



## CASE REPORT

# Four cats with fungal rhinitis

Beth L Whitney<sup>1\*</sup>, John Broussard<sup>2</sup>, Joseph D Stefanacci<sup>1</sup>

<sup>1</sup>Veterinary Referral and Emergency Center, 123 West Cedar Street, Norwalk, CT, USA

<sup>2</sup>The Animal Medical Center, 510 East 62nd Street, New York, NY 10021, USA

Fungal rhinitis is uncommon in the cat and cases of nasal aspergillosis—penicilliosis have been rarely reported. Signs of fungal rhinitis include epistaxis, sneezing, mucopurulent nasal discharge and exophthalmous. Brachycephalic feline breeds seem to be at increased risk for development of nasal aspergillosis—penicilliosis. Computed tomography (CT) imaging and rhinoscopy are useful in assessing the extent of the disease and in obtaining diagnostic samples. Fungal culture may lead to false negative or positive results and must be used in conjunction with other diagnostic tests. Serological testing was not useful in two cats tested. The cats in this study were treated with oral itraconazole therapy. When itraconazole therapy was discontinued prematurely, clinical signs recurred. Hepatotoxicosis is a possible sequel to itraconazole therapy.

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An 8-year-old, indoor-only, male castrated domestic shorthair cat weighing 14.5 lb (6.6 kg) was evaluated for sneezing and bilateral epistaxis of 3 weeks duration. A small amount of dried blood in the left nostril and a slight swelling of the left side of the nose were present. A complete blood count (CBC), serum biochemistry profile and total serum thyroxine (T<sub>4</sub>) were within reference range. A cryptococcus latex agglutination antigen titer (IDEXX Laboratory, Totowa, NJ), feline leukemia antigen titer by ELISA (FeLV) and a feline immunodeficiency virus (FIV) antibody titer were negative. Thoracic radiographs were interpreted as normal.

The cat was anesthetized using ketamine (2.2 mg/kg IV) and valium (0.2 mg/kg IV) for induction and isoflurane for maintenance of anesthesia. Computed tomography (CT) was performed revealing a mass-like soft tissue density extending through the left nasal cavity into the nasopharynx. The mass appeared to be attached to the lateral nasal wall along the left maxilla. Mucosal thickening was apparent throughout the nasopharynx and into the caudal nasal recess. There was no apparent erosion of the left frontal bone, cribiform plate, orbital bone,

and no invasion into the brain was noted. A round, white mass was visualized at the left choanae with a rhinoscope; a biopsy was taken using Poppin forceps. Histopathologic examination of the samples revealed a mild lymphocytic infiltration. Because these samples were considered non-diagnostic, a sinus trephination was performed of the left nasal sinus under general anesthesia. Biopsies were submitted for histopathology and bacterial culture. Histopathologic examination of the trephine biopsy specimen revealed multifocal and focally extensive neutrophilic, lymphocytic and plasmacytic rhinitis. Abundant exudate was present on the mucosal surfaces that consisted mostly of neutrophils and cellular debris. Numerous large colonies of thin-walled and branching fungi were present. These findings were consistent with marked chronic, active rhinitis presumably caused by fungal disease such as *Aspergillus* or *Penicillium* species. The culture revealed marked growth of *Pseudomonas aeruginosa*, sensitive to ciprofloxacin, amikacin and gentamycin. This infection was thought to be an opportunistic infection.

The cat was treated with ciprofloxacin, 5 mg/kg (2.3 mg/lb) body weight, PO, q 24 h for 21 days for the *Pseudomonas* species infection and itraconazole (Sporanox; Janssen Pharmaceutica, Tutusville, NJ) at 10 mg/kg (4.5 mg/lb) body

\*Corresponding author. E-mail: bethwhitney@hotmail.com

weight, PO, q 24 h for 4 months. A CBC and serum biochemistry profile were repeated 1, 2 and 4 months after initiation of itraconazole treatment. Results remained within reference range. The epistaxis and sneezing resolved 2 weeks into therapy and the facial swelling resolved over a 1 month period. A CT scan repeated 4 months after initiation of itraconazole therapy revealed that the soft tissue density in the left nasal cavity was smaller than previously. The right cavity was unchanged. There was still no evidence of invasion of the cribiform plate, brain, or orbit. A bone defect was noted in the dorsal left frontal bone from the trephine biopsy. A biopsy of the soft tissue opacity was offered but declined by the owner. The cat remains asymptomatic 8 months after stopping the itraconazole therapy.

