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JOURNAL TITLE: Journal of the American Veterinary Medical Association

VOLUME/EDITION: 250/3

PUBLISHER: American Veterinary Medical Association

PUBLICATION DATE: February 2017

DOI: 10.2460/javma.250.3.309

Topical treatment of mycotic rhinitis-rhinosinusitis in dogs with meticulous debridement and 1% clotrimazole cream: 64 cases (2007–2014)

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OBJECTIVE
To evaluate outcomes for dogs with mycotic rhinitis-rhinosinusitis (MRR) treated by meticulous debridement and topical application of 1% clotrimazole cream and investigate potential prognostic factors that could help predict whether 1 or multiple treatments would be needed for clinical resolution of the condition.

DESIGN
Retrospective case series.

ANIMALS
64 dogs.

PROCEDURES
Medical records were reviewed to identify dogs treated for MRR by meticulous debridement and topical application of 1% clotrimazole cream. Signalment, clinical signs, previous treatments, CT findings, presence of unilateral or bilateral disease, predisposing factors, number and type of treatments, and complications were recorded. Outcome information was obtained from records or by telephone interview with owners. Association of selected factors with the number of treatments needed for clinical resolution was evaluated.

RESULTS
Clotrimazole was instilled via the trephination site (n = 42) or under endoscopic guidance (22). Thirteen dogs underwent a 5-minute flush with 1% clotrimazole solution prior to cream application, and 34 received adjunctive oral itraconazole treatment. The MRR was deemed resolved in 58 dogs, and clinical signs persisted in 1 dog. Five dogs died (2 of causes unrelated to MRR) ≤ 1 month after treatment. The first treatment was successful in 42 of 62 (68%) dogs; overall success rate was 58 of 62 (94%). No prognostic factors for the number of treatments needed to provide clinical resolution were identified. Seven dogs with reinfection were successfully retreated.

CONCLUSIONS AND CLINICAL RELEVANCE
Topical treatment by meticulous debridement and 1% clotrimazole cream application had results similar to or better than those described in other studies of dogs with MRR. Trephination or adjunctive itraconazole treatment did not influence the number of treatments needed for a successful outcome. (*J Am Vet Med Assoc* 2017;250:309–315)

Mycotic rhinitis-rhinosinusitis, most commonly caused by *Aspergillus fumigatus*,[1] is a common cause of chronic nasal discharge in dogs.[2] Chronic mucopurulent nasal discharge, nasal pain, and ulceration and depigmentation of the nasal planum are typical clinical signs on evaluation; epistaxis might also be present.[3] Diagnosis is made on the basis of endoscopic visualization of fungal plaques in the nasal cavity, frontal sinuses, or both as well as results of a combination of further diagnostic tests such as CT, biopsy, fungal culture, cytologic examination, and serologic testing.[4] Orally and topically administered antifungal agents have been used to treat MRR with variable success. Clinical improvement was observed in 20 of 47 and 6 of 10 of dogs that were treated with oral antifungal agents.[5,6] Topical antifungal agents (enilconazole, clotrimazole, bifonazole) are available in various formulations (eg, creams or solutions with various concentrations of the active compounds). These are administered directly into the nasal cavity, frontal sinuses, or both through means such as surgically implanted indwelling catheters in the frontal sinuses,[7] temporary trephination of the frontal sinuses,[8–12] temporary frontal sinus catheters placed under endoscopic guidance,[13–15] or temporary catheters placed blindly

ABBREVIATIONS

HU	Hounsfield unit
MRR	Mycotic rhinitis-rhinosinusitis

into the nasal cavities.[8,11-14,16] Topical administration of antifungal agents is usually preceded by removal of fungal plaques and necrotic tissue. Although several treatment regimens have been described, an optimal treatment is unknown, and the disease course is often frustrating for clinicians and owners because multiple treatments can be necessary.[3]

The purpose of the study reported here was to retrospectively evaluate the outcomes for dogs that underwent treatment of MRR by meticulous debridement and instillation of clotrimazole cream with endoscopic guidance or through a trephination site. A second aim was to identify potential prognostic factors that could help to predict whether 1 or multiple treatments would be necessary for clinical resolution of the condition.

