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Sinonasal aspergillosis: Outcome after topical treatment in dogs with cribriform plate lysis

Beatriz Belda[1] | Nicholas Petrovitch[2] | Kyle G. Mathews[1]

[1]Department of Clinical Sciences, College of Veterinary Medicine, North Carolina State University, Raleigh, North Carolina

[2]Department of Molecular Biomedical Sciences, College of Veterinary Medicine, North Carolina State University, Raleigh, North Carolina

Correspondence
Kyle G. Mathews, DVM, MS, North Carolina State University, College of Veterinary Medicine, Department of Clinical Sciences, 1052 William Moore Drive, Raleigh, NC 27607.
Email: kmathews@ncsu.edu

Background: Cribriform lysis has been considered a contraindication for topical treatment of sinonasal aspergillosis (SNA) because of concerns about drug extravasation with resultant neurologic signs or death.

Objective/Hypothesis: To describe dogs with SNA and cribriform plate lysis treated with topical antifungal medications. Our hypothesis was that the conventional dogma that topical therapy should be avoided in these cases is incorrect.

Animals: Nine client-owned dogs with SNA and lysis of the cribriform plate, lysis of the floor of a frontal sinus or both detected by computed tomography (CT).

Methods: A retrospective review of medical records was performed. Dogs that met inclusion criteria (ie, SNA confirmed by at least 1 laboratory test, braincase affected on CT, and topical treatment applied) were included. Size of lesions, ancillary diagnostic test results, topical therapy, and adjuvant PO treatments were recorded. Outcome was determined by phone calls.

Results: Four dogs were alive at the time of the manuscript submission with follow-up ranging from 188 to 684 days without neurological signs observed. All dogs were discharged without major complication 1-7 days postoperatively. One dog that had presented with a history of seizures experienced seizure activity 2 months after treatment.

Conclusions and Clinical Importance: Topical therapy did not result in complications in these dogs in which lytic regions as large as 16 × 22 mm^2 were noted. Sinonasal aspergillosis associated lysis of the cribriform plate; lysis of the floor of a frontal sinus or both detected on CT is not necessarily a contraindication to topical therapy.

KEYWORDS
aspergillus, cribriform plate, lytic, nasal

1 | INTRODUCTION

Aspergillus fumigatus is a common cause of rhinitis and sinusitis in dogs and has been found in 12%-34% of dogs evaluated for chronic sinonasal disease.[1–5] Diagnosis is confirmed by a combination of rhinoscopy, computed tomography (CT), cytology or histology, fungal culture, and serology.[2–6]

Topically applied drugs have become the standard treatment for fungal rhinitis in dogs. Numerous topical medications have been investigated including enilconazole solution, bifonazole cream, clotrimazole solution, clotrimazole cream, clotrimazole gel, and iodine cadexomer dressings.[1,6–18] Various procedures have been developed to administer topical antifungal medications. They vary in invasiveness and ease of performance and include surgically implanted sinus tubes, nonsurgically placed tubes for intranasal therapy under general anesthesia, and sinus trephination or sinusotomy. Numerous studies have concluded that

Abbreviations: CT, computed tomography; SNA, sinonasal aspergillosis.

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meticulous debridement of fungal plaques and granulomas before topical treatment increases efficacy, with resolution in approximately one-half to two-thirds of patients after a single treatment.[6,8,11,12]

It has been stated that topical therapy in patients with cribriform plate lysis should be avoided because of concern about potential drug extravasation across the damaged cribriform plate into the brain, resulting in seizure activity or death.[19,20] This concern has resulted in some dogs with evidence of lysis being treated less aggressively by systemic therapy alone, or being euthanized because systemic therapy has a lower success rate, especially in patients with bulky sinonasal fungal disease.[21–23] However, topical treatment of patients with lysis of the cribriform plate of the ethmoid bones or the internal surface of the frontal bones (floor of the frontal sinuses) has been reported infrequently, and therefore these concerns currently are hypothetical.[12]

Few publications describe dogs with cribriform plate lysis secondary to sinonasal aspergillosis (SNA) that were treated topically. Two reports describe 3 dogs with cribriform lysis that were treated with topical enilconazole with no apparent complications.[8,9] In another report, 2 dogs with minor cribriform plate involvement also were treated topically with 1% clotrimazole solution without apparent complications.[6] The extent of cribriform or frontal sinus involvement and follow-up in these patients were not provided.[6,8,9] More recently, a case report described neurological complications (ie, pneumocephalus, pneumorrachis, and meningoencephalitis) after fungal granuloma debridement via dorsal rhinotomy. In this case, topical treatment was not applied, the complications were not considered severe, and the patient improved with supportive care.[24]

The goal of our retrospective study was to determine if dogs with cribriform plate lysis, lysis of the floor of a frontal sinus or both that were treated with topical antifungal medications had any complications associated with treatment. Our hypothesis was that the majority of these cases would have resolution of their clinical signs without complications, including increase in seizure activity, or death.

