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A Case of Nasal Cryptococcosis in a Domestic Shorthair Cat

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Abstract : An 8-year-old spayed female domestic shorthair cat was presented with a chief complaint of chronic nasal discharge and dyspnea. Physical examination revealed pyohemorrhagic nasal discharge, inspiratory dyspnea and stertor, and an enlarged right mandibular lymph node. Abnormalities of blood works and serum chemistry included mildly increased hematocrit, and globulin concentration. Serologic tests for FeLV and FIV, and a panel of polymerase chain reaction tests for *Chlamydophila felis*, Feline Calicivirus, Herpesvirus, *Bordetella*, *Mycoplasma felis*, and H1N1 influenza was all negative. Only radiographic finding showed increasing soft tissue density in the right nasal cavity and computed tomography disclosed soft tissue/fluid opacification in the right nasal cavity, paranasal sinus, and pharyinx along with slight deviation to the right of the osseous nasal septum. Focal lysis of ventral nasal septum was also suspected in CT scan. Cytological evaluation of fine needle aspirate smears of the enlarged mandibular lymph nodes revealed numerous fungal yeasts having variably thick capsule both extracellularly and intracellularly with low numbers of macrophages. Some yeasts showed narrow based budding, which was a consistent finding with *Cryptococcus* organisms. Serum protein electrophoresis was a polyclonal consistent with chronic infection and serum was submitted for a fungal serology panel test. In serologic tests *Cryptococcus* antigen titer was 1 : 32,768. In vitro culture was unsuccessful. Treatment was initiated with administration of fluconazole, clindamycin, and tocopherol. Clinical signs resolved within 3 days after the initial treatment. The cat was discharged and scheduled for periodic evaluation and continued therapy, but was lost to follow-up thereafter.

Key words **:** Nasal discharge, Cryptococcosis, cat.

Introduction

Cryptococcosis is the most common systemic mycosis in cats and known species included *Cryptococcus neoformans, Cryptococcus gattii, Cryptococcus magnus,* and *Cryptococcus albidus*, among which the last has been known to be associated with immune compromised patients (14,16). No known predisposing conditions are confirmed yet, although retroviral status, sex, and breed predilections have been controversially postulated (2,11,16). Indoor cats can also be affected in spite of the fact that *Cryptococcus* organisms are isolated from environmental sources such as soil, weathered pigeon excreta or *Eucalyptus* tree species (11,16).

Feline cryptococcosis has been most frequently reported in Australia, western Canada, and the western United States, and less prevalently in other countries including UK. In Korea sporadic cases have been reported in human medicine (4), but no known feline cases have been documented so far. Recently three strains of *Cryptococcus gattii* have also been isolated in clinical samples from human patients in Korea (3).

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The present report describes first clinical case of feline cryptococcosis with chronic duration of upper respiratory signs diagnosed according to high serum antigen titer, and cytological findings consistent with cryptococcosis. To the best of the authours' knowledge this is the first case of feline cryptococcosis in Korea.

Case

An 8-year-old spayed female Domestic shorthair cat was referred with a chief complaint of chronic nasal discharge and dyspnea unresponsive to antibiotics and prednisolone. In physical examination unilateral pyohemorrhagic nasal discharge and epiphora in the right nasal eye, inspiratory dyspnea and stertor, and right mandibular lymph node enlargement were observed. The cat showed right nasal discharge since 2002 when the owner adopted as a stray. In 2005 nasal discharge became purulent and the cat began to sneeze. The cat was diagnosed at a local hospital with sinusitis and pneumonia, and an antibiotic therapy was instituted according to the susceptibility test. But the cat was not responsive. The cat readmitted in 2007 in other two primary hospitals with worsened clinical signs and an antibiotic plus prednisolone was given with little improvement. One day before admission to

