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Transcatheter Intravascular Stent Placement in a Shih Tzu Dog with Refractory Pulmonic Stenosis

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Abstract : A 4-year-old intact male Shih Tzu dog (5.4 kg of body weight) was referred with primary complaints of heart murmur and exercise intolerance. Diagnostic studies found severe valvular pulmonic stenosis (peak velocity of 6.4 m/s, pressure gradient 165 mmHg). The dog was treated with 3 cm (length) × 1.5 cm (diameter) of Palmaz biliary stent. The outcome of stent placement was favorable and remarkably reduced the severity of PS (6.4 m/s to 3.0 m/s of peak velocity). Clinical condition was remarkably improved with the absence of cardiac murmur, although mild pulmonic regurgitation existed from the day of stent placement. To our best knowledge, this case is the first clinical trial for treating PS with intravascular stent in Korea.

Key words **:** pulmonic stenosis, stent, transcatheter, dog, PS.

Introduction

Pulmonic stenosis (PS) is one of commonly occurred congenital cardiac defects in dogs and causes clinical manifestation secondary to pressure overload of the right ventricle. Due to the right ventricular concentric hypertrophy, the right ventricular compliance and dispensability may be reduced in direct proportion to the severity of the right ventricular outflow (RVOF) obstruction. Generally, > 5 m/s of the peak velocity of jet flow at RVOF (pressure gradient over 100 mmHg) is regarded as severe and is needed for immediate surgical or transcatheter cardiac intervention. Clinical signs associated with PS are varied by the severity, but are related to right heart failure including ascites, hepatomegaly, syncope and exercise intolerance (11).

Medical treatment for PS should be directed to improve diastolic function and to ameliorate clinical signs associated with right heart failure (15), but is often frustrating for severe PS. Therefore, more ultimate therapeutic strategy such as surgical correction (19) or balloon valvuloplasty (2,4,9,10) may be required in severe PS. Although balloon dilation has rapidly become the standard of care in veterinary practice for treatment of valvular pulmonic stenosis, the application of balloon dilation is limited to valvular pulmonic stenosis where commissural fusion is the major abnormality. Furthermore, surgical intervention are only reserved for those animals in which balloon dilation has either failed or is not applicable, although many surgical options exist for treatment of pulmonic stenosis, due to the increased morbidity and mortality of surgical intervention.

Recently, intravascular stents have been used to alleviate peripheral or main pulmonary artery stenosis in humans (12,18) and shown to result in a greater increase in stenotic vessel diameter, decreased acute complication rate and decreased failure rate, compared to balloon valvuloplasty (12,18). Successful application of pulmonic stenting has been also reported in dogs with supravalvular pulmonic stenosis (7).

This case report describes the first clinical trial of intravascular stent in a dog with refractory infundibular type of pulmonic stenosis.

CASE

A 4-year-old intact male Shih Tzu dog (5.4 kg of body weight) was referred to Veterinary Teaching Hospital of Kangwon National University with primary complaints of heart murmur and exercise intolerance. Clinical signs of heart failure were obvious for the last 6 month before presentation. According to the referring veterinarians, the clinical signs were medically manageable with calcium channel blocker (diltiazem, 0.5 mg/kg, PO, BID, Herben, Jeil Pharmaceutical, Korea) and beta-adrenergic blocker (propranolol, 0.5 mg/kg, PO, BID, indenol, Dongkwang Pharmaceutical, Korea). However, clinical signs were worsen recently. Thus the dog was referred for balloon valvuloplasty. At presentation, the grade V/VI ejection quality-systolic murmur was detected at the left base (Fig 1A). Although the femoral arterial pulses were normal (130 mmHg systolic pressure at Doppler method), the jugular vein was markedly distended

