Aspergillus otitis in small animals – a retrospective study of 17 cases

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Background – Aspergillus spp. are saprophytic opportunistic fungal organisms and are a common cause of oto-mycosis in humans. Although there have been case reports of Aspergillus otitis externa in dogs, to the best of the authors’ knowledge, this is the first retrospective case series describing Aspergillus otitis in dogs and cats.

Objective – To characterize signalment, putative risk factors, treatments and outcomes of a case series of dogs and cats with Aspergillus otitis.

Animals – Eight dogs and nine cats diagnosed with Aspergillus otitis.

Methods – A retrospective review of medical records from 1989 to 2014 identified animals diagnosed with Aspergillus otitis based on culture.

Results – All dogs weighed greater than 23 kg. The most common putative risk factors identified in this study were concurrent diseases, therapy causing immunosuppression or a history of an otic foreign body. Aspergillus otitis was unilateral in all study dogs and most cats. Concurrent otitis media was confirmed in three dogs and one cat, and suspected in two additional cats. Aspergillus fumigatus was the most common isolate overall and was the dominant isolate in cats. Aspergillus niger and A. terreus were more commonly isolated from dogs. Animals received various topical and systemic antifungal medications; however, otic lavage under anesthesia and/or surgical intervention increased the likelihood of resolution of the fungal infection.

Conclusion – Aspergillus otitis is uncommon, typically seen as unilateral otitis externa in cats and larger breed dogs with possible risk factors that include immunosuppression and otic foreign bodies; previous antibiotic usage was common.

Introduction

Otitis externa – inflammation of the external ear canal and sometimes the pinna – is a common ailment in small animals, occurring in 4.6% of the canine case population in one hospital based study.1 Otomycosis, a fungal infection of the ear, was diagnosed in 26.7% of those cases.1 The most common organism to cause otomycosis in dogs is Malassezia pachydermatis.1–4

In humans otomycosis is diagnosed most commonly in warm, humid climates.5,6 Predisposing factors include immune compromise, cleansing the ear with sticks/swabs, prior otology procedures, swimming, use of non-sterile oil in the ear, wearing head coverings, pruritus elsewhere on the body and the use of topical antibiotics or steroids.6–11 Aspergillus spp. and Candida spp. are the most common fungi implicated in otomycosis in people.6,7,10–15

Aspergillus spp. are saprophytic environmental fungi that occasionally cause opportunistic infections in small animals. In dog and cats sino-nasal and sino-orbital aspergillosis are the most common manifestations.16–20 Less commonly, and particularly in immunocompromised individuals or German shepherd dogs, the fungal organism may cause disseminated disease.21 Dissemination is most commonly associated with A. terreus; whereas the sino-nasal form is more commonly associated with A. fumigatus.18,21,22

Two case reports of dogs with Aspergillus otomycomosis have been published describing treatment and outcome.23,24 To the best of the authors’ knowledge there are no studies that have evaluated Aspergillus otitis in a series of small animals. This retrospective study evaluated the clinical presentation, possible risk factors and outcomes of Aspergillus otitis in dogs and cats seen at a university teaching hospital over a 25 year period.

Materials and methods

The University of California, Davis, veterinary medical teaching hospital records system was searched for cases presented between 1 June 1989 and 1 June 2014 using the words “Aspergillus otitis”. The inclusion criterion was a clinical diagnosis of Aspergillus otitis (otitis externa and/or media), confirmed by identification of the organism on culture from samples obtained from the ear canal and/or identifica-
tion of the organism on histopathology. The study population included both cats and dogs, although separate descriptive statistics were done for each species. The signalment, age of onset, weight of the animal, extent of disease (otitis externa versus otitis media; unilateral versus bilateral), description of the ears on physical and otoscopic examination, and concurrent/predisposing diseases were recorded for each case. Clinical data including results of cytological examination of ear canal exudate, bacterial and fungal cultures, histopathology, treatment protocols, response to therapy and time to resolution (if available) were also recorded. Resolution was defined as absence of inflammation and exudate within the ear on physical examination, and negative cytological exam and/or fungal culture of swabs obtained from the external canal.

Results
The initial search identified 33 cases, of which 17 met the criteria for inclusion in the study. There were eight dogs and nine cats included in the study.

