Case Report

Terbutaline Responsiveness in a Cat with Sinus Arrest

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Abstract

An 8-year-old neutered male Persian breed cat presented at the private practice for investigation of seizure-like episodes. An echocardiography revealed mild enlargement of the left atrium (La/AO: 1.73) with spontaneous echo contrast and mitral regurgitation. A left anterior fascicular block was also detected in the electrocardiogram. The cat had no response to the atropine response test. Aminophylline, pimobendan, clopidogrel, and furosemide were initially prescribed at the private clinic, and then the cat was referred to Prasu Arthon Animal Hospital, Faculty of Veterinary Science, Mahidol University, Thailand. Repeated echocardiogram and electrocardiogram demonstrated left atrium enlargement (La/AO: 1.85) and sinus arrest, respectively. The cat was diagnosed with feline nonspecific phenotype cardiomyopathy. As the cat has no improvement after aminophylline administration and the owners declined further management with pacemaker implantation, therefore, terbutaline at 0.625 mg/cat PO q12h was given to replace aminophylline. The cat responded well to this prescription. The mean interval of each syncope episode was markedly increased. Terbutaline increased the mean syncopal episode interval from 8.4 days of aminophylline treatment to 15.5 days. In this case, terbutaline could increase the mean heart rate (MHR) to 190 bpm, which might be an advantage over aminophylline, which increased the MHR to 165 bpm. Unfortunately, the cat died 62 days after starting a new medication. The objective of this case report is to describe medical management in a cat with sinus arrest without atropine responsiveness by using oral terbutaline.

Keywords: Sinus arrest, Terbutaline, Feline nonspecific phenotype cardiomyopathy

การตอบสนองต่อเทอร์บูทาลีนในแมวที่มีภาวะการหยุดเต้นของปุ่มไซนัสหัวใจห้องบน

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บทคัดย่อ

แมวพันธุ์เปอร์เซียอายุแปดปีเพศผู้ทำหมันแล้วเข้ารับการรักษาที่โรงพยาบาลสัตว์เอกชนเพื่อวินิจฉัยอาการคล้ายชัก การตรวจหัวใจด้วยคลื่นเสียงความถี่สูงเผยให้เห็นการขยายตัวในระดับต่ำของหัวใจห้องบนซ้าย (La/AO: 1.73) พร้อมด้วยการไหลเวียนเลือดผิดปกติ ลักษณะคล้ายควันบุหรี่ไหลวนและลิ้นไมตรัลรั่ว จากการตรวจคลื่นไฟฟ้าหัวใจพบภาวะแขนงประสาทข้างซ้ายส่วนหน้าของการนำไฟฟ้าในหัวใจผิดปกติ (left anterior fascicular block) แมวไม่ตอบสนองต่อการทดสอบการตอบสนองต่อยาอะโทรปีน และได้รับการรักษาจากโรงพยาบาลสัตว์เอกชนด้วยยาอะมิโนฟิลลีน พิโมเบนแดนโคลพิโดเกรล และฟูโรซีไมด์ จากนั้นแมวถูกส่งตัวไปยังโรงพยาบาลสัตว์ปศุอาทร คณะสัตวแพทยศาสตร์ มหาวิทยาลัยมหิดล ประเทศไทย การตรวจหัวใจด้วยคลื่นเสียงความถี่สูงและคลื่นไฟฟ้าหัวใจซ้ำแสดงให้เห็นถึงการขยายตัวของหัวใจห้องบนซ้าย (La/AO: 1.85) และภาวะการหยุดเต้นของปุ่มไซนัสหัวใจห้องบนตามลำดับ สัตว์ได้รับการวินิจฉัยว่ามีภาวะ feline nonspecific phenotype cardiomyopathy เนื่องจากอาการของแมวไม่ดีขึ้นหลังจากให้ยาอะมิโนฟิลลีน และเจ้าของปฏิเสธที่จะรักษาต่อด้วยการฝังเครื่องกระตุ้นหัวใจ ดังนั้นยาเทอร์บูทาลีนที่ขนาด 0.625 มิลลิกรัมต่อตัวแมว รับประทานทุก 12 ชั่วโมง จึงถูกนำมาใช้แทนที่ยาอะมิโนฟิลลีน แมวตอบสนองต่อยาตัวใหม่เป็นอย่างดี ค่าเฉลี่ยระยะห่างของอาการเป็นลมหมดสติเพิ่มขึ้นอย่างเห็นได้ชัด เทอร์บูทาลีนช่วยเพิ่มค่าเฉลี่ยระยะห่างของการเป็นลมหมดสติได้จาก 8.5 วันของการใช้อะมิโนฟิลลีน เป็น 15.5 วัน และสามารถเพิ่มอัตราการเต้นหัวใจเฉลี่ยได้ที่ 190 ครั้งต่อนาที ซึ่งอาจดีกว่าอะมิโนฟิลลีนที่ 165 ครั้งต่อนาที แต่แมวเสียชีวิต 62 วันหลังจากเริ่มใช้ยาตัวใหม่ วัตถุประสงค์ของรายงานสัตว์ป่วยนี้คือ เพื่อนำเสนอการจัดการทางยาในแมวที่มีภาวะการหยุดเต้นของปุ่มไซนัสหัวใจห้องบนซึ่งไม่ตอบสนองต่อการทดสอบด้วยยาอะโทรปีน โดยการให้ยาเทอร์บูทาลีนแบบรับประทาน

