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# Invasive Mould Infections of the Naso-Orbital Region of Cats: A Case Involving *Aspergillus fumigatus* and an Aetiological Review

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## Abstract

### Case and context

This report describes a cat diagnosed with sinonasal-orbital Aspergillus fumigatus infection using advanced imaging, histopathology and culture. Aetiology, clinical aspects and treatment of this rare and devastating infection are discussed with reference to a literature review of invasive mould (ie, filamentous fungal) infections involving tissues of the naso-orbital region of cats.

### Presentations

Invasive fungal infections can present with different localisations (nasal passages, sinuses, orbits, subcutaneous space, palate, etc) depending on the species involved and its means of introduction into the tissues. Localised subcutaneous lesions (swellings, ulcerations, masses, nodules, etc), without concomitant signs of nasal/orbital disease, generally result from traumatic injuries and subsequent inoculation of fungal spores into the subcutaneous space. In contrast, naso-ocular involvement and concurrent signs of nasal disease (nasal discharge, sneezing, masses protruding from the nostrils) generally result from inhalation of spores, with subsequent spread of infection into the nasal planum or penetration of overlying bone and invasion of the subcutaneous space. Aspergillus species typically show such an invasion mechanism and frequently affect orbital tissues. Dematiaceous fungi (ie, filamentous fungi with brown/black hyphae) are reported to cause solitary, less invasive, slowly developing lesions, probably as a result of traumatic injuries with inoculation of fungal propagules. Accordingly, the subcutaneous space is more frequently primarily involved.

### Treatment and outcome

Whatever the mould species, reported treatment options include surgery and a series of antifungal drugs. The outcome is frequently poor, especially for Aspergillus infections, although various measures can be taken to maximise the chances of success, as discussed in this report.

## Case history

A 4-year-old indoor /outdoor male neutered domestic shorthair cat was referred for an ophthalmic evaluation due to protrusion of the right eye, accompanied by a decreased appetite and difficulty eating.

### General and ophthalmic examination

The eye was exophthalmic and dorsotemporally deviated, while the nictitating membrane was thickened and partially elevated (Fig 1). Retropulsion of the globe was decreased but not painful. There was evidence of moderate pain on opening the mouth, a soft swelling in the soft palate (Fig 2), and regional lymph node enlargement. No other physical abnormalities were detected. The results of a complete blood count and urinalysis were within reference intervals. Feline leukaemia virus antigen and feline immunodeficiency antibody tests (Snap Combo Test; Idexx Laboratories, USA) were negative. Ultrasonographic examination of the abdomen and thoracic radiographs showed no abnormalities.

Marked conjunctival hyperaemia, ulcerative exposure keratitis and severe corneal oedema were present in the right eye, precluding an examination of the anterior chamber and eye fundus. Fluorescein uptake was positive in the central part of the cornea and results of a Schirmer tear test were 0 mm/min. Using applanation tonometry, the intraocular pressure (IOP) was 14 mm/Hg (normal IOP in the cat: 15–25 mmHg). The palpebral reflex was normal and the menace response was negative in the right eye (OD); the direct right pupillary light reflex (PLR) could not be evaluated because of the corneal opacity, nor could the consensual left PLR to OD. The left eye did not show any abnormalities. An ocular ultrasound examination (curved array 7.5 MHz, MyLab 30; Esaote Biomedical, Milan, Italy) of the right eye showed a 1.8 × 2 cm hyperechoic lesion within the orbit. Cytology of fine needle aspiration (FNA) biopsies of the mass and soft palate swelling revealed a population of neutrophils, macrophages and lymphocytes, interspersed with a few plasma cells.

Given the failure to identify an underlying aetiological agent or neoplastic cells, the initial diagnosis reached was that of a non-specific inflammation. The cat was prescribed amoxicillin/clavulanate (15 mg/kg PO q12h, Synulox; Pfizer), enrofloxacin (5 mg/kg PO q24h, Baytril; Bayer) and tobramycin (ocular drops q6h for 2 weeks, Stilbiotic; Trebifarma, Italy).

### Imaging and surgical findings — 1 week post-presentation

A computed tomography (CT) scan performed 1 week later revealed a lack of response to treatment and confirmed an infiltrative lesion of 2.3 × 3 cm within the right orbit, causing dorsotemporal deviation of the globe and extending through the palatine bone and pharyngeal region (Fig 3).

Cytological samples from CT-guided FNA biopsies of the retro bulbar and palatine lesions and right mandibular lymph node revealed a mixed inflammatory cell population with no neoplastic cells. Bacterial and fungal cultures were negative.

