Acta Scientiae Veterinariae, 2023. 51(Suppl 1): 869.

CASE REPORT
Pub. 869

ISSN 1679-9216

Epididymal Primary Mast Cell Tumor in a Dog

Geórgia Modé Magalhães[1], Elzylene Léga[2], Rafael Torres-Neto[3], Valéria Amorim Conforti[4], Renée Laufer Amorim[5], Camila Ângela Marques[6], Thaís Gomes Rocha[6] & Cristiane dos Santos Honsho[6]

ABSTRACT

***Background*:** In the literature, there are a few descriptions of epididymis neoplasia in domestic animals, especially considering primary tumors. In the few reports found in literature, the lesions were a consequence of the invasion of testicular or paratesticular neoplasia, as a papillar carcinoma in a dog's and a bull's epididymis, and mesenchymal tumors - fibrome/fibrosarcoma, leiomyoma/leiosarcome. On the other hand, mast cell tumors are the second most prevalent neoplasia in dogs in Brazil, affecting especially the skin. The aim of this report is to describe for the first time a low malignancy mast cell tumor in a mixed-breed dog's epididymis, without metastasis or recurrence in a 2-year follow-up period.

***Case*:** A 10-year-old male mixed-breed dog was presented for pre-surgical evaluation for elective orchiectomy. In the physical examination, an increase in the volume of approximately 2 cm with an irregular appearance was identified on palpation in the cranial pole of the left testis. In the trans surgical period, an increase in testicular volume (4 cm long x 2 cm wide) was observed, with a firm consistency in the region of the vas deferens with macroscopic changes in the region. The testis was sectioned, and the fragments were sent for histopathological evaluation in 10% buffered formaldehyde. There was a fairly cellular circumscribed neoplastic infiltrate, distributed in a sheet and separated by fibrovascular stroma, and rounded neoplastic cells with a moderate amount of basophilic cytoplasmic granulation, and discrete anisocytosis and anisokaryosis. The nuclei were rounded with vesicular chromatin with 1 or 2 distinct nucleoli. No mitosis figures were observed in 10 high power fields (400x). Few eosinophils were distributed throughout the neoplastic cell population. Immunohistochemistry demonstrated immunostaining for KIT protein with perimembranous staining in 95% of neoplastic mast cells, giving a KIT 1 pattern. There was no positive nuclear staining for Ki67 in any cell of the histological sections examined. A grade II mast cell tumor (low grade of malignancy) was diagnosed. After diagnosis, the animal underwent radiographic evaluation of the chest and abdominal ultrasound, and a new physical inspection in search of nodules, plaques, skin lesions, or subcutaneous masses. There were no metastases in the thorax and abdominal cavity, nor physical alterations, and it can be inferred that the epididymis was the primary site of the mast cell tumor. After 2 years of orchiectomy, there were no recurrences, and no chemotherapy treatment was performed.

***Discussion*:** Extracutaneous mast cell tumors are uncommon in animals, but have been reported in oral and nasal mucosa, nasopharynx, larynx, trachea, intestine, visceral lymph nodes, spleen, liver, spinal cord, intestine, ureter, conjunctiva, lung and more recently in tear gland of the third eyelid. However, in the authors' assessment, this is the first description of mast cell tumor in the epididymis in dogs. The diagnosis was established by histopathological examination, which revealed a grade II epididymal mast cell tumor and immunohistochemical evaluation (KIT and Ki-67) as being of low aggressiveness. The diagnosis of a primary tumor was confirmed since the staging was established after the histopathological diagnosis, involving chest radiography, abdominal ultrasound, cutaneous evaluation in search of nodules, plaques, cutaneous and subcutaneous lesions, and did not reveal other abnormalities or metastases not identified in the preoperative evaluation. In addition, immunostaining with KIT and Ki-67 reaffirmed the low degree of malignancy and the potential for metastases, which can be observed by the asymptomatic follow-up of the patient 2 years after the surgical excision.

Keywords: tumoral, neoplasm, carcinoma, metastases, histopathology, immunohistochemistry.

