



Case Report

Visceral Mast Cell Tumor and Mastocythemia in a Dog

Fernanda G. Grano¹, José Eduardo S. Silva¹, Guilherme D. Melo¹, Augusto Schweigert¹, Paulo C. Ciarlini¹, Gisele F. Machado¹*

Department of Animal Clinics, Surgery and Reproduction, College of Veterinary Medicine, UNESP - Univ Estadual Paulista, Araçatuba, Brazil

*Corresponding Author: Gisele F. Machado, Departamento de Clínica, Cirurgia e Reprodução Animal, Faculdade de Medicina Veterinária, UNESP – Universidade Estadual Paulista "Júlio de Mesquita Filho", Rua Clóvis Pestana 793, CEP 16050-680, Araçatuba, São Paulo, Brazil. E-mail: giselem@fmva.unesp.br

Submitted July 3rd 2012, Accepted September 20th 2012

Abstract

Mast cell tumor manifests as a localized proliferation of mast cells in the skin, or less frequently as a systemic disorder, which may be accompanied by the presence of neoplastic mast cells in the peripheral blood (mastocythemia). In some cases, the neoplastic circulating mast cells originate in the bone marrow, designated as mast cell leukemia, rarely observed in dogs, or the cells may arise from visceral mast cell tumors, characterizing systemic mastocytosis. The aim of this report was to describe a case of a six-year-old female German shepherd dog presenting with history of anorexia, hematemesis and diarrhea. The blood work revealed intense mastocythemia (43%), with degranulated mast cells, and anisocytosis. At necropsy, white nodular lesions in the thymic region and an infiltrative mass in mesenteric and abdominal lymph nodes were observed. Those lymph nodes were enlarged and off-white. Histopathological examination revealed neoplastic mast cells in the liver, spleen, lymph nodes, kidneys, lungs, gastric and enteric mucosae, and adrenal glands. The clinical, hematological and histopathological findings were compatible with mastocythemia, associated with a moderately differentiated visceral mast cell tumor.

Key words: canine, mastocytoma, myeloproliferative disorder, neoplasm.

Case Report

A six-year-old, female German shepherd dog was referred to the Veterinary Teaching Hospital of the College of Veterinary Medicine, UNESP-Araçatuba-SP, Brazil, with a day history of anorexia, hematemesis and diarrhea during two days. Physical examination revealed dehydration of 8% and congestion of oral and ocular mucosae. Cutaneous nodules were not observed. A complete blood work was performed. No changes were noticed in the erythrogram, however, leukogram changes included leukocytosis (65,300 leukocytes/μL), neutrophilia (28,732 neutrophils/μL) with regenerative left shift (3,265 band cells/μL), monocytosis (3,265 monocytes/µL) and evident mastocythemia (43%, corresponding to 28,079 cells/µL). Most of mast cells in the blood smear were degranulated, with moderate

anisocytosis and karyolysis (Figure 1). The dog died on the next day. At necropsy, multiple nodules were observed in the thymic region, and both mesenteric and abdominal lymph nodes were enlarged. For histopathological examination, the neoplastic nodules and samples of other tissues were collected, fixed in 10% neutral buffered formalin, and stained with hematoxylin-eosin (H&E). Slightly pleomorphic roundish cells with scant cytoplasmic granules, round to polymorphic nucleus with small nucleoli were observed in the nodules. There was low mitotic activity (less than 1 mitotic figure per highpower microscopic field). Tissue sections were further stained with toluidine blue and cytoplasmic granules stained metachromatic, characteristic of mast cells. Cells with the same pattern were also observed in the hepatic sinusoids and forming islands in the portal area (Figure 2a), spleen, pulmonary alveolar capillaries (Figure 2b),

adrenal glands (Figure 2c), renal interstitial and glomerular capillaries, and intestinal and gastric mucosae (Figure 2d). Eosinophils were not associated with the infiltrating neoplastic cells. The hematological and histopathological findings were compatible with mastocythemia associated with a moderately differentiated visceral mast cell tumor.