Due to progressive deterioration in the cat's condition, the owner agreed to an orbital exenteration with excision of the regional lymph nodes. A large (2.5 × 3 cm) multi-lobulated friable mass was evident adherent to the lateral sclera. Histological examination showed multifocal to coalescing granulomas characterised by a large central zone of coagulative necrosis, with hyaline fungal hyphae (Figs 4 and 5) heavily infiltrating the third eyelid cartilage; the hyphae were parallel-walled, dichotomously branching, regularly septated, and 4–6 μm in width. Inflammatory infiltration effaced the orbital skeletal muscles. Regional lymph nodes showed intense follicular hyperplasia but no hyphae. Unfortunately, cultures were not possible at the time because accidentally all of the specimens were fixed in formalin.

Based on these findings, treatment with oral itraconazole (10 mg/kg PO q24h, Sporanox; Janssen-Cilag, Italy) was instituted.

**Fungal studies — 3 weeks post-presentation**

Two weeks later, two soft subcutaneous painless swellings in the right frontal and maxillary regions were evident, accompanied by nasal discharge and crust around the nares. The palatine mass appeared enlarged (Fig 6). Nasal tissue samples obtained by rhinoscopy and incision biopsies from the frontal and maxillary regions and soft palate were cultured on Sabouraud dextrose agar with chloramphenicol and gentamicin. Fungal colonies grew from all samples within 48–72 h at 37°C.

Microscopic examination revealed hyphae with swollen apical vesicles lacking a basal septum. These were covered by phial-shaped cells (phialides) producing conidia. These components form the so-called conidial head, typical of Aspergillus species. Morphological features of subcultures on Czapek agar1 were consistent with Aspergillus fumigatus (ie, smoky grey-green colonies with a pale reverse; erect unbranched conidiophores supporting swollen dome-shaped apical vesicles 20–30 μm in diameter; conidiogenous cells occurring only on the upper portion of the vesicles). Bacterial cultures were negative.

Antifungal susceptibility tests (microdilution method) yielded minimum inhibitory concentration (MIC) values of 0.25, 0.5 and 4 μg/ml for posaconazole, itraconazole and amphotericin B, respectively. Because of the high cost of posaconazole, the cat was treated with itraconazole (10 mg/kg PO q24h, Sporanox) and terbinafine (5 mg/kg PO q24h, Lamisil; Novartis, Italy). The choice was based on previously published data regarding the in vitro synergy of this combinaton against A fumigatus.2,3

**Funduscopic examination — 4 weeks post-presentation**

One week later, the cat was re-examined for blindness of 1 day's duration. The left eye was mydriatic, with a non-responsive pupil and negative menace response. Funduscopic evaluation by indirect ophthalmoscopy showed a swollen optic disc and multifocal linear areas of oedema in both the tapetal and non-tapetal regions. The other ocular structures were normal. The therapeutic approach was considered inadequate, allowing progression of the fungal infection to the contralateral eye, resulting in optic neuritis and chorioretinitis. Therefore, the combination therapy

was replaced by oral posaconazole (5 mg/kg PO q12h, Noxafil; kindly donated by Schering-Plough, Milan, Italy).

After 7 days of treatment, the cat regained vision, the pupil diameter returned to normal, a menace response was present and the optic disc appeared to be normal. The multifocal oedematous areas within the retina were markedly reduced. A further ophthalmic examination 2 weeks later did not reveal any abnormalities. Additionally, the facial and palatine swellings were no longer evident.

### MRI studies — 6 months post-presentation

Six months after initial presentation the cat, which was still receiving posaconazole, was re-examined for an episode of intermittent miotic pupil and elevated third eyelid in the remaining (left) eye, with a right head tilt and ataxia that lasted for 12 h. Ophthalmic and neurological examinations did not reveal any abnormalities; however, central nervous system involvement was suspected. Therefore, magnetic resonance imaging (MRI) of the skull was performed. This revealed right-sided otitis media, left-sided frontal sinusitis and aggressive, infiltrative right orbital disease with involvement of the brain, right pterygoid muscle (and possibly soft palate) and sphenoid sinus (Fig 7). A bony defect was present at the base of the skull in the region of the foramen ovale/foramen rotundum. No obvious turbinate destruction or cribriform plate abnormalities were detected.

Cytology from samples obtained by flushing the right bulla revealed pyogranulomatous inflammation with rods and cocci, without fungal hyphae. Staphylococcus intermedius and Proteus species were isolated. Fungal cultures were negative. The cat was given two doses of cefovecin (8 mg/kg SC 15 days apart, Convenia; Pfizer, Italy) and maintained on oral posaconazole.

One month later, a moderate left eye exophthalmos with lateral globe deviation was noted. Ocular ultrasound revealed a 0.7 × 1 cm hyper echogenic nodule in the orbit, and FNA cytology showed sparse fungal hyphae. At that time, the owner decided to seek a second opinion and went on to pursue a different therapeutic approach. The cat was given amphotericin B liposomal complex (AmBisome; Gilead Sciences, Rome, Italy), diluted to 1 mg/ml in 5% dextrose (D5W), which was intravenously infused at a con centration of 1 mg/kg for 1–2 h 3 days/week (10 treatments).

