Two cases of feline pyothorax: medical versus surgical treatment and associated challenges

Twee gevallen van feliene pyothorax: medicamenteuze versus chirurgische behandeling en geassocieerde uitdagingen

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ABSTRACT

Pyothorax is a rare disease in cats. Underlying causes and treatment recommendations vary greatly between cases. In this case series, the management of two challenging cases of feline pyothorax is discussed. In the first case, a nine-year-old female spayed European shorthair cat with pyothorax caused by *Bacteroides fragilis* is described. At the time of presentation, she was diagnosed with feline immunodeficiency virus as well. The pyothorax was succesfully managed medically. Unfortunately, the cat relapsed after three months and the owner elected euthanasia. The second case involved a ten-year-old male castrated British shorthair cat with identification of filamentous bacteria on pleural fluid cytology. This cat underwent surgical intervention because thoracic drainage was very difficult. Eventually, he recovered well and did not relapse up to two months postoperatively. The challenges in the decision process and treatment complications are discussed.

SAMENVATTING

Pyothorax is een aandoening die niet vaak voorkomt bij katten. De onderliggende oorzaken en behandelingskeuze variëren sterk naargelang het geval. In het voorliggende artikel worden twee uitdagende casussen van pyothorax bij de kat besproken. In de eerste casus wordt een vrouwelijke, gesteriliseerde Europese korthaar van negen jaar met pyothorax ten gevolge van *Bacteroides fragilis* besproken. Bij presentatie van de kat op de Faculteit Diergeneeskunde (UGent) werd bij het dier bovendien het feliene immunodeficiëntie virus gediagnosticeerd. De pyothorax werd succesvol behandeld met medicamenteuze therapie, maar de kat herviel drie maanden nadien en werd geëuthanaseerd. In de tweede casus wordt een mannelijke, gecastreerde Britse korthaar van tien jaar beschreven, waarbij op het cytologisch onderzoek van de pleurale effusie filamenteuze bacteriën geïdentificeerd werden. De kat onderging een chirurgische ingreep, herstelde uiteindelijk goed en vertoonde geen tekenen van recidief tot twee maanden postoperatief. De uitdagingen bij het maken van belangrijke beslissingen en de complicaties tijdens de behandeling worden besproken.

INTRODUCTION

Pyothorax is characterized by an accumulation of septic exudate in the thoracic cavity (Ettinger and Feldman, 2010). Most commonly, oropharyngeal flora is isolated in the pleural fluid (Walker et al., 2000; Demetriou et al., 2002). While infection of the thoracic cavity through penetrating bite wounds or parapneumonic spread after aspiration of oropharyngeal flora, e.g. after dental procedures, seem to occur most often in cats, the underlying cause remains unknown in 30-65% of cases (Waddell et al., 2002; Barrs et al., 2005; MacPhail, 2007; Barrs and Beatty, 2009a). The treatment approach of pyothorax remains controversial, but can be broadly divided into two groups: medical and/or surgical management. Medical treatment usu-

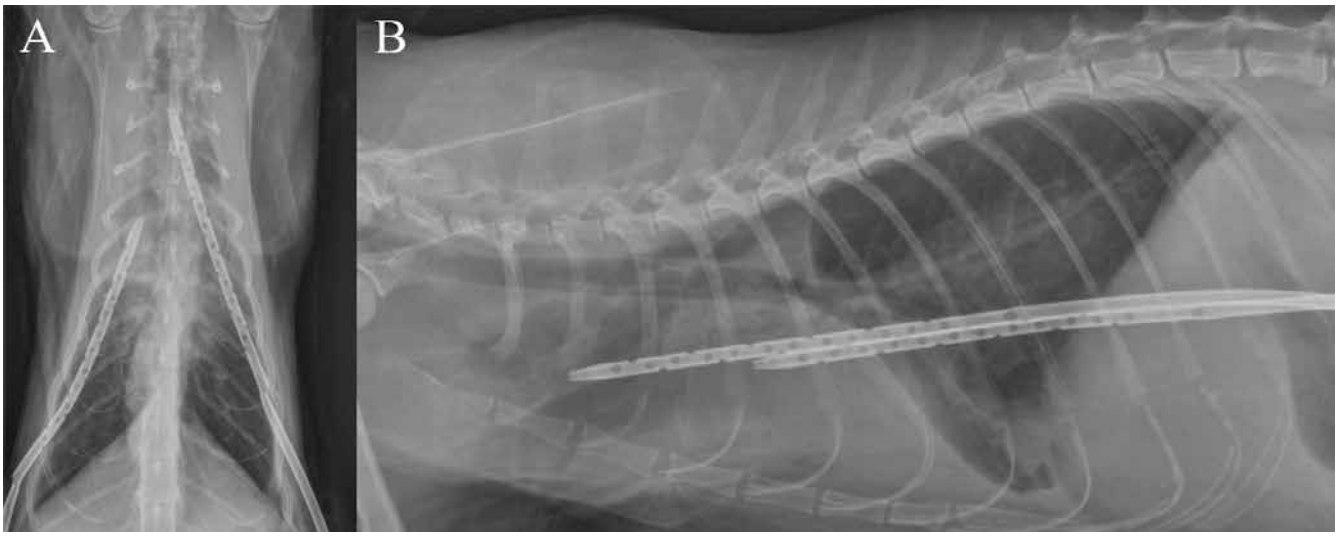
ally includes broad spectrum antibiotic treatment and thoracic drainage through thoracostomy tubes and often provides a good outcome in uncomplicated cases. In contrast, surgical treatment should be considered in cases that respond inadequately to the placement of thoracostomy tubes, in cases with isolation of filamentous bacteria in the pleural fluid, in cases of suspicion of or confirmed foreign body, and in cases with medical treatment failure after 2-7 days (Demetriou et al., 2002; Barrs et al., 2005; Monnet, 2009; Boothe et al., 2010; Murphy and Papasouliotis, 2011a; Stillion and Letendre, 2015). In this article, two cases of feline pyothorax are reported, enabling a thorough discussion of the differences between medical and surgical management and several factors influencing the clinician's decision process. The cat described in the first case tested positive for feline immunodeficiency virus (FIV). The compromised immune status of the cat required special measures to overcome pleural infection. In the pleural fluid of the second case, filamentous bacteria were isolated, complicating the general approach due to the associated pyogranulomatous reaction. The isolation of filamentous bacteria is one of the most common indications for early surgical intervention in pyothorax.