DOI: 10.22456/1679-9216.126619

Received: 17 November 2022 Accepted: 24 March 2023 Published: 9 May 2023

[1]Federal Institute of Education, Science and Technology of the South of Minas Gerais (IFSULDEMINAS), Muzambinho, MG, Brazil. [2]Educational Foundation of Ituverava (FEI), Ituverava, SP, Brazil. [3]VETMOL - Diagnóstico em Patologia Molecular Veterinária e Pesquisa, Botucatu, SP. [4]Washington State University (WSU), Pullman, WA, USA. [5]São Paulo State University (Unesp), Botucatu. [6]University Vila Velha (UVV), Vila Velha, ES, Brazil. CORRESPONDENCE: C.S. Honsho [crishonsho@yahoo.com.br]. University of Vila Velha - UVV. Campus Biopráticas. Rua São João n. 48. CEP 29101-420 Vila Velha, ES, Brazil.

INTRODUCTION

Epididymal neoplasms are extremely uncommon in domestic animals [6,14] and when present, they usually result from the invasion of testicular or paratesticular tumors [14,24]. There are reports of papillary carcinoma in the epididymis of dogs [1,6,14,21] and a bull [14], and of mesenchymal tumors, fibroma/fibrosarcoma, and leiomyoma/leiomyosarcoma [1,14,22].

The aim of this study is to report the first occurrence of primary mast cell tumor in the epididymis, of low malignancy, in a mixed breed dog with no metastasis nor recurrence 2 years after tumor excision.

CASE

A 10-year-old male mongrel dog was presented for a pre-surgical evaluation for elective orchiectomy. On physical examination, the animal was normal except for the identification of an increase of volume of approximately 2 cm, with an irregular aspect in the cranial pole of the left testicle, observed on physical examination. The animal was submitted to routine preoperative examinations: complete blood count, biochemical evaluation with hepatic and renal profile, electrocardiogram, and echodopplercardiography. With the exams within the normal range, orchiectomy was scheduled.

During the transurgical period, an increased volume in the testicular area (4 cm long x 2 cm wide) was observed, with a firm consistency in the region of the vas deferens and macroscopic changes in the region. After excision of the testis, the lesion was sectioned into one-centimeter fragments, which were immersed in a 10% formaldehyde buffered solution and sent for histopathological evaluation.

The fragment had a fairly cellular circumscribed neoplastic infiltrate, distributed in a sheet (Figure 1) separated by a fibrovascular stroma. The neoplastic cells were rounded and had a moderate amount of basophilic cytoplasmic granulation. Discrete anisocytosis and anisokaryosis were observed. The nuclei were rounded, occasionally edentulous, with vesicular chromatin presenting 1 or 2 distinct nucleoli. No mitosis figures were observed in 10 high power fields (400x). Few eosinophils were distributed throughout the neoplastic cell population. The margins of the histological sections showed neoplastic involvement.

Immunohistochemistry was performed with markers for cell differentiation and proliferation. The result demonstrated immunostaining for KIT[1] protein with perimembranous staining in 95% of neoplastic mast cells, giving a KIT 1 pattern. There was no positive nuclear staining for Ki67[1] in any cell of the histological sections examined. A diagnosis of grade II (low grade of malignancy) mast cell tumor was made [11].

