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Abstract

Case summary An 11-year-old male neutered cat was referred to The Ohio State University's Veterinary Teaching Hospital after being diagnosed with pleural effusion by a referral veterinarian. After thoracocentesis, analysis of the effusion was consistent with chyle. Echocardiography, radiographs and bloodwork were used to diagnose hypertrophic cardiomyopathy phenotype and left-sided congestive heart failure, suspected to be secondary to uncontrolled hyperthyroidism. While initiating medical therapy, repeated thoracocenteses were required. A severe pneumothorax developed, necessitating placement of bilateral thoracostomy tubes. A thoracic CT scan did not reveal a cause for the pneumothorax; therefore, it was suspected to have occurred secondarily to an iatrogenic laceration of the parenchyma during thoracocentesis. An autologous blood patch pleurodesis was considered contraindicated so instead the cat was administered a blood patch using blood from a canine blood donor. The cat's respiratory status remained stable without additional intervention. At 30h after blood patch pleurodesis, the thoracostomy tubes were removed and thoracic radiographs revealed near resolution of the pleural effusion and pneumothorax. The cat remained subclinical and was discharged from the hospital 48h after the blood patch pleurodesis. Upon follow-up at 4 and 8 weeks after discharge, the cat was alive and had no complications or adverse reactions from the blood patch pleurodesis.

Relevance and novel information This case documents the first report of a xeno-blood patch pleurodesis performed in a cat using blood from a canine donor. The cat had a successful discharge from the hospital with no adverse reactions from the xeno-blood patch pleurodesis.

Keywords: Blood patch pleurodesis; continuous pneumothorax; thoracocentesis; thoracostomy tube

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Case description

An 11-year-old neutered male domestic shorthair cat was referred to The Ohio State University's Veterinary Teaching Hospital for increased respiratory rate and effort. The cat, historically hyperthyroid and treated with diet alone, was presented to his primary veterinarian for respiratory distress and found to have pleural effusion (PLUR) on thoracic radiographs (TXRs), prompting referral.

On presentation, the cat had a gallop rhythm, absent bilateral bronchovesicular sounds ventrally, tachypnea

(50 breaths/min) with abdominal effort, weighed 2.6 kg with a body condition score of 2/9 and was estimated to be 5–7% dehydrated, with tacky mucous membranes and a prolonged skin tent. The cat was

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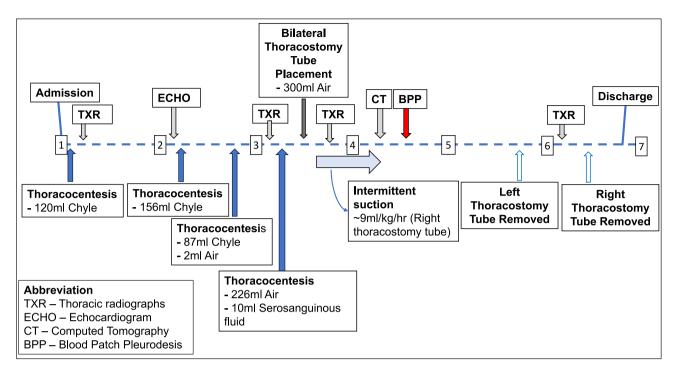


Figure 1 Timeline from admission to discharge represented by a dashed line with hospitalization days listed as numbers in boxes. Blue arrows represent thoracocentesis interventions; light gray arrows represent diagnostics; the dark gray arrow represents placement of thoracostomy tubes; the red arrow represents administration of xeno-blood patch pleurodesis; and white arrows represent removal of thoracostomy tubes

placed in an oxygen kennel (Snyder Intensive Care Units; Snyder Manufacturing) and an intravenous catheter was placed after respiratory improvement. Bilateral thoracocenteses were performed with sedation (butorphanol tartrate 0.3 mg/kg; Zoetis and alfaxalone 0.7 mg/kg IV; Convetrus). Opaque fluid totaling 120 ml was obtained, stabilizing the respiratory status (Figure 1). Fluid analysis (white blood count 6830/ul, predominantly small lymphocytes) and paired triglycerides (blood 45 mg/dl, effusion 401 mg/dl) confirmed a diagnosis of chyle.

TXRs (Figure 2) revealed residual PLUR (L>R), left cranial lung lobe atelectasis and cardiomegaly. Basic bloodwork and thyroid testing supported a diagnosis of uncontrolled hyperthyroidism (Table 1). The cat was hospitalized for oxygen, sedation (butorphanol tartrate 0.1–0.3 mg/kg IV; Zoetis) and fluid rehydration. Maintenance fluids were initiated with 0.45% sodium chloride 2 ml/kg/h (sodium chloride 1000 ml; Baxter), in addition to Plasmalyte-148 (Baxter) for replacement of 5% dehydration over 24h (total fluids 4 ml/kg/h). The cat was weaned from oxygen with clinical improvement and remained stable overnight with no other interventions.