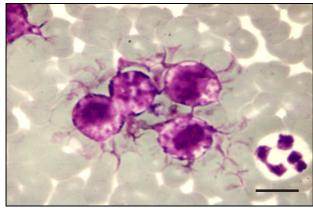
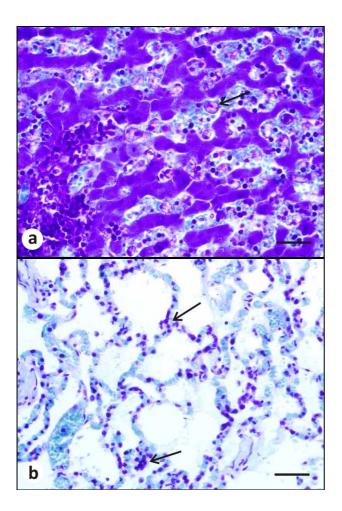


Figure 1 – Degranulated mast cells, with presence of karyolysis in canine blood smear. Panoptic stain. Bar = 10 µm.



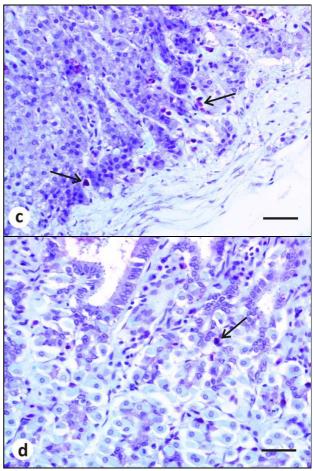


Figure 2 – Histochemical features of a visceral moderately differentiated mast cell tumor associated with peripheral mastocythemia in a dog. Note the presence of neoplastic mast cells (arrow) in the hepatic sinusoids (a), in the pulmonary alveolar capillaries (b), in the adrenal glands (c) and in the gastric mucosa (d). Toluidine blue. Scale bar = $50 \, \mu m$.

Discussion

Herein we report a case of visceral mast cell tumor and mastocythemia in a dog. Gross examination revealed multiple nodules mostly in abdominal lymph nodes. Mast cell neoplasms manifest as mast cells proliferation in the skin or less frequently as a systemic disorder with mast cells disseminating to internal organs. Neoplastic mast cells infiltrates may occur in lymph nodes, spleen, liver, gastrointestinal tract and bone marrow (1, 2, 20). Many of the clinical signs and paraneoplastic syndromes associated with disseminated mast cell tumors are attributed to the releasing of vasoactive substances produced by mast cells. These signs include anorexia, hematemesis and diarrhea, as presented in this report, and also vomiting, melena and abdominal pain as a result of gastrointestinal ulceration due to stimulation of H2 receptors of parietal cells in the stomach by high levels of histamine (6, 15, 22, 23).

In dogs, neoplastic mast cells may appear in large numbers in the peripheral blood (mastocythemia), due to systemic mastocytosis or mast cell leukemia (5). Although mast cell tumor is a common disorder in dogs, it is rarely observed accompanied by leukemic mastocytosis. In this type of leukemia, the neoplastic mast cells in the blood may appear in large numbers with systemic manifestations, more commonly reported in cats than in dogs (12, 20). Specific criteria to diagnose mast cells leukemia have not yet been established in animals with systemic mastocytosis. However, veterinary reports document a number of circulating mast cells higher than 10%, like in humans (20, 26). In this report, blood analysis detected 43% of circulating mast cells, in accordance with descriptions in the literature.

In human patients, the diagnosis of mast cell leukemia is based on the percentage of atypical mast cells, when the amount of these cells is higher than 10% in the bloodstream (26). Animals that have mast cell leukemia concomitant with systemic mastocytosis may also present moderate to severe leukocytosis due to the high number of mast cells (20). The rapid evolution of the disease is compatible with systemic mastocytosis, which usually presents a more aggressive behavior and a more unfavorable prognosis than the cutaneous form, especially when associated with mast cell leukemia (22).

