BJVP
Brazilian Journal of Veterinary Pathology
ISSN 1983-0246

Case Report

Immunohistochemical and Morphopathological Features of Multiple Cutaneous Mast Cell Tumor in a Cow

Azizollah Khodakaram-Tafti[1*], Morteza Eshraghi[2], Bita Geramizadeh[3], Hanieh Shaterzadeh-Yazdi[1], Taghi Taghipur-Bazargani[4]

[1]Department of Pathology, School of Veterinary Medicine, Shiraz University, Shiraz, Iran.
[2]Veterinary Practitioner, Foudeh Dairy Farm, Esfahan, Iran.
[3]Department of Pathology, Transplant Research Center, Shiraz University of Medical Sciences, Shiraz, Iran.
[4]Department of Clinical Sciences, Faculty of Veterinary Medicine, Tehran University, Tehran, Iran.
* **Corresponding Author:** Department of Pathology, School of Veterinary Medicine, Shiraz University, Shiraz, Iran. E-mail: tafti@shirazu.ac.ir.

Submitted February 25th 2015, Accepted April 11th 2015

Abstract

A 4 year old female Holstein cow with multiple skin lesions was referred for clinical examination. Grossly, approximately 60 discrete cutaneous nodules and masses with variable sizes ranging from 1 to 5 cm were observed on both sides of flunks, shoulders, neck, back, and mammary glands. Histopathologically, the masses were composed of non-encapsulated accumulation of neoplastic round cells contained moderate to abundant amounts of finely eosinophilic granules in the cytoplasm. Cellular or nuclear pleomorphism and mitotic figures were not remarkable. Metachromasia was seen in cytoplasmic granules stained with toluidine blue. In the immunohistochemical staining, the neoplastic cells were positive for vimentin and c-kit. No immunoreactivity was seen for cytokeratin and HMB - 45. Based on these findings, multiple cutaneous mast cell tumor was diagnosed. Immunohistochemical features of mast cell tumor have not been reported previously in cattle.

Key words: multiple mast cell tumor, pathology, immunohistochemistry, cattle.

Introduction

Mast cells are normal components of connective tissues throughout the body. These cells originate from CD34 progenitor cells in bone marrow and then migrate to tissues such as skin, lung, and digestive tract (11, 18). A characteristic feature of mature mast cells is the presence of cytoplasmic granules which contain many biological mediators such as histamine, heparin, proteolytic enzymes, leukotrienes, and prostaglandins (8, 10, 17).

Mast cells appear to play a central role in many inflammatory and immune reactions. These cells when stained with Toluidine blue or Giemsa show a characteristic color change known as metachromasia that is caused by hexasaccharides, the fundamental unit of heparin (12, 17). Accumulation and proliferation of mast cells occur in a variety of allergic, inflammatory, parasitic, or idiopathic conditions. However, the presence of pure population of these cells with no evidence of predisposing etiology is termed mast cell tumor (16).

Mast cell tumors or mastocytomas are seen most commonly in dogs, less frequently in cats and rarely in cattle, horses and pigs (1, 7, 17). Many of cutaneous forms are prone to local recurrence and lymphogenous metastasis. Mast cell tumors can cause the death of animal due to consequences of paraneoplastic disorders such as anaphylaxis or gastroduodenal ulceration and perforation (9, 10).

In cattle, pathological findings of mast cell tumors in cutaneous and visceral locations have been reported infrequently but there is no information about immunohistochemical characteristics of the tumor in this species. This report describes the clinical, morphopathological and immunohistochemical findings of multiple cutaneous mast cell tumor in an adult cow.

 All rights reserved 2007.

Case report

A 4 year old female Holstein cow with numerous skin lesions including approximately 60 raised plaques and nodules, were referred for clinical examination. The cow was in good body condition and all vital signs were normal in physical examination. There was no abnormal change in superficial lymph nodes by palpation. For histopathological examination, several biopsies of the masses were taken, fixed in 10% neutral buffered formalin and referred to the Pathology Department of the School of Veterinary Medicine, Shiraz University, Shiraz, Iran. After fixation, Tissue samples were routinely processed, and stained with hematoxylin and eosin (HE) and toluidine blue for light microscopic examination. Sections of formalin-fixed paraffin-embedded tissue were immunohistochemically stained for vimentin (Biocare, pre diluted), cytokeratin AE1/AE3 (Biocare, pre diluted), c-kit (polyclonal, Rabbit PCAb, Genova, pre diluted) and HMB-45 (NCL-L-HMB45, Novocastra, 1:50 dilution) using the avidin-biotin peroxidase complex detection technique (DAKO, Denmark), with diaminobenzidine (DAB) as the chromogen.

