Cryptococcosis is a systemic fungal infection that affects both humans and animals worldwide, with many reported infections belonging to the Cryptococcus neoformans species and Cryptococcus gattii species complexes. Cryptococcus isolates are further divided into 9 or more molecular types. The more detailed taxonomy is complicated and controversial, and we elect to retain the older, more traditional nomenclature. Of the species, C. neoformans

**OBJECTIVE**
To describe the CT findings of Australian dogs and cats with nasal cryptococcosis over a 12-year period.

**ANIMALS**
12 dogs and 9 cats diagnosed with nasal cryptococcosis from 2008 through 2020.

**METHODS**
CT findings were compared among enrolled cases from Australian veterinary referral centers. Disease severity was compared between a subset of patients with cryptococcal speciation performed (n = 6 dogs; n = 3 cats) and geographic domicile.

**RESULTS**
Dogs demonstrated diffuse disease affecting numerous nasal regions and sinuses. Cats displayed more focal nasal and nasopharyngeal disease. Dogs were more likely to have a nasal mass, whereas cats were more likely to have a nasopharyngeal mass. Cribriform plate lysis was common in dogs but not observed in cats. Sinonasal osteolysis was a common feature in both species. Mandibular lymph nodes were commonly enlarged in dogs, whereas in cats, the retropharyngeal lymph nodes were more likely enlarged. There was no obvious difference in disease severity or lesion distribution in relation to the causal species of Cryptococcus, although to determine if this finding is robust, an appropriately powered prospective study is warranted.

**CLINICAL RELEVANCE**
There are numerous studies describing the clinical features, treatment, and outcomes of dogs and cats with cryptococcosis. To the best of our knowledge, there is only 1 previous study describing the CT features of nasal cryptococcosis, undertaken in one part of North America. Our study describes the CT features of nasal Cryptococcus sp in an Australian canine and feline cohort, adding new pertinent observations while reinforcing reported radiological observations.

**Keywords:** cryptococcosis, CT, Australian, nasal, mycosis

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Cryptococcus sp. The authors hypothesized that if there was a difference in lesion severity between populations. The secondary aim was to determine if disease presentation differs between geographical areas – especially between Western Australia, where C gattii molecular biotypes VGI and II account for up to 55% and 50% of feline and canine infections, respectively. C gattii VGIa and VGIb predominate in the Pacific Northwest of the United States and Canada, whereas VGGII is prevalent in California, especially in cats.

Inhalation of basidiospores or desiccated yeast cells from the environment allows colonization of the nasal cavity and subsequent mucosal invasion; this is why the nasal passages and sinuses are thought to be a primary site of cryptococcal infection in most animals. In cats, cryptococcal rhinitis and upper respiratory tract (URT) signs (nasal discharge, sneezing, stridor/stertor) are commonly seen, with infections typically localizing for a protracted period before invading surrounding structures. Although rare, pulmonary involvement can occasionally occur. URT signs are also seen in dogs but can be clinically subtle or even inapparent. Neurologic involvement occurs earlier in the clinical course in dogs compared to cats, following local invasion and lysis of the cribriform plate or ventral wall of the frontal sinus, resulting in signs of meningoencephalitis. Other affected body systems include the skin, optic nerve(s), orbit(s), and regional lymph nodes (LN). Diagnosis is based on the presence of consistent history and clinical signs, serological antigen tests (latex cryptococcal antigen agglutination test [LCAT] and lateral flow assays [LFA]), and identification of the organism in cytological or histological preparations. Definitive diagnosis relies on positive fungal culture and/or identification of organisms on cytology smears, or histopathologic sections (or combinations thereof).

Cross-sectional imaging, particularly CT, is an important diagnostic tool for investigating patients with URT signs, and for visualization of the nasal cavity and neurocranium. It is useful for identifying masses. Although rare, pulmonary involvement can occasionally occur. URT signs are also seen in dogs but can be clinically subtle or even inapparent. Neurologic involvement occurs earlier in the clinical course in dogs compared to cats, following local invasion and lysis of the cribriform plate or ventral wall of the frontal sinus, resulting in signs of meningoencephalitis. Other affected body systems include the skin, optic nerve(s), orbit(s), and regional lymph nodes (LN).

CT images of the head were obtained with different helical CT scanners depending on the practice (Somatom Scope, Go UP, Sensation 64, Emotions Duo, Emotions 16; Siemens; GE Lightspeed Qx, Lightspeed, Brightspeed; GE HealthCare Technologies Inc). Precontrast and postcontrast studies were performed following the administration of iohexol (1 to 2 mL/kg, IV).

