

Primary Mast Cell Tumor in the Palpebral Conjunctiva in a Dog

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ABSTRACT

Background: Mastocytoma is the neoplastic proliferation of mast cells. This neoplasia exhibits a mild to extremely aggressive biological behaviour and can develop in any anatomical location. It is considered one of the most clinically relevant oncodermatological disorders in veterinary medicine, although it is considered rare in the conjunctiva of dogs. The objective of this work is to describe the case and highlight the importance of cytological examination in the diagnosis and treatment.

Case: A 13-year-old mixed-breed neutered dog was brought to the Veterinary Teaching Hospital for presenting a nodule in the lower palpebral conjunctiva of the right eye for the past 3 months. The patient had good body condition and was clinically healthy. At the ophthalmic examination, a nodular and whitish enlargement with a smooth surface was observed on the lower palpebral conjunctiva of the right eye. No impairment of vision or ocular reflexes or any other alterations in the left eye were noted. Material obtained from the lesion with swab for cytological examination and stained with Diff Quick and allowed to obtain the diagnosis of mastocytoma. The cellularity was low to moderate and composed of round cells. The cytoplasm appeared indistinct with numerous metachromatic granules. The nucleus was rounded, paracentral, with condensed chromatin and inconspicuous nucleoli. Moderate anisocytosis and anisokaryosis were also observed. Complete blood count and serum biochemistry results were performed, and the results obtained were within reference values. The treatment consisted of surgical excision of the nodule with a margin of 0.5 mm on all edges followed by compressive hemostasis. The material obtained by the surgical excision was sent for histopathological analysis to confirm the cytological diagnosis and for surgical margin delimitation. On macroscopy, two eyelid fragments were identified. The tissue was firm and uniformly whitish. The smaller fragment was irregular and whitish. Microscopically, in the palpebral conjunctiva, beneath the surface epithelium, a non-circumscribed, non-encapsulated, and densely cellular infiltrative neoplastic proliferation was observed. The cells were round, with moderate amount of cytoplasm, a large number of intracytoplasmic basophilic granules, and well-defined cytoplasmic borders. The nuclei were round, with condensed chromatin and inconspicuous nucleoli. Cellular and nuclear pleomorphism was classified as moderate, and, after evaluation 10 fields at a magnification of 400x, no mitoses were seen. Toluidine blue staining improved the observation of cytoplasmic granules. Additionally, a multifocal and pronounced inflammatory infiltrate of eosinophils was noted. Histopathology findings confirmed the cytological diagnosis of mastocytoma. The patient showed good recovery after the surgical procedure with no local recurrence of the tumor after 60 days.

Discussion: In clinical routine, to obtain an adequate sample for diagnosis is not always easy. The less traumatic and invasive technique should be preferred to minimize complications related to physical or chemical restraint. The time to obtain diagnostic information is also crucial for the treatment outcome. Cytological examination of a specimen obtained by swab and stained with Diff Quick staining proved to be effective for the diagnosis of a mastocytoma in the palpebral conjunctiva, a very unusual site of this tumor, demonstrating the relevance of this technique.

Keywords: mast cells, cytology, histopathology, dog, oncology.

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INTRODUCTION

Mastocytoma is considered one of the most clinically relevant disorders in small animal practice [3]. It can develop anywhere in the body, and mainly affected are cutaneous and subcutaneous tissues. The tumor biological behaviour can vary from low metastatic potential to extremely aggressive lesions [6] and its location is defined as an important prognostic indicator [24]. Fine-needle aspiration (FNA) is diagnostic for 92-96% of tumors [3], while histopathological examination is necessary for precise results and is required to determine the biological behaviour of mast cell tumors in dogs.

Ocular tumors in dogs and cats are relatively rare [7]. Among canine orbital neoplasms, the majority are mesenchymal tumors (40%), followed by epithelial origin (35%), neural origin (8%), and round cell or other types of tumors (17%). Of these, most are lymphomas, followed by melanomas and rare mastocytomas [9]. Among ocular surface/appendage neoplasms originating in the conjunctiva are melanocytic neoplasms; vascular neoplasms (hemangiomas and hemangiosarcomas); adenoma/adenocarcinoma of the third eyelid gland; and, less commonly, mastocytomas [13]. In this context, due to the low prevalence of conjunctival mastocytomas, the aim of this report is to describe a mast cell tumor diagnosed by cytology in the lower right palpebral conjunctiva.

