report describes transient atrioventricular block as the etiology for syncopal events in a 6-year-old male German shepherd dog with atrial fibrillation and dilated cardiomyopathy. The arrhythmia diagnosis was obtained via Holter monitoring. Medical treatment with a sustained-release preparation of theophylline, as an additive to the standard congestive heart failure treatment (benazepril, furosemide and pimobendan) may have contributed to temporary remission of the syncopal events. However, the congestive heart failure progressed and the dog was euthanized. Veterinarians should be aware of the possibility of transient atrioventricular block causing syncope in dogs with DCM and AF and should be careful in empirically lowering the ventricular response rate if these dogs present with syncopal episodes.

Introduction

Syncope is defined as a sudden loss of consciousness with a loss of postural tone and is always associated with a spontaneous recovery.[1,2] Cardiac disease is the most common cause of syncope in small animals and arrhythmias represent one of the most frequently reported etiologies.[1,2] Atrial fibrillation (AF), ventricular premature complexes and ventricular tachycardia are common arrhythmias in dogs with dilated cardiomyopathy (DCM) and have been associated with syncope.[1—4] However, arrhythmias are not the only mechanism responsible for syncope[5—7] and efforts to document or exclude an arrhythmogenic substrate for the syncopal events are important. Holter monitoring and event

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doi:10.1016/j.jvc.2005.12.003

recorders play an important role in documenting the presence or absence of cardiac arrhythmias and guiding therapeutic recommendations in dogs presenting with syncope.

Case history

A 6-year-old, 50 kg, male German shepherd dog (GSD) was referred to the Hospital for Small Animals of the University of Liège because it had undergone 5 unexplained syncopal events within a week prior to presentation. Each event occurred when the dog was at rest in a recumbent position and was characterized by a sudden transient loss of consciousness, associated with opisthotonus and urinary incontinence. After a few seconds, the dog regained consciousness and resumed normal activity. Tonic–clonic limb motions, facial tremors, hypersalivation and defecation were not observed. The owners did not report a pre-ictal or post-ictal period and the dog was completely normal between episodes. Pertinent past medical history included lethargy of 1 year duration and the presence of intermittent polypnea for 6 months.

On presentation, the dog was in good body condition and was bright, alert and responsive with a normal respiratory pattern. Mucous membranes were pink and the capillary refill time was less than 2 s. Cardiac auscultation revealed a chaotic heart rhythm, varying from 130 to 140 beats per minute (bpm), associated with 30% pulse deficits. There were no audible heart murmurs and pulmonary auscultation was normal. The rest of the physical examination was unremarkable, including a full neurological assessment.

Initially an electrocardiogram (ECG), systemic blood pressure measurement, thoracic radiographs, echocardiogram, and routine laboratory work were performed. The ECG confirmed the presence of AF with a ventricular response rate of 140–160 bpm. Systolic systemic arterial blood pressure measured indirectly by the Doppler method[c] was 130 mmHg. Thoracic radiographs revealed cardiomegaly (vertebral heart size[8] of 11.5 vertebrae) with mild left atrial enlargement. The pulmonary veins were prominent and wider than the accompanying pulmonary arteries indicating venous congestion. The pulmonary parenchyma showed a generalized mild broncho-interstitial pattern. Two-dimensional and M-mode echocardiography showed the presence of a dilated left ventricle [left ventricular internal diameters in diastole and systole = 60.6 mm (range: 47.6–53) and 54.9 mm (range: 29.9–33.8), respectively], with poor contractility (fractional shortening = 9%, range: 25–44%). The left atrium (LA) was mildly dilated (right parasternal long axis four chamber view[9]: LA = 48 mm, range: <42 mm; two-dimensional short axis view[10]: LA/aortic diameter = 36.8 mm/23.6 mm = 1.6, range: <1.6). Color and continuous wave spectral Doppler revealed the presence of mild mitral valve insufficiency with no tricuspid valve insufficiency. The peak aortic (0.7 m/s, range: <1.5–1.7 m/s) and pulmonary arterial (0.5 m/s, range: <1.3 m/s) velocities were within normal limits. Hematology, biochemistry (including baseline serum total T4 and endogenous TSH), and urinalysis were within normal limits. Plasma taurine (53 nmol/L, range: >50 nmol/L) and plasma total carnitine (24 μmol/L, range: 12–38 μmol/L) were subsequently measured and determined to be within reference ranges.[11] Based on the history, physical examination and ancillary diagnostic tests, mild congestive heart failure (CHF) secondary to DCM was diagnosed. Therapy with benazepril[d] (0.25 mg/kg SID) and pimobendan[e] (0.3 mg/kg BID) was instituted. During the following days the dog developed mild dyspnea and new thoracic radiographs obtained by the referral veterinarian identified pulmonary edema. Consequently, furosemide[f] (1 mg/kg BID) was added to the treatment.