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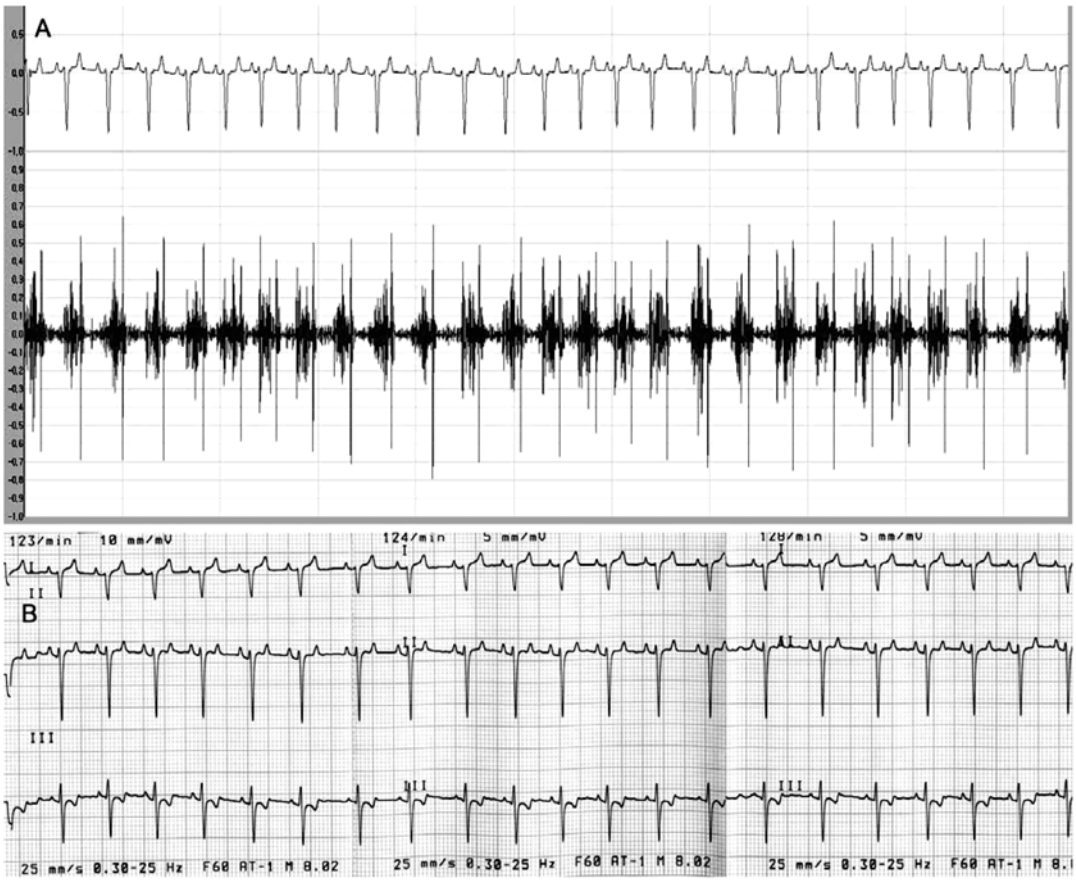

Fig 1. Phonocardiogram and electrocardiogram of this case. A: The grade V/VI ejection quality-systolic murmur was heard at the left base. B: The electrocardiogram showed normal sinus rhythm (120 - 125 beats per min) with right ventricular enlargement (presence S wave in leads I, II, and III).