Canine cases
There were four spayed female and four castrated male dogs. All dogs in this sample represented large breeds. There were two golden retrievers, two Border collies, and one each of the following: Labrador retriever, Vizsla, Doberman and Rhodesian ridgeback. The mean body weight of these dogs was 34.7 kg (range 23.8–48.6 kg). The average age at the time of diagnosis was 6.75 years (range 3–10 yr) and the mean duration of clinical signs prior to diagnosis was 2.5 months (range 0.3–6 month).

History and clinical findings in canine cases
All dogs had a unilateral otitis externa and three were diagnosed with otitis media of the affected ear via either computed tomography (two cases) or otoscopic observation of a ruptured tympanum (one case). Five of eight dogs had undergone computed tomographic examination. Potential risk factors included grass awn foreign body (three cases), concurrent immunosuppression (two cases; one due to chemotherapy for neoplasia and one that had received glucocorticoids for immune-mediated thrombocytopenia), a mass in the external canal (one case) and ear lavage with aural haematoma repair (one case). One dog had no identifiable risk factors. Five of eight dogs had been treated with systemic antibacterials prior to diagnosis and four dogs had received topical otic preparations containing antibacterial agents. Three dogs had received a combination of topical and systemic antibacterial therapy.

Four dogs had results of cytological evaluation of otic exudate available for review. Only two of the four dogs had observable fungal hyphae on cytology (Table 1). All dogs had Aspergillus species isolated on samples of otic exudate submitted for either bacterial cultures and/or fungal cultures, and some reported mixed populations of micro-organisms (Table 1). Several different species of Aspergillus were cultured from either the bacterial or the fungal culture submissions: three each were A. niger and A. terreus, and one each was A. fumigatus and A. awamori. No dog had more than one species of Aspergillus cultured. One dog underwent ventral bulla osteotomy and biopsy of the otic canal; histopathology revealed fungal hyphae and these were confirmed by fungal culture to represent A. fumigatus. A second dog was negative for fungal organisms on histopathology of a biopsied mass from the tympanic bulla.

Table 1. Laboratory data and physical examination at time of diagnosis of Aspergillus ear infection – canine cases

<table>
<thead>
<tr>
<th>Case number</th>
<th>Physical examination</th>
<th>Otoscopic examination</th>
<th>Cytological results</th>
<th>Bacterial culture</th>
<th>Fungal culture</th>
<th>Histopathology</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dog 1</td>
<td>Purulent exudate</td>
<td>n.a.</td>
<td>n.a.</td>
<td>Aspergillus niger</td>
<td>n.a.</td>
<td>Aspergillus niger</td>
</tr>
<tr>
<td>Dog 2</td>
<td>Brown ceruminous debris</td>
<td>Yellow fluid</td>
<td>Hyphae, yeast*, inflammatory cells</td>
<td>No growth</td>
<td>Aspergillus fumigatus</td>
<td>Fungal hyphae</td>
</tr>
<tr>
<td>Dog 3</td>
<td>Brown ceruminous debris and purulent exudate</td>
<td>Yellow fluid, ruptured tympanic membrane, stenosis, ulceration</td>
<td>n.a.</td>
<td>Staphylococcus pseudintermedius</td>
<td>Aspergillus terreus</td>
<td></td>
</tr>
<tr>
<td>Dog 4</td>
<td>Brown ceruminous debris</td>
<td>White plaques, ruptured tympanic membrane, stenosis</td>
<td>Inflammatory cells, cocci bacteria</td>
<td>Aspergillus fumigatus</td>
<td>Fungal hyphae</td>
<td></td>
</tr>
<tr>
<td>Dog 5</td>
<td>Brown ceruminous debris and purulent exudate</td>
<td>Yellow fluid, mass</td>
<td>n.a.</td>
<td>Aspergillus awamori</td>
<td>n.a.</td>
<td></td>
</tr>
<tr>
<td>Dog 7</td>
<td>Brown ceruminous debris</td>
<td>Stenosis</td>
<td>RBC, neutrophils, mixed bacteria</td>
<td>Aspergillus terreus</td>
<td>Corynebacterium sp. and Enterococcus sp.</td>
<td>Aspergillus terreus</td>
</tr>
<tr>
<td>Dog 8</td>
<td>Brown ceruminous debris and purulent exudate, ulceration, mass</td>
<td>n.a.</td>
<td>RBC, neutrophils, mixed bacteria</td>
<td>Aspergillus terreus</td>
<td>Corynebacterium sp. and Enterococcus sp.</td>
<td>Aspergillus terreus</td>
</tr>
</tbody>
</table>

RBC, red blood cells.