Materials and Methods

Case selection

Electronic medical records of a university veterinary teaching hospital (Small Animal Clinic, Justus-Liebig-University Giessen) and a veterinary referral hospital (Tierklinik Hofheim) were searched to identify dogs with a diagnosis of MRR that underwent treatment between September 28, 2007, and September 2, 2014. Each dog was included in the study only once. Dogs treated by meticulous debridement followed by application of 1% clotrimazole cream into the nasal cavities and frontal sinuses via trephination or via antegrade rhinoscopy were eligible for study inclusion. Dogs that received additional topical treatment by flushing with a 1% clotrimazole solution for 5 minutes, oral antifungal treatment, or both were included in the study. Dogs treated by soaking the affected region with clotrimazole solution for an hour were excluded.

Diagnosis of MRR was made on the basis of endoscopic visualization of fungal plaques in nasal cavities, frontal sinuses, or both, with associated nasal turbinate destruction.[13,17] Additional diagnostic procedures included CT, histologic examination of nasal biopsy samples, fungal culture, and cytologic examination of imprints of nasal biopsy samples, as determined by the attending clinician. The CT images were evaluated at the time of examination by a board-certified radiologist or national specialist in diagnostic imaging. In these reports, destruction of the turbinates with presence of abnormal soft tissue in the nasal passages, thickening of the mucosa, and hyperostosis or lysis of surrounding bone were considered suggestive of fungal rhinitis.[18] Frontal sinus involvement was suspected if mucosal thickening, presence of abnormal soft tissue within a frontal sinus, hyperostosis or lysis affecting frontal bones, or a combination of these findings was identified on CT images.[18]

Medical records review

Information obtained from medical records included signalment (age, breed, and sex), duration and types of clinical signs (eg, presence of unilateral or bilateral nasal discharge or epistaxis), previous treatments (corticosteroid or antimicrobial administration [including previous antifungal treatment]), CT findings (eg, involvement of frontal sinus or disruption of the cribriform plate), presence of unilateral or bilateral nasal disease (determined by evaluation of CT images, rhinoscopy findings, or both), and presence of any predisposing factors (eg, foreign body, previous head trauma, dental disease, or systemic immunosuppression). The number and type of topical clotrimazole treatments, type and dosage of antifungal medications administered orally after topical treatment (if applicable), complications attributed to treatment, and patient outcome (eg, number of treatments necessary until clinical resolution, persistence of mild serous nasal discharge after treatment, duration of follow-up, and whether reinfection was diagnosed) were also recorded.

Procedures

Computed tomography (when used) and rhinoscopy were performed in patients under general anesthesia. For analgesia, an opioid agent (eg, buprenorphine, methadone, or fentanyl), regional (infraorbital nerve) blockade with lidocaine, or both were provided. Dogs were placed in sternal recumbency. For CT, a helical CT scanner[a] (technical settings of 120 kV, 350 mA, and slice thickness of 2 mm) was used to obtain images of the affected region. The images were viewed with soft tissue (window level, 70 HUs; window width, 400 HUs) and bone (window level, 900 HUs; window width, 2,200 HUs) settings. Retrograde rhinoscopy was performed with a bronchoscope (5.2 mm × 85 cm)[b] or a rigid endoscope (4 mm × 18 cm; 120° view)[c] and followed by anterograde rhinoscopy with a multipurpose rigid endoscope (2.7 mm × 18 cm, 30° or 0° view)[d,e] or bronchoscope (3.0 mm × 100 cm or 5.2 mm × 85 cm).[b,f] Rhinoscopy, trephination, and treatment at the referral hospital were performed by one of the authors (CS). At the university teaching hospital, several clinicians with various experience levels performed the rhinoscopy and treatment procedures; however, this was supervised by one of the authors (RN).

After diagnostic rhinoscopy, most dogs treated at the university teaching hospital underwent trephination irrespective of evidence of frontal sinus involvement on CT. Rolled cotton gauze was placed in the pharynx, and trephination was performed midway between the zygomatic process of the frontal bone and 1 cm lateral to the midline with a 6-mm bone drill.

For dogs seen at the referral hospital, the decision to trephine the frontal sinuses was made on the basis of evidence of frontal sinus involvement on CT and endoscopic accessibility of the sinuses; in dogs with severe turbinate destruction, debridement of the frontal sinus was possible rhinoscopically with an antegrade approach. If the frontal sinus could not

be accessed via rhinoscopy in dogs that had frontal sinus involvement identified by CT, trephination was performed.

