Feline Idiopathic Pulmonary Fibrosis

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ABSTRACT

Background: Feline idiopathic pulmonary fibrosis is an irreversible disease that is rarely reported in veterinary clinical routine, with this case as the second reported in Brazil. This study aimed to describe a case of idiopathic pulmonary fibrosis in a domestic cat.

Case: A 10-year-old female cat with a history of respiratory distress was treated at the Veterinary Hospital of the State University of Santa Cruz (HV-UESC). The first signs were observed three months before clinical care, characterized mainly by dyspnea that was more pronounced during nighttime. There was no history of previous illnesses or prior drug use. The cat lived with two other domiciled cats, did not have access to the street, and had restricted access to the terrace of the building, from where other animals could have possibly entered. Physical examination showed a poor body condition with a temperature of 37°C and dehydration estimated at 9%. The animal was observed to remain in an orthopedic position, with tachypnea (109 mvm), wheezing through the mouth, and severe expiratory dyspnea. Pulmonary auscultation detected fine discontinuous adventitious noises. There were no changes in the cardiac function in terms of rhythm, frequency, or auscultation. Oxygen therapy and slow administration of 0.9% NaCl solution were performed; moreover, blood was collected for complete blood count, in which no abnormalities were observed. Thoracic radiography was performed on the cat, and the results showed a mixed pulmonary pattern characterized by bronchiectasis, thickening of the bronchiolar wall, and an unstructured interstitial pattern throughout the pulmonary area. Shortly after the beginning of the clinical care, the animal died due to respiratory arrest and was necropsied. The main macroscopic finding was pulmonary edema. Lung samples were subjected to microscopic evaluation, which revealed extensive multifocal areas of alveolar septa thickening characterized by smooth muscle hyperplasia, hypertrophy associated with intense fibroplasia, type II pneumocyte hyperplasia, and discrete intra-alveolar and interstitial lymphohistiocytic inflammatory infiltrate. Based on the clinical, radiographic, macroscopic, and histopathological findings, the diagnosis of idiopathic pulmonary fibrosis was established.

Discussion: This is the second case of feline idiopathic pulmonary fibrosis reported in Brazil. The observations in the physical examination, namely, the orthopedic positioning, dyspnea, and mouth breathing, are characteristic of respiratory distress and showed the severity of the lesions in the respiratory system. The clinical manifestation of idiopathic pulmonary fibrosis in cats reveals that gas exchange had already been compromised, which indicates an advanced stage of disease. In addition to respiratory signs, systemic signs such as apathy, anorexia, weight loss, and dehydration also confirm the severity of the condition. Because of the severity of the clinical condition at the time of the clinical care, it was not possible to adopt a more aggressive therapeutic approach, and the animal eventually died. Taken together, the clinical, radiographic, macroscopic, and histopathological findings led to the diagnosis of idiopathic pulmonary fibrosis. Literature states that the diagnosis of idiopathic pulmonary fibrosis requires clinical, radiographic, and histopathological findings consistent with the alterations observed in this cat. Much remains to be understood with regard to idiopathic pulmonary fibrosis in felines, since the currently available information is sparse and divergent. The description of these cases is extremely important to increase the available knowledge and to improve the prognosis and therapy for this serious disease.

Keywords: Felis catus, lung, fibroplasias, smooth muscle hyperplasia.
INTRODUCTION

Idiopathic pulmonary fibrosis is among the group of lung interstitial diseases that affect both humans and animals [1,5]. In humans, specific alterations associated with usual interstitial pneumonia are known, and these characteristics are similar to those described for idiopathic pulmonary fibrosis in felines [2,3,8]. The microscopic findings are interstitial fibrosis with foci of fibroblasts and myofibroblasts (“honeycomb lung”), epithelium metaplasia with type II pneumocyte hyperplasia, and smooth muscle metaplasia/hyperplasia [1-3,10,11].

In addition to the similar histopathological features between feline idiopathic pulmonary fibrosis and the usual interstitial pneumonia of humans, there are several other similarities. In both human interstitial pneumonia and feline idiopathic pulmonary fibrosis, there is a lack of knowledge about their etiopathogenesis; moreover, both diseases exhibit heterogeneity of clinical manifestations, poor response to therapies, and a high mortality rate [2,8,10,11].

In light of the severity of interstitial lung diseases and the inefficiency of response to therapies, comparisons of the diseases that affect humans and animals have been established. In this context, spontaneous idiopathic pulmonary fibrosis in felines has been used as a model for the study of usual interstitial pneumonia [8,10]. However, information is limited to a few case reports found in literature [2,3,5,10], and in Brazil, there is only one previous case report on feline idiopathic pulmonary fibrosis [6].

