

<Case Report>

Orbital exenteration for a third eyelid gland carcinoma in a dog

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Abstract: A 13-year-old neutered male Poodle dog was presented with a third eyelid mass in the left eye. The dog had undergone local resection of the mass about a year prior in a private practice. On cytological examination, the mass was diagnosed as adenocarcinoma. Although lung and lymph node metastases were suspected, based upon the computed tomographic results, exenteration was performed to relieve chronic pain and to improve the dog's quality of life. Exenteration carried a good prognosis with no tumor recurrence until 1 year and 10 months after surgery, when local recurrence occurred near the left zygomatic arch.

Keywords: Poodle, dogs, exenteration, metastasis, third eyelid gland carcinoma

Orbital neoplasms are known as a common cause of orbital disease in dogs [8]. They usually cause displacements of globe. Almost of orbital tumors are reported as malignant with high local recurrence risk [4, 5]. Primary orbital tumors are major cause in dogs and could be originated from any tissues within orbit such as osteochondrosarcoma and squamous cell carcinoma [4, 10]. It is difficult to confirm the origin of tumors without histological examination, but third eyelid tumors are suspected by their location [10]. Various types of tumors have been reported including adenocarcinoma, adenoma and squamous cell carcinoma in the third eyelid [3]. The most common type has been known as adenocarcinoma in dogs [3]. It is generally localized, firm and shows red swelling [5]. Histologically, poor differentiation, cellular anaplasia, locally invasive behavior or vascular invasion indicates malignancy of tumor and possibility of metastasis [3]. Treatment for third eyelid adenocarcinoma is a surgical excision of the third eyelid gland including tumor before invasion or metastasis [10]. The purpose of this case study was to present a case of third eyelid adenocarcinoma undergoing exenteration to improve the quality of life although the dog had already pulmonary and lymph nodes metastasis and to discuss treatments of third eyelid tumors.

A 13-year-old, castrated male, Poodle dog was referred to the Veterinary Medical Teaching Hospital at Seoul National University (VMTH-SNU) for a third eyelid mass in the left eye (OS) (Fig. 1A). Referring veterinarian partially resected

the mass and adenocarcinoma of third eyelid was diagnosed on the cytological examination. As the tumor was rapidly growing during one year after the resection, complete surgical resection was considered. Prior to the surgery, a computed tomography (CT) was performed.

The CT findings showed that an oval mass of soft tissue density was located ventrally in the left orbit and the eyeball was displaced and pressed upward and outward by the orbital mass with a diameter of 25 × 23 mm (Fig. 2A). The adjacent lacrimal, maxillary, and frontal bones was thinned, meaning the possibility of invasion into surrounding tissues (Fig. 2B). In addition, many pulmonary nodules were found in the lung and the left axillary lymph node was enlarged, meaning that pulmonary and lymph node metastasis was strongly suspected. Intraabdominal metastasis was not detected.

At first presentation to the VMTH-SNU, the OS globe could not be examined because a red enlarged mass at the third eyelid masked the eye. In the right eye, ophthalmic examinations, including a tear production test (Schirmer Tear Test; MSD, USA), neuro-ophthalmic examinations and rebound tonometry (Icare TonoVet; Icare Finland Oy, Finland), were performed and abnormalities were not detected.

Because the mass was continuously induced inflammation and bleeding, a surgery or other medical managements were considered. Because of the dog's age, 13 years old, and metastasis, the conservative therapy was decided by the owner at first. Partial tarsorrhaphy was performed to prevent

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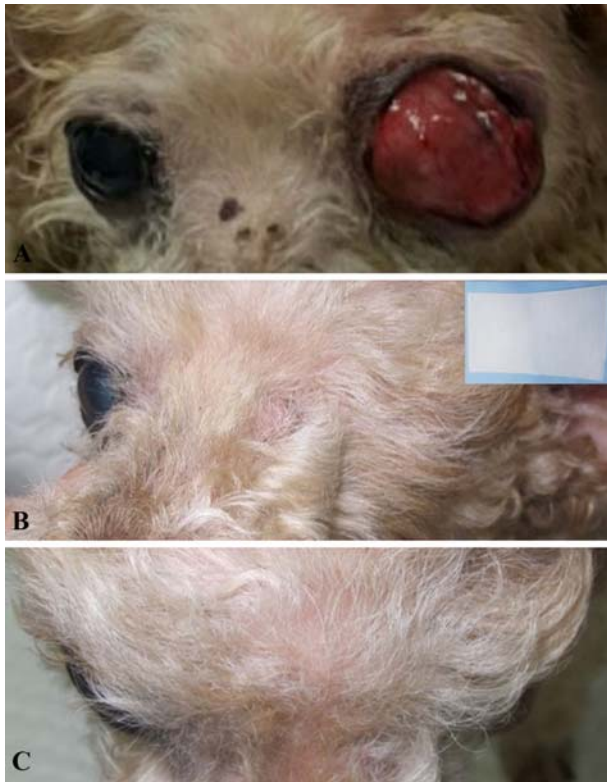