Any samples for cytologic or histologic examination or fungal culture were obtained prior to debridement and application of topical antifungal medication. The first part of the treatment consisted of meticulous debridement. If trephination was performed, fungal plaques were loosened with a curette and removed from the affected frontal sinus mostly by use of suction. The remaining material was flushed out through the nasal opening with copious amounts of balanced electrolyte solution (up to 5 L). If no trephination was performed, fungal plaques and necrotic material in the sinus were loosened with forceps under endoscopic guidance and then flushed out. Once there was no evidence of fungal material left in the frontal sinus, flushing and suction were continued in the nasal cavity. This procedure of flushing and suctioning, lasting up to 2 hours, was performed until all visible fungal material and necrotic tissue were removed.

Subsequently, 1% clotrimazole cream[g] was instilled via a 9F feeding tube[h] into each affected frontal sinus until cream could be seen leaking from the nares. Depending on the dog's size and head conformation, 30 to 100 mL of the cream was used for each sinus and nasal cavity. In some dogs, administration of the cream was preceded by a short flush with 1% clotrimazole solution[i] (50 mL in dogs weighing ≤ 20 kg [44 lb] and 100 mL in dogs weighing > 20 kg). The use of clotrimazole cream and clotrimazole solution for treatment of MRR in dogs was extralabel, because no product was licensed for this indication in Germany.

Some dogs received a course of oral antifungal agent administration beginning at the time of hospitalization for debridement and topical treatment. The decision of whether or not to treat systemically in addition to the topical treatment was made at the attending clinician's discretion.

Recheck rhinoscopy was performed 3 to 8 weeks after debridement and topical treatment to confirm resolution of MRR or to repeat treatment in dogs with persistent clinical signs and visible fungal plaques. Resolution of MRR was defined as absence of visible fungal plaques with no or negligible amounts of necrotic turbinate material present. The latter, if present, was nevertheless removed endoscopically. Some dogs that had follow-up rhinoscopy received an additional treatment with clotrimazole cream in the absence of visible fungal plaques if deemed appropriate by the attending clinician, on the basis of the knowledge that microscopic residual disease cannot be ruled out by endoscopic visualization. Because the additional treatment was not administered on the basis of the presence of visible fungal plaques, it was not included in calculations of the number of treatments necessary until clinical resolution.[11] In dogs that did not have follow-up rhinoscopy performed, MRR was considered to have resolved if no clinical signs or only mild serous nasal discharge was present for > 6 months[9] after the treatment on the basis of information collected from the owners by telephone. Reinfection was defined as recurrence of mucopurulent or hemorrhagic nasal discharge (or both) and the presence of fungal plaques on rhinoscopy ≥ 12 months after the initial infection was deemed resolved.

Statistical analysis

Distribution of the data was assessed by the Kolmogorov-Smirnov test; the data were found to be nonnormally distributed. The associations of various factors (patient age; duration of clinical signs; presence of unilateral or bilateral disease, epistaxis, or frontal sinus involvement; whether oral antifungal treatment was administered; whether trephination was performed; and the treating institution) with the number of treatments necessary until clinical resolution (1 vs > 1) were tested by the Mann-Whitney *U* test (for numeric variables) and Fisher exact test (for categorical variables). Values of $P < 0.05$ were accepted as significant. Commercially available statistical software[j] was used for all analyses.

Results

Eighty dogs (24 at the university teaching hospital and 56 at the referral hospital) were treated for MRR during the study period. Sixteen dogs (all treated at the referral hospital) were excluded because they were treated by methods other than those under evaluation. The median age of the 64 dogs included in the study was 5.2 years (range, 0.4 to 14.75 years). Forty-four were male and 20 were female. Forty-five were purebred dogs, with Golden Retriever (n = 8), German Shepherd Dog (4), and Labrador Retriever (3) being the most commonly represented breeds. Eighteen dogs were of mixed breeding, and the breed was not recorded for 1. Forty dogs had unilateral and 20 had bilateral nasal discharge, and for 4 dogs this information was not recorded. Thirty-eight dogs had epistaxis. Median duration of clinical signs was 2.5 months (range, 0.5 to 24 months).