คำสำคัญ : การหยุดเต้นของปุ่มไซนัสหัวใจห้องบน เทอร์บูทาลีน Feline nonspecific phenotype cardiomyopathy

Introduction

Sinus arrest is a condition occurring when the discharge from SA node fails to deliver, leading to the absence of the heart rhythm. The pause may be due at least twice R-R interval or last 5-12 seconds if severe. Ventricular escape complex or normal complex will end the pause for survival. There are many causes including fibrosis of SA nodal tissue, enormously increased vagal stimulation, drugs and neoplasia. Sick sinus syndrome (SSS) is the most common cause of symptomatic sinus arrest in dogs. It is characterized by a variety of arrhythmias such as sinus bradycardia, sinus arrest, paroxysmal atrial tachycardia (bradycardia-tachycardia syndrome) and intermittent AV nodal block (Madron 2000). Miniature Schnauzers, Cocker Spaniels, Dachshunds, Pugs and West Highland White Terriers are breeds predisposed to this condition. Clinical signs associated with sinus arrest may present with intermittent weakness and syncope if the pause is severe and frequent (Tilley et al., 2008).

Medical management of sinus arrest is indicated in asymptomatic patients. The atropine response test might help select candidates that would respond to the prescription. Atropine 0.02 mg/kg IM or IV will increase 50% of baseline HR within 5-10 minutes after injection. Even if the patients have partial response to atropine, they are one of good candidates for medical management. Initially, the medication will start with parasympatholytic therapy followed by sympathomimetic drugs (Côté 2001). Atropine 0.04 mg/kg IV might be used to elevate heart rate. In normal dogs, a lower dose (0.02 mg/kg) of atropine showed ineffectively parasympathetic blockage (Rishniw et al., 2023). Beta-1 agonist drugs can be given in addition to speeding ventricular escape rate. The most common drug is isoproterenol in dogs. Dopamine is another option in cats and dogs (Côté 2001). Dobutamine might be one of the choices, but its positive chronotropic effect is less than dopamine. Sinus bradycardia or sick sinus syndrome can be managed with medicine in unstable patients or if pacemaker therapy is not an option. Treatment options aimed at breaking high vagal tone by using vagolytic drugs, such as propantheline, hyoscyamine sulfate, or phosphodiesterase inhibitor, theophylline, aminophylline. Sympathomimetic drugs, albuterol, terbutaline, could be prescribed as an alternative. In the case of symptomatic patients such as syncope or episodic weakness, artificial pacemaker therapy is indicated (Tilley et al., 2008).

Terbutaline, a selective beta 2 agonist, has been studied for its effect on the cardiovascular system. It increases in cardiac output, heart rate and systolic blood pressure, but decreases in diastolic blood pressure and total peripheral resistance (Kendall et al., 1982). Terbutaline does not impact on pulmonary vascular resistance or pressure. The beta 2 receptors are predominantly found in the bronchi and peripheral arteries, but few in the heart. Canine coronary vascular sympathetic receptors are classified as a constricting alpha 2 receptor and a vasodilating beta 2 receptor. The selective beta 2 agonist indirectly decreases myocardial blood flow as a result of systemic vasodilation and directly affects myocardial perfusion by enhancing vasodilation on coronary circulation. This helps protect a heart from ischemic events by enhance myocardial response to an increased oxygen demand for external work. Terbutaline induces tachycardia through a baroreceptor reflex mechanism. It is useful in heart failure condition by reducing the left ventricular afterload per se (Hansen et al., 1988).

There is only one case report of terbutaline usage for treating feline cardiomyopathy (Penning et al., 2009), but they neither do atropine response test nor provide the follow-up after treated. The objective of this case report is

to describe medical management in a cat with sinus arrest without atropine responsive by using terbutaline.

