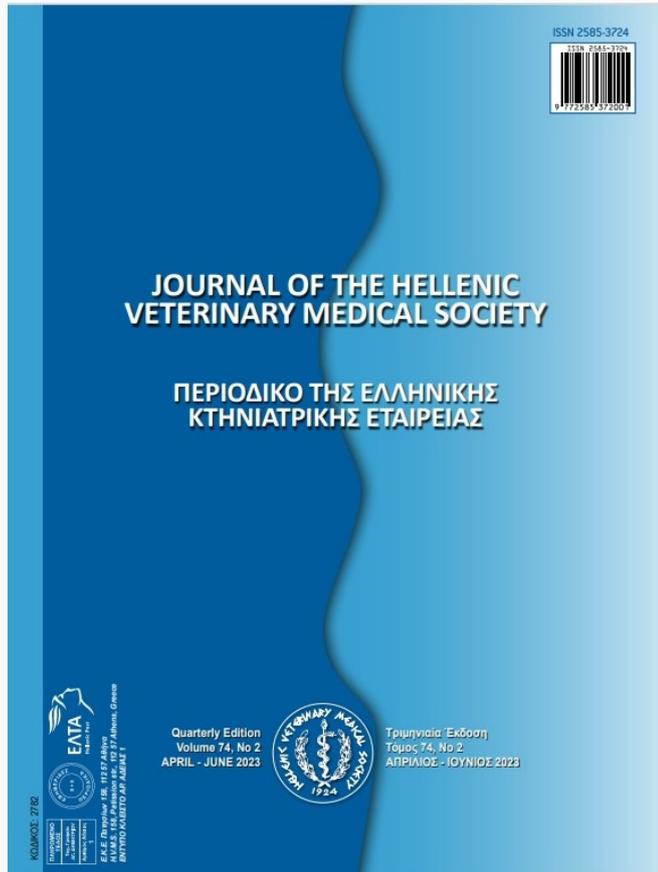


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Negative Pressure Pulmonary Edema due to Upper Airway Obstruction in Two Dogs

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ABSTRACT: Two dogs were referred because of chronic cough and respiratory distress. One dog (Case 1) showed severe respiratory distress and mild interstitial patterns on the thoracic radiographs after external ring prostheses were placed to support a collapsing cervical trachea. The dog had received 1 mg/kg of furosemide three times daily for 2 days to treat pulmonary edema. Although appropriate treatment was provided to resolve pulmonary edema, persistent pulmonary edema and respiratory distress were still present. There was no evidence of cardiogenic pulmonary edema based on the physical, radiographic, and echocardiographic examinations. The other dog (Case 2) was diagnosed with tracheal collapse and bronchomalacia. In addition, mild interstitial patterns were detected on the thoracic radiographs. There was no evidence of cardiac disease based on the physical and radiographic examinations. Because these findings were suspected to indicate negative pressure pulmonary edema due to airway obstruction, Case 1 was immediately given dexamethasone for 2 days to relieve postoperative swelling. Case 2 received 0.05 mg/kg of acepromazine for sedation and endotracheal intubation with positive-pressure ventilation for 2 days. All abnormal signs, including pulmonary edema, disappeared in Case 1, but Case 2 was discharged with a mild cough. This report describes the clinical course of negative pressure pulmonary edema due to airway obstruction in two dogs. Clinicians should be aware that airway obstruction can cause fulminant non-cardiogenic pulmonary edema in dogs.

Keywords: canine, postobstructive pulmonary edema, respiratory distress, tracheal collapse.

