Radiation therapy for tumors of the nasal cavity and paranasal sinuses in dogs

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Tumors of the nasal cavity and paranasal sinuses (sinonasal tumors) in dogs account for only approximately 1% of all neoplasia; however, over 80% are malignant, and they carry a poor long-term prognosis (1). Although these tumors are slow to metastasize, they are locally invasive, and, without treatment, euthanasia is generally elected within a few months due to progression of local disease. Sinonasal tumors usually occur in older dogs, with the average age at diagnosis between 8.7 to 10.7 y (1). Of all sinonasal tumors, approximately 2/3 are carcinomas and 1/3 are sarcomas (1,2). Round cell tumors of the sinonasal cavity, such as lymphoma or mast cell tumors, can carry a better prognosis than carcinomas and sarcomas and are not considered in this article.

Dogs are commonly presented for nasal discharge, which may be hemorrhagic or mucopurulent. Other presenting complaints include facial deformity (Figure 1A), ocular discharge, sneezing, stertor, dyspnea, exophthalmos, and, if the tumor has invaded through the cribiform plate, potentially neurologic signs (1–3). Differential diagnoses that should be considered include bleeding disorders, fungal or bacterial rhinitis, foreign body, and trauma (2,3).

While the role of various environmental contaminants remains unclear in the development of canine sinonasal neoplasia, it has been shown that dolichocephalic breeds kept indoors and exposed to environmental tobacco smoke are at an increased risk (4). Brachycephalic breeds (with the exception of the Boston terrier) are at a decreased risk for the development of sinonasal cancer (1).

A presumptive diagnosis of neoplasia may be made based on skull radiographs, but a definitive diagnosis requires a biopsy. Radiographic signs consistent with sinonasal neoplasia include the presence of soft-tissue densities within the nasal cavity as well as bony destruction and proliferation (3) (Figure 2). Tissue samples for histology may be obtained via rhinoscopy, rhinotomy, or transnostril blind biopsy (2). Prior to passing any instrument through the naris, the distance from the naris to the medial canthus of the eye should be measured externally and marked with tape on the biopsy instrument, to prevent accidental penetration of the cribiform plate (2). Before performing a biopsy, a clotting profile (including buccal mucosal bleeding time, prothrombin time, and activated partial thromboplastin time) should be performed (2,3). A computed tomography

Figure 1. A 10-year-old Dachshund with facial deformity resulting from a nasal carcinoma (1A). A pre-contrast computed tomographic transverse image of the nasal cavity (1B) reveals a soft tissue density mass occupying most of the nasal cavity with lysis of the dorsal right aspect of the nasal and maxillary bones.
(CT) scan is strongly recommended to support the diagnosis and evaluate the extent of the tumor, and is essential for tumor staging. Computed tomographic changes consistent with canine sinonasal neoplasia include destruction of bone and abnormal soft tissue density (Figure 1B) (2). A CT scan can also assess whether there has been extension of the tumor through the cribriform plate.

Despite the fact that, at time of diagnosis, only approximately 6% of dogs have detectable regional lymph node metastasis, and pulmonary metastasis is rare (3), full staging is nonetheless required prior to initiating treatment. Staging will affect the recommended treatment plan for a patient, and also has been shown in some studies to predict outcome with treatment. Staging is the assessment of the anatomical extent of disease, and uses the World Health Organization (WHO) TNM classification system that evaluates the primary tumor (T), regional lymph nodes (N) and presence or absence of distant metastasis (M) (Table 1) (5). Additionally, dogs with sinonasal tumors may be further classified under Théon’s Modified Staging System, which is used to indicate the extent of the tumor and the degree of bony erosion (6). A complete pretreatment workup for canine sinonasal tumors involves a CT scan of the nasal cavities and paranasal sinuses, palpation of the regional lymph nodes, thoracic radiographs, blood work (CBC and serum biochemistry analysis), and urinalysis. If the regional lymph nodes are enlarged, cytology and/or histology are recommended. At the Western College of Veterinary Medicine, an abdominal ultrasound is performed prior to full course radiation therapy, in order to screen for concurrent disease that may affect a patient’s life expectancy.

