CASE REPORT

Pyothorax caused by *Nocardia* sp. in a cat – Case report

Piotórax causado por *Nocardia* sp. em gato – Relato de caso

Juliana de Moraes Intrieri[1], Gabriela Pereira Salça de Almeida[2], Isabelle Vilela Bonfim[3], Fernando Rocha Miranda[2], Andressa Aparecida Lima Reis[2], So Yin Nak[1], Gabriele Bernardo do Amaral[1], Mário Mendes Bonci[4] & Diefrey Ribeiro Campos[5]

[1] Veterinarian. Autonomus, Rio de Janeiro, RJ, Brazil
[2] Veterinarian, MSc., Programa de Pós-Graduação em Ciências Veterinárias (PPGCV), Departamento de Parasitologia Animal (DPA). Intituto de Veterinária (IV), Universidade Federal Rural do Rio de Janeiro (UFRRJ). *Campus* Seropédica, RJ. Brazil.
[3] Veterinarian, PPGCV, DPA, IV, UFRRJ. *Campus* Seropédica, RJ, Brazil.
[4] Veterinarian, MSc., Programa de Pós-Graduação em Diagnóstico Bucal, Radiologia Odontológica e Imaginologia da Faculdade de Odontologia da Universidade de São Paulo. São Paulo, SP, Brazil.
[5] Veterinarian, DSc. PPGCV, DPA. IV, UFRRJ. *Campus* Seropédica, RJ. Brazil.

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Abstract

Nocardiosis is an infection caused by ubiquitous opportunistic bacteria and is rare in felines. In retrospective studies of the infection in the species, pyothorax was found in only about 5% of the cases described, with the most frequent forms being cutaneous and subcutaneous. This report describes *Nocardia* spp. as an etiologic agent of pyothorax in a feline leukemia virus (FeLV)-positive female cat. A 10-year-old female mixed-breed cat, positive for FeLV, with chronic kidney disease IRIS stage 2, was examined with a severe dyspneic onset, suspected of pleural effusion. It also had skin lesions in the interscapular region. The patient underwent thoracentesis, and a dense, creamy, fetid, and flocculated liquid was collected. Radiography was performed after draining the pleural fluid, which showed images suggestive of atelectasis of the left lung lobes and pneumonia. The collected material was sent for analysis, which found that it was a septic exudate. In addition, it was referred for bacterial culture in a special medium due to suspicion of nocardiosis. Long-term treatment with amoxicillin + clavulanic acid resolved the clinical case.

Keywords: nocardiosis, dyspnea, pleural effusion, retrovirus.

Resumo

A nocardiose é uma infecção causada por bactérias oportunistas ubíquas e é rara em gatos. Em estudos retrospectivos da infecção na espécie, o piotórax foi encontrado em apenas cerca de 5% dos casos descritos, sendo as formas mais frequentes a cutânea e a subcutânea. Este relato descreve *Nocardia* spp. como agente etiológico do piotórax em um gato vírus da leucemia felina (FeLV)-positivo. Um gato mestiço de 10 anos de idade, positivo para o FeLV, com doença renal crônica IRIS estágio 2, foi examinado com dispneia grave, com suspeita de derrame pleural. Apresentava lesões cutâneas na região dorsal entre as escápulas. Após sedação, tricotomia e antissepsia, o paciente foi submetido à toracocentese e coletado líquido denso, cremoso, fétido e floculado. A radiografia foi realizada após drenagem do líquido pleural, que mostrou imagens sugestivas de atelectasia dos lobos pulmonares esquerdos e pneumonia. O material coletado foi encaminhado para análise, que constatou tratar-se de exsudato séptico. Além disso, foi encaminhado para cultura bacteriana em meio especial por suspeita de nocardiose. O tratamento prolongado com amoxicilina + ácido clavulânico foi suficiente para a resolução do caso clínico.

Palavras-chave: nocardiose, dispneia, efusão pleural, retrovirus.