CASE 1

A nine-year-old female spayed European shorthair cat was presented at the referring veterinarian with chronic complaints of dyspnea, weight loss and lethargy and complete anorexia for three days. Upon examination, the cat had a fever. Antibiotics and non-steroidal anti-inflammatory drugs were initiated, but without clinical improvement. The following day, a thoracocentesis was performed due to muffled lung sounds on auscultation. Thick, yellow fluid was aspirated and the cat was referred (day 0) to the Small Animal Department, Faculty of Veterinary Medicine (Ghent University) for further diagnostic work-up and treatment.

Upon admission, the cat reacted aggressively to manipulation. She was tachypneic (70/min) and presented with an inspiratory dyspnea without stridor. Lung auscultation was muffled ventrally on both sides, but more pronounced on the left hemithorax. The remaining vital parameters were within normal limits. The cat showed mild muscle atrophy and severe dental plaque, tartar and gingivitis. The left eye showed remnants of an infection with feline herpes virus (FHV) as a kitten. The cat was kept strictly indoors, but the other cat in the household was allowed to go outside, and both cats did not get along very well.

The cat was admitted to the intensive care unit and supplemented with humidified oxygen in an oxygen cage. Quick in-house cytological evaluation of the pleural fluid provided by the referring veterinarian suggested pyothorax, based on the macroscopic appearance of the effusion and the presence of degenerated neutrophils and suspicion of intracellular bacteria on cytology. An intravenous (IV) catheter was placed and the cat was sedated with butorphanol (Dolorex®, Intervet International BV, Boxmeer, the Netherlands; 0.4 mg/kg IV), dexmedetomedine (Dexdomitor®, Orion Corporation, Espoo, Finland; 3 µg/kg IV) and midazolam (Dormicum®, NV Roche SA, Brussels, Belgium; 0.2 mg/kg IV). Afterwards, propofol (Propovet Multidose®, Zoetis Belgium SA, Louvain-la-Neuve, Belgium) was administered IV to effect, to allow placement of bilateral thoracic drains (Surgivet® Pneumothorax Set (10 Fr); Smiths Medical ASD Inc., Minnesota, United States of America). About 290 mL of pleural effusion was removed and correct positioning of the chest tubes was radiographically evaluated (Figures 1A and 1B). Thoracic radiographs did not reveal significant changes of the lung



Figures 1A and B. Control radiographs after the placing of bilateral thoracic drains in the cat of the first case. The right drain ends at the level of the fifth rib and was advanced slightly further afterwards. The left drain correctly ends at the level of the second rib. There is a moderate amount of pleural effusion present, characterized by the rounded lung lobes and the soft tissue opacity silhouetting with the heart.

Table 1. Blood results of both cases at presentation (day 0).

	Case 1	Reference values case 1	Case 2	Reference values case 2
Erythrocytes	**5.66**	6.54 – 12.2 x 10^{12}/L	**4.44**	5.00 – 10.00 x 10^{12}/L
Hematocrit	**23.1**	30.3 – 52.3 %	**22.9**	30.0 – 45.0 %
Hemoglobin	**8.1**	9.8 – 16.2 g/dL	10.7	9.0 – 15.1 g/dL
MCV	40.8	35.9 – 53.1 fL	51.6	41.0 – 58.0 fL
MCH	**14.3**	21.2 – 25.9 pg	**24.2**	12.0 – 20.0 pg
MCHC	35.1	28.1 – 35.8 g/dL	-	29.0 – 37.5 g/dL
RDW	23.1	15 – 27 %	20.9	17.3 – 22.0 %
Leukocytes	11.75	2.87 – 17.02 x 10^9/L	**38.01**	5.50 – 19.50 x 10^9/L
Neutrophils	**0.88**	1.48 – 10.29 x 10^9/L	**33.59**	2.50 – 12.50 x 10^9/L
Lymphocytes	**8.40**	0.92 – 6.88 x 10^9/L	1.00	0.40 – 6.80 x 10^9/L
Monocytes	**2.42**	0.05 – 0.67 x 10^9/L	1.58	0.15 – 1.70 x 10^9/L
Basophils	0.03	0.01 – 0.26 x 10^9/L	0.10	0.00 – 0.10 x 10^9/L
Eosinophils	**0.02**	0.17 – 1.57 x 10^9/L	**1.74**	0.10 – 0.79 x 10^9/L
Platelets	**19**	151 – 600 x 10^3/µL	**835**	175 – 600 µL x 10^3
Reticulocytes	**1.1**	3 – 50 x 10^3/µL	49.5	10 – 110 µL x 10^3
Urea	**14.3**	5.7 – 12.9 mmol/L	8	5.7 – 12.9 mmol/L
Creatinine	67	71 – 212 µmol/L	69	71 – 212 µmol/L
Total protein	66	57 – 89 g/L	60	57 – 89 g/L
Albumin	24	23 – 39 g/L	**18**	23 – 39 g/L
Globulin	42	28 – 51 g/L	42	28 – 51 g/L
ALT	21	12 – 130 U/L	101	12 – 130 U/L
ALP	14	14 – 111 U/L	37	14 – 111 U/L
Total bilirubin	-	-	**77**	0 – 15 µmol/L
Glucose	6.8	3.95 – 8.84 mmol/L	7.24	3.95 – 8.84 mmol/L
Sodium	**149**	150 – 165 mmol/L	161	150 – 165 mmol/L
Potassium	4	3.5 – 5.8 mmol/L	4.7	3.5 – 5.8 mmol/L
Chloride	-	-	122	112 – 129 mmol/L

MCV = mean corpuscular volume; MCH = mean corpuscular hemoglobin; MCHC = mean corpuscular hemoglobin concentration; RDW = red cell distribution width; ALT = serum alanine transferase activity; ALP = serum alkaline phosphatase activity.

field. The aspirated fluid grossly appeared yellow and opaque with large amounts of flocculent material. Pleural fluid cytology revealed a high cellularity, predominantly consisting of severely degenerated neutrophils and macrophages. Many extracellular and intracellular rod-shaped bacteria were present, confirming the suspected pyothorax. Total protein and total nucleated cell count (TNCC) were not performed since cytological examination was sufficient for diagnosis. A sample of the pleural effusion was submitted for aerobic and anaerobic culture.

A complete blood count (CBC) and serum biochemistry profile were performed, showing mild, non-regenerative anemia, mild lymphocytosis, severe neutropenia, pseudothrombocytopenia and slightly elevated urea (Table 1). Blood smear revealed moderate neutrophilia with left shift. The neutropenia seen on CBC can be explained as a laboratory error, in which the automated cell counts probably miscounted band neutrophils as lymphocytes. Given that the cat belonged to a multi-cat household with a history of intercat aggression, additional testing for feline immunodeficiency virus (FIV) and feline leukemia virus (FeLV) was performed (SNAP® COMBO FeLV Ag/FIV Ab TEST KIT, Idexx Laboratories Inc., Maine, United States of America); the cat tested positive for FIV.