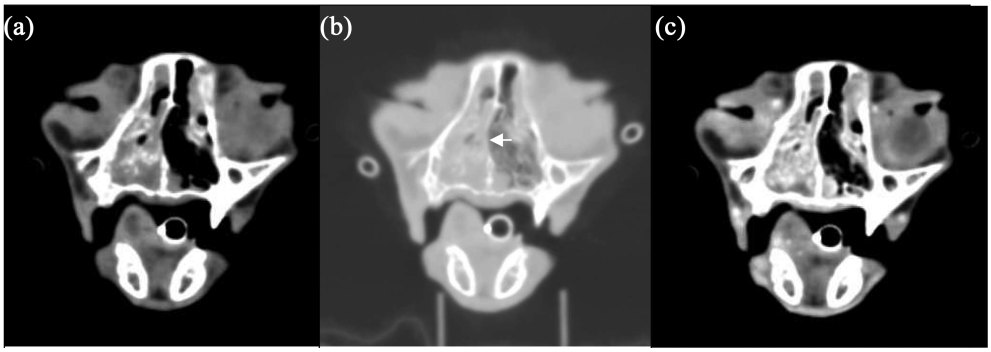

Fig 1. CT scan. Transverse computed tomographic image made at the level of the orbits using soft-tissue window level (a), lung window level (b) and with contrast enhancement (c). Soft tissue/fluid opacification with contrast enhancement was seen in right and left nasal cavity, right side is more apparent. Turbinate structure was preserved, however nasal septum was slightly deviated with focal lysis to the right side (b).

referral hospital clinical signs became severe with open-mouth respiration and the cat was presented on emergency.

After stabilizing the patient routine laboratory tests were performed, and abnormalities in blood works and serum chemistry included mildly increased hematocrit (50.8%, reference range 30-45%), and mild hyperglobulinemia (5.6 g/dl, reference range 2.8-5.1 g/dl). Radiography revealed only increased soft tissue density in the right nasal cavity (Fig 1). Cytological evaluations of the nasal swab smears were unproductive. Computed tomography was performed for more accurate evaluation of the nasal cavity and paranasal sinus. Soft tissue/fluid opacification with contrast enhancement was seen in the right nasal cavity, paranasal sinus and pharynx. A little soft tissue/fluid ossification was also seen in the left ventral nasal cavity. There was no turbinate destruction, mass or foreign body. However, the osseous nasal septum was slightly deviated to the right side. Focal lysis of ventral nasal septum was also suspected (Fig 1). The possibility of fungal infection or nasal tumor was considered.

Additional tests were performed including serological tests for FeLV and FIV, a panel of polymerase chain reaction (PCR) tests covering *Chlamydophila felis*, Feline Calicivirus, Herpesvirus, *Bordetella*, *Mycoplasma felis*, and H1N1 influenza, serum protein electrophoresis, and fine needle aspiration of the enlarged mandibular lymph nodes. Serologic tests and PCR tests results were all negative. Serum protein electrophoresis showed polyclonal gammopathy consistent with chronic infection. In cytological smears of the lymph nodes there were found numerous yeasts with thick negative capsule with a few narrow budding yeasts, moderate numbers of macrophages phagocytizing yeasts, and low numbers of eosinophils (Fig 2). Yeasts were periodic acid Schiff stain positive (Fig 3). Cytological findings were most consistent with *Cryptococcus* infection, and patient serum was submitted for serologic antigen test and lymph node aspirates were re-obtained for fungal culture. *Cryptococcus* antigen titer was 1 : 32,768 but in vitro culture was unsuccessful. Based on cytological findings and significantly increased cryptococcal antigen titer, final diagnosis of Cryptococcal upper respiratory infection was made.