One month later, because of a deterioration in its physical condition and the development of seizures, the cat was euthanased at the owner's request. A necropsy was declined.

## Discussion

### Fungi infecting the naso-orbital region of cats

To review the aetiology of mould infections of the naso-orbital region in cats, the available published reports were screened and cases were recruited if invasive fungi affecting the nasal passages, sinuses, orbits, palate and naso-orbital subcutaneous space were demonstrated histologically.4–36 The fungi could be conveniently divided into two main groups: hyalohyphomycetes, comprising hyaline septate hyphal tissue forms (cases 1–30, Table 1), and phaeohyphomycetes, comprising pigmented septate hyphal forms (cases 31–58, Table 2). The characteristic pigmentation of phaeohyphomycetes (dematiaceous fungi), due to the melanin in their cell wall, is typically seen on microscopic examination of infected tissues and always in cultures.37

Zygomycetes are excluded from both groups because their hyphae in tissues, as well as in culture, are aseptate.37

All these fungi are environmental saprophytes, causing infections in the presence of predisposing local or systemic factors. Moreover, most of these fungi cause similar sinonasal-orbital disease, and also disseminated infections in humans.38,39 Importantly, none of them can be considered a zoonotic agent, as has erroneously been described elsewhere.40

Some fungal species are more frequently reported than others, and this might reflect their adaptation to a sporadically parasitic aptitude, along with their proportionately higher abundance in the environment.37,41 Thereafter, the tissue invasion pattern seems to depend on the fungal agent's preferred route of entry and on its subsequent ability to invade tissues.26 In the present case, the fungal disease showed progressive involvement of different naso-orbital structures, thus confirming the locally invasive nature of A fumigatus; in agreement with previous reports, infection did not disseminate. Many cases (including the present one) caused by A fumigatus and closely related species — all of which are part of the so-called Aspergillus section Fumigati42 — present with an orbital localisation (Table 1); therefore, it is possible that this fungal group demonstrates a ‘tropism’ towards this anatomical site in cats. Interestingly, Cryptococcus neoformans, the most frequent fungal species causing sinonasal pathology in cats, has the potential to spread through the cribriform plate from sinonasal structures to the olfactory bulbs, tracts and optic nerve, but does not involve the orbit.43–47 By contrast, in the dog, sinonasal cryptococcosis can spread to the orbit, as Aspergillus does in cats, whereas retrobulbar localisation is extremely rare.48

With regard to the dematiaceous fungi (cases 31–58, Table 2), orbital involvement is much more rarely reported and, in the only case in which it occurred (case 31), a traumatic pathogenesis with a plant foreign body was demonstrated.20 In fact, in cats dematiaceous fungal infections generally localize to the subcutaneous space due to traumatic injuries and subsequent inoculation of fungal propagules.26 Compared with Aspergillus and other hyalohyphomycete infections, non-facial cutaneous sites have been more frequently reported, thus confirming the traumatic pathogenesis.26,35

Some strains (cases 20–27) that possessed, in culture, morphological features consistent with A fumigatus were subsequently identified, by PCR, as Neosartorya species, Aspergillus lentulus and Aspergillus udagawae.

As mentioned above, they form, together with ‘true’ A fumigatus, the Aspergillus section Fumigati. In fact, molecular studies have revealed frequent misidentification of A fumigatus by morphotyping,49 and this could eventually apply to cases 16–19, as well as the present case, since in none of these instances was molecular confirmation obtained. Conversely, some fungal strains recovered from dogs with sinonasal forms without orbital involvement (the analogous canine fungal syndrome rarely involves the orbit and tends to be less locally aggressive)50,51 have previously been confirmed as ‘true’ A fumigatus by molecular techniques.30

The difference in aggressiveness of these fungal forms noted between cats and dogs could be due to features of their muzzle morphology. It has been hypothesised that the brachycephalic conformation of Persian and Himalayan cats may be an important risk factor, causing mucosal oedema, and

influencing airflow and mucociliary clearance, thus increasing their susceptibility to invasive fungal infection.21,25,28,33

The findings in the present case support the conclusion of previous authors that an orbital Aspergillus localisation in cats is likely to be part of a more extensive disease process involving the nose and paranasal cavities.26,29–31,33 Infection of the orbital region may have occurred after initial colonisation of nasal/paranasal tissues by spores. The positive fungal culture of nasal tissues, together with the bony defect in the region of the foramen ovale/foramen rotundum identified on MR images, support this hypothesis. However, because evidence of nasal involvement appeared after orbital involvement, and no abnormalities of the cribriform plate were detected by MRI, the possibility of descending infection should also be considered. Spores that are normally part of the commensal cutaneous and mucosal microflora may have entered the orbit through a periorbital or conjunctival wound caused by a foreign body or penetrating injury, overwhelming the nonspecific local host defence mechanisms. However, no foreign body was identified on CT scans, MR images or histopathology slides; nor were any wounds discovered in the orbital region. Swellings in the frontal and maxillary regions appeared after sinonasal-orbital signs and presumably derived from the spread of infection through the bones, with colonisation of the subcutaneous space. Regardless of the route of entry, the present case confirms that orbital disease can represent the first clinical sign of such fungal disease in cats.

