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Sinonasal mycosis following transfrontal craniotomy in three dogs

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CASE DESCRIPTION
Three dogs were presented for investigation of chronic nasal discharge and epistaxis 141, 250, and 357 days after undergoing transfrontal craniotomy to treat an intracranial meningioma (2 dogs) or a meningoencephalocele (1 dog).

CLINICAL FINDINGS
CT findings were consistent with destructive rhinitis and frontal sinusitis in all 3 dogs, with results of histologic examination and fungal culture of samples obtained during frontal sinusotomy confirming mycotic infection. Frontal sinusotomy revealed fungal plaques covering a combination of bone and residual surgical tissue adhesive at the site of the previous craniotomy in all 3 dogs. *Aspergillus* spp were identified in all 3 dogs, and *Chrysosporium* sp was also identified in 1 dog.

TREATMENT AND OUTCOME
Surgical curettage was followed by antifungal treatment (topical clotrimazole in 2 dogs and oral itraconazole for 3 months in 1 dog). Nasal discharge improved in the short-term but recurred in all dogs 99, 118, and 110 days after frontal sinusotomy. One dog received no further treatment, 1 dog received an additional 8.5 months of oral itraconazole treatment, and 1 dog underwent 2 additional surgical debridement procedures. At last follow-up, 2 dogs were alive 311 and 481 days after frontal sinusotomy; the third dog was euthanized because of status epilepticus 223 days after frontal sinusotomy.

CLINICAL RELEVANCE
Sinonasal mycosis should be considered as a potential complication in dogs developing persistent mucopurulent nasal discharge, intermittent epistaxis, and intermittent sneezing following transfrontal craniotomy. The pathophysiology may be multifactorial, and potential risk factors, including use of surgical tissue adhesive in the frontal sinus, require further investigation.

A 12-year-old 27-kg neutered male Airedale Terrier (dog 1) was evaluated at the Small Animal Referrals Hospital at the Royal Veterinary College (SARH-RVC), London, England, for investigation of mucopurulent nasal discharge with intermittent mild epistaxis of 26-weeks' duration. The dog had undergone transfrontal craniotomy 56 months prior to this presentation for resection of a right-sided frontal lobe meningioma that had been causing seizures. A modified bilateral transfrontal approach had been performed, as described previously.[1] Briefly, an oscillating saw was used to make a diamond-shaped external frontal bone flap overlying the frontal sinus. Sinus septa and ethmoturbinates were removed with rongeurs, and a pneumatic drill with a round burr was used to access the dura mater underlying the internal table of the frontal bone. After a durotomy was performed, the mass was removed with careful blunt dissection and use of an ultrasonic aspirator. A swab sample was collected from the frontal sinus for aerobic and anaerobic bacterial culture and antimicrobial susceptibility testing. The dura mater was closed with an autologous graft of temporalis muscle fascia that was secured to the edges of the defect with a cyanoacrylate surgical tissue adhesive (Histoacryl; B. Braun Medical Ltd). The external frontal bone flap was replaced and secured with size-0 synthetic non-absorbable monofilament polypropylene suture material (Prolene; Johnson & Johnson Medical Ltd) passed through holes predrilled into the bone flap and adjacent external table of the frontal bone with a 2-mm burr. Bone wax (S.M.I. AG) was placed to fill all gaps on the periphery to make the seal airtight. The periosteum and subcutaneous tissues were closed with synthetic absorbable monofilament suture material (PDS Plus Antibacterial; Johnson & Johnson Int), and the skin was closed routinely. Histologic examination of

the excised frontal lobe mass confirmed a diagnosis of grade I transitional meningioma.

The dog recovered well from the transfrontal craniotomy procedure, but 3 weeks after surgery, it developed intermittent sneezing and an increased frequency of swallowing. There was a partial response to amoxicillin–clavulanate (19.6 mg/kg, PO, q 12 h for 10 days), after which the swallowing was deemed self-limiting as it occurred predominantly in the evening and no more than once daily. A second course of amoxicillin–clavulanate (18.8 mg/kg, PO, q 12 h for 15 days) was administered 3 months later because increased swallowing recurred, and fenbendazole (53 mg/kg, PO, q 24 h for 5 days) was also prescribed. No nasal discharge was reported at this time, and following this treatment, the frequency of swallowing reduced to once every 14 days.

