Case Report

Reversible pulmonary hypertension secondary to bronchopneumonia in a kitten

Jidapa Tosuwan[1] Sirilak Disatian Surachetpong[1*]

Abstract

A five-month-old Siamese kitten was presented with acute respiratory distress. The kitten had respiratory acidosis. The result of the feline N-terminal prohormone of brain natriuretic peptide (NT-proBNP) test kit was abnormal. Thoracic radiography revealed patchy lung infiltration and cardiomegaly. Severe right heart enlargement and an intermediate probability of pulmonary hypertension were suggested from echocardiography. Pulmonary hypertension secondary to severe pneumonia was suspected. The kitten was treated with oxygen supplementation, antibiotics and pimobendan. The clinical signs, radiography and echocardiography returned to normal after 30 days of treatment.

Keywords: feline, pneumonia, pulmonary hypertension

[1]*Department of Veterinary Medicine, Faculty of Veterinary Science, Chulalongkorn University, Henri Dunant Rd., Bangkok, 10330, Thailand*

****Correspondence****: sirilakd27@gmail.com* (S. D. Surachetpong)

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Introduction

Pulmonary hypertension (PH) is defined as abnormally increased pressure within the pulmonary vasculature (Reinero *et al*., 2020). A few studies have reported PH in cats including PH associated with Eisenmenger's syndrome in congenital heart disease, pulmonary thromboembolism, pulmonary capillary hemangiomatosis, pulmonary fibrosis, heartworm disease, lungworm disease and chronic upper airway obstruction (Jaffey *et al*., 2017, Vezzosi and Schober, 2019). A recent consensus classified PH in dogs into six categories including pulmonary arterial hypertension, PH due to left heart disease, respiratory diseases and/or hypoxemia, thromboembolic pulmonary hypertension and parasitic diseases, and PH with unclear multifactorial mechanisms (Reinero *et al*., 2020). Referring to PH due to respiratory diseases, treating the underlying cause should decrease the severity of the clinical signs and attenuate or delay the progression of PH. This report describes curative PH in a cat affected with severe acute pneumonia.

Materials and Methods

Signalment and history: A five-month-old 2.95 kg male Siamese kitten was presented with acute respiratory distress at the emergency unit of the Small Animal Teaching Hospital, Faculty of Veterinary Science of Chulalongkorn University, Thailand. The kitten had no history of previous illness before it developed a sudden increased respiratory effort.

Physical examination: At presentation, the kitten had severe mixed inspiratory and expiratory dyspnea without loud breathing sounds. The respiratory rate was 72 breaths/min. The rectal temperature was 99 ^{o}F. The kitten had pale pink mucous membranes, a capillary refilling time of less than 2 seconds, increased lung sounds and a systolic murmur heart sound grade 3/6 with the point of maximal intensity at the right apex. The heart rate was 198 beats/minute without pulse deficit and the systolic blood pressure was 82 mmHg. The kitten was 7% dehydrated. Palpable lymph nodes were within the normal limit. No other abnormality was found from the physical examination.

Diagnostic plan, initial treatment plan and outcome: Blood was collected for a complete blood count (CBC), serum biochemistry and blood gas analysis when the kitten was more stable after resting in an oxygen cage. The CBC and blood chemistry parameters were within the normal range of the laboratory reference range of the Small Animal Hospital, Faculty of Veterinary Science, Chulalongkorn University, except for mild elevation of alkaline phosphatase and blood urea nitrogen (Table 1). The alkaline phosphatase elevation might have occurred from the active bone growth in a young cat and the mild increase blood urea nitrogen could have been from dehydrated status. Arterial blood gas analysis could not be performed. Therefore, venous blood gas analysis was done instead (Table 2). The result showed respiratory acidosis suggesting a primary respiratory disorder. The feline NT-proBNP ELISA test kit (SNAP Feline proBNP Test; IDEXX Laboratories, Westbrook, Maine, USA) result was abnormal. The cat was initially treated with intravenous furosemide injection 1 mg/kg. A full cardiovascular examination including radiography, electrocardiography and echocardiography was performed, when the cat could breathe better. The electrocardiography showed normal sinus rhythm. Thoracic radiography showed diffused interstitial and alveolar lung infiltration and cardiomegaly (Figure 1).