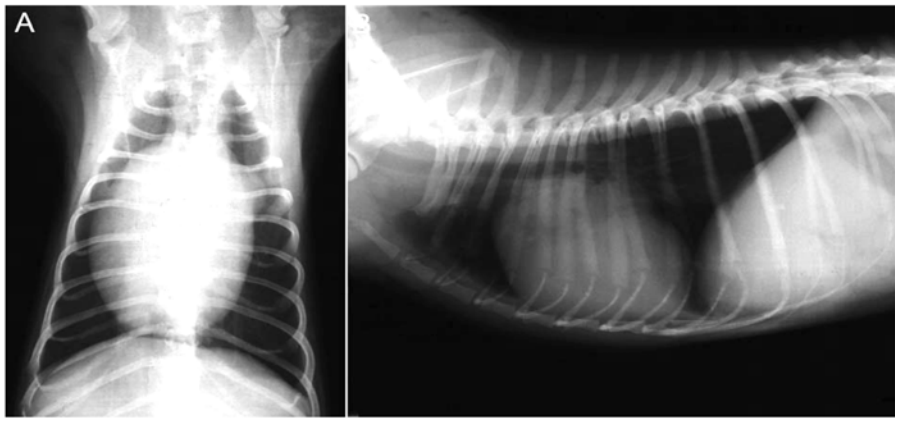

Fig 2. Thoracic radiography of this case. A: Dorsoventral projection of thoracic radiography showed a bulging of main pulmonary artery (MPA) with generalized cardiomegaly. B: Lateral projection of thoracic radiography showed right sided cardiomegaly (vertebral heart scale 11.2) with enlarged MPA, distended caudal vena cava and hepatomegaly.

with positive hepato-jugular reflex.

Complete blood cell count (CBC) and serum chemistry profiles revealed hypoalbuminemia (2.5 g/dL, reference range 3.1 - 4.1), decreased hematocrit (31.2%, reference range 37 - 55%) and mean corpuscular volume (52.3 fL, reference range 60 - 77). On the day of presentation, electrocardiographic (ECG) studies revealed normal sinus rhythm (120 - 125 beats per min) with right ventricular enlargement (presence S wave in leads I, II, and III; Fig 1B). Dorsoventral projection of thoracic radiography showed bulging of main pulmonary artery

(MPA) with generalized cardiomegaly (Fig 2A), whereas lateral projection of thoracic radiography showed right sided cardiomegaly (vertebral heart scale 11.2) with enlarged MPA, distended caudal vena cava and hepatomegaly (Fig 2B). The 2-dimensional (2D) echocardiography in right parasternal short axis view revealed markedly thickened right ventricular free wall (RVFW) and interventricular septum and narrowed left ventricular dimension at systole and diastole (Fig 3A). The 2D left apical four chamber view revealed markedly enlarged right atrium and ventricle and relatively narrowed left atrium and ventricle (Fig 3B). The color and continuous spectral Doppler studies at right ventricular outflow tract (RVOT) level showed severe jet quality turbulent flow (Fig 3C) at peak velocity of 6.4 m/s (pressure gradient 165 mmHg; Fig 3D) and narrowed RVOT (0.22 cm), suggesting severe pulmonic stenosis, since the pressure gradient in stenotic pulmonic valve area was higher than 100 mmHg. Interestingly, the stenosis occurred not by valvular dysplasia but by thickened and narrowed pulmonic annulus (Fig 3C). Therefore, the intravascular stenting for widening the pulmonic annulus was applied for this case, rather than balloon dilation therapy.

For the intravascular stent placement, surgical anesthesia was achieved with propofol (4 mg/kg IV for induction then 0.4 mg/kg/min CRI for maintenance; Myeongmoon Pharmaceutical, Korea) after the premedication with atropine (0.05 mg/kg SC; Daewoo Pharmaceutical, Korea), diazepam (0.1 mg/kg IV; Daewon Pharmaceutical, Korea) and butorphanol (0.05 mg/kg IV; Hanlim pharmaceutical, Korea) with oxygen supply through intra-tracheal tube. The venipuncture was performed at right jugular vein with an 18G needle. A guidewire (Fixed Core Wire Guides Safe-T-J® Curved, COOK, Bloomington, USA) was inserted into the needle and located at pulmonary artery. An introducer sheath (Check-Flo Performer® Introducer, COOK, Bloomington, USA) is inserted to the right external jugular vein with guidance of pre-placed guidewire (Fig 4A). The sizing balloon catheter (Activator™ Balloon catherter, Cordis®, Johnson & Johnson, Miami, USA; Fig 4B) was then inserted and measured the stenotic annulus more correctly. The stenotic annulus was 0.25 cm, while the intact supravalvular annulus was 1.25 cm. Therefore 3 cm (length) × 1.5 cm (diameter) of Palmaz genesis transhepatic biliary stent (Cordis®, Johnson & Johnson, Miami, USA) was selected. For the placement of the stent, the stent catheter was inserted with the guidance of pre-placed guidewire at the stenotic annulus. With inflation