The diagnosis of well differentiated mast cell tumors is easily performed in histopathological sections, while less differentiated mast cell tumors may be confused with other round cell tumors (28). Most of the neoplastic mast cells in dogs contain cytoplasmic granules that stain light grayish blue with H&E or purple with metachromatic dyes, such as toluidine blue (10, 24), enabling the differentiation of mast cell tumor from other round cell tumors (13, 17). Cellular morphology as differentiation of the cells, color and shape of the nucleus, number of nucleoli and number of mitotic figures, was used for malignancy evaluation, and based on it the final diagnosis of the neoplasm was a moderately differentiated visceral mast cell tumor.

Mast cell tumor metastases usually affect initially the local lymph nodes followed by the spleen (46%), liver (41%) or other visceral organs; the involvement of the lungs is not common (3, 9, 16, 25). In severe systemic dissemination, neoplastic mast cells may be present in the bone marrow and in the peripheral blood (25). In a report of grade III mast cell tumor in dogs, the involvement of lymph nodes, was similar to the observed in the case reported herein; in such cases is fundamental to determine the prognosis of the affected dogs: dogs with lymph node metastases by the time they are diagnosed had lower survival rates than those with absence of metastases (11). In disseminated mastocytosis, generally the visceral form of a mast cell tumor occurs secondary to an undifferentiated primary cutaneous mast cell tumor (8, 14, 25), which was not observed in this case.

Primary visceral tumors are rare in dogs and there are few reports of mast cell tumors detected primarily in the thoracic cavity (4, 21) or abdominal cavity (19), without cutaneous nodules, presentation more commonly described in cats than in dogs. Dogs with visceral mast cell tumor can present eosinophilia, basophilia, and mastocythemia (4, 21). In this case basophilia and eosinophilia were not detected, although mastocythemia was evident. Clinical, hematological and histopathological findings of the reported case are compatible with mastocythemia, likely due to systemic mastocytosis, associated with a moderately differentiated visceral mast cell tumor.

References

- AMMANN RW., VETTER, D., DEYHLE, P. et al. Gastrointestinal involvement in systemic mastocytosis. Gut., 1976, 17, 107-112.
- BENDEL WL., RACE GH. Urticaria pigmentosa with bone involvement. J. Bone Joint Surg., 1963, 45A, 1043-1056.
- CONROY JD. Canine skin tumors. J. Am. Vet. Med. Assoc., 1983, 19, 91–114.
- DAVIES AP., HAYDEN DW., PERMAN V. Noncutaneous systemic mastocytosis and mast cell leukemia in a dog: case report and literature review. J. Am. Anim. Hosp. Assoc., 1981, 17, 361–368.
- DE BOSSCHERE H., DELOOSE S. Mast cell leukemia in a dog [abstract]. Vlaams Diergeneeskundig Tijdschriftz, Jan 2009, 78(1), 49-52.
- DOBSON JM., SCASE TJ. Advances in the diagnosis and management of cutaneous mast cell tumours in dogs. J. Small Anim. Pract., 2007, 48, 424–31.
- GIL DA COSTA RM., MATOS E., REMA A. et al. CD117 immunoexpression in canine mast cell tumours: correlations with pathological variables and proliferation markers. BMC Vet. Res, 2007, 3, 19.
- 8. GOVIER SM. Principles of treatment for mast cell tumors. Clin. Tech. Small Anim. Pract., 2003, 18, 103–6.
- GROSS TL., IHRKE P., WALDER EJ., AFFOLTER VK. Mast cell tumors. Skin Diseases of the Dog and Cat: Clinical and Histopathologic Diagnosis, 2 ed. Oxford: Blackwell, 2005: 853–65.
- 10. HENDRICK MJ, MAHAFFEY EA, MOORE FM, VOS JH, WALDER EJ. World Health Organization. Histological classification of mesenchymal tumors of skin and soft tissues of domestic animals. 2 ed. Washington: Armed Forces Institute of Pathology; 1998: 29.
- 11. HUME CT., KIUPEL M., RIGATTI L. et al. Outcomes of Dogs with Grade 3 Mast Cell Tumors: 43 Cases (1997–2007). J. Am. Anim. Hosp. Assoc., Jan/Feb 2011, 47, 1.
- 12. JAIN NC. Essentials of Veterinary Hematology. 1 ed. Philadelphia: Lea & Febiger; 1993.
- KLATT EC, LUKES RJ, MEYER PR. Benign and malignant mast cell proliferations: diagnosis and separation using a pHdependent toluidine blue stain in tissue section. Cancer, 1983, 51, 1119-1124.
- LEMARIE RJ., LEMARIE SL., HEDLUND CS. MAST CELL tumors: clinical management. Comp. Cont. Educ. Pract. Vet., 1995, 17, 1085–1101.
- LONDON CA., SEGUIM B. Mast cell tumors in dog. Vet. Clin. Small Anim., 2003, 33, 473-489.