This study aimed to report a case of idiopathic pulmonary fibrosis in a domestic cat, which died a few hours after the start of its care.

CASE

A 10-year-old female domestic cat, weighing 3.9 kg, was brought to the Veterinary Hospital of the State University of Santa Cruz (HV-UESC), and was exhibiting signs of fatigue and respiratory distress. The first signs were observed three months before clinical care, as the cat was reported to have dyspnea that was more pronounced during nighttime. The clinical picture evolved to show continuous respiratory discomfort, which was manifested by apathy, anorexia, and weight loss. There was no history of previous illnesses or drug use. The cat did not have access to the street, lived with two other domiciled cats, and had restricted access to the building terrace, from where other animals could possibly enter.

Physical examination showed poor body condition, a temperature of 37°C, and dehydration estimated at 9%. The animal was observed to remain in an orthopedic position, with tachypnea (109 mmHg), wheezing through the mouth, and severe expiratory dyspnea. Pulmonary auscultation detected fine discontinuous adventitious noises (fine crepitations). There were no changes in the cardiac function in terms of rhythm, frequency, or auscultation. Because of the emergency situation, oxygen therapy was performed, followed by cannulation of the cephalic vein, and maintenance by administering 0.9% NaCl solution. In order to perform a complete blood count, 2 mL of blood was collected through jugular vein puncture, and was stored in tubes containing EDTA. All the analyzed parameters were within the reference values for this species.

In addition, a radiograph of the thoracic region was obtained. In the dorsoventral and left lateral positions, a mixed pulmonary pattern characterized by bronchial dilatation (bronchiectasis), thickened bronchial wall (suggestive of peribronchial infiltrate), and non-structured interstitial pattern in all lung areas (Figure 1A) were observed. The radiographic images suggested interstitial or fungal pneumonia associated with bronchiectasis. After two hours of clinical care, the condition evolved to death due to respiratory arrest.

The animal was referred to the HV-UESC Necropsy Service. During post-mortem examination, the lungs were observed to have a firm consistency and an irregular surface with multifocal areas showing plaque-like thickening. Elevated areas with characteristics compatible with alveolar emphysema were evident at the edges of the pulmonary lobes (Figure 1B). In addition, edema was observed by parenchyma cutting. No significant lesions were observed on the other organs. Samples of the lungs, heart, kidneys, and liver were collected, fixed in 10% formalin solution, and sent to the HV-UESC Histopathology Laboratory for histopathological analysis. Microscopically, there were extensive areas with thickening of the alveolar septa with type II pneumocyte hyperplasia and intense smooth muscle tissue hyperplasia/hypertrophy of the alveolar walls. In addition, extensive fibroplasia was noted in the interstitium in association with moderate multifocal lymphocytic inflammatory infiltrate. Moderate multifocal hyperemia and hemorrhage were also observed. In addition, thickening and fibrosis of the pleura were observed (Figure 2). The other organs did...
not present any significant lesions. Based on the clinical, radiographic, macroscopic, and histopathological findings, the diagnosis of idiopathic pulmonary fibrosis was confirmed.

**DISCUSSION**

The report describes a case of feline idiopathic pulmonary fibrosis, a disease rarely reported in veterinary clinical practice [1-3], with this being only the second case described in Brazil [6]. The cat was 10 years old, which is within the age range described for this disease [1-3,6].

In the majority of interstitial lung diseases, there is an association with an etiological (usually infectious) agent, which include toxic compounds, reactions to drugs, neoplastic compounds, and immunomediated compounds. In the case of idiopathic pulmonary fibrosis, there is no identification of an agent that triggers this disease [2], which was also observed in our study.

According to the history, clinical manifestations began three months before the clinical care and progressively worsened, with the cat exhibiting severe dyspnea associated with apathy, anorexia, and weight loss. In the literature, there is heterogeneity of data about the clinical presentation of idiopathic pulmonary fibrosis in felines. The duration of the symptoms may vary from days to years, and sudden death can occur with no marked clinical manifestations [2,10].

The changes observed in the physical examination showed the severity of the lesions in the respiratory system, which was also evident in the observed symptoms, namely, orthopedic positioning, dyspnea, and mouth breathing, which all characterize respiratory distress. According to Cohn et al. [2], the clinical manifestation of idiopathic pulmonary fibrosis in cats reveals that gas exchange is already compromised, which indicates an advanced stage of disease. The fine discontinuous adventitious sounds, audible in the pulmonary auscultation, are produced as a result of the opening of small airways during inhalation and indicate that the pulmonary compliance is diminished by the presence of fibrous tissue, which is consistent with the case reported in this study [4]. In addition to respiratory signs, systemic signs of apathy, anorexia, weight loss and dehydration also corroborate the severity of the condition and have been described by other authors in cases of feline idiopathic pulmonary fibrosis [3].