Introduction

Pyothorax is a clinical condition caused by the accumulation of pus in the pleural cavity (Norsworthy, 2018). The cause of feline pyothorax is not clear yet in the literature, but the main ones reported include parapneumonic infections, foreign body migrations, hematogenous dissemination or bacterial inoculation through penetrating chest wounds. The main clinical signs observed include a restrictive breathing pattern, tachypnea, fever, anorexia, cough and lethargy, which can potentially progress to a fatal septic condition. Characteristics such as the presence of flocculating material and foul odor support the diagnosis, which is confirmed through cytology

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***Correspondence**
Juliana de Moraes Intrieri
Departamento de Parasitologia Animal, Instituto de Veterinária, Universidade Federal Rural do Rio de Janeiro – UFRRJ
Rodovia BR 465, Km 7, Campus Universitário, Bairro Zona Rural
CEP 23897-000 - Seropédica (RJ), Brasil
E-mail: julianaintrieri25@gmail.com

and analysis of pleural fluid plus bacterial culture (Epstein & Balsa, 2020). Cytology should show degenerative neutrophilis, macrophages, and occasionally bacteria (Norsworthy, 2018).

Nocardiosis is caused by aerobic gram-positive filamentous bacteria of the order Actinomycetales (Lipovan et al., 2015). They are ubiquitous and saprophytic and can be found in soil, organic matter, plants, sand and water (Sykes, 2012). There is a great variety in the predominant species and their virulence around the world (Norsworthy, 2018) with *N. africana* being the main one reported in Brazil (Lipovan et al., 2015). It is less frequently diagnosed than actinomycosis, bacteria of the same order, but the cases are rising in association with an increase of immunocompromised hosts (Sykes, 2012).

Clinical signs may present as pulmonary, systemic or solitary extrapulmonary forms (Lipovan et al., 2015). Cutaneous and subcutaneous forms are the most common in cats, corresponding to about 75% of cases in literature reports (Sykes, 2012). Respiratory affections can involve the lungs or only the pleural cavity (Norsworthy, 2018). The systemic form, in many cases, is associated with lung diseases that spread through the bloodstream (Sykes, 2012). Pyothorax as a form of infection in a retrospective study of nocardiosis in felines corresponded just about 5% of patients (Malik et al., 2006). About 60% of patients affected by the bacterium in humans had immunosuppressive diseases concurrent with an infection such as human immunodeficiency virus (HIV) (Javaly et al., 1992). In cats, the main concomitant diseases observed in that study were retroviruses, with the main ones being the feline leukemia virus (FeLV) and feline immunodeficiency virus (FIV) (Sykes, 2012).

Diagnosis isolates the agent from skin lesions or respiratory tract samples, such as pleural effusions. The samples must be cultured in aerobic and anaerobic media to distinguish nocardiosis from actinomycosis, considering that they are clinically indistinguishable from each other. Microscopically, *Nocardia* species appear as branched filaments that break into rod or coccoid shapes (Sykes, 2012).

Treatment consists of pleural fluid drainage and long-term systemic antibiotic therapy (Barrs, 2011). The radiographic examination can be performed by stabilizing the patient's clinical condition and helping diagnose pleural effusions (Beatty & Barrs, 2010). The objective of this study was to report a case of pyothorax caused by *Nocardia* species in a FeLV-positive cat.

Case description

A 10-year-old female mixed-breed cat, FeLV-positive (determined by ELISA [SNAP FIV/FeLV Combo; IDEXX]) with chronic kidney disease IRIS stage 2 was treated in Seropédica, in the state of Rio de Janeiro, Brazil. The patient had severe dyspnea and muffled heart sounds during auscultation. Thoracentesis was performed based on clinical signs of pleural effusion, and 120 ml of foul-smelling fluid was drained from the right side and 230 ml from the left side, with rosy color and flocculated appearance (Figure 1).

After thoracentesis and patient stabilization, an increase in body temperature (40.1 °C), heart rate of 260 bpm, respiratory rate of 82 bpm, and normal colored mucosa were observed. In addition, circular lesions with an alopecic area with papules and crusts were observed in the interscapular region (Figure 2). Skin samples were collected and sent for histopathological examination and diagnosed as eosinophilic plaques

Radiography was then performed to elucidate the case better. The images revealed an alveolar pattern, especially in the left lung lobes, suggestive of atelectasis of the left lung lobes and pneumonia. were observed., associated with the left lateral displacement of the cardiac silhouette. No images were suggestive of remnant pleural effusion (Figure 3).

