

Surgical and Localized Radiation Therapy for an Intranasal Adenocarcinoma in a Rabbit

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ABSTRACT. An 8-year-old spayed female Netherland Dwarf rabbit presented with a two-month history of dyspnea and snoring. A computed tomography (CT) scan of the head revealed mass lesions in the right nasal cavity. Surgical exenteration of the lesions was performed, and the histopathological diagnosis was an intranasal adenocarcinoma. On the basis of this diagnosis, radiotherapy was planned and consisted of eight fractions of 6 Gy administered once a week. After the completion of radiation therapy, the soft tissue density in the right nasal cavity, as detected by CT, significantly decreased. The prognosis has remained good for over 3 years after treatment. This paper is the first to describe the clinical and pathological features of an intranasal tumor in a rabbit.

KEY WORDS: adenocarcinoma, intranasal tumor, rabbit, radiation therapy

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Numerous infectious agents cause upper respiratory tract diseases in rabbits, and these include mainly bacterial organisms, such as *Pasteurella multocida*, *Bordetella bronchiseptica* and *Pseudomonas* species; however, some cases may involve viral, fungal or parasitic pathogens as well. Noninfectious causes of upper respiratory tract disorders include traumatic injury and dental disease. The only neoplastic disease of the nasal cavity reported in rabbits is an anecdotal report of a carcinoma of the nasal turbinates [7].

In dogs, intranasal tumors reportedly accounted for about 1% of all tumors [8], and epithelial tumors, including adenocarcinomas and squamous cell carcinomas, accounted for about 60% of intranasal tumors [11]. In general, the biological behavior of malignant intranasal tumors is characterized by progressive local invasion, with the incidence of lymphatic metastasis being as low as 10% at the initial diagnosis [11]. The first choice of therapy for intranasal tumors in dogs and cats is either radiation therapy alone or a combination of surgery and radiation therapy [1, 9, 12, 14]. Additionally, chemotherapy has been used as the primary treatment [2, 6] and as an adjuvant therapy [3, 4].

However, there have been no reports of nasal tumors in rabbits, and the therapeutic efficacy, biological behavior and prognosis are unknown.

Here, the authors evaluated a rabbit presenting with dyspnea and snoring, and an intranasal mass detected by

computed tomography (CT) was histologically diagnosed as an adenocarcinoma. This report describes the treatment of this case, which has been maintained successfully for a long period by a combination of exenteration of the intranasal mass and localized radiotherapy.

An 8-year-old spayed female Netherland Dwarf rabbit, weighing 1.36 kg, presented with dyspnea and snoring that began 2 months earlier. Another private veterinary clinic had administered antibiotics via a subcutaneous injection and nebulization. The rabbit's snoring improved, but not the dyspnea. Three weeks later, discharge from the right nasal cavity was observed during consultation, and a sample collected for bacterial culture yielded a negative result. Because of the worsening dyspnea, a CT scan was performed under anesthesia for evaluation of the nasal cavity. Images from the CT scan revealed two mass lesions of soft tissue density within the right nasal cavity (Fig. 1). Thereafter, the rabbit was referred to our clinic for further treatment. On physical examination, the rabbit was dyspneic and produced a snoring sound, although there was no abnormality in the rabbit's external appearance, including the maxilla, nasal bridge and orbits. A complete blood cell count and serum biochemical profile showed no abnormal findings. Thoracic and abdominal radiographs revealed no abnormal findings, including no evidence of pulmonary metastasis. Based on the CT images, exenteration of the intranasal mass lesions was performed.

Following premedication with an intramuscular injection of a combination of medetomidine (100 µg/kg) and ketamine (5 mg/kg), isoflurane was administered to the rabbit via a face mask. Subsequently, tracheal intubation was performed by a tracheostomy, with the rabbit retained in the abdominal position. Exenteration of the intranasal mass lesions and trephination of nasal bone were performed through a dorsal rhinotomy. In brief, the nasal cavity was entered

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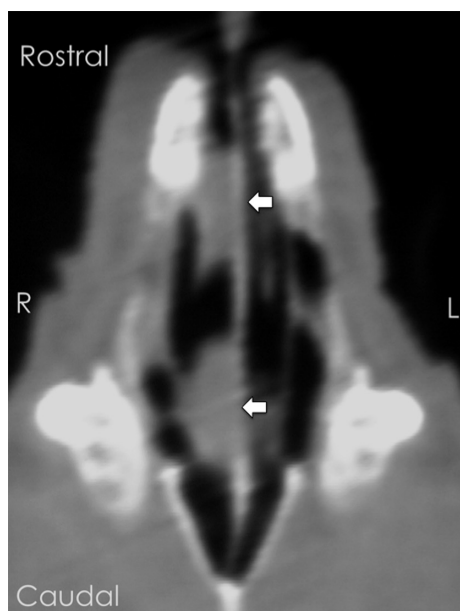


Fig. 1. Computed tomography (CT) scan of the head of the rabbit. The soft tissue density of two mass lesions (arrows) within the right nasal cavity is shown in the coronal aspect.

through a dorsal midline approach, in which the nasal bone was carbonized using a carbon dioxide laser to expose the nasal turbinates and nasal cavity. The stoma was extended using a rongeur, and the mass attached to the nasal septum and turbinates lining the nasal cavity was extirpated (Fig. 2). No obvious bone invasion or destruction was observed. The other rostral mass detected by CT was determined to be nasal discharge. Hemostasis was achieved with gauze pressure packing and cauterization. After excision of all the neoplastic tissue in the right nasal cavity, the subcutaneous tissue and skin were not closed, and a trephination orifice was made. The tracheostomy was closed routinely.