A 9-year-old, indoor-only, 11.4 lb (5.2 kg) male castrated Persian cat was evaluated for purulent nasal discharge and a periorbital swelling. Ophthalmic examination revealed chemosis and supraorbital swelling over the left eye with a purulent nasal discharge. Thoracic radiographs were interpreted as normal. CBC and biochemistry profile were within normal limits; FeLV antigen and FIV antibody tests were negative. A CT scan was performed after the cat was anesthetized with ketamine (2.2 mg/kg IV) and valium (0.2 mg/kg IV) for induction and isoflurane for maintenance of anesthesia. The CT scan revealed a mixed fluid/soft tissue density throughout the left nasal cavity with extension into the nasopharynx. No cribiform or brain invasion was seen although there was punctate bone lysis in the rostral left nasal and periorbital bone. Rhinoscopy demonstrated a white, fluffy mass in the choanae. A biopsy of the mass was performed using the rhinoscope. The biopsy sample was submitted for histopathology and aerobic and anaerobic culture and sensitivity. Histopathologic evaluation of the biopsy revealed lymphocytic-plasmacytic rhinitis. Based on the non-specific findings of the mass-effect seen on CT and rhinoscope, a trephine biopsy was performed of the left frontal sinus. This biopsy specimen revealed chronic active inflammation with bone loss and numerous fungal hyphae consistent with *Aspergillus* or *Penicillium* species. A serum anti-*Aspergillus* species immunodiffusion antibody test was negative (IDEXX Laboratory, Totowa, NJ). The cat was treated with itraconazole, 10 mg/kg (4.5 mg/lb), PO, q 24 h. Upon re-evaluation 1 month later, the cat was doing well with decreased periorbital

swelling and nasal discharge. Serum biochemistry abnormalities at that time included mildly elevated alanine aminotransferase, aspartate aminotransferase and a mild lymphopenia. Treatment with itraconazole was continued. Serum biochemistry profile was checked 1 and 6 months later and was normal. The cat remained asymptomatic for the rhinitis. Against medical recommendation, the owner decided to discontinue therapy at 10 weeks because of resolution of clinical signs.

The cat was evaluated 8 months later for exophthalmos and recurrence of nasal discharge from the left nostril. A CBC and biochemistry profile at this time were within normal limits. A repeat CT scan revealed soft tissue infiltration into the left nasal sinus and destruction of the left nasal conchae and ethmoid turbinates. A nasal biopsy was obtained with Poppin forceps for histopathologic examination, bacterial and fungal culture. The cat was treated with fluconazole (Sporanox; Janssen Pharmaceutica) 10 mg/kg (4.5 mg/lb), PO, q 12 h for presumptive recurrence of fungal rhinitis. The biopsy revealed marked suppurative rhinitis with exudation and fungal hyphae consistent with *Aspergillus* species or *Penicillium* species. Bacterial and fungal cultures were negative. The cat was monitored monthly, and 8 months after beginning the fluconazole therapy the cat was asymptomatic for the rhinitis but was experiencing miliary dermatitis on the left flank and face with facial excoriations. Because this was thought potentially to be secondary to the fluconazole therapy, this drug was discontinued at this time. The miliary dermatitis resolved after discontinuation of the fluconazole. Miliary dermatitis has not been described as a side effect of fluconazole in the literature. The cat is asymptomatic 1 year after discontinuation of therapy.