Eleven months after the transfrontal craniotomy procedure, the dog began shaking its head and again had an increased frequency of swallowing. CT imaging demonstrated that the external frontal bone flap had displaced into the frontal sinus **(Figure 1)**, and the dog underwent frontal sinusotomy to remove the necrotic bone flap 12 months after the initial surgery, with the soft tissues and skin closed routinely without a replacement for the bone flap. Swab samples from the frontal sinus at this time yielded profuse growth of *Pseudomonas aeruginosa* and *Enterococcus faecium*. After a 5-week course of enrofloxacin (19.4 mg/kg, PO, q 12 h), the sneezing stopped, and all associated clinical signs had resolved at a reexamination 6 months later.

The dog was again examined 44 months after the transfrontal craniotomy procedure because of a recurrence of seizures. CT imaging of the skull revealed regrowth of the transitional meningioma as well as a smaller, extra-axial, left-sided parietal lobe mass. A second transfrontal craniotomy was performed to excise the parietal lobe mass and debulk the frontal lobe meningioma. To access the parietal mass, a pneumatic drill with a round burr was used to enlarge the previous surgical site. Prior to durotomy, all previous cyanoacrylate surgical tissue adhesive appeared grossly normal and was removed. A temporalis muscle fascia graft from the opposite side was used to close the dura mater and was sealed with the same cyanoacrylate surgical tissue adhesive. Routine closure of the soft tissues and skin overlying the frontal sinus was performed in the absence of a bone flap.

Histologic examination of the parietal lobe mass revealed a grade I psammomatous meningioma; examination of the recurrent frontal lobe mass matched the previous diagnosis of a grade I transitional meningioma. No fungal plaques were visible intraoperatively, and aerobic and anaerobic bacterial culture and antimicrobial susceptibility testing of a frontal sinus swab sample obtained at the time of surgery yielded *Staphylococcus pseudointermedius* and *Escherichia coli*. The dog was administered amoxicillin–clavulanate (18.8 mg/kg, PO, q 12 h for 14 days); no nasal discharge was noted postoperatively.

Two months after the second transfrontal craniotomy, the dog started sneezing and developed a mucopurulent nasal discharge. Temporary resolution was achieved with 3 separate courses of amoxicil-