On day 2, an echocardiogram confirmed a hypertrophic cardiomyopathy phenotype, American College of Veterinary Internal Medicine (ACVIM) stage C, active left-sided congestive heart failure (CHF), with a moderate amount of PLUR. Severe left atrial enlargements and left ventricular concentric hypertrophy were diagnosed, consistent with a thyrotoxic cardiomyopathy.1 Furosemide 1.5 mg/kg IV (VetOne) was administered for CHF. Bilateral thoracentesis was repeated (Figure 1) after administration of midazolam 0.2 mg/kg IV (Cardinal) and methadone 0.2 mg/kg IV (Cardinal). The treatment plan was amended to discontinue fluids and include furosemide 1 mg/kg IV q8h (VetOne) and clopidogrel 6.5 mg/kg PO q24h (Cardinal). Methimazole 0.87 mg/kg PO q12h (Felimazole; Dechra) was also initiated to treat hyperthyroidism. Despite initial treatment, the cat's respiratory status worsened, necessitating repeated bilateral thoracocenteses (midazolam 0.4 mg/kg IV [Cardinal], alfaxalone 0.7 mg/kg IV [Vetcove] and methadone 0.2 mg/kg IV [Cardinal]), achieving a normal respiratory rate (Figure 1).

On day 3, TXRs (Figure 3) were repeated owing to the return of tachypnea and dyspnea. Persistent cardiomegaly with unstructured pulmonary infiltrates, resolving PLUR, and a moderate, bilateral pneumothorax was visualized and confirmed with thoracocenteses (Figure 1). Oxygen support was continued; however, 3h later, tachypnea and dyspnea returned. A repeat TXR (Figure 4) revealed a severe pneumothorax (R>L), pulmonary atelectasis and static PLUR. Bilateral thoracocenteses

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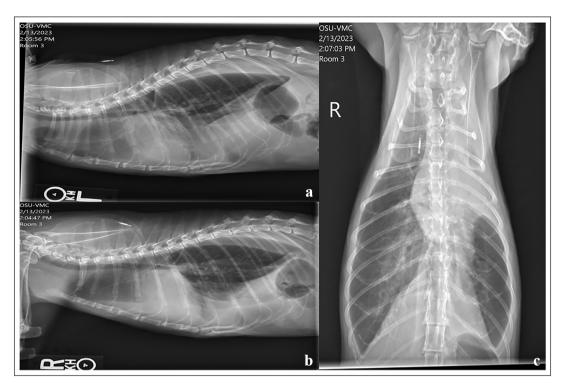


Figure 2 Three-view thoracic radiographs on the day of presentation, after thoracocentesis: (a) left lateral view; (b) right lateral view; and (c) ventrodorsal view. Bilateral pleural effusion was noted, which was worse on the left with left cranial lung lobe atelectasis, and cardiomegaly is seen

Table 1 Initial bloodwork performed on presentation

Test	Results	Reference interval
Н	7.316	7.265–7.424
HCT (%)	39	36–50%
Hb (g/dl)	13.5	4.0-24.0
RBC ($\times 10^{12}$ /I)	9.71	6.3–10.6
Platelet (×109/I)	190	128–444
Leukocyte (×109/l)	10.03	2.3–18.4
Segmented neutrophils (×10 ^s	7.92	1.4–11.8
Lymphocytes (×109/I)	1.2	0.6–5.7
Monocytes (×109/I)	0.50	0.0–0.6
Eosinophils (×109/I)	0.40	0.0–1.5
Na (mmol/l)	151.90	146.2–156.2
K (mmol/l)	3.77	3.42-4.71
CI (mmol/I)	116.70	117–125
iCa (mg/dl)	5.14	4.7–5.4
iMg (mg/dl)	1.2	0.80-1.19
Glucose (mg/dl)	129	72–132
Lactate (mmol/l)	3.6	1.1–3.5
BUN (mg/dl)	25	22–33
Creatinine (mg/dl)	0.66	0.7–1.9
HCO ₃ (mmol/I)	15.94	17.6–22.2
ALT (IU/I)	100	24–115
AST (IU/I)	93	12–45
ALP (IU/I)	69	10–61

(Continued)

Table 1 (Continued)