**Diagnostic challenges and developments**

It can be difficult to diagnose this rare and devastating infection without a high index of suspicion for a fungal aetiology, especially considering that no single test result may be deemed definitive. Cytology from the right location may help to demonstrate fungal hyphae and eventually guide intraoperative resection of abnormal tissues. However, it might yield an inflammatory cell population and, therefore, prove relatively insensitive if used as the sole diagnostic tool. In the present case, FNA biopsies from the mass, palatine swelling and regional lymph nodes yielded negative results for fungal hyphae, both initially and at the time of CT scanning. In retrospect, in the light of a thorough knowledge of the literature, a fungal aetiology should have been considered highly likely given the recovered inflammatory pattern. Cytology was not consistent with an acute suppurative inflammation or lymphoma; moreover, a retrobulbar abscess without fever and severe pain would appear unlikely, as would a neoplasm in a young adult cat.

Histopathology is another diagnostic tool with a variable sensitivity depending on the distribution of fungal hyphae within tissues and sample collection. Moreover, without a high index of suspicion for a fungal aetiology, a common error is to put all material in formalin, thereby preventing the possibility of subsequent definitive mycological identification by culture, as happened initially in the present case.

It may still be possible to determine the aetiology using a panfungal PCR from both fresh tissue samples and paraffin-embedded (PE) sections, as illustrated by a recent study.52 In the present case, since the fungal strain failed to grow on subculture, such an approach was attempted at a later date to obtain a molecular confirmation of the culture-based identification. In order to retrieve fungal DNA from paraffin blocks, multiple sections, 10 μm thick, were obtained. Sections were cut with a

sterile blade and placed in a sterile container. Panfungal PCR was performed in the Mycology Laboratory at Westmead Hospital, Australia. In the event, PCR failed to detect fungal DNA in the PE specimens. A 60–65% success rate for the retrieval of fungal DNA from a PE section in which fungal elements were seen by microscopy is reported by the laboratory and in the literature.52 Prolonged storage of the PE specimens had probably led to DNA deterioration and might explain the negative result.

Culture is more sensitive than cytology and is the only means of obtaining definitive identification, but may yield negative results because of the lack or poor vitality of the fungal organisms within the specimens,41 as in the present case. With respect to the reviewed veterinary literature, a definitive identification is lacking for 12 cases (Tables 1 and 2), in which cultures were either not performed or yielded negative results. Conversely, because fungal infection can occur secondarily to other pathological processes, and environmental fungal spores can physiologically colonise some tissues such as nasal mucosa, clinical specimens might contain fungal spores. Furthermore, culture dishes can be contaminated, especially if samples are handled and put in culture without using a sterile biological hood. For these reasons, the pathogenic role of an isolated mould may be debatable and should always be interpreted along with cytology/hystology.50

In the present case, a fungal culture at initial presentation was omitted in error and the diagnosis of fungal infection was made on histology after orbital exenteration. The fungus was cultured only at a later date, thus preventing an earlier diagnosis, earlier antifungal treatment and a possible better clinical outcome. Given these considerations, FNAs, biopsies or surgical specimens from cats with retrobulbar masses and/or sinonasal signs should always be submitted for culture as early as possible.

In recent years progress has been made to expedite the diagnosis of fungal infections with the development of highly sensitive serodiagnostic assays for fungal antigen detection, such as galactomannan or beta-D-glucan assays. They are routinely used in humans,53 but only sporadically in veterinary medicine.31,54 Ideally, they should have been used in the present case and would have raised a suspicion of a fungal aetiology at an early stage.

**Treatment options**

Treatment options reported in the literature include systemic therapy combined with surgical removal of the lesions in order to reduce as much as possible of the fungal load. Clearly, a better clinical outcome follows a radical surgical excision.4–36 An effective standardised protocol is not yet available and treatment failures or relapses are commonly described.

In the present case, itraconazole therapy was instituted first because of its documented efficacy, relative safety, ease of administration and affordability.55–57 However, its clinical effect, alone and in combination with terbinafine, was poor, despite their in vitro synergy.2,3 Posaconazole was then administered because it was active against the fungal isolate in vitro, and because of its efficacy in human patients,58,59 as well as a published report of its efficacy in a case of feline orbital aspergillosis.29 It possesses a broad spectrum of activity, is palatable and easier to use due to the reduced risk of liver toxicity with high doses compared with other antifungal drugs.60 The owner's financial constraints did not allow access to the drug until Schering-Plough Animal Health

generously supplied it. In the light of the long remission of clinical signs, even with its delayed administration, it should have been the drug of choice. The disease, however, relapsed.