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CASE HISTORY

Case 1

A 7-year-old, intact female Pomeranian weighing 2.35 kg was referred because of severe respiratory distress following surgery in which external ring prostheses were placed to support a collapsing cervical trachea. Upon physical examination, the dog showed stridor, tachypnea, inspiratory dyspnea, and bilateral crackles during lung auscultation. No heart murmur was detected. No remarkable signs were found in complete blood count values. The serum biochemistry profile showed a decreased serum albumin concentration (2.4 g/dL; Reference interval (RI) = 2.6-3.3 g/dL) and a decreased serum globulin concentration (2.5 g/dL; RI = 2.7-4.4 g/dL). The serum concentrations of electrolytes were normal, except for a decreased serum total calcium concentration (6.7 mg/dL; RI = 9-11.3 mg/dL). Blood gas analysis of venous blood showed respiratory acidosis based on

pH (7.296; RI = 7.35-7.45) and increased P_{CO_2} (45.6 mmHg; RI = 34-40 mmHg). Thoracic radiographs revealed mild interstitial patterns in the caudal part of the left cranial, the right cranial, and the right middle lung lobe and widening of the pulmonary artery to the right caudal lung lobe (Figure 1). In the echocardiographic examination, the suspicion of pulmonary hypertension was raised based on increased tricuspid regurgitation velocity (4.48 m/s) and a mildly dilated right atrium chamber but there was no evidence of cardiac remodeling or a decrease in cardiac output or contractility. The dog had received 1 mg/kg of furosemide three times daily and supplemental oxygen to treat pulmonary edema (PE) for the previous 2 days. Although prompt treatment was provided to resolve PE, the dog continued to suffer from PE and respiratory distress. Because of poor response to previous treatments and the physical, radiographic, and echocardiographic examination results, negative pressure

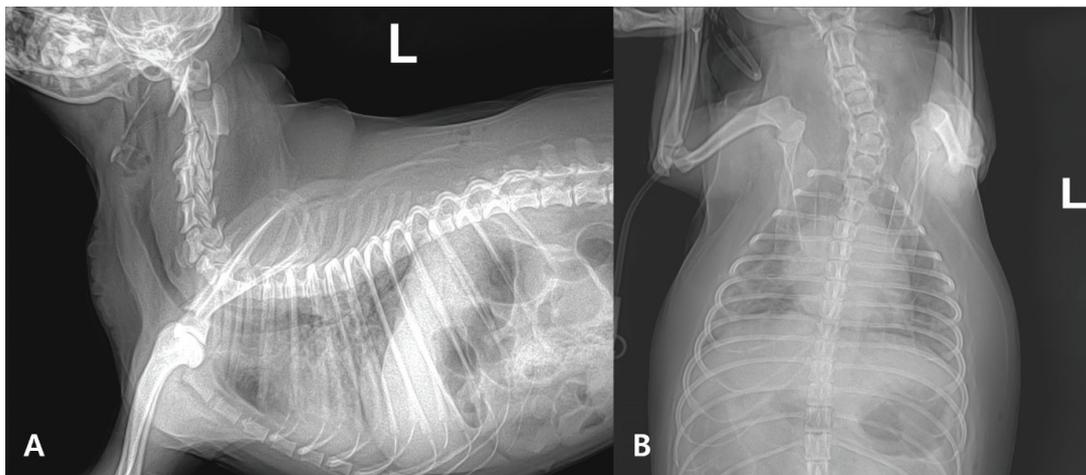


Figure 1. Left (A) lateral and (B) ventrodorsal views of the thoracic radiograph reveals mild interstitial patterns in a dog (Case 1) with severe respiratory distress