Case description

An 8-year-old neutered male Persian breed cat presented at a private practice for investigation of seizure-like episodes. The owner took the cat to the first animal hospital. The veterinarian found bradycardia (HR 66 bpm), normal heart sound, tachypnea (RR 67 bpm), increased lung sound and weak femoral pulse with pulse deficit on physical examination. The cat fell into lateral recumbency and had all limbs increased in tonicity during the examination for 5 seconds. Consciousness was impaired during the episode. The complete blood count (CBC) and blood chemistry were normal. Thoracic radiography revealed cardiomegaly (VHS 9.48). The cat was referred to perform echocardiogram and electrocardiogram at the second private practice. They found mildly enlargement of left atrium (La/AO: 1.73) with spontaneous echo contrast (SEC) and functional mitral regurgitation were found. The left anterior fascicular block (LAFB) was suspected on electrocardiogram, according to their discharge report. The cat had no response to the atropine response test. Due to the financial constraints of the owner, the oral medications were prescribed from the private practice with aminophylline, pimobendan, clopidogrel and furosemide at 5.32 mg/kg PO q12h, 0.26 mg/kg PO q8h, 18.75 mg/cat q24h and 2.12 mg/kg PO q24h, respectively on day 0. The cat showed no improvement in clinical signs. Therefore, the owner took the cat to Prasu Arthon Animal Hospital (PAAH), Faculty of veterinary science, Mahidol University, Thailand the next day.

On physical examination, the cat was conscious and his mental status was still responsive. The vital signs and neurological examination were unremarkable. A CBC found mild leukocytosis (19.89x10^3/uL; reference range [RR], 5.5-19x10^3/uL) and thrombocytopenia (PLT, 27x10^3/uL; RR 300-600x10^3/uL) because of platelet clumping in blood smear. Mild increased creatinine (1.96 mg/dL; RR 0.80-2.40 mg/dL) presented on blood chemistry. Cardiomegaly (VHS 8.5) and bronchial lung pattern are shown in thoracic radiography (Figure 1 and 2). Repeated echocardiogram and electrocardiogram indicated left atrium enlargement (La/AO: 1.85) and sinus bradycardia (HR 100 bpm) with triplet ventricular beats (Figure 3), respectively. Feline nonspecific phenotype cardiomyopathy (NCM) was a tentative diagnosis in this case. The owner refused further diagnosis with 24-hour ECG (Holter monitoring) and further management with a pacemaker implantation because of financial difficulties. The medication continued with pimobendan, clopidogrel, aminophylline and furosemide without adjusting doses.

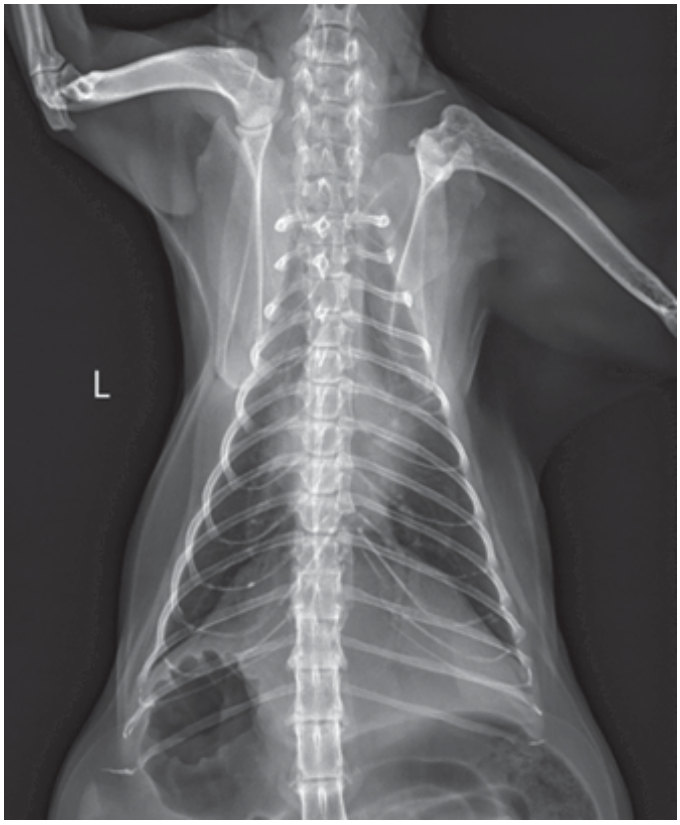

Figure 1. Thoracic radiography on ventrodorsal view revealed generalized bronchial lung pattern.