CASE

A 13-year-old mixed-breed medium-sized, male, neutered dog was brought to the Veterinary Teaching Hospital of the Federal University of Santa Maria due to a volume enlargement in the right palpebral conjunctiva for the past 3 months. The patient was in good body condition, and no abnormalities were found during the clinical examination. In the ophthalmic examination, a nodular, whitish enlargement with a smooth surface was observed on the lower palpebral conjunctiva of the right eye, which was more prominent when the eyelid was retracted (Figure 1). No impairment of vision or reflexes, or other alterations were observed in the left eye.

After physical restraint of the patient, the sample for cytology was obtained with the aid of a sterile cotton swab, rotating it under the nodule. The material was transferred to glass slides for microscopy by rolling the swab. The slides were air-dried, and

subsequently stained with a Diff-Quick stain¹. The samples were evaluated at magnifications of 100x and 400x and revealed low to moderate cellularity, composed of round cells morphologically consistent with mast cells. The cytoplasm appeared indistinct with numerous metachromatic granules. The nuclei were rounded, paracentral, with condensed chromatin and inconspicuous nucleoli. Moderate anisocytosis and anisokaryosis were also observed. The samples also contained squamous epithelial cells with melanin granules inside the cytoplasm (Figure 2). Eosinophils were not observed. Cytology findings suggested mastocytoma, and histopathological examination was performed for confirmation and classification.

Based on the cytological diagnosis, the decision was to remove the tumor. Biochemical tests (blood ureic nitrogen (BUN), creatinine, alanine aminotransferase, albumin, total proteins, serum alkaline phosphatase) and a complete blood count were within reference values [21].

The surgical procedure was performed after pre-anaesthetic medication with methadone² [Mytedom® - 0.3 mg/kg, IM]. Induction was carried out by administration of diazepam³ [Diazepam® - 0.2 mg/kg, IV] and propofol³ [Provide® - 2.5 mg/kg, IV], and inhaled anaesthetic maintenance with isoflurane was used at concentrations adjusted to maintain the



Figure 1. Nodular volume enlargement (arrow) located in the lower palpebral conjunctiva of the eye right of a dog.

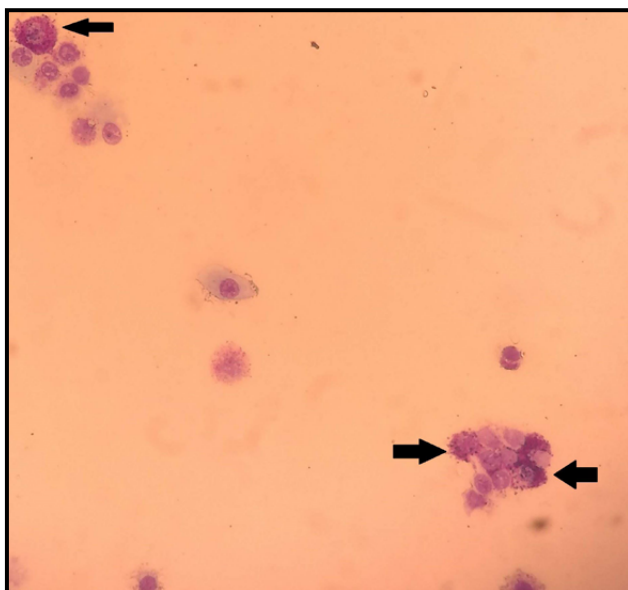


Figure 2. Cytological sample collected of lower palpebral conjunctiva of the eye right of a dog using the swab technique and stained with Diff-Quick. Note round cells (arrow) with notable presence of intracytoplasmic metachromatic granules. [400x].

anaesthetic plane. Surgical excision of the nodule was done with a margin of 0.5 mm on all edges, followed by mechanical compression for approximately 5 min until complete haemostasis, which was effective, and sutures were not required. Prophylactic antibiotic therapy consisted of cephalexin³ [Cefalexina[®] - 30 mg/kg, IV], and analgesic/anti-inflammatory treatment included dipyrone³ [Analges V[®] - 25 mg/kg, IV] and dexamethasone³ [Acetato de dexametasona[®] - 0.25 mg/kg, IV].