While the long-term prognosis for canine sinonasal tumors is poor, radiation therapy has been shown to improve survival times. On the other hand, with no treatment, or if surgery, chemotherapy, immunotherapy or cryosurgery is performed as a sole treatment, the median survival time is 3 to 6 mo, as progressive local invasion of the tumor leads to increasingly severe clinical signs, and owners generally opt for euthanasia (Figure 3) (7). With full-course megavoltage radiation therapy, median survival times ranging from approximately 12 to 16 mo have been reported (6,8). Patients that have undergone full course radiation therapy may still continue to show clinical signs related to the tumor (such as nasal discharge or sneezing), although these signs are usually less severe than before treatment. One study found that only 39% of dogs were completely free of clinical signs after radiation (9).

There is conflicting evidence as to various prognostic indicators for canine sinonasal neoplasia. While 1 study reported a relative risk of relapse 3.3-fold higher for dogs with carcinomas than for dogs with sarcomas, other studies have failed to show any difference in median survival times between the 2 histologic types (6,10,11). Nonkeratinizing squamous cell carcinomas were found to have a shorter median survival time than those

**Figure 2.** An intraoral dorsoventral radiograph of the nasal cavities in a dog with a sinonasal carcinoma, showing loss of turbinate bone detail (2A). A radiograph of a normal dog is shown for comparison (2B).
Additional factors that may adversely affect prognosis include stage of disease (6,8,10,11,13). Stage 1 disease in one study; however, other studies have not reported for other histologic types: full-course radiation resulted in a median survival time of 15.8 mo (8). Local reaction to the intramuscular slow release cisplatin polymer may occur. This can range from a mild reaction that responds to antibiotic therapy to moderate to severe reactions that require removal of the implant and tissue debridement (8). Reactions may occur up to 6 mo after implant (8). Other side-effects of cisplatin include bone marrow suppression and renal toxicity.

Table 1. Staging systems for canine sinonasal tumors

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<thead>
<tr>
<th>TNM World Health Organization Staging (5)</th>
<th>Théon Modified Staging System (6)</th>
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<tr>
<td>T — Primary Tumor</td>
<td>S1 unilateral or bilateral neoplasm confined to the nasal passage without extension into the frontal sinus</td>
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<tr>
<td>T&lt;sub&gt;0&lt;/sub&gt;</td>
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<tr>
<td>T&lt;sub&gt;1&lt;/sub&gt;</td>
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<td>T&lt;sub&gt;4&lt;/sub&gt;</td>
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<td>T&lt;sub&gt;5&lt;/sub&gt;</td>
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<tr>
<td>N — Regional Lymph Node (RLN)</td>
<td>S2 bilateral neoplasm extending into the frontal sinuses with erosion of any bone of the nasal passage</td>
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<tr>
<td>N&lt;sub&gt;0&lt;/sub&gt; No evidence of RLN involvement</td>
<td></td>
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<tr>
<td>N&lt;sub&gt;1&lt;/sub&gt; Movable ipsilateral nodes</td>
<td></td>
</tr>
<tr>
<td>N&lt;sub&gt;2&lt;/sub&gt; Movable contralateral or bilateral nodes</td>
<td></td>
</tr>
<tr>
<td>N&lt;sub&gt;3&lt;/sub&gt; Fixed nodes</td>
<td></td>
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<tr>
<td>M — Distant Metastasis</td>
<td></td>
</tr>
<tr>
<td>M&lt;sub&gt;0&lt;/sub&gt; No evidence of distant metastasis</td>
<td></td>
</tr>
<tr>
<td>M&lt;sub&gt;1&lt;/sub&gt; Distant metastasis cannot be assessed</td>
<td></td>
</tr>
<tr>
<td>M&lt;sub&gt;x&lt;/sub&gt; Distant metastasis detected</td>
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Théon Modified Staging System (6)

- S1 unilateral or bilateral neoplasm confined to the nasal passage without extension into the frontal sinus
- S2 bilateral neoplasm extending into the frontal sinuses with erosion of any bone of the nasal passage

reported for other histologic types: full-course radiation resulted in a median survival time of only 5.5 mo (12). Using Théon’s modified staging system, dogs with Stage 2 disease had a 2.3-fold higher risk of relapse after radiation therapy than dogs with Stage 1 disease in one study; however, other studies have not found that stage of disease impacted prognosis (6,8,10,11,13).