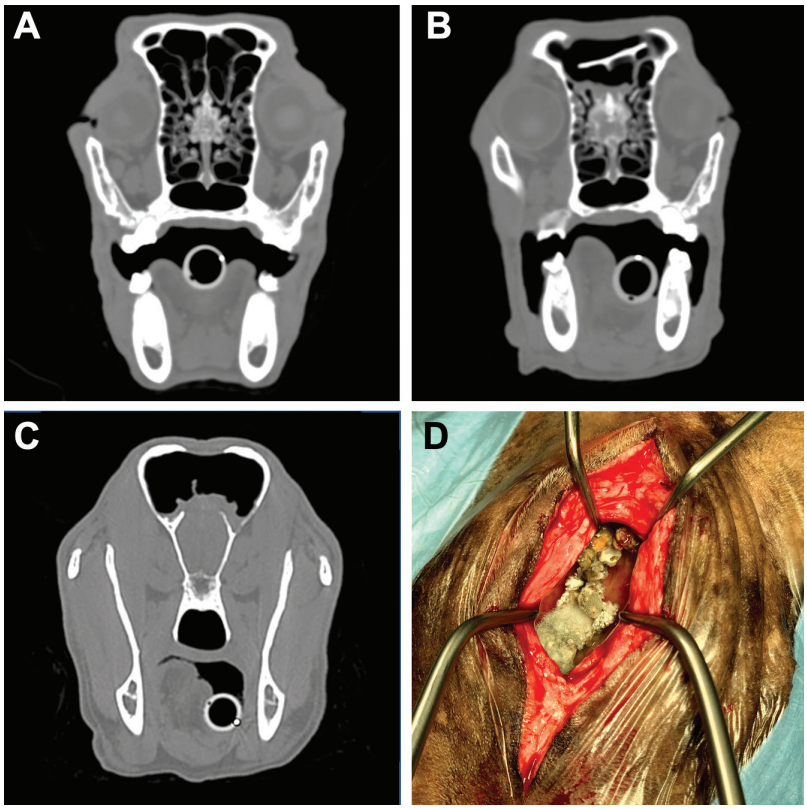

Figure 1—Transverse CT images viewed in bone windows (A through C) and an intraoperative photograph (D) of a 12-year-old Airedale Terrier (dog 1) that underwent transfrontal craniotomy for resection of a right-sided frontal lobe meningioma and 56 months later was examined because of mucopurulent nasal discharge with intermittent epistaxis. A—On a CT image acquired before the transfrontal craniotomy, bony septa within the frontal sinus appear intact. B—Eleven months after the transfrontal craniotomy, there is displacement of the external frontal bone flap into the frontal sinus and iatrogenic loss of the bony architecture; frontal sinusotomy was performed to remove the necrotic bone flap. C—Forty-four months after the transfrontal craniotomy, there was ventral accumulation of soft tissue–attenuating material within the frontal sinus overlying the defect in the internal table of the frontal bone. D—During a frontal sinusotomy 56 months after the original transfrontal craniotomy, a large green-white fungal plaque could be seen peripherally around the edges of the fascial graft overlying the internal table defect and appeared to be attached to the cyanoacrylate surgical tissue adhesive that had been used to hold the graft in place.

lin–clavulanate (13.9 mg/kg, PO, q 12 h for 14 days and for 35 days and 18.5 mg/kg, PO, q 12 h for 15 days) and a single course of doxycycline (11.1 mg/kg, PO, q 24 h for 10 days). After approximately 20 weeks, the mucopurulent discharge was bilateral and had developed a hemorrhagic appearance, with streaks of blood appearing intermittently. Hematologic testing revealed mild monocytosis (1.7 X 10^9 cells/L; reference interval, 0.15 to 1.5 X 10^9 cells/L), and serum biochemical testing revealed moderate hypoalbuminemia (17.9 g/L; reference interval, 26.3 to 38.2 g/L) and slightly high inorganic phosphorus (1.93 mmol/L; reference interval, 0.8 to 1.6 mmol/L) and cholesterol (8.96 mmol/L; reference interval, 3.2 to 6.2 mmol/L) concentrations and amylase (1,632 U/L; reference interval, 100 to 1,200 U/L) and alkaline phosphatase (352 U/L; reference interval, 0 to 130 U/L) activities. Results of a bile acid stimulation test and urine protein-to-creatinine concentration ratio were both normal.

Multiphase CT imaging of the head revealed a ventral accumulation of soft tissue–attenuating material in the frontal sinus, overlying the defect in the internal table of the frontal bone (Figure 1). There was also evidence of maxillary turbinate destruction, along with regrowth of the intracranial meningiomas. Rhinoscopy performed under general anesthesia identified mucus in both nasal cavities but no visible fungal plaques. Blind nasal biopsies were performed, and histologic examination revealed multifocal, moderate lymphoplasmacytic rhinitis with submucosal edema and a suppurative exudate.

Owing to the clinical suspicion of sinonasal mycosis, frontal sinusotomy was performed, revealing a large green-white plaque within the combined frontal sinus (Figure 1). The plaque was distributed peripherally around the edges of the fascial graft overlying the internal table defect and appeared to be attached to the cyanoacrylate surgical tissue adhesive. During sinusotomy, the abnormal material was removed by gentle curettage. The sinuses were flushed with copious volumes of warm saline (0.9% NaCl) solution, and 200 mg of clotrimazole 1% solution (Canesten Solution; Bayer) was instilled in the frontal sinuses. Prior to closure of the overlying soft tissues, 400 mg of clotrimazole 1% cream (Canesten Antifungal Cream; Bayer) was deposited in the frontal sinus. Fungal culture of the plaque yielded *Aspergillus fumigatus* complex and an isolate from the genus *Chrysosporium*.

Dog 1 was reexamined 118 days after sinonasal mycosis had been diagnosed because of recurrence of the nasal discharge. The discharge resolved without treatment within 2 weeks. The dog was euthanized because of status epilepticus 223 days after sinonasal mycosis had been diagnosed.