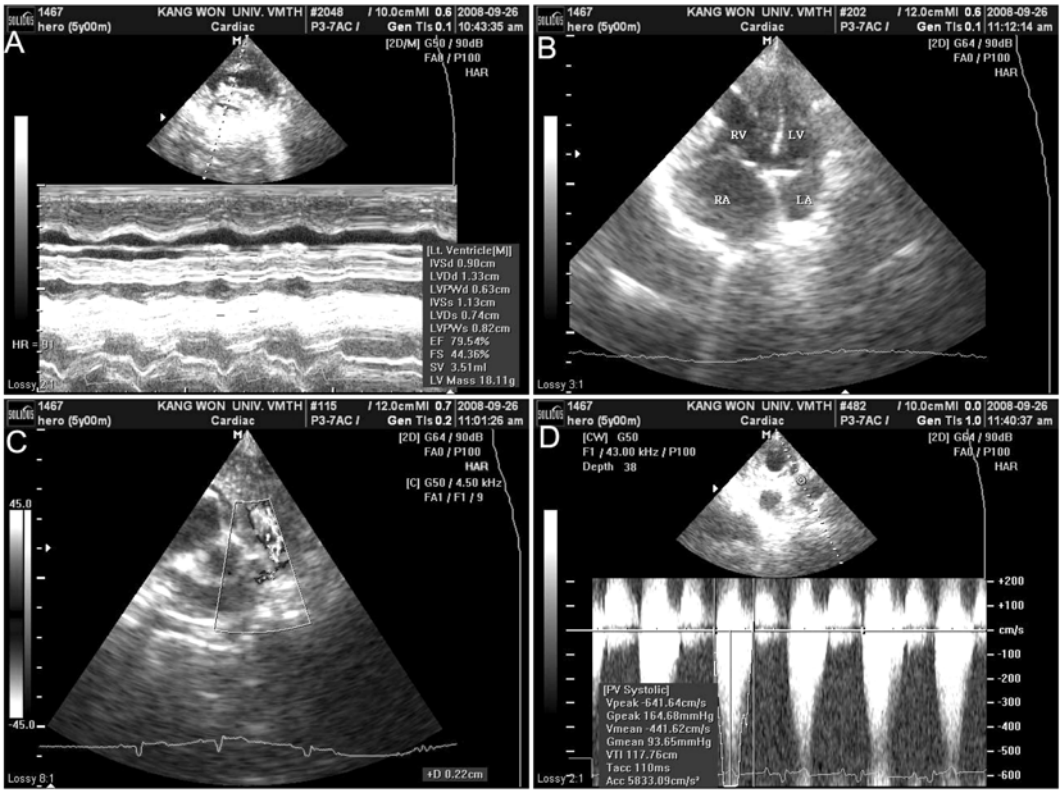

Fig 3. Echocardiography of this case. A: The 2-dimensional (2D) echocardiography in right parasternal short axis view revealed markedly thickened right ventricular free wall (RVFW) and interventricular septum and narrowed left ventricular dimension at systole and diastole. B: The 2D left apical four chamber view revealed markedly enlarged right atrium and ventricle and relatively narrowed left atrium and ventricle. C: The color Doppler studies at right ventricular outflow tract (RVOT) level showed severe jet quality turbulent flow and narrowed RVOT (0.22 cm). D: The continuous spectral Doppler studies at RVOT level showed jet flow at peak velocity of 6.4 m/s (pressure gradient 165 mmHg), suggesting severe pulmonic stenosis.