Images were assessed using bone (window width, 1,500; window level, 300) and soft tissue (window width, 400; window level, 60) algorithms and their associated windowing. Features were divided into different categories, including soft tissue or fluid attenuation, within nasal regions and involvement of surrounding structures, including turbinates, the choanae and nasopharynx (NP), and frontal and sphenoidal sinuses. To describe the extent of disease, the regions within the nasal cavity were divided into 3 areas in dorsal (dorsal, middle, and ventral) and axial (rostral, middle, and caudal) planes. Structural changes were described as unilateral or bilateral, and whether an entire discrete nasal region was involved. Disease severity was
determined based on the extent of disease extension within nasal regions and/or sinuses (Table 1). Other affected regions were categorized as cutaneous/subcutaneous and retrobulbar/orbital. The presence or absence of fluid within the tympanic bullae was recorded. Nasal and NP masses were identified based on the presence of destructive concholysis and soft tissue attenuation, resulting in a mass effect. Masses were categorized as contrast enhancing or non–contrast enhancing. If there was ambiguity in differentiating a non–contrast-enhancing mass from fluid, these cases were classified as not having a nasal or nasopharyngeal mass. Lesion size was measured but not included in the results as lesions were often constrained by anatomic cavities and related to the size and anatomical variation of the animal. Osteolysis of the cribiform plate and sphenoidal and sinonasal bones was recorded when detected.

Mandibular and retropharyngeal LNs were described as enlarged (mild or moderate/severe) or normal in size (Table 1). Lymphadenomegaly was based on reference intervals from previous descriptive studies. LNs were defined as normal if they were ovoid, well defined, homogenous, and non–contrast enhancing and had a width less than 6 mm in cats and 10 mm in dogs (mandibular LNs) or 5 mm in cats and 10 mm in dogs (retropharyngeal LNs). Mild lymphadenomegaly indicated a 10% to 20% increase in width above reference intervals, and moderate/severe lymphadenomegaly indicated a > 20% increase in width above reference intervals. Intracranial disease extension was defined as the presence of a URT lesion with evidence of neurocranial or cribiform plate osteolysis or a contrast-enhancing lesion within the neurocranium and meningeal enhancement.