In addition to rhinoscopic examination, procedures performed to confirm or support the diagnosis or further assess the extent of disease included CT (n = 62), histologic examination of nasal biopsy samples (35), fungal culture (30), and cytologic examination of imprints from nasal biopsy samples (19). The CT examination revealed evidence of unilateral MRR in 46 dogs, involvement of the frontal sinus in 41, and disruption of the cribriform plate in 8. Rhinoscopy was suggestive of unilateral MRR in 47 dogs. For 6 dogs, there was discordance between rhinoscopic and CT findings regarding the presence of unilateral or bilateral disease. The disease in these dogs was considered bilateral on the basis of evidence of bilateral involvement with one of the diagnostic modalities. For 3 dogs, fungal plaques were found unilaterally on rhinoscopy but typical turbinate destruction

was present bilaterally on CT, and the opposite findings were recorded for the remaining 3 dogs.

Possible predisposing factors were identified for 17 dogs. These included head trauma, dental disease, foreign body, and systemic immunosuppression or systemic immunosuppressive treatment. Head trauma was reported by the owners of 4 dogs, and supportive evidence was present on CT examination (eg, evidence of previous fractures) in all 4. Where dental disease was present and considered a possible predisposing factor (n = 4), it was treated as appropriate (eg, by tooth extraction). A foreign body (plant material) was identified on initial endoscopic evaluation in 4 dogs and removed in all 4. Immunosuppressive treatment was discontinued prior to examination at the university teaching hospital or referral hospital for 3 dogs, and for 1 dog, this was not possible owing to relapse of the immune-mediated disease (polyarthritis). One dog was found to be neutropenic, but the underlying condition was unknown.

Nine dogs had received oral antifungal treatments (itraconazole [n = 7] or ketoconazole [2]) prior to examination and treatment at the authors' institutions; these medications had been discontinued prior to evaluation. Seven dogs had previously received local treatment (soak with an antifungal agent [n = 5] or rhinotomy [2]).

Most (42/64 [66%]) dogs underwent trephination. Seven of these dogs had the procedure performed despite the lack of evidence of frontal sinus involvement on CT. Fungal plaques were not found in the sinuses in any of these dogs, but were present in the nasal cavities in all 7. Twenty-two dogs had no trephination performed because of either rhinoscopic accessibility of the frontal sinuses (n = 8) or lack of evidence of sinus involvement on CT (14). A short flushing procedure with 1% clotrimazole solution was performed for 13 dogs after trephination and prior to instillation of the 1% clotrimazole cream. Thirty-four dogs (5 treated at the university teaching hospital and 29 treated at the referral hospital) received a 3-month course of treatment with itraconazole (5 mg/kg [2.3 mg/lb], PO, q 24 h) beginning at the time of the first topical treatment.

Recheck rhinoscopy was performed for 50 dogs 3 to 8 weeks after the initial clotrimazole treatment. Resolution of MRR was confirmed in 32 of 50 dogs at that time (including 24 that received a follow-up clotrimazole cream treatment in the absence of visible fungal plaques). The remaining 18 dogs underwent repeated treatment at this visit because of persistent clinical signs and residual fungal plaques.

Overall, MRR was deemed resolved in 58 of 64 (91%) dogs; 9 of these 58 (16%) underwent flushing with clotrimazole solution prior to the cream instillation, and 49 (84%) did not. Resolution of the disease was confirmed with rhinoscopy for 38 dogs; 32 of these needed 1 treatment, 5 needed 2 treatments, and 1 needed 3 treatments. Resolution of the disease was reported on the basis of telephone interview with the owners for the remaining 20 dogs. Mild serous nasal discharge persisted after resolution of MRR in 20 dogs; 16 of these 20 had clinical resolution confirmed by follow-up rhinoscopy. Mucopurulent nasal discharge persisted in 1 dog, and 5 dogs died ≤ 1 month after the treatment, before resolution could be evaluated. Two dogs were reported to have died from conditions unrelated to the infection (splenic tumor and pancytopenia of unknown origin), and 3 died of conditions possibly associated with the disease or its treatment. Excluding the 2 dogs that died of unrelated causes, treatment was successful in 58 of 62 (94%) dogs overall. Forty-two of 58 (72%) dogs that were successfully treated required only 1 treatment for clinical resolution of the disease. Among successfully treated dogs, infection was deemed resolved after only 1 treatment for 5 of 9 dogs that received the combination of a brief clotrimazole solution flush and clotrimazole cream, compared with 37 of 49 (76%) of dogs with this outcome following treatment with the cream only. Use of the clotrimazole flush prior to the application of the cream was not significantly associated with the number of treatments required for clinical resolution of the infection **(Table 1)**. Furthermore, there were no significant differences between dogs that needed 1 versus ≥ 2 treatments in regard to age, duration of clinical signs, presence of unilateral versus bilateral disease, presence of epistaxis, additional systemic itraconazole treatment, frontal sinus involvement on CT, treatment approach through trephination, or institution where the treatment was performed.