In the authors' opinion, the eventual clinical inefficacy might be explained either by poor tissue penetration of the drug within the lesion or unattained therapeutic blood levels. As no pharmacokinetics on posaconazole are currently available for cats, and the dosage for its use in cats has been empirically extrapolated from other species,61 a dose rate based on a previous report was used in the present case.29 Therapeutic drug monitoring, involving measurement of posaconazole serum concentration, was not performed, but would have been useful.

For many years, amphotericin B was considered the drug of choice for severe deep mycoses, because of its broad spectrum of activity. Further, the lipid formulations have been associated with decreased renal toxicity.62 It can be administered intravenously, subcutaneously63 or intralesionally. In human medicine, its intralesional use has been documented for both cutaneous and retrobulbar fungal lesions.64,65 In veterinary medicine, a recent report describes its successful intralesional use in a refractory case of feline sporotrichosis,66 thus adding a worthwhile therapeutic option for frustrating mycotic infections. Feline sino-orbital fungal infections may eventually benefit from this intra-lesional orbital approach, although, due to the limited retrobulbar space and proximity of the meninges and optic nerve, care should be taken in order to avoid toxicity and iatrogenic damage.67 In the present case, systemic amphotericin B administration was chosen as the last option, due to high MIC values. However, it should be emphasised that favourable MIC values have been shown to be poorly predictive of the in vivo response for itraconazole and posaconazole, which were used in this case.

Voriconazole and caspofungin could be alternative effective drugs. The former is the agent of choice for the treatment of most Aspergillus species infections in human patients.68 It has recently been used in two cats affected by orbital mycosis (cases 2 and 19); although it was apparently effective, almost immediately, against the fungal organisms, it also resulted in adverse reactions.36 The latter has proven to be effective in a case of canine systemic aspergillosis,69 but no studies have been performed in cats to date.

**KEY POINTS**

Rational management in cases of feline naso-orbital aspergillosis requires that rapid diagnosis through serology, along with fungal culture from FNA biopsies, is attempted.

Given the severity of this syndrome, and the need for long courses of therapy, it is very important to obtain representative material in order to allow accurate species identification and generate in vitro susceptibility data. Thus, a proportion of biopsy/surgical specimens should be withheld from formalin fixation, allowing additional cultures where necessary.

For the best chance of a successful outcome, as much infected tissue as possible should be debrided (not just in the naso-orbital region, but also from the oral cavity if disease has extended there) after 1–2 weeks of posaconazole therapy. By removing abnormal tissues, high levels of antifungals are likely to be obtained postoperatively. Such therapeutic intervention requires a team approach, with intraoperative cytology available as a guide.

Finally, an aggressive combination therapy with posaconazole and amphotericin B and/or terbinafine — eventually with the measurement of serum drug concentrations — offers the best prospects of success.

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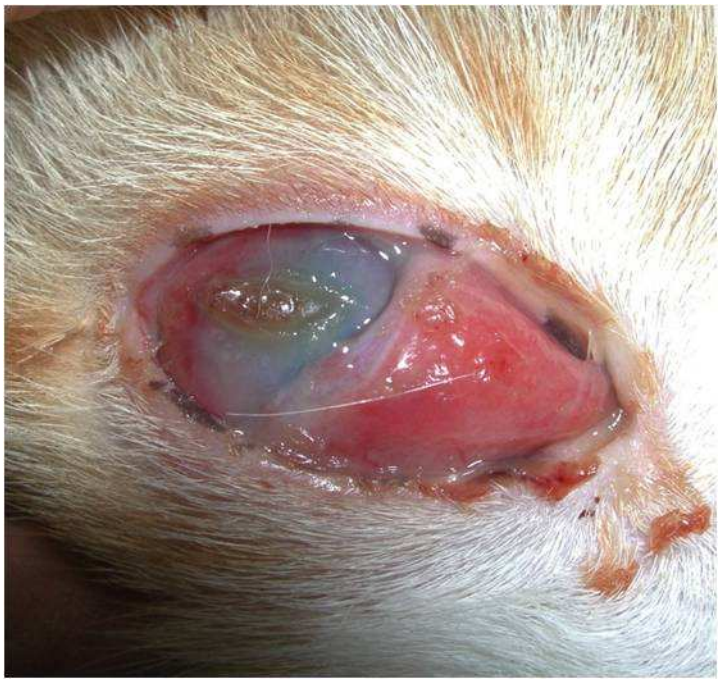