For treatment fluconazole (50 mg/kg, bid, PO), clindamycin (10 mg/kg, bid, PO), and tocopherol (1 capsule, sid, PO)

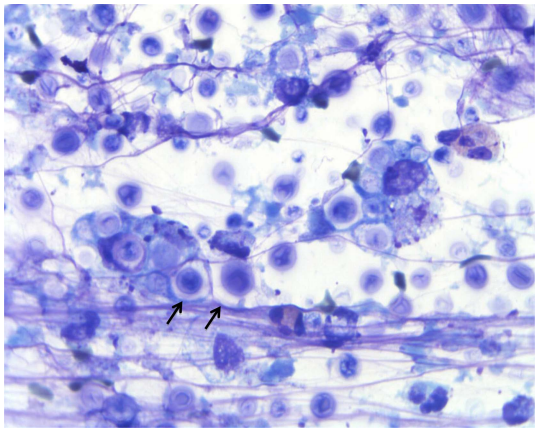

Fig 2. Fine-needle aspirate of lymph node. Note the numerous yeasts and the variably thick negative capsule of the organisms (arrow). Diff-Quik, × 400.

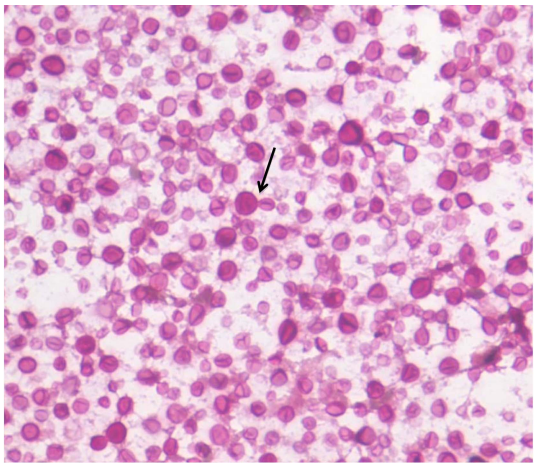

Fig 3. Periodic acid Schiff stain. Note the characteristic narrow based budding for Cryptococcus sp. (arrow). × 400.

was instituted. The cat improved uneventfully in three days after initiation of anti-fungal therapy. The owner was notified that prognosis was still guarded even in the favorably recovering cases and it should take months to years with regular checkup of serum antigen titer. However, the owner elected discharge after the clinical signs resolved and the patient was lost to followup.

Discussion

Cryptococcosis can be diagnosed by cytology or histopathology with or without fungal culture (6,16). Cryptococcal polysaccharide capsular antigen titer assay is also available for diagnosis. Cytologically *Cryptococcus* organisms are characterized by the presence of thick negative capsule which are variable in size, and narrow based budding yeasts (16). *Blastomyces* organisms are similar in appearance but having broad based budding is different to *Cryptococcus spp.*. Recognition of capsule is made easy with India ink preparation of fine needle aspiration of the affected organ. In recent reports cytological diagnosis was the only method of identifying the *Cryptococcus* organisms in approximately 40% of the cases (8,11). Cytological examination of lymph nodes, nasal samples, cytocentrifuged CSF, urine sediments, or other samples in the affected area should be done in suspected cases. In the present case CT scan of the nasal cavity was helpful to rule in the possibility of fungal disease, and fungal infection could be confirmed after cytological identification of the organisms in enlarged lymph node smears. Cytological evaluation of the lesions is useful, quick, inexpensive and sensitive means of diagnosing cryptococcosis (16).

Culture of *Cryptococcus* is easy and cryptococcal organisms grow quickly on birdseed agar, Sabrouraud-dextrose and cornmeal agar but not on dermatophyte media because of cycloheximide that inhibits growth of this organim (7). *C. neoformans* and *C. gattii* can be differentiated by using L-Canavanine glycine bromothymol blue media (6). Samples obtained by nasal swabs, and fine needle aspiration, CSF, lymph nodes, pleural and abdominal fluids, and urine sediments can be used for culture. In the present case lymph node aspirates and nasal swabs were intended for culture, but it was known later that lymph node samples were mistakenly omitted during the shipping, and culture of only nasal swab sample was unyielding. Recollecting samples was not tried because antifungal therapy was already initiated. Initial cytological evaluation of the nasal swab before submitting sample for culture was unrewarding. Culture should be done for classifying serotypes and molecular types.