### Outcomes
Cases were categorized as either alive, dead, or euthanized (referred to as “died”) or lost to follow-up.

<table>
<thead>
<tr>
<th>CT feature</th>
<th>Location and severity of features</th>
<th>Dogs (%)</th>
<th>Cats (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Soft tissue or fluid attenuation in the nasal cavity</td>
<td>Rostral (rostral to the roots of the maxillary canine teeth)</td>
<td>10/12 (83)</td>
<td>8/9 (89)</td>
</tr>
<tr>
<td>Nasal region involvement</td>
<td>Middle (in between the maxillary and carnassial teeth)</td>
<td>5/10 (50)</td>
<td>0/8 (0)</td>
</tr>
<tr>
<td></td>
<td>Caudal (caudal to maxillary carnassial teeth)</td>
<td>5/10 (50)</td>
<td>5/8 (63)</td>
</tr>
<tr>
<td>Severity</td>
<td>Mild</td>
<td>0/10 (0)</td>
<td>4/8 (50)</td>
</tr>
<tr>
<td></td>
<td>Moderate</td>
<td>3/10 (30)</td>
<td>0/8 (0)</td>
</tr>
<tr>
<td></td>
<td>Severe</td>
<td>7/10 (70)</td>
<td>4/8 (50)</td>
</tr>
<tr>
<td>Lateralization</td>
<td>Unilateral</td>
<td>1/10 (10)</td>
<td>5/8 (63)</td>
</tr>
<tr>
<td></td>
<td>Bilateral</td>
<td>9/10 (90)</td>
<td>3/8 (37)</td>
</tr>
<tr>
<td>Soft tissue or fluid attenuation in the sinuses</td>
<td>Frontal</td>
<td>9/12 (75)</td>
<td>4/9 (44)</td>
</tr>
<tr>
<td>Individual sinus involvement</td>
<td>Sphenoidal</td>
<td>2/9 (22)</td>
<td>0/4 (0)</td>
</tr>
<tr>
<td></td>
<td>Multiple sinus involvement</td>
<td>Frontal and sphenoidal</td>
<td>5/9 (56)</td>
</tr>
<tr>
<td>Turbinate involvement</td>
<td>7/12 (58)</td>
<td>6/9 (67)</td>
<td></td>
</tr>
<tr>
<td>Choana involvement</td>
<td>4/12 (33)</td>
<td>4/9 (44)</td>
<td></td>
</tr>
<tr>
<td>NP involvement</td>
<td>3/12 (25)</td>
<td>6/9 (67)</td>
<td></td>
</tr>
<tr>
<td>NP mass</td>
<td>0/12 (0)</td>
<td>5/9 (56)</td>
<td></td>
</tr>
<tr>
<td>Disease extension</td>
<td>Cutaneous/subcutaneous tissue</td>
<td>4/12 (33)</td>
<td>1/9 (11)</td>
</tr>
<tr>
<td></td>
<td>Retrobulbar</td>
<td>4/12 (33)</td>
<td>1/9 (11)</td>
</tr>
<tr>
<td></td>
<td>Unilateral</td>
<td>0/12 (0)</td>
<td>1/9 (11)</td>
</tr>
<tr>
<td></td>
<td>Bilateral</td>
<td>1/12 (8)</td>
<td>1/9 (11)</td>
</tr>
<tr>
<td>Lymphadenomegaly</td>
<td>Mandibular</td>
<td>10/11 (91)</td>
<td>6/9 (67)</td>
</tr>
<tr>
<td>Individual lymphadenomegaly</td>
<td>Retropharyngeal</td>
<td>7/10 (70)</td>
<td>1/6 (16)</td>
</tr>
<tr>
<td></td>
<td>Mandibular and retropharyngeal</td>
<td>2/10 (20)</td>
<td>4/6 (67)</td>
</tr>
<tr>
<td>Generalized lymphadenomegaly</td>
<td>Mild</td>
<td>1/10 (10)</td>
<td>1/6 (16)</td>
</tr>
<tr>
<td></td>
<td>Moderate/severe</td>
<td>2/10 (20)</td>
<td>4/6 (67)</td>
</tr>
<tr>
<td>Nasal cavity mass</td>
<td>8/10 (80)</td>
<td>2/6 (33)</td>
<td></td>
</tr>
<tr>
<td>Contrast enhancing</td>
<td>3/12 (25)</td>
<td>1/9 (11)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>2/3 (67)</td>
<td>1/1 (100)</td>
<td></td>
</tr>
</tbody>
</table>

NP = Nasopharyngeal.

*Evidence of disease involving the nasal region in an axial plane. *Evidence of disease involving the nasal region in a dorsal plane. *Evidence of disease involving an entire individual nasal region. *Evidence of disease involving only 1 nasal region and/or sinus. *Evidence of disease involving at least 2 nasal regions and/or sinuses but not more than 3. *Evidence of disease involving more than 3 nasal regions and/or sinuses.
follow-up (LTFU) at the time of enrollment into the study. Alive cases were identified as (1) cured if they were subclinical and had a negative reciprocal LCAT titer (< 2) or (2) under treatment if they were still receiving antifungal treatment. Cases that died were divided into causes related to cryptococcosis (based on signs associated with cryptococcosis and a lack of other concurrent diseases that could contribute to mortality) or unrelated to cryptococcosis. Cases were classified as LTFU if they were not known to be dead but did not return for follow-up at the participating hospitals and referring practitioner data could not be obtained. Days to outcome was based on the last date of entry on medical records within participating hospitals or on the last date of communication with referring veterinarians or owners, with day 1 being the date of initial presentation.

**Statistical analysis**

Collected data from imaging studies were analyzed and tabulated and frequencies of occurrence (and percentages) were calculated with Excel (version 16.79.2; Microsoft Corp). SPSS Statistics (version 29, IBM Corp) was used to conduct a two-tailed Fisher-Freeman-Halton exact test to determine whether the categorical variable of disease severity differed between *C gattii* and *C neoformans* infections in culture-positive cases.

**Results**

Twelve dogs and 9 cats across 6 referral centers had head CT imaging performed and were included in this study. There were no cases from 6 of the remaining referral centers that met the inclusion criteria. Procedural protocols, including induction, general anesthetic maintenance, CT scanners used, patient positioning, and postprocedural recovery, were institution dependent.

**Dogs**

The median age at presentation was 2.5 years (range, 1.5 to 9 years), and median weight was 20.8 kg (range, 4.1 to 37.1 kg). Six of 12 (50%) dogs were spayed females, 4 of 12 (33%) were intact females, and 2 were male (1 intact; 1 neutered). Numerous breeds were represented: Staffordshire Bull Terriers (2/12) and 1 each of the following: Miniature Schnauzer, Border Collie, Maltese, Jack Russell Terrier, Poodle, Kelpie, Cocker Spaniel, Doberman Pinscher, Dalmatian, and English Pointer.