Peripheral blood was collected for hemogram and blood chemistry, which indicated leukocytosis, neutrophilia with left shift, lymphopenia, and thrombocytopenia (Table 1). Blood biochemistry was performed, and the only alteration found was azotemia compatible with the previously diagnosed chronic kidney disease stage. Intramuscular administration of tramadol chlorhydrate at a dosage of 1 mg/kg every 12 hours, along with subcutaneous administration of dipyrone at a dosage of 25 mg/kg every 12 hours, and oral administration of amoxicillin + clavulanic acid at the dosage of 22 mg/kg every 8 hours, and metronidazole at a dosage of 15 mg/kg every 12 hours, was prescribed, all during five days.

Figure 1. Fluid collected from the pleural cavity, with a pinkish color, viscous, foul odor and flocculated appearance.

Figure 2. Dermal lesions located between the shoulder blades. Diagnosis of eosinophilic plaques was confirmed after cutaneous cytology.

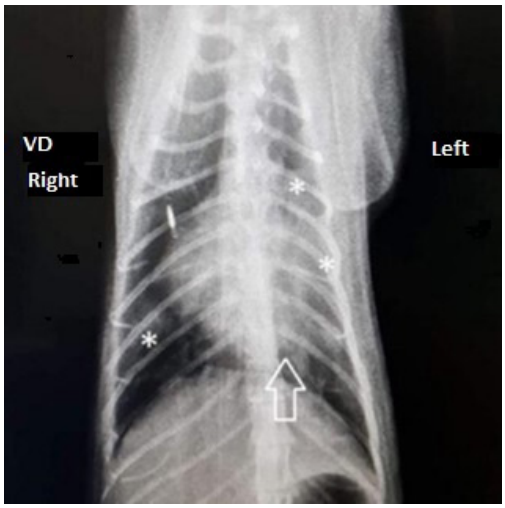

Figure 3. Ventrodorsal (VD) radiographic projection, showing an alveolar pattern (asterisk / *) and left lateral displacement of the cardiac silhouette (arrow). Courtesy of the Diagnostic Imaging Service, Small Animal Veterinary Hospital, UFRRJ.

Table 1. Hematological parameters of the cat with pyothorax on the day of diagnosis (Day 0) and follow-up during treatment.

Hemogram	Day 0	Day 3	Day 7	Month 1	Month 3	Month 5	Reference Range*
Red Blood Cells ($x10^6$ cells/µL)	6.9	6.6	6.6	6.0	9.9	10.0	5.0 - 10.0
Hemoglobin (g/dL)	9.0	8.0	8.0	10.0	13.5	13.6	8.0 - 15.0
Hematocrit (%)	28.7	26.2	25.6	30.0	44.7	44.4	24.0 - 45.0
MCV (fL)	41.4	39.8	38.9	50.0	45.2	44.1	39.0 - 55.0
MCHC (g/dL)	31.4	30.5	31.3	33.3	30.2	30.6	30.0 - 36.0
White Blood Cells (cells/µL)	36400	24800	16800	13500	9500	6800	5500 - 19500
Metamyelocytes (cells/µL)	0	0	0	0	0	0	0
Myelocytes (cells/µL)	0	0	0	0	0	0	0
Banded neutrophil (cells/µL)	1092	248	0	0	0	0	0 - 300
Neutrophil (cells/µL)	32396	23604	15120	13500	5985	3740	2500 - 12500
Lymphocytes (cells/µL)	1092	1240	1176	9585	2280	2108	1500 - 7000
Monocytes (cells/µL)	728	248	168	2160	380	204	0 - 850
Eosinophils (cells/µL)	1092	0	336	135	855	748	0 - 1500
Basophils (cells/µL)	0	0	0	0	0	0	0
Platelets (units/µL)	147000	156000	360000	508000	297000	375000	230000 - 680000

MCV = mean corpuscular volume; MCHC = mean corpuscular hemoglobin concentration; *Brooks et al. (2022).