2 | MATERIALS AND METHODS

2.1 | Criteria for selection cases

A search of the North Carolina State University College of Veterinary Medicine's medical records, surgery, internal medicine, and pathology databases for dogs diagnosed with SNA between January 2001 and July 2017 was performed. Cases with the following criteria initially were included: destructive rhinitis evident on CT (the majority of patients also having rhinoscopy) and confirmed by at least 1 laboratory test (cytology, serology, fungal culture or histopathology) consistent with a diagnosis of aspergillosis. Among these patients, medical records of those that had mention of lysis of the cribriform plate of the ethmoid bones or the internal surface of the frontal bones (ie, floor of the frontal sinuses) in the CT report and that underwent treatment (topical, systemic, or both) then were evaluated.

The following information was retrieved from the medical record: signalment, history, physical examination findings, CT results, rhinoscopic and surgical findings, clinical laboratory results (cytology, serology, fungal and bacterial culture, and histopathology), number of topical treatments performed, and postoperative medications. Length of follow-up available in the medical record or communication log was recorded. Additional follow-up then was completed by telephone with referral veterinarians, followed by a similar conversation with the owner using a standardized questionnaire (see Supporting Information Materials).

2.2 | Procedures

All dogs were anesthetized for CT (with or without rhinoscopy) and surgery using an anesthetic protocol at the discretion of a board-certified anesthesiologist. Typically, general anesthesia consisted of premedication with hydromorphone (0.04-0.07 mg/kg IV), induction with midazolam (0.1-0.2 mg/kg IV), and propofol (4–6 mg/kg IV) and maintenance with isoflurane in oxygen. During surgery, analgesia often was managed with a fentanyl infusion (0.1-0.4 μg/kg/min IV).

2.2.1 | Computed tomography

Computed tomography was performed in all patients. Three different CT units were used over the period included in the present study (GE Single Slice Sytec Sri; GE Healthcare, Washington DC; Siemens 16 Slice Sensation, and Siemens 64 Slice Perspective; Siemens Healthcare, Malvern, PA). Dogs were positioned in sternal recumbency. A 1 mm transverse slice dataset was acquired and reconstructed preadministration and postadministration of contrast medium (iohexol at 770 mg I/kg). Sagittal and dorsal plane sequences were reconstructed after administration of contrast medium in all cases. Digital CT images were retrospectively reviewed by a board-certified radiologist (Nicholas Petrovitch) unaware of treatment or outcome. Follow-up CT studies also were evaluated if performed, and the timing between the studies was recorded. Multiplanar reconstructions from the transverse series were created to assess the lytic regions in both transverse and sagittal planes. Cribriform or frontal bone lytic lesions that affected the braincase were measured and classified as either permeative or geographical. Permeative lysis was defined as a region of bone that contained multifocal punctate hypoattenuations, but retained its overall shape throughout the region (Figure 1). Geographical lysis was defined as a region of bone that contained a single, large, well-defined hypoattenuating zone (Figure 2).

2.2.2 | Rhinoscopy

Rhinoscopic evaluation of the nasal cavity also was performed in all dogs suspected to have SNA unless rhinoscopy and confirmation of the diagnosis with laboratory test results was performed before referral. During rhinoscopy, biopsy specimens were collected for microbial culture, cytologic evaluation, and histologic examination. Removal of fungal material was not performed endoscopically other than for diagnostic confirmation.