During the evening, the respiratory rate decreased to acceptable limits (36 to 44 breaths/min), the dyspnea resolved and the oxygen supplementation was stopped. The cat received maintenance fluid therapy (Sterofundin B®, B. Braun Melsungen AG, Melsungen, Germany; 70 mL/kg/day IV) as well as Hartmann's infusion (Vetivex Hartmann's Solution®, Dechra Limited, Staffordshire, United Kingdom; 35 mL/kg/day IV) for rehydration and to compensate for loss of fluids through thoracic drainage. The chest tubes were emptied every four hours and thoracic lavage with Hartmann's solution was performed every eight hours (initially 10 mL/kg, thereafter 20 mL/kg). Antibiotic therapy was initiated with amoxicillin-clavulanic acid (Augmentin®, GlaxoSmithKline Pharmaceuticals SA/NV, Waver, Belgium; 20 mg/kg q8h IV) and enrofloxacine (Baytril 2.5%®, Bayer SA/NV, Diegem, Belgium; 5 mg/kg q24h SC). Buprenorphine (Vetergesic®, Alstoe Limited, York, United Kingdom; 10 µg/kg q8h IV) was initiated for pain management.

On day 1, the cat remained mildly tachypneic but the lung sounds were less muffled. The general condition was improved, but the cat remained anorexic. Omeprazole (Losec®, AstraZeneca SA/NV, Brussels, Belgium; 1 mg/kg q24h IV) was initiated. The thoracic drains were still highly productive with a total of 34.6 mL/kg/day.

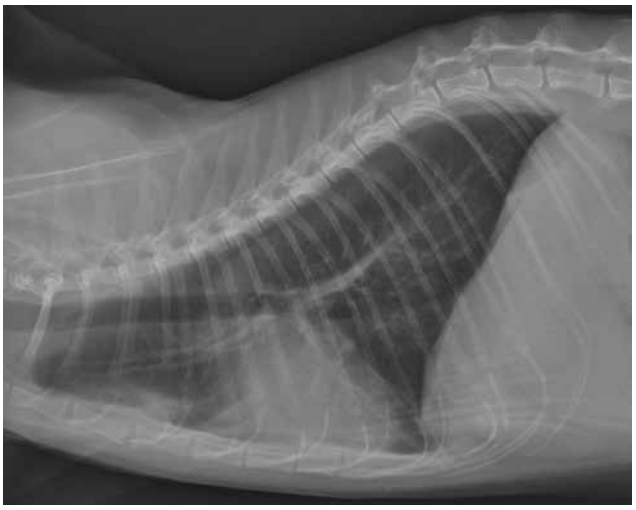


Figure 2. Right lateral thoracic radiograph of the European shorthair cat two weeks after discharge, showing marked improvement of the pleural effusion. There are some pleural fissure lines present, most likely indicating thickening of the pleura due to scar tissue.

Over the next days, the cat's respiratory pattern normalized. Repeated pleural fluid cytology revealed decreasing numbers of neutrophils, macrophages and intracellular bacteria. By day 3, chest tube production had decreased to 6.4 mL/kg/day and bacteria were only rarely detected on pleural fluid cytology. Unfortunately, the cat's good clinical response coincided with more aggressive behavior, which was an important factor in the cat's further management. The cat was sedated with butorphanol (Dolorex®; 0.3 mg/kg IV) and both thoracic drains were removed. Because the cat still showed poor appetite, a naso-esophageal feeding tube was placed and tube feeding was started. On day 4, bacteriological culture of the pleural fluid came back positive for *Bacteroides fragilis,* sensitive to amoxicillin-clavulanic acid, and enrofloxacine was discontinued. Biochemistry was repeated and revealed normalization of the serum urea concentration. The cat regained appetite and was discharged on day 5 with amoxicillin-clavulanic acid (Kesium®, SOGEVAL, Laval, France; 20 mg/kg q12h PO) for a minimum of four weeks.

Recheck thoracic radiographs were advised one week after discharge, but the cat was presented two weeks later. At this point, she was still on antibiotics and showed no clinical signs of recurrence. She was eating well and had no respiratory complaints. On physical examination, there was neither tachypnea nor dyspnea. Auscultation of the lung field was normal, but a systolic heart murmur of 2/6 was detected at the level of the sternum. Due to the cat's uncooperative behavior, only one lateral view was performed and revealed pleural fissure lines, most likely indica-ting thickening of the pleura (scar tissue) associated with the pyothorax (Figure 2). The antibiotics were continued until the next control visit two to three weeks later. Echocardiography was offered, but declined by the owner.

Further follow-up was performed by the referring veterinarian. The antibiotic therapy was prolonged for several additional weeks and the cat remained clinically stable. Unfortunately, three months after discharge, pyothorax recurred. The owners decided not to treat again and the cat was euthanized.

CASE 2

A ten-year-old male castrated British shorthair cat was presented to the referring veterinarian for detartration. Afterwards, he was lethargic and completely anorexic for two days. He remained partially anorexic