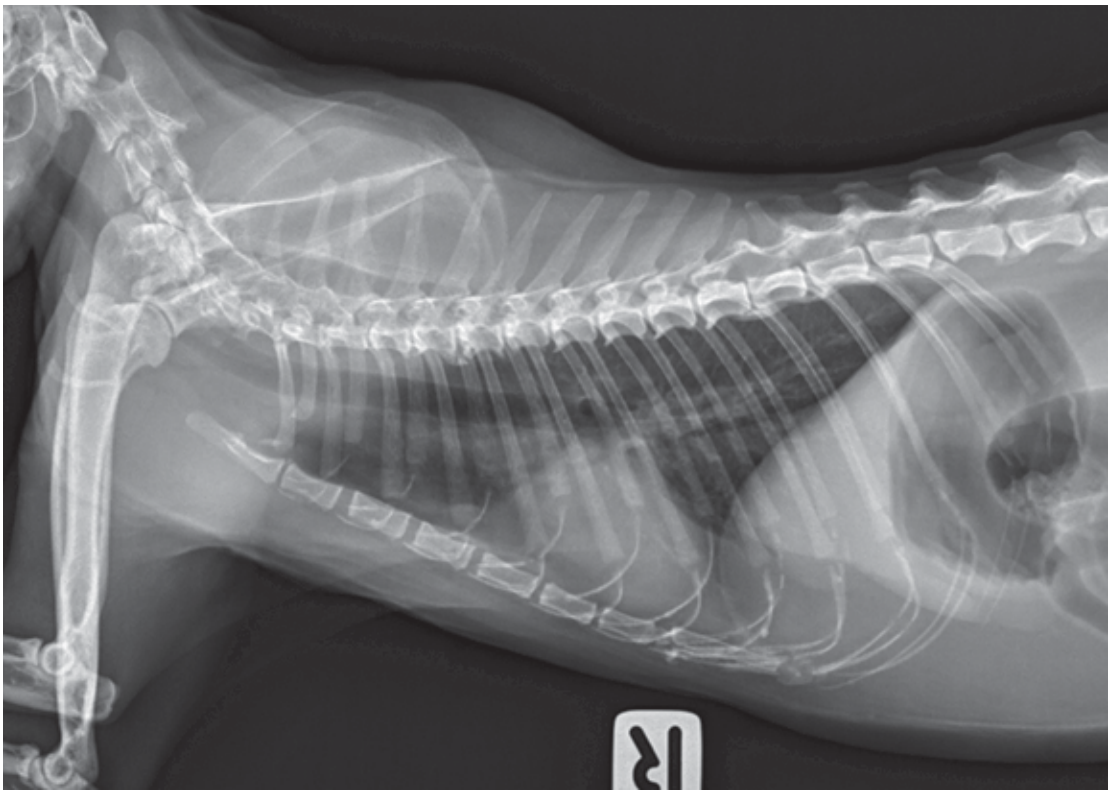

Figure 2. Thoracic radiography on lateral view revealed cardiomegaly (VHS 8.2) and bronchial lung pattern.

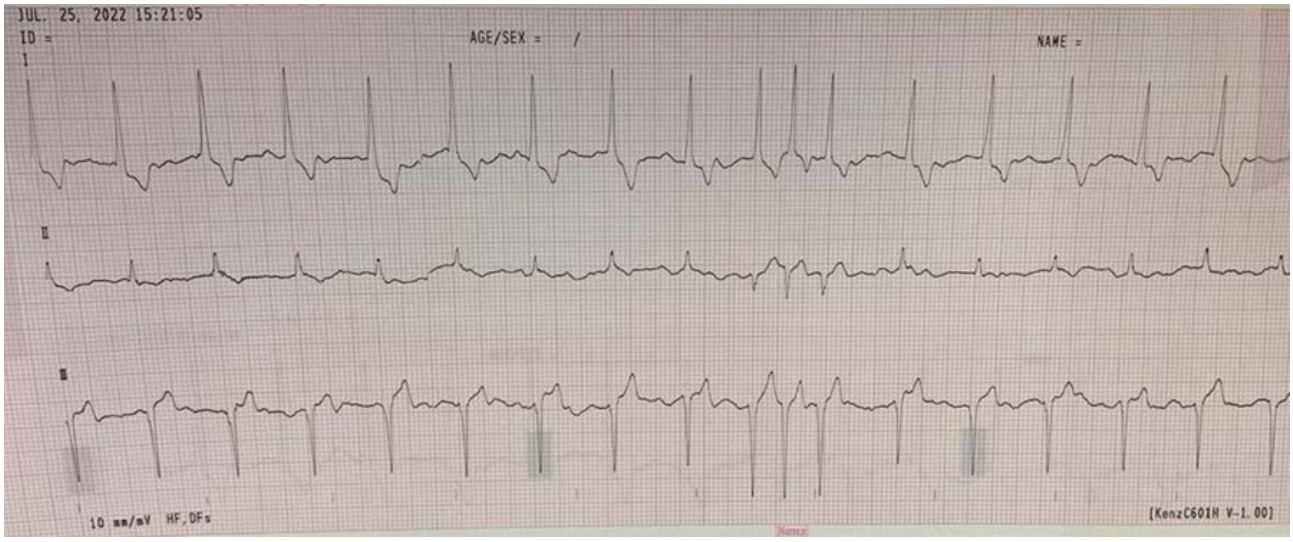

Figure 3. Sinus bradycardia (HR 100 bpm) with triplet ventricular beats (red box) found on ECG (25 mm/s and 10 mm/mV).