2.2.3 | Surgery

All dogs were positioned in sternal recumbency before sinusotomy. A 20 Fr Foley catheter was inserted retrograde around the soft palate into the nasopharynx. The balloon was inflated with air, and laparotomy sponges placed in the oropharynx so that the balloon blocked the

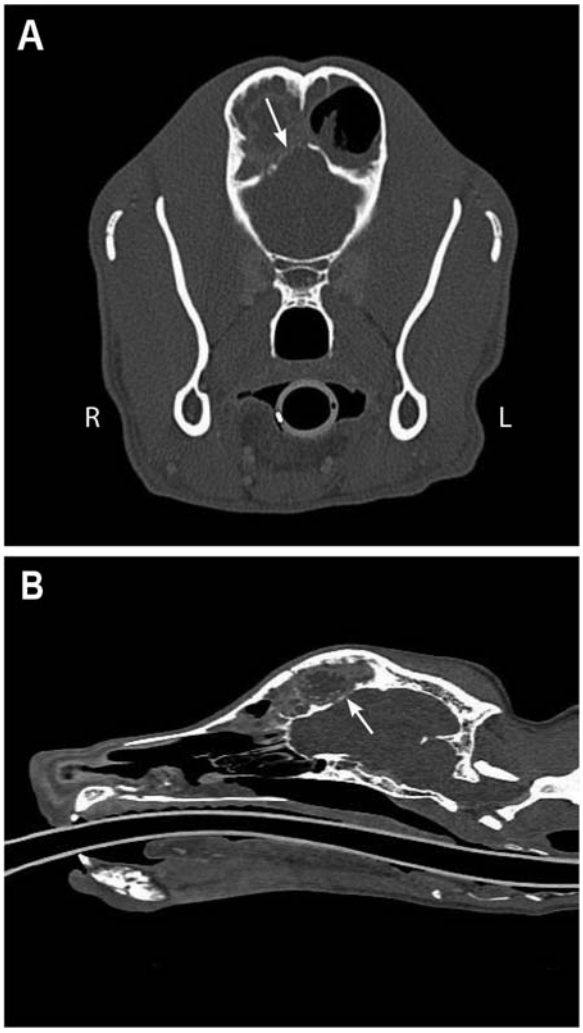

FIGURE 1 Transverse (A) and sagittal (B) computed tomographic images of dog 5 with permeative lysis of the right frontal sinus (arrows)

nasopharynx at the junction between the hard and soft palates. In patients treated with clotrimazole solution, additional 10 Fr Foley catheters were placed in each nostril and inflated with air to prevent drug from exiting the nasal cavity during treatment. The frontal and nasal bones were aseptically prepared and a dorsal midline skin incision was made extending from near the temporal ridge to just rostral to the medial canthi. Subcutaneous tissues and periosteum were incised on midline and periosteum was elevated and reflected laterally. A trephination site was made over the right or left sinus using an intramedullary pin. The trephination site was enlarged as needed based on CT findings using Love-Kerrison rongeurs to expose fungal granulomas. Fungal plaques and granulomas were removed and the region gently debrided taking care not to disrupt tissues on the floor of the frontal sinuses. Gentle saline irrigation and removal of saline with suction was performed before topical antifungal drug administration.

2.2.4 | Topical therapy

Five different topical protocols were used during this period (Supporting Information Table S1): (1) compounded 1% enilconazole (Clinapharm EC; Merck Animal Health, Madison, NJ) through indwelling sinus catheters (6 mL bilaterally q12h × 7d; n = 1); (2) instillation of 1% clotrimazole (Clotrimazole 1% topical solution; Taro Pharmaceuticals, Brampton, Ontario, Canada) topical solution over 60 minutes followed by its removal (n = 2); (3) instillation of 1% clotrimazole topical solution over 60 minutes followed by its removal and instillation of 1% clotrimazole cream (Clotrimazole 1% cream; Taro Pharmaceuticals, Brampton, Ontario, Canada) before closure (n = 3); (4) instillation of 1% clotrimazole topical solution over 60 minutes followed by its removal and instillation of compounded sterile 1% clotrimazole in poloxamer 25% (pluronic) gel (Poloxamer 407 NF; Letco Medical, Decatur, AL) before closure (n = 1); and, (5) instillation of compounded sterile 1% clotrimazole pluronic gel alone (n = 4). All dogs had a single topical treatment via sinusotomy except for 1 dog that received 3 treatments with the clotrimazole solution and cream combination spaced 2 and 6 months apart. All compounding was performed at the North Carolina State University College of Veterinary Medicine Pharmacy. Clotrimazole topical solution, when applied, was injected via the sinusotomy sites and filled the nasal cavity and sinuses. When clotrimazole topical cream or gel was used, it was injected into the frontal sinuses using a syringe and shortened polyvinyl