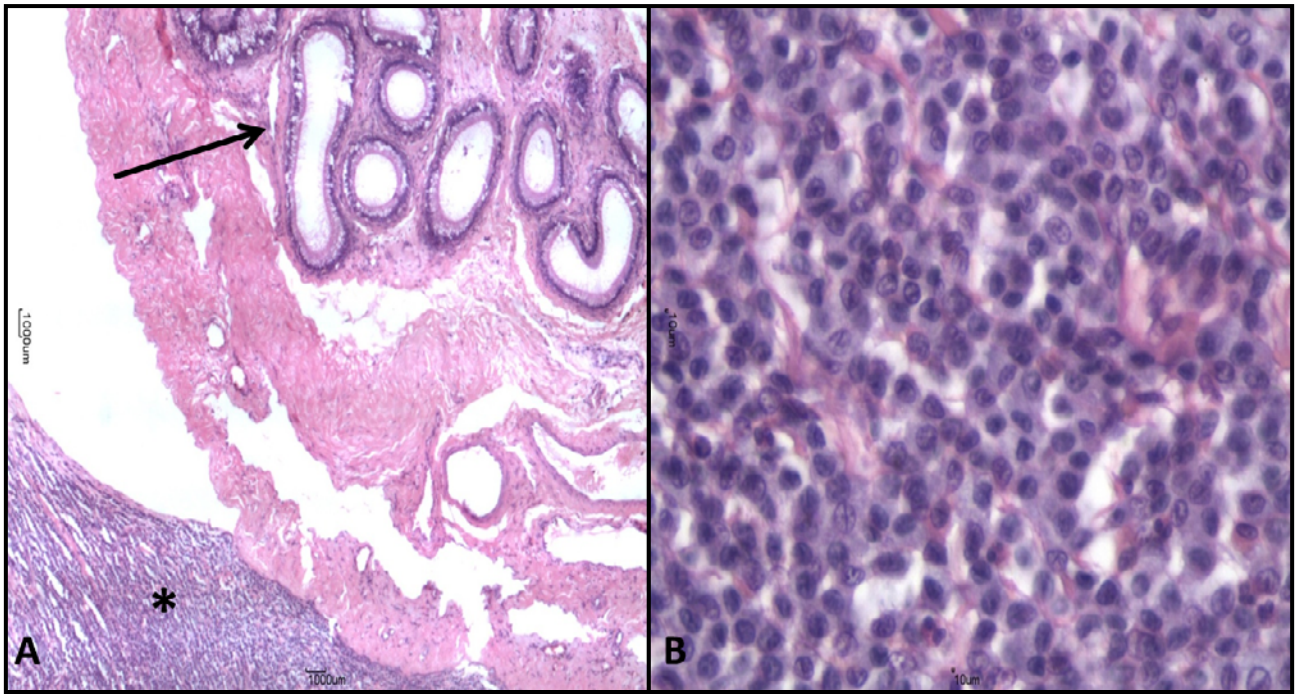

Figure 1. Photomicrograph of mast cell tumor grade II and low grade of malignancy in the dog's epididymis. A- Epididymis (arrow) and the presence of proliferation of mast cells in (*) [HE; obj.10]. B- Proliferation of neoplastic mast cells with little cellular pleomorphism [HE; obj.40].

After the diagnosis, the animal underwent radiographic evaluation of the chest and abdominal ultrasound, and a new physical inspection in search of nodules, plaques, skin lesions, or subcutaneous masses. There were no physical changes nor metastases in the chest and abdominal cavity, which leads to the conclusion that the epididymis was the primary site of the mast cell tumor.

Two years after orchiectomy and tumor excision, there were no recurrences, and no chemotherapy treatment was performed. This was a report of a primary mast cell tumor of the epididymis with C-Kit 1 immunophenotype, therefore, non-aggressive.

DISCUSSION

Mast cell tumors are divided into 2 subtypes: connective tissue mast cell tumors and mucosal mast cell tumors. Connective tissue cells are found mainly in the skin, peritoneal cavity, non-mucosal portion of the gastrointestinal tract, and the fibrous capsule of internal organs. Mucosal mast cell tumors are in the lamina propria of the gastrointestinal tract and lungs [10,18]. Cutaneous mast cell tumors are malignant and the most commonly diagnosed in dogs worldwide [7,9,11,13], while extracutaneous mast cell tumors are less common, but have been reported in oral and nasal mucosa, nasopharynx, larynx, trachea, intestine, lymph nodes, visceral [10,20], spleen, liver [13], spinal cord [17], intestine [15], ureter [25], conjunctiva [2,12]; lung [4] and more recently in the lacrimal gland of the third eyelid [8]. However, to the authors' knowledge, this is the first report of mast cell tumor in a dog's epididymis.

Animals over 9 years of age are the most affected by mast cell tumors [3,7,13,27] - as the animal in this report - despite having already been identified in young animals [13,15,23]. There is no predisposition regarding gender [3,7,13,24,28].

There are many reports of mast cell tumor in mixed-breed patients, such as the case of the animal in this study, but it is more frequent in pure breeds such as Boxers, Pugs, Labrador Retrievers and Golden Retrievers, Weimaraners, French Bulldogs, Dachshunds, Boston, Bull and Staffordshire terriers, and Shar-peis, among others [3,7,13].