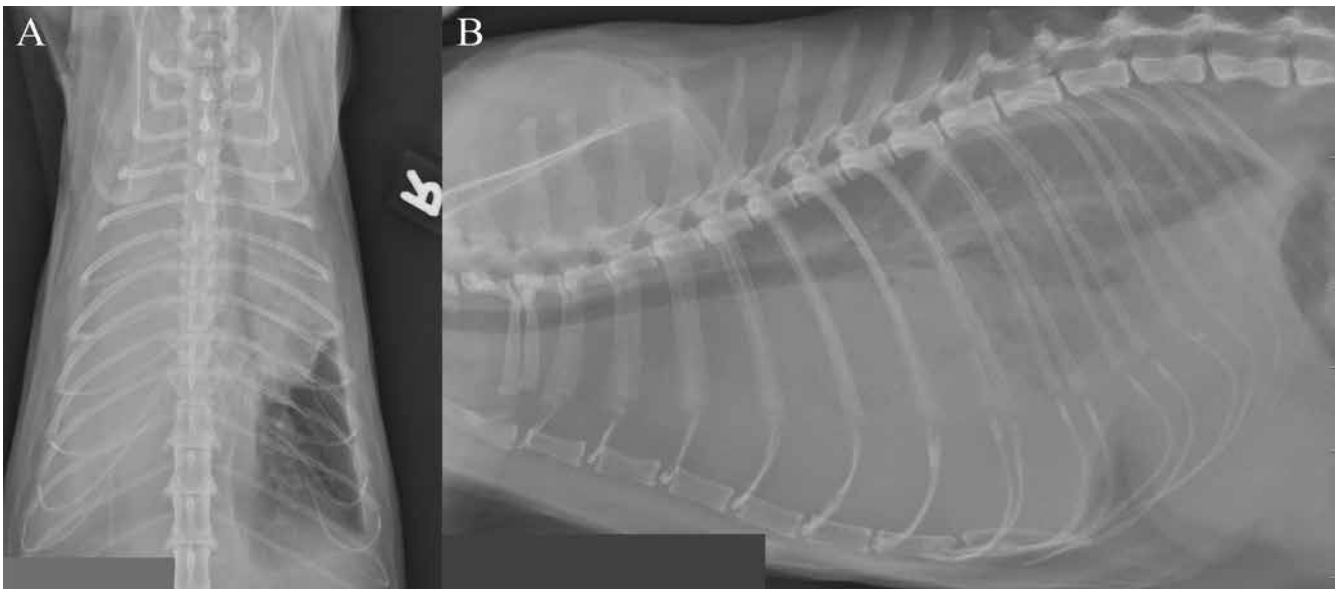


Figure 3. A. Right lateral and B. dorsoventral thoracic radiographs of the cat of the second case, showing very severe pleural effusion, more pronounced in the left hemithorax. The cardiac silhouette is masked by the soft tissue opacity of the free fluid and the trachea is displaced dorsally. The lungs are severely displaced caudodorsally on the lateral projection. There is an alveolar pattern present in the right cranial lung lobe.

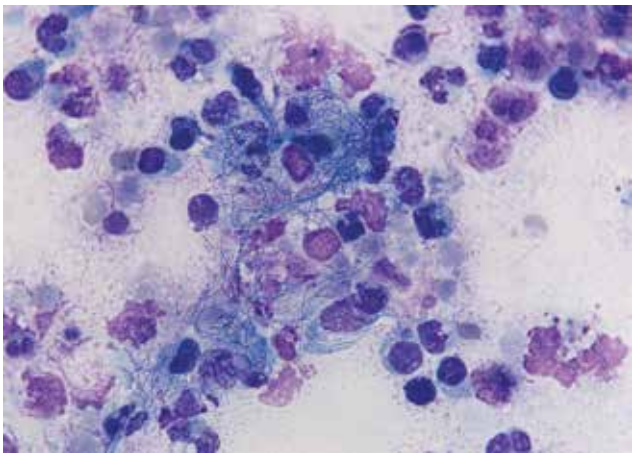


Figure 4. Hematoxylin and eosin stain of the pleural fluid of the British shorthair cat, showing large clusters of filamentous bacteria and large amounts of degenerated neutrophils and macrophages.

over the following three weeks and lost 600 grams. At that point, tachypnea, dyspnea and a fever of 40°C were identified. The cat received tolfenaminic acid (Tolfedine® 4%, Vétoquinol BV, 's-Hertogenbosch, Belgium; 4 mg/kg IM) and cefovecin (Convenia®, Zoetis Belgium SA, Louvain-La-Neuve, Belgium; 8 mg/kg IM), without improvement. Two days later, thoracic radiographs revealed the presence of mainly left-sided pleural effusion. Only a small amount of thick fluid was removed by thoracocentesis. Therefore, the cat was referred (day 0) to the Small Animal Department of the Faculty of Veterinary Medicine (Ghent University).

Physical examination revealed tachypnea with severe dyspnea – mainly inspiratory – without stridor, tachycardia and lethargy. Muffled lung- and heart sounds were auscultated, especially on the left hemithorax. The cat had pale pink mucous membranes with normal capillary refill time, and femoral pulses were weak. The blood pressure (BP), measured with the Doppler ultrasonic technique, was within normal limits (96 mmHg). CBC and serum biochemistry revealed mild, non-regenerative anemia, moderate leukocytosis, consisting of moderate neutrophilia and mild eosinophilia, mild thrombocytosis, moderate hypoalbuminemia and marked hyperbilirubinemia (Table 1). After stabilization with humidified oxygen delivered through a face mask, thoracic radiographs showed severe pleural effusion with asymmetric distribution, more pronounced in the left hemithorax. An alveolar pattern in the left cranial lung lobe was suspected, but this was to be re-evaluated after removal of the pleural fluid (Figures 3A and 3B).

Bilateral thoracocentesis was performed, removing 50 mL of thick, yellow pus containing flocculent material. On cytology, the pleural fluid showed a high cellularity and contained mostly degenerate neutrophils with smaller numbers of macrophages and areas of necrotic material. These findings were consistent with a purulent exudate. Large clusters of filamentous

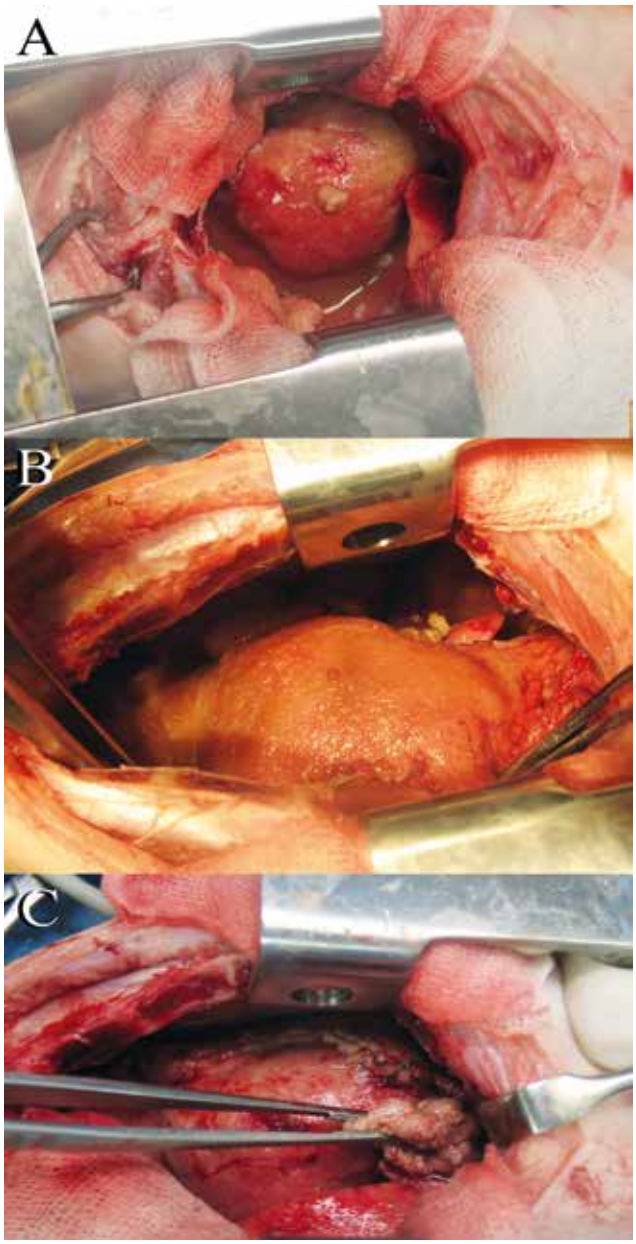


Figure 5. Intraoperative images showing A. a large amount of thick, pleural effusion with flocculent and fibrinous material B. left hemithorax with collaps of the lung lobes, covered with fibrinous material and C. a severely reactive and thickened mediastinum.