The radiographic findings were also consistent with those described in the literature for felines affected by this condition [3]. Thus, all the findings led to the diagnosis of interstitial pneumonia, which was further confirmed by the microscopic findings.

Due to the severity of the clinical picture at the time of clinical care, it was not possible to adopt a more aggressive therapeutic approach, since efforts were made to establish a precise diagnosis. Oxygen therapy was not effective in improving the cat’s respiratory condition, and the animal died two hours after the beginning of clinical care. Several therapeutic approaches have been proposed for idiopathic pulmonary fibrosis, including corticosteroids with or without the association of cytotoxic agents. Despite several therapeutic attempts, there is no evidence of clinical improvement or increased survival after treatment, either in human or veterinary medicine [2,8,11].

The macroscopic and microscopic alterations reported in this case are in accordance with the literature [2]. However, owing to the similarity between the histopathological findings, feline asthma or parasitism by *Aelurostrongylus abstrusus* was firstly considered as differential diagnoses. Asthma was discarded since it usually exhibits the association of eosinophilic infiltrate with other microscopic findings; however, this was not observed in the samples evaluated. In addition, *A. abstrusus* parasitism was ruled out due to the observations of intense fibroplasia and fibrosis, as well as the hyperplasia of type II pneumocytes, which are characteristics that are not consistent with *A. abstrusus* parasitism. In addition, no parasites were observed on the slides analyzed, although this factor alone cannot be considered as a criterion for exclusion, since the animal may have eliminated the parasite while the parasite-induced lesions remain [9].

In idiopathic pulmonary fibrosis, it is believed that the lesion begins in type I pneumocytes, which cover most of the alveolar surface. Thus, when these cells are damaged, type II pneumocytes proliferate in order to cover the exposed basement membrane. When the repair occurs successfully, some type II pneumocytes die while others differentiate into type I pneumocytes. However, under pathological conditions such as idiopathic fibrosis, transforming growth factor beta (TGFβ) mediates the replacement of this process by the proliferation of fibroblasts, which differentiate into myofibroblasts, which secrete collagen and other proteins [7].
Figure 1. Feline idiopathic pulmonary fibrosis. A- Right lateral thoracic radiograph showing bronchiectasis (→), thickening of the bronchiolar wall (→), and unstructured interstitial pattern throughout the lung area. B- Lungs. Irregular surface with multifocal areas showing plaque-like thickening, in addition to firm consistency; elevated areas with characteristics compatible with alveolar emphysema were evident at the edges of the pulmonary lobes.

Figure 2. Feline idiopathic pulmonary fibrosis. A- Lung. Photomicrography evidencing extensive multifocal areas of thickening of the alveolar septa characterized by hyperplasia and smooth muscle hypertrophy associated with intense fibroplasia and moderate lymphocytic inflammatory infiltrate [HE; 10x]. B- Lung. Photomicrography evidencing moderate lymphocytic inflammatory infiltrate [HE; 40x]. C- Lung. Photomicrography smooth muscle hypertrophy (red) associated with intense fibroplasia (blue) [Masson’s trichrome; 20x]. D- Pleura. Photomicrography thickening and fibrosis of the pleura (blue) [Masson’s trichrome; 10x].
The pattern of the inflammatory infiltrate, which was composed mainly by lymphocytes and plasma cells, was probably due to continuous antigenic stimulus that leads to an intense and progressive immune response, especially with regard to light chain immunoglobulins [7].

Thus, clinical, radiographic, macroscopic, and histopathological findings have led to the diagnosis of idiopathic pulmonary fibrosis, as indicated by the literature, which states that the establishment of this diagnosis is made through clinical, radiographic, and histopathological findings consistent with this alteration [2].

Much remains to be understood with regard to idiopathic pulmonary fibrosis in felines, since the currently available information is sparse and divergent. One of the factors that hinders the understanding of the data is the absence of criteria that standardize the classification of interstitial lung diseases in feline medicine, whereas these criteria exist in human medicine. This fact makes it difficult to determine the true incidence of idiopathic pulmonary fibrosis in this species [8,10]. The description of these cases is extremely important to improve the availability of knowledge and to advance the prospects of prognosis and therapy for this serious disease.

Since this disease is progressive and still does not have effective therapies [2], the affected animals die, which occurred with the cat of the present report, due to the severity and the evolution of the clinical picture.

Declaration of interest. The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

REFERENCES

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