Of the 12 dogs, 5 (41%) presented with URT signs (eg, stertor, respiratory distress, or nasal discharge), 2 (6%) had CNS signs (nystagmus, proprioception deficits, hyperesthesia, hyperreflexia and ataxia), 2 (16%) had a combination of URT signs and CNS signs, 1 (9%) had both URT signs and ocular signs (ocular discharge), 1 (9%) had lymphadenomegaly and URT signs, and 1 (9%) had lymphadenomegaly alone. The dog with ocular signs had reduced retropropulsion of the left eye, suggestive of retrobulbar disease. The median duration of clinical signs was 3.4 weeks (range, 1 to 32 weeks).

*Cryptococcus* organisms were identified in cytological preparations for 5 of 12 (41%) dogs. Two of 5 (40%) dogs had cryptococcal organisms identified on cytological smears from regional LN aspirates (1 mandibular, 1 retropharyngeal). The remaining 3 dogs had cryptococcal organisms identified in a cytocentrifuged specimen of CSF, a smear from a nasal swab, and an aspirate of the right frontal sinus, respectively. Five of 12 dogs (41%) had histopathologic confirmation of cryptococcosis using biopsies from a nasal mass (3/12 [25%]), 1 of 12 (9%) from the right retropharyngeal LN, and 2 of 12 (16%) from material within the frontal sinus. A serum LCAT was performed in all but 1 case, with a positive result in 10 of 11 (90%) cases, with reciprocal titers ranging from 16 to 4,096 (median titer, 1:256). Fungal cultures were performed in 9 of 12 (75%) dogs using material harvested from mandibular LNs (2/9), CSF (1/9), a nasal mass (3/9), nasal flushes (2/9), and the mass above the left eye in the dog with ocular discharge (1/9). Six of 9 (67%) fungal cultures yielded isolates, with 4 of 6 (67%) identified as *C neoformans* and 2 of 6 (33%) as *C gattii*. Culture media were not standardized among laboratories and not specifically stated in mycology reports. Molecular typing was performed in only a single dog (*C gattii* VGI).

Ten of 12 (83%) dogs had soft tissue or fluid attenuation distributed among multiple regions of the nasal cavity (Table 1). Soft tissue or fluid accumulation was identified in the entire cross-sectional area of the dorsal, middle, and ventral nasal regions in 2 of 10 (20%) dogs, with the remaining 8 of 10 (80%) dogs having disease across the entire cross-sectional area of the nasal cavity in at least 1 region or in a combination of regions. One dog had unilateral nasal involvement, but the remaining 9 had bilateral involvement. Nine of 12 (75%) dogs had frontal and/or sphenoidal sinus involvement.

Based on the classification of severity, 3 of 10 (30%) had moderate disease, whereas the remaining 7 of 10 (70%) had severe disease. No dogs had mild disease. Turbinate involvement was evident in 7 of 12 (58%) dogs, choana involvement in 4 of 12 (33%) dogs, and NP involvement in 3 of 12 (25%) dogs. Disease extension into cutaneous and subcutaneous tissue was described in 4 of 12 (33%) dogs. Four of 12 (33%) dogs had disease extension into the retrobulbar/orbital structures, and 1 dog had extension into both tympanic bullae.

Lymphadenomegaly was described in 10 of 12 (83%) dogs (Table 1). A nasal mass was identified in 3 of 12 (25%) dogs. One dog had a mass lesion in the left caudal nasal region and soft tissue attenuation diffusely dispersed through the left ventral nasal region (Figure 1). The other 2 dogs had a contrast-enhancing mass with associated turbinate lysis and extension into the frontal and sphenoidal sinuses. No dogs had evidence of a discrete NP mass.

Osteolysis of the cribriform plate or sphenoidal or sinonasal bones was seen in 10 of 12 (83%) dogs, either individually affected or in combination
The affected bones included nasal and ethmoid conchae and turbinates (Figure 1) and the frontal, maxillary, and lacrimal bones. Five of 12 (42%) dogs had evidence of neurocranial lysis and an intracranial mass effect independent of a nasal mass (5/7 [71%] dogs with cribriform plate lysis did not have a nasal mass). Although CT findings related to CNS cryptococcosis are out of the scope of this study, they are described in a separate study.