Fig.1

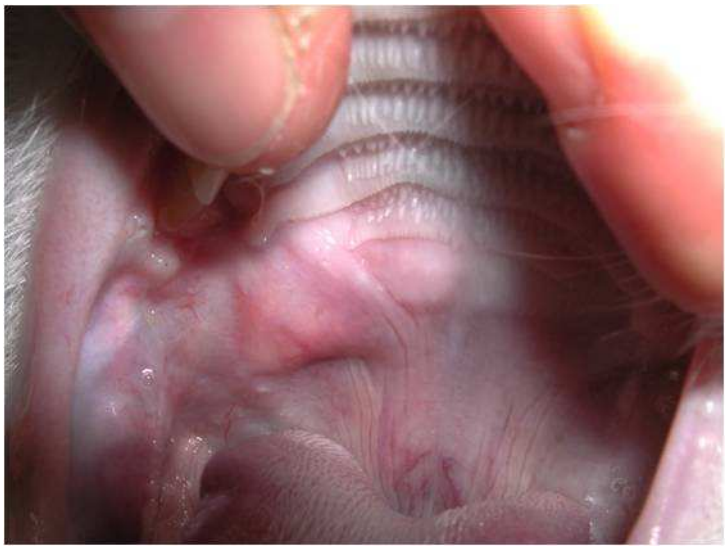
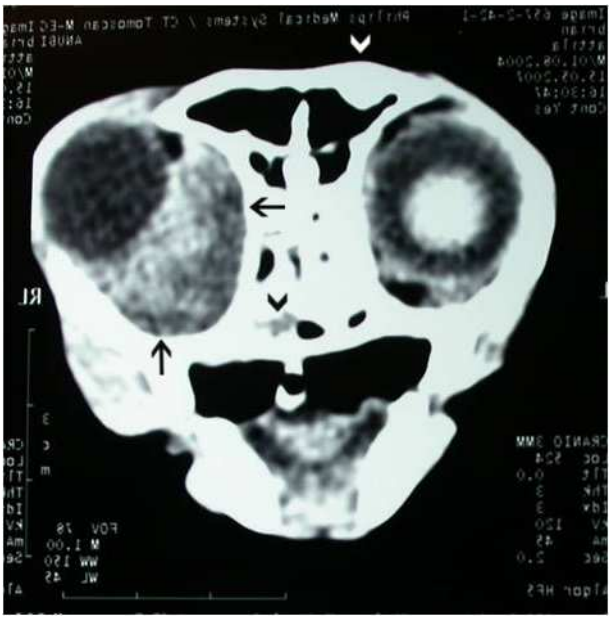


Fig. 2



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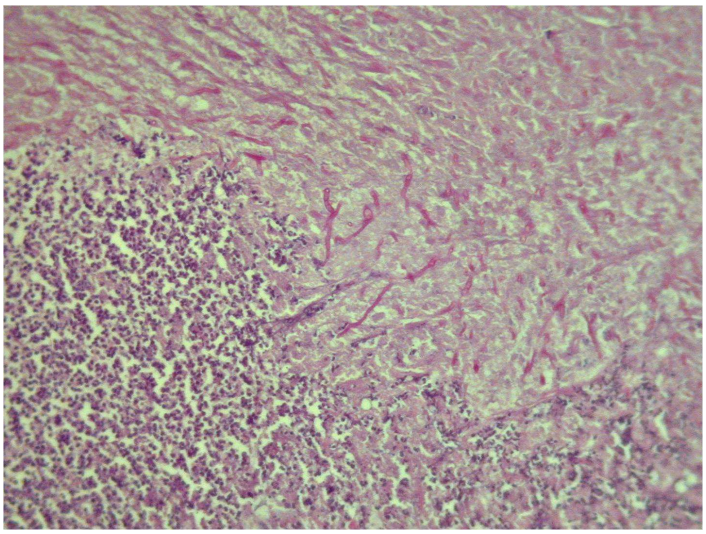

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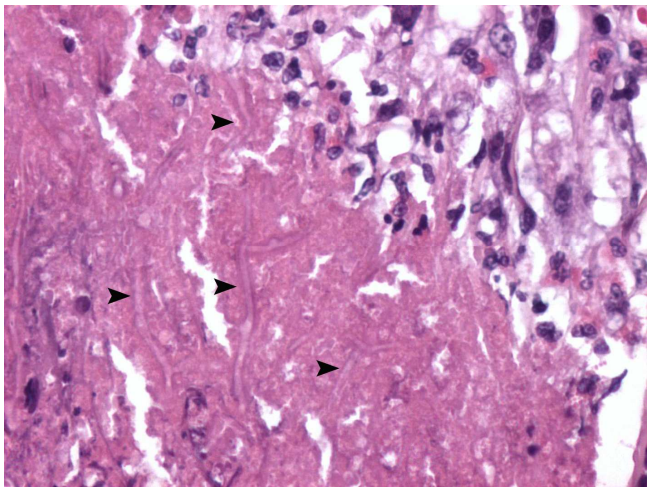