The overall treatment complication rate was 12 of 64 (19%) when deaths possibly attributable to MRR or its treatment were included; the rate for non–life-threatening complications was 9 of 64 (14%). Most of the treatment complications were mild and temporary. Mild swelling was noted after trephination in 7 dogs, and 1 dog had an abscess at the trephination site necessitating surgical debridement. One dog developed aspiration pneumonia and recovered with antimicrobial treatment. Of the 3 dogs with deaths considered attributable to the fungal disease or treatment complications, 1 dog that initially improved after the sole treatment died suddenly after recurrence of nasal discharge within a few weeks. One dog with previous head trauma and seizures continued having seizures after the treatment and was euthanized. This dog had evidence of disruption of the cribriform plate and pneumocephalus identified by MRI at the time of initial examination. The third dog had severe epistaxis on the day after treatment that necessitated blood transfusion and was eventually euthanized.

One dog had persistent nasal discharge after 1 treatment, but further treatment was declined by the owner. This dog was subsequently euthanized because of persistent clinical signs and was categorized as having treatment failure.

Seven dogs had reinfection diagnosed a median of 18 months (range, 12 to 30 months) after treatment (or last treatment for dogs that needed > 1 treatment). All 7 dogs had received a 3-month course of itraconazole at the time of their initial treatment for MRR. The reinfection occurred on the same side of the nasal cavity in dogs with unilateral disease at the time of the first evaluation (n =

Table 1—Results of analysis for association of variables of interest with the number of topical treatments (1 vs > 1 application of 1% clotrimazole cream through a trephination site or by rhinoscopic methods) needed until clinical resolution of MRR in 58 dogs treated at 2 hospitals.

Variable	No. of treatments		*P* value
	1 (n = 42)	2–3 (n = 16)	
Age (y)	5.5 (0.4–14.75)	4.6 (0.5–12.5)	0.281
Duration of clinical signs (mo)	2.5 (0.5–24.0)	2 (0.5–18.0)	0.746
Epistaxis	23	12	0.359
Distribution			0.052
Unilateral disease	33	8	
Bilateral disease	9	8	
Frontal sinus involvement	28	10	0.642
Systemic treatment with itraconazole	23	9	1.0
Trephination	24	12	0.243
Brief clotrimazole flush	5	4	0.243
Treating institution			0.373
University teaching hospital	13	7	
Referral hospital	29	9	

Data are absolute values or median (range). Sixty-four dogs that underwent treatment by application of clotrimazole cream with or without a brief (5-minute) flush with 1% clotrimazole solution immediately prior to instillation of the cream were included in the retrospective study; 6 dogs were excluded from this analysis because the disease was not considered resolved (owing to persistent nasal discharge following treatment [n = 1] or death for MRR-related [3] or unrelated causes [2] ≤ 1 month after the initial treatment). Disease resolution was confirmed by follow-up rhinoscopy of 38 dogs and was concluded on the basis of information obtained in telephone interviews with the owners of 20 dogs.

6) and bilaterally in 1 dog with bilateral involvement on initial examination. In all 7 dogs, there was frontal sinus involvement in both episodes of infection. Five of these dogs had received 1 clotrimazole treatment before clinical resolution of the initial infection, and 2 had required ≥ 2 treatments before clinical resolution was achieved. Clinical resolution of the disease had been confirmed by rhinoscopy in 5 of these dogs. All 7 dogs with reinfection were successfully treated again.

Discussion

The present study identified a high success rate for the treatment of MRR by meticulous debridement and application of 1% clotrimazole cream. Most (42/62 [68%]) dogs had clinical resolution after only 1 treatment, and the overall success rate (including dogs that underwent 2 or 3 treatments) was 58 of 62 (94%) after exclusion of 2 dogs that died of causes unrelated to MRR or its treatment. This compares favorably to most previous reports of topical antifungal treatment in dogs for this condition, where success rates after the first treatment of 39 of 85 (46%) to 12 of 14 (86%) and overall success rates from 59 of 85 (69%) to 24 of 26 (92%) were found.[8–13,15] However, direct comparison of treatment success among these studies is difficult because of the variation in methods of outcome evaluation (eg, endoscopic examination, clinical reexamination, or telephone reports).