Cats

Nine cats were included in this study. Their median age at presentation was 6 years (range, 2 to 16.3 years), and their median weight was 4.6 kg (range, 2.71 to 5.9 kg). Four of 9 cats (44%) were spayed females, and 5 of 9 (56%) were castrated males. Domestic Shorthair cats comprised 6 of 9 cases, with 1 each of Domestic Longhair, Ragdoll, and Birman cats.

All 9 cats (100%) presented with increased respiratory effort; 3 of 9 (33%) had inspiratory stridor, and the remaining 6 of 9 (67%) had stertor. Two of 9 cats (22%) had concurrent ocular signs: 1 cat had periorbital swelling, and the other had unilateral (oculus sinister) mydriasis in conjunction with an absent ipsilateral pupillary light reflex, reduced ipsilateral menace response (suggesting left-sided optic neuritis), and diffuse spinal pain on palpation. One cat (1/9 [11%]) had right retropharyngeal lymphadenomegaly. The median duration of clinical signs was 6 weeks (range, 1 to 24 weeks).

Diagnosis of nasal cryptococcosis was based on histological assessment of the affected tissue in 6 of 9 (67%) cats (nasal mucosa in 4/6, NP mass in 16, and right medial retropharyngeal LN in 1/6). Two of 9 (22%) cats had cryptococci identified in cytological preparations of a nasal flush and a smear from mucous lining the nasal mucosa. In the final cat, diagnosis was based on a positive serum LCAT (reciprocal titer 512).

Six of 9 cats (67%) had a serum LCAT performed, all with positive results. Reciprocal titers
Fungal cultures were performed in 3 of 9 (33%) cats; 2 of 3 (67%) returned positive growth of *C. gattii*, and the remaining cat had a positive culture for *C. neoformans*. Subtyping was not performed for any cat.

The distribution of soft tissue or fluid attenuation within nasal regions in cats was highly variable. Eight of 9 (89%) cats had a soft tissue density or fluid attenuation detected within nasal regions; 5 of 8 (63%) had unilateral involvement, and 3 of 8 (37%) had bilateral nasal involvement (Table 1). Four of 8 (50%) cats had disease distributed amongst several nasal regions, and 4 of 8 (50%) had focal disease. Of the cats with focal disease, 75% had involvement of the caudal nasal region alone, and 25% had involvement of the rostral nasal region. Of the cats with multiple nasal regions affected, 2 of 4 (50%) cats had involvement of the rostral, caudal, and ventral nasal regions, 1 (25%) cat had involvement of the entire ventral nasal region, and the final cat had involvement of all nasal regions. Four of 9 cats (44%) had sinus involvement, with 75% involving the sphenoidal sinus alone and 25% of cases with both sphenoidal and frontal sinus extension. Based on the classification of severity, 4 of 8 (50%) had mild disease, and 4 of 8 (50%) had severe disease.

Turbinate lysis was described in 6 of 9 (67%) cats, choanae involvement in 4 of 9 (44%) cats, and NP involvement in 6 of 9 (67%) cats. Disease extension into cutaneous/subcutaneous tissue was described in 1 cat (11%). One cat (11%) had disease extension into the retrobulbar structures, and 2 of 9 cats (22%) had soft tissue density or fluid within the tympanic bullae (unilateral in 1 cat and bilateral in the other). Lymphadenomegaly was identified in 6 of 9 (67%) cats. Four of 6 cats (67%) had retropharyngeal lymphadenomegaly. One cat had normal retropharyngeal LNs but mild left mandibular lymphadenomegaly (11 mm wide). The remaining cat had bilateral mandibular lymphadenomegaly. A contrast-enhancing NP mass was identified in 5 of 9 (56%) cats and a nasal mass (contrast enhancing; 20 X 9 mm) in only 1 (11%) cat.

Osteolysis of the sphenoidal and sinonasal bones was seen in 6 of 9 cats (66%) as a combination or occurring separately (Figure 2). The affected bones included the palatine (Figure 3), maxillary, nasal, and lacrimal bones. There was no evidence of cribriform plate osteolysis in any cat. Three of 9 (33%) cats had evidence of neurocranial lysis (sphenoidal and sinonasal bones) and intracranial mass effect. Further descriptions of CNS findings of cryptococcosis have been reported in a separate study.15

**Geographic location, Cryptococcus sp, and disease severity**

Twenty-one animals were included from referral hospitals along the east and west coasts of Australia; 9 of 21 (42%) animals were from Sydney and Newcastle in New South Wales, 7 of 21 (33%) were from Perth in Western Australia, and 5 of 21 (23%) were from Brisbane and the Gold Coast in Queensland. There
were no cases from the other states and territories. **Table 2** describes the distribution of culture-positive dogs and cats, the species cultured, and the degree of severity based on CT images. There were no obvious differences in severity (mild, moderate, or severe) between *Cryptococcus* sp, with a similar number of dogs and cats in each group (**Table 3**).