Mast cell tumors present a variable and unpredictable biological behavior, ranging from benign to metastatic and potentially fatal tumors [5,11,18]. In dogs, the anatomical location has already been used as a predictive factor of the biological behavior of mast cell tumors, attributing greater aggressiveness to those located in the gastrointestinal tract, digits, and viscera, which is probably associated with greater systemic involvement of mast cell tumors, with involvement of lymph nodes and distant metastases [19,26]. Normally, this presentation is preceded by aggressive primary lesions that lead the animal to death within 6 months [13,19], different from what was observed in this patient, in which in a 2-year follow-up of the diagnosis no physical, radiographic, and ultrasonographic evidence of metastases or involvement of abdominal lymph nodes was found.

Iwata *et al*. [10] reported more aggressive growth in extracutaneous mast cell tumors compared to cutaneous ones, however, other authors have already reported the opposite [7,9,13]. Thus, histological classification using a cell differentiation scale is the main tool for veterinary pathologists to assess the biological behavior of canine mast cell tumors and their prognosis [11,13,16,21]. For tumors classified as low grade, the use of proliferation markers, KIT expression, and Ki-67 are essential to determine the risk of metastases and select the best treatment [11,13,16,27]. In this report, the identification of the mast cell tumor and its classification as grade II according to the histological characteristics were important to guide the clinician in the search for other abnormalities not identified in the pre-surgical evaluation and the establishment of their staging by means of abdominal ultrasound and chest radiography. In addition, immunostaining with KIT and Ki-67 reaffirmed the low degree of malignancy and the potential for metastases, which can be observed by the asymptomatic follow-up of the patient 2 years after the surgical excision.

Symptoms related to patients with mast cell tumors are often nonspecific, including anorexia, emesis, diarrhea, melena, and signs of depression, which are described as promoted by the release of histamine, heparin, and other vasoactive amines by the tumor, leading to gastrointestinal ulcerations [13,16,27]. Anemia, eosinophilia, and neutrophilia have been reported in patients with visceral mast cell tumors [28]. In the dog of this report, specifically, the lesion of irregular appearance was identified during the physical inspection, although the owner observed no symptomatology prior to the consultation. The pre-surgical exams (blood count, renal and hepatic biochemistry, electrocardiography, and echodopplercardiography) did not reveal alterations, as

well as the exams performed for staging after receiving the diagnosis and during the 2-year follow-up.

In conclusion, the definitive diagnosis of mast cell tumor was established by histopathological examination, however, the inclusion of other evaluations such as immunohistochemistry and tumor location contributed to the determination of the prognosis and the safety of the established treatment. In addition, it is worth emphasizing the importance of tumor staging, including radiographic and ultrasound assessments in patient follow-up.

MANUFACTURER

[1]Dako North America Inc. Carpinteria, CA, USA.

Declaration of interest. The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

REFERENCES

1 **Balao C.S., Gómez L.G., Cuesta Gerveno J.M., Ortega-Ferrusola C., Martín-Muñoz P., Duque F.J.C., Parejo C. & Peña Vega F. 2019.** A Rare Case of a Primary Unilateral Low-Grade Paratesticular Leiomyosarcoma in a 2 Years Old Dog. *Frontiers in Veterinary Science*. 6: 83. DOI: 10.3389/fvets.2019.00083.

2 **Barsotti G., Marchetti V. & Abramo F. 2007.** Primary conjunctival mast cell tumor in a Labrador Retriever. *Veterinary Ophthalmology*. 10(1): 60-64. DOI: 10.1111/j.1463-5224.2007.00502.x.

3 **Blackwood L., Murphy S., Buracco P., De Vos J.P., De Fornel-Thibaud P., Hirschberger J., Kessler M., Pastor J., Ponce F., Savary-Bataille K. & Argyle D.J. 2012.** European consensus document on mast cell tumours in dogs and cats. *Veterinary and Comparative Oncology*. 10(3): e1-e29. DOI: 10.1111/j.1476-5829.2012.00341.x.

4 **Campbell O., Lorimier L.P., Beauregard G., Overvelde S. & Johnson S. 2017.** Presumptive primary pulmonary mast cell tumor in 2 dogs. *The Canadian Veterinary Journal*. 58(6): 591-596.