None of the pretreatment factors evaluated (patient age, duration of clinical signs, unilateral vs bilateral disease, presence of epistaxis, or frontal sinus involvement) or factors associated with treatment (access by trephination vs rhinoscopy, use of a 5-minute flush with 1% clotrimazole solution before application of the cream, oral itraconazole administration, or facility where the procedures were performed) significantly influenced the number of treatments needed for clinical resolution of MRR among dogs that had a successful outcome. Although clotrimazole solution might cause some chemical irritation of the mucosa and, in this way, possibly contribute to debridement, we did not identify any association between its use and the number of treatments required for clinical resolution. However, this result could have been attributable to the low number of dogs that received a 5-minute clotrimazole flush in the present study (9 for which treatment was successful). The main difference among the treatment protocols for individual dogs in this study was in the technique for accessing the frontal sinus. Trephination also did not influence the number of treatments necessary for resolution of the disease among dogs with successful outcomes. Importantly, no fungal plaques were found in frontal sinuses of 7 dogs that had trephination despite the lack of evidence of sinus involvement on CT. These findings suggest that trephination may not be needed in dogs without evidence of frontal sinus involvement on CT. Although trephination might enable better access to the frontal sinus, we do not consider this technique to be an essential part of the treatment as long as meticulous debridement and application of clotrimazole cream can be performed via endoscopic methods. In agree-

ment with others,[11,13,15] we regard debridement as an important part of the treatment. However, some investigators did not specify debridement as a part of their treatment protocols[9,10] and achieved treatment success rates comparable to those of our study. Only 1 preliminary report specifically addressed the importance of completeness of the debridement.[19] In that study,[19] a significantly higher percentage (22/28 [79%]) of dogs was cured with only 1 treatment when debridement was complete, compared with dogs that had incomplete debridement (8/20 [40%]). It could be argued that debridement prolongs anesthetic time; however, this potential disadvantage could be outweighed if its use might obviate further treatment. Additional research in this area is warranted.

Clotrimazole cream was chosen as the topical antifungal agent for dogs in the present study for a variety of reasons. The cream was previously shown to have good distribution in the nasal cavities and frontal sinuses of canine cadavers.[20,21] Prolonged retention of the cream was shown in a cadaver study,[20] whereas poor retention of the irrigation solution was found in client-owned dogs with MRR.[22] Prolonged retention would enable prolonged contact time of the antifungal agent with any residual fungal particles. It is currently unknown whether the contact time achieved by the application of clotrimazole cream yields results superior to those that can be achieved with an alternative method in which the affected region is soaked for 1 hour with the antifungal agent in solution. However, with the latter treatment, the anesthetic time would be approximately 1 hour longer than that needed for instillation of the cream under endoscopic guidance or after trephination. Considering the substantial amount of time that might have already been spent on debridement prior to the application of the antifungal agent, choosing a faster method might be preferable, especially in older or debilitated dogs.

Younger dogs were identified as having a greater chance of treatment success in a previous study.[12] In that same study,[12] there was no significant association between frontal sinus involvement or duration of clinical signs and treatment success. In the present study, none of these factors were significantly associated with the number of treatments (1 vs 2 or 3) needed for clinical resolution in the 58 dogs that had a successful outcome. Adjunctive treatment with orally administered antifungal agents was associated with treatment failure in the aforementioned study,[12] but our study found no association between adjunctive treatment with oral itraconazole administration and the number of treatments until clinical resolution. Oral itraconazole treatment did not prevent reinfection in the present study; all 7 dogs that had reinfection received oral itraconazole at the time of their initial clotrimazole treatment. The limited effect of systemic antifungal treatment likely reflects the histologic findings associated with MRR, indicating that fungal elements are found on the mucosal surface rather than invading the mucosa.[23]

Mild swelling and abscess formation at the trephination site occurred in the present study and in previous studies[8,10]; however, in general, the treatment was well tolerated. One dog in our study developed severe epistaxis the day after treatment necessitating a blood transfusion, and was eventually euthanized. It cannot be ruled out that the epistaxis was associated with the treatment, but it was considered unlikely given that this did not occur during or immediately after the treatment. Severe epistaxis was reported[13] in 2 dogs treated by infusion and soaking of affected nasal passages with enilconazole; however, this occurred immediately after removal of the nasal catheters used for the treatment.