Test	Results	Reference interval
CK (IU/I)	465	68–538
Cholesterol (mg/dl)	206	77–264
Total bilirubin (mg/dl)	0.00	0.0-0.1
Total protein (g/dl)	6.8	5.3-8.5
Albumin (g/dl)	3.5	2.8-4.1
Globulin (g/dl)	3.3	2.2-5.3
Glucose (mg/dl)	125	75–211
T4 (μg/dL)	4.64	1.0–3.0

Values in bold are outside of the reference interval

ALP=alkaline phosphatase; ALT=alanine transaminase; AST=aspartate aminotransferase; BUN=blood urea nitrogen; CI=chloride; CK=creatine kinase; Hb=hemoglobin; HCO₃=Bicarbonate; HCT=hematocrit; iCa=ionized calcium; iMg=ionized magnesium; K=potassium;

Na=sodium; RBC=red blood cell, T4=thyroxine

(methadone 0.2 mg/kg IV [Cardinal] and midazolam 0.5 mg/kg IV [Cardinal]) were repeated, followed by placement of an aseptic bilateral thoracostomy tube (TT) (Catheter $14\,\mathrm{G} \times 20\,\mathrm{cm}$; MILA) under general anesthesia (Figure 1). TXR to confirm adequate TT placement showed minimal residual bilateral pneumothorax and PLUR. Methadone $0.2\,\mathrm{mg/kg}$ IV q6h (Cardinal) was added to the treatment plan. Frequent aspirations of the TTs yielded approximately $9\,\mathrm{ml/kg/h}$ of air from the right TT, while the left was minimally productive (Figure 1).

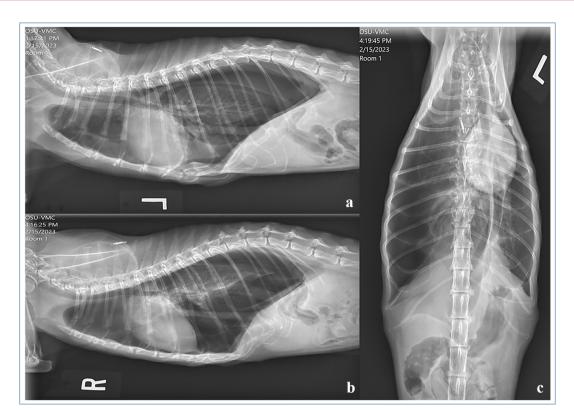


Figure 3 Three-view thoracic radiographs on day 3 of hospitalization: (a) left lateral view; (b) right lateral view; and (c) ventrodorsal view. Moderate bilateral pneumothorax, with resolving pleural effusion, generalized cardiomegaly consistent with reported hypertrophic cardiomyopathy and unstructured pulmonary infiltrates (atelectasis or cardiogenic pulmonary edema) are seen

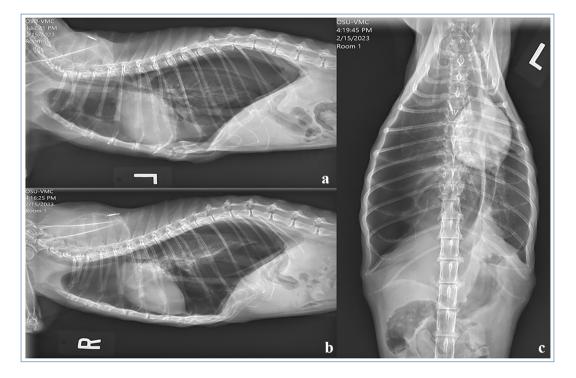


Figure 4 Repeat three-view thoracic radiographs on day 3 of hospitalization: (a) left lateral view; (b) right lateral view; and (c) ventrodorsal view. Severe right tension pneumothorax and moderate left pneumothorax, with pulmonary atelectasis and resolving pleural effusion are seen. Similar generalized cardiomegaly remains present, consistent with reported hypertrophic cardiomyopathy

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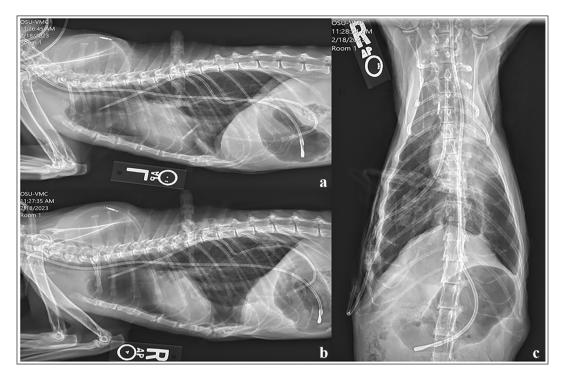