Grossly, numerous discrete cutaneous nodules and masses ranging from 1 to 5 cm in diameter were observed on both sides of flunks, shoulders, neck, back, and mammary glands. There was no evidence of metastasis to superficial lymph nodes. Prior to definitive diagnosis, the animal was sent to slaughterhouse by owner and it was not possible to evaluate any metastasis to internal organs. The subcutaneous smaller masses of approximately 1 cm in diameter and covered by hair were not easy to observe but were palpable as firm nodules. The larger nodules had raised and hairless surfaces. The surfaces of a few of large masses were ulcerated. The largest mass had approximately 5 cm in diameter. It was ulcerated, firm, and on cut section it was white to tan, and associated with unusual hemorrhage (Fig. 1).



Figure 1. Multiple cutaneous mast cell tumor in a cow. The largest mass was ulcerated and hemorrhagic.

Microscopically, the nodules and masses were composed of a nonencapsulated but well circumscribed moderate to dense accumulation of well differentiated neoplastic mast cells in the dermis. In the large masses, overlying epidermis was ulcerated. The neoplastic mast cells were round with distinct borders, and contained moderate to abundant amounts of finely eosinphilic granules in the cytoplasm (Fig. 2). The nuclei of these cells were round to oval, hypochromatic and often with prominent single nucleolus. Cellular and nuclear pleomorphism and mitotic figures were not remarkable. Metachromasia was seen in cytoplasmic granules of neoplastic cells stained with toluidine blue (Fig. 3). In the immunohistochemical staining, the neoplastic cells were positive for vimentin (Fig. 4). Also, diffuse cytoplasmic expression of c-kit was observed (Fig. 5). No immunoreactivity was seen to cytokeratin (Fig. 6) and HMB-45 (Fig. 7). Cytokeratin was stained by the normal overlying epithelium. Based on the pathological, histochemical and immunohistochemical findings, multiple cutaneous mast cell tumor was diagnosed.

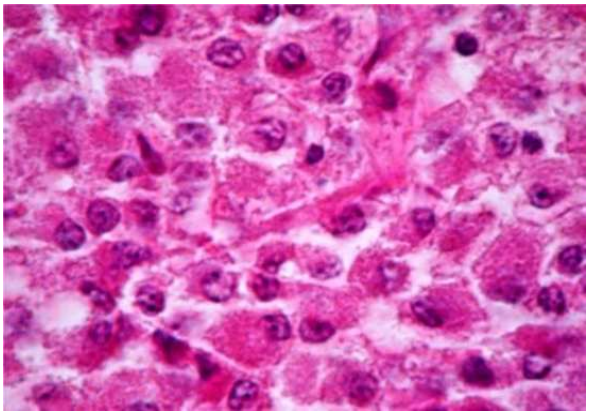


Figure 2. Multiple cutaneous mast cell tumor. The neoplastic mast cells were well differentiated round cells with distinct borders contained finely eosinphilic granules in the cytoplasm (H&E).

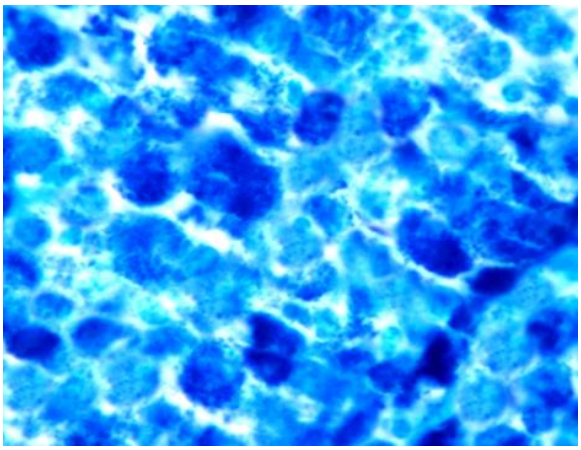


Figure 3. Multiple cutaneous mast cell tumor. Metachromasia of cytoplasmic granules of neoplastic mast cells were seen (Toluidine blue).