Serum antigen titer test is highly sensitive and specific, and detects all known serotypes (16). As low as 1 : 2 can be significant and can be extremely high (> 1 : 60,000). In this case the titer was 1 : 32,768, confirming the diagnosis. Therapy should be continued until the titer become negative. However negative titer does not necessarily guarantee no relapse or reinfection (6). Antigen titers can be maintained high in spite of clinical improvements in some cats.

Treatment is required for months to years, which may be economic constraint for many owners and results in decreased owner compliance and early relapse or worsening of clinical signs after transient improvements. Fluconazole is currently accepted as the initial drug of choice for cats with localized cutaneous or nasal disease (16). Itraconazole and ketoconazole are also effective, and itraconazole can be used for cats with cryptococcal meningitis (9,10,16). Amphotericin B should be given in cats with CNS involvment or disseminated disease, and less nephrotoxic form of newer amphotericin B is also available (16). Prognosis is variable and in one study 60% of cats were uneventfully recovered after an initial course of therapy, but replases were found in one third of cats with favorable response to treatment (5,11,12). In cats with CNS involvement altered mental status was known as a negative prognostic factor. Prognosis of cats with seizures or high titers was not significantly different (15). Anti inflammatory doses of glucocorticoid in conjunction of antifungal drug treatment can be effective even in severely obtunded or seizuring cats (15). In the present case the clinical signs were improved in three days after initiation of anti fungal therapy using fluconazole. The cat was scheduled for serial monitoring of the antigen titer on regular visits, but the owner was not compliant.

In conclusion feline cryptococcosis was diagnosed in a cat with chronic upper respiratory signs on the basis of cytological identification of the organism, serum *Cryptococcus* antigen titer, and treatment response. Cryptococcus should be included in the differentials for feline patients with nasal disease.

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코리안 쇼트헤어 고양이에서 발생한 크립토코쿠스 감염증 의심 1증례

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요 약 : 8세 중성화 암컷 고양이가 만성 비강 삼출과 호흡곤란으로 내원하였다. 신체검사에서 오른쪽 비강의 출혈농성 삼출이 관찰되었고, 흡기성 호흡곤란과 코골기 증상, 종대된 오른쪽 하악 림프절이 확인되었다. 전혈검사와 혈청화학 검사에서 미약하게 증가한 헤마토크리트 값과 고글로불린혈증이 나타났으며, 혈청학적 및 PCR 기법을 이용한FeLV, FIV, *Chlamydophila felis*, Feline Calicivirus, Herpesvirus, *Bordetella*, *Mycoplasma felis*, H1N1 influenza 검사에서는 모두 음성이었다. 방사선 검사에서는 오른쪽 비강의 연조직 밀도 상승이 관찰되었고, CT촬영에서는 비중격의 위축과 골 용해가 확인되었다. 추가 검사로 실시한 하악 림프절 세포학 검사에서는 다양한 두께의 염색이 안 되는 협막을 갖는 곰팡이가 관찰되었으며, narrow based budding을 보이는 곰팡이도 관찰되어 크립토코쿠스 감염증으로 잠정진단하였다. 혈청학적 검사에서 크립토코쿠스 항원가는 1 : 32,768로 매우 높게 나왔다. 검사결과에 기초해서 곰팡이 감염 치료를 위해 fluconazole, clindamycin, tocopherol투여를 실시했으며 약물 투여 후 3일 이내에 환자의 증상은 극적으로 개선되었다. 장기적인 관찰과 추가 항원역가 검사를 실시하고자 하였으나 환자는 증상 개선 후 퇴원하여 재 내원하지 않았다.

주요어 : 비강 삼출, 크립토코쿠스, 고양이