- O'KEEFE DA. Canine mast cell tumors. Vet. Clin. North Am.: Small An. Pract., 1990, 20, 1105–15.
- OZAKI K., YAMAGAMI T., NOMURA, K. et al. Mast Cell Tumors of the Gastrointestinal Tract in 39 Dogs. Vet. Pathol., 2002, 39, 557-564.
- PATNAIK AK., EHLER WJ., MACEWEN EG. Canine cutaneous mast cell tumor: morphologic grading and survival time in 83 dogs. Vet. Pathol., 1984, 21, 469-474.
- PATNAIK AK., TWEDT DC., MARRETTA SM. Intestinal mast cell tumour in a dog. J. Small Anim. Pract., 1980, 21, 207–212.
- PLIER ML., MAC WILLIAMS PS. Systemic mastocytosis and mast cell leukemia. In: FELDMAN BF., ZINKL JG., JAIN NC. Eds. Schalm's Veterinary Hematology. 5ed. Philadelphia: Lippincott Williams & Wilkins, 2000: 747-754.
- POLLACK MJ., FLANDERS JA., JOHNSON RC. Disseminated malignant mastocytoma in a dog. J. Am. Anim. Hosp. Assoc., 1991, 27, 435–440.
- ROCHA TM., FARIAS MR., WOUK AFPF. et al. Mastocitoma em cães – revisão. Clin Vet., 2004, IX (52), 42-54.

- 23. ROGERS KS. Mast cell tumors, dilemmas of diagnosis and treatment. **Controv. Clin. Onc.**,1996, 26(1), 87-102.
- SIMOES JPC, SCHONING, P. Canine mast cell tumors: a comparison of staining techniques. J. Vet. Diagn. Invest., 1994, 6, 458-465.
- 25. THAMM DH, VAIL DM. Mast cell tumors. In: WITHROW SJ., VAIL DM. Withrow & MacEwen's Small Animal Clinical Oncology, Eds. 4 ed. St Louis, MO: Saunders Elsevier, 2007: 402–24.
- TORREY E., SIMPSON K., WILBUR S., MUNOZ P., SKIKNE B. Malignant mastocytosis with circulating mast cells. Am. J. Hemat., 1990, 34 (4), 283-286.
- 27. WEBSTER JD., YUZBASIYAN-GURKAN V., MILLER RA. et al. Cellular proliferation in canine cutaneous mast cell tumors: associations with c-KIT and its role in prognostication. **Vet. Pathol.**, 2007, 44, 298–308.
- 28. YAGER JA., WILCOCK BP. Color atlas and text of surgical pathology of the dog and cat: dermatopathology and skin tumors. 1ed. London: Mosby-Year Book, 1994: 273-286.