At representation 2 weeks later, the dyspnea had resolved but the dog had become more lethargic and the owners reported 5 more syncopal events at rest. Physical examination, ECG, systolic blood pressure measurement, thoracic radiographs, echocardiography, and serum biochemistry showed neither aggravation nor improvement from the previous evaluation. A 24-hour ambulatory ECG monitor (Holter)[g] was performed to try and determine the cause of the syncopal events. Holter analysis revealed AF with an average ventricular response rate of 160 bpm and a transient episode of extended (8.27 s) AV block followed by ventricular escape complexes (Fig. 1). The episode of AV block corresponded with the sole syncopal event reported by the owners. Five other pauses of more than 2 s and less than 3 s (mean 2.33 s) and frequent relative pauses (less than 2 s) were also recorded by the Holter.

After determining the syncopal episodes were presumably secondary to transient AV block,

[c] Ultrasonic Doppler Flow Detector (model 811-B), Parks Medical Electronics Inc., Oregon, USA.

[d] Fortekor, Novartis, Brussels, Belgium.

[e] Vetmedin, Boehringer Ingelheim, Brussels, Belgium.

[f] Lasix, Aventis, Paris, France.

[g] Vista, Novacor, Rueil-Malmaison, France.

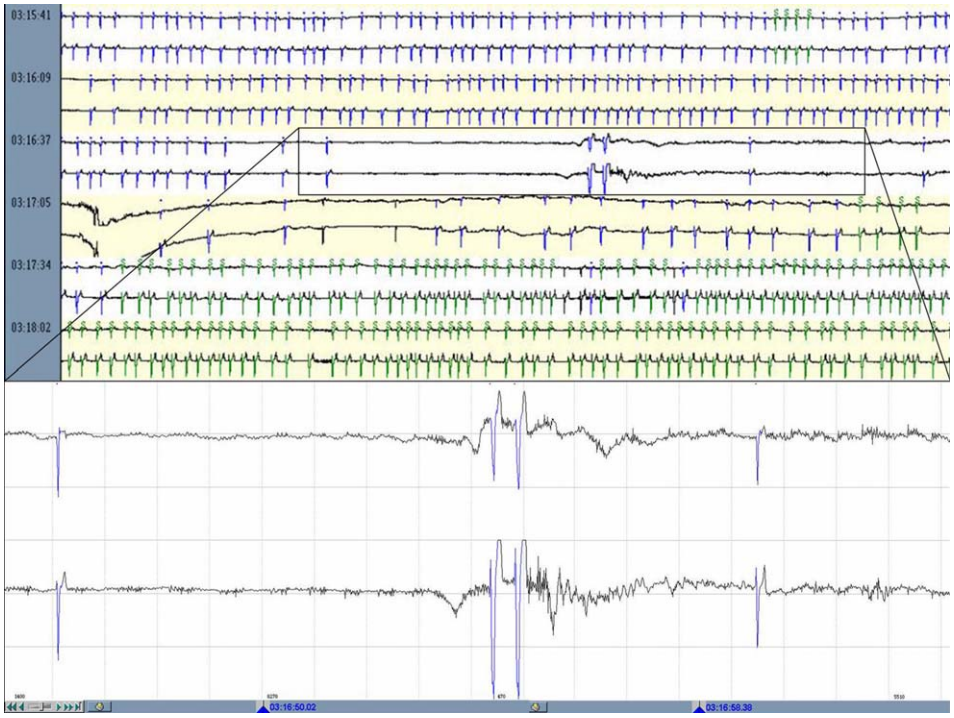

Figure 1 Holter recording showing the transient AV block resulting in ventricular asystole (duration 8.27 s) followed by two ventricular escape complexes.

pacemaker implantation was discussed as the treatment of choice with the owners. Unfortunately due to monetary constraints the owners opted to try medical therapy with a sustained-release preparation of theophylline[h] (20 mg/kg SID) added to the previously prescribed regimen for DCM. No further syncopal events occurred during the following week, but because of the occurrence of side effects (i.e., diarrhea and restlessness), the dosage of theophylline was reduced to 10 mg/kg SID. The dosage reduction was accompanied by resolution of the side effects without recurrence of the syncopal events. During the following months, the dog displayed more energy and regained a normal quality of life (i.e., absence of lethargy, dyspnea and syncopal events) according to the owners. A second Holter to confirm resolution or reduction of the transient AV block was proposed, but refused by the owners for financial reasons. Consequently, electrocardiographic resolution of the transient AV block as the means for the reported clinical resolution of the syncopal events following the addition of theophylline could not be confirmed.

