Case Report: Syringeal Aspergillosis in a Grey Parrot (*Psittacus erithacus erithacus*)

Bob Doneley BVSc FACVSc (Avian Medicine)

West Toowoomba Veterinary Surgery, 194 West Street, Toowoomba QLD 4350

Abbreviations

SID – once daily
BID – twice daily
TID – three times daily
IM – intramuscular
PO – orally
PCV – Packed Cell Volume

Introduction

Aspergillus spp are ubiquitous environmental fungi found world-wide, widely distributed in the environment, growing readily in bird faeces and warm, moist environments, and in substrates such as wood shavings, corn cob bedding, and seed hulls. *A fumigatus* is the species most commonly associated with birds, although *A flavus*, *A glaucus*, *A niger*, *A terreus* and *A nidulans* have also been reported.[1]

Aspergillus is an opportunistic pathogen, often associated with disesidase in immuno-compromised individuals. Several species appear to be particularly susceptible to infection; amongst the psittacids, the Grey Parrot (*Psittacus erithacus erithacus*) appears to be prominent amongst reported cases (author's observations).

Infection can occur in the skin, the respiratory tract, and the digestive tract, although haematogenous spread can blur these distinctions and lead to disease in other organ systems including muscles, bone and the nervous system. Respiratory infection, the most common presentation in birds, can localise in the sinuses, the trachea, the lungs or the air sacs. Acute respiratory distress can occur when an infection localises in syrinx, where the trachea bifurcates into the bronchi.[1]

Treatment of aspergillosis is often frustrating, especially when an individual is acutely compromised. This paper reports a successful treatment of an Aspergillus granuloma in the syrinx of a Grey Parrot (*P erithacus erithacus*).

Case Report

Max, an 8 year-old male Grey Parrot (*P erithacus erithacus*) was presented for an unusual respiratory noise noted that morning by the owner. The bird was housed indoors with another Grey Parrot, a pair of Eclectus Parrots (*Eclectus roratus polychloros*) an Alexandrine Parrot *(Psittacula eupatoria)* and 2 cockatiels *(Nymphicus hollandicus)*, all in separate cages in the same room. Its daily diet consisted of a formulated diet (Roudybush®), fruit (apple, grape, and passionfruit), vegetables (peas, corn and carrot), spouted seed and 1 almond nut. It was handled daily by the owners and was tame and easily managed.

On examination the bird weighed 488g, and was in good body condition. At rest it displayed no evidence of respiratory disease - there was no mouth breathing, increased sternal lift or respiratory noise. However, while been examined it exhibited moist inspiratory rales and a mildly increased respiratory effort. On auscultation moist rales were readily discernible. Haematology performed at this time revealed a mild increase in his white cell count (PCV 46%, estimated white cell count 21.75 x 10^9/L; heterophils 86%, lymphocytes 12%, monocytes 2%, cellular morphology normal).

The bird was admitted and started on piperacillin-tazobactam (Tazocin®, Wyeth: 100mg/kg IM BID). The respiratory noise and increased respiratory effort worsened over the next 24 hours, although it was not noticeable when the bird was left undisturbed. Itraconazole (Sporonox®, Janssen Cilag) was begun at 2.5mg/kg BID PO.

Forty-eight hours after presentation the bird was anaesthetized (mask induction with isoflurane), radiographed and examined endoscopically. Radiographs suggested air saculitis, but coelioscopy showed no lesions in the thoracic or abdominal air sacs. Tracheoscopy revealed a large white, glistening granuloma occluding approximately 85% of the tracheal lumen at the level of the syrinx. Given the high incidence of Aspergillosis in this species, a tentative diagnosis of a syringeal Aspergillus granuloma was made. Cytology of an aspirate, showing branching fungal hyphae, confirmed this diagnosis.

An air sac catheter was placed in the left caudal thoracic air sac and sutured in place. Treatment at this time was piperacillin-tazobactam 100mg/kg IM BID; itraconazole 2.5mg/kg PO BID, nebulisation with Amphotericin B (Fungizone®, Bristol-Myers, Squib Australia) and acetylcysteine (Mucomyst®, Bristol-Myers, Squib Australia) TID and Amphotericin B 1mg/kg diluted in saline and injected intra-tracheally SID. Several unsuccessful attempts were made endoscopically on two alternate days to debride the granuloma; the resultant tracheitis lead to the addition of meloxicam (Metacam®, Boehringer 0.3mg/kg PO BID) to the treatment regimen.