Fig. 1. Pre- and post-operative appearances. (A) Pre-operative appearance showing red enlarged third eyelid gland mass in the left eye. (B) Frontal view; 3 months after exenteration. Inserted surgical mesh was shown at the top right inset. (C) Dorsal view; 3 months after exenteration. Left side orbit shows no depression of skin.

continuous ulceration and bleeding of the mass, and intralesional injections of 5-fluorouracil (5-FU) at a dosage of 10 mg (5-FU inj.; JW Pharmaceutical, Korea) were administered at weekly intervals for 35 days with systemic medications; piroxicam (0.3 mg/kg per orally [PO], once a day [SID]; Crown Pharm, Korea), cephalexin (30 mg/kg PO, twice a day [BID]; Donghwa Pharmaceutical, Korea), famotidine (0.5 mg/kg PO, BID; Nelson Pharmacy, Korea), and misoprostol (5 µg/kg PO, BID; Unimed Pharm, Korea) [11]. Topical 1% 5-FU diluted with artificial tear and neomycin-polymyxin B-dexamethasone eye drops (Maxitrol; Alcon, Belgium) four times daily were also administered [1, 2, 8]. The size of the mass was slightly reduced after the 2nd and 3rd 5-FU injections. But after the 4th 5-FU injection, it was increased again. After discussion with the owner for more severe pain from ulceration of eyelid skin and the mass, exenteration of OS was decided to improve the patient's quality of life although the mass was already spread to other organs.

The patient was sedated with midazolam (0.2 mg/kg; Bukwang Pharm, Korea) and hydromorphone (0.075 mg/kg; Hana Pharm, Korea). Propofol (6 mg/kg; Myungmoon Pharm, Korea) and isoflurane (Terrell; Piramal Critical Care, USA) were used for anesthetic induction and maintenance, respectively.

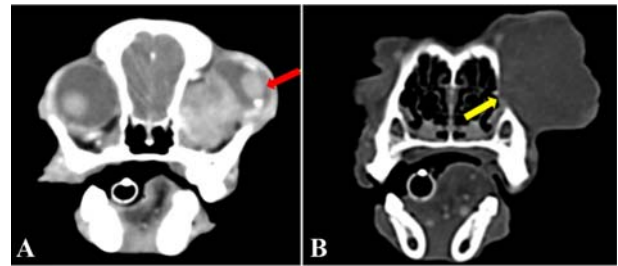


Fig. 2. Computed tomography (CT) images. (A) Soft tissue window. Contrast-enhanced CT images show a displacement of the globe (red arrow) by the intraorbital tumor. (B) Bone window. An invasion into the adjacent orbital bone (yellow arrow).

After positioning the dog in right recumbency, the surgical site was prepared aseptically. Exenteration of OS was performed and the surgical mesh (Bard Mesh; Davol, USA) was inserted after trimming to prevent contracture of orbital space (Fig. 1B) [6, 10]. The globe and orbital contents were placed in 10% formalin for fixation. On histologic examination, solid carcinoma of the gland of the third eyelid extended into orbital adipose tissue was confirmed. The exenteration site was stable and dog's general health condition was improved (Fig. 1B and C). Other re-examination about metastasis was recommended but declined by the owner. At 1 year and 10 months post-surgery, the dog have recurrence near the left zygomatic arch bone. Additional examination or surgery about recurrence were refused by the owner.

Abnormal massive lesions of third eyelid include cysts, neoplasia and inflammatory disease [10]. Third eyelid gland neoplasia is uncommon in dogs [3, 10, 12]. In a review of 127 canine third eyelid neoplasm, adenocarcinoma is the most common third eyelid tumor (108/127; 85.0%), followed by adenoma (18/127; 14.2%) and squamous cell carcinoma (1/127; 0.8%) [3]. The breed distribution of Poodle, same as this case, was 2.3% (n = 3) which was relatively high rate [3]. In 54 cases of third eyelid adenocarcinoma with follow-up available, metastasis rate was 9.3% (n = 5) and local recurrence rate was 13.0% (n = 7) [3]. The average survival time (SurvT) was significantly more decreased with metastasis than with no metastasis [3]. Also, the SurvT was 438.94 days for cases with incomplete margins [3]. In this case, the dog already had lung and lymph node metastasis and considered incomplete margins. So, this dog's SurvT had been suspected less than 438 days.

Intralesional 5-FU injections were reported for the treatment of squamous cell carcinoma of eyelid in horses and cutaneous neoplasms in humans [7, 9, 11]. In horses, volume of drug injected per lesion depended on mass size and 5-FU intralesional injection was successful in reducing tumor size and improving clinical signs in all patients [11]. Topical application of 1% 5-FU was also reported for the treatment of conjunctival squamous cell carcinoma of the eyelid, conjunctiva and cornea in humans [1, 2, 8]. However, in this case, the tumor size was not markedly decreased after four

times of intralesional 5-FU injection and topical instillation, but rather slightly increased. We considered that different type of tumor, insufficient number of injections and not enough time for regression made it not effective to reduce the tumor size. Additional research is needed to document the intralesional injection therapy using 5-FU for third eyelid tumor in dogs.

