## Sick Sinus Syndrome (SSS) in a Maltese Dog Concurrent with Mitral Valve Endocardiosis (MVE)

Chul Park, Dong-in Jung, Ha-Jung Kim, Byeong-Teck Kang, Ju-Won Kim, Chae-Young Lim, Jong-Hyun Yoo\*, and Hee-Myung Park!

Department of veterinary internal medicine, College of veterinary medicine, Konkuk University,
#1 Hwayang-dong, Kwangjin-gu, Seoul 143-701, Korea
\*Department of veterinary internal medicine, College of veterinary medicine, Seoul National University

**Abstract:** A 13-year old, female Maltese dog was presented due to a five-month history of episodic syncope. A diagnosis of sick sinus syndrome (SSS) with mitral valve endocardiosis (MVE) was made based on history takings, physical and cardiac examination, complete blood count (CBC), serum chemistry profiles, radiography, electrocardiography (ECG), atropine response test, hormonal assay, and echocardiography. In this case, SSS was definitely diagnosed by evaluation of ECG recording following atropine administration. Clinical signs were improved with medical management of theophylline (THEOLAN®, KunWha Pharm, Seoul, Korea, 20 mg/kg, PO, BID). After 10 more month survival, the dog died of respiratory distress and shock during the operation of abdominal mass removal in local animal hospital. Unfortunately, we were not able to perform necropsy after death due to owner's decline. This case demonstrates that theophylline can be used in management of dog with SSS.

Key words: sick sinus syndrome, syncope, atropine response test.

### Introduction

Sick sinus syndrome (SSS) is the term used to describe primary conduction abnormalities that produce erratic, inconsistent sinoatrial (SA) depolarizations, inadequate subsidiary escape rhythms, and clinical signs of bradycardia. These abnormalities include inappropriate sinus bradycardia, severe sinus arrest and/or SA block, which are important causes of clinical bradycardia<sup>6,13</sup>. The most common clinical signs are episodic weakness and syncope because a reduction in cardiac output may result in hypoperfusion of vital organs, like brain<sup>14</sup>. The cardiac event recorder is particularly useful in small-breed dogs and cats that would be encumbered by a Holter monitor, and in patients with a history of more than one syncopal episode a week4. Syncope or fainting refers to a sudden, yet transient loss of consciousness due to a deprivation of energy substrate, either oxygen or glucose, that briefly impairs the cerebral metabolism. Many dogs and people with SSS also appear to have coexisting dysfunction of the atrioventricular (AV) nodal and intraventricular subsidiary pacemakers, resulting in a failure to generate appropriate escape rhythms<sup>1,15</sup>.

The condition has been reported in many breeds of dog, but female miniature Schnauzers appear to be more susceptible than other breeds<sup>5</sup>. The definitive diagnosis for SSS has been performed through atropine response test. A poor response (less than 50 percent increase in heart rate) may support SSS<sup>14</sup>. If the animal is asymptomatic or has mild clinical signs, no therapy is required. Only severe, symptomatic bradycardias

(syncope, malaise) warrant specific treatment with drugs or pacemaker implantation.

This case report was performed to describe clinical and electrocardiographic characteristics in dogs with SSS.

#### Case Report

A 13-year-old, female Maltese dog weighing 6.04 kg was investigated for frequent syncopal episodes. The syncopal episodes were first noted around five months before presentation, which were progressively increasing in frequency. Upon initial presentation to our animal hospital, the dog was dyspneic and leaned towards obesity (body condition score; 4/ 5). She was evaluated by physical and cardiac examination, a complete blood count (CBC), a standard biochemistry profile, electrocardiography (ECG-NIHON KOHDEN Cardiofax GEM (ECG-9020K)-), thoracic radiography, hormonal assay, and echocardiography. Atropine response test was applied for the definitive diagnosis. Weak femoral pulses were detected during physical examination and the heart beats were decreased between 50 and 70 beats per minute (bpm). With respect to the cardiovascular system, the dog had a grade II to III/VI left-sided systolic regurgitant murmur. CBC and serum biochemical analyses revealed elevated alkaline phosphatase (ALP, 903 U/L; reference range, 0 to 140 U/L). Radiography of the thorax showed mild cardiomegaly (Vertebral heart score; VHS=12.0) without evidence of pulmonary venous congestion or congestive heart failure (Fig 1). Sternal contact was increased on thoracic radiographic findings, which are suggestive of right atrial enlargement (Fig 1).

