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Primary Pulmonary Hypertension in a Maltese Dog

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Abstract : A 1-year-old castrated male Maltese dog (weighing 2.4 kg) was presented with primary complaints of occasional coughing, dyspnea and exercise intolerance. Based on diagnostic findings including paradoxical split S2, diastolic regurgitant murmur, marked dilation of pulmonary artery, right ventricular eccentric hypertrophy with thickening of ventricular septum, severe tricuspid and pulmonic regurgitation (5.4 m/sec and 3.4 m/sec, respectively) and the absence of any congenital intracardiac shunting, obstructive pulmonary diseases and systemic diseases associated with right ventricular pressure overload or pulmonary hyperperfusion, the case was tentatively diagnosed as primary pulmonary hypertension. The dog was treated with furosemide, aspirin and oxygen supplementation. This case report described a rare case of primary pulmonary hypertension in a Maltese dog.

Key words **:** pulmonary hypertension, tricuspid, regurgitation, paradoxical split S2.

Introduction

Pulmonary hypertension (PHT) is defined as a clinical condition if the systolic pressure of pulmonary artery exceeds over 30 mmHg (15). PHT can be occurred by either primary or secondary disease of the pulmonary vasculatures. The main causes of secondary PHT include diseases causing the increased pulmonary blood flow, increased pulmonary vascular resistance, or chronic elevations of left atrial pressure (7,11,15). The most well known cause of PHT in dogs was dirofilariasis (heartworm). Primary PHT is often called as idiopathic PHT and is occurred by abnormal pulmonary arterial hypertension of unknown etiologies in humans and dogs (5,16). However primary PHT has been rarely reported in veterinary literature. Histopathological feature of primary PHT is an abnormal thickening of tunica media of muscular pulmonary arteries, which is often called as a plexogenic pulmonary arteriopathy in human (3). Although the differentiation of primary PHT from secondary causes is sometimes difficult, the diagnosis of primary PH should exclude secondary causes which can increase the pulmonary blood pressure (e.g. chronic obstructive pulmonary disease, heartworm infestation, obliteration of pulmonary vasculature, right-to left cardiac shunts, obstructive valvular diseases) in dogs (7,8,11,15).

Invasive cardiac catheterization for measuring pulmonary arterial pressure and pulmonary wedge pressure was required to evaluate the pressure overload in pulmonary artery and right cardiac chambers, and to predict the disease progression and prognosis of PHT in dogs (15). Thanks to recent development of Doppler echocardiography, non-invasive Doppler method using the modified Bernoulli equation ($\Delta P = 4 \times velocity^2$) has been developed and is widely used to determine the severity of PHT (2,4,8,11). In the absence of pulmonic stenosis, systolic or diastolic pulmonary arterial pressure can be measured by application of the modified Bernoulli equation to the maximal velocity of tricuspid regurgitation or pulmonic insufficiency, respectively (9). Diagnostic criteria for PHT based on Doppler echocardiographical findings are a peak tricuspid regurgitant velocity 2.8 m/sec or pulmonic insufficiency velocity 2.2 m/sec. PHT can be further classified mild (< 50 mmHg), moderate (51-75 mmHg), or severe (> 75 mmHg), based on the pressure gradient between right atrium (RA) and right ventricle (RV) in dogs (11). This is a case report of primary PHT occurred in a Maltese dog.

Case Report

A 1-year-old castrated male Maltese dog (weighing 2.4 kg) was presented at the Veterinary Teaching Hospital, Kangwon National University with primary complaints of occasional coughing, dyspnea and exercise intolerance. The dog had history of heart murmur and exercise intolerance from the early of life. In the physical examination, split S2 and a grade IV/VI regurgitant murmur were heard over the right apex and base (Fig 1). The 12-lead electrocardiogram showed bi-ventricular enlargement (Tall QRS and deep S wave in lead II) with sinus tachycardia (180-200 bpm) and occasional sinus arrest. The systolic blood pressure measured by Doppler method in the forelimb was 105 mmHg. The capillary refill time was delayed (over 3.5 sec). On the day of presentation, no significant abnormalities were observed in routine hematology and

