

## Histiocytic sarcoma complex in the palpebral conjunctiva of a seven-month-old dog

*Histiocytair sarcoom in de palpebrale conjunctiva bij een zeven maanden oude hond*

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### ABSTRACT

A seven-month-old, intact, female Anatolian Shepherd dog was referred for treatment of swelling and redness of the left eye. Ophthalmological examination revealed a pea-sized mass in the palpebral conjunctiva of the left lower eyelid. Ulcerative keratitis and blepharospasm were detected due to the irritation caused by the mass. Fluorescein staining was positive and the Schirmer tear test result was 13 mm/min. No other masses were detected in other parts of the patient's body, and its general condition was good. The mass was removed surgically and was interpreted as histiocytic sarcoma. During a three-year, post-operative follow-up period, no recurrence of the mass was observed.

### SAMENVATTING

Een zeven maanden oude, intacte, vrouwelijke Anatolische herder werd aangeboden met zwelling en roodheid aan het linkeroog. Tijdens het oftalmologisch onderzoek werd een massa ter grootte van een erwtenaantoon in de palpebrale conjunctiva van het linker onderste ooglid. Ulceratieve keratitis en blefarospasmen werden vastgesteld wegens irritatie veroorzaakt door de massa. Er werden geen andere massa's in andere delen van het lichaam aangetoond. De hond was in goede algemene conditie. De massa werd chirurgisch verwijderd en gediagnosticeerd als histiocytair sarcoom. Gedurende een postoperatieve opvolgingsperiode van drie jaar werd geen recidief waargenomen.

### INTRODUCTION

Histiocytic proliferative diseases include several disorders identified in dogs. They are classified according to their clinical appearance and pathological differences as follows: canine cutaneous histiocytoma, canine reactive histiocytosis (cutaneous and systemic forms), and histiocytic sarcoma complex (HSC) (localized, disseminated histiocytic sarcoma and malignant histiocytosis) (Naranjo et al., 2007).

Historically, malignant histiocytic sarcoma (HS) has been recognized in the Bernese Mountain dog as a hereditary disease, but has later been described in other breeds as well (Rahj et al., 2018). Eyelid involvement has been shown in cutaneous histiocytomas; involve-

ment of eye and adnexal structures has been described in systemic histiocytosis (Gelatt, 1975; Moore, 1984; Scherlie et al., 1992; Patterson et al., 1995). Cutaneous histiocytomas regress spontaneously and reactive histiocytosis usually responds to immunosuppressive therapy. However, HS is considered a malignant neoplasm of histiocytic origin with a poor prognosis (Naranjo et al., 2007).

The mass mostly resembles the clinical manifestation of eyelid tumors. Epiphora and blepharospasm occur due to the corneal irritation caused by the conjunctival mass. If the tumor grows to such an extent that it impairs the function of the eyelids, more serious ocular findings such as ulcerative keratitis may be observed (Hedlund, 2007; Finn et al., 2008).

Secondary ocular neoplasms are rarely encountered but the clinician must be aware that tumor metastasis may cause clinical ocular disease. In dogs, excluding lymphoma, histiocytic sarcoma is the most common tumor that metastasizes to the globe. This tumor in the eye has the same breed predilection as it has when found in other parts of the body. Hemangiosarcoma, mammary adenocarcinoma and malignant oral melanoma can also be the metastatic ocular neoplasms (Dubielzig, 2017).

In cats, HS is very rare. Scurrel et al. (2013) reported an intraocular histiocytic sarcoma complex in a thirteen-year-old, male, British Blue cat.

In this case report, the clinical, surgical and histopathological findings of a histiocytic sarcoma localized in the palpebral conjunctiva of a young dog are described.

### Case description

A seven-month-old, intact, female Anatolian Shepherd dog was presented to the surgery clinic of the Faculty of Veterinary Medicine (Aksaray University, Turkey) with complaints of swelling and redness of the left eye.

The patient's history was taken, physical and ophthalmological examinations were performed. Fluorescein staining was positive. Since the Schirmer tear test result was 13 mm/min, the patient was considered suspicious for dry eye. Epiphora, mucopurulent discharge and corneal vascularization were seen in the left eye. A pea-sized mass was observed in the palpebral conjunctiva of the left lower eyelid. The onset of ulcerative keratitis and blepharospasm were caused by the irritation of the mass and the patient's scratching.

Therefore, it was decided to directly remove the mass operatively rather than taking a biopsy. Ofloxacin (Exocin 0.3% ophthalmic drops, Allergan, Turkey) was applied as a local antibiotic, 1-2 drops four times

a day, until the day of surgery. Before the operation, a thoracic radiograph was taken to evaluate the suitability for anesthesia and possible metastases. The owners declined abdominal ultrasonography. Food and water were withheld for eight hours and two hours, respectively. The dog was premedicated with xylazine HCl (XylazinBio 2%, Interhas, Turkey) intramuscularly (IM) at a dose of 2mg/kg. Anesthesia induction was achieved by administering ketamine HCl (Ketazol 10%, Interhas, Turkey) IM at a dose of 10mg/kg. The patient was intubated orotracheally with an appropriate intubation tube. Maintenance of general anesthesia was provided with isoflurane (Isoflurane USP 100%, USA) in 100% oxygen with the end-tidal isoflurane concentration between 1% and 3%. The patient was ventilated via intermittent positive pressure ventilation in the pressure-control mode to maintain the end-tidal CO<sub>2</sub> level between 35-45 mmHg.