*Most likely Malassezia spp.
ment (343 d in duration) and one was lost to follow-up. Three of these six dogs underwent otic lavage under general anaesthesia and two had ventral bulla osteotomies.

**Feline cases**

There were seven spayed female and two castrated male cats. Six domestic shorthair, one domestic longhair, one domestic medium hair and one Persian cross-bred cat were represented. The mean body weight was 6.5 kg (range 3.6–7.8 kg). The mean age at the time of diagnosis was 9.1 years (range 2–13 yr), and the mean duration of clinical signs before diagnosis was 9.9 months (range 1–36 month). Four cats lived indoors only and five cats were also allowed outside.

**History and clinical findings of feline cases**

Two cats had bilateral otitis externa and seven cats had unilateral otitis externa. One cat was confirmed to have otitis media on computed tomography and two additional cats were suspected to have otitis media. Potential risk factors included diabetes mellitus (two cats), immunosuppressive therapy (one cat) and allergic dermatitis (two cats). Three of nine cats had been tested for feline leukaemia virus and feline immunodeficiency virus, and all were negative. Eight of nine cats had been treated with systemic antibacterial agents prior to diagnosis and five had received topical otic preparations containing antibacterials. Five cats had received a combination of topical and systemic antibacterial therapy.

Seventeen of nine cats had cytological evaluation of otic exudate samples recorded. Only two had visible fungal hyphae on cytology evaluation (Table 3). Results of bacterial and fungal culture are given in Table 1. Several different species of *Aspergillus* were isolated from either the bacterial or fungal cultures. Five isolates were identified as *A. fumigatus*, three as only *Aspergillus* sp., and one each as *A. niger* and *A. flavus*. One cat had both *A. flavus* and *A. niger* isolated. One cat underwent biopsy of nodules noted in the external otic canal; histopathology revealed intralesional mycelia which were confirmed by fungal culture to represent *A. fumigatus*.

**Treatments and outcomes of cats**

Eight cats were treated with topical medications following diagnosis of otitis and eight were treated with systemic drugs (Table 4). No cat underwent surgical treatment (beyond a tissue biopsy) or lavage under anaesthesia. The otitis in five of nine cats resolved with a mean time of 94 days (range 38–196 d). One of these five cats relapsed 2 months after treatment was discontinued and the otitis could not be resolved after 293 days at which time the cat was lost to follow up. The cat which received immunosuppressive therapy for control of an immune-mediated disease had not resolved after 493 days and developed metastatic neoplasia. Two cats were lost to follow-up, one immediately following initiation of treatment and the other after 149 days. One cat was still undergoing treatment at the time of writing (370 d).

**Discussion**

We have identified only 17 cases of *Aspergillus* otitis from a hospital population over a 25 year period. The majority of cases were unilateral, consistent with previously reported cases of *Aspergillus* otitis in dogs23,24 and humans.13–15 In humans bilateral otomycosis is more commonly seen in immunocompromised patients.12 In the present study two cats presented with bilateral
disease. One was being profoundly immunosuppressed for immune-mediated skin disease and thrombocytopenia, but the other had no identifiable cause for immune suppression. None of the dogs presented with bilateral otitis.

Fungal otitis media has been reported in humans, although less commonly than fungal otitis externa. In our study population otitis media was identified on computed tomographic findings or observation of a ruptured tympanic membrane in three dogs and one cat, and two cats were suspected of having otitis media. The confirmed cases had *Aspergillus* cultured from samples collected from the middle ear (obtained via ventral bulla osteotomy in two dogs, aspiration of fluid from middle ear).
ear in one dog with a ruptured tympanic membrane and myringotomy in one cat). One cat and one dog with Aspergillus otitis media were immunocompromised which could explain the more invasive nature of the infection. Another dog with otitis media had a prior grass awn foreign body found in the ear, which may have penetrated the tympanic membrane causing the otitis media. No potential risk factors were identified in one cat and one dog with otitis media. All dogs in the current study represented large breeds, but there were no obvious breed predilections. However, the sample size was very small and not compared to the general hospital population. Interestingly, no German shepherd dogs were involved. This breed is predisposed to the development of systemic aspergillosis.