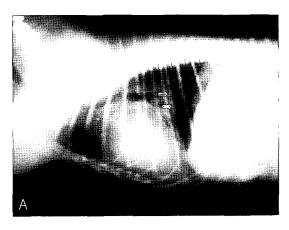
The dog had regular sinus bradycardia with sinus arrest or block and occasional ventricular escape rhythms were present

<sup>1</sup>Corresponding author.

E-mail: parkhee@konkuk.ac.kr

(Fig 2). Frequently, prolonged RR intervals and notched R waves with slurring T waves were evident (Fig 2). For the definitive diagnosis, the patient was given atropine (Atropine sulfate; Je il pharm Co, Daegu, Korea, 0.04 mg/kg, intravenously). Her heart rate and rhythm were monitored by ECG

20 minutes after atropine administration. The dog responded with blunted increases of less than 50 percent in heart rate (Fig 3). Hypothyroidism was ruled out through the thyroid hormonal assay. Total T4 concentration was  $1.71 \,\mu\text{g/dl}$  (reference range;  $1.0 \, \text{to} \, 4.0 \,\mu\text{g/dl}$ ) and thyroid-stimulating hor-



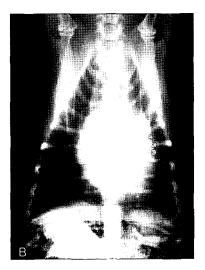


Fig 1. Right lateral (A) and ventrodorsal (B) thoracic radiographs with mild biatrial enlargement. A, The enlarged left auricle is seen (thin arrows), and there is mild sternal contact. B, Note the bulge in the left cardiac border at the 3 o'clock position (small arrowheads).

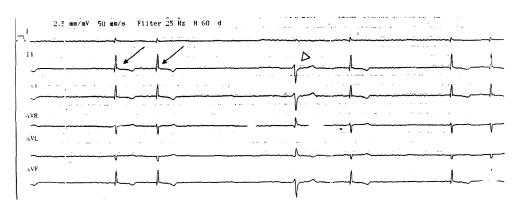


Fig 2. Resting electrocardiography shows ventricular escape rhythm (arrow head), sinus block, and sinus bradycardia. Notched R (thin arrows) waves are illustrated every QRS complex on lead II electrocardiographic recording.

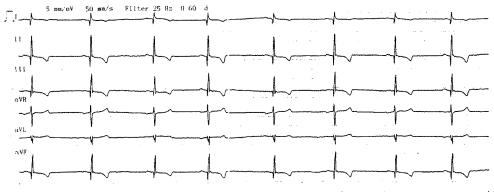


Fig 3. Electrocardiography taken 20 minutes after the IV administration of atropine shows only a poor response with an increase in the heart rate to 86 bpm and the suppression of periods of sinus block.

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mone (TSH) stimulation test revealed normal response (preinjection of TSH;  $2.1 \mu g/dl$  in total T4 and 6 hours after TSH injection;  $6.4 \mu g/dl$  in total T4), which is not suggestive of hypothyroidism.

On echocardiographic examination, the mitral valve was thickened and nodular, and there was mild left atrial enlargement (Fig 4). However, mitral valvular prolapse and regurgitation were not remarkable. Fractional shortening (FS) was 68%, indicating impaired cardiac function.