After an initial improvement of 4 months, the dog's clinical status deteriorated again with recurrence of lethargy and dyspnea. Based on clinical examination and thoracic radiographs, the referral veterinarian documented progression of the DCM and recurrence of CHF. The dosage of furosemide was progressively increased to 4 mg/kg BID with only temporary remission of clinical signs. Two weeks later, the syncopal events recurred despite the continued administration of theophylline, and the owners opted for euthanasia. Unfortunately, a post-mortem examination was not allowed.

[h] Theolair, 3M, Diegem, Belgium.

Discussion

Atrial fibrillation was the dominating arrhythmia in this dog, but since the syncopal events were most commonly observed at rest, there was concern that the AF was not solely responsible for the clinical presentation in this case. Atrial fibrillation is one of the most common arrhythmias diagnosed in dogs and is most commonly associated with severe underlying cardiac disease resulting in atrial enlargement, like DCM, severe mitral valve regurgitation and congenital malformations.[12] Other possible causes of AF are severe ischemia or shock, atrial tumors, electrolyte disturbances, hypothermia and anesthesia.[13] In this case the AF was considered to be due to mild atrial dilation secondary to advanced DCM. Although there was only mild left atrial enlargement a host of other factors, like critical atrial mass, alteration in the

autonomic tone, chronic changes in atrial wall tension, and atrial myocardial lesions, may contribute to the development of AF.[14] The rationale, optimum time, and therapeutic modality to treat AF are debatable, but in general it is recommended that therapy should be instituted when the average ventricular response rate exceeds 140–160 bpm.[12,15]

Treatment options include restoring and maintaining sinus rhythm with electrical or pharmacological cardioversion (i.e., rhythm control) or controlling the ventricular rate with antiarrhythmic drugs (i.e., rate control).[12] Digoxin has traditionally been considered the first choice for lowering the ventricular response rate below 140–160 bpm in cases of DCM complicated by atrial fibrillation.[12] However, digoxin may contribute to fatal ventricular arrhythmias and aggravate pre-existing conduction blocks.[16] Digoxin was withheld and further diagnostics were recommended in this case because the dog did not have a resting heart rate of >160 bpm and the history (i.e., syncope at rest) provided concern that the AF was not responsible for the syncopal events.

Indeed, ventricular premature complexes and ventricular tachycardia/fibrillation are commonly reported in canine DCM and can be responsible for syncopal events and even sudden death.[4,17] Sinus bradycardia and cardiac asystole, resembling neurocardiogenic syncope, have also been reported in cardiomyopathic Doberman pinschers and Boxers.[17,18] Another potential etiology for the syncopal events in this dog was an acceleration of the ventricular response rate of AF. Finally, a recent study reported a relatively high frequency of 3rd degree AV block in GSD that may account for otherwise unexplained syncope.[19]

With the goal of most appropriately diagnosing and managing the syncopal events in this case a Holter recording was obtained. Surprisingly, the single observed syncopal event during the 24-h recording coincided with a transient, prolonged episode of high-grade AV block. Since a Holter recording was not performed prior to initiating therapy with benazepril and pimobendan it is impossible to determine if the same etiology (i.e., the transient AV block) was responsible for the pre-treatment and post-treatment syncopal events. However, since the owners did not report any differences in the frequency or presentation of the episodes before and after the initiation of treatment, we feel it is unlikely that the benazepril or pimobendan contributed to the syncopal events.

Atrioventricular block has been reported in canine DCM but it is less common than other arrhythmias like AF and ventricular tachyarrhythmias.[3] Other conditions that have been associated with 3rd degree AV block include congenital disorders (ventricular septal defect, congenital AV block), myocarditis (inflammatory, infectious), cardiac neoplasia, cardiomyopathies (hypertrophic, restrictive), myocardial trauma, myocardial ischemia or infarction, electrolyte abnormalities (hyper/hypokalemia), strong vagal stimulation, and intoxication by several drugs (digoxin, β-blockers, calcium channel blockers, quinidine, doxorubicin). In most cases, however, AV blocks are probably the result of idiopathic fibrosis in geriatric dogs.[13,16] In this case, because post-mortem examination was not allowed, the exact etiology of the transient AV block could not be determined.