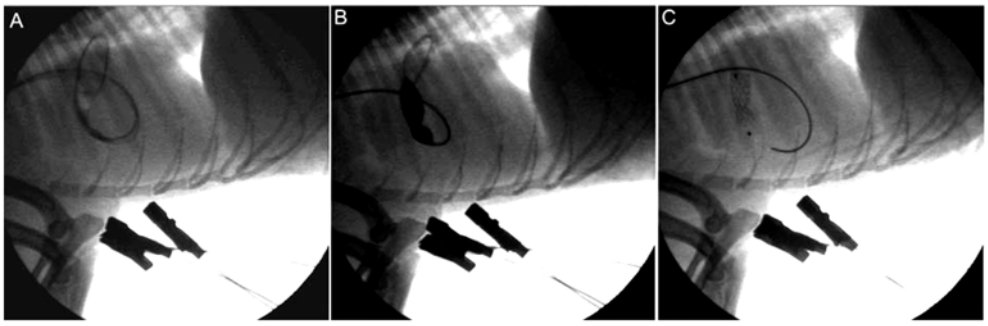

Fig 4. Procedure of transcatheter pulmonic stent placement. A: A guidewire (Fixed Core Wire Guides Safe-T-J® Curved, COOK, Bloomington, USA) was inserted into the needle and located at pulmonary artery. B: The sizing balloon catheter (Activator™ Balloon catherter, Cordis®, Johnson & Johnson, Miami, USA; Fig 4B) was then inserted and measured the stenotic annulus. C: 3 cm (length) × 1.5 cm (diameter) of Palmaz genesis transhepatic biliary stent (Cordis®, Johnson & Johnson, Miami, USA) was deployed at the stenotic pulmonic annulus.