A 9-year-old 43-kg spayed female crossbreed dog (dog 2) was presented for investigation of a 2-week history of bilateral mucopurulent nasal discharge with intermittent mild epistaxis. The discharge had developed 12 months after transfrontal craniotomy at the SARH-RVC for resection of a right-sided frontal lobe meningioma. A modified bilateral transfrontal approach had been performed, following the same technique as described for dog 1 with the exception that the external frontal bone flap was not replaced. Recovery had been uncomplicated. The discharge partially improved with administration of doxycycline (10.5 mg/kg, PO, q 24 h for 10 days).

At the time of presentation for nasal discharge, hematologic testing revealed no abnormalities, and serum biochemical testing revealed mild hypoalbuminemia (25.1 g/L; reference interval, 26.3 to 38.2 g/L), high cholesterol concentration (10.42 mmol/L; reference interval, 3.2 to 6.2 mmol/L), and high alkaline phosphatase activity (845 U/L; reference interval, 0 to 130 U/L). Rhinoscopy, histologic examination of nasal biopsy samples, and fungal culture of the mucopurulent nasal discharge did not identify fungal organisms. Results of serologic testing for *Aspergillus* spp (Axiom Veterinary Laboratories Ltd) were positive, indicating exposure to the fungus. CT imaging of the skull revealed bilateral nasal turbinate lysis and a broad-based heterogeneously contrast-enhancing soft tissue density overlying the floor of the frontal sinus. Additionally, an extra-axial homogeneously contrast-enhancing frontal lobe mass consistent with either residual or recurrent meningioma was identified.

Owing to the CT findings suggestive of destructive sinonasal disease, frontal sinusotomy was performed, revealing a large, gray-brown fungal plaque in the combined frontal sinus **(Figure 2)**. As in dog 1, the abnormal material appeared to overlie the defect

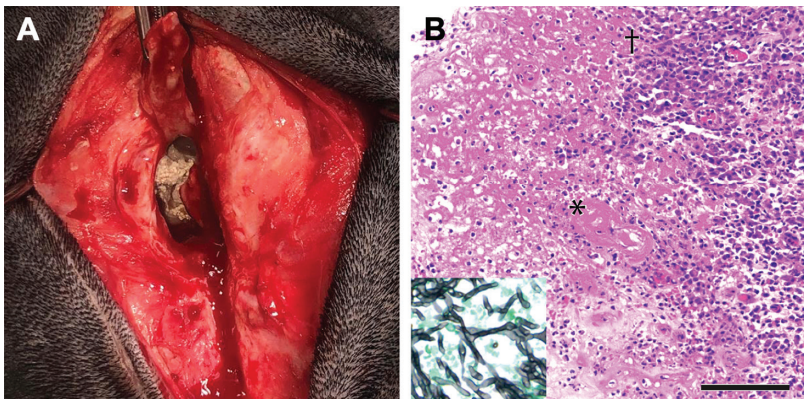

Figure 2—Photograph acquired during frontal sinusotomy of 9-year-old crossbreed dog (dog 2) with a 2-week history of bilateral mucopurulent nasal discharge with intermittent mild epistaxis that developed 12 months after transfrontal craniotomy (A), and a photomicrograph of biopsy tissue obtained during the sinusotomy (B). A—A large gray-brown fungal plaque can be seen overlying the site of the transfrontal craniotomy performed 12 months previously. B—Histologic examination revealed marked necrosuppurative inflammation (asterisk) with adjacent dense lymphoplasmacytic infiltrates (dagger); H&E stain; bar = 200 µm. Inset—Intralesional fungal hyphae with parallel walls and dichotomous branching can be seen. Grocott stain.

in the internal table of the frontal bone and was associated with the cyanoacrylate surgical tissue adhesive. During sinusotomy, all grossly abnormal material and surgical tissue adhesive was removed by gentle curettage, along with sections of necrotic turbinate bone. The periosteum and subcutaneous tissues were closed with synthetic absorbable monofilament suture material, and the skin was closed routinely. Fluconazole solution (200 mg; Fresenius Kabi Ltd) was instilled once daily for 4 days into the frontal sinus via an indwelling catheter. On the fifth day of treatment, clotrimazole 1% cream (200 mg) was deposited in the sinus, and the catheter was removed.

Fungal culture of the plaque yielded *Aspergillus fumigatus*, and histologic examination of the plaque and necrotic bone demonstrated marked necrosuppurative and lymphoplasmacytic sinusitis with intralesional fungal hyphae (Figure 2). Six weeks later, the discharge was reported to be intermittent, bilateral, and clear.