After the surgery, cytological imprints were made with the obtained fragments, and material was collected by fine-needle aspiration for cytological re-evaluation. The Diff-Quick stained samples showed moderate to marked cellularity, mainly consisting of mast cells, confirming the cytological diagnosis of mastocytoma at a magnification of 400x. Subsequently, tissue fragments were fixed in 10% formalin and sent for histopathological and histochemical evaluation.

During macroscopic examination, the presence of 2 eyelid fragments was noted. The larger fragment measured 1.0 x 0.6 x 0.4 cm, nodular, with an irregular surface and a diameter of 0.5 cm. On cutting, it was firm and uniformly whitish. The smaller fragment was irregular and whitish (Figure 3). Microscopically, in the palpebral conjunctiva, beneath the surface epithelium, infiltrative neoplastic proliferation, non-circumscribed, non-encapsulated, and densely cellular was observed.



Figure 3. Macroscopic view of 2 tissue fragments, showing a white nodular mass located in the lower palpebral conjunctiva of the right eye of a dog.

The cells were round, with moderate cytoplasm, a large amount of intracytoplasmic basophilic granules, and well-defined cytoplasmic boundaries. The nuclei were round, with condensed chromatin and inconspicuous nucleoli. There was moderate cellular and nuclear pleomorphism, and no mitoses were observed after evaluating 10 fields at a magnification of 400x (Figure 4A). Toluidine blue staining was also performed, facilitating the observation of cytoplasmic granules (Figure 4B). Additionally, a multifocal and pronounced inflammatory infiltrate of eosinophils was noted. The histopathological diagnosis was mastocytoma.

The patient had a good recovery after the surgical procedure and was discharged with a prescription for dexamethasone eye drops³, [Cylcort[®] Colírio - one drop every 8 h for 10 days], and oral dipyrone⁴ [Dipirona monoidratada[®] - 25 mg/kg, VO, every 8 h for 3 days]. After 60 days, there was no tumor growth.

DISCUSSION

Fine-needle aspiration cytology (FNAC) is diagnostic for 92-96% of mast cell tumors [3] and is also used in the diagnosis of tumors in the ocular conjunctiva in dogs [8]. However, it was considered unviable at the time of the consultation because of the affected region, which was too close to the eye, representing a risk of ophthalmic injury during FNAC. Thus, a swab of the lower palpebral conjunctiva over the nodule was chosen. Given that the normal cytological pattern of healthy canine conjunctiva consists of superficial, intermediate, and basal epithelial cells, sometimes containing melanin granules, as well as goblet cells, leukocytes, and mucus [4], the slight to moderate presence of mast cells observed in cytology, probably due to the ease by which these cells exfoliate [3], allowed for a suggestive diagnosis of mastocytoma.