A 4-year-old 3.5 kg (7.7 lb) male castrated indoor-only Himalayan cat was evaluated for evaluation of chronic purulent nasal discharge of several months. A CBC and serum biochemistry profile were within normal limits and the cat was seronegative for FeLV antigen and FIV antibody. A CT scan was performed using a propofol (Diflucan; Roerig Pharmaceutical, New York, NY) induction (3 mg/kg) and isoflurane for maintenance of anesthesia. The CT showed bilateral fluid accumulation and soft tissue densities throughout the nasal cavities and into the nasopharynx and caudal nasal recesses. No cribiform, orbital, or frontal bone lysis was seen. Invasion into the brain or frontal sinuses was not

seen. Areas of punctate lysis were seen in the right palatine bones. A blind biopsy of the nasal passage was performed using Poppin forceps. Rhinoscopy was not performed on this patient. Histopathologic examination of the biopsy revealed the presence of fungal hyphae consistent with *Aspergillus* species (or *Penicillium* species). A fungal culture of this tissue was positive for *Aspergillus niger*. A serum anti-*Aspergillus* species immunodiffusion antibody test was negative, however. The cat was treated with itraconazole, 5 mg/kg (2.3 mg/lb), PO, q 12 h. The cat was admitted to the hospital after 2 months of itraconazole therapy for anorexia, icterus and weight loss. A serum biochemistry profile was performed which revealed an elevated alkaline phosphatase (111 IU/l; reference range 0–62 IU/l), alanine aminotransferase (394 IU/l; reference range 28–76 IU/l), aspartate aminotransferase (161 IU/l; reference range 5–55), and total bilirubin (8.6 mg/dl; reference range 0.0–0.4 mg/dl). An abdominal ultrasound revealed a hyperechoic liver of normal size. The rest of the ultrasound examination was within normal limits. The owners declined an ultrasound-guided biopsy of the liver at this time. The cat was treated with supportive therapy for presumed itraconazole toxicity with intravenous fluids and nutritional support. The itraconazole therapy was discontinued and an esophagostomy feeding tube was placed by a technique previously described (Codner et al 1993). The anorexia and icterus resolved in 5 days and liver enzymes returned to normal. The owners opted not to restart the antifungal medication at that time. The cat was evaluated for recurrence of nasal discharge and sneezing 9 months after initial diagnosis. A CT scan repeated at this time was unchanged from the original CT scan. A biopsy using rhinoscopy and blind biopsies with Poppin forceps revealed rhinitis (lymphocytic/plasmacytic infiltration) but no fungal elements. Fungal and bacterial cultures were negative. No treatment was initiated at this time as per the owner's request.

An 8-year-old 3.8 kg (8.4 lb) indoor-only Himalayan cat presented for evaluation of sneezing and unilateral (right-sided) epistaxis of 2 weeks duration. The cat tested negative for FeLV antigen and FIV antibody. A CBC, biochemistry profile, and a coagulation profile (prothrombin time and activated partial thromboplastin time) were within normal limits. The cat was sedated with propofol (4 mg/kg) and isoflurane was used for maintenance of anesthesia. A CT scan

revealed a mass-like soft tissue density in both nasal cavities that extended into the nasopharynx and right caudal nasal recess, obliterating the nasal septum. No lysis of the orbit, frontal bones or cribriform plate was seen and no invasion of the brain was noted. Rhinoscopy was performed revealing a white rounded mass effect in the left naris that was biopsied. Histopathologic examination of the biopsy specimen showed infiltration with lymphocytes consistent with rhinitis and fungal hyphae consistent with *Aspergillus* or *Penicillium* species. This cat was recently diagnosed and follow-up is not yet available. Treatment consists of itraconazole 5 mg/kg (2.3 mg/lb) PO, q 12 h.

## Discussion

Fungal mycoses, especially of *Aspergillus* species, are rare in the cat and *Cryptococcus neoformans* is the organism typically encountered with nasal mycoses. Only two cases of sinusitis with orbital involvement and four cases of nasal aspergillosis have been described in the literature (Wilkinson et al 1982, Goodall et al 1984, Hamilton et al 2000, Tomsa et al 2003). Disseminated fungal disease has been reported more frequently, predominantly involving the lung, skin, bone and gastrointestinal tract (Sautter et al 1955, Pakes et al 1967, Fox et al 1978, Ossent 1987, Davies and Troy 1996). The four cases described here are cats with rhinitis and sinusitis, with one having orbital involvement.