When all cases are considered, the most common putative risk factors were immunosuppression (endogenous or iatrogenic; 3 of 8 dogs and 3 of 9 cats) and grass awn foreign bodies (3 of 9 dogs). Otic foreign bodies have not been specifically identified as a predisposing cause of otomycosis in humans, but the use of ear sticks for otic cleansing has been identified as a predisposing cause in people. This is presumably because the Aspergillus sp. is introduced into the ear by the foreign body, which may also cause concurrent physical trauma to the ear at the time of its entry. Three different species of Aspergillus were isolated from the three dogs with grass awn foreign bodies. Unfortunately, due to the small sample size it is not possible to determine if there was a statistically significant association between these potential risk factors and development of Aspergillus otitis.

In humans there has been some suggestion that fluoroquinolones contribute to the development of otomycosis. Antimicrobial use prior to the diagnosis of otomycosis was very common among the cases in our study, and three dogs and seven cats had previously been treated with a topical and/or systemic fluoroquinolone prior to diagnosis with Aspergillus otitis. However, many other antibacterial classes were also represented, so it is therefore not possible to determine if fluoroquinolone exposure specifically increased the risk of Aspergillus otitis.

The species most commonly isolated in this case population was A. fumigatus (five cats and one dog). Aspergillus fumigatus is also the most common species involved in feline and canine rhinosinusitis. In dogs A. niger and A. terreus were each isolated from three cases. Aspergillus niger has previously been documented as a cause of otitis externa in dogs, and Aspergillus otomycosis in humans is most commonly caused by A. fumigatus and A. niger. In humans with invasive aspergillosis, A. terreus is associated with a poorer prognosis when compared to other species of Aspergillus. Aspergillus terreus is also frequently associated with resistance to amphotericin B, but not azole antifungal medications. In two of three dogs from which A. terreus was isolated, the otomycosis did not resolve in one case and a total ear canal ablation and bullae osteotomy was required in the other. The third dog was lost to follow-up. Based on this case series, dogs may have a better prognosis; 75% of dogs were treated successfully compared to only 56% of cats. This may be due to the fact that more dogs were treated with otic lavages under anaesthesia or surgical removal of infected material via a total ear canal ablation and/or ventral bulla osteotomy. None of the cats received these treatments. In dogs with sino-nasal aspergillosis, meticulous rhinoscopic or surgical debridement is recommended before infusing topical antifungal medication into the nasal cavity and sinuses. Concurrent systemic antifungal medication administration is also recommended. In humans with otomycosis, thorough mechanical debridement of fungal elements is recommended prior to instituting topical therapy.

Clotrimazole is often recommended to manage otomycosis in humans because of its broad spectrum of activity and lack of ototoxicity. Resistance of Aspergillus spp. to antifungal agents has been reported. In this study all animals that received systemic itraconazole had the infection resolved, whereas only 75% of those treated with systemic fluconazole resolved. This may reflect the fact that Aspergillus spp. are commonly resistant to fluconazole, or could be related to other case specific factors. Posaconazole and voriconazole may prove to be useful for cases of Aspergillus otomycosis nonresponsive to other antifungal medications. Voriconazole has been used in cats with systemic fungal disease but has been associated with renal and neurological toxicity. These adverse effects were not seen in a dog treated with voriconazole. Voriconazole has also been used with fewer adverse effects in cats.

Major limitations of this study include its retrospective nature and the small sample size. Case investigations and management were not consistent due to the retrospective design and the rarity of this infection makes it difficult to accumulate a sample size large enough to determine the statistical significance of putative risk factors. It is also important to note that Aspergillus spp. are environmental saprophytes and growth on culture does not prove causation. Aspergillus spp. is the most common cause of “false positive” fungal cultures. Identification of intraleisional hyphae by histopathology provides the best evidence of pathological effect and visualization of hyphae on cytological exam is supportive.