organisms confirmed the diagnosis of pyothorax (Figure 4). The cat was sedated with fentanyl (Fentadon®, Dechra, Bladel, the Netherlands; 5 µg/kg IV) and a local intercostal block was performed with lidocaine (Xylocaïne® 2%, AstraZeneca BV, Zoetermeer, the Netherlands; 4 mg/kg) to allow the placement of two thoracic drains. About 200 mL of red-brownish fluid with flocculent material was removed over the next ten hours, but drainage remained difficult. The cat was hospitalized and was started on crystalloid infusion (Vetivex Hartmann's Solution®; 90 mL/kg/24h), amoxicillin-clavulanic acid (Augmentin®; 20 mg/kg q8h IV) and enrofloxacine (Baytril 2.5%®; 5 mg/kg q24h IV). For analgesia, buprenorphine (Vetergesic®; 20 µg/kg q6h IV) was administered.

Table 2. Follow-up blood results during the hospitalization of case 2.

	Day 2	Day 3	Day 4	Day 5	Day 7	Day 9	Reference values
Erythrocytes	**3.37**	**4.36**	5.26	5.42	5.01	5.26	5.00 – 10.00 x 10^{12}/L
Hematocrit	**17.6**	**22.6**	**27.3**	**28.6**	**26.0**	**26.5**	30.0 – 45.0 %
Hemoglobin	**6.5**	9.6	9.5	10.4	9.7	9.7	9.0 – 15.1 g/dL
MCV	52.2	51.9	51.9	52.8	51.8	50.4	41.0 – 58.0 fL
MCH	19.3	**22.1**	18.2	19.3	19.3	18.4	12.0 – 20.0 pg
MCHC	37.0	-	35.0	36.5	37.3	36.5	29.0 – 37.5 g/dL
RDW	19.6	20.0	18.7	19.1	19.4	20.3	17.3 – 22.0 %
Leukocytes	**60.3**	**56.48**	**36.99**	**27.76**	**33.34**	**29.94**	5.50 – 19.50 x 10^9/L
Neutrophils	**54.72**	**50.22**	**31.91**	**24.41**	**30.03**	**20.37**	2.50 – 12.50 x 10^9/L
Lymfocytes	0.41	0.48	1.03	0.88	0.51	0.72	0.40 – 6.80 x 10^9/L
Monocytes	**2.75**	**3.94**	**2.20**	1.22	1.48	1.24	0.15 – 1.70 x 10^9/L
Basophils	**0.23**	0.09	**0.20**	**0.16**	**0.22**	**0.19**	0.00 – 0.10 x 10^9/L
Eosinophils	**2.19**	**1.76**	**1.65**	**1.09**	**1.10**	**2.42**	0.10 – 0.79 x 10^9/L
Platelets	403	**642**	524	575	434	**783**	175 – 600 x 10^3/µL
Reticulocytes	41.1	33.5	40.8	82.7	34.0	58.7	10 – 110 x 10^3/µL
Urea	-	-	-	-	2.5	-	5.7 - 12.9 mmol/L
Creatinine	69	74	-	-	73	-	71 – 212 µmol/L
Total protein	**43**	**56**	-	-	65	-	57 – 89 g/L
Albumin	**10**	**16**	**17**	-	**20**	**22**	23 – 39 g/L
Globulin	33	40	-	-	45	-	28 – 51 g/L
ALT	-	-	-	-	116	-	12 – 130 U/L
ALP	-	-	-	-	**135**	-	14 – 111 U/L
Total bilirubin	**63**	**62**	-	**46**	-	-	0 – 15 µmol/L
Glucose	-	-	-	-	7.43	-	3.94 – 8.83 mmol/L
Sodium	156	159	158	-	163	161	150 – 165 mmol/L
Potassium	4.3	**3.3**	3.7	-	-	4.5	3.5 – 5.8 mmol/L
Chloride	125	120	118	-	120	117	112 – 129 mmol/L
Phosphorus	-	-	1.49	1.71	-	-	1.00 – 2.42 mmol/L

MCV = mean corpuscular volume; MCH = mean corpuscular hemoglobin; MCHC = mean corpuscular hemoglobin concentration; RDW = red cell distribution width; ALT = serum alanine transferase activity; ALP = serum alkaline phosphatase activity.

The next day (day 1), the cat remained tachypneic with mild inspiratory dyspnea and muffled lung sounds. Because drainage through the thoracic drains was difficult and filamentous bacteria were seen on cytology, the cat underwent an exploratory sternotomy. He received fentanyl (Fentadon®, Dechra, Bladel, the Netherlands; 5 µg/kg IV) as premedication, and anesthesia was induced with alfaxalone (Alfaxan®, Jurox (UK) Limited, Worcestershire, United Kingdom; 3 mg/kg IV) and maintained with isoflurane (IsoFlo®, Zoetis Belgium SA, Louvain-La-Neuve, Belgium) vaporized in oxygen using a rebreathing system, combined with a constant rate infusion (CRI) of fentanyl (Fentadon®, Dechra, Bladel, the Netherlands; 5 µg/kg/h IV). Inspection of the pleural cavity showed a large quantity of thick, yellow fluid. In the left hemithorax, all lung lobes were collapsed and covered with fibrous material. The right hemithorax showed no collapsed lung lobes, but adhesions between the lung and the parietal pleura were present. The mediastinum was severely reactive and thickened and was removed for the most part (Figure 5). Samples for aerobic and anaerobic bacteriologic and histologic examination were taken and submitted to the lab. A new thoracic drain was placed and secured with a Chinese finger trap suture. An esophageal feeding tube was placed to ensure adequate nutritional support. Additionally, a fentanyl patch (Duragesic®, Janssen Pharmaceutica Products, L.P., New Jersey, United States of America) was placed onto shaved and cleaned skin to provide analgesia during hospitalization.