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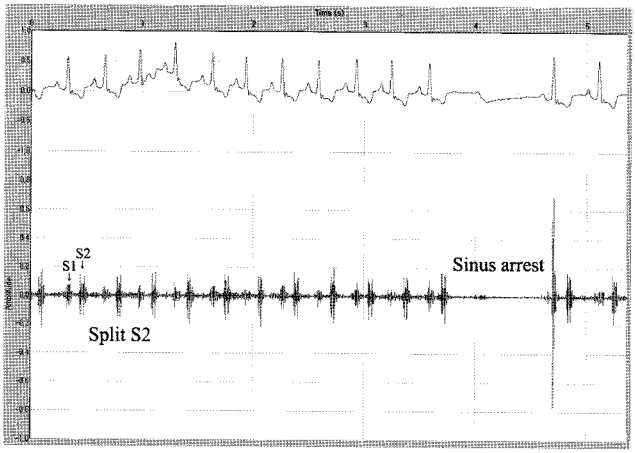

Fig 1. The phonocardiogram. The phonocardiogram revealed a paradoxical split S2, systolic (tricuspid regurgitation) and diastolic (pulmonic regurgitation) regurgitant murmur, and a sinus arrest.

blood chemistry except severe polycythemia (70% of packed cell volume; normal range: 37-55%) and increased level of blood urea (45 mg/dL). In this dog, negative results were obtained from heartworm antigen test (SNAP, Idexx, USA) and modified Knott's test.

Radiographic studies of the thoracic and abdominal cavities revealed a marked right-sided cardiomegaly, enlarged pulmonary arteries (a marked bulging of pulmonary artery), distended posterior vena cava, and an enlarged hepatic shadow (Fig 2, 3).

Two-dimensional and M-mode echocardiography revealed severe right ventricular eccentric hypertrophy, small left ventricle and marked thickening and flattening of ventricular

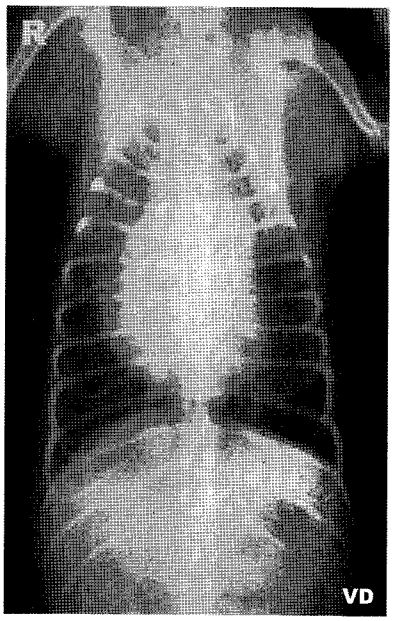

Fig 2. Thoracic radiography (ventrodorsal projection). Thoracic radiography revealed a marked bulging of pulmonary artery and right-sided cardiac enlargement.

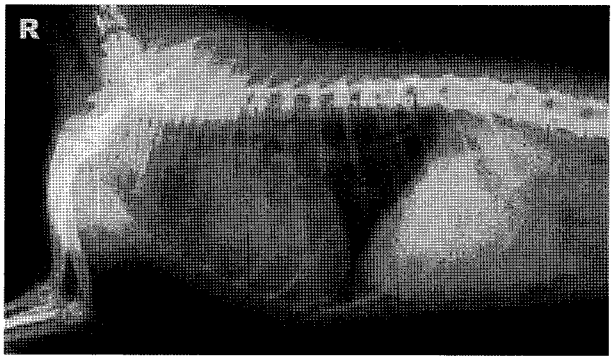

Fig 3. Thoracic radiography (lateral projection). Thoracic radiography revealed enlarged pulmonary arteries, distended posterior vena cava, right-sided cardiomegaly, and an enlarged hepatic shadow.

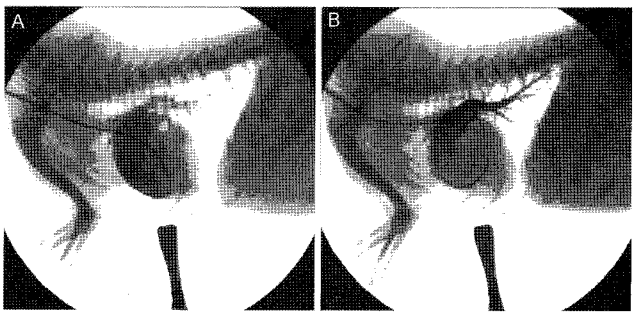

Fig 4. Angiography. There was marked enlargement of pulmonary root (A). However there was no narrowing of pulmonary annulus. Subsequent angiography also revealed there was no physical shunting between pulmonary artery and descending aorta (B).