Throughout this treatment the bird remained alert and retained its appetite. There was an approximately 10% weight loss. Respiratory noises and effort were only noticed when it was disturbed. The air sac catheter remained patent but was replaced after 5 days, this time in the right caudal thoracic air sac. Concerns about the bird's psychological status led to its discharge after 7 days to be treated on an out-patient basis. The bird was examined once daily to ensure patency of the air sac catheter, monitor weight and give the intra-tracheal Amphotericin B.

Nine days after commencing this treat regimen the owner reported that the previous night the bird had developed marked respiratory distress and increased noise. It then appeared to 'cough' something up, and immediately afterwards the bird's respiratory effort returned to normal and the noise abated. Tracheal endoscopy revealed that the syringeal granuloma had all but disappeared, although traces of it could be seen in one bronchus. The air sac catheter was left in place; 2 days later it was capped and 24 hours later, with no evidence of dyspnoea, it was removed.

The bird was then discharged, with the owner treating at home with nebulising (as above) BID, voriconazole (Vfend®, Pfizer: 15mg/kg PO BID) and meloxicam 0.3mg/kg PO BID. Three weeks later the bird was presented for re-evaluation. No problems had been noted and the bird was accepting the medication well. Haematology at this time showed a normal PCV (43%) and white cell count (8.5 x 10^9/L), although a monocytosis was apparent (heterophils 54%, lymphocytes 38%, monocytes 8%). Biochemistry showed no evidence of renal or hepatic dysfunction. Tracheal endoscopy showed no evidence of the granuloma, although the syringeal membranes appeared slightly oedematous. Whole body radiographs showed moderate air saculitis.

At the time of writing the bird remains clinically normal. It is still been nebulised with Amphotericin B once daily and receives voriconazole twice daily. It is planned to discontinue the nebulisation in the near future, but to continue the voriconazole for at least 6 months. Monthly rechecks are scheduled for 12 months.

Discussion

Aspergillosis is a non-contagious opportunistic infection caused by members of the fungal genus *Aspergillus*. These fungi are widespread in the environment, with avian exposure occurring frequently and regularly. It is unclear why infection develops in some individuals. Healthy birds exposed to high concentrations of fungal spores can develop disease, as can immuno-compromised individuals exposed to lower concentrations. Some species of birds e.g. the Grey Parrot, the Pionus Parrot (*Pionus* spp), ostriches (*Struthio camelus*), penguins (*Sphenisciformes* spp), waterfowl, and many raptors appear to be particularly prone to infection and disease.[1]

The most common site for infection in birds is the respiratory tract, following the inhalation of high concentrations of spores. The infection may develop anywhere along the respiratory tract, from the sinuses to the air sacs. Localised invasion and haematogenous dissemination can see the infection developing in other organs including the muscles, bones and CNS. Both acute and chronic forms of disease are recognised; acute infection, with miliary abscess formation in the parenchyma of the lung, is almost invariably fatal.[1] More chronic infections (in the sinuses, trachea and air sacs) are treatable if diagnosed early and treated aggressively.

Ante-mortem diagnosis can be difficult. As with many clinical conditions, the combination of a detailed history and thorough physical examination, augmented by radiology, haematology and endoscopy can lead the clinician to a tentative diagnosis of aspergillosis. Serological tests may be misleading and should not be used in isolation, especially at an individual level.[1] In this bird the initial haematology was misleading, with nothing to suggest a chronic granulomatous disease was present. Whether this was due to the location and nature of the lesion, or to laboratory error, remains uncertain. Radiology was suggestive of air sacculitis, but endoscopy and cytology were the principal means of achieving a diagnosis.

The objectives in treating this bird were: to relieve the tracheal obstruction by removing the granuloma; to provide an alternate means for the bird to breathe (via an air sac catheter) until the obstruction was cleared; and to prevent recurrence by clearing the body of any remaining fungal elements.