Treatment of third eyelid adenocarcinoma is a surgical excision [10]. According to clinical signs, invasiveness of tumor and existence of metastasis lesion, a surgery could be planned and an adequate extent of resection is determined [10]. Because the presence of metastasis was associated with significantly shorter SurvT [3], evaluation including thoracic radiography and abdominal imaging and early complete surgical resection is recommended [10]. In this case, the third eyelid tumor invaded to the surrounding tissues and bones, so partial or total orbitectomy techniques could be considered [10]. However, because of pulmonary and lymph nodes metastasis and risks associated with anaesthesia, the owner decided to do exenteration without orbitectomy.

Orbital implantation was safe and inexpensive methods for improving cosmetic appearance after enucleation or exenteration in dogs [6, 10]. However, orbital implants are contraindicated in dogs that have neoplasms extended outside the globe and infection involving the ocular surface [10]. In this case, a surgical mesh was inserted in the orbit following exenteration to prevent postoperative depression of the skin and extension outside, even though the dog had a tumor of the third eyelid. After surgery, the owner's satisfaction with the cosmetically surgical outcome was high and the dog had no recurrence until 1 year and 10 months. Therefore, our findings suggest that, even though dogs had neoplasms in the orbit, orbital implants could be considered to prevent depression of the skin.

As the case already had regional lymph node and pulmonary metastasis, surgical intervention was not considered for the first option. However, a medical therapy was not effective against the tumor and the dog had chronic pain and continuously discomfort. Although the case was old age and had a distant metastasis, a surgical removal of the tumor was performed and had a good prognosis. The dog's life quality was very improved and the owner was satisfied with the surgical outcome. Before the surgery, the expected survival time of the case had been considered less than 438 days. But the case has lived longer than expected lifetimes with no tumor recurrence until 1 year and 10 months after surgery.

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References

1. **Al-Barrag A, Al-Shaer M, Al-Matary N, Al-Hamdani M.** 5-Fluorouracil for the treatment of intraepithelial neoplasia and squamous cell carcinoma of the conjunctiva, and cornea. *Clin Ophthalmol* 2010, **4**, 801-808.
2. **De Keizer RJW, De Wolff-Rouendaal D, Van Delft JL.** Topical application of 5-fluorouracil in premalignant lesions of cornea, conjunctiva and eyelid. *Doc Ophthalmol* 1986, **64**, 31-42.
3. **Dees DD, Schobert CS, Dubielzig RR, Stein TJ.** Third eyelid gland neoplasms of dogs and cats: a retrospective histopathologic study of 145 cases. *Vet Ophthalmol* 2016, **19**, 138-143.
4. **Gelatt KN, Whitley RD.** Surgery of the orbit. In: Gelatt KN, Gelatt JP (eds.). *Veterinary Ophthalmic Surgery*. 1st ed. pp.51-87, Elsevier Saunders, Maryland Height, 2011.
5. **Gelatt KN, Gilger BC, Kern TJ.** *Veterinary Ophthalmology*. 5th ed. pp. 945-968, Wiley, Ames, 2013.
6. **Hamor RE, Roberts SM, Severin GA.** Use of orbital implants after enucleation in dogs, horses, and cats: 161 cases (1980-1990). *J Am Vet Med Assoc* 1993, **203**, 701-706.
7. **Kirby JS, Miller CJ.** Intralesional chemotherapy for nonmelanoma skin cancer: a practical review. *J Am Acad Dermatol* 2010, **63**, 689-702.
8. **Midena E, Angeli CD, Valenti M, de Belvis V, Boccato P.** Treatment of conjunctival squamous cell carcinoma with topical 5-fluorouracil. *Br J Ophthalmol* 2000, **84**, 268-272.
9. **Nanda S, Reddy BSN.** Intralesional 5-fluorouracil as a treatment modality of keloids. *Dermatol Surg* 2004, **30**, 54-57.
10. **Peruccio C.** Diseases of the third eyelid. In: Maggs DJ, Miller P, Ofri R (eds.). *Slatter's Fundamentals of Veterinary Ophthalmology*. 6th ed. pp. 178-185, Elsevier, St. Louis, 2018.
11. **Pucket JD, Gilmour MA.** Intralesional 5-fluorouracil (5-FU) for the treatment of eyelid squamous cell carcinoma in 5 horses. *Equine Vet Educ* 2014, **26**, 331-335.
12. **Wilcock B, Peiffer R Jr.** Adenocarcinoma of the gland of the third eyelid in seven dogs. *J Am Vet Med Assoc* 1988, **193**, 1549-1550.