Feline disseminated cryptococcosis
Spodsberg, Eva-Maria Hohneck; Aalbæk, Bent; McEvoy, Fintan

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**Introduction**
Cryptococcosis is an opportunistic systemic fungal infection and occurs worldwide, caused by several Cryptococcus (C.) species, which are saprophytic, round, basidiomycetous yeasts with C. neoformans most commonly causing disease (1, 2, 3). Infection occurs in the environment through e.g. pigeon droppings and soil rich primarily via inhalation through the respiratory system.

Cryptococcal basidiospores are considered the main infectious particles due to their small size of 2-3 µm, compared to vegetative, encapsulated cells (4, 5). In the desiccated state, the Cryptococcus organism may be no larger than 1 µm and may survive up to 2 years (2). In infected tissue, and often when cultured, the organism is a variable-sized yeast (3.5 to 7 µm) with a large heteropolysaccharide capsule (1 to 30 µm) (2). The majority of yeasts settle out in the nasal cavity or nasopharynx, where they can produce disease or result in animals becoming asymptomatic carriers of the organism (2).

**Summary**
Disseminated cryptococcosis was diagnosed in a cat presenting with severe dyspnoea and multiple cutaneous nodules based on cytology, serology and culture. A 3.5 years old male, castrated, domestic shorthaired cat presented with an acute history of progressive dyspnoea, tachypnoea and anorexia and a history of chronic continuous stridor, stertor and recurrent cutaneous masses.

Nasal and thoracic radiographs showed an increased opacity in the nasal cavity, a diffuse pulmonary infiltrate and a suspected cranial mediastinal mass. Thoracic ultrasound confirmed the presence of several cranial mediastinal masses. Fine needle aspiration of the cutaneous and mediastinal masses revealed the presence of encapsulated yeast cells. Culture confirmed infection with Cryptococcus neoformans. Latex cryptococcal antigen test was highly positive with a titer of >1:8192. The cat was treated with fluconazole for 15 months until the titer was below detectable levels.

**Feline disseminated cryptococcosis**

**A case report**

SPODSBERG, E.H.1*, AALBÆK, B.2, MCEVOY, F.J.1

1 UNIVERSITY HOSPITAL FOR COMPANION ANIMALS, DEPARTMENT OF VETERINARY CLINICAL AND ANIMAL SCIENCES, FACULTY OF HEALTH AND MEDICAL SCIENCES, UNIVERSITY OF COPENHAGEN, DENMARK
2 DEPARTMENT OF VETERINARY DISEASE BIOLOGY, FACULTY OF HEALTH AND MEDICAL SCIENCES, UNIVERSITY OF COPENHAGEN, DENMARK
*CORRESPONDING AUTHOR

**Sammendrag**
En kat med svær dyspnø og multiple kutane masser blev diagnosticeret med dissemineret cryptococcosese på basis af cytologiske og serologiske undersøgelser samt mykologisk dyrkning.

not more common in cats with retroviral infections (7, 8, 10, 11). Diagnostic options of cryptococcosis include cytologic examination, capsular antigen detection, and culture. Cytological finding in aspirates of encapsulated yeast cells is suggestive. Capsular antigen can be demonstrated by Latex Cryptococcus Agglutination Test (LCAAT) (12). Aetiological diagnosis is obtained by culture and mycological characterisation of the isolate.

Case History
A 3.5 years old male castrated, domestic shorthaired cat presented to the University Hospital for Companion Animals at the University of Copenhagen with a 5-days history of progressing dyspnoea, tachypnoea and anorexia. The cat was born and raised in California, USA and was imported to Denmark one year previously. It had a history of long-standing respiratory symptoms, described as continuous stridor and stertor and occasionally dyspnoea, and recurrent cutaneous masses, some of which had been surgically removed. There was no history of nasal discharge and cough was only occasionally observed. The cat had been kept indoors for the past year, but had been an outdoor cat prior to that. It was current on vaccinations, but it had not been wormed for the last year. It had been treated with amoxicillin/clavulanic acid (12.5 mg/kg q12h per os) without response for the previous three days.

Physical examination confirmed tachypnoea (respiratory rate 50 breaths/minute) with an increased inspiratory and expiratory effort. Auscultation of the lungs was difficult due to pronounced stridor and stertor. Mucous membranes were pale pink with a capillary refill time of two seconds. The cat had multiple cutaneous, indolent, mobile, firm masses of varying size with a raised, smooth surface, dispersed over the whole body.