On day 35, the cat returned to PAAH due to syncope recurrence more than 6 times per day. The CBC found mild leukocytosis (19.23x10^3/uL; RR 5.5-19x10^3/uL). Hypokalemia (K, 2.7 mmol/L; RR 2.9-4.2 mmol/L) was also detected. Potassium chloride tablets (KCl) were added using dose 60 mEq PO q24h. The cat was admitted at PAAH on day 35-37. During hospitalization, pimobendan and furosemide were increased to high dose of 0.53 mg/kg PO q12h and 2 mg/kg IV q12h, respectively, because the disease progressed. On day 35, electrocardiogram demonstrated left anterior fascicular block with two atrial premature contraction (APC) and sinus arrest (Figure 4). The cat recovered to normal after correcting hypokalemia. The furosemide dosage decreased to 1.4 mg/kg PO q12h as the result of hypokalemia on day 37 and the cat was discharged.

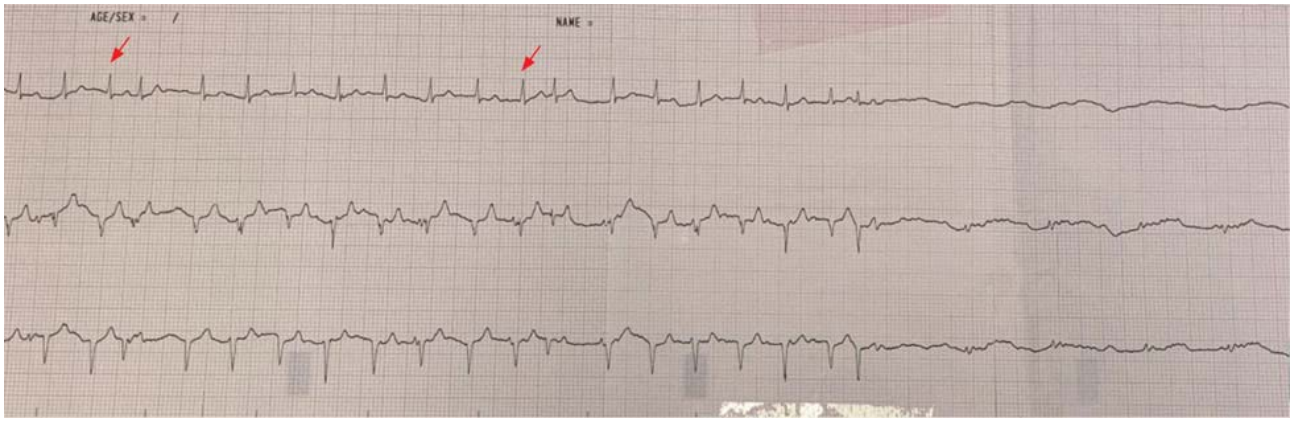

Figure 4. ECG demonstrated left anterior fascicular block with two APC (red arrow) and sinus arrest (25 mm/s and 10 mm/mV).

On day 41, syncope occurred more than 45 times per day in total and hypokalemia was returned, so the cat was admitted on day 41-46 at PAAH. Terbutaline 0.625 mg/cat PO q24h was tested as an alternative to aminophylline to increase heart rate on day 44. Surprisingly, the cat had no syncope at all after changing medication for 48 hours. Spironolactone 2 mg/kg PO q24h was used for potassium-sparing effects. Electrocardiogram was detected right on time as syncope occurred on day 44 and it showed sinus arrest followed by ventricular rhythm (Figure 5). Intermittent hypokalemia was generally found in old cats with hyperaldosteronism, so abdominal ultrasonography was evaluated. The results discovered chronic hepatopathy, cholestasis with bile sludge, bilateral nephropathy with renal insufficiency and no abdominal mass were found. On day 46, the cat had no syncope episodes for 48 hours so we discharged him with terbutaline, clopidogrel, pimobendan, furosemide, KCl and spironolactone. The cats had an appointment for a recheck of clinical signs on day 51 at PAAH, but the owner missed the appointment.

Figure 5. ECG showed sinus arrest, followed by ventricular rhythm, correlated with syncope (50 mm/s and 10 mm/mV).

On day 80, the cat came back with syncope estimated more than 20 times per day. The potassium level was normal. Terbutaline was increased to the maximum dose using 1.25 mg/cat PO q12h. No syncope occurred after adjusting the dose. On day 86, an electrocardiogram found first-degree AV block even though the cat had no clinical signs. Unfortunately, the cat died after syncope recurred on day 106. Survival time since started terbutaline was 62 days in this case. The owner was inconvenienced to allow necropsy the cat.

Table 1. Chronological summary of vital signs, potassium, clinical signs and treatment in a cat with sinus arrest.