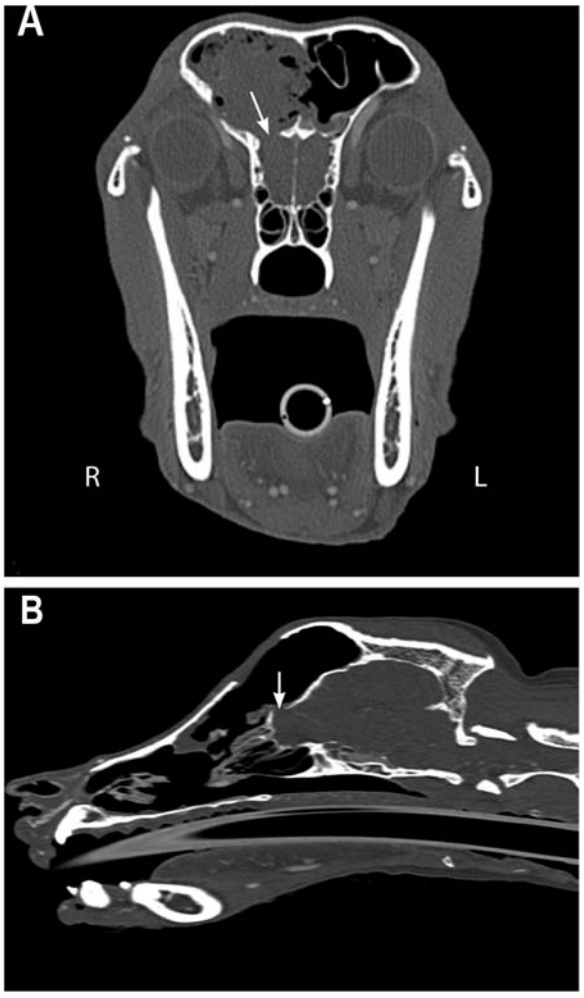

FIGURE 2 Transverse (A) and sagittal (B) computed tomographic images of dog 7 with geographic lysis of the right dorsal cribriform plate and floor of the right frontal sinus (arrows)

catheter until the caudal nasal cavity and sinuses were full. Subcutaneous and skin layers were closed routinely.

2.2.5 | Oral antifungal therapy

All dogs were treated with an oral antifungal medication after the procedure (see Supplemental Materials). These included itraconazole (3–7 mg/kg PO q24h; n = 5); terbinafine (14–30 mg/kg PO q24h; n = 2); both terbinafine (30 mg/kg PO q24h) and itraconazole (7 mg/kg PO q24h; n = 1); and, posaconazole 13 mg/kg PO twice weekly; n = 1). Duration of treatment varied from 10 days (lost to follow-up) to 7 years (referring veterinarian's decision).

3 | RESULTS

3.1 | Signalment

Fifty patients with SNA were identified. Eleven of them had evidence of cribriform plate or frontal bone lysis, of which 9 were treated topically. One dog was euthanized at the time of diagnosis. One dog had a sinusotomy and fungal granuloma removal followed by saline flush of the sinuses but no topical antifungal was administered. The group of 9 topically treated dogs with braincase lysis was composed of 6 castrated males and 3 spayed females. Median age was 7 years (range, 1–12 years). Median body weight was 28.2 kg (range, 7.6–36.4 kg). Golden retriever was the most common breed, accounting for 5/9 cases, followed by 1 each of the following: Miniature schnauzer, Rottweiler, Old English Sheepdog, and mixed breed dog.

3.2 | Clinical presentation

The most common presenting owner complaints of dogs with SNA with cribriform plate involvement were serous to purulent nasal discharge (9/9), epistaxis (4/9), ocular discharge (2/9), and nasal planum depigmentation (2/9). The chronicity of the nasal discharge was described by owners as > 1 year before presentation in 2 dogs (22%), between 6 and 11 months in 2 dogs (22%) and < 3 months in 6 dogs (67%). One dog was reported to have had seizures 1 week before referral, which were not treated.

3.3 | Computed tomographic findings

Sixteen CT studies were reviewed. Five dogs had 2 CTs performed, and 1 had 3 CTs performed. Repeat CTs were performed at re-evaluations to confirm absence of fungal granulomas (2 dogs), recurrence of nasal discharge (2 dogs), stertor secondary to nasopharyngeal stenosis (1 dog), and recurrent seizures (1 dog).