Figure 5 Three-view thoracic radiographs, day 6 of hospitalization, 30 h after pleurodesis, and immediately after removal of the left thoracostomy tube: (a) left lateral view; (b) right lateral view; and (c) ventrodorsal view. Mild persistent bilateral pneumothorax (right>left), pleural effusion and pulmonary atelectasis (worse in the left cranial lung lobe) are shown. Similar generalized cardiomegaly is seen. Right lateral thoracic body wall subcutaneous emphysema associated with TT placement is also seen. Nasogastric tube placement is also noted along with aerophagia

On day 4, a thoracic CT scan was performed under general anesthesia to evaluate for underlying etiology; a moderate right pneumothorax, scant left pneumothorax and PLUR were visualized. No underlying lung pathology or source was identified so an iatrogenic pneumothorax was suspected. A nasogastric tube was placed to facilitate administration of enteral nutrition and water.

As a result of the persistent, continuous pneumothorax, thoracotomy was discussed to diagnose and address the cause. Given the lack of CT scan findings, comorbidities, poor body condition, advanced age, invasiveness and expense of the procedure, this was declined. Continued medical management was also discussed. Euthanasia was considered because of the unpredictability of the length of hospitalization, rising cost and poor long-term prognosis. Alternatively, a blood patch pleurodesis (BPP) was elected after 24h as a last alternative to hasten resolution. Because of tachypnea, dyspnea, resolving CHF and under-conditioning, autologous blood was deemed unsafe. Allogenic-BPP was unavailable. Instead, the cat was administered a BPP using blood from a previously screened canine donor (DEA 1.1–). Whole blood was aseptically collected from the dog's external jugular vein into a non-anticoagulated 30 ml syringe. Simultaneously, the cat was administered midazolam 0.2 mg/kg IV (Cardinal) and methadone 0.2 mg/ kg IV (Cardinal) and the TTs were evacuated to negative. Immediately after blood collection, 30 ml (cat dose of

11 ml/kg) of donor blood was aseptically instilled via the TTs. Because the right TT had been more productive, 20 ml of blood was instilled in the right and 10 ml in the left. The cat was then rotated to allow dispersion of the BPP across all pleural surfaces. After pleurodesis, the cat's respiratory status was monitored, without aspirations of the TTs. The cat remained subclinical, with a normal respiratory rate recorded hourly. With resolution of clinical signs, the left TT was negative on aspiration and removed on day 5 (methadone 0.2 mg/kg IV; Cardinal), approximately 30h after pleurodesis (Figure 1).

The cat continued to be eupneic on day 6. TXRs (Figure 5) revealed a mild, bilateral pneumothorax and PLUR. The right TT was consequently negative on aspiration and removed (methadone 0.2 mg/kg IV; Cardinal). The cat was discharged from the hospital with furosemide 1.75 mg/kg PO q12h (Furosemide; Leading), clopidogrel 6.5 mg/kg q24h (Cardinal) and methimazole 0.87 mg/kg q12h (Felimazole; Dechra). At 4 and 8 weeks after discharge, the cat was alive and had no complications or adverse reactions from the BPP.

Discussion

Pneumothorax is the accumulation of free air within the pleural space, between the visceral and parietal pleura of the chest wall.² Iatrogenic pneumothorax can occur after thoracocentesis, fine-needle aspiration, TT placement or barotrauma during positive pressure ventilation.^{3,4} This

cat was diagnosed with CHF and chylothorax. No primary lung disease was identified; therefore, the pneumothorax was considered iatrogenic.

Cats with pneumothorax can often be treated successfully with medical management alone.3 Stabilization includes thoracocentesis, sedation and oxygen support. Standard medical management is typically required for 2-3 days and may include thoracocentesis, placement of TTs, oxygen, supportive care and treatment of underlying primary disease.2 Cats failing medical management are recommended to have diagnostics to rule out surgical disease.2 Thoracotomy can be both diagnostic and therapeutic. This invasive procedure, necessitating increased surgical skill and resources, may also result in increased morbidity and has financial ramifications for the owner. Surgery does not guarantee resolution and may not be a feasible option for all animals. Continuing medical management can also be lengthy, expensive and frustrating, often requiring extended hospital stays with no promise of resolution and the potential for recurrence.