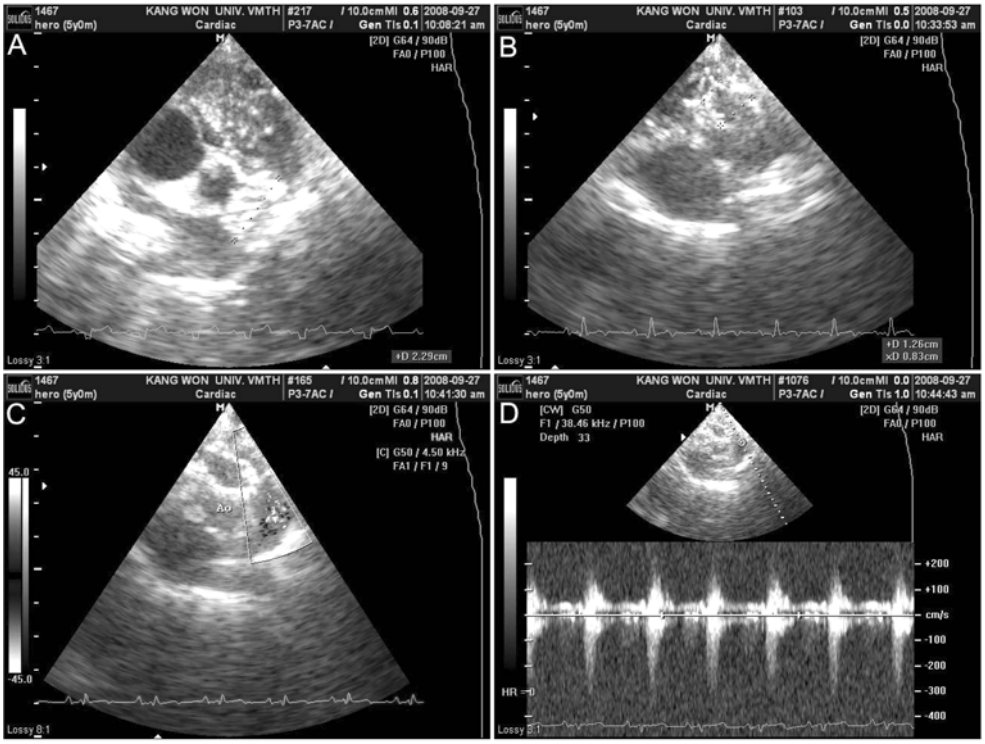

Fig 5. Echocardiography taken 1 day after stent placement. A: The 2-dimensional (2D) echocardiography at right ventricular outflow tract (RVOT) level showed appropriate positioning of the stent (dotted line). B: At the same level of echocardiography, the diameter of annulus, where the stent was deployed, was measured 0.83 cm at the narrowest point and 1.26 cm at the widest point. C: Color Doppler studies at RVOT level showed mild pulmonic regurgitation. D: Continuous wave spectral Doppler study at RVOT level showed remarkably reduced pulmonic jet measured at peak velocity of ~ 3.0 m/s (pressure gradient 36 mmHg).

device (Sphere™ Inflation device, COOK, Bloomington, USA), the stent was expanded by inflating balloon of the stent catheter. After then the stent was expanded further with larger diameter of balloon dilation catheter (Activator™ Balloon catherter, Cordis®, Johnson & Johnson, Miami, USA). After achieving stent expansion, the dilation catheter was then removed (Fig 4C). Total time for stent implantation took only 30 min after surgical anesthesia. After the stent implantation, the peak pulmonic velocity at the RVOT was reduced to ~ 3 m/s (pressure gradient 36 mmHg) and successfully reduced the severity of disease to mild stenosis (Fig. 5D). On the echocardiographical examination, the stent was placed at pulmonic annulus (Fig 5A) and the diameter of annulus was measured ranged from 0.83 to 1.26 cm (Fig 5B). Color Doppler studies showed mild pulmonic regurgitation (Fig. 5C). Medical treatment was directed to prevent thromboembolism and pre-existing concentric hypertrophy using clopidogrel (10 mg/kg, PO, SID, Plavix, Sanofi-Aventis, Korea), dilt-

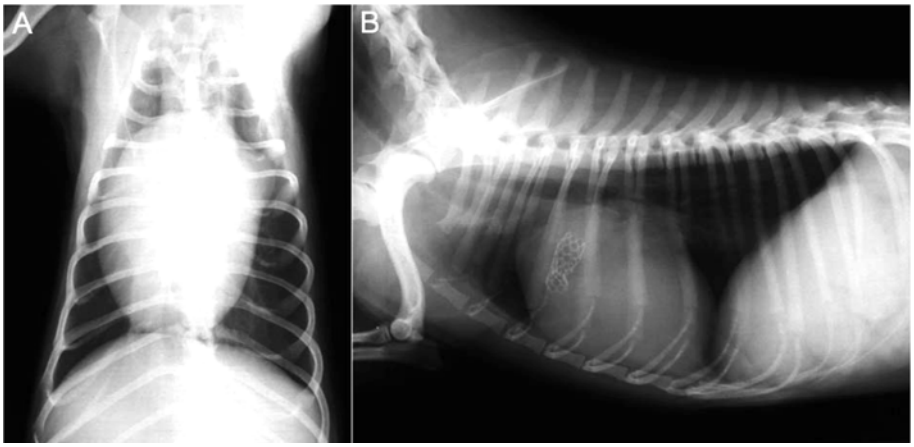

Fig 6. Thoracic radiography taken a month after stent placement. Dorsoventral (A) and lateral (B) projection of radiography showed that the location and diameter of stent was not much changed.

iazem (0.5 mg/kg, PO SID; Keunwha Pharmaceutical, Korea) and prescription diet (Hill's h/d, USA). Periodic re-evaluations performed in monthly interval revealed no further deterioration of PS (maintained ~ 3 m/s of maximal velocity). The thoracic radiography taken at a month after the stent placement showed the location and diameter of stent was not much changed (Fig 6). The dog did not showed cardiac murmur and played well with other dogs (no exercise intolerance).