 All rights reserved 2007.

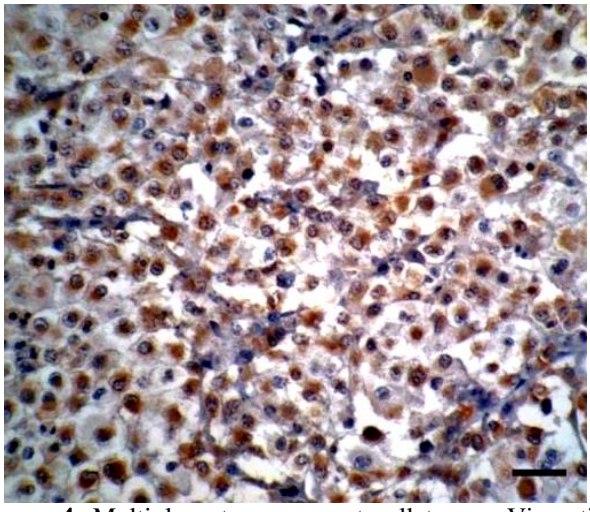


Figure 4. Multiple cutaneous mast cell tumor. Vimentin was detected in the cytoplasm of neoplastic cells (bar=50 µm).

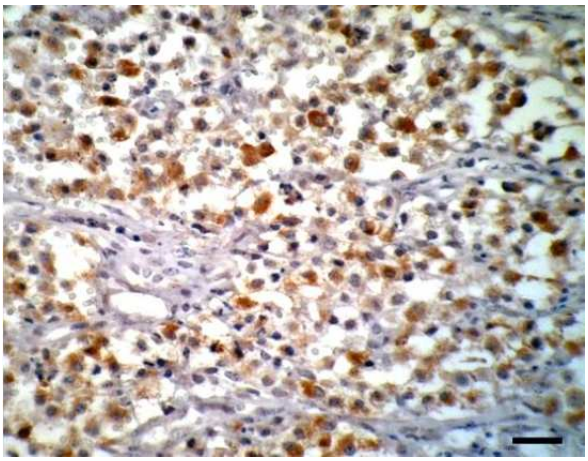


Figure 5. Multiple cutaneous mast cell tumor. Diffuse cytoplasmic expression of c-kit in the tumoral cells (bar=50 µm).

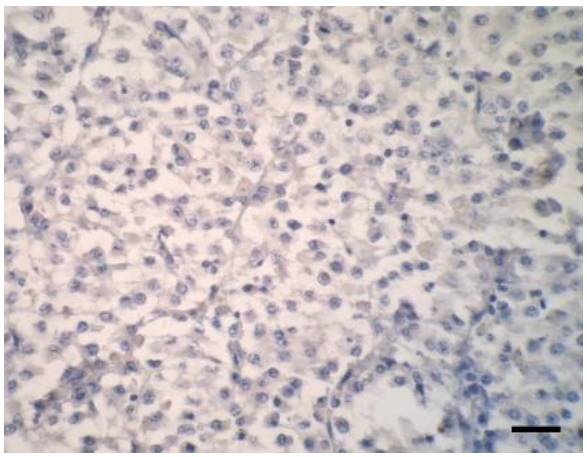


Figure 6. Multiple cutaneous mast cell tumor. No immunoreactivity to cytokeratin in the tumoral cells (bar=50 µm).