septum (Fig 5). The mitral and aortic valves were intact. No turbulent blood flows were detected in the left ventricular outflow tract. Furthermore atrial and ventricular septa were intact. Color and spectral Doppler echocardiography detected high-velocity regurgitation jet flow across the tricuspid and pulmonic valves (Fig 6). The peak tricuspid regurgitant velocity was 5.4 m/s (Fig 6D), whereas pulmonic insufficiency velocity was 3.4 m/s (Fig 6B). Based on the modified Bernoulli equation ($\Delta P = 4 \times \text{velocity}^2$), the pressure gradient between RA and RV was over 110 mm/Hg, indicating severe pulmonary hypertension. Since no other abnormalities causing PHT have been identified, the case was tentatively diagnosed as primary PHT, based on diagnostic findings including paradoxical split S2, diastolic regurgitant murmur, marked dilation of pulmonary artery, right ventricular eccentric hypertrophy with thickening of ventricular septum, severe tricuspid and pulmonic regurgitation and the absence of any congenital intracardiac shunting, obstructive pulmonary diseases and systemic diseases associated with right ventricular pressure overload or pulmonary hyperperfusion.

Subsequent angiographical studies under general anesthesia found neither obstructive right ventricular obstructive diseases

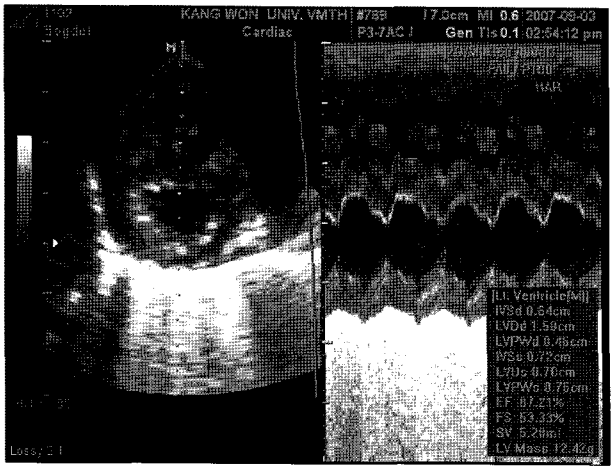

Fig 5. The echocardiography. The 2-dimensional and M-mode echocardiography revealed severe right ventricular eccentric hypertrophy, small left ventricle, and marked thickening and flattening of ventricular septum.

(e.g. pulmonic stenosis) nor shunt flow from right-to-left chambers (e.g. patent ductus arteriosus) (Fig 4).

The dog was initially treated with oxygen (oxygen cage, 5 L/min), furosemide (2 mg/kg/day, PO), and aspirin (5 mg/kg/day, PO). Since the dog's systolic blood pressure was lower than normal reference range, vasodilators were not administered. The clinical condition was deteriorated rapidly despite the intensive medical treatment. The dog died three days after the presentation. Because the owner refused the postmortem examination, unfortunately, further histopathological examination was not able to perform.

Discussion

Exclusion of secondary causes of PHT in this dog was difficult and complicated. However, the right ventricular hypertrophy and right atrial dilation in this dog implied the PHT was moderate to severe and was not occurred recently. No evidence of pulmonary disease in CBC, lung sound auscultation and chest X-ray ruled out primary lung diseases. If dog has acute pulmonary disease causing cyanosis, the dog might not have right sided cardiac remodeling (e.g. RA dilation or RV hypertrophy). If the dog had chronic obstructive pulmonary diseases, there would be evidence(s) in CBC, lung sound auscultation and chest X-ray. Polycythemia and lower arterial oxygen tension were only secondary findings occurred by poor pulmonary ventilation and perfusion. Those finding could be happened by any kind of chronic pulmonary dis-