**Table 2**—*Cryptococcus* sp identified (by fungal culture) per state in dogs and cats.

<table>
<thead>
<tr>
<th>Australian state</th>
<th><em>C gattii</em></th>
<th><em>C neoformans</em></th>
</tr>
</thead>
<tbody>
<tr>
<td>New South Wales (NSW)</td>
<td>Dogs: 0 (0%)</td>
<td>Dogs: 2 (33%)</td>
</tr>
<tr>
<td></td>
<td>Cats: 1 (33%)</td>
<td>Cats: 0 (0%)</td>
</tr>
<tr>
<td>Queensland (QLD)</td>
<td>Dogs: 2 (33%)</td>
<td>Dogs: 0 (0%)</td>
</tr>
<tr>
<td></td>
<td>Cats: 1 (33%)</td>
<td>Cats: 1 (33%)</td>
</tr>
<tr>
<td>Western Australia (WA)</td>
<td>Dogs: 0 (0%)</td>
<td>Dogs: 2 (33%)</td>
</tr>
<tr>
<td></td>
<td>Cats: 0 (0%)</td>
<td>Cats: 0 (0%)</td>
</tr>
</tbody>
</table>

**Table 3**—Number of patients with speciation of *Cryptococcus* performed and disease severity based on CT features.

<table>
<thead>
<tr>
<th><em>Cryptococcus</em> sp</th>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>C neoformans</em></td>
<td>1</td>
<td>3</td>
<td>5</td>
<td>9</td>
</tr>
<tr>
<td><em>C gattii</em></td>
<td>1</td>
<td>2</td>
<td>1</td>
<td>4</td>
</tr>
<tr>
<td>Total</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>9</td>
</tr>
</tbody>
</table>

*Evidence of disease involving only 1 nasal region and/or sinus. Evidence of disease involving at least 2 nasal regions and/or sinuses but not more than 3. Evidence of disease involving more than 3 nasal regions and/or sinuses.

**Outcomes**

Ten cases were LTFU; hence, the outcomes of only 11 cases (6 dogs, 5 cats) were described. Of the 11 cases, 5 of 11 (45%) cases (3/6 [50%] dogs; 2/5 [40%] cats) were alive. All 3 dogs were receiving treatment with amphotericin B and a triazole but were not cured. Both cats received fluconazole alone; 1 cat was defined as cured and the other under treatment.

Six of 11 (54%) cases (3/6 [50%] dogs; 3/5 [60%] cats) died. One dog went into cardiac arrest 1 day after diagnosis, presumably attributable to cryptococcosis. The other 2 were euthanized: 1 the day after diagnosis and the other 678 days after diagnosis, both associated with progressive clinical signs (nasal discharge and neurological deterioration, respectively). Of the dogs that died within 1 day of diagnosis, 1 dog was started on a triazole, and the other did not receive any antifungals. The dog that died > 1 year after diagnosis received a combination of amphotericin B and fluconazole therapy and had a marked improvement in clinical signs before late acute deterioration. All 3 cats were euthanized secondary to disease unrelated to cryptococcosis (abdominal neoplasia, a forebrain lesion [suspected meningioma], and lymphoma). Of these cats, 2 were documented to have achieved a cure prior to euthanasia; all cats were treated with fluconazole alone.

All cases, prior to being LTFU, were treated with combination antifungal therapy or a triazole alone. At their last follow-up, all cases were documented to have improved or had resolving clinical signs and were receiving ongoing antifungal therapy. Cases were...
LTFU between 50 and 966 days; all were documented to be alive at the time of their last follow-up, although long-term outcome could not be established.

Discussion

This study describes CT findings for an Australian population of dogs and cats with nasal cryptococcosis. In dogs, the distribution of soft tissue densities or fluid attenuation within nasal cavities was highly variable. Dogs tended to have extensive disease. Changes were often observed in numerous nasal regions, contiguous sinus(es), and the NP. Seventy-five percent of dogs in this study had soft tissue or fluid attenuation in their sinuses, with over half having involvement of the frontal and sphenoidal sinuses.