A total of 17 lytic braincase lesions was identified in these 9 dogs on pretreatment CTs (see Supporting Information Materials). Nine were classified as geographic with 5 affecting the cribriform plate and 4 affecting the floor of a frontal sinus. Eight were classified as permeative with 1 affecting the cribriform plate, and 7 affecting the floor of a frontal sinus.

Sizes of the defects ranged from 2.2 × 3 mm to 10 × 17.8 mm for geographic lesions, and 2.8 × 3.1 mm to 22 × 16 mm for permeative lesions. Subjectively, no difference in lesion size was found between initial and re-evaluation CTs. Contrast enhancement of underlying meninges and neural parenchyma was found in 1 dog on both pre- and post-treatment CT scans.

3.4 | Outcome

All dogs recovered uneventfully from anesthesia and were discharged a median of 2 days (range, 1–7 days) postoperatively. Discounting the 1 dog treated with enilconazole via indwelling tubes for 7 days, the median hospital stay was 1 day postoperatively.

Two dogs were euthanized because of recurrence of nasal signs (n = 1) or seizures (n = 1) 38 and 120 days postoperatively, respectively (see Supporting Information Materials). Postoperative seizures only occurred in the 1 dog for which seizures were reported preoperatively. One dog died 11 days postoperatively from presumed gastric dilatation-volvulus and no necropsy was performed. Four dogs were alive with no clinical signs associated with fungal rhinitis 188–684 days postoperatively.

Only 1 dog had > 1 topical treatment for SNA after referral because of recurrence of nasal discharge. Treatments were separated by 2 and 6 months. This dog was euthanized 2,541 days postoperatively for presumed appendicular osteosarcoma. During the follow-up period, this dog developed mild intermittent episodes of nasal discharge that responded to multiple 2 week courses of an antimicrobial (sulfamethoxazole/trimethoprim, 14 mg/kg PO q24h). This dog also was kept on itraconazole PO by the referring veterinarian.

Infusion of 1% clotrimazole pluronic gel alone was the most recently used protocol. This protocol was used in 4 dogs of which 3 were still alive with no recurrence of clinical signs at the time of manuscript submission, with a follow-up of 297, 441, and 188 days, respectively.

Infusion of 1% clotrimazole solution followed by 1% clotrimazole pluronic gel was used in 1 dog, which was still alive with no recurrence of clinical signs at the time of manuscript submission with a follow-up time of 684 days.

4 | DISCUSSION

Despite previous concerns about potential neurologic complications associated with topical therapy in canine SNA patients with cribriform lysis, no immediate complications, neurologic or otherwise, were noted in any of our patients. The 1 dog that had seizures after treatment had a history of a previous seizure and additional seizures were not observed until they occurred 2 and 3 months after topical therapy. Therefore, the seizures in this dog were not considered to be complications of treatment. Although our study was focused primarily on the safety of topical therapy in this sub-group of patients, and not on success of treatment, for those 5 patients with > 6 months of follow-up, only 1/5 required > 1 topical treatment based on absence of clinical signs. This response rate is comparable to those of previous studies where approximately 50%-65% cases resolved after a single topical treatment.[6,12] Confirmation of resolution cannot be confirmed

however without re-evaluation rhinoscopic examination, and although repeat rhinoscopy was discussed with all owners, only 3 elected to have it performed.[10]

Cribriform plate lysis has been described in 5%-20% of dogs with SNA, similar to our study prevalence of 22% (11/50).[3,25,26] It has been our experience that the finding of braincase lysis (cribriform plate or internal surface of the frontal bones) on CT may result in euthanasia of the patient. The exact location and size of these lesions has not been documented in the past. All of the patients in our study had bulky disease in the frontal sinuses. Because of this finding, a surgical approach to the sinuses was elected to remove fungal granulomas. Granulomas were gently removed before topical therapy. No obvious defects in the braincase were noted by the attending surgeons.