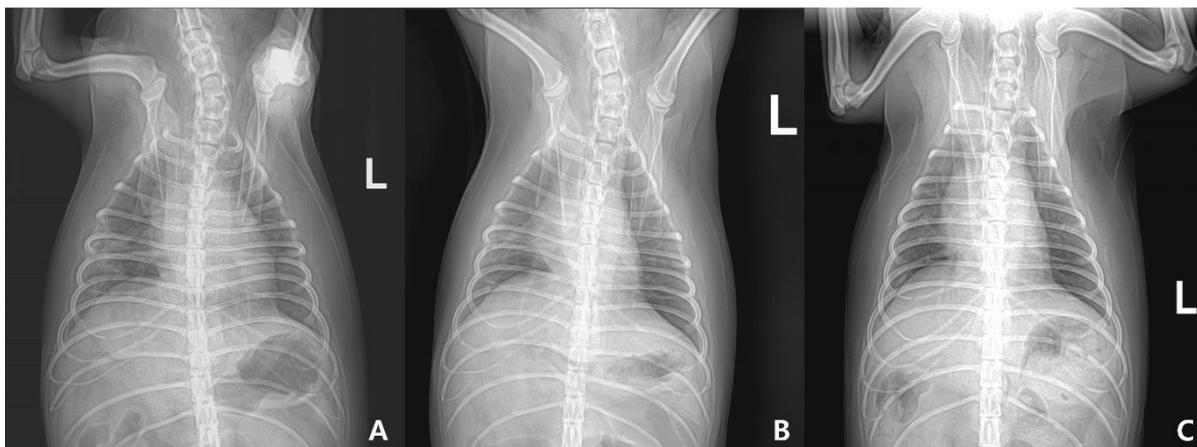


Figure 2. Interstitial patterns on the thoracic radiograph disappears in the dog (Case1) after treatments. From the day of treatment; (A) day 1, (B) day 2, (C) day 5

PE (NPPE) due to upper airway obstruction was suspected. Therefore, additional medications such as sildenafil (1.25 mg/kg PO, q 12 h) for managing pulmonary hypertension, theophylline (10 mg/kg PO, q 12 h), ambroxol (2 mg/kg PO, q 12 h), and butorphanol (0.2 mg/kg IV, q 6-8 h) for relief of respiratory distress were administered. Dexamethasone (0.3 mg/kg IV, q 12 h) was also administered for 2 days to relieve postoperative cervical swelling. After 5 days of treatment, all clinical signs and interstitial patterns on the thoracic radiograph disappeared (Figure 2).

Case 2

A 9-year-old, intact male Maltese weighting 4.0 kg was presented in a state of collapse and non-responsive (coma). The dog had a history of chronic coughing and inspiratory dyspnea with a goose honking sound. On

physical examination, spontaneous respiration was confirmed. There was no heart murmur during heart auscultation. Relevant physical examination findings included tachypnea with increased bronchovesicular sounds during lung auscultation, and tachycardia with no heart murmur and normal systolic blood pressure (130 mmHg; Doppler method). Low arterial oxygen hemoglobin saturation ($SpO_2 < 90\%$) was detected on pulse oximetry, and oxygen was immediately supplemented using face mask. Furthermore, an intravenous catheter was placed for fluid therapy and medications. Upon a brief neurologic examination, weak pupillary light reflex, and loss of palpebral reflex and menace response were observed. No remarkable findings were noted in the complete blood count values or serum biochemistry profile results. Thoracic radiography including inspiratory and expiratory lateral view