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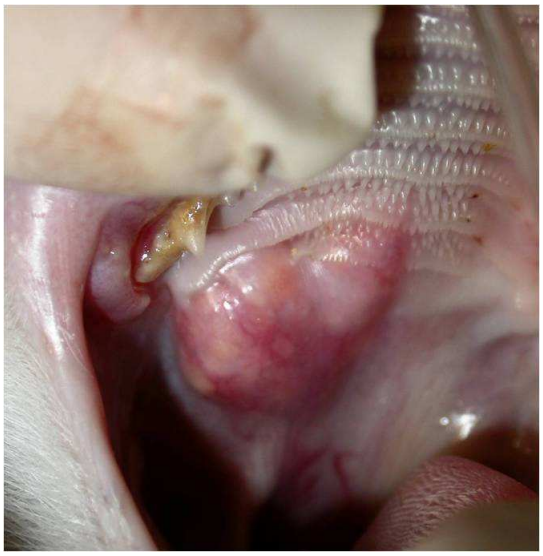

Fig. 6

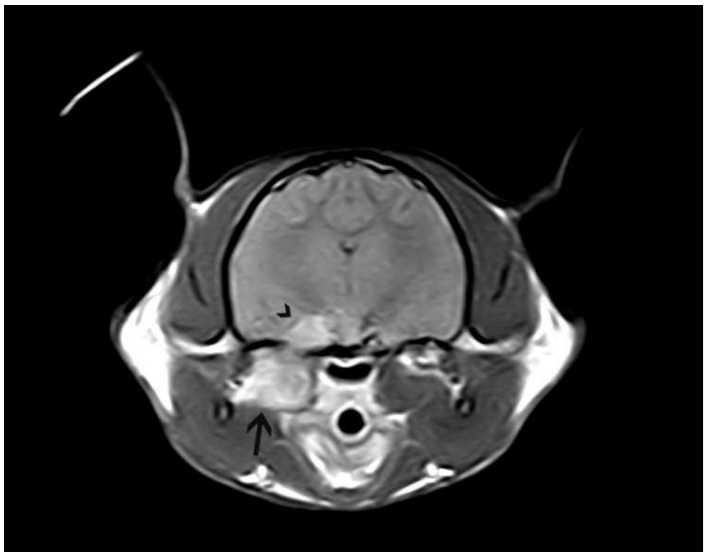

Fig. 7

Figure legends

**Figure 1**: Right eye exophthalmos with dorsal and temporal deviation of the globe, third eyelid protrusion and severe central exposure keratitis

**Figure 2**: Palate region at initial presentation exhibiting a swelling in the right pterygopalatine fossa

**Figure 3**: Transverse CT of the head at the level of the lens of the eye (brain window) after intravenous contrast medium administration. A right orbital space occupyng lesion showing heterogeneous contrast enhancement (black arrows) displaces dorsolaterally the right eye. A mild amount of material with moderate density is visible on the right sidde of the nasopharynx (black arrowhead). The left frontal bone seems to be mildly thickened (white arrowhead)

**Figure 4**: H&E, original magnification 4x. A large, irregular zone of coagulative necrosis is rimmed by a thick inflammatory cell infiltration

**Figure 5**: H&E, original magnification 400x. At high power field numerous, negative stained, parallel walled, dichotomously branching, 4-6 microns wide fungal hyphae were evident (arrowheads) within coagulative necrosis. A rim of macrophages and epithelioid cells admixed with eosinophils and neutrophils surrounded necrotic focus

**Figure 6**: Palate region after 4 weeks therapy with oral itraconazole. Note the enlargement of the palate swelling

**Figure 7**: Transverse, T1W MR image post contrast through the skull immediately rostral to the tympanic bullae. The right medial pterigoyd muscle is slightly larger than the contralateral one and shows increased, heterogeneous contrast uptake (arrow). Note the focal area of increased contrast uptake in the right temporal lobe adjacent to the skull base in the region of the trigeminal canal (arrowhead)