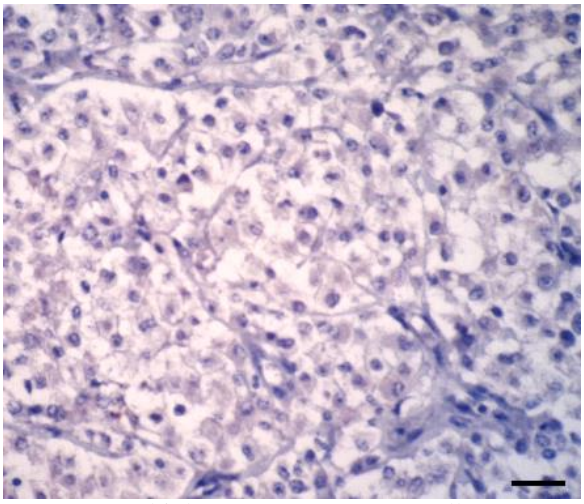


Figure 7. Multiple cutaneous mast cell tumor. No immunoreactivity to HMB-45 in the tumoral cells (bar=50 µm).

Discussion

Mastocytomas have been rarely reported in cattle. These case reports did not describe any immunohistochemical findings. Mast cell tumors should be differentiated from the other round cell tumors such as histiocytoma, lymphoma, plasma cell tumor and melanoma (17). Using of immunohistochemistry technique can be help to access more diagnostic data to definitive identify of neoplasms (14) and can be helpful in mast cell tumors in which toluidine blue stains were negative. In this study, we used cytokeratin, vimentin, c-kit and HMB-45 as the markers of epithelial cells, mesenchymal cells, mast cells and melanocytic cells, respectively.

Vimentin and cytokeratin have been considered as the markers in diagnosis of round cell tumors. Vimentin, as a mesenchymal marker, is expressed in the mast cell tumors, plasma cell tumors, localized histiocytomas and melanomas while cytokeratin AE1/AE3 is expressed by tumor cells originated from epithelium such as carcinomas (2, 14). In the present study, neoplastic cells were positive to vimentin but no immunoreactivity was seen to cytokeratin. Based on these findings, mesenchymal origin of the tumor cells was confirmed.

CD-117 (kit or c-kit) is a growth factor receptor that encoded by the c-kit proto-oncogene. It is expressed in mast cells and it is thought to play in mast cell tumor pathogenesis (3, 8, 17). Gp100 is specific for melanocytic distinction which is detected by the antibody HMB-45 (13). In this study, diffuse cytoplasmic expression of the c-kit was seen in tumoral cells. This finding showed that the origin of neoplastic cells may be melanocytes or mast cells. However, considering the metachromasia of cytoplasmic granules of neoplastic cells in toluidine blue and negative results of expression of HMB-45, the mast cell origin of the neoplastic cells was confirmed.

 All rights reserved 2007.

In this case, most of histopathological and histochemical characteristics of this tumor were similar to previous findings. The reports about pathological findings showed that most of the mast cell tumors in cow were composed of well differentiated cells with variable eosinophilic cytoplasmic granules metachromatically stained with toluidine blue and Giemsa (5, 6). Also, all tumors were nonencapsulated, and mitotic figures were not common. The eosinophils infiltration in the tumor had been commonly reported (1, 7, 10, 17) but we have not seen remarkable infiltration of these cells in the tumor. Other findings sometimes reported were necrosis, fibrosis and calcification in these tumors (1, 7) but fibrosis and mineralization were not seen in the present study.

In cattle, the tissues most commonly involved were skin, lymph node, liver, spleen, tongue, lung, skeletal muscle, heart, kidney, omentum, pleura, pericardium, peritoneum and uterus (1, 4, 7, 15). Since most cases of bovine mastocytoma were multicentric, it is impossible to determine the primary site and it is possible that there is no primary site for the tumor. However, the most common site for mast cell tumor in cattle appears was the skin as single or multiple cutaneous nodules (7). These tumors manifest as a heterogenous disease, which is highly unpredictable in its biological behavior. In cows with metastases, the neoplastic cells were well differentiated without mitotic figures. Bovine mastocytomas may occur in the skin with or without visceral metastasis, but visceral involvement with no skin lesions has also been reported. Furthermore, congenital mastocytomas have been reported in calves (12, 16).

In conclusion, the present report showed multiple cutaneous mast cell tumor without fibrosis, mineralization and infiltration of eosinophils in a cow. Immunohistochemical staining demonstrated that the neoplastic cells were positive to vimentin and c-kit and negative to cytokeratin and HMB-45. Immunohistochemical features of mast cell tumor have not been reported previously in cattle.