One aspect of medical management previously explored is pleurodesis, a procedure aimed to stop the recurrence of fluid or air within the pleural space.⁵ Pleurodesis obliterates the pleural space while simultaneously resolving the source of the leaking air. This is performed by mechanical abrasion, via thoracotomy or thoracoscopy, or by instilling a sclerosant into the pleural space causing inflammation and fibrosis, resulting in adhesions between the pleural membranes.^{6,7} In dogs and cats, BPP has been a documented cost-effective and successful pleurodesis method in situations where surgery has been declined or where persistent pneumothorax occurs.^{8–15}

During a BPP, whole venous blood is removed from the dog and aseptically delivered into the pleural space. Adhesion of clotted blood onto the affected pleural surface seals air leaking and triggers inflammation and fibrosis, resulting in adhesion of the pleurae.^{2,16} Autologous BPPs have few reported complications, including transient fever, infection, empyema and PLUR.¹⁷

Recently, four separate reports describe the successful use of BPP for pneumothorax in cats. 17–20 Three of these reports used autologous blood and one case series describes the successful use of allogenic BPP for treatment. 17 With allogenic BPP, there is added concern for immunologic blood transfusion reactions, none of which were reported. 17 A clear list of complications has not been reported.

Variable dosing strategies were employed in each feline BPP report. Dosages were in the range of 2–10 ml/kg.^{17–20} Each report described success at their respective dosages, making standard dosing desirable.^{17–20} Recognizing the limitations of small populations reported, variability in animal size, heterogeneous etiologies and limitations in available feline blood products, readily

available alternatives to autologous and allogenic BPP for cats is desirable. In this case, a xeno-BPP at a dose of 11 ml/kg for the cat was performed. This dose equated to approximately 1 ml/kg of the canine donor. This dose reduces morbidity risk to the larger donor, while providing ample BPP resources to the recipient and was similar to previous feline BPP reports. ^{17–20} If an autologous or allogeneic BPP was performed, this dose would have presumably been significantly lower, owing to the smaller donor size and higher donor morbidity.

Consideration was given to compatibility testing between the canine donor blood and the cat recipient. In the cat AB blood group systems, cats have clinically important anti-A and anti-B alloantibodies. To the authors' knowledge, clear published guidelines to support or refute compatibility testing between these two species do not exist and no information is available on the compatibility of blood used in xeno-BPP. In a study on xenotransfusion of anemic cats with canine blood, major crossmatching of feline plasma control samples with DEA 1.1+ and 1.1- canine red blood cells (RBCs) resulted in both positive and negative reactions, in a catdependent manner, while minor crossmatching showed mostly incompatibility.²¹ Crossmatching therefore may not predict transfusion reactions.21 In this case, no compatibility testing was performed. Adverse transfusion reactions, including immunologic acute and delayed hypersensitivity reactions, were discussed. Prophylactic medications to treat hypersensitivity reactions (corticosteroids or diphenhydramine) were considered but not given. Given the lack of allogenic BPP and consideration for euthanasia, the benefit of a xeno-BPP appeared to outweigh the risk. While some cats have alloantibodies, it is more likely that cats will develop antibodies to canine RBCs after exposure. 21,22 As a result of likely systemic absorption of the canine blood, repeated xeno-BPP would increase the risk for immunologic reactions. Further research is needed. No acute or delayed adverse reactions were identified in this case.

This report has some limitations. Initially, the CHF diagnosis was minimized. Had this been more strongly considered, an emergency echocardiogram could have been provided. Slower rehydration via the gastrointestinal tract would be safer. Diuretic therapy should have been initiated. It is uncertain if fluid therapy led to increased PLUR but cannot be excluded. Although butorphanol is effective for sedation, it may counteract the benefit of pure mu opioid agonist for better analgesia, hence why the thoracocentesis sedation protocol was changed on day 2.

The long-term outcome and complications associated with xeno-BPP remain unknown. Future investigation into ideal dosing and complications is necessary to recommend xeno-BPP for standard medical treatment involving pleurodesis.

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Conclusions

The report describes the successful use of canine blood for a BPP to treat a continuous pneumothorax in a cat. To the authors' knowledge, a xeno-BPP in a cat has never been reported. Xeno-BPP may be a viable option for the medical management of continuous pneumothorax in feline patients when autologous or allogenic feline blood cannot be used.

Conflict of interest The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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Ethical approval The work described in this manuscript involved the use of non-experimental (owned or unowned) animals. Established internationally recognized high standards ('best practice') of veterinary clinical care for the individual patient were always followed and/or this work involved the use of cadavers. Ethical approval from a committee was therefore not specifically required for publication in *JFMS Open Reports*. Although not required, where ethical approval was still obtained, it is stated in the manuscript.

Informed consent Informed consent (verbal or written) was obtained from the owner or legal custodian of all animal(s) described in this work (experimental or non-experimental animals, including cadavers) for all procedure(s) undertaken (prospective or retrospective studies). No animals or people are identifiable within this publication, and therefore additional informed consent for publication was not required.

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