Persistence of mild serous nasal discharge, occasional sneezing, or both was reported in approximately half (9/20 and 14/27) of successfully treated dogs in 2 studies,[9,14] and mild serous nasal discharge was identified in 20 of 58 (34%) dogs in the present study. Irreversible turbinate destruction predisposing the dogs to develop bacterial rhinitis and persistent lymphoplasmacytic rhinitis after successful treatment of MRR have been discussed as possible reasons for these mild persistent signs.[14]

Reinfection was identified in 7 successfully treated dogs in the present study. The reinfection rate (7/58 [12%]) was similar to results of previous reports in which 3 of 15 (20%) and 3 of 27 (11%) dogs, respectively, had recurrence of MRR.[11,14] Although the same side of the nasal cavity was affected at the time of recurrence and persistence of fungal disease could not be completely ruled out, it was considered less likely given the time interval between the last treatment and recurrence of clinical signs. It has been suggested that turbinate destruction could make the nasal cavity more susceptible to reinfection.[11] All 7 dogs that had reinfection in this study, as well as 3 of 3 dogs described in another report,[11] had frontal sinus involvement. However, it is unclear whether this finding has clinical relevance.

A major limitation of this study was its retrospective character, which caused some data to be missing. Considering the study design and inclusion of dogs from 2 hospitals, the treatments might not have been uniform in all dogs. Performing trephination in some but not all dogs with frontal sinus involvement could have been a source of bias. Furthermore, treatments performed at the university teaching hospital might not have been completely standardized because several clinicians with various degrees of experience performed the treatments, although the procedure was supervised by one of the authors (RN). As there was no standardized way of describing rhinoscopic findings and the treatment procedure itself, it was not always possible to evaluate the extent and severity of MRR, which might have influenced treatment outcome. Another limitation was that the resolution of MRR was not confirmed rhinoscopically in 20 of 58 (34%) dogs that were deemed to have successful treatment. However, removing dogs without endoscopic reassessment had no influence on the results

of the statistical analysis (data not shown). Furthermore, even in dogs that had follow-up rhinoscopy performed, no culture or histologic evaluation of nasal biopsy specimens was performed to confirm resolution of MRR. This might have been particularly important in dogs with small amounts of necrotic turbinate material present on follow-up endoscopy. In these dogs, necrotic material was visually differentiated from fungal plaques on the basis of the premise that necrotic parts of the turbinates can be easily separated from the mucosa by touching with the endoscope or forceps. However, culture or histologic examination of what was considered necrotic material from these patients might have enabled more reliable differentiation than visual inspection. Although unlikely, if fungal particles were mistaken for necrotic material, the application of clotrimazole cream at the follow-up endoscopy would have been necessary to achieve resolution of the disease and would have to be calculated in the number of treatments needed for this outcome. In this case, the 7 dogs that had negligible amounts of necrotic material on follow-up rhinoscopy would have been considered successfully treated after 2 treatments, rather than 1 treatment.

Overall, topical treatment by meticulous debridement and application of 1% clotrimazole cream either via a trephination site or endoscopically into the affected frontal sinuses and nasal cavities had a successful result in most dogs after the first treatment. The overall success rate (58/62 [94%]) was considered excellent, and the treatment was well tolerated in most dogs.

Acknowledgments

The study was not supported by a grant.

The authors declare that there were no conflicts of interest.

Presented as an oral abstract at the 23rd Annual Meeting of Internal Medicine and Clinical Pathology Specialists, Leipzig, Germany, January 2015.

Footnotes

a. CT scanner Brilliance 16, Philips Healthcare, Best, The Netherlands.
b. Broncho-Fiberscope, catalogue No. 60001 VL1, Karl Storz, Tuttlingen, Germany.
c. HOPKINS II Retrograde Telescope 120°, Karl Storz, Tuttlingen, Germany.
d. HOPKINS II Straight Forward Telescope 0°, Karl Storz, Tuttlingen, Germany.
e. HOPKINS II Forward-Oblique Telescope 30°, Karl Storz, Tuttlingen, Germany.
f. Broncho-Fiberscope, Karl Storz, Tuttlingen, Germany.
g. Canesten Crème, Bayer, Leverkusen, Germany.
h. Feeding tube, B. Braun, Melsungen, Germany.
i. Fungizid Pumpspray, Ratiopharm, Ulm, Germany.
j. SPSS, version 22.0, IBM, Armonk, NY.

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