Thoracic radiographs were taken to ensure the correct placement of the esophageal feeding tube as well as the thoracic drain. Postoperatively, the cat suffered from severe hypotension (BP of 74 mmHg), and serum biochemistry revealed severe hypoalbuminemia (Table 2). He received two boluses of colloids (HAES-steril 6%®, Fresenius Kabi NV/SA, Schelle, Belgium; 2.5 mL/kg IV) and was placed on a CRI of colloids (HAES-steril 6%®; 0.8 mL/kg/h IV). Because the blood pressure (BP) did not improve, a CRI of norepinephrine (Levophed®, Hospira Benelux BVBA, Antwerp, Belgium; 0.1 µg/kg/min IV) was started. After gradually increasing the dose to 0.18 µg/kg/min, the BP increased to normal values (90-92 mmHg). The thoracic drain was emptied every four hours and a total of 68 mL (15.1 mL/kg/day) was collected on day 1. Buprenorphine was replaced by methadone

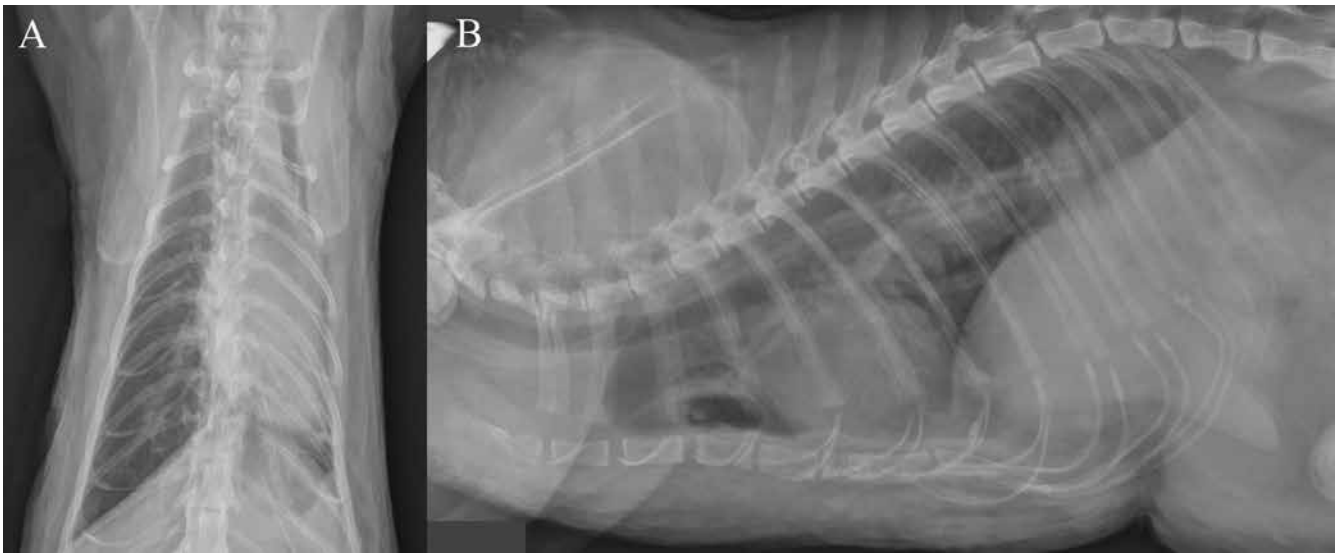


Figure 6A. Lateral and B. dorsoventral thoracic radiographs of the British shorthair cat on day 9. The radiographs show improvement of the atelectasis of the left cranial lung lobe, which had previously been seen. A left-shift of the mediastinum and the cardiac silhouette is still present due to remaining decreased volume of the left lung. A focal area of pleural effusion persists at the level of the left costodiaphragmatic angle.

(Comfortan®, Eurovet Animal Health BV, Bladel, the Netherlands; 0.3 mg/kg q4h IV) until sufficient activity of the fentanyl patch could be reached and meloxicam (Metacam®, Boehringer Ingelheim Vetmedica GmbH, Ingelheim/Rhein, Germany; 0.1 mg/kg SID SC) was added to the therapy.

On day 2, the BP decreased again (75-84 mmHg). Therefore, meloxicam was not repeated, and the CRI of norepinephrine was increased to 0.22 µg/kg/min. Blood examination revealed persistent hypoalbuminemia and more severe anemia (Table 3). A compatible whole blood transfusion was administered without complications. During the day, a total of 86 mL (20.2 mL/kg/day) of pleural effusion was collected. The neutrophils still showed signs of degeneration, but less than on the initial smears. The macrophages were strongly vacuolated. Only a few rod-shaped intracellular bacteria were seen, but no more chains of filamentous bacteria were present. Tube feeding was started in the evening. Methadone was discontinued, further therapy remained the same.

The next day (day 3), the hypoalbuminemia and anemia had slightly improved (Table 3). Because the cat developed hypokalemia, the Hartmann infusion was supplemented with potassium (Kali-Sterop®, Laboratoria STEROP NV; Brussels, Belgium; 30 mEq/L). The CRI of colloids and norepinephrine could be decreased gradually while maintaining normal BP, and both were discontinued eventually. The total amount of pleural effusion aspirated decreased to 28 mL (6.4 mL/kg/day).

On day 4, thoracic radiographs showed small remnants of pleural effusion, but an iatrogenic pneumothorax was caused, because the three way-stop valve got detached. Fortunately, this was quickly resolved. The hypokalemia normalized and the potassium supplementation was stopped. The hypoalbuminemia, anemia and leukocytosis kept on improving and total aspirated pleural fluid decreased to 18 mL (3.9 mL/kg/day) (Table 3). The pleural fluid had a lower cellularity than the days before and no more bacteria were seen. Despite the cytological presence of filamentous organisms, bacterial culture after three days of growth came back negative. Histological examination revealed reactive proliferations, most likely in response to bacterial antigens, with rod-shaped bacteria in a single area. No filamentous bacteria were seen and acid-fast stains were negative.

During the following days, the cat remained stable, but calm and anorexic. On day 5, the thoracic drain was removed and on day 6, the antibiotics were changed from intravenous to oral administration. Enrofloxacine (Xeden®, SOGEVAL, Laval, France; 5 mg/kg SID PO) and amoxicillin clavulanic acid (Clavubactin®, Le Vet BV, Oudewater, the Netherlands; 12.5 mg/kg BID PO) were administered. The Hartmann infusion was continued at maintenance rate. The next day (day 7), definitive bacterial cultures came back negative as well. It was decided to add trimethoprim-sulphadiazine (Tribrissen®, Intervet International BV, Boxmeer, the Netherlands; 15 mg/kg SID PO), because the clinical condition of the cat did not improve sufficiently, suggesting ongoing infection despite negative culture results. Afterwards, the cat became more active. Blood results improved further and thoracic radiographs were repeated on day 9, which showed improvement of the atelectasis of the left cranial lung lobe and little remaining pleural effusion (Table 2; Figures 6A and 6B).