5 **Casanova M., Branco S., Veiga I.B., Barros A. & Faísca P. 2021.** Stereology in Grading and Prognosis of Canine Cutaneous Mast Cell Tumours. *Veterinary Pathology*. 58(3): 483-490. DOI: 10.1177/0300985820985138.

6 **De Bosschere H., Desplenter N., De Naegel K. 2009.** Epididymal carcinoma in a dog. *Vlaams Diergeneeskundig Tijdschrift*. 78: 440-442.

7 **De Nardi A.B., Santos Horta R., Fonseca-Alves C.E., Paiva F.N., Linhares L.C.M., Firmo B.F., Ruiz Sueiro F.A., Oliveira K.D., Lourenço S.V., Francisco Strefezzi R., Brunner C.H.M., Rangel M.M.M., Jark P.C., Castro J.L.C., Ubukata R., Batschinski K., Sobral R.A., Cruz N.O., Nishiya A.T., Fernandes S.C., Santos S.C., Gerardi D.G., Challoub G.S.G., Biondi L.R., Laufer-Amorim R., Oliveira P.R., Lavalle G.E., Huppes R.R., Grandi F., Vasconcellos C.H.C., Anjos D.S., Luzo Â.C.M., Matera J.M., Vozdova M. & Dagli M.L.Z. 2022.** Diagnosis, prognosis and treatment of canine cutaneous and subcutaneous mast cell tumours. *Cells*. 11(4): 618. DOI: 10.3390/cells11040618.

8 **Demir A., Sevim Karagözo lu G., Yüzba io lu G. & Firat I. 2020.** Mast cell tumour of the third eyelid gland in a Kangal Dog. In: *20th International Continuing Education Congress* (Istanbul, Turkey). *Journal of Istanbul Veterinary Sciences*. 4(Suppl 1): [abstract PS01].

9 **Horta R.S., Lavalle G.E., Monteiro L.N., Souza M.C.C., Cassali G.D. & Araújo R.R. 2018.** Assessment of canine mast cell tumour mortality risk based on clinical, histologic, immunohistochemical, and molecular features. *Veterinary Pathology.* 55(2): 212-223. DOI: 10.1177/0300985817747325.

10 **Iwata N., Ochiai K., Kadosawa T., Takiguchi M. & Umemura T. 2000.** Canine extracutaneous mast-cell tumours consisting of connective tissue mast cells. *Journal of Comparative Pathology.* 123(4): 306-310. DOI: 10.1053/jcpa.2000.0420.

11 **Kiupel M., Webster J.D., Bailey K.L., Best S., DeLay J., Detrisac C.J., Fitzgerald S.D., Gamble D., Ginn P.E., Goldschmidt M.H., Hendrick M.J., Howerth E.W., Janovitz E.B., Langohr I., Lenz S.D., Lipscomb T.P., Miller M.A., Misdorp W., Moroff S., Mullaney T.P., Neyens I., O'Toole D., Ramos-Vara J., Scase T.J., Schulman F.Y., Sledge D., Smedley R.C., Smith K., W Snyder P., Southorn E., Stedman N.L., Steficek B.A., Stromberg P.C., Valli V.E., Weisbrode S.E., Yager J., Heller J. & Miller R. 2011.** Proposal of a 2-tier histologic grading system for canine cutaneous mast cell tumours to more accurately predict biological behavior. *Veterinary Pathology*. 48(1): 147-155. DOI: 10.1177/0300985810386469.

12 **Lee J.Y. & Jeong S.M. 2013.** Primary conjunctival mast cell tumor in a Korean native Jindo Dog. *Journal of Veterinary Clinics*. 30(2): 131-133.

13 **London C.A. & Thamm D.H. 2020**. Mast cell tumors. In: Vail D.M., Thamm D.H. & Liptak J.M. (Eds). *Withrow & MacEwen's Small Animal Clinical Oncology*. 6th edn. St. Louis: Elsevier, pp.382-403.

14 **MacLachlan N.J. & Kennedy P.C. 2002.** Tumours of the genital systems. In: Meuten D.J. (Ed). *Tumours in Domestic Animals*. Ames: Iowa State Press, pp.547-574.