Two days after the surgery, the rabbit was doing well, but on the third day postoperatively, her respiratory condition became unstable, because of obstruction of the trephination orifice by crustae. Treatment to remove the crustae and maintain patency of the trephination orifice was repeated for 2 weeks, and the respiratory condition gradually improved, except for mild nasal snoring. The rabbit was prescribed enrofloxacin (10 mg/kg once a day orally), metoclopramide hydrochloride (0.5 mg/kg twice a day orally) and cyproheptadine hydrochloride hydrate (0.4 mg/kg twice a day orally) for 4 weeks. The trephination orifice closed naturally, but the respiratory condition remained normal.

Histopathological evaluation of the nasal tissues revealed a glandular proliferation of atypical columnar epithelial cells with severe lymphocytic infiltration and interstitial hemorrhage. Tumor cells had clear to slightly eosinophilic cytoplasm and a pale oval nucleus with mild anisokaryosis. Nucleoli were prominent in occasional tumor cells, and there were 1 to 2 mitotic figures per 400 \times field. Based on the histopathological findings, the diagnosis was an intranasal

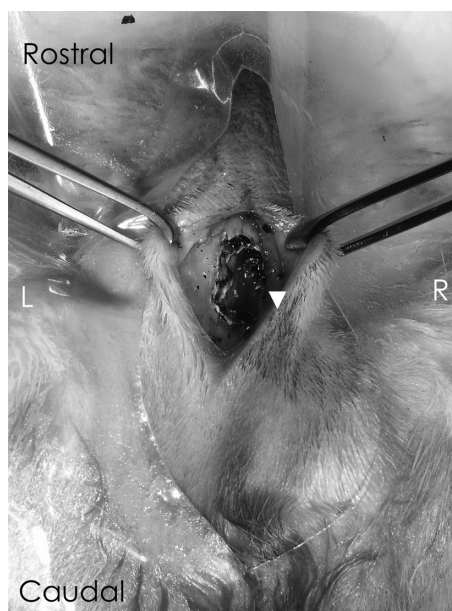


Fig. 2. The extirpation of the intranasal mass lesion. The nasal cavity was exposed by means of a dorsal midline approach using a carbon dioxide laser, and the mass attached to the nasal septum (arrowhead) and turbinates lining the nasal cavity was extirpated. No obvious bone invasion or destruction was observed. The other rostral mass detected by computed tomography (CT) (Fig. 1) was determined to be nasal discharge.

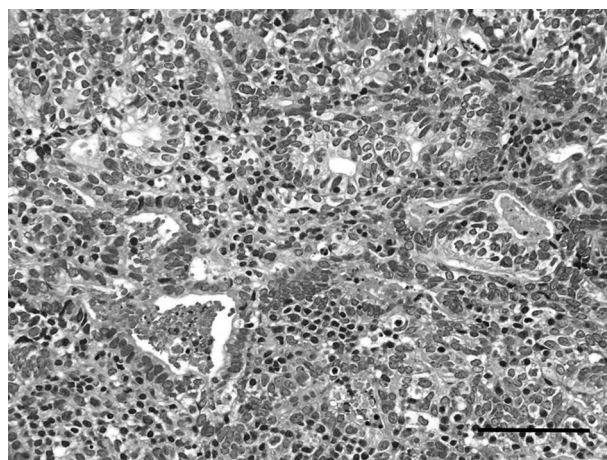


Fig. 3. Histopathological findings of the intranasal mass. Glandular proliferation of atypical columnar cells with severe lymphocytic infiltration and interstitial hemorrhage was observed. Hematoxylin and Eosin stain. Bar=100 μ m.

adenocarcinoma (Fig. 3).

Radiation therapy was planned using an orthovoltage unit (MS-320R-2; Hitachi Medical Corporation, Tokyo, Japan). Radiotherapy was initiated 4 weeks after surgery and consisted of once weekly administration of eight fractions of 6 Gy each over 8 consecutive weeks. The radiation was