The cat was discharged on oral antibiotics (enrofloxacine, amoxicillin clavulanic acid and thrimethoprim-sulphadiazine), and feeding through the esophageal feeding tube were continued at home. Fortunately, the cat quickly started eating spontaneously at home

and the esophageal feeding tube could be removed. Two months after discharge, the cat was active, had a good appetite and had already gained some weight. Recheck thoracic radiographs were taken by the referring veterinarian, which showed no more pleural effusion and further improvement of the atelectasis of the left lung lobes. Unfortunately, the cat was lost to further follow-up.

DISCUSSION

In this article, both medical and surgical treatments of pyothorax in cats are discussed based on the description of two different cases. It is obvious that the treatment approach should be adjusted according to each individual case. The first case showed no immediate indication for surgical intervention. Medical treatment was started and the cat rapidly responded. The second case was diagnosed with a more complex pyothorax from the beginning, characterized by inadequate drainage through thoracostomy tubes and cytological detection of filamentous bacteria. It was quickly decided that surgical exploration would be necessary to provide a good outcome. Not all cases of pyothorax are this clearly divided into those that need surgery and those that do not. Therefore, all cases of pyothorax should undergo thorough work-up, minimally consisting of thoracic radiographs after fluid drainage and cytological evaluation and bacteriological culture of the pleural fluid, to assess whether or not any complicating factors could be present (MacPhail, 2007).

Although in case 1, straightforward medical treatment of pyothorax is described, the treatment approach was in fact complicated by the FIV-positive status of the cat. An association between pyothorax and FIV-positive cats could be expected, given that both can be attained through bite wounds. Moreover, the immuosuppression caused by FIV might be a predisposing factor for bacterial infections, possibly leading to pyothorax. Currently, no direct relationship between pyothorax and FIV seems to be present. The prevalence of FIV in cats with pyothorax seems to be low (1.5%), although only 50 of 128 affected cats have actually been tested (Demetriou et al., 2002; Waddell et al., 2002; Barrs et al., 2005). Given that the cat was only diagnosed with FIV at presentation for pyothorax, it is difficult to assess the influence of FIV on the pleural space disease process. The anamnesis did not reveal any relevant medical history, but the acute phase of infection with FIV, characterized by transient sickness, often goes unnoticed by the owners. This suggests that at presentation, the cat was either in the subclinical phase of FIV-infection, undergoing progressive immunosuppression, or in the terminal phase, with the bacterial infection of the pleural space as an opportunistic infection (Sykes, 2014a).

The cat in this case responded well to conservative treatment, consisting of analgesia, thoracic drainage with lavage and antibiotic therapy. Initially, amoxicillin-clavulanic acid and enrofloxacine were administered. In light of increasing antibiotic resistance, it would have been better to initiate therapy with amoxicillin-clavulanic acid or amoxicillin only, given that the obligate anaerobic bacteria most frequently isolated from pyothorax in cats, are often susceptible to penicilline derivates (Walker et al., 2000; Demetriou et al., 2002; Barrs et al., 2005; Barrs and Beatty, 2009b). However, the veterinary clinicians in this case report take increasing antibiotic resistance into consideration through the use of de-escalation therapy, i.e. discontinuation of ineffective antibiotics after susceptibility testing or based on clinical response (Weese et al., 2015). In human medicine, de-escalation therapy has been successfully used in order to minimize antibiotic resistance and no negative impact on clinical condition has been seen (Gonzalez et al., 2013; Mokart et al., 2014). In the cat of this case report, the isolated bacteria were susceptible to amoxicillin-clavulanic acid and therefore, enrofloxacine was discontinued. By doing so, the development of antibiotic resistance might have been be minimized (Weese et al., 2015).

In the literature, there is no general consensus as to when thoracic drains are ideally removed in cases of pyothorax. Most commonly, drain removal is advised when fluid production is declining, cytological evidence of infection resolution is present and the patient is responding well clinically. Ideally, bacterial culture results should confirm appropriate antibiotic therapy prior to removal (Demetriou et al., 2002; Klainbart et al., 2007; Barrs and Beatty, 2009b; Marques et al., 2009; Murphy and Papasouliotis, 2011b). Several external factors took part in the decision to prematurely remove the drains in this case. The cat was difficult to manipulate, especially regarding thoracic drainage and lavage, and the owners were financially limited. Given that drain production was low, clinical response was good and significant cytological improvement of infection was seen, the thoracic drains were removed in spite of few bacteria still being present on cytology of the pleural fluid. In this case, the results of culture and susceptibility testing were not available yet, to confirm appropriate antibiotic treatment.

This case sets a good example for treating FIV-positive cats. Although these cats are more susceptible to opportunistic infections, they may be as capable as FIV-negative cats in fighting infections. However, it might be necessary to prolong antibiotic therapy or to treat more aggressively to enable full recovery (Hosie et al., 2009). In one case, a cat tested positive for FIV when being presented for recurrence of pyothorax (Demetriou et al., 2002). It can be suggested that there is a link between FIV and recurrence rates, but data supporting this belief are insufficient and recurrence is a known complication of pyothorax in cats, regardless of the immune status (Demetriou et

al., 2002; Waddell et al., 2002; Boothe et al., 2010). In the cat of this case report, the pyothorax relapsed three months after discharge, but it remains uncertain whether this can be attributed to the FIV-positive status of the cat.

In case two, a complex example of pyothorax in cats caused by filamentous organisms is described. Filamentous bacteria most commonly isolated in pyothorax include *Actinomyces* spp. and *Nocardia* spp. (Demetriou et al., 2002; Waddell et al., 2002; Barrs et al., 2005). Most commonly, *Nocardia* spp. are acid-fast whereas *Actinomyces* spp. are not. However, when the infecting strain of *Nocardia* is not acid-fast, differentiation between both may be difficult (Sykes, 2014b). Although *Nocardia* spp. are usually not difficult to isolate on most routine bacteriologic media (Saubolle and Sussland, 2003), the culture results came back negative, hence, definitive diagnosis and susceptibility testing were not possible in this case. In this case, acid-fast stains on the histological samples came back negative, but the cat was suspected to be infected with *Nocardia* spp. based on poor response to initiated antibiotic therapy. *Nocardia* spp. are gram-positive filamentous saprophytes that are found in dust, organic material and water. Infection occurs through inhalation or through inoculation of skin wounds. Nocardiosis is often seen as an opportunistic infection in immunocompromised patients (Malik et al., 2006; Sykes, 2014b). The cat in case 2 did not undergo FIV/FeLV-testing because he was strictly kept indoors and had no contact with other cats, making infection unlikely. There were no reasons to assume that the cat was immunocompromised. Typically, nocardiosis is divided into three clinical syndromes: cutaneous, pulmonary and disseminated nocardiosis (Malik et al., 2006; Sykes, 2014b). In pulmonary nocardiosis, infection most likely occurs through inhalation, and intra- and/or extrapulmonary masses are formed, possibly leading to pyothorax (Sykes, 2014b). In this case, it is important to acknowledge dental procedures as a possible underlying cause of pyothorax. In most cases of pyothorax, oropharyngeal flora is isolated. These bacteria can be aspirated during dental procedures (Demetriou et al., 2002; Barrs et al., 2005). This cat had recently undergone detartration, but it was difficult to confirm a causal relationship. *Actinomyces* spp. may form part of the normal oropharyngeal flora in cats, whereas *Nocardia* spp. do not (Walker et al., 2002; Barrs et al., 2005).