Four months after sinusotomy, the dog was reexamined because of a 1-week history of bilateral mucopurulent nasal discharge. Frontal sinusotomy was performed without further diagnostic testing. The right side of the frontal sinus again contained fungal plaques, and the left side contained smooth pink tissue consistent with granulation tissue. Both the fungal plaques and granulation tissue were removed, after which the frontal sinuses and nasal chambers were copiously flushed bilaterally with saline solutions. The nares were each occluded with the bulb of a Foley catheter to enable soaking of the nasal chambers and frontal sinuses for 30 minutes with clotrimazole 1% solution (600 mg), after which time clotrimazole 1% cream (400 mg) was instilled.

After initial resolution of the discharge, the bilateral mucopurulent nasal discharge recurred again 10 weeks later, at which time the dog underwent a third frontal sinusotomy procedure. Fungal plaques were again debrided, followed by copious flushing with saline solution. An indwelling 10F Foley catheter was placed in the combined frontal sinus, and indwelling 8F Foley catheters were placed in the middle portion of the right and left nasal cavities. The frontal sinus catheter and each nasal catheter were infused with clotrimazole 1% solution (200 mg and 100 mg, respectively). For the next 4 days, all 3 indwelling catheters were thoroughly flushed with saline solution and clotrimazole 1% solution was again infused. On the fifth day of treatment, clotrimazole 1% cream (400 mg) was infused into the sinus catheter prior to the removal of all 3 catheters.

Six weeks following this procedure, the nasal discharge recurred. At this time, given the ongoing recurrence of clinical signs and quality of life concerns, a decision was made to not perform further invasive treatment and to euthanize the dog if its condition deteriorated. At last follow-up 481 days after the diagnosis of sinonasal mycosis was first made, the dog was alive with persistent purulent nasal discharge considered refractory to treatment and infrequent seizures that were controlled with phenobarbital (2.1 mg/kg, PO, q 12 h).

A 3-year-old 30-kg sexually intact male Tamaskan dog (dog 3) was presented to the IVC Evidensia Referral Hospital in Helsingborg, Sweden, with a 3-week history of unilateral mucopurulent nasal discharge. The dog had undergone transfrontal craniotomy for resection of an ethmoidal meningoencephalocele and closure of the defect 5 months earlier, having initially been examined because of generalized seizures. A modified bilateral transfrontal approach was performed as described for dog 1, with the frontal bone flap replaced.

Four months after surgery, the dog was reported to be sneezing with increased frequency in addition to rubbing its muzzle. Five weeks after this, the dog was reported to have developed a mucopurulent nasal discharge with an intermittent, hemorrhagic component. At this time, cytologic examination of the discharge showed a mixed population of bacteria, and broad-spectrum antimicrobial treatment was initiated with amoxicillin–clavulanate (12.5 mg/kg, PO, q 8 h for 6 days).

Owing to ongoing nasal discharge, CT imaging of the skull was performed, which revealed marked bilateral nasal turbinate lysis with irregular regions of soft tissue–attenuating material, in addition to depression of the frontal bone flap. Results of serologic testing for *Aspergillus* spp (NationWide Laboratories; Microgen Bioproducts Ltd) were negative. A frontal sinusotomy was performed, which identified 2 loose pieces of bone coated in gray-green fungoid material **(Figure 3)** within the sinus cavity as well as purulent material on the floor of the sinus. Dur-

