



INFECTIOUS DISEASE

Chronic Invasive Pulmonary Aspergillosis in Two Cats with Diabetes Mellitus

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Summary

Human patients with diabetes mellitus are at increased risk of fungal infections. Diabetes mellitus has also been implicated as a predisposing factor in the establishment of fungal lung infections in cats. Two diabetic cats of different origins presented with severe acute respiratory conditions that resulted in their death. At necropsy examination there was friable, black material in the main bronchi that obstructed the bronchial lumina. Microscopical examination of the lungs revealed the presence of pneumonia, calcium oxalate crystals and a large quantity of fungal hyphae and conidial heads. Fungal infection was confirmed with Grocott's methenamine silver stain. The results of the mycology analysis were compatible with *Aspergillus* section *Nigri*.

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Aspergillosis is an infection caused by *Aspergillus* spp., a fungus that is ubiquitous in nature and is usually introduced to the body by inhalation. *Aspergillus* spp. are widely distributed and have been observed in a broad range of habitats because these organisms colonize a wide variety of substrates (Tell, 2005). In man, the most common organism isolated from patients with invasive or disseminated aspergillosis is *Aspergillus fumigatus* (Latgé, 1999). *A. fumigatus* has been rarely reported to cause pneumonia in cats (Degi et al., 2011; Hazell et al., 2011). In cats, *A. fumigatus* and *Aspergillus niger* are the most common causes of sinonasal aspergillosis (Barrs and Talbot, 2014). In apparently immunocompetent cats, invasive sino-orbital aspergillosis is the most common disease, and the causative organisms are *Aspergillus felis* and *Aspergillus udagawae*; both species belong to the *Fumigati* section (Barrs et al., 2012).

Immunocompetent mammals rarely develop pulmonary aspergillosis unless they are exposed to high

doses of infective conidia (Charlton et al., 2008). We report two cases of pneumonia caused by *Aspergillus* section *Nigri* in domestic cats with diabetes mellitus.

The first case, a 16-year-old, 2 kg neutered female domestic crossbred cat, was referred to a veterinary hospital. The cat had polyuria, polydipsia, inappetence, severe dyspnoea, lethargy and progressive weight loss. In addition, anaemia (haematocrit 21%, reference range [RR] 24–45%), leucopenia ($4.0 \times 10^9/l$; RR $5.0\text{--}19.5 \times 10^9/l$), neutropenia ($1.07 \times 10^9/l$; RR $2.5\text{--}12.5 \times 10^9/l$) and increased fructosamine (533.7 $\mu\text{mol/l}$; RR 219–247 $\mu\text{mol/l}$) and glucose (46.0 mmol/l; RR 4.05–7.43 mmol/l) levels were found. Urinalysis showed a moderate level of protein and a high level of glucose, with a specific gravity of 1.018 (RR >1.035). An ultrasound examination revealed a diffuse increase in the size and echogenicity of the liver and pancreas, probably due to hepatic lipidosis secondary to diabetes mellitus and pancreatitis. In light of the clinical signs, a diagnosis of uncontrolled diabetes mellitus was suspected. The cat was hospitalized and treated to correct the

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fluid deficit and the increased electrolyte levels and received intramuscular insulin treatment (0.2 IU/kg q24h). On the 10th day of hospitalization, after the acute onset of severe dyspnoea, the cat died.

The second case, a 12-year-old, 3 kg neutered male domestic crossbred cat, was referred to a veterinary hospital. The owner reported that the cat had polyuria, polydipsia, inappetence, severe dyspnoea, lethargy and vomiting. The cat had diabetes mellitus and had been treated with NPH insulin subcutaneously (1.0 IU/kg q24h) for the last 6 years. Mature neutrophilia ($20.9 \times 10^9/l$) and lymphopenia ($9.0 \times 10^9/l$; RR $1.5\text{--}7.0 \times 10^9/l$), as well as increased glucose levels (21.6 mmol/l), were found. Urinalysis showed moderate levels of protein, high levels of glucose and a specific gravity of 1.020. In light of these results, a diagnosis of uncontrolled diabetes mellitus was suspected. The cat was hospitalized and treated similarly to the previous case. On the 3rd day of hospitalization, hyperglycaemia was stabilized with the use of regular insulin; however, the cat experienced an acute onset of severe dyspnoea and died.