The dog was treated with furosemide (Lasix®, Handok Phama Co, Chungbuk, Korea, 2 mg/kg, PO, BID), enalapril (Emalein®, Poongrim Pharm, Seoul, Korea, 0.5 mg/kg, PO, BID), and theophylline (THEOLAN®, KunWha Pharm, Seoul, Korea, 20 mg/kg, PO, BID). The patient's clinical signs had been improved by administering oral theophylline. ECG was regularly recorded during therapy, showing mildly improved heart rate without ventricular escape rhythms (Fig 5). How-

ever, she died during the operation of abdominal mass removal in local animal hospital.

#### Discussion

SSS is a progressive heart disease characterized by a variety of arrhythmias, including sinus bradycardia, sinus arrest, paroxysmal atrial tachycardia, intermittent AV nodal block, and lack of ventricular escape complexes. The pathophysiological basis of the syndrome has yet to be fully elucidated, with most cases being deemed idiopathic<sup>7,13</sup>. In this case, the electrocardiographic abnormalities included sinus bradycardia, intermittent sinus arrest or block and ventricular escape rhythms. Clinical signs of the disease are variable with dogs being asymptomatic or showing syncope, seizures, and episodic weakness<sup>5,7,11</sup>. This patient had had syncopal episode and fainting and these clinical signs of the dog were referable to a

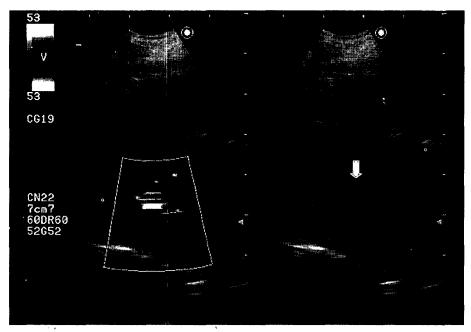


Fig 4. Echocardiographic examination of right parasternal long axis view with color flow imaging shows mild thickening of mitral valve leaflets (arrow). The left atrium is also dilated. However, mitral valvular prolapse and regurgitation were not remarkable.

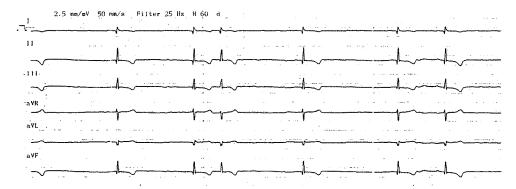


Fig 5. Regular electrocardiography recording was performed during therapy. Heart rates were mildly increased from 80 bpm to 90 bpm and ventricular escape rhythms were disappeared.

decrease in cardiac output and hypoperfusion of the brain, heart and skeletal muscle. Notched R waves and deep slurring T waves might support myocardial ischemia and even infarction on the ECG records of this patient. Also, atropine induces vagal inhibition by promoting a parasympatholytic effect and atropine response test principally demonstrates that a bradycardia is of sinus origin. In spite of unclear understanding, possible causes of SSS include ischaemic heart disease affecting the sinus node artery, or the replacement of the sinus node and atrioventricular tissue with fibrous connective tissue 8. Fibrosis of the node or perinodal tissues is found in a substantial proportion of elderly human patients<sup>12</sup>.

There are several non-cardiac conditions that could result in signs of bradycardia. Hypothyroidism may cause various degrees of sinus dysfunction, decreasing cardiac contractility and conduction. Enhanced vagal tone in hypothyroidism also slows the heart rate and accentuates sinus arrhythmias. In the present case, hypothyroidism was primary differential diagnosis and ruled out by performing TSH stimulation test. Digitalis toxicity can cause electrocardiographic changes consistent with SSS<sup>13</sup>. A chronic respiratory syndrome, idiopathic pulmonary fibrosis (IPF), has recently been recognized and characterized in the West Highland white terrier<sup>3</sup>. In this case report, however, the patient didn't show any clinical signs of respiratory disease. According to a report<sup>9</sup>, if the relationship between the clinical signs and significant electrocardiographic abnormalities is clear, the diagnosis of SSS can be established. We used atropine to evaluate the function of the sinus node and the dog showed only poor response to atropine, meaning sinus dysfunction and SSS.