Table 1 The complete blood count and blood chemistry profiles of the kitten on day 1 and day 4.

Parameter	Day 1	Day 4	Reference range
Complete blood count			
RBC (x10^6 per ul)	8.94	8	4.95-10.53
Hemoglobin (g/dl)	13.6	12.1	8.5-14.4
Hematocrit (%)	40.2	32.4	25.8-41.8
Platelet (x10^3 per ul)	128	68	160-660
WBC (x10^3 per ul)	13.22	10.74	3.8-19
Neutrophils (x10^3 per ul)	10.18	6.77	2.5-12.5
Eosinophils (x10^3 per ul)	0.30	0.95	0-1.5
Basophils (x10^3 per ul)	0.0	0.0	Rare
Lymphocyte (x10^3 per ul)	2.60	2.72	1.5-7.0
Monocytes (x10^3 per ul)	0.13	0.30	0-0.85
Blood chemistry			
ALT (Units)	67	74	13-75
ALP (Units)	131	78	3-61
BUN (mg%)	32	22.1	10-30
Creatinine (mg%)	0.6	1	0.8-20
Total protein (g%)	6.0	6.9	6.1-8.8
Albumin (g%)	3.0	3.2	2.6-4.3

ALT: alanine aminotransferase; ALP: alkaline phosphatase; BUN: blood urea nitrogen; RBC: red blood cell count; WBC: white blood cell count

Table 2 The echocardiographic result on Day 2 and Day 30

Parameter	Day 2	Day 30
B-mode Measurements		
LA (mm)	8.91	10.7
Ao (mm)	5.9	7.0
LA:Ao	1.51	1.52
M-mode measurements		
IVSd (mm)	3.2	3.9
IVSs (mm)	4.5	4.2
LVIDd (mm)	11.9	13.6
LVIDs (mm)	7.0	8.8
LVPWd (mm)	3.3	3.9
LVPWs (mm)	6.1	5.3
FS (%)	41.24	35.19
Doppler measurement		
TV Vmax (m/s)	2.11	-
TV Δp (mmHg)	17.73	-
PV Vmax (m/s)	0.81	1.06

LA: left atrial; Ao: aorta; Δp: pressure gradient; FS: fractional shortening; IVSd: interventricular septum thickness at end-diastole; IVSs: interventricular septum thickness at end-systole; LA:Ao: ratio of the left atrial dimension to the aortic annulus dimension; LVIDd: left ventricular internal dimension at end-diastole; LVIDs: left ventricular internal dimension at end-systole; LVPWd: left ventricular posterior wall thickness at end-diastole; LVPWs: left ventricular posterior wall thickness at end-systole; PV: pulmonary valve; TV: tricuspid valve; Vmax: peak velocity

Transthoracic echocardiography was performed using an ultrasound machine (Mindray, M9, Shenzhen, P.R. China). Two-dimensional echocardiography showed right atrial and ventricular enlargement. Color-flow echocardiography revealed moderate tricuspid regurgitation. Mid-systolic notching of the pulmonary artery Doppler flow profile was found. Systolic pulmonary arterial pressure (PAP) was 27.73 mmHg estimated from tricuspid regurgitant flow velocity measured by continuous-wave Doppler echocardiography plus an estimated right atrial pressure. The intermediate probability of PH was determined based on the American College of Veterinary Internal Medicine (ACVIM) consensus guideline for diagnosis of PH in dogs (Reinero *et al*., 2020). The echocardiographic results are shown in Table 2 and Figure 2. The kitten was suspected of being affected by PH secondary to severe pneumonia.

The kitten was admitted to the critical care unit and kept in an oxygen cage. Amoxicillin/clavulanic acid was administered at a dose of 24 mg/kg intravenously every 8 h. Pimobendan and aminophylline were given every 12 h per oral (PO) at doses of 0.2 mg/kg and 8 mg/kg, respectively.

On Day 3, thoracic radiography showed an improvement of lung infiltration in the caudal lung lobes. However, alveolar lung infiltration was still observed in the cranial and middle lung lobes (Figure 2).