A cavitary fluid sample was sent for analysis, culture, and antibiogram. It was found to be a septic exudate due to high cellularity, with most of it composed of neutrophils with a tendency to degenerate, hypersegmented, small, and without reactivity. Microscopic analysis showed filamentous bacteria phagocytosed by neutrophils and macrophages, compatible with *Nocardia* species (Figure 4).

The microbiological culture was carried out in two Petri dishes containing chocolate agar. Ten microliters of cavity fluid were deposited on each plate. One plate was incubated under aerobic conditions and the second under anaerobic conditions in an oven at 36 °C. The plate under anaerobic conditions did not allow the development of microorganisms, discarding the hypothesis of actinomycosis. However, after five days, the sample incubated in aerobiosis generated colonies of a vivid white, gaining a powdery appearance on the seventh day. These colonies were seeded on Sabouraud agar, where, after seven days, colonies with a dry and yellowish appearance were obtained. The colonies did not present a characteristic earthy odor, ruling out the possibility of *Streptomyces* spp. Under microscopy, the colonies showed Gram-positive filaments and coccobacilli, and when stained by the Ziehl-Neelsen technique, reddish filaments (MZN-positive) were observed. No other microorganisms were isolated. The Kirby-Bauer method (Bauer et al., 1966) of bacterial sensitivity to antibiotics detected sensitivity to amoxicillin + clavulanic acid and resistance to metronidazole.

After three days, there was a new dyspnea onset. Thoracentesis was performed, and 150mL was drained from the left side only. Based on culture and antibiogram, only amoxicillin + clavulanic acid was prescribed for five months. During treatment, new radiographic examinations were performed monthly and attenuation of the previously described pulmonary patterns was observed. At the end of the therapeutic protocol, the patient was discharged without clinical recurrence.

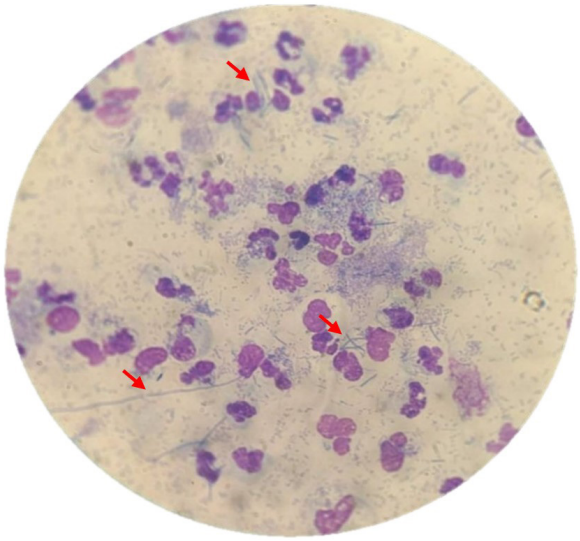

Figure 4. Cellular predominance of mildly degenerated neutrophils and high presence of phagocytosed filamentous bacteria at the bottom of the slide (red arrows). Fast panoptic staining was used for optical microscopy with 1000x magnification.

Discussion

The most commonly observed form of nocardiosis in domestic animals is cutaneous, although in humans, the pulmonary is the most frequent (Silkworth et al., 2019). Because nocardiosis is an uncommon cause of pyothorax in cats (De Souza, 2003), reports of its occurrence are still scarce. However, it is known as a bacterium present in the environment, and there are reports of zoonotic events of the disease, so new data and integration of species results are needed to advance knowledge about the bacterium and all its pathogenic potential (Silkworth et al., 2019).

It can occur through inhaling aerosols, including lung infections, only in the pleural cavity or through contact with skin lesions with contaminated sites. In cases of suspected pyothorax due to environmental contamination through chest wounds, species of saprophytic bacteria such as *Nocardia* species, *Pseudomonas* species, and mycobacteria have been found (Barrs et al., 2005). In the cat reported here, there were only chronic eosinophilic plaques in the dorsal region, previously diagnosed by cutaneous histopathological examination. There was no history of recent skin perforation. Clinical signs were compatible with pleural effusion, such as muffled heart sounds, inspiratory dyspnea (Souza, 2003), and elevated temperature (Norsworthy, 2018), along with an alveolar pattern of the left lung lobes detected through chest radiography, commonly associated with bacterial pneumonia (Holland & Hudson, 2020).