The distribution of soft tissue and fluid attenuation was generally quite different in cats. When multifocally distributed disease was identified, it tended to involve all nasal regions, whereas focal disease was mostly localized to the caudal nasal region. If multiple sinuses were involved, the sphenoid sinus was invariably affected. Only 1 cat had frontal sinus involvement, and this was in conjunction with sphenoidal sinus infection. This differs to recent studies where frontal sinus involvement was more commonly identified in dogs and cats in 1 study and in 50% of cats in another study. This may reflect the tendency in Australia to sample subcutaneous involvement over the frontal sinus with needle aspiration, thereby negating the requirement for cross-sectional imaging to obtain a diagnosis of cryptococcosis. Regardless, cross-sectional imaging is still recommended to determine the extent of disease given that sinonasal involvement is so common.

All cats in this study presented with URT signs. Such historical findings suggest that cats tend to present with signs of nasal cavity disease alone and that the URT is the primary site of infection following inhalation, with extension to contiguous anatomical structures. This is consistent with CT changes mainly affecting the rostral and ventral nasal cavity, the sites where particulate material would first be filtered after inhalation assuming laminar flow of inspired air. This contrasts to humans, in which the primary site of infection is suspected to be the lower respiratory tract due to differences in size, anatomical architecture, physiology, and behavior. In humans, as a generalization, fungal cells are either cleared from the airways by mucociliary transport or restricted to granulomas in the lung or regional hilar LNs, persisting for months or indefinitely, typically in an arrested state. When immunocompromise develops, dormant cryptococcal cells can be reactivated and multiply locally, with subsequent hematogenous dissemination to cause systemic infection involving tissues with a tropism for this pathogen, including the CNS.

In contrast, dogs presented with a combination of signs, predominantly CNS signs. Less than half the canine cohort presented with URT signs alone. This observation is supported by previous studies highlighting the importance of nasal cavity infection but also a high prevalence of early CNS involvement and disseminated disease in dogs. Although CT abnormalities of the CNS were not included in this study, 70% of dogs in this study had evidence of cribiform plate lysis, a likely pathway for CNS extension. Although the nasal cavity is believed to be the primary site of infection in dogs, as in cats, hematogenous spread to the CNS and other tissues is another plausible route for dissemination.

The species of Cryptococcus also potentially plays a role in disease severity and CNS extension; in California, dogs with C gattii had nasal cavity and cribiform plate involvement at necropsy, whereas dogs with C neoformans infections had disseminated disease without cribiform plate involvement. This suggests that hematogenous spread to the CNS is the more likely route of extension for C neoformans, although rapid spread to the CNS without osteolysis is also possible.

Interestingly, of the dogs from which C neoformans was isolated, only 25% had CNS signs, although this may not be truly representative due the small cohort with positive fungal cultures. In the University of California, Davis study, the CNS was the most commonly identified body system infected in dogs as opposed to nasal tissue in cats. Nevertheless, cats still develop CNS disease, and it is thought to result from localized spread through the cribiform plate to the meninges, olfactory bulbs, and optic nerves, which have a close anatomical relationship. The single cat in this study with CNS abnormalities had evidence of optic nerve dysfunction, with an absent ipsilateral pupillary light reflex and absent menace response. Cribiform plate lysis was not detected using CT in any cat; thus, osteolysis of the sphenoidal sinus or hematogenous spread are both plausible routes of intracranial entry.

No dogs were identified with a discrete NP mass, although they were more likely to have a nasal mass than cats. Our CT observations are comparable to a recent case series where most dogs had nasal masses extending into the rostral NP, whereas most cats with a discrete NP mass had no evidence of concurrent nasal mass lesions. Neoplasia (especially lymphoma, benign polyps) should also be considered when an NP mass is present, although the number of cats with osteolysis, particularly frontal bone lysis, appears to be higher in the face of mycotic disease compared to neoplasia. No cats in this study had evidence of cribiform plate lysis; instead, they typically had sphenoidal and sinonasal bony lysis. This differed from the canine cohort, where cribiform plate lysis was identified in 70% of cases and sinonasal and sphenoidal osteolysis in 80% of cases, emphasizing the prevalence of osteolysis in cases of canine cryptococcosis, even in the absence of a nasal mass. Fewer feline cases displayed osteolysis on head CT, in accord with the recent case series from Oregon. Despite this, significant osteolysis of paranasal bones, turbinate destruction, and nasal septum lysis occur with both feline sinonasal neoplasia and nonmycotic rhinitis, underscoring that overlapping CT features exist between numerous sinonasal diseases.