All blood profile values on Day 4 were within the normal range. The kitten was discharged at Day 4 at the owner's request. Oral medications including amoxicillin/ clavulanic acid (dose 25 mg/kg q8h PO), pimobendan (dose 0.2 mg/kg q12h PO) and aminophylline (dose 8 mg/kg q12h PO) were prescribed. Oxygen supplementation was done in an oxygen tank at home.

On Day 7, the kitten was brought back to the hospital for follow-up. At home, the kitten stayed within the oxygen tank all the time. On examination, the kitten was still depressed and anorexic. Thoracic radiographs showed an alveolar lung infiltration but it was better than that on Day 4 (Figure 2). The antibiotic was changed from amoxicillin/clavulanic acid to doxycycline (dose 10 mg/kg q24h PO), and pimobendan was continued (dose 0.2 mg/kg q12h PO). On Day 10, the kitten was weaned off oxygen. The respiration returned to normal. Doxycycline and pimobendan were continued for 18 more days.

Thoracic radiography on Day 28 showed clear lung fields (Figure 2). Echocardiography was reperformed and revealed normal cardiac chamber size. The tricuspid regurgitation had disappeared. All anatomic changes secondary to PH, including right atrial enlargement and mid-systolic notching of the pulmonary artery Doppler flow profile, had returned to normal (Figure 3). The kitten completely recovered and all medications were discontinued.

Results and Discussion

The kitten in this case report had acute respiratory distress. The radiography suggested pneumonia. Organisms that have been reported as lower respiratory pathogens of cats include *Pasteurell*a spp, *Escherichia coli*, *Staphylococcus* spp, *Streptococcus* spp, *Pseudomonas* spp, *B. bronchiseptica*, and *Mycoplasma* spp (Shaver and Bastarache, 2014). Although imaging is essential to investigate lung disease, it is usually insufficient to confirm a specific disease. Bronchoalveolar lavage with bacterial culture and cytologic examination are required for a definitive diagnosis (Bichot and Bienzle, 2021). However, this technique is invasive and was not suitable for this kitten because it had severe respiratory distress.