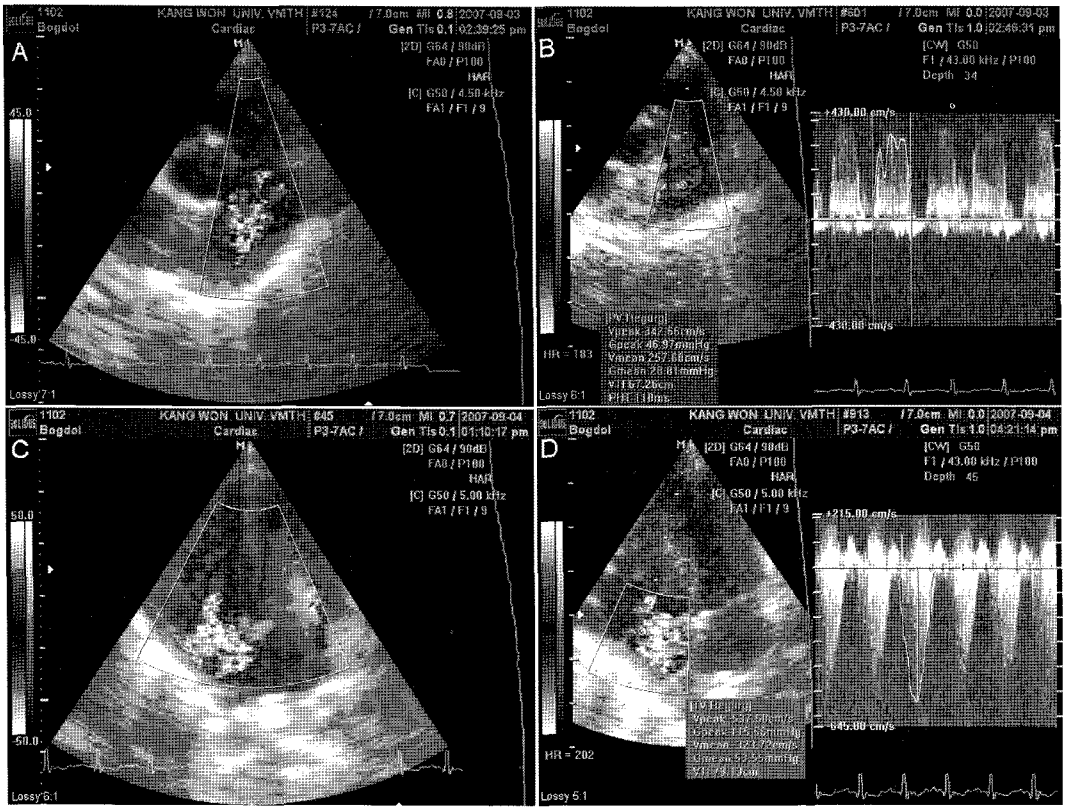

Fig 6. The color and spectral Doppler echocardiography. The color and spectral Doppler echocardiography of this case detected high-velocity regurgitation jet flow across the pulmonic (A) and tricuspid valves (C). The peak pulmonic insufficiency velocity was 3.4 m/s (B), whereas tricuspid regurgitant velocity was 5.4 m/s (D). The pressure gradient between pulmonary artery and right ventricle was 46 mmg/Hg, while the pressure gradient between right atrium and ventricle was 116 mmg/Hg.

eases and right-to-left intracardiac shunts. Those findings were not informative for ruling out etiology of PHT in this case. Our angiographic study clearly ruled out cardiac diseases causing right-to-left intracardiac shunt. Primary cause of pulmonary thromboembolism in dogs is heartworm infestation. However, the dog was negative in heartworm antigen test and modified Knott's test. Ultrasonographical study also failed to reveal heartworm infestation in this case. Considering patient's age, the primary cause for PHT might be congenital or idiopathic. However, our angiography clearly revealed no abnormalities in pulmonary vasculatures. Generally speaking, primary PHT is characterized by abnormal pulmonary arterial hypertension of unknown etiologies. Excluding primary cardiac and pulmonary diseases for this case, we believed the cause of PHT is probably primary.