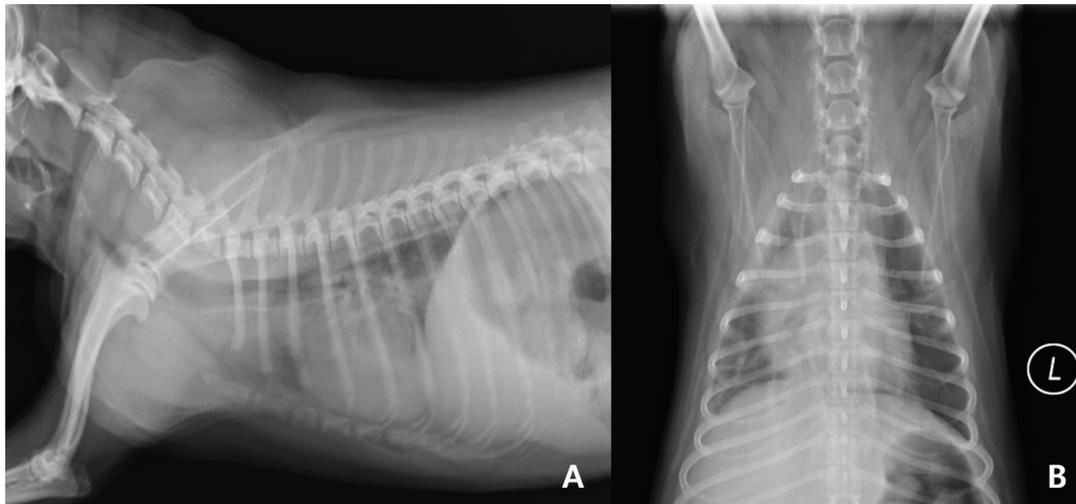


Figure 3. Right (A) lateral and (B) ventrodorsal views of the thoracic radiograph shows mild interstitial patterns in a dog (Case 2) at admission

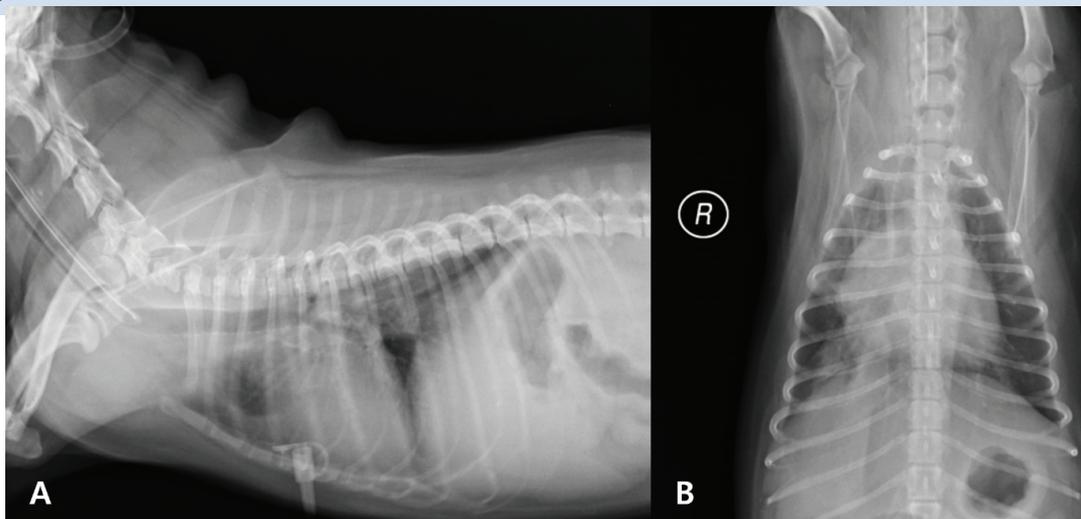


Figure 4. Right (A) lateral and (B) dorsoventral views of the thoracic radiograph shows improved interstitial patterns in the dog (Case 2) after treatments