Day	Heart rate (beats/min)	Respiratory rate (breaths/min)	Systolic blood pressure (mmHg)	Potassium (mmol/L)	Syncope (Yes/No)	Treatment (PO)
1	66	67	N/A	3.5	Y	Aminophylline 5.32 mg/kg q12h Clopidogrel 18.75 mg/cat q24h Pimobendan 0.26 mg/kg q8h Furosemide 2.12 mg/kg q24h
2	140	36	N/A	N/A	Y	Aminophylline 5.32 mg/kg q12h Clopidogrel 18.75 mg/catq24h Pimobendan 0.26 mg/kg q8h Furosemide 2.12 mg/kg q24h
35	150	42	130	2.7	Y	Aminophylline 5.32 mg/kg q12h Clopidogrel 18.75 mg/cat q24h Pimobendan 0.53 mg/kg q12h Furosemide 2 mg/kg q12h KCl 60 mEq q24h
36	190	24	110	4.06	N	Aminophylline 5.32 mg/kg q12h Clopidogrel 18.75 mg/cat q24h Pimobendan 0.53 mg/kg q12h Furosemide 2 mg/kg q12h KCl 60 mEq 24h
37	180	40	110	N/A	N	Aminophylline 5.32 mg/kg q12h Clopidogrel 18.75 mg/cat q24h Pimobendan 0.53 mg/kg q12h Furosemide 1.4 mg/kg q12h KCl 60 mEq 24h
41	168	60	100	2.92	Y	Aminophylline 5.32 mg/kg q12h Clopidogrel 18.75 mg/cat q24h Pimobendan 0.53 mg/kg q12h Furosemide 1.4 mg/kg q12h KCl 60 mEq 24h
42	250	48	120	3.23	N	Aminophylline 5.32 mg/kg q12h Clopidogrel 18.75 mg/cat q24h Pimobendan 0.53 mg/kg q12h Furosemide 1.4 mg/kg q12h KCl 60 mEq 24h

Table 1. Chronological summary of vital signs, potassium, clinical signs and treatment in a cat with sinus arrest. (Cont.)

Day	Heart rate (beats/min)	Respiratory rate (breaths/min)	Systolic blood pressure (mmHg)	Potassium (mmol/L)	Syncope (Yes/No)	Treatment (PO)
43	180	30	110	2.51	Y	Aminophylline 5.32 mg/kg q12h Clopidogrel 18.75 mg/cat q24h Pimobendan 0.53 mg/kg q12h Furosemide 1.4 mg/kg q12h KCl 60 mEq 24h
44	220	40	120	3.18	Y	Terbutaline 0.625 mg/cat q12h Clopidogrel 18.75 mg/cat q24h Pimobendan 0.53 mg/kg q12h Furosemide 1.4 mg/kg q12h KCl 60 mEq q24h
45	210	25	140	4.14	N	Terbutaline 0.625 mg/cat q12h Clopidogrel 18.75 mg/cat q24h Pimobendan 0.53 mg/kg q12h Furosemide 1.4 mg/kg q12h KCl 60 mEq q24h
46	200	20	110	3.79	N	Terbutaline 0.625 mg/cat q12h Clopidogrel 18.75 mg/kg q24h Pimobendan 0.53 mg/kg q12h Furosemide 1.4 mg/kg q12h KCl 60 mEq q24h Spironolactone 2 mg/kg q24h
80	160	40	100	3.81	Y	Terbutaline 0.625 mg/cat q12h Clopidogrel 18.75 mg/kg q24h Pimobendan 0.3 mg/kg q12h Furosemide 1.4 mg/kg q12h KCl 60 mEq q24h Spironolactone 2 mg/kg q24h
81	180	28	120	N/A	Y	Terbutaline 1.25 mg/cat q12h Clopidogrel 18.75 mg/cat q24h Pimobendan 0.3 mg/kg q12h Furosemide 1.4 mg/kg q12h KCl 60 mEq q24h Spironolactone 2 mg/kg q24h

Table 1. Chronological summary of vital signs, potassium, clinical signs and treatment in a cat with sinus arrest. (Cont.)

Day	Heart rate (beats/min)	Respiratory rate (breaths/min)	Systolic blood pressure (mmHg)	Potassium (mmol/L)	Syncope (Yes/No)	Treatment (PO)
82	160	40	N/A	N/A	N	Terbutaline 1.25 mg/cat q12h Clopidogrel 18.75 mg/cat q24h Pimobendan 0.3 mg/kg q12h Furosemide 1.4 mg/kg q12h KCl 60 mEq q24h Spironolactone 2 mg/kg q24h
86	200	24	N/A	N/A	N	Terbutaline 1.25 mg/cat q12h Clopidogrel 18.75 mg/cat q24h Pimobendan 0.3 mg/kg q12h Furosemide 1.4 mg/kg q12h KCl 60 mEq q24h Spironolactone 2 mg/kg q24h
106	Cardiac arrest	N/A	N/A	N/A	Y	Terbutaline 1.25 mg/cat q12h Clopidogrel 18.75 mg/cat q24h Pimobendan 0.3 mg/kg q12h Furosemide 1.4 mg/kg q12h KCl 60 mEq q24h Spironolactone 2 mg/kg q24h

N/A = not available

Table 2. The mean of heart rate, syncopal events, and the mean syncopal episodes interval when using aminophylline in comparison with terbutaline.