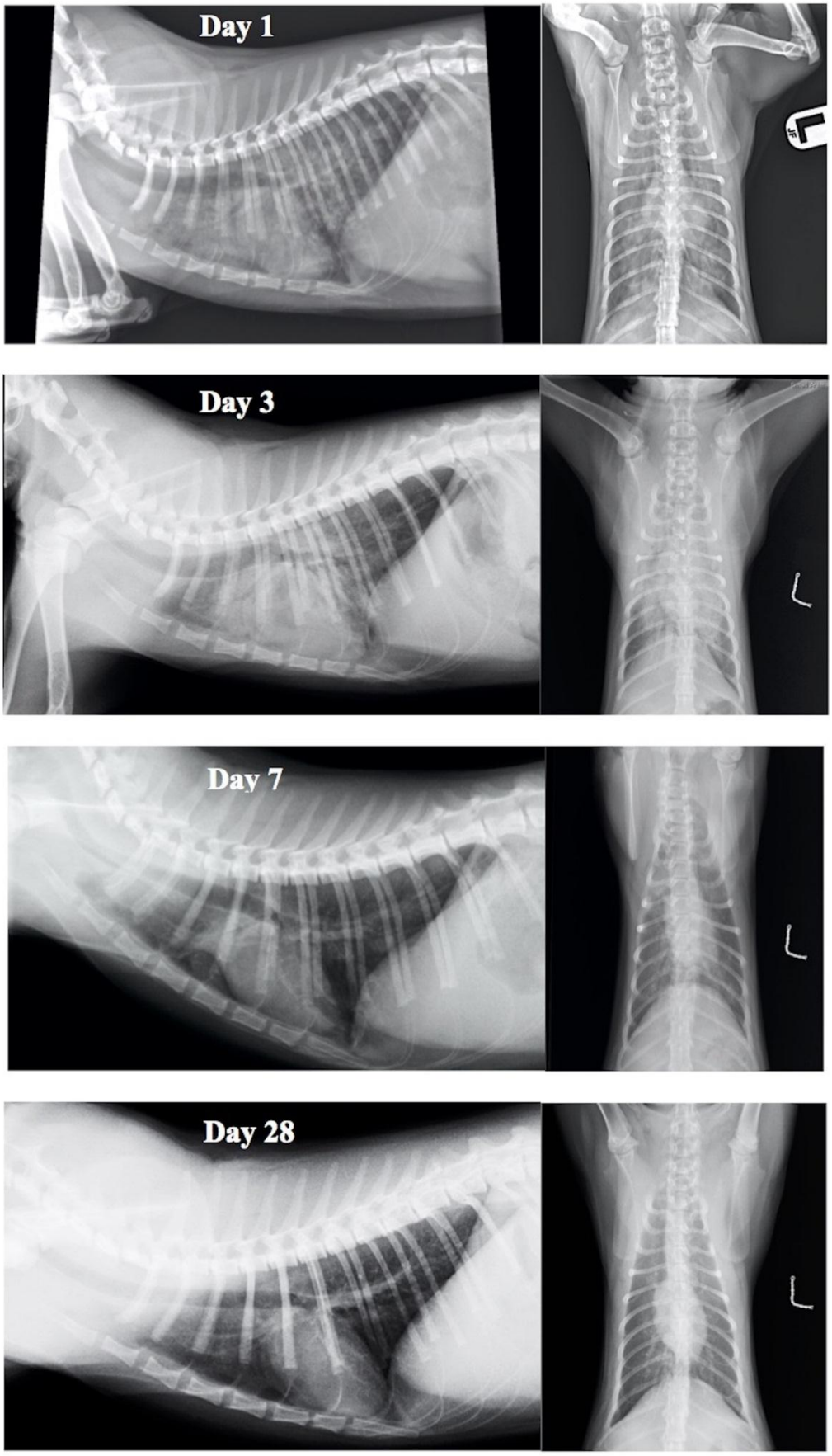

Figure 1 Right lateral thoracic radiographs (Right), Ventrodorsal thoracic radiographs (Left). Radiography show alveolar lung infiltration that was reduced during treatment from at Days 1, 3 and 7. Radiography on Day 28 shows a normal cardiac silhouette and lung field.