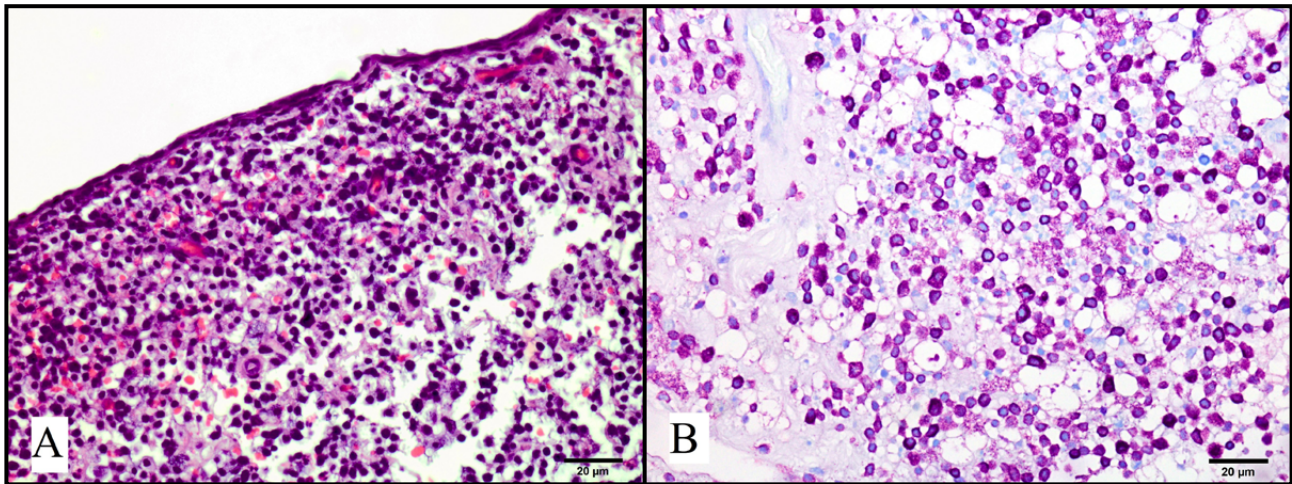


Figure 4. A- Histopathological sample of lower palpebral conjunctiva of the eye right of a dog showing high cellularity composed by mast cells and eosinophils [HE; 100x]. B- Histopathological sample of lower palpebral conjunctiva of the eye right of the same dog with a high presence of intracytoplasmic metachromatic granules [Toluidine Blue staining; 100x].

Cytology suggested that the tumor in this case could be considered less aggressive, because the cells were well differentiated (due to the presence of cytoplasmic granules). However, cytological classification is considered auxiliary for initial clinical decision-making, with histological classification required for the identification of high-grade neoplasms [12].

The histopathology also confirmed mastocytoma and suggested a less aggressive behaviour due to the small size of the tumor (less than 3 cm) and the absence of mitotic figures. The mitotic index is strongly predictive of the tumor biological behaviour and survival and can be used as a prognostic indicator [19], as also reported in subcutaneous mastocytomas in dogs [22]. Additionally, patients with tumors smaller or equal to 3 cm in maximum diameter survive longer [10], they have a better prognosis.

The tumor was not graded because the classification system which is used to grade cutaneous mast cell tumors in dogs [11,16] is not applicable to tumors located in the conjunctiva. The histological grade does not interfere with the prognosis of patients with mastocytomas in this location [8].

The presence of a pronounced eosinophilic inflammatory infiltrate in the histopathological examination may be related to the release of inflammatory mediators such as IL-5 (interleukin 5), produced by mast cells, which can attract these cells to the site of the lesion [14]. The presence of an eosinophilic infiltrate is usually observed in the histopathological examination of cutaneous mastocytomas [18], as well as in ocular conjunctiva mastocytomas [2]. The absence

of eosinophils in cytological samples is likely related to the collection technique (conjunctival swab), where there was no access to the internal regions of the tumor.

Additional tests such as abdominal ultrasound, chest radiography, and cytology of liver, spleen, and bone marrow were not performed as the histopathology suggested less aggressive behaviour. Sentinel lymph node cytology is always recommended, even in cases of low-grade mast cell tumors [25]. In this case, this procedure was not performed. Additional examinations are typically recommended in cutaneous mastocytomas [3,6], in cases presenting clinical signs, concurrent disease, or high-grade tumors [17].

The surgical excision of the nodule is considered the primary treatment for all cases of mastocytomas in the conjunctiva [8]. The excision of the nodule, performed with a margin of 0.5 mm on all edges, can be considered satisfactory due to the location, which makes extensive surgical excision impractical [5]. A study reported that surgical margins of 5 mm or less for cutaneous mast cell tumors in challenging locations (distal limbs) were associated with a 93% recurrence-free rate at 2 years in most cases [8]. In most cases of conjunctival mastocytomas, dogs are disease-free after surgical excision. Only two cases in the literature describe local recurrence [8]. Adjuvant therapies to the surgical procedure, such as radiotherapy and chemotherapy, were not performed because surgical excision was considered satisfactory, the tumor burden was low, and the patient did not show signs of metastasis [3].

Postoperatively, a glucocorticoid eye drop (dexamethasone) was prescribed due to its depressive

effects on proliferation, reduction in mast cell degranulation capacity, and cytokine production [1]. The use of glucocorticoids during and after surgery is also justified by their anti-inflammatory effects [23], and it usually yields good results in the treatment of canine cutaneous mastocytomas [15,20].

The prognosis of the patient can be considered favourable, given the absence of local recurrence 60 days after surgical removal, the absence of clinical signs, and the low probability of metastasis, as observed in conjunctival mastocytomas in dogs [8]. Cytology of a conjunctival mast cell tumor stained with Diff Quick proved to be a fast, easy to perform and reliable

method for screening in an uncommon site. The therapy was guided by the cytological results and grading of the tumor was obtained by histopathology of the excised tumor and confirmed the cytological findings.

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Declaration of Interest. The authors report no conflicts of interest. The authors alone are responsible for the contents of the paper.

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