In summary, this case series suggests that Aspergillus spp. are uncommon causes of otitis externa with or without concurrent otitis media in small animals, with a predisposition for unilateral disease. There may be a predisposition for large dogs, and immunosuppression and otic grass awn foreign bodies may be risk factors. Prior antibacterial therapy was very common amongst these cases, as might be expected in a referral population. Analysis of a larger group of cases will be necessary to assess whether thorough otic lavage or surgery is indicated in cases of Aspergillus otitis and whether use of systemic itraconazole provides a therapeutic advantage.

References

Résumé

Contexte – Aspergillus spp. est un organisme fongique opportuniste saprophytique, cause fréquente d’otomycose chez l’homme. Bien que des cas d’otite externe liée à Aspergillus chez le chien soient décrits, à la connaissance des auteurs, ceci est la première étude rétrospective de cas décrivant des otites à Aspergillus chez le chien et le chat.
**Aspergillus otitis in small animals**

**Objectifs** – Déterminer le signalement, les facteurs de risque, les traitements et l’évolution d’une série de cas de chiens et de chats atteints d’otite à Aspergillus.

**Sujets** – Huit chiens et neufs chats atteints d’otite aspergillaire.

**Méthodes** – Une revue rétrospective des données médicales de 1989 à 2014 ont identifiés les animaux atteints d’otite aspergillaire à la culture.

**Résultats** – Tous les chiens pesaient plus de 23 kg. Les facteurs de risque principaux identifiés dans cette étude étaient les maladies concurrentes, les traitements immunosupresseurs ou des commémoratifs d’otite à corps étranger. Une otite aspergillaire était unilatérale pour tous les chiens de l’étude et la plupart des chats. Une otite moyenne a été confirmée pour trois chiens et un chat et suspectée pour deux autres chats. Aspergillus fumigatus était fréquent et le plus fréquemment isolé chez le chat. Aspergillus niger et terreus étaient plus fréquents chez le chien. Les animaux recevaient de traitements topiques et systémiques antifongiques; cependant, un lavage auriculaire sous anesthésie et/ou intervention chirurgicale augmentaient la probabilité de résolution de l’infection fongique.

**Conclusion** – L’otite aspergillaire est rare, typiquement observée en tant qu’otite unilatérale externe chez les chats et les chiens de grande race avec des facteurs de risque qui regroupent une immunsuppression et des corps étranger auriculaires; un traitement antibiotique précédent était fréquent.

**Resumen**

**Introducción** – Aspergillus spp. son hongos saprofiticos oportunistas que son una causa común de otomícosis en humanos. Aunque se han descrito algunos casos de otitis causadas por Aspergillus en perros, a nuestro entender este es el primer estudio retrospectivo de casos descritos de otitis externa causadas por Aspergillus en perros y gatos.

**Objetivo** – caracterizar la anamnesis, factores de riesgo, tratamientos y resultados de una serie de casos de perros y gatos con otitis causada por Aspergillus.

**Animales** – ocho perros y nueve gatos diagnosticados con otitis causada por Aspergillus.

**Métodos** – una revisión retrospectiva de los historiales clínicos desde 1989 al 2014 identificados con animales diagnosticados por otitis causada por Aspergillus basado en resultados del cultivo.

**Resultados** – todos los perros pesaron más de 23 kilos. Los posibles factores de riesgo más comunes identificados en este estudio fueron enfermedades concomitantes, terapia causando inmunosupresión, o historia de un cuerpo extraño en el oído. La otitis causada por Aspergillus fue unilateral en todos los perros de este estudio y en la mayoría de los gatos. Se confirmó además otitis media en tres perros y un gato, y se sospechó en otros 2 gatos. Aspergillus fumigatus fue el aislado más frecuente en general, y fue el dominante en gatos. Aspergillus niger y Aspergillus terreus fueron aislados más comúnmente en perros. Los animales recibieron varias medicaciones tópicas sistémicas antifúngicas, sin embargo el lavado ótico bajo anestesia y/o la intervención quirúrgica incrementaron la posibilidad de resolución de la infección fúngica.