*Aspergillus* species are ubiquitous in the environment and they are considered opportunistic invaders. Two distinct forms of *Aspergillus* species infection occur in dogs and cats, the localized nasal form and disseminated disease. Disseminated disease in dogs typically does not develop in association with the paranasal form of the disease (Lanthier and Chalifoux 1991). In dogs, *Aspergillus fumigatus* is the most common species encountered with nasal infection. Destruction and necrosis of the nasal mucosa and underlying turbinate bones usually occurs with canine nasal aspergillosis. This is believed to be caused by a vasculitis and vascular necrosis of the submucosal vessels. *A. fumigatus* has been shown to produce an endotoxin that is hemolytic and dermonecrotic (Tilden et al 1961).

The classical clinical signs of canine nasal aspergillus are profuse mucopurulent nasal discharge, epistaxis, facial pain and ulceration of the nares. Two cats in this series were evaluated for epistaxis and two for purulent

nasal discharge, but ulceration of the nares and facial pain were not recognized. One cat had orbital involvement and one had facial swelling.

Disseminated aspergillosis is apparently an opportunist in immunosuppressed cats and tends to be secondary to immunosuppressive disorders such as diabetes mellitus, infections (FeLV, FIV, or feline panleukopenia virus), or prior use of glucocorticoids or antibiotics (Davies and Troy 1996). Nasal aspergillosis in dogs, however, usually occurs without an immunocompromising condition in otherwise healthy animals (Sharp et al 1991). Lane et al (1974) described five canine nasal aspergillus cases that had previous trauma and secondary aspergillus infection. The four cats in this report were otherwise healthy, middle-aged, retrovirus negative patients with no previous history of glucocorticoid or antibiotic therapy, or trauma. No possible predisposing factors such as a history of upper airway infections or dental disease were identified in these cats.

Most cases of canine nasal aspergillus occur in dolicocephalic breeds yet three out of four of these cats were brachycephalic breeds. German shepherd dogs are predisposed to invasive systemic aspergillosis; this may be due to an immune deficiency. It is interesting that two of the cats in this report are Himalayan and one is Persian and these breeds are genetically related. Persian cats were shown to have an increased incidence of *Aspergillus* species infection in a previous study (Davies and Troy 1996). That study showed no sex predisposition but all four cats in this report are male. It has been theorized that brachycephalic cats are susceptible to fungal infections because of alterations in nasal airflow and mucociliary clearance (Lanthier and Chali-foux 1991). This contrasts with the aforementioned predisposition of dolicocephalic dogs.

Diagnosis of *Aspergillus*–*Penicillium* species infection ante mortem can be challenging because all tests can have false positives or false negative results. In dogs, a positive diagnosis of nasal aspergillosis should include at least two of the following criteria (Sharp 1998): radiographic features typical of fungal rhinitis; visualization of fungal plaques with rhinoscopy, *Aspergillus* species identification on histology, culture, or cytology; or positive serology.

Because of its ability to generate cross-sectional images, CT has proven to be superior to conventional radiography in demonstrating the extent of pathology and in differentiating infectious rhinitis from nasal neoplasia in dogs

(Codner et al 1993, Saunders et al 2002). The typical CT findings described in dogs with nasal aspergillosis include destruction of the conchae and turbinates, increased radiolucency within the nasal passages and frontal sinus osteomyelitis. Except for frontal sinus involvement, CT findings in these cats were consistent with the findings described in dogs with nasal aspergillosis.

Fungal plaques can be visualized with rhinoscopy and appear as white, yellow or green mold in the turbinates. Rhinoscopy was performed in three out of four cats and a white mass effect was seen in all three. Histopathology has been used as the primary means of diagnosing feline *Aspergillus* species ante mortem (Davies and Troy 1996). Histopathology reveals the characteristic dichotamous branching septate hyphae often with accompanying infiltrates of macrophages, lymphocytes, and neutrophils. It is often difficult to obtain a conclusive biopsy because superficial biopsies will show rhinitis without revealing the fungal organism. In two of these cases, the cats had to undergo more invasive biopsy procedures for an accurate diagnosis.