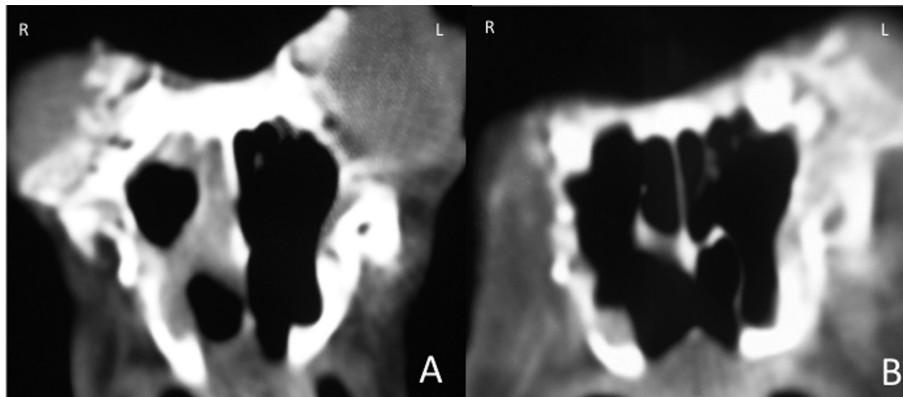


Fig. 4. Computed tomography (CT) scan of the head in the rabbit diagnosed with an intranasal adenocarcinoma. A soft tissue density in the transverse aspect within the right nasal cavity prior to radiation therapy (A) was significantly reduced after the completion of the radiation therapy (B).

single field irradiation, and the radiation field size was 4×4 cm (source to skin distance [SSD], 40 cm). The eyes of the rabbit were shielded with lead plates during the irradiation procedure. A CT scan (Asteion™ Super4; Toshiba Medical Systems Corporation) of the nasal cavity before irradiation revealed a small lesion of soft tissue density within the right nasal cavity extending to the rhinopharynx and an intact nasal septum in the transverse aspect (Fig. 4A). A contrast CT study was not performed, because of the small size of the mass; hence, the CT images were strongly affected by a partial volume effect. Moreover, since the mass adhered to the mucosal surface of nasal cavity, it was likely affected by artifact from the nasal bone and nasal septum. After the completion of radiation therapy, the CT images taken at the last radiation therapy visit revealed that the soft tissue density was markedly reduced (Fig. 4B). Mild binocular cataracts and whitening and coarsening of the fur on the nasal crest were observed during radiation therapy. Metoclopramide hydrochloride (0.5 mg/kg twice a day orally) and cyproheptadine hydrochloride hydrate (0.4 mg/kg twice a day orally) were prescribed as appetite enhancers, with the instructions to use them if necessary. The altered color and texture of the fur on the nasal crest improved gradually within a few months, and the mild binocular cataracts did not progress.

There were no obvious abnormalities on follow-up CT examinations performed at 1, 6 and 12 months after radiation therapy. This patient has remained in good condition, without tumor recurrence or delayed side effects of radiation (late-onset radiation damage) for more than 3 years after the initial presentation.

Intranasal tumors are extremely rare in rabbits. Bacterial infections cause most upper respiratory diseases and often have a chronic course. The principal symptom in this rabbit was dyspnea, whereas clinical signs associated with intranasal tumors in dogs include sneezing, epistaxis and/or swelling of nasal crest, with dyspnea rarely reported [1, 5, 9, 12]. Since rabbits are obligate nasal breathers, because of the position of the elongated epiglottis over the caudal margin of the soft palate [7], upper respiratory tract diseases are more

severe and cause dyspnea more easily in rabbits than in other animal species. Therefore, in contrast to dogs, initial clinical signs of intranasal tumors may include dyspnea in rabbits. Thus, intranasal tumors should be on the list of differential diagnoses for rabbits presenting with dyspnea, and advanced diagnostic imaging, such as CT or magnetic resonance imaging (MRI), is recommended.

In dogs, radiotherapy is the treatment of choice for intranasal tumors [9, 12, 14]. In one report on dogs, exenteration of nasal tumors with radiation therapy significantly prolonged survival time compared with radiation therapy alone [1]. Since CT contrast studies were not performed before and after radiation therapy, it was unknown whether the small lesion of soft tissue density within the right nasal cavity was a recurrence of the carcinoma or nasal discharge, but a combination of surgery and radiation therapy was similarly effective and resulted in a good prognosis for more than 3 years in this case.

Mild binocular cataracts and altered color and texture of the fur on the nasal crest were suspected side effects of acute radiation in this case. In dogs, acute phase side effects of radiation are often noted. Specifically, rhinitis, dermatitis and mucositis can be severe and can persist up to 4–8 weeks after treatment [5]. Moreover, keratoconjunctivitis sicca, corneal ulceration and cataracts are common secondary ocular changes occurring during radiation therapy [5]. In general, use of multi-fractionated irradiation can prevent these radiation side effects [13], but the stress resulting from frequent visits and the risk of repeated anesthesia should be considered in rabbits. Rabbits in particular are prone to stress-induced anorexia, which may be deadly. As to the radiation protocol, although we have used similar protocol for a few tumor cases in rabbits without remarkable side effects, considering TDF (Time, dose and Fractionation factor) which is indicated not exceed 100 in dogs and cats [10], TDF 112 in the present case might be excessive radiation dose. Based on these results, additional studies are necessary to evaluate the therapeutic efficacies including radiation protocol and the prognosis of intranasal tumors in rabbits.

In conclusion, to the authors' knowledge, this is the first report of an intranasal adenocarcinoma in a rabbit. The authors suggest that an intranasal tumor should be considered as a differential diagnosis for rabbits presenting with dyspnea.

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