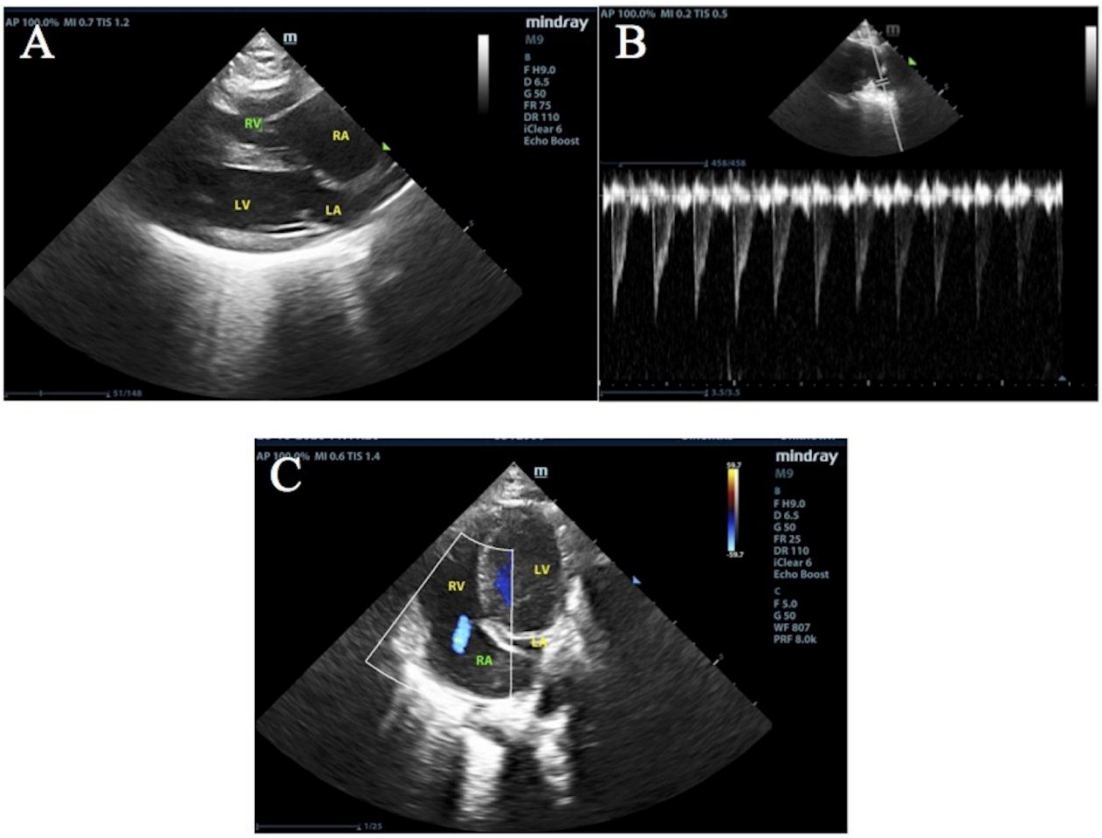

Figure 2 Echocardiography Day 1: (a) Right parasternal long axis view shows right heart enlargement, (b) Pulsed-wave Doppler echocardiography shows dagger flow profile of the pulmonary artery, (c) Left apical four chambers view shows tricuspid regurgitation tricuspid regurgitation