Discussion

Problem encountering balloon dilation for treating PS in dogs is that the balloon dilation is only consistently responded well in PS occurred with commissural fusion, although it has been widely reported usefulness of balloon dilation therapy in the veterinary literature (2,13). In those patients in which balloon dilation is not appropriate, only palliative surgical procedures was applicable, although the morbidity and mortality associated with surgery is significantly greater than that of catheter based procedures, regardless of procedure (5,13,14).

Transcatheter intravascular stent placement has been reported for the correction of both acquired and congenital supravalvular pulmonic stenosis in humans and dogs (1,7,12). According to human literatures, stent placement found to be result in a greater increase in stenotic vessel diameter, decreased acute complication rate and decreased failure rate (1,8,12,18). Criteria for appropriate balloon diameter in the treatment of valvular pulmonic stenosis found to be 1.2 - 1.5 times greater than the annular diameter. (3,17). Larger balloon sizes often causes tearing of the arterial wall with either rupture or aneurysm formation. However, because the stent used in this case was expandable, the correct sizing of stent was more easily achieved with the sizing balloon. Furthermore, the stent could be further expandable with larger diameter of balloon catheter, if necessary, with minimal risk of vascular tearing. The balloon in stent catheter was designed for engages (expands) the stent inside of catheter. This mechanism is designed to prevent stent dislocation and to allow optimization of stent positioning prior to full deployment on inflation of the outer balloon.

Re-stenosis due to continued external compression leading to failure of the prosthesis or intimal hyperplasia is a major complications reported in humans (16,20), although it is manageable with re-dilation of the stent. Severe pulmonic regurgitation and stent fracture has been reported in humans treating valvular pulmonic stenosis (6). The cause of stent fracture is associated with the repetitive cyclic loading placed on the stent by the muscular right ventricular outflow tract (6). Thus better transcatheter pulmonic valvular replacement techniques are currently being investigated in humans. However, in this case, the integrity of stent lasted longer (no fracture), even though it placed from muscular part of RVOT. Although pulmonic insufficiency existed immediately after the stent placement, the severity was mild so that medical treatment was not required. However, periodic monitoring for checking stent integrity and position should be conducted.

To our best knowledge, this case is the first clinical trial for treating PS with intravascular stent in Korea. The outcome of stent placement was favorable and remarkably reduced the severity of PS (6.4 m/s to 3.0 m/s of peak velocity at RVOT). Clinical condition was remarkably improved with the absence of cardiac murmur, although mild pulmonic regurgitation was existed from the day of stent placement. Since the total time for stent placement took only 30 min in this case, the inhalation anesthesia was not necessary. Because, unfortunately, pulmonic stent placement has been recently applied, there is limited information related to the stent (e.g. long term clinical outcome, disadvantage and advantage). Further study should be directed to establishment and optimization of this procedure, since this procedure has rarely done in veterinary fields. In addition, long-term complications associated with this procedure is currently monitoring in this case.

Acknowledgement

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카테터를 통한 혈관스텐트 장착을 통한 심한 폐동맥협착증 치료 1례

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요 약 : 4 년령 시쭈개 (체중 5.4 kg)가 심잡음과 운동불내성으로 내원하였다. 진단검사상 심한 폐동맥협착증으로 진단되었다 (우심실 유출로의 peak velocity of 6.4 m/s, 압력구배 165 mmHg). 본 환견은 3 cm (길이) × 1.5 cm (직경)의 Palmaz biliary stent를 이용하여 치료하였다. 시술후 환견의 폐동맥 협착증은 상당히 많이 개선되었다 (우심실 유출로의 of peak velocity가 3.0 m/s로 감소). 내원전 보였던 임상증상은 더 이상 보이지 않았지만 경미한 폐동맥 패쇄부전이 관찰되었다. 본 증례는 우리나라에서 최초로 시도된 스텐트를 이용한 폐동맥 협착증 증례이다.

주요어 : 폐동맥 협착증, 스텐트, 카테터, 개, PS