to increase the chance of detecting airway collapse with screening for identifying pulmonary infiltrates was performed. The dog was diagnosed with tracheal collapse based on the thoracic radiographs. In addition, mild interstitial patterns were detected in the right middle lung lobe and the right caudal lung lobe without any evidence of cardiac enlargement (Figure 3). There was no evidence of cardiogenic PE (CPE) based on physical, thoracic radiographic examination and emergency echocardiography. These findings indicated that NPPE was caused by tracheal collapse, resulting in severe respiratory distress and hypoxic brain injury. Although treatments such as supplemental oxygen, nebulized fluticasone and salbutamol (fluticasone 1 mL and salbutamol 1 mL with N/S 3 mL), and aminophylline (10 mg/kg IV) were provided to resolve respiratory distress at presentation, the dog had no response. Therefore, acepromazine (0.05 mg/kg IV) was administered followed by propofol (4 mg/kg IV) for induction of anesthesia and endotracheal intubation, and a propofol CRI (0.1 to 0.6 mg/kg/min) was used to facilitate positive-pressure ventilation (PPV) via an anesthesia ventilator (MATRX MODEL 3000, MIDMARK®, USA) for 2 days. Tidal volume and respiratory frequency were adjusted to maintain End-tidal CO₂ values between 35 and 40 in capnography. These were controlled between 10-15 ml/kg, 8-15/min, respectively. Peak airway pressure was kept at 20-30 cmH₂O. To prevent oxygen toxicity, the fraction of inspired oxygen (FiO₂) was monitored to not exceed 0.6. After the treatments, including mechanical ventilation for 2 days, approach to weaning was based on oxygenation levels (SpO₂ 98% and FiO₂ 0.5). After successful weaning from PPV, previous neurologic deficits including weak pupillary light reflex and loss of palpebral reflex greatly improved. The dog was discharged with a mild cough, but interstitial patterns on the right middle and caudal lung lobe on the thoracic radiographs improved (Figure 4). From the day of discharge, theophylline (10 mg/kg PO, q 12 h), N-acetylcysteine (50 mg/kg PO, q 12 h), tramadol (4 mg/kg PO, q 12 h), and bromhexine (2 mg/kg PO, q 12 h) were administered for 2 weeks to improve respiratory distress. Additionally, prednisolone (0.5 mg/kg PO, q 24h for 7 days, and 0.3 mg/kg PO, q 24 h for 7 days) was given to prevent the intratracheal swelling that resulted from endotracheal intubation.

DISCUSSION

PE is defined as fluid accumulation in the interstitial or alveolar space of the lung and is classified into

two categories depending on the underlying causes: cardiogenic (CPE) and non-cardiogenic PE (NCPE) (Bouyssou et al, 2017; Glaus et al, 2010). NPPE is a well-known type of NCPE caused by upper airway obstruction such as chock, strangulation, tumors, or laryngospasms in humans (Bhattacharya et al, 2016; Lonergan et al, 2021; Herrick et al, 1990). Nevertheless, it could be a life-threatening emergency, and early diagnosis followed by rapid treatment of NPPE is still challenging because of the clinical similarities with other types of PE (Perina, 2003; Liu et al, 2019). In addition, it is important to distinguish between NCPE and CPE because these conditions have different treatments (Glaus et al, 2010). In humans, the prevalence of NPPE as a result of laryngospasms related to extubation of the endotracheal tube after general anesthesia is only 0.05% to 0.1% (Liu et al, 2019). Treatments such as ventilation with continuous positive airway pressure and ways of controlling the underlying causes are reported (Budhathoki and Wu, 2020; Liu et al, 2019). However, in veterinary medicine, there has been only one report of a horse with NPPE as a postanesthetic complication (Tute, et al, 1996). Therefore, the present report for case 1 is the first to describe the clinical course of NPPE following surgery in which external ring prostheses were placed to support a collapsing cervical trachea. In addition, the report for case 2 is about successful treatment of NPPE using PPV.

Case 1 presented with acute respiratory distress accompanied by respiratory acidosis based on blood gas analysis after surgery in which external ring prostheses were placed to support a collapsing cervical trachea. First, the possibility of aspiration pneumonia, which is one of the differential diagnoses and most common complications of general anesthesia, was relatively low based on a history of strict fasting before surgery and absence of aspiration during the perioperative period although silent aspiration could not be completely ruled out. No evidence of cardiac disease was found based on physical examination, thoracic radiograph, and echocardiogram. Pulmonary edema and respiratory distress persisted despite the use of diuretic drugs to reduce pulmonary hydrostatic pressure. Thus, the possibility of CPE and fluid overload was ruled out. In addition, increased pulmonary opacity is more often asymmetric, unilateral, and dorsal for NPPE than it is for other types of NCPE (Bouyssou et al, 2017). In this case, bilateral, but asymmetrically increased, pulmonary opacity was observed in the lungs on the ventrodorsal view (Fig-