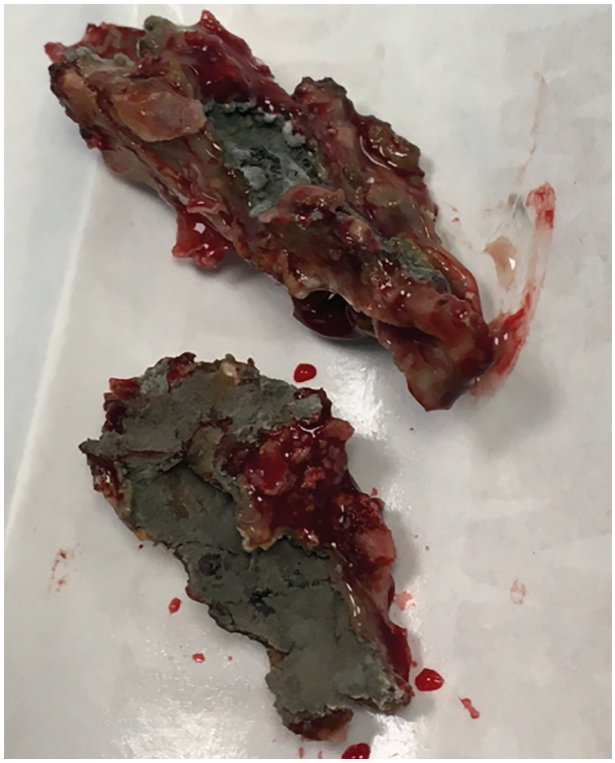

Figure 3—Photograph of 2 bone fragments coated in gray-green fungal material removed during frontal sinusotomy in a 3-year-old Tamaskan dog (dog 3) with a 3-week history of chronic mucopurulent nasal discharge 5 months after undergoing transfrontal craniotomy.

ing frontal sinusotomy, the depressed frontal bone flap, loose bone fragments, and cyanoacrylate surgical tissue adhesive were removed. The frontal sinus was flushed with copious volumes of saline solution. Histologic examination revealed marked necrosuppurative sinusitis with intralesional fungal hyphae. Cytologic examination revealed conidia consistent with *Aspergillus* spp. Bacterial culture yielded *Enterobacter aerogenes*.

Following surgery, the dog was treated with itraconazole (6.7 mg/kg, PO, q 12 h for 3 months). Clinical signs initially improved, with all sneezing and discharge resolving after 4 weeks. However, 2 days after cessation of itraconazole, sneezing recurred, and consequently, treatment was reinitiated at the previous dosage for an additional 4.5 months after which the dosage was tapered by 25% of the original dosage each month. Serum biochemical testing was performed 1 and 4 months after initiation of itraconazole treatment, with no abnormalities documented. Repeated CT imaging of the skull 7 months after frontal sinusotomy revealed resolution of previous soft tissue–attenuating material, and the destructive rhinitis appeared static with respect to the degree of turbinate destruction. Cytologic and histologic examination of samples obtained via rhinoscopy did not reveal any fungal organisms.

At last follow-up 311 days after the diagnosis of sinonasal mycosis had been made, there was no recurrence of clinical signs, and the dog was receiving the final dosage of itraconazole (3.3 mg/kg, PO, q 24 h for 1 month). The frequency of seizures had remained unchanged from the frequency prior to transfrontal craniotomy, and the dog was being treated with phenobarbitone (8.3 mg/kg, PO, q 12 h) and potassium bromide (10.8 mg/kg, PO, q 12 h). Higher dosages of anticonvulsant medications were declined by the owner owing to excessive adverse effects.

Discussion

Transfrontal craniotomy, by allowing an approach through the internal table of the frontal bone, enables surgical access to the structures of the rostrodorsal aspect of the cranial cavity.[1] Common indications for this surgical approach include intracranial mass resection and tissue biopsy in the region of the frontal lobes and olfactory bulbs.[2] The main limitation of earlier surgical techniques was restricted surgical access to the frontal lobes and olfactory bulbs,[3,4] but a more recent technique described by Glass et al[1] that uses a modified bilateral transfrontal approach provides greater visualization of these structures while sparing the cribriform plate. Regardless of the specific technique used, surgical access involves exposure of the surgical field to commensal microbes of the frontal sinus. Previously reported complications following transfrontal craniotomy in dogs include surgical site infection, subcutaneous emphysema, aspiration pneumonia, meningeal defects leading to rhinorrhea, post-operative seizures, tension pneumocephalus, and neurologic deterioration.[4–7] There is a single report[3] of a surgical site abscess causing persistent nasal discharge; however, to our knowledge, the present clinical report was the first to describe the development of sinonasal mycosis following transfrontal craniotomy in dogs.