Drugs	The mean of heart rate (bpm)	Syncopal events* (times)	The mean syncopal episodes interval (days)
Aminophylline	165	5	8.4
Terbutaline	190	4	15.5

*The frequency of syncope was counted in 43 days follow-up in each treatment as shown in table 1

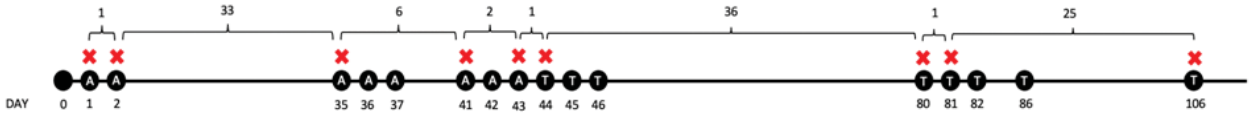

Figure 6. Timelines summary of cardiac syncopal events and interval of each syncopal episodes for aminophylline (A) and terbutaline (T) treatment.

Discussion

Syncope is a subset of collapse, a loss of postural tone suddenly, but includes loss of consciousness. Insufficient blood flow to the brain is the main cause of syncope. This can be classified as cardiogenic syncope and neurocardiogenic syncope. Cardiogenic syncope is associated with cardiogenic arrhythmias or neurocardiogenic reflexes causing hypotension. Blood pressure is estimated to fall at least 50%. Cardiac arrythmia has to be profound and sustained enough to originate systemic arterial hypotension. Asystole, such as bradyarrhythmia from sinus arrest, or a marked reduction in cardiac output could produce much degree of arrhythmias causing systemic arterial hypotension. This condition can be intermittent and might be detected only on Holter. It is fortunate that this case, we could detect the absence of electrical signal during episode of syncope simultaneously. We assume that the cause of sinus arrest in this case is because of primary cardiac disease, but the neurological cause could not be ruled out, even though the neurological examination was nonremarkable. There is limitation of the financial constraints of animal owners, making it impossible to diagnose further. Neurocardiogenic syncope is well-known as vasovagal syncope in small animals. It is the consequence of a profound bradyarrhythmia combine with reflex vasodilation generating hypotension. The mechanism is believed that autonomic nervous system was sudden failed, sympathetic tone terminated and rapid increase in vagal tone took place. The explicit mechanism remains unknown. Triggering events are usually associated with intense excitement situation as greeting owner etc. Structural heart disease, for example aortic stenosis, stimulating high left ventricular pressure which promote ventricular pressure receptors and trigger this reflex (Martin 2016).

Feline nonspecific phenotype cardiomyopathy (NCM) is a feline cardiomyopathy category that describes an abnormal echocardiographic pattern which does not match of all common cardiomyopathies in cat including hypertrophic cardiomyopathy (HCM), dilated cardiomyopathy (DCM), restrictive cardiomyopathy (RCM) and arrhythmogenic right ventricular cardiomyopathy (ARVC). It is formerly known as unclassified cardiomyopathy. NCM was originally described as an echocardiographic finding of a large left atrium (LA) and a common figure of the left ventricle without abnormal diastolic function (Kittleson and Côté 2021). The echocardiographic finding in this case showed left atrial enlargement (La/AO: 1.85) with normal systolic and diastolic function. Parameters including NLVIDd (0.89), %FS (58.15), MV E:A ratio (1.54), IVSDd (0.43 cm.) and LVPWd (0.44 cm.). It is not compatible with another category of feline cardiomyopathy so the cat has cardiomyopathy-nonspecific phenotype.

Sick sinus syndrome (SSS) is the most common cause of symptomatic sinus arrest. This condition is often found in many dog breeds including Miniature Schnauzers, Cocker Spaniel, West Highland White Terrier and