Initial attempts were made to manually debride the granuloma endoscopically; these attempts were unsuccessful due to the location of the lesion. Iatrogenic tracheitis precluded further attempts and necessitated the use of meloxicam as an anti-inflammatory agent. A tracheotomy was contemplated but was decided against due to the risk of stricture formation and the difficulty in achieving adequate access. It appears that early mycotic granulomas, before becoming organised and fibrotic, may absorb moisture and 'dissolve' (Brian Speer, personal communication). Intra-tracheal injections of diluted Amphotericin B, combined with nebulisation, were employed to not only deliver therapeutic concentrations of an anti-fungal drug at the infection site, but also to increase the humidity around the granuloma in an attempt to dissolve it. The episode of increasing dyspnoea followed by the bird 'coughing' may have been due to the granuloma swelling prior to dissolution. This reaction has been seen by other clinicians (Speer, personal communication) and, while alarming to the observer, should be survivable as long as the air sac catheter is patent and the granuloma does not extend extensively into both bronchi.

The unique anatomy and physiology of the avian respiratory tract makes placement of an air sac catheter a life-saving technique in birds with tracheal obstructions. Although usually thought to remain effective for only 3-4 days, both catheters employed in this bird were left in place for 5 days; neither was occluded when removed. Certainly, if the catheter was not patent at the moment of granuloma dissolution, the outcome of this case would almost certainly have been fatal. The subsequent air sacculitis around the catheter site has not proven to be detrimental to the bird.

Eliminating fungal elements from the bird's body required the use of systemic and aerosolised antifungal drugs. Amphotericin B is an amphoteric poloyene macrolide anti-fungal agent; it is fungicidal to a wide range of fungi including *Aspergillus*, *Candida*, *Blastomyces*, *Coccidioides*, *Histoplasma*, *Sporothrix* and *Mucor*

spp.[1] It has been used extensively in birds and may be administered intra-tracheally, intravenously, through sinus irrigation and by nebulisation. Its potential for nephrotoxicity limits the duration of parenteral treatment times, but poor absorption from the gastrointestinal and respiratory tracts allows treatment by these routes with minimal complications. It is tissue irritant and must be diluted to minimise iatrogenic inflammation.

Itraconazole is widely used in the treatment of fungal infections. It has greater efficacy than ketoconazole or fluconazole against Aspergillus, and is potentially less toxic than Amphotericin B. Given orally, it takes 5 days of twice daily dosing to achieve therapeutic tissue levels which can then be maintained by once daily dosing. It is eliminated by hepatic metabolism, but Grey Parrots are reported to be sensitive to this drug; consequently, lower doses (2.5-5mg/kg) are recommended in this species.[1]

Concern about the long-term use of itraconazole in this patient led to the use of voriconazole as a replacement therapeutic. Voriconazole is a relatively new antifungal medication in veterinary medicine. A triazole antifungal, it exhibits potent *in vivo* and *in vitro* activity against many fungi including Aspergillus. Flammer (2006)[2] suggests that a dose of 18mg/kg PO will achieve therapeutic tissue levels in Grey Parrots with no observable side-effects. Schmidt et al (2006)[3] found that 12.5mg/kg PO BID achieved therapeutic tissue levels in falcons. Accordingly, this patient was placed on voriconazole at 15mg/kg PO BID, with no adverse effects noted at the time of writing.

Syringeal granulomas have long carried a guarded to poor prognosis. However, early diagnosis and aggressive treatment using appropriate medications can change this bleak outcome. Speer (personal communication) reports that, if diagnosed and treated aggressively, 76% of Grey Parrots with syringeal granulomas can survive this disease and recover fully. The use of an air sac catheter is a key element of treatment; without it, affected birds would most likely suffocate before therapeutic or surgical intervention could relieve the obstruction.

References

1. Dahlhausen RD. Implications of mycoses in clinical disorders, in Harrison GJ, Lightfoot TL (eds) Clinical Avian Medicine, Vol II. Spix Publishing, Fl; 2006: 691-704.
2. Flammer K. Antifungal drug update, in Proc Annu Conf Assoc Avian Vet 2007: 3-5
3. Schmidt V, Demiraj F, Di Somma A, Bailey T, Ungemach FR, Krautwald-Junghanns M-E . Plasma concentrations of voriconazole in falcons, in Proc Annu Conf Assoc Avian Vet 2007: 323-326