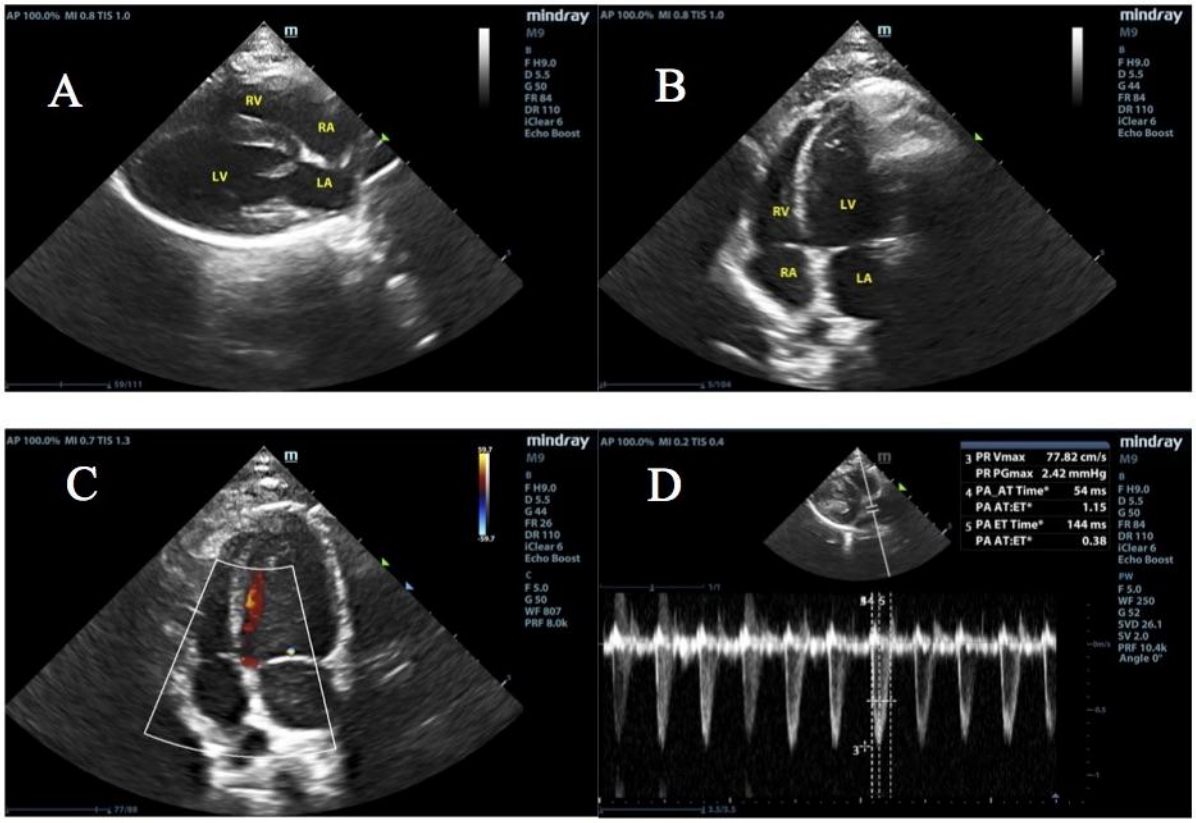

Figure 3 Echocardiography Day 28: (a) Right parasternal long axis view shows normal cardiac size and structure, (b) Left apical four chambers view shows normal cardiac size and structure, (c) Left apical four chamber view shows no tricuspid valve regurgitation, (d) Pulse-wave Doppler measurement of pulmonary artery

Systolic murmurs and cardiomegaly assessed from radiography suggested cardiac problems. The abnormal result of the feline NT-proBNP ELISA test kit indicated increased stretch and stress of the myocardium, suggesting cardiac disease (Baisan *et al*., 2016). Right-sided heart enlargement secondary to pulmonary hypertension was confirmed by echocardiography. In dogs, an increased NT-proBNP concentration has been reported in dogs with precapillary PH (Kellihan *et al*., 2011) An elevation of NT-proBNP concentration has been reported in a cat model with PH (Wallner *et al*., 2017). However, to the authors' knowledge, an association of NT-proBNP and naturally occurring PH in cats has not been reported.

Oxygen supplementation is most important in cats with moderate to severe hypoxia. Supplemental oxygen at 40% to 60% should be provided until respiratory difficulty disappears, and the animals can be weaned off it to room air. As bacterial pneumonia was suspected and a bronchoalveolar lavage could not be performed in this kitten, we decided to treat the kitten with empirical antibiotics. An injectable amoxicillin/clavulanic acid was first used, regardless of the severity of the lung lesions based on the thoracic radiographs. Once the lung lesions had worsened, doxycycline was prescribed instead. After the resolution of clinical and radiographic signs, doxycycline was continued for three weeks. The antimicrobial use guideline by the International Society for Companion Animal Infectious Diseases recommends re-evaluating animals with pneumonia 10-14 days after starting treatment. The decision to extend or stop treatment depends on clinical, hematological and radiographic findings (Lappin *et al*., 2017).

Pimobendan is a positive inotrope (calcium sensitizer) and vasodilator (phosphodiesterase-III inhibitor) (Harris *et al*., 2016). This drug has survival benefits in dogs with several heart diseases but there is no consensus in existence regarding off-label use of pimobendan in cats. Pimobendan has therapeutic benefits in hypertrophic cardiomyopathic cats with systolic dysfunction and congestive heart failure (Ward *et al*., 2020). Pimobendan was added to this kitten because of the expectation of improving cardiac contraction and dilating the pulmonary vessels and reducing PAP. The kitten tolerated pimobendan well and right-sided congestive heart failure secondary to PH did not develop during the course of treatment.

Since few reports describe PH in cats, the clinical characteristics and specific echocardiographic findings of PH remain undefined. One study revealed that PH in cats is usually associated with right-sided heart enlargement (Vezzosi and Schober, 2019). Using the ACVIM consensus guidelines for diagnosis of PH in dogs, the intermediate probability of PH was defined for the kitten in this report. There are two previous publications reporting reversible PH in cats. The first case was reported in 2011, where the cat was diagnosed with congestive heart failure and pulmonary thromboembolism. After treatment for 28 days, the clinical signs and echocardiographic evidence of PH were completely resolved (Baron *et al*., 2011). Another report was published in 2012, concerning heartworm-induced PH in a kitten. PH was completely reversed after four months of treatment (Dirven *et al*., 2012). To the authors' knowledge, this is the first report of reversible PH secondary to pneumonia in cats.

In conclusion, PH can develop suddenly in cats with severe pneumonia. Successful treatment of pneumonia can completely reverse PH to normal. PH in cats may be overlooked as the estimated PAP assessed by echocardiography may not be measured or underestimated. Using anatomic sites of echocardiographic signs of PH, as used in dogs, can help to assess the probability of PH in cats. However, the clinical characteristics of PH in cats may be different from dogs. A guideline should be developed for the management of cats with PH.

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