A retrospective study reported that 75% of 28 cases of pyothorax analyzed in cats corresponded to pulmonary alterations. In bacterial cultures, no case of *Nocardia* species was found in the 13 described species (Sim et al., 2021). In suspected cases of nocardiosis, the laboratory must be informed so that the sample will be cultured in a proper medium, and the samples must be transported in anaerobic tubes. It must be submitted to aerobic and anaerobic environments, differentiating from actinomycosis, which is clinically indistinguishable from nocardiosis. Gram staining is often misleading, so an acid-resistant type should be performed (Norsworthy, 2018) In that case, the sample was adequately sent for culture in a particular medium, followed by adequate staining for *Nocardia* species, due to suspicion based on the clinical examination. It highlights the possibility that bacterial prevalence is more significant than routinely observed due to diagnostic particularities that make its identification difficult.

Another possible contributor to bacterial prevalence was FeLV, an immunosuppressive virus. FeLV is an infection often associated with immunodeficiency due to its immunosuppressive character. It is caused by a retrovirus that carries the enzyme reverse transcriptase, which is responsible for integrating viral RNA into the host's genome (Hofmann-Lehmann & Hartmann, 2020). In humans, a correlation has been found between infections by *Nocardia* species with

the presence of the human immunodeficiency virus, with the lung as the main organ affected (Javaly et al., 1992). In the present report, FeLV was an important immunosuppressive agent, enabling infection by an opportunistic bacterium.

Treatment of the pathology consists of removing the fluid from the pleural cavity by thoracentesis and antibiotic therapy, according to the bacterial culture. Prolonged antibiotic therapy for four to six weeks is essential due to the high recurrence rate (Barrs & Beatty, 2009). The use of amoxicillin-clavulanate represents an alternative for treatment, reaching clinical and microbiological cure in about 70% of the cases described in a study (Bonifaz et al., 2007) and 100% effectiveness on a more recent one that used disk-diffusion antimicrobial susceptibility test (Condas et al., 2015). In addition, radiographic control is necessary to monitor the involution of previously observed lung lesions (Bonifaz et al., 2007). In this case, after thoracentesis, the fluid was found to be *Nocardia*-positive, and the antibiotic treatment with satisfactory sensitivity was amoxicillin + clavulanic acid, instituted for five months. At the end of the therapeutic protocol, the patient was discharged without clinical relapses for 60 months

Conclusions

Nocardia species are etiologic agents of pyothorax in felines, especially in those immunosuppressed by FeLV. It is rare, and diagnostic particularities make its identification difficult. There are already reports of zoonotic events of the disease. New species data are needed to advance knowledge of all their pathogenic potential. Prolonged treatment with amoxicillin + clavulanic acid resolved the reported clinical case.

Ethics statement

All procediments were consented by the animal owner (for case reports).

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Conflict of interests

JMI, GPSA, IVB, FRM, AALR, MMB, SYN, GBA, DRC – none.

Authors' contributions

JMI and DRC – preparation and writing the initial draft. GPSA, IVB, SYN and FRM – clinical procedures. AALR - performed and interpretation of laboratorial analysis. MMB - performed and interpretation of microbiological analysis. GAB – performed and interpretation of imaging exams. DRC – Writing, Review and Editing manuscript

Availability of complementary results

The authors must identify where readers can access any complementary information available, such as in an online repository or from the authors on request. We suggest consulting https://wp.scielo.org/wp-content/uploads/Lista-de-Repositorios-Recomendados_pt.pdf

The study was carried out at Laboratório de Quimioterapia Experimental em Parasitologia Veterinária, Departamento de Parasitologia Animal do Instituto de Veterinária, Universidade Federal Rural do Rio de Janeiro, Seropédica, RJ, Brasil.

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