The two cats were submitted for routine necropsy examination. The lungs were swollen and heavy with a firm elastic consistency and were severely congested and slightly haemorrhagic. At the entrance to the right and left main bronchi there was a large quantity of friable, black material, interspersed with yellow foci, that obstructed the bronchial lumina (Fig. 1). The livers of both cats were enlarged, with rounded edges, and the cut surfaces were soft and yellow. In addition, in the caudal lobe of the right lung of the first cat, there was an asymmetric

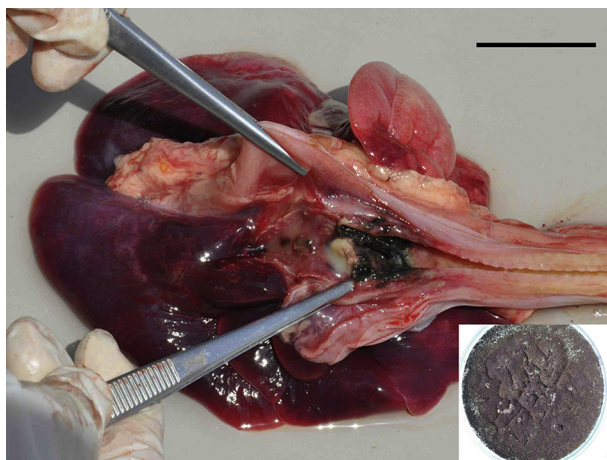


Fig. 1. The lungs from cat number 2. The lungs are swollen and congested. At the entrance to the left main bronchus there is a large quantity of friable, black material, interspersed with yellow foci, that obstructs the bronchial lumen. Bar, 3 cm. Inset: *Aspergillus* section *Nigri* after 7 days of incubation; the colony has black and densely stippled appearance.

infiltrating grey–white mass, raised slightly over the pleural surface. This mass had firm consistency and a solid cut surface and measured 3.0 cm in diameter. All tissue samples obtained at necropsy examination were fixed in 10% neutral buffered formalin and processed routinely. Sections were stained by haematoxylin and eosin (HE).

Microscopical examination of the pulmonary parenchyma and bronchial lumina revealed a large quantity of septate, acute-angled or dichotomous branching hyphae (3–4 μm diameter). In addition, biserial conidial heads with brown phialides and metulae, encompassing the entire surface, as well as smooth-walled, hyaline or darkened conidiophores, were found (Fig. 2). The metulae developed in a double series and produced dark brown to black globose to subglobose conidia with rough walls (3–4 μm diameter) (Fig. 3). Septate hyphae occupied numerous air spaces and infiltrated the alveolar septa. An intense infiltrate that consisted predominantly of neutrophils with fibrin deposition, associated with necrosis of the bronchial epithelium, was also observed. A methenamine silver stain was performed on the lung sections to highlight the fungi. Sections of the pulmonary parenchyma and bronchi were viewed under polarized light and revealed a high number of birefringent crystals with radiating spokes, consistent with calcium oxalate (Fig. 4). In both cases, severe diffuse fatty degeneration of the liver, vacuolation of the epithelium of the pancreatic ducts and accumulation of glycogen in the renal proximal tubules were observed. These findings were consistent with the diagnosis of diabetes mellitus. The histological appearance of the mass in the caudal lobe of the right lung of the first cat was

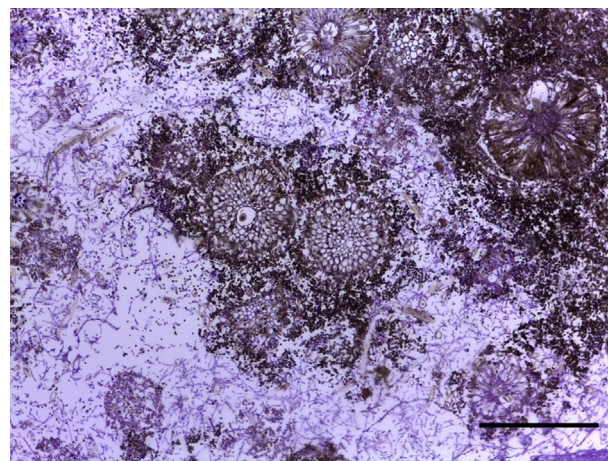


Fig. 2. Section of lung from cat number 1 showing conidial heads and dichotomous branching hyphae of *A. section Nigri*. HE. Bar, 100 μm .

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