Accurate measurement of pressure gradient in the RA-to-RV or the RV-to-pulmonary artery (PA) is important to predict the prognosis of the patient. Although measuring pulmonary wedge pressure or pulmonary arterial pressure is the single most important test for measuring pressure gradient in the RA-to-RV or the RV-to-PA (15), those methods were not popularly applied in clinical situation, because those methods are required the invasive cardiac catheterization and expensive measuring equipment. In clinical situation, Doppler echocardiography and application of Bernoulli equation to the maximal velocity of jet flows (to calculate RV-to-RA and PA-to-RV pressure gradients) are more widely used and has been proven effective and accurate in humans and dogs (2,4,8,11). This method was also effective for our case. Based on the Bernoulli equation to the maximal velocity of jet flows in tricuspid and pulmonary valves, the severity of PHT in our case was severe pulmonary hypertension (RV-to-RA gradient 116.64 mmHg, PA-to-RV pressure gradient 46.24 mmHg).

Therapeutic aims of PHT are i) correcting the specific hemodynamic abnormalities (addressing underlying causes), ii) reducing pulmonary vascular resistance, and iii) reducing right ventricular pressure overload (12). However, there is no perfect cure for primary pulmonary hypertension. Oxygen is the most potent vasodilator. Therefore oxygen therapy is essential for any type of PHT. Although diuretics are useful for reducing right ventricular preload, aggressive diuresis should be avoided because it can compromise cardiac output by excessively reducing preload (12). Although the pharmacological benefits of anticoagulants in nonthromboembolic pulmonary hypertension have not been clearly defined, survival rate in idiopathic PHT was significantly increased in human patients receiving anticoagulant therapy (6,14). Calcium channel blockers (CCB) are the first choice of drug for PHT in human (13). However recent case study in dogs found that the use of CCB was not favorable, because this medication often induced profound systemic hypertension (12). Short-acting vasodilators (adenosine, inhaled nitric oxide, or prostaglandin I_2 [PGI_2]) are also useful to reduce blood pressure in pulmonary artery, although no studies have evaluated short-acting pulmonary vasodilator trials and subsequent therapy with calcium channel blockers in veterinary fields. Intravenous PGI_2 (Prostacyclin) has been shown to improve exercise capacity, hemodynamics, vascular remodeling, and short- and long-term survival in humans (10). Clinical effect of prostacyclin or its analogs are currently being investigated in human (10). Other promising pulmonary vasodilators being researched for primary and secondary PHT include endothelin receptor antagonists (bosentan) and phosphodiesterase inhibitors (sildenafil) (10). One veterinary study has found that sildenafil was effective for controlling PHT in dogs (1). Although there were several options for treating our case, our medical treatment was not favorable. Use of prostacyclin and sildenafil may retard the disease progression in our case. However, we could not obtain those drugs at that time, because of the strict regulation for use of sildenafil in Korea. The therapeutic rationales for oxygen therapy and furosemide were to increase pulmonary perfusion and tissue oxygenation, and to reduce preload in right cardiac chambers, respectively. Aspirin was administered to prevent thromboembolism after angiography and to prevent fibrosis in pulmonary arterial vasculatures.

Although the prognosis for PHT depends on the underlying cause, the severity of pulmonary hypertension, and reversibility of vascular pathology, in general, prognosis of idiopathic (primary) PHT is poor to grave (12). Medical treatment for PHT only provides short-term relief and retardation of disease progression.

In conclusion, this case study described clinical and diagnostic features of primary PHT in a dog. This is the case report describing primary PHT in a Maltese dog.

Acknowledgements

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말티즈 견에서 발생한 원발성 폐동맥 고혈압증

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요 약 : 중성화된 1년령 말티즈 개(2.4 kg)가 간헐적인 기침, 호흡곤란, 운동 불내성을 주요 증상으로 내원하였다. 신체검사 시 제 2음 모순 분열, 확장기 역류성 잡음이 관찰되었으며, 심장초음파에서 주폐동맥의 확장, 심실 중격 비대를 동반한 우심실 편심성 비대, 심각한 삼첨판 역류증과 폐동맥 역류증 (5.4 m/sec, 3.4 m/sec)이 관찰되었다. 이러한 진단검사 결과를 바탕으로, 본 증례를 선천성 심장 내 단락, 폐쇄성 폐질환, 그리고 우심계의 압력 과부하 또는 폐혈관계 과관류와 관련된 전신질환과 감별하여 원발성 폐동맥 고혈압증으로 잠정진단 하였다. 환자는 furosemide와 aspirin을 투여하여, 산소요법을 실시하였다. 본 증례는 드물게 발생하는 개의 원발성 폐동맥 고혈압이다.

주요어 : 폐성고혈압, 삼첨판, 역류, 제 2음 모순 분열