Pyothorax caused by filamentous organisms generally does not respond well to medical therapy because of the associated pyogranulomatous inflammatory response, complicating sufficient drainage of the pleural exudate (Sivacolundhu et al., 2001; Malik et al., 2006). In this case, drainage through thoracostomy tubes was indeed very difficult. Thoracic radiographs revealed an alveolar pattern, and computed tomography (CT) was proposed to the owners to provide more detailed information regarding the cause. The owners did not consent to this scan and decided on early exploratory surgery instead. The performed mediastinectomy was necessary to enable adequate thoracic drainage, which is one of the cornerstones of successful treatment of pyothorax (Piek and Robben, 2000; Rooney and Monnet, 2002; Boothe et al., 2010).

Postoperatively, the cat in case 2 did not recover without complications. The cat developed severe hypotension. In cats with pyothorax, this is most commonly seen due to the development of sepsis (Brady et al., 2002). Most common complications after thoracic surgery include pain and/or wound dehiscence and discharge. Postoperative hypotension has not been thoroughly described, but recovery after thoracic surgery seems to be more guarded for cats than for dogs (Moores et al., 2007; Tilson, 2016). In general, the mortality rates of cats and dogs undergoing thoracic surgery vary according to underlying disease, with an intermediate survival rate (60-70%) for cats and dogs undergoing thoracic surgery for pleural effusion (Bellenger et al., 1996; Tilson, 2016). Severe complications, including death, seem to be associated more often with the underlying cause than with the surgery itself (Moores et al., 2007). Postoperatively, the cat in case two was hemodynamically unstable and the prognosis did seem more guarded at that time point. Intensive treatment with fluid therapy and vasopressors was necessary to gradually restore normal blood pressure. Only after two days, the colloids and norepinephrine could be discontinued and the cat was able to maintain normal blood pressure. Meloxicam was administered for perioperative pain management, when blood pressure was normalized. The use of non-steroidal anti-inflammatory drugs in a hypotensive patient is contraindicated because of the increased risk of adverse reactions, such as renal injury. Such drugs should be used cautiously in the presence of hypotension (Berry, 2015; Hunt et al., 2015). Therefore, when the blood pressure lowered again later on, meloxicam was discontinued. Further, on day 4, iatrogenic pneumothorax was caused through detachment of the three-way stop valve while taking thoracic control radiographs. Luckily, there were no other injuries to the thoracic cavity, the intrathoracic air was quickly evacuated through the intact thoracic drain and the cat did not suffer from any consequences afterwards. The long-term presence of thoracostomy tubes is not without risk. It has been reported that cats with chest tubes develop a variety of complications in over half of cases, ranging from local irritation to nerve damage, hemorrhage and pneumothorax (Barrs et al., 2005).

It was difficult to assess appropriate antibiotic therapy in this case, because there was no culture or susceptibility testing to account for. When there is a suspicion of *Nocardia* spp., first-choice antibiotics consist of trimethoprim-sulfonamides (TMS), but these are often disguarded due to the potential side effects, such as nausea, anorexia and myelosuppression, which may occur when treating at high dosages

for a long period of time, which is usually required for the treatment of pyothorax (Malik et al., 2006; Sykes, 2014b). Further, different strains of *Nocardia* spp. respond to different types of antibiotics and a broad-spectrum approach is for that reason often initiated instead. Studies in cats have shown that antimicrobial resistance of the most common strains of *Nocardia* to fluoroquinolones and amoxicillin-clavulanic acid is high and therefore, both should not be recommended for treating nocardiosis (Malik et al., 2006; Govendir et al., 2011). While waiting for culture results, the antibiotic therapy of the case discussed above initially consisted of the combination of amoxicillin-clavulanic acid and enrofloxacine. Although this is not the first choice for treating nocardiosis, it is generally effective for the treatment of other bacteria causing pyothorax, including *Actinomyces* spp. (Sivacolundhu et al., 2001; Rooney and Monnet, 2002; MacPhail, 2007). Unfortunately, nocardiosis could never be confirmed. The culture results came back negative and repeated cultures were not performed as it was unlikely to yield positive results after treatment with broad-spectrum antibiotics for several days. The insufficient improvement of the clinical condition of the cat raised suspicion and after six days, TMS were added to the therapy. According to de-escalation therapy, amoxicillin-clavulanic acid and enrofloxacine should have been discontinued and replaced by TMS (Weese et al., 2015). The lack of culture and susceptibility testing in this case made it difficult to safely adjust antibiotic therapy. Therefore de-escalation therapy was not applied. Furthermore, it is difficult to attribute the progression of the clinical condition to the initiation of TMS, because clinical improvement of nocardiosis is often only seen after approximately seven days of antibiotic treatment (Sykes, 2014b).

After discharge, the cat recovered well and was treated with long-term antibiotics. The cat did not show any signs of recurrence two months after discharge. It is not clear for how long the antibiotic therapy was prolonged and if all antibiotics were continued long-term. Nocardiosis usually has a guarded long-term prognosis because of high recurrence rates (Malik et al., 2006). Data concerning the appropriate duration of antibiotic treatment of pyothorax caused by *Nocardia* spp. in cats is scarce. The total duration of antibiotic treatment should be three to six months, but it may be required for up to a year to prevent the patient from relapsing (Sivacolundhu et al., 2001; Malik et al., 2006; Yildiz and Doganay, 2006).

CONCLUSION

In this case series, one case of pyothorax that was medically managed and one case that required surgical treatment are described. These two cases show that treatment approach should always be assessed individually in order to provide a good outcome and that challenges occur in cats with pyothorax. Recurrence is a common complication of pyothorax, which was of significant importance in the first case, describing pyothorax in an immunocompromised patient. In this case, prolongation of antibiotic therapy should be advised. The second case involved filamentous bacteria, causing an intrathoracic pyogranulomatous inflammatory response. Antibiotic therapy should be long-term in this case as well. In both cases, there was no clear consensus as to when the antibiotic therapy could be safely terminated.

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