This patient had increased FS of 68%. Usually, FS may be increased in early mitral valve endocardiosis (MVE) and hypertrophic cardiomyopathy and the dog was in early stage of MVE based on no signs of congestive heart failure (CHF) and mitral regurgitation. Both ECG and echocardiography showed hypertrophied left ventricle. Dogs with any degree of mitral valve insufficiency (MVI) from mild to severe, whether or not they are in CHF, will have FSs greater than 50% if they have no myocardial dysfunction<sup>2</sup>.

Treatment for those cases that are aclinical or showing minimal clinical signs is not usually implemented<sup>15</sup>. If there are severe clinical problems, injectable atropine or other oral anticholinergic agents and theophylline may alleviate these signs. Anticholinergies may cause undesirable side effects of conspitation, papillary dilation, and eye and mucous membrane dryness<sup>7</sup>. Alternatively, a sympathomimetic agent can be administered. Oral theophylline has been used successfully in people with SSS<sup>10</sup>. Therefore, this dog was treated with theophylline for long-term base. An artificial ventricular-demand pacemaker is required for long-term control of bradycardias. A pacemaker should be implanted when a causal relationship has been demonstrated between the bradycardia and the clinical signs<sup>9</sup>. Actually, the pacemaker option was not feasible in this patient because the patient was well responsive to medical therapy and pacemaker implantation was highly expensive.

This report describes SSS in an old female Maltese dog that was considered to have concurrent MVE.

#### **Conclusions**

We diagnosed this patient with SSS concurrent with MVE based on history takings, physical examination, CBC, serum chemistry, radiography, echocardiography, ECG, hormonal assay, and atropine response test. This case represents that ECG recordings and atropine response test were sensitive, specific, and accurate methods for the diagnosis of SSS in this patient. Differential diagnosis was necessary for a definitive diagnosis. Medical management may be successful in some cases, but the implantation of a pacemaker can provide more effective long-term control. In this case, the owner didn't want to take pacemaker implantation due to high expense. The patient had survived for 10 more months with medical therapy.

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# 말티즈견에서 발생한 Mitral Valve Endocardiosis (MVE)를 동반한 Sick Sinus Syndrome (SSS)에 대한 증례

박 철ㆍ정동인ㆍ김하정ㆍ강병택ㆍ김주원ㆍ임채영ㆍ유종현\*ㆍ박희명

건국대학교 수의과대학 수의내과학교실 \*서울대학교 수의과대학 수의내과학교실

요 약: 13년령의 암컷 말티즈견이 5개월간의 일시적인 기절현상 (syncope) 을 주증상으로 내원하였다. 환축은 병력 청취, 신체검사, 심장검사, 총혈액검사, 혈액 화학적 검사, 방사선학적 검사, 심전도 검사, 아트로핀 반응 검사 (atropine response test), 호르몬 검사, 심전도 검사 등을 통해 심장의 문제가 있는 것으로 진단 되었다. 본 증례에서 심전도 검사는 아트로핀 투여에 의한 심전도 기록을 통해 sick sinus syndrome을 확진 하는데 중요한 역할을 하였다. 임상 증상은 테오필린 (THEOLAN®, 근화제약, 서울, 한국, 20 mg/kg, 경구 투여, 1일 2회)을 복용하면서 개선되었다. 환축은 10개월을 생존하였으나 지역 병원에서 복강의 종괴를 제거하는 수술을 받는 중 호흡곤란과 쇼크로 사망하였다. 사망 후보호자의 반대로 부검은 이루어 지지 않았다.

주요어: sick sinus syndrome, syncope, atropine response test.