Treatment protocols changed over time and were based on surgeon preference and information available in the scientific literature over the last 20 years. Numerous authors have studied the distribution of different antifungal compounds.[16,18,27,28] Four of the last 5 dogs were treated with surgical debridement of fungal granulomas followed by instillation of clotrimazole pluronic gel alone. Poloxamer 25% gel is a unique polymeric drug carrier that undergoes reverse gelation (gels as it warms to body temperature) and likely remains in the frontal sinuses longer than the commercially available cream.[16] It has been shown to be safe when placed in the frontal sinuses of normal dogs, and appears to be safe when placed in dogs with cribriform lysis based on the results of our study.[16] The preparation of compounded clotrimazole in poloxamer gel has been described, and many compounding pharmacies that supply sterile preparations are able to provide this product.[16] This method of topical therapy is relatively rapid compared with those involving a 1-hour infusion of clotrimazole solution. Theoretically, clotrimazole gel or cream would be less likely to cross any lytic lesions in the braincase compared with the solution, but no negative effects of the solution were noted in our case series, which may be because the solution was placed at surgery via an open sinusotomy. It is not known if intranasal administration of solution results in increased intranasal pressure, potentially resulting in increased risk of intracranial extravasation in patients with braincase lysis on CT.

Although sample size was small, patients that had larger lytic defects did not appear to have worse outcome than those that had smaller defects. Only 1 dog with permeative lysis of the frontal sinuses had evidence of cerebral contrast enhancement, and we therefore cannot comment on the importance of this finding (this dog had no neurologic complications). Upon review of re-evaluation CTs, when available, no changes in size of the defect were found, suggesting that remineralization of the lytic lesions, if it occurs, is a slow process.

As with many retrospective studies, the lack of standardized treatment, follow-up and small sample size suggest that the results be interpreted with caution. Regardless, many of our patients responded well to treatment, and no immediate postoperative complications were observed. Neurologic complications only occurred in the 1 patient with a history of seizures, and these occurred long after discharge from the hospital.

In conclusion, topical treatment, as described here, may be offered as a therapeutic option to owners of some dogs with SNA that have evidence of braincase lysis as long as potential adverse effects are considered. Further prospective studies with standardized topical protocols and follow-up are warranted.

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CONFLICT OF INTEREST DECLARATION

Authors declare no conflict of interest.

OFF-LABEL ANTIMICROBIAL DECLARATION

There are no FDA-approved products for the topical treatment of sinonasal aspergillosis; therefore, all use of topical antifungals in this retrospective review was off-label.

INSTITUTIONAL ANIMAL CARE AND USE COMMITTEE (IACUC) OR OTHER APPROVAL DECLARATION

Authors declare no IACUC or other approval was needed.

ORCID

Kyle G. Mathews http://orcid.org/0000-0003-3431-6049

REFERENCES

[1] Sharp NJ, Sullivan M, Harvey CE. Treatment of canine nasal aspergillosis with enilconazole. *J Vet Intern Med*. 1993;7:40–43.

[2] Saunders JH, Clercx C, Snaps FR, et al. Radiographic, magnetic resonance imaging, computed tomographic, and rhinoscopic features of nasal aspergillosis in dogs. *J Am Vet Med Assoc*. 2004;225:1703–1712.

[3] Johnson LR, Drazenovich TL, Herrera MA, Wisner ER. Results of rhinoscopy alone or in conjunction with sinuscopy in dogs with aspergillosis: 46 cases (2001–2004). *J Am Vet Med Assoc*. 2006;228:738–742.

[4] De Lorenzi D, Bonfanti U, Masserdotti C, Caldin M, Furlanello T. Diagnosis of canine nasal aspergillosis by cytological examination: a comparison of four different collection techniques. *J Small Anim Pract*. 2006;47:316–319.

[5] Peeters D, Clercx C. Update on canine sinonasal aspergillosis. *Vet Clin North Am Small Anim Pract*. 2007;37:901–916.

[6] Pomrantz JS, Johnson LR. Repeated rhinoscopic and serologic assessment of the effectiveness of intranasally administered clotrimazole for the treatment of nasal aspergillosis in dogs. *J Am Vet Med Assoc*. 2010;236:757–762.

[7] Sharp NJ, Sullivan M. Treatment of canine nasal aspergillosis with systemic ketoconazole and topical enilconazole. *Vet Rec*. 1986;118:560–561.

[8] Zonderland JL, Störk CK, Saunders JH, Hamaide AJ, Balligand MH, Clercx CM. Intranasal infusion of enilconazole for treatment of sinonasal aspergillosis in dogs. *J Am Vet Med Assoc*. 2002;221:1421–1425.

[9] Saunders JH, Duchateau L, Störk C, van Bree H. Use of computed tomography to predict the outcome of a nonivasive intranasal infusion in dogs with nasal aspergillosis. *Can Vet J*. 2003;44:305–311.