As a preoperative antibiotic, cefazolin sodium (25 mg/kg) was administered intravenously. Throughout the operation, a 0.9% NaCl solution was administered intravenously. The patient was placed in right lateral recumbency and prepared for routine aseptic surgery by clipping the hair around the surgical site (Figure 1A). The site was scrubbed with benzalkonium chloride 20% and povidone-iodine, then rinsed with alcohol carefully avoiding contact with the globe. The mass was circumscribed with chalazion forceps, then 1 mm clean margins were taken. The incision line was sutured, taking care to appose the eyelid border correctly. A continuous suture pattern was performed on only one plane by using a monofilament absorbable suture material (Figure 1B).

During the postoperative period, ofloxacin (Exocin 0.3% ophthalmic drops, Allergan, Turkey) three drops four times a day, oxytetracycline hydrochloride and polymyxin b sulfate ophthalmic ointment (Terramycin ophthalmic ointment, Pfizer, Turkey) twice a day and a lubricant (Viscotears ophthalmic gel, Bausch & Lomb) were administered. An Elizabethan

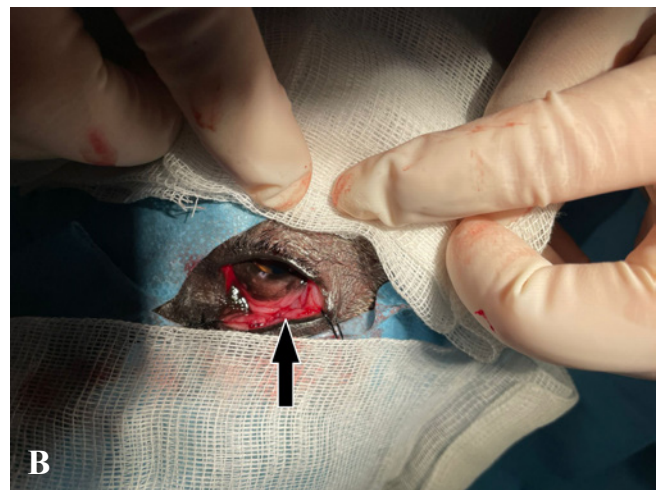


Figure 1. A. Preoperative image of the mass (white arrow). B. Perioperative image of the eyelid and conjunctiva (black arrow showing the suture line)



collar was placed to prevent the dog from scratching and to protect the surgical wound. Amoxicillin clavulanic acid (Synulox, 50 mL; Zoetis, NJ, USA) 20 mg/kg/day was administered subcutaneously for seven days postoperatively. The patient recovered uneventfully. Postoperative follow-up was conducted in the first month and every six months during the next three years. No recurrence was observed for 36 months.

The mass was fixed in 10% formalin for 48 hours. Routine histological tissue processing was performed on the tissues. The tissues whose processing was completed, were blocked into paraffin wax. Five  $\mu\text{m}$  thick sections were taken from the blocks for histopathological examination. They were stained with hematoxylin and eosin, and examined under a light microscope.

Histopathological examinations revealed that the cells forming the tumor were mostly atypical histiocytes with a round-like structure, with large cytoplasm and prominent and large basophilic nuclei (Figure 2). Some tumor cells contained vacuoles and substances such as erythrocytes and hemosiderin in the cytoplasm they phagocytosed (Figure 3). Lymphocyte infiltrates with basophilic nuclei were frequently observed among the tumor cells (Figure 4).

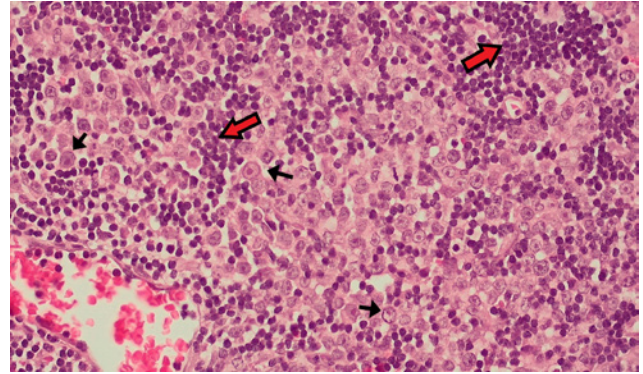
## DISCUSSION

Eyelid tumors are common in middle-aged and older dogs (Aquino, 2007; Wilcock, 2008). In a retrospective study by Kaya et al. (2018), it was shown that the age range of tumor cases was situated in the middle and older age groups. In the present case, the dog was seven months old, and the histiocytic sarcoma complex was diagnosed at a young age.