Sinonasal mycosis is a broad term referring to fungal infections of the sinus and nasal cavities. The most commonly encountered fungal genus is *Aspergillus*,[8] which was identified in all 3 dogs in the present report. A provisional diagnosis of sinonasal mycosis was achieved through a combination of clinical signs, diagnostic imaging, and serologic testing. Confirmation of the diagnosis was made following frontal sinusotomy, with visualization of fungal plaques and subsequent fungal culture. *Aspergillus* serologic testing was performed in 2 dogs, with result being negative in 1 (dog 3). Given the fungal culture and histologic findings in dog 3, however, the negative serologic result likely represented a false-negative result, and a low test sensitivity has previously been reported.[9]

In dog 1, an isolate belonging to the *Chrysosporium* genus was also cultured. This fungal genus has been infrequently reported in the veterinary literature, with disseminated,[10,11] dermatotropic,[12] and ocular forms[13] having been described. *Chrysosporium* infection of the sinonasal cavities has been reported once previously in the human literature[14] but not, to our knowledge, in dogs.

Previously reported clinical signs associated with sinonasal mycosis in dogs include mucopurulent nasal discharge, sneezing, nasal planum depigmentation and ulceration, epistaxis, nasal pain, and, in severe cases, facial deformity.[15] In the 3 dogs in the present report, only mucopurulent nasal discharge, sneezing, and intermittent mild epistaxis were observed, which may all be considered non-specific signs of sinonasal disease, as opposed to specifically indicating mycosis. The absence of other characteristic clinical signs, such as epistaxis, may reflect differences in the underlying anatomy as a result of the prior transfrontal craniotomy. We speculate that surgical removal of vascular bony structures such as ethmoturbinates and associated mucosa from the frontal sinuses and nasal cavity may have reduced the tendency to develop epistaxis in these dogs.

Routine serum biochemical testing revealed mild to moderate hypoalbuminemia and increased alanine phosphatase activities in dogs 1 and 2 in the present report; however, the cause of these changes was not identified. Hypoalbuminemia is the most frequently documented abnormality in dogs with systemic blastomycosis and histoplasmosis,[16] but dogs with sinonasal mycosis often do not have systemic signs.[17] Although an immunodeficiency is not believed to underlie sinonasal mycosis, it is possible that an impaired local or systemic immune response may be involved to some extent.[18] Still, the etiopathogenesis of sinonasal aspergillosis is yet to be fully elucidated, with alternative predisposing factors occasionally reported such as nasal foreign bodies and facial trauma,[8] suggesting that a multifactorial pathogenesis underlies opportunistic overgrowth of these ubiquitous fungi. It is also important to note that middle-aged, mesaticephalic and dolichocephalic dogs, such as those included in the present report, are overrepresented in reports of sinonasal aspergillosis.[15,19]

Transfrontal craniotomy irreversibly alters the local anatomy, with the bony septa and caudal extent of the ethmoturbinates removed to allow access the inner table of the frontal sinus.[1] Disruption of this architecture might impact the efficacy of mucociliary

clearance, which forms a key part of the innate immune defense, increasing the risk of fungal infection.[15] Because of their complex and fragile structure, resection of the turbinates could lead to the inadvertent creation of sequestra. Sequestra were found in the frontal sinuses of all 3 dogs in the present report. In the 2 dogs that had the external table of the frontal bone replaced following frontal sinusotomy, the bone flap itself was displaced into the frontal sinus postoperatively. This suggests a failure of the anchorage system involving suture material and burred holes and may provide support for non-replacement of the bone flap as in dog 2 or the use of alternative techniques, such as a recently described rivet-like titanium clamp system.[20] The sinus anatomy was further altered in the dogs in the present report through the use of an autologous temporalis muscle fascial graft and surgical tissue adhesive to seal the cranial cavity and durotomy.

At the time of sinusotomy and debridement, fungal plaques in the sinus were centered on the craniotomy site in dogs 1 and 2 and followed the distribution of the peripherally located surgical tissue adhesive. The use of surgical tissue adhesives such as cyanoacrylate glue in the frontal sinuses of dogs has not previously been evaluated. However, in the human literature there is a recent case report[21] of cyanoacrylate glue causing chronic rhinosinusitis following a transsphenoidal hypophysectomy, although microbial culture was not performed. The antibacterial effect of cyanoacrylate has been described previously,[22] and it is possible that cyanoacrylate may have a local effect on the commensal microbiota of the sinus cavity and provide a potentially suitable surface for fungal colonization. However, an in vitro study[23] showed that cyanoacrylate reduced *Candida* biofilm formation on acrylic dental resins.

