Canine Sinonasal Aspergillosis

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*Aspergillus fumigatus* is a ubiquitous soil saprophyte, and a cause of chronic rhinitis in dogs. Infection of the nasal cavity may develop following inhalation of a large number of fungal spores. The disease spreads throughout the nasal cavity and often extends into the frontal sinuses. Rarely, infection disseminates throughout the body. Sinonasal aspergillosis most often affects young to middle age dolichocephalic and mesocephalic dogs.

**History and clinical signs:**

Nasal discharge is typically unilateral, but can progress to bilateral with chronic infection. The discharge is typically mucopurulent in nature, but may become hemorrhagic. Sneezing, epistaxis, pawing at the nose, and ulceration or depigmentation of the nasal planum can be seen. Advanced cases may develop facial deformity due to paranasal extension or inflammation. Systemic signs such as lethargy and anorexia may be present.

**Diagnosis:**

Aspergillosis is often suspected based on the signalment, history and clinical signs. Identification of fungal plaques or fungal organisms should be done to make a diagnosis. Unfortunately, a sensitive, noninvasive diagnostic test for the disease is not available. Confirmation of the diagnosis often requires multiple tests because the organism may be difficult to identify.

*CT scan or MRI* is far superior to nasal radiographs as a diagnostic tool and defines the extent of the disease. Advanced imaging by either method has high sensitivity and specificity for the diagnosis. Findings suggestive of aspergillosis include: turbinate lysis, nasal soft tissue or fluid opacity, reactive bone remodeling or osteolysis, and the presence of a mixed opacity in the frontal sinus or nasal cavity suggestive of a fungal granuloma. Cribiform plate destruction may also be seen, which is a key finding when considering treatment. Abnormalities are usually unilateral, but bilateral involvement is noted in 15-20% of advanced imaging cases.

*Rhinoscopy* is performed following the CT scan/MRI. Atrophy of turbinates and mucopurulent discharge are frequently seen. Identification of fungal plaques is strongly supportive of the diagnosis. These plaques are white, yellow or black in color and have an almost fuzzy surface. CT/MRI images can serve as a guide to locating fungal plaques and turbinate destruction. Examination of the frontal sinus via rhinoscopy is difficult to perform. Frontal sinus trephination is typically needed to evaluate the sinuses, and is recommended in dogs with sinus involvement on CT/MRI images.

Cytology and histopathology can allow for identification of fungal hyphae. Collection technique is critical. Impression smears of nasal discharge, blind nasal swabs and blind biopsies have very low sensitivity. Fungal hyphae are best identified cytologically using mucosal brushings or impression smears of a plaque collected using direct endoscopic visualization. Similarly, biopsy of a fungal plaque and surrounding mucosa using visual guidance offers a high diagnostic yield. Surrounding inflammation, often lymphoplasmacytic to neutrophilic, is also present.
Fungal culture of nasal tissue can be done, but results may not be available for 1-2 weeks. As with cytology and histopathology, a fungal plaque should be obtained for culture. Aspergillus fumigatus was cultured from a high percentage of dogs with histologically confirmed cases in separate studies. Culture is often not performed in cases with typical advanced imaging and rhinoscopic findings.

Serologic testing of serum for antifungal (aspergillosis) antibodies performed by agar gel immunodiffusion is available. This test has poor sensitivity, but good specificity for the diagnosis. The clinical usefulness of this test is considered low since the results are unpredictable. Serology can be considered in cases with a high index of suspicion but a nondiagnostic work-up. Polymerase chain reaction (PCR) testing for aspergillosis has also been reported. Although the specificity was shown to be high, the sensitivity is poor, and this test is not recommended.

Treatment:

Oral therapy with antifungal medications has a low success rate of clearing the disease, but may lessen the clinical signs. Some of the newer generation –azole agents have been shown to have good activity against Aspergillosis. Voriconazole can be tried at 4-5 mg/kg PO BID as well as posaconazole at 5 mg/kg/day given with food. Unfortunately, these medications are usually cost-prohibitive and treatment duration is lengthy. These drugs are options for dogs with cribiform plate destruction or as adjunctive therapy.

Topical treatment with an anti-fungal agent is the treatment of choice for nasal aspergillosis. The synthetic imidazole clotrimazole is used as a 1% solution or cream depot with the patient under general anesthesia. Eniconazole has also been used with similar success. Both invasive and noninvasive techniques have been described, and a clear benefit of one technique over others has not been properly established. No matter which technique is used, fungal plaques in the nasal cavity and frontal sinus should be debrided via curettage and lavage with a saline solution prior to therapy.

A non-invasive, 1 hour nasal cavity soak has become a favored treatment, and the technique has been described in great detail. This therapy hopes to maximize contact time of the clotrimazole solution with the nasal mucosa, prevents early leakage of the solution out of the nose, and also prevents aspiration of the solution. The problem with this technique is that the frontal sinus infection is usually not addressed. In addition, this technique seems to be associated with more single treatment failures. As a result, modifications to the non-invasive soak technique have been made.

When frontal sinus involvement is present, trephination in combination with a clotrimazole soak infused through tubes placed into the sinus and nasal cavity may allow for better treatment success. A short (5 min) and a long (1 hour) soak followed by placement of a cream depot into the frontal sinus have been described. These techniques appear to improve one-time and overall treatment success rate.

Clotrimazole infusion and depot therapy are generally well tolerated and side effects are infrequent. Pharyngitis may develop but is usually transient. Infusion of the solution in a dog with destruction of the cribiform plate will lead to neurologic signs and potentially death.
Follow-up:

Success rates for one time treatment using various invasive and non-invasive techniques have ranged from 40-100% and overall success rates from 65-100%. However, standards have not been established for evaluating response to treatment and treatment success. Resolution of the nasal discharge should not be used as the sole criteria of success. Ideally, rhinoscopy should be repeated 3-6 weeks after the 1st treatment. Repeat treatments are often required. The absence of plaques, negative histopathology and negative culture indicate treatment success.

References