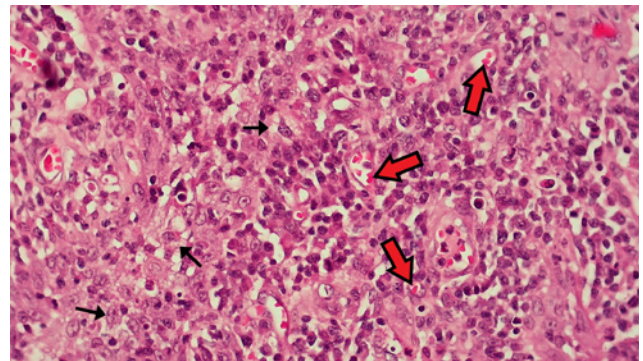
Eyelid involvement in cutaneous histiocytomas and attachment organs, and intraocular involvement in systemic histiocytosis have been reported (Scherlie et al. 1992). Cutaneous histiocytomas regress spontaneously, and reactive forms (cutaneous and systemic histiocytosis) usually respond to immunosuppressive therapy. However, histiocytic sarcoma complex is a malignant neoplasm of histiocytic origin with a poor prognosis (Naranjo et al. 2007).

In a study by Liu et al. (2019), a histiocytic sarcoma complex was detected on the eyelid of a 72-year-old person. In a case report by Rahj et al. (2018), a disseminated histiocytic sarcoma with intraocular involvement was described in a ten-year-old, female Rottweiler. The results of a study by Naranjo et al. (2007) conducted on 26 dogs revealed that the affected tissues of patients diagnosed with histiocytic sarcoma were anterior and posterior uvea, sclera, choroid, vitreous, and orbit. Although the dogs initially showed ocular clinical signs, most of the patients died due to complications arising from disseminated histiocytic sarcoma (Naranjo et al. 2007).

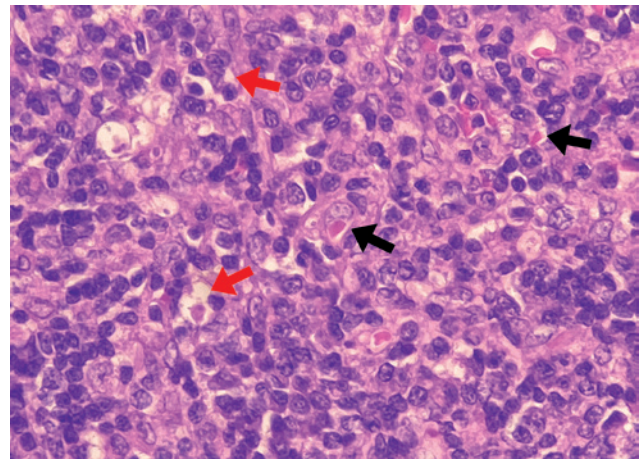
Histiocytic sarcoma cases have been reported in



**Figure 2.** Atypical histiocytes (black arrows) form the tumor and dense lymphocyte infiltrates (red arrows) between these cells (x200, HE).



**Figure 3.** Intracytoplasmic vacuole structures (black arrows) and newly formed blood vessels (red arrows) in atypical histiocytes (x200, HE).



**Figure 4.** Phagocytosed erythrocytes (black arrows) and intracytoplasmic vacuole formations (red arrows) in the tumor cells (x400, HE).

the spleen, liver, lung, subcutis, skeletal muscles and even the brain, but to the authors' knowledge, no case of HSC in the palpebral conjunctiva has been reported so far (Affolter and Moore, 2002; Şahinduran et al., 2016). HSC can be localized or disseminated in dogs. Both types can show aggressive behavior, but it has been reported that localized HSC has a better prognosis than disseminated HSC (Fulmer and Mauldin,

2007). While the term ‘localized’ refers to the development of the tumor in one region, regional lymph nodes and other distant metastases refer to the term ‘disseminated’. Histologically, there are tumoral cases in which large round cells predominate and cases in which spindle-shaped tumor cells predominate (Goldschmidt and Goldschmidt, 2017). In the present report, the tumor cells were mostly round oval-shaped cells with prominent cytoplasm, containing erythrocytes and vacuoles. It has been reported that the origin of localized HSC cases in dogs is mostly the presence of myeloid dendritic antigen-presenting cells (Affolter and Moore, 2002). However, further studies are required to determine the exact origin of the tumor.

## CONCLUSION

Histopathological evaluation is essential for the diagnosis of localized and disseminated histiocytic sarcomas in dogs. To the authors’ knowledge, this is the first case report of histiocytic sarcoma complex in the palpebral conjunctiva in a dog. No other masses were detected in other parts of the patient’s body, and its general condition was good. During the three-year post-operative follow-up period, no recurrence of the mass was observed. It was concluded that the early diagnosis of histiocytic sarcoma complex in the palpebral conjunctiva of the young dog without breed predisposition, and the surgical removal of the mass prevented possible recurrences and increased the patient’s welfare.

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