The initial therapeutic approach was aimed at addressing the respiratory distress with oxygen supplementation. After the initial stabilization, blood was collected for complete blood count (CBC), serum biochemistry, acid-base chemistry (venous blood sample) and Idexx SNAP® FIV/FeLV Combo Test. CBC and biochemistry did not show any abnormalities except for a mild stress-induced hyperglycemia. Acid-base chemistry did not show any abnormalities either, but as venous blood was used, blood oxygenation could not be assessed. Lactate was in the reference range. FIV and FELV tests were negative.

Nasal and thoracic radiographs showed an increased opacity in the nasal cavity and a diffuse pulmonary infiltrate with a broncho-interstitial pattern is visible. Auscultation of the lungs was difficult due to pronounced stridor and stertor. Mucous membranes were pale pink with a capillary refill time of two seconds. The cat had multiple cutaneous, indolent, mobile, firm masses of varying size with a raised, smooth surface, dispersed over the whole body.

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Marcy-l’Etoile, France) according to the manufacturer’s instructions. Latex Cryptococcus agglutination antigen test (LCAAT), performed on blood serum at Athens University, Georgia, USA, was highly positive with a titer of >1:8192.

Discussion
This presentation of a young cat with chronic respiratory symptoms and cutaneous nodules due to disseminated cryptococcosis represents a rare case in Denmark, though the disease is described to have worldwide significance. In all likelihood, the infection had been acquired during the cat’s stay in California, USA, as it had a history of long-standing respiratory signs. Regarding the cat’s history, systemic mycoses were important differential diagnoses due to a high prevalence in certain regions in the USA. All findings including the history of long-standing continuous upper respiratory tract noise and chronic recurrent cutaneous nodules could be explained by chronic disseminated cryptococcosis with intranasal, intrathoracic and cutaneous involvement.

The severe findings on radiography and CT indicated irreversible chronic intranasal changes and marked pulmonary pathology with intrathoracic granulomata which might prevent full recovery, so that ongoing respiratory sounds and decreased lung capacity would be expected. The presence of CNS disease caused by cryptococcosis is the major factor described to influence outcome in cats (13). In our case, the cat did not show any signs of CNS involvement, but as imaging studies of those regions were not performed, this could not be definitely ruled out. Our patient had a LCAAT titer >1:8192 which correlated positively with the disseminated distribution of the disease, as patients with disseminated skin and/or lymph node involvement have significantly higher titers (12).

Although the prognosis of cryptococcosis should be considered as guarded, a majority of cats can be expected to be cured, but treatment is protracted and expensive (13). We initiated treatment with fluconazole, an azole antifungal, which is described to be very effective in the treatment of feline cryptococcosis, including cases with advanced, longstanding, or disseminated disease (2, 13, 14). Furthermore, this drug can be given orally. Side effects in cats can be inappetence and, rarely, increased liver enzyme activity and hepatic toxicity (14). On follow-up visits, liver enzyme activity and LCAAT titers were measured to monitor progress, evaluate prognosis, and guide cessation of treatment (2, 12, 15, 16). The cat responded well to treatment and no side effects were observed. Antifungal therapy was continued until the LCAAT titer declined to an undetectable level after 15 months of continued therapy. This was a significantly longer treatment period than described in a previous study where the median duration of treatment with fluconazole in cats

Figure 4. CT nasal cavity and thorax (2 mm slice thickness). A: Nasal cavity: soft tissue filling bilaterally in the nasal cavity and in the left frontal sinus, bilateral nasal turbinate destruction and deviation of the nasal septum. B: Thorax: soft tissues nodules distributed throughout the lungs and significant consolidation of the lungs in the ventral lung field.

Figure 5. Culture on Sabouraud dextrose agar of isolate from aspirated material from a cutaneous nodule, incubated at for 30°C for 6 days, showing mucoid, grey-white colonies.
with less severe cryptococcosis was 4 months with a range of 1 to 8 months (13). Due to the advanced disease progression in our patient, a longer treatment period was expected. Despite clinical improvement, resolution of the cutaneous masses and a finally undetectable LCAAT titer, a full recovery with resolution of all respiratory symptoms seems unlikely due to the severe intranasal anatomical changes.

This case report emphasises that it is important to consider cryptococcosis in cats with respiratory symptoms with or without cutaneous involvement due to its worldwide significance, particularly in cats from countries with a high prevalence of cryptococcosis.

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Reference