NP involvement in cats was 3-fold more common compared to dogs in this study, with an NP mass...
documented in 56% of cases. Soft tissue densities or fluid attenuation within the tympanic bullae can be associated with NP masses, secondary to auditory tube obstruction or ascending infections, with a previous study documenting bullae effusion in up to 28% of cats with sinonasal neoplasia or inflammatory disease, although only 2% of cats in that study had myotic sinonasal disease. In another study, only 12% of cats with nasal aspergillosis had tympanic bullae involvement, and changes were considered incidental. Only 2 cats (22%) in our study had CT changes involving the tympanic bullae, which contrasts to 60% in the recent comparable study. Therefore, involvement of the tympanic bullae secondary to myotic nasal disease is variable, and fungal extension cannot be confirmed without direct sampling of the material within the tympanic bullae.

Lymphadenomegaly was commonly identified in both dogs and cats, though this was more common in dogs as observed in a previous study from California. Similar to previous studies, there was no specific pattern between LN changes in dogs and cats. LNs represent an easy and often accessible site for sampling via needle aspiration, facilitating a cytological diagnosis of cryptococcosis and an accessible sterile site to culture.

Aspergillosis is a common mycotic disease in dogs and, to a much lesser extent, in cats. In cats, however, CT findings of aspergillosis can present similar to cryptococcosis. Aspergillosis usually presents in 2 forms, either as sinonasal (the most common form in dogs) or sino-orbital (SOA; the most common form in cats), although this artificial construct really reflects a spectrum of presentations. The former presents with CT findings, including cavitated turbinate lysis, soft tissue attenuation, and reactive bone changes, particularly involving the frontal sinus and maxillary recess. Cats with SOA had similar changes, although turbinate lysis is less cavitory and severe, and sphenoidal sinus and paranasal bone involvement is more common. Differentiating between the 2 mycotic diseases can be difficult with CT alone; however, to date there have been no reports of a nasal mass associated with aspergillosis in dogs. This contrasts to cats as nasal and nasopharyngeal masses have been documented in both SOA and sinonasal cases (more often in SOA cases). Severe cavitated turbinate lysis occurs, more so in sinonasal in cats. This reinforces the notion that a diagnosis of cryptococcosis should always be obtained with laboratory support and not based on a single positive diagnostic result or CT findings alone.

Of the cases with follow-up, just under half were alive at the time of enrollment, with a median follow-up time of 542 days. The median survival time of deceased cases was 678 days, and cause of death in all cats was another disease. Furthermore, 2 cats were documented to have achieved a cure with antifungal therapy (triazoles alone) prior to death. Successful treatment of nasal cryptococcosis with antifungals has been described in previous studies. Despite the numerous cases LTFU, the documented improvement or resolution of clinical signs in our cohort stresses the importance of antifungal therapy, although a cure often requires prolonged periods and high doses of antifungal treatment, and often combination drug therapy, to achieve appropriate concentrations in poorly perfused areas, including sinuses. Unfortunately, too few patients had cryptococcal speciation performed to execute appropriately powered statistical analyses associated with disease severity, Cryptococcus sp, and survival status. Regardless, there were no obvious differences in disease severity based on CT images nor survival status, stressing the importance that positive outcomes are observed even in the face of severe disease detected with cross-sectional imaging.

One aim of this study was to identify commonly isolated species of Cryptococcus along the coastlines of Australia and to determine if there was a significant difference in the severity of disease based on CT findings between C neoformans and C gattii. Unfortunately, there were too few cases with positive cultures to make a meaningful comparison with previous studies or to comment on potential disease associations. Despite the low number of cases with fungal cultures, there was no obvious association between Cryptococcus sp and disease severity, which is in accord with a previous study indicating that Cryptococcus sp did not influence the observed clinical picture in either dogs or cats.

The limitations of this study were in relation to its retrospective nature in combination with small case numbers in some subgroups, which resulted in underpowered statistical comparisons. CT images were reviewed by a nonblinded radiologist or resident under supervision, resulting in potential interpretation bias. In addition, given that ambiguous cases were identified as not having a nasal or nasopharyngeal mass, certain cases could have been misclassified. CT features of cryptococcosis can overlap with other diseases, and although all included cases had a diagnosis of cryptococcosis, the method of diagnosis was not standardized. Thus, concomitant disease resulting in the presumed changes on head CT could not be excluded. Fungal cultures to identify species and molecular type were not obtained in most cases.

This study highlights the CT findings in a cohort of Australian dogs and cats with nasal cryptococcosis. Nasal cryptococcosis presents differently in dogs versus cats and to other mycotic diseases. There was no significant difference in disease severity between C neoformans and C gattii infection arising in different regions of Australia nor in outcomes for this cohort.

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Disclosures

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References