Still, regardless of any antimicrobial effects the surgical tissue adhesive may have had, its physical contribution to the abnormal sinus environment, along with the findings in the dogs of the present report, raises concerns regarding its use in the frontal sinus during transfrontal craniotomy in dogs. Further investigation into the use of surgical tissue adhesives in the frontal sinuses of dogs would be useful to establish the wider relevance of the findings for the 3 dogs in the present report.

Similarly, it is conceivable that perioperative antimicrobial administration may destabilize the commensal sinus microbiota. A pilot study[24] in mice demonstrated that antimicrobial-mediated sinus microbe depletion augmented the pathogenicity of otherwise commensal bacteria. However, a recent study[25] found that antimicrobial administration had no impact on overall human sinus microbiome diversity in healthy and diseased patients. The impact of perioperative antimicrobial administration on the sinus commensal microbial population in dogs has not been reported, to our knowledge.

The creation of abnormal sinus anatomy during transfrontal craniotomy created challenges to the diagnosis of sinonasal mycosis in the dogs in the present report. Although a provisional diagnosis of sinonasal mycosis can typically be made in dogs on the basis of clinical signs and results of diagnostic testing, including endoscopy, biopsy, and serologic testing, characteristic CT imaging findings are the most supportive.[26] On CT imaging, a destructive pattern of the nasal turbinates may indicate mycosis. However, with resection of the sinus septa and ethmoturbinates during transfrontal craniotomy, this sentinel anatomy is often largely removed. Further, some degree of sinus fluid accumulation is likely following surgery owing to development of inflammatory sinusitis,[27] which could mask subtle fungal plaque formation, as was the case in dog 1. Consequently, in the present report, the diagnosis of sinonasal mycosis was confirmed only after frontal sinusotomy and direct visualization of fungal plaques, followed by subsequent fungal culture and histologic examination. As a result, in dogs with mucopurulent nasal discharge following transfrontal craniotomy, sinonasal mycosis should not be confirmed or excluded on the basis of clinical signs and diagnostic imaging findings alone.

Fungal plaque debridement in combination with topical administration of an imidazole antifungal agent such as clotrimazole is typically considered first-line treatment for sinonasal mycosis.[28–30] However, a consensus protocol does not exist, and various debridement and local antifungal treatments have been described.[15] All dogs in the present study underwent meticulous surgical curettage of fungal material and cyanoacrylate surgical tissue adhesive, with dogs 1 and 2 concurrently receiving topical treatment. At the time of the first sinonasal mycosis treatment in dog 2, clotrimazole solution was unavailable, so fluconazole was used owing to its favorable safety profile.[31] The owner of dog 3 elected for systemic treatment because of concerns regarding communication between the frontal sinus and cranial cavity. Although oral antifungal administration is reported to be inferior to topical administration for sinonasal mycosis, its use has been suggested when there are concerns regarding potential extension of topical agents into the CNS and subsequent chemically-induced meningoencephalitis.[32,33] However, recent studies[34–36] have reported no neurologic complications when topical treatment was used despite concurrent lysis of the cribriform plate or sinus ventral floor. No neurologic complications were encountered with the topical use of clotrimazole in 2 dogs in the present report, providing further support for this finding.

Although the present report describes only 3 dogs, these cases provide some important findings and highlight areas for future research. Further investigations might include a larger scale study evaluating the incidence of sinonasal disease following transfrontal craniotomy as well as a study evaluating the impact of various methods of surgical closure of the internal table of the frontal bone, including the use of tissue adhesives.

In conclusion, these cases highlight sinonasal mycosis as a potential complication following transfrontal craniotomy in dogs. Sinonasal mycosis should represent an important differential diagnosis in any dog that develops persistent mucopurulent nasal discharge, intermittent epistaxis, and intermittent sneezing following transfrontal craniotomy. The pathophysiology may be multifactorial, with use of surgical tissue adhesive, disruption of the normal bony structures and vascular supply, and destabilization of the local immune system and intranasal fauna all contributing to disruption of the normal sinus environment. Fur-

ther investigation may be useful to better understand the underlying causes and risk factors, including the use of surgical tissue adhesive in the frontal sinus.

Acknowledgments

The authors declare that there were no conflicts of interest.

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