**Conclusion** – la otitis causada por Aspergillus es poco frecuente, típicamente observada como una otitis unilateral externa en gatos y en perros de raza grande con posibles factores de riesgo incluyendo inmunosupresión y cuerpos extraños en el oído; terapia previa con antibióticos fue también común.

**Zusammenfassung**

**Hintergrund** – Aspergillus spp. sind saprophytische opportunistische Organismen, die eine häufige Ursache für eine Ototymyose beim Menschen darstellen. Obwohl es Fallberichte über Aspergillus Otitis externa bei Hunden gibt, handelt es sich hierbei nach bestem Wissen der Autoren um eine erste retrospektive Fallserie, die Aspergillus Otitiden bei Hunden und Katzen beschreibt.


**Tiere** – Acht Hunde und neun Katzen mit der Diagnose einer Aspergillus Otitis.


**Schlussfolgerung** – Eine Aspergillus Otitis kommt selten vor, tritt typischerweise als unilaterale Otitis externa bei Katzen und Hunden größerer Rassen mit möglichen Risikofaktoren, wie Immunsuppression und einem Fremdkörper im Ohr auf; vorherige Verwendung von Antibiotika war häufig.
要約
背景 — Aspergillus sppは日和見腐敗性真菌で、ヒトにおいて耳真菌症の一般的な原因の一つである。イヌにおいてAspergillus外耳炎の症例報告はあるものの、筆者の知るところによれば、これはイヌとネコのアスペルギルス外耳炎を解説し初めての回顧的な症例である。
目的 — 連のAspergillus耳炎のイヌとネコの症例の症状、推定されるリスクファクター、治療法および治療結果を特徴づけることである。
供与動物 — Aspergillus耳炎の8頭のイヌおよび9頭のネコ
方法 — 1989年から2014年に培養検査でAspergillus耳炎と診断された動物の医療記録の回顧的再検討
結果 — すべてのイヌの体重は23kg以上であった。この研究で特定された、最も一般的な推定されるリスクファクターは併発疾患、免疫抑制を生じる治療、あるいは耳述内異物の履歴であった。Aspergillus耳炎は調査したすべてのイヌとほとんどのネコにおいて片側性であった。中耳炎の併発が3頭のイヌと1頭のネコで確認され、さらに2頭のネコで疑われた。Aspergillus fumigatusが全体で最も多く分離され、ネコでは大部分を占めていた。Aspergillus nigerとA. terreusがイヌで多く分離された。動物は様々な外用療法や全身性抗真菌療法を受けたが、麻酔下での耳洗浄や、あるいは外科的な介在により真菌感染症の治癒の可能性が増加した。
結論 — Aspergillus耳炎は一般的ではなく、免疫抑制や耳述内異物を含むリスクファクターを持つネコおよび大型犬種のイヌにおいて、典型的には片側性の外耳炎が認められ、過去の抗菌剤使用が共通していた。

摘要
背景 — 曲菌属は腐生条件致病性真菌性微生物、常可引起人耳真菌病。尽管有过多例犬感染曲霉菌性外耳炎的病例报告，但就作者所知，这是第一篇回顾性描述犬猫曲霉菌性外耳炎的报告。
目的 — 描述犬猫曲霉菌性外耳炎病征、推测的风险因素、治疗及其效果。
动物 — 诊断为曲霉菌性耳炎的八只犬和九只猫。
方法 — 回顾分析1989年到2014年通过真菌培养诊断为曲霉菌性耳炎的病例。
结果 — 所有犬体重均大于23公斤。该研究中常见的致病因素为并发疾病，治疗产生的免疫抑制或耳部异物病史。该研究中所有犬和大部分猫曲霉菌性耳炎是单独的。三只犬、一只猫并发了中耳炎，另两只猫疑为中耳炎。黑曲霉和土曲霉最常感染犬，动物接受了多种外耳和全身性抗真菌药物;然而，麻醉下耳道灌洗和/或外科的介入，增加了真菌感染治愈的几率。
结果 — 曲菌性耳炎不常见，特点为犬和猫的单侧外耳炎，可能增加感染的因素有免疫抑制和耳道异物; 之前通常有抗生素治疗史。

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