Additional factors that may adversely affect prognosis include the presence of facial deformity at the time of presentation, age over 10 years, and the presence of regional lymph node metastasis at time of diagnosis (9,10).

Cisplatin is a chemotherapeutic agent known to increase tumor cell kill when used in conjunction with radiation therapy, in part due to decreasing the ability of the tumor cells to repair DNA damage caused by ionizing radiation (14). When combined with full-course radiation, cisplatin may improve median survival times for canine sinonasal tumors (7,8). In a 1997 study involving 13 dogs, Lana et al (7) found that the use of a slow-release cisplatin polymer was well tolerated, and that it may improve the median survival time in dogs with sinonasal tumors treated with radiotherapy. This finding was supported in a 2nd, retrospective analysis of 51 dogs with malignant sinonasal tumors, where the authors found that the use of full course radiation therapy in combination with slow-release cisplatin resulted in a median survival time of 15.8 mo (8). Local reaction to the intramuscular slow release cisplatin polymer may occur. This can range from a mild reaction that responds to antibiotic therapy to moderate to severe reactions that require removal of the implant and tissue debridement (8). Reactions may occur up to 6 mo after implant (8). Other side-effects of cisplatin include bone marrow suppression and renal toxicity.

One recent study involving 53 dogs showed that, if the tumor recurs after full course radiation therapy, exenteration of the nasal cavity significantly improves the median survival time (44.7 mo as compared with 19.7 mo with radiation only) (15). However, the dogs in the group that received post-radiation surgical treatment of recurrence did experience a significantly higher rate of delayed complications, including chronic rhinitis, osteomyelitis, and osteonecrosis (15). In the radiation and surgery group, 5 of the 13 dogs (38%) developed recurrent or chronic rhinitis that developed into osteomyelitis; in the surgery-only group, only 4 of the 40 dogs (10%) developed chronic rhinitis (15). Further studies need to be done to confirm the benefit of surgery for recurrent disease after radiation treatment and to better define the level of risk of severe delayed effects.

The current recommended treatment for canine sinonasal tumors at the Western College of Veterinary Medicine is full-course radiation therapy in combination with a slow-release cisplatin polymer that is administered intramuscularly on the first day of radiation treatment. Radiation generally involves 18–20 fractions, which are given under general anaesthesia Monday to Friday for 3½ to 4 wk as an out-patient procedure.

As with all full-course radiation treatments, acute effects will occur to varying degrees. Potential acute effects include oral mucositis, skin erythema and desquamation, conjunctivitis, and keratoconjunctivitis sicca (8). Pain is controlled through oral medications such as nonsteroidal anti-inflammatories and opioids, as well as daily local anaesthetic blocks and oral rinses. Acute side effects of radiation usually begin to develop during the 2nd to 3rd week of treatment, are at their worst at 2 wk after finishing treatment, and are generally completely healed by 4 wk post-treatment.

With full-course radiation treatment there is a low risk, typically less than 5%, of serious side effects occurring months to years after radiation therapy in normal tissues that are included in the radiation field. This risk is accepted in order to administer a sufficient dose to the tumor to result in a good probability of long-term tumor control. Late effects that may be seen months to years after radiation if the eyes are within the treatment field include keratoconjunctivitis sicca, keratitis, corneal vascularization, and cataract formation (8). Skin pigmentation changes, alopecia, and coat color changes are also commonly seen within the radiation field.

In conclusion, while sinonasal tumors in dogs are rarely cured, radiation therapy can significantly improve the expected median survival time, and is the treatment of choice. A full workup should be performed for any older dog presenting with...
chronic nasal discharge, and referral to a radiation oncology center is recommended once the diagnosis of sinonasal neoplasia has been made.

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References