ure 1). Furthermore, the serum biochemistry profile showed hypoproteinemia which might result from increased pulmonary vascular permeability and leakage of protein-rich fluid into the alveolar air sacs (Perina, 2003). Therefore, this feature could support the suspicion of NPPE in dogs with upper airway obstruction showing acute respiratory distress, because the dog had no evidence of massive bleeding, pleural/peritoneal effusion, vasculitis or other diseases that cause panhypoproteinemia such as protein-losing enteropathy. Additionally, there was no allergic reaction such as generalized erythema, hypotension, or swelling of the cervical area including the larynx and pharynx associated with drug administration during the perioperative period.

Laryngeal edema, and oropharynx and tracheal damage are frequent complications of endotracheal intubation under general anesthesia in humans. Interestingly, a previous report suggested that head, neck, and oropharyngeal surgery, which may be involved with the sensitive dilator muscles of the upper airway, increases the risk of NPPE in human patients (Liu et al, 2019). Case 1 underwent neck surgery in which external ring prostheses were placed to support a collapsing trachea. Considering the above factors, NPPE after tracheal intubation or cervical surgery, although it was performed to relieve tracheal collapse, was most suspected. Some studies report that steroids can be useful for the prevention and treatment of such complications, including laryngeal edema (Wittekamp et al, 2009). Subsequently, Case 1 was immediately given dexamethasone for 2 days to relieve postoperative tracheal swelling and recovered quickly after treatment.

In Case 2, increased pulmonary opacity was asymmetric and unilateral according to the radiographic examination of the lungs in the ventrodorsal view, and there was no evidence of cardiac disease. Because upper airway obstruction can cause NPPE, and tracheal collapse is the most common cause of upper airway obstruction in dogs (Algren et al, 1993; Bouyssou et al, 2017), NPPE due to tracheal collapse was most suspected. The neurologic deficits noted were likely the result of brain damage related to NPPE and hypoxia. Furthermore, there was no history of fluid therapy that could be related to fluid overload and no reason to suspect drug-induced anaphylaxis. De-

spite providing oxygen, nebulizer, and aminophylline, there was no improvement of the clinical signs. Thus, PPV, the most useful strategy for successful treatment of NPPE in humans (Perina, 2003; Liu et al, 2019), was performed. A previous study found that the survival-to-discharge rate for respiratory distress treated with PPV was 62.5% in 16 dogs, although the cause of respiratory distress was congestive heart failure (Edwards et al, 2014). Human patients who have upper airway obstruction attempt to inspire against the obstruction (Herrick et al, 1990; Lonergan et al, 2021). This effort generates very low intrathoracic pressure, which results in increased venous return from systemic circulation and preload that causes PE (Herrick et al, 1990; Bhattacharya et al, 2016). In addition, negative intrathoracic pressure decreases alveolar-capillary pressure, causing damage to the alveolar epithelial and capillary barriers. This damage leads to accumulation of protein-rich fluid in the alveolar sac (Budhathoki et al, 2020). Therefore, PPV can counteract and ameliorate the pathophysiology of NPPE as seen in Case 2 with fulminant PE.

In conclusion, veterinary clinicians should be aware that upper airway obstruction or surgery, especially associated with head and neck under general anesthesia, can cause fulminant NPPE in dogs. Furthermore, dogs with NPPE can be successfully treated using PPV and other treatments for underlying airway obstructions as in human patients. When NPPE occurs, swift recognition prompts clinical suspicion and adequate treatments of NPPE. In other words, understanding the etiology and pathophysiology of NPPE due to upper airway obstruction and early diagnosis with rapid intervention helps reduce mortality in dogs.

ACKNOWLEDGEMENTS

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