[10] Schuller S, Clercx C. Long-term outcomes in dogs with sinonasal aspergillosis treated with intranasal infusions of enilconazole. *J Am Anim Hosp Assoc*. 2007;43:33–38.

[11] Billen F, Guieu LV, Bernaerts F, et al. Efficacy of intrasinusal administration of bifonazole cream alone or in combination with enilconazole irrigation in canine sino-nasal aspergillosis: 17 cases. *Can Vet J*. 2010;51:164–168.

[12] Mathews KG, Davidson AP, Koblik PD, et al. Comparison of topical administration of clotrimazole through surgically placed versus non-surgically placed catheters for treatment of nasal aspergillosis in dogs: 60 cases (1990–1996). *J Am Vet Med Assoc*. 1998;213:501–506.

[13] Friend EJ, Williams JM, White RA. Invasive treatment of canine nasal aspergillosis with topical clotrimazole. *Vet Rec*. 2002;151:298–299.

[14] Sharman M, Paul A, Davies D, et al. Multi-centre assessment of mycotic rhinosinusitis in dogs: a retrospective study of initial treatment success (1998 to 2008). *J Small Anim Pract*. 2010;51:423–427.

[15] Sissener TR, Bacon NJ, Friend E, Anderson DM, White RA. Combined clotrimazole irrigation and depot therapy for canine nasal aspergillosis. *J Small Anim Pract*. 2006;47:312–315.

[16] Mathews KG, Linder KE, Davidson GS, Goldman RB, Papich MG. Assessment of clotrimazole gels for in vitro stability and in vivo retention in the frontal sinus of dogs. *Am J Vet Res*. 2009;70:640–647.

[17] Preston TJ, Hosgood GL, Paul A. Surgical management of refractory nasal aspergillosis using iodine cadexomer dressings in three dogs. *Aust Vet J*. 2016;94:405–410.

[18] Hayes GM, Demetriou JL. Distribution and persistence of topical clotrimazole after sinus infusion in normal canine cadavers. *J Small Anim Pract*. 2012;53:95–100.

[19] Mathews KG, Koblik PD, Richardson EF, Davidson AP, Pappagianis D. Computed tomographic assessment of noninvasive intranasal infusions in dogs with fungal rhinitis. *Vet Surg*. 1996;25:309–319.

[20] Day MJ, Peeters D, Clercx C. Canine sinonasal aspergillosis-penicilliosis. In: Greene CE, ed. *Infectious Diseases of the Dog and Cat*. 4th ed. St. Louis, MO: Saunders Elsevier; 2012:657–658.

[21] Eliasjirjoss I, Paulo K, Osvaldoprado C. Nasal aspergillosis and penicilliosis in dogs: results of treatment with thiabendazole. *Rev Assoc Med Bras*. 2002;48:184–150.

[22] Sharp NJH, Sullivan M. Use of ketoconazole in the treatment of canine nasal aspergillosis. *J Am Vet Med Assoc*. 1989;194:782–786.

[23] Sharp NJH, Harvey CE, O'Brien JA. Treatment of canine nasal aspergillosis/penicilliosis with fluconazole (UK-49,858). *J Small Anim Pract*. 1991;32:513–516.

[24] Launcelott ZA, Palmisano MP, Stefanacci JD, Whitney BL. Ventricular pneumocephalus, cervical subarachnoid pneumorrhachis, and meningoencephalitis in a dog following rhinotomy for chronic fungal rhinitis. *J Am Vet Med Assoc*. 2016;248:430–435.

[25] Saunders JH, Zonderland J-L, Clercx C, et al. Computed tomographic findings in 35 dogs with nasal aspergillosis. *Vet Radiol Ultrasound*. 2002;43:5–9.

[26] Saunders JH, van Bree H, Gielen I, de Rooster H. Diagnostic value of computed tomography in dogs with chronic nasal disease. *Vet Radiol Ultrasound*. 2003;44:409–413.

[27] Sharman M, Lenard Z, Hosgood G, Mansfield C. Clotrimazole and enilconazole distribution within the frontal sinuses and nasal cavity of nine dogs with sinonasal aspergillosis. *J Small Anim Pract*. 2012;53:161–167.

[28] Burrow R, Baker M, White L, McConnell JF. Trephination of the frontal sinuses and instillation of clotrimazole cream: a computed tomographic study in canine cadavers. *Vet Surg*. 2013;42:322–328.

SUPPORTING INFORMATION

Additional Supporting Information may be found online in the supporting information tab for this article.

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