Dachshunds, rare in cats (Tilley et al., 2008). The disturbance is not only affected in sinus activity, but also involved in those of other cardiac conductive tissues such as AV conduction, supraventricular and ventricular excitability. The cause is still unknown. The histological finding of SSS in dogs showed extensive depletion of nodal cells with fatty or fibrofatty tissue replacement (Machida and Hirakawa 2021). In human, they believe that the most common cause of intrinsic changes in the SA node is degenerative fibrosis of nodal tissue producing sick sinus syndrome. The diagnosis is maybe difficult. It relies on repeated and sufficiently long ECG, approximately 2-3 minutes. Sinus bradycardia maybe only present in the early stage. The dysrhythmias of the syndrome are hardly detected if the patient is asymptomatic. Holter monitoring is the most common method used in diagnosis (Adán and Crown 2003). Severe hyperkalemia, a serum potassium level of >7.5-8mEq/L, might be one of the causes inducing cardiac arrest, but this case experienced intermittent hypokalemia, as shown in table 1, which we presume it was a consequence of furosemide administration after investigating possible causes and no abnormalities were found. If there were smaller and biphasic T waves presented on ECG, it is the result of hypokalemia (Madron 2000). An atropine response test could predict the ability of the heart to respond to vagolytic drugs and long-term drug management success. Propantheline or hyoscyamine or aminophylline/theophylline help improving the condition by reducing bradycardia episodes and sinus arrest. Median survival time of dogs with SSS was 538 days. 54% of SSS dogs were successfully syncope controlled by using positive chronotropic drugs (Ward et al., 2016). Canine and feline bradyarrhythmia are considered pacemaker implantation as a first line therapy in most cases, improving quality of life and survival time (Santilli et al., 2019).

Aminophylline was initially prescribed in order to increase cardiac output. It is a methylated xanthine derivative which combine theophylline and ethylenediamine. A previous study of aminophylline on cardiovascular effects demonstrated myocardial contractility stimulation effects not only depend on dose, but also depend on route of administration (Rutherford et al., 1981), and it could temporary increase cardiac output (Howarth et al., 1947). Aminophylline, used to manage SSS, is recommended at dose 6-10 mg/kg PO q8h (Madron 2000). The unresponsiveness of using aminophylline in this case might be depended on dose.

Terbutaline 0.3 mg PO q8h was prescribed in a cat with history of bradycardia. The cat was reported to respond well after started terbutaline and had no additional event of collapsing after discharged for 3 months. There was no additional follow-up data (Penning et al., 2009). Ward et al. (2016) prescribed oral positive chronotropic drugs including theophylline, propantheline, hyoscyamine and terbutaline. The specific those of drugs chosen did not affect the treatment responsiveness. Terbutaline stimulates systemic vascular effect inducing heart rate and cardiac output (Hansen et al., 1988). Cilostazol is other medical choices to increase heart rate and prolong survival time in cats with syncope. High-grade atrioventricular block in a cat was reported using long-term management with cilostazol, an antiplatelet aggregation with phosphodiesterase III inhibitor, at 8-10 mg/kg PO q12h. It prolonged survival time for 650 days without surgical correction (Iwasa et al., 2019).

Pimobendan is a benzimidazole pyridazinone drug, act as positive inotrope and balanced vasodilatory effect. It improved left atrial function in HCM cats with CHF, but did not worsen HOCM (Oldach et al., 2019). Pimobendan 0.075-0.5 mg/kg PO q12h showed significant advantage in survival time not only in HCM-affected cat, but also

HOCM-affected cat (Reina-Doreste et al., 2014). The most common dose prescription of pimobendan is 1.25 mg PO q12h per cat (median initially total daily dose of 0.56 mg/kg/day; range 0.12-1.74 mg/kg/day). The cats with CHF, regardless of HCM or HOCM, are safe and well tolerated to pimobendan (Ward et al., 2020). Study has shown that high and standard doses of pimobendan do not differ in cardiac performance of dogs with natural-occurring myxomatous mitral valve disease (MMVD) (Kaplan et al., 2022). On the other hand, experimentally induced mitral regurgitation (MR) had proved to be benefit on using the high dose of pimobendan. They found that pimobendan has dose-dependent manner to decrease left atrial pressure caused by experimental MR (Suzuki et al., 2011). Further studies evaluating high dose pimobendan on long-term clinical benefit for animals with congestive heart disease are warranted.

In conclusion, this case report mainly describes medical management in a cat with sinus arrest without atropine response by using terbutaline. In this case, terbutaline can increase the mean of heart rate to 190 bpm which might advantage over aminophylline that is 165 bpm. Terbutaline also helps increasing mean syncopal episodes interval from 8.4 days of aminophylline treatment to 15.5 days of terbutaline treatment, as shown in table 2, and prolonging survival time for 62 days. Timelines summary of cardiac syncopal events and interval of each syncopal episodes for aminophylline and terbutaline treatment is shown in Figure 6. Atropine response test was negative but the cat still responded well to terbutaline. The syncope recurred even though we maximize the terbutaline and pimobendan dosage, but the effectiveness of pimobendan is not dose dependent in natural-occurring heart disease, as mentioned above. Therefore, we assumed that terbutaline improves the clinical symptoms. We hypotheses the recurrences might be the consequence of cerebral hypoxia during the episodes. MRI should be done to investigate brain lesions. A limitation of this study is the lack of Holter-monitoring. It could detect any electrical abnormalities more precisely, especially when the cat is in normal condition.

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