15 **Mahler S. 2012.** Mast cell tumour in a young boxer dog. *Veterinary Record*. 171(7): 182. DOI: 10.1136/vr.e5551.

16 **Misdorp W. 2004.** Mast cells and canine mast cell tumours. A review. *The Veterinary quarterly*. 26(4): 156-169. DOI: 10.1080/01652176.2004.9695178.

17 **Moore T.W., Bentley R.T., Moore S.A., Provencher M., Warry E.E., Kohnken R. & Heng H.G. 2017.** Spinal mast cell tumours in dogs: imaging features and clinical outcome of four cases. *Veterinary Radioliology & Ultrasound*. 58(1): 44-52. DOI: 10.1111/vru.12429,

18 **O'Connell K. & Thomson M. 2013.** Evaluation of prognostic indicators in dogs with multiple, simultaneously occurring cutaneous mast cell tumours: 63 cases. *Veterinary and Comparative Oncology.* 11(1): 51-62. DOI: 10.1111/j.1476--5829.2011.00301.x.

19 **Ozaki K., Yamagami T., Nomura K. & Narama I. 2002.** Mast cell tumours of the gastrointestinal tract in 39 dogs. *Veterinary Pathology*. 39(5): 557-564. DOI: 10.1354/vp.39-5-557.

20 **Patnaik A.K., MacEwen E.G., Black A.P. & Luckow S. 1982.** Extracutaneous mast-cell tumour in the dog. *Veterinary Pathology*. 19(6): 608-615. DOI: 10.1177/030098588201900603.

21 **Patnaik K., Ehler W.J. & MacEwen E.G. 1984.** Canine cutaneous mast cell tumour: morphologic grading and survival time. *Veterinary Pathology*. 21(5): 469-474. DOI: 10.1177/030098588402100503.

22 **Ramírez G.A., Suárez-Bonnet A., Sánchez-Salguero X. & Molín J. 2020.** Primary verocay body-rich epididymal leiomyosarcoma in a dog. *Journal of Comparative Pathology*. 178: 27-31. DOI: 10.1016/j.jcpa.2020.06.005.

23 **Rigas K., Biasoli D., Polton G., Finotello R., Murphy S., Di Palma S., Starkey M. & Verganti S. 2012.** Mast cell tumours in dogs less than 12 months of age: a multi-institutional retrospective study. *Journal Small Animal Practice*. 61(7): 449-457. DOI: 10.1111/jsap.13181.

24 **Śmiech A., Ślaska B., Łopuszyński W., Jasik A., Bochyńska D. & Dąbrowski R. 2018.** Epidemiological assessment of the risk of canine mast cell tumours based on the Kiupel two-grade malignancy classification. *Acta Veterinaria Scandinavica*. 60(1): 70. DOI: 10.1186/s13028-018-0424-2.

25 **Son N.V., Chambers J.K., Shiga T., Kishimoto T.E., Kikuhara S., Saeki K., Fujiwara R., Tsuboi M., Nishimura R., Uchida K. & Nakayama H. 2018.** Sarcomatoid mesothelioma of tunica vaginalis testis in the right scrotum of a dog. *The Journal of Veterinary Medical Science.* 80(7): 1125-1128. DOI: 10.1292/jvms.18-0186.

26 **Steffey M., Rassnick K.M., Porter B. & Njaa B.L. 2004.** Ureteral mast cell tumour in a dog. *Journal of the American Animal Hospital Association*. 40(1): 82-85. DOI: 10.5326/0400082.

27 **Takahashi T., Kadosawa T., Nagase M., Matsunaga S., Mochizuki M., Nishimura R. & Sasaki N. 2000.** Visceral mast cell tumours in dogs: 10 cases (1982-1997). *Journal of the American Veterinary Medical Association.* 216(2): 222-226. DOI: 10.2460/javma.2000.216.222.

28 **Welle M.M., Bley C.R., Howard J. & Rüfenacht S. 2008.** Canine mast cell tumours: a review of the pathogenesis, clinical features, pathology, and treatment. *Veterinary Dermatology*. 19(6): 321-339. DOI: 10.1111/j.1365--3164.2008.00694.x.