| | Fungal species | Cat | invasion pattern | | | | | | OL |
|---|---|---|---|---|---|---|---|---|---|
| **HYALOHYPHOMYCETES (N = 30)** | *culture not performed* | 1 [28] | or | sin | na | sc n | sc f | pal | N |
| | | 2 [36] | or | sin | na | sc n | sc f | pal | N |
| | *negative culture* | 3 [17] | or | sin | na | sc n | sc f | pal | N |
| | | 4 [25] | or | sin | na | sc n | sc f | pal | N |
| | | 5 [25] | or | sin | na | sc n | sc f | pal | N |
| | | 6 [25] | or | sin | na | sc n | sc f | pal | N |
| | | 7 [28] | or | sin | na | sc n | sc f | pal | N |
| | | 8 [28] | or | sin | na | sc n | sc f | pal | N |
| | | 9 [36] | or | sin | na | sc n | sc f | pal | N |
| | *Aspergillus spp.* | 10 [5] | or | sin | na | sc n | sc f | pal | N |
| | | 11 [21] | or | sin | na | sc n | sc f | pal | N |
| | | 12 [34] | or | sin | na | sc n | sc f | pal | N |
| | *Aspergillus niger* | 13 [34] | or | sin | na | sc n | sc f | pal | N |
| | | 14 [28] | or | sin | na | sc n | sc f | pal | N |
| | *Aspergillus flavus* | 15 [26] | or | sin | na | sc n | sc f | pal | N |
| | *Aspergillus fumigatus* | 16 [10] | or | sin | na | sc n | sc f | pal | N |
| | | 17 [29] | or | sin | na | sc n | sc f | pal | N |
| | | 18 [33] | or | sin | na | sc n | sc f | pal | N |
| | | 19 [36] | or | sin | na | sc n | sc f | pal | N |
| | Aspergillus Section Fumigati | 20 [31] | or | sin | na | sc n | sc f | pal | N |
| | | 21 [30] | or | sin | na | sc n | sc f | pal | N |
| | | 22 [30] | or | sin | na | sc n | sc f | pal | N |
| | | 23 [30] | or | sin | na | sc n | sc f | pal | N |
| | | 24 [30] | or | sin | na | sc n | sc f | pal | N |
| | | 25 [30] | or | sin | na | sc n | sc f | pal | N |
| | | 26 [30] | or | sin | na | sc n | sc f | pal | N |
| | | 27 [30] | or | sin | na | sc n | sc f | pal | brain |
| | *Paecilomyces fumosoreus* | 28 [8] | or | sin | na | sc n | sc f | pal | digit, liver |
| | *Paecilomyces lilacinus* | 29 [26] | or | sin | na | sc n | sc f | pal | N |
| | *Penicillium spp.* | 30 [4] | or | sin | na | sc n | sc f | pal | lungs |

Table 1

| | Fungal species | **cat** | Invasion pattern | | | | | | OL |
|---|---|---|---|---|---|---|---|---|---|
| **PHAEOHYPHOMYCETES (N = 28)** | *culture not performed* | 31 [20] | or | sin | na | sc n | sc f | pal | N |
| | | 32 [18] | or | sin | na | sc n | sc f | pal | foreleg |
| | | 33 [12] | or | sin | na | sc n | sc f | pal | N |
| | *Alternaria alternata* | 34 [19] | or | sin | na | sc n | sc f | pal | N |
| | | 35 [23] | or | sin | na | sc n | sc f | pal | N |
| | *Alternaria infectoria* | 36 [15] | or | sin | na | sc n | sc f | pal | tail,pinna,digits |
| | *Alternaria spp .* | 37 [27] | or | sin | na | sc n | sc f | pal | N |
| | | 38 [27] | or | sin | na | sc n | sc f | pal | N |
| | | 39 [35] | or | sin | na | sc n | sc f | pal | N |
| | | 40 [35] | or | sin | na | sc n | sc f | pal | N |
| | | 41 [35] | or | sin | na | sc n | sc f | pal | N |
| | | 42 [35] | or | sin | na | sc n | sc f | pal | N |
| | | 43 [35] | or | sin | na | sc n | sc f | pal | N |
| | | 44 [35] | or | sin | na | sc n | sc f | pal | pinna |
| | | 45 [35] | or | sin | na | sc n | sc f | pal | paw |
| | | 46 [35] | or | sin | na | sc n | sc f | pal | tail, pinna, digits |
| | *Exophiala jeanselmei* | 47 [26] | or | sin | na | sc n | sc f | pal | N |
| | | 48 [26] | or | sin | na | sc n | sc f | pal | N |
| | | 49 [6] | or | sin | na | sc n | sc f | pal | N |
| | | 50 [13] | or | sin | na | sc n | sc f | pal | N |
| | | 51 [14] | or | sin | na | sc n | sc f | pal | N |
| | *Exophiala spinifera* | 52 [11] | or | sin | na | sc n | sc f | pal | N |
| | | 53 [17] | or | sin | na | sc n | sc f | pal | N |
| | *Cladophialophora bantiana* | 54 [24] | or | sin | na | sc n | sc f | pal | N |
| | *Dissitimurus exedrus* | 55 [16] | or | sin | na | sc n | sc f | pal | N |
| | *Fonsecea pedrosoi* | 56 [22] | or | sin | na | sc n | sc f | pal | N |
| | *Phialophora verrucosa* | 57 [7] | or | sin | na | sc n | sc f | pal | N |
| | *Ulocladium spp.* | 58 [32] | or | sin | na | sc n | sc f | pal | N |

Table 2

Table 1 and 2 legend

Etiology of invasive molds infections involving tissues of the naso/ocular region of cats.

**Invasion pattern**: or = orbit; sin = paranasal sinus; nas = nasal passage; sc f = facial subcutaneous space (cheek, periorbital, forehead etc.) ; sc n = perinasal/nasal bridge/nasal planum subcutaneous space; pal = palate. Grey cells indicate involvement of the anatomical site.

**OL** = other localizations (N = No)