Acknowledgements

We thank Mrs. S. Jowkar from the Department of Pathology of the Veterinary School, Shiraz University and Mrs. Heidari from the Department of Pathology of the Namazi Hospital, Shiraz University of Medical Sciences, Shiraz, Iran, for their technical assistance.

References

1. AMES T., O'LEARY T. Mastocytoma in a cow: a case report. **Can. J. Comp. Med.**, 1984, 48, 115-117.
2. ARAÚJO MR., PREIS IS., LAVALLE GE., CASSALI GD., ECCO R. Histomorphological and immunohistochemical characterization of 172 cutaneous round cell tumours in dogs. **Pesq. Vet. Bras.**, 2012, 32, 772-780.
3. DA COSTA RMG., MATOS E., REMA A., LOPES C., PIRES MA., GÄRTNER F. CD117 immunoexpression in canine mast cell tumours: correlations with pathological variables and proliferation markers. **BMC Vet. Res.**, 2007, 3, 19.
4. DODD DC. Mastocytoma of the tongue of a calf. **Vet. Pathol.**, 1964, 1, 69-72.
5. DUNCAN J., PRASSE K. Cytology of Canine Cutaneous Round Cell Tumors Mast Cell Tumor, Histiocytoma, Lymphosarcoma and Transmissible Venereal Tumor. **Vet. Pathol.**, 1979, 16, 673-679.
6. HARGIS AN., EVE GINN P. The integument. ZACHARY JF., MACGAVIN MD. (Ed). **Pathologic basis of veterinary disease.** Mosby Elsevier, St. Louis 2011:1082.
7. HILL J., LANGHEINRICH K., KELLEY L. Prevalence and location of mast cell tumors in slaughter cattle. **Vet. Pathol.**, 1991, 28, 449-450.
8. LEON A., CEAUŞU Z., CEAUŞU M., ARDELEANU C., MEHEDINTI R. Mast cells and dendritic cells in basal cell carcinoma. **Rom. J. Morphol. Embryol.**, 2009, 50, 85-90.
9. MISDORP W. Congenital tumours and tumour-like lesions in domestic animals. 1. Cattle a review. **Vet. Q.**, 2002, 24, 1-11.
10. MISDORP W. Mast cells and canine mast cell tumours. A review. **Vet. Q.**, 2004, 26, 156-159.
11. NORTHRUP NC., HARMON BG., GIEGER TL., BROWN CA., CARMICHAEL KP., GARCIA A., LATIMER KS., MUNDAY JS., RAKICH PM., RICHEY LJ, STEDMAN NL., CHENG AL., HOWERTH EW. Variation among pathologists in histologic grading of canine cutaneous mast cell tumors. **J. Vet. Diagn. Invest.**, 2005, 17, 245-248.
12. PÉREZ V., ESPÍ A., CORPA JM., ARIAS M., PRIETO M., ALVAREZ VM., GARCÍA MARÍN JF. Multiple cutaneous mast cell tumour in a calf. **Vet. Rec.**, 1999, 145, 81-82.
13. PRIETO VG., SHEA CR. Immunohistochemistry of melanocytic proliferations. **Arch. Pathol. Lab. Med.**, 2011, 135, 853-859.
14. SANDUSKY G., CARLTON W., WIGHTMAN K. Diagnostic immunohistochemistry of canine round cell tumors. **Vet. Pathol.**, 1987, 24, 495-499.
15. SHAW D., BUOEN L., WEISS D. Multicentric mast cell tumor in a cow. **Vet. Pathol.**, 1991, 28, 450-452.
16. SMITH BI., PHILLIPS LA. Congenital mastocytomas in a Holstein calf. **Can. Vet. J.**, 2001, 42, 635.
17. STREFEZZI RF., KLEEB SR., XAVIER JG., CATÃO-DIAS JL. Prognostic indicators for mast cell tumors. **Differentiation**, 2009, 58, 81.
18. WELLE MM., BLEY CR., HOWARD J., RÜFENACHT S. Canine mast cell tumours: a review of the pathogenesis, clinical features, pathology and treatment. **Vet. Dermatol.**, 2008, 19, 321-339.

 All rights reserved 2007.