Some thoughts on sinonasal aspergillosis in dogs and cats

Richard Malik DVSc FACVSc FASM
Post Graduate Foundation of Veterinary Science, Building B22, The University of Sydney, 2006

When a consensus about the treatment of a disease has been reached, it is generally possible to conclude that the condition is well understood and therapy guidelines are based on secure knowledge and clinical experience with good follow-up.

On the other hand, when there are many disparate schools of thought on diagnosis and therapy, and new treatment regimens are continually being developed, one must be suspicious that no one treatment regimen is suitable for the management of all cases. This would appear to be the case for nasal aspergillosis in both the dog and the cat, although I have the sense that people are now doing a ‘better job’ in thinking about the pathogenesis of this disease spectrum.

I believe part of the problem is that the term aspergillosis does not really signify what is happening within the nasal cavity and contiguous sinuses, and the recent trend to categorise cases using a classification scheme adapted from humans seems to be helpful. Thus, cases should be described as having:

1. Non-invasive mycotic rhinitis
2. Non-invasive destructive/erosive mycotic rhinitis
3. Chronic invasive mycotic rhinitis

Non-invasive disease (aspergilloma) is known to occur in man, but is rarely encountered in cats and dogs, and represents the formation of a fungal ball within the nasal cavity or sinus, but without tissue invasion or turbinate atrophy.

Non-invasive destructive disease is typically seen in the dog, and is the result of long standing infections where fungal hyphae grow into blood vessels supplying the turbinates causing ischaemic necrosis and turbinate atrophy. This turbinate erosion and distortion are the hallmark of this condition rhinoscopically (especially when plaques of fungal mats can be seen concurrently), and accounts also for the lesions seen in plain radiographs and with cross sectional imaging.

Chronic invasive aspergillosis takes the disease complex one step further, in that the infection penetrates through the bones surrounding the nasal cavity to involve soft tissues in the orbit, the hard palate, the bridge of the nose or the nasopharynx.

All these infections most likely represent localised disease (variably invasive) in an immune competent host.
Clearly, the extent of tissue invasion has a huge impact on the recommendation for therapy, as a fungal ball can be treated by simple surgical extraction, whereas non-invasive destructive disease requires at least local (topical) antifungal strategies, while invasive disease requires systemic administration of effective antifungal drugs (perhaps in concert with topical therapy and sometimes accompanied by appropriate surgical debridement).

In my experience, cats in Australia usually get invasive disease and for this reason we have placed much more emphasis on systemic drug strategies (e.g. using oral itraconazole and subcutaneous amphotericin B) rather than topical intranasal therapy in this species. This approach has, however, not been adopted by colleagues overseas. In contrast, invasive disease is less common in the dog, although approximately one quarter of dogs with aspergillosis have some destruction of the cribriform plate.

Over the past few years, the most popular treatment regimens advocated for treating canine cases of non-invasive destructive aspergillosis have revolved around “soaking” the nasal cavity and sinuses with clotrimazole during one or more prolonged sessions under general anaesthesia. Recent refinements have involved placing tubes into the sinuses endoscopically, or using depot preparations which release clotrimazole over a greater duration of time. This type of approach has become more popular than the once or twice daily flushes with enilconazole through indwelling tubes in the sinonasal cavities; a treatment regimen that is defensible based on principles of antifungal therapy and has the best recorded success rate, albeit with high morbidity.

There seems little interest in systemic therapy in canine patients, despite high recorded success rate for both fluconazole and itraconazole therapy in the literature.

As a clinician interested in infectious diseases, the evolution of treatment regimens has been *ad hoc* from my perspective. Furthermore, it has been undertaken principally by surgeons, a very worrying precedence! It is noteworthy that there has been little attention paid to principles widely accepted in the treatment of other chronic infectious diseases.

I offer the following comments in the spirit of being provocative, stimulating discussion, and to encourage people to conduct more basic and clinical research in relation to this fascinating condition:

1. Not all mycotic infections are caused by *Aspergillus fumigatus*. In some places *Aspergillus flavus* or *Aspergillus fisherii* are likely to be involved and other species of filamentous fungi such as *Scedosporium apipserumum* or *Penicillium spp* or even algal forms such as *Pythium spp* may be the culprits. **For this reason, species identification is of great importance, as most of these saprophytes have a relatively predictable susceptibility pattern to antifungal agents, once you know their phenotype.** Furthermore panfungal PCR primers can be used to produce a rapid diagnosis via sequence analysis (contact Dr Catriona Halliday at ICPMR, Westmead Hospital). Susceptibility testing at a reference lab is further recommended. It may be that agents other than itraconazole may be drugs of
choice e.g. terbinafine, voriconazole, posaconazole. Also, don’t forget that you can also get nasal cryptococcosis in both cats and dogs.

2. Early diagnosis of cases in general practice and **speedy implementation of therapy can result in a rapid and complete response to therapy with itraconazole**. I have had three success stories with rapid resolution over the last 3 years. This may not be the cases in patients treated inappropriately for many months with antibiotics (and sometimes glucocorticoids!) in the absence of any demonstrable clinical response. Referral clinicians may be getting to see cases that are difficult to treat because of their chronicity. **Generalists should have a high suspicion for this diagnosis when there is unilateral nasal discharge with depigmentation of the naris.**

3. I believe most cases start in the nasal cavity, not in the sinuses. The role of grass seeds, awns and similar foreign bodies deserves more attention in relation to disease prevention.

4. Most cases of invasive disease caused by a microbial pathogen require high levels of the therapeutic agent to be present in the tissues for sufficient time for the agent to be cleared by phagocytosis. Thus, expecting a one-off treatment, e.g. clotrimazole/vehicle nasal soak, to cure all patients is naive in the extreme.

5. **It must be born in mind that perhaps one quarter of dogs with sinonasal aspergillosis have some destruction of the cribriform plate**, and are therefore at risk for the development of neurological sequellae following soaking the nasal cavity with clotrimazole dissolved in solvents likely to be highly irritant to the meninges.

6. **Clotrimazole is an inferior antifungal.** I am at a loss why we persevere in using it for these infections when much more potent, fungicidal agents are available. The polyenes amphotericin B and natamycin deserve appraisal as topical agents, especially if they can be formulated into depot preparations which can be instilled into the frontal sinuses to provide long lasting local levels in the nasal cavity. High doses of polyenes can be used as they are largely unabsorbed from the alimentary tract.

7. It may be worth combining systemic therapy using itraconazole with daily nebulisation therapy using natamycin, amphotericin B or enilconazole. Enilconazole is available in two interesting commercial formulations (in addition to Imaverol rinse) – one that produces non-toxic smoke (“Clinafarm Smoke”®), the other that uses DOSS as a dispersal agent (“Clinafarm spray”®). Both are inexpensive.

8. The pool biocide polyhexamethylene biguanide (“Baquacil”®) as a 0.02% solution (or higher) may prove useful for topical therapy, depot therapy and nebulisation therapy. This is a potent antifungal to which resistance has not been
shown to develop. It is inexpensive and is non-toxic enough to have been used in human patients with mastoiditis and corneal infections.

References