A positive fungal culture must be interpreted with caution because 30–40% of normal dogs or those with nasal neoplasia have been shown to culture fungal positive (Sharp 1998). False negatives can also occur and one of the two cats that had fungal cultures in this study was negative. It is possible that the samples sent for fungal culture lacked the fungal colony. Negative fungal cultures have been observed in human patients and in a previous report of cats with fungal rhinitis (Tomsa et al 2003). This report considered histologic findings diagnostic and found culture to be an ineffective means of diagnosis. Serology has also been used as a diagnostic tool using agar gel immunodiffusion (AGID), counterimmunoelectrophoresis (CIE), and ELISA techniques to detect fungi-specific serum antibodies. Two cats were tested for *Aspergillus* species antibodies and both were negative. One of the cats with a negative titer had a positive culture for *Aspergillus* species. Serum immunoelectrophoresis for antibodies against *A. fumigatus* were positive in two of the three cases in a previous report (Tomsa et al 2003). Therefore, serology alone cannot be used to definitively rule out or rule in an *Aspergillus* species infection.

Effective treatment of nasal aspergillosis has proven difficult. Several systemic anti-fungal drugs have been used to treat nasal aspergillus



in the past. The best results have been achieved using itraconazole and fluconazole, and even these only obtaining cure rates of 50–60% in canine patients (Tomsa et al 2003). Five percent of dogs treated with itraconazole experience hepatotoxicity (Legendre 1995). It is, therefore, very important to monitor liver enzymes in these patients. All cats in this report were treated with itraconazole and two of the four cats had relapses of clinical signs after itraconazole therapy was discontinued. Two cats had elevated liver enzymes, one cat required discontinuation of itraconazole therapy and hospitalization with supportive care. The other cat was asymptomatic and liver enzymes returned to normal levels in a month despite continuation of itraconazole therapy.

Topical therapy with a non-invasive infusion of clotrimazole is considered the treatment of choice for canine nasal aspergillosis. The cure rate has been as high as 94% (Mathews et al 1998). Potential adverse side effects of topical clotrimazole include patient discomfort, pharyngitis/pharyngeal edema, aspiration of clotrimazole leading to fatal inhalation pneumonia, and leakage of medication across an interrupted cribiform plate potentially leading to slow anesthetic recovery and neurological deficits. Side effects can be avoided by using a French Foley catheter with an inflated balloon and placing laparotomy sponges in the pharynx, using the 1-h infusion protocol with a form of clotrimazole that does not contain alcohol or propylene glycol, and performing a CT before the procedure to evaluate for cribiform plate destruction. This procedure has been described in the literature for use in dogs (Mathews et al 1995). Recently use of this technique has been reported in a cat with fungal rhinitis (Tomsa et al 2003). This procedure may be of benefit in cats with recurrent disease or in cats that develop itraconazole related hepatotoxicity. Studies are needed to evaluate its efficacy in cats. Rhinotomy and turbinectomy are no longer considered beneficial in treating nasal aspergillus and may be detrimental (Lanthier and Chalifoux 1991, Sharp et al 1991, Watt et al 1995).

Nasal aspergillosis/penicilliosis is rare in the cat. It is unclear if this group of cats represents an emerging disease, an underdiagnosed disease, or a coincidental cluster of cases. Clinical signs included mucopurulent nasal discharge, epistaxis and exophthalmos. A diagnostic work-up of these cases included bloodwork (CBC, biochemistry panel, FeLV antigen and FIV

antibody tests), chest radiographs, CT scan and rhinoscopy with biopsies. It is sometimes necessary to perform a rhinotomy to obtain diagnostic samples if the samples obtained with rhinoscopy are inadequate. Oral anti-fungal therapy was variably effective. One cat was asymptomatic after 4 months of itraconazole, one cat had recurrence of signs subsequent to discontinuation after a 10 week course of treatment and one cat had recurrence of signs after a 2 month course of itraconazole. Non-invasive infusion of clotrimazole may be a better alternative to oral therapy.

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