Similarly the exact cause of the DCM could not be determined. Primary, idiopathic DCM was the most plausible diagnosis in this case but other numerous etiologies of secondary DCM exist in dogs.[15,20] Since an inflammatory origin can lead to chronic myocardial failure (secondary DCM) and 3rd degree AV block, a chronic form of myocarditis could have been present in this case.[i,13,15,21] Inflammatory responses to infectious agents such as viruses, bacteria, fungi, Rickettsiae, spirochetes, protozoa and Bartonellosis have all been reported in the pathogenesis of myocarditis.[i,15,21,22] This dog showed no hematological evidence of an inflammatory response but unfortunately these are not always present, particularly in cases of chronic myocarditis.[i] Chronic myocardial inflammation is often only confirmed via gross and histopathologic examinations so the inability to perform a necropsy in this dog limits our ability to exclude this etiology as contributing to the DCM and transient AV block.[i]

As we discussed with the owners, the only effective long-term treatment in symptomatic patients with high-grade AV block is permanent cardiac pacemaker implantation.[13] Because of the general poor prognosis of DCM, the severity of the systolic dysfunction in this case and the reluctance of the owners for pacemaker implantation, medical treatment was attempted.[20] A sustained-release formulation of theophylline was used in this case and potentially contributed to temporary remission of the syncopal events.

Theophylline competitively inhibits phosphodiesterases (PDE) nonspecifically thereby increasing the intracellular levels of cyclic AMP (cAMP). Increased cAMP has a direct sympathetic effect

[i] Meurs KM. Myocarditis in the canine and feline patient. Proceedings of the 17th ACVIM Congress, Chicago, 1999: 136–7 (abstract).

by releasing epinephrine from adrenergic nerve terminals and the adrenal medulla and further contributes to an increase in intracellular calcium influx via phosphorylation of calcium channels. An increase in calcium influx in nodal tissue (sinus node and AV node) and myocardial tissue results in a positive chronotropic and inotropic effect, respectively.[23–25] However, this PDE mediated mechanism is controversial since theophylline does not inhibit PDE at therapeutic concentrations.[24,26]

Adverse effects of theophylline include restlessness, hyperexcitability, nausea and vomiting, diarrhea, sinus tachycardia, and ventricular arrhythmias.[23,25] Central nervous system excitement and gastrointestinal signs are not uncommon when starting the therapy but generally resolve over time and cardiac arrhythmias have been reported only to occur at high plasma levels.[23,25] Restlessness and diarrhea were reported in this case and resolved after reducing the dosage. Whether the appearance of these side effects at the recommended dosage was due to the concurrent use of pimobendan or whether the bioavailability of theophylline was relatively higher in this dog is uncertain.[23]

A final point of discussion is that pimobendan also increases the intracellular levels of cAMP via PDE inhibition. In contrast to theophylline, which inhibits PDE nonspecifically, pimobendan only inhibits PDE III and V.[20,27] Consequently, the increase in intracellular cAMP mediated by pimobendan may not be enough to enhance AV nodal conduction. We therefore believe that it was unlikely pimobendan contributed to the clinical resolution of the syncopal events, if they were indeed due to transient AV block. Moreover, in the face of myocardial failure, the PDE III inhibition by pimobendan is attenuated.[28]

Conclusion

To the authors' knowledge, this is the first report of syncope associated with transient AV block in a dog with underlying AF and DCM. We believe a sustained, oral formulation of theophylline, administered because of the inability to implant a permanent pacemaker, contributed to the temporary remission of syncopal events. Serial Holters, displaying resolution of the transient AV block after institution of theophylline and recurrence of the AV block following discontinuation of the drug, would have provided further support for its efficacy, but owners' constraints limited these diagnostics. Ultimately, the underlying myocardial failure progressed and the dog was euthanized for worsening CHF and recurrence of syncope. A postmortem examination was declined therefore evaluation of the cardiac conduction system and differentiation between primary idiopathic DCM and secondary DCM (myocarditis) could not be performed.

This report highlights that veterinarians should be aware of the possibility of transient, high-grade AV block producing syncope in dogs with DCM and AF. Therapy aimed at empirically lowering the ventricular response rate in these dogs, without consideration of performing a Holter monitor in an attempt to characterize the etiology for the syncope, should be undertaken with caution.

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