Grade II mast cell tumor and its surgical management in a Bhotia Dog: A case study

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Abstract
The objective of the present study was to remove surgically 1.3 kg tumor mass successfully under general anaesthesia (Ketamine with Diazepam) after proper sedation with pre-anaeasthetics like Atropine and Xylazine. A ten-year-old 40 kg male Bhotia dog was presented to Animal Birth Control Centre (ABCC) Nagar Nigam Dehradun Uttarakhand India in August, 2017 with a huge firm irregular superficial mass present in the left axillary region since one year. Further, pre- scapular lymph nodes were greatly enlarged and the dog was not eating properly besides showing reluctance to stand. Histopathological findings revealed presence of round cells which were identical to mast cells showing high nucleo-cytoplasmatic ratio, nuclear pleomorphism and hyperchromasia, grayish to bluish cytoplasmic granules, few mitotic figures and nuclear binucleation along with moderate eosinophilic and lymphocytic infiltration confirming the mast cell tumor diagnosis. The thoracic radiography did not revealed any sign of metastasis of the tumor to any visceral organ.

Keywords: Eosinophilic, hyperchromasia, lymphocytic, mast cell tumor, nucleo-cytoplasmatic ratio, pleomorphism

Introduction
Mast Cell Tumors (MCTs) or mastocytomas are common tumors, particularly in the skin of dogs, where they manifest as a heterogeneous disease, which is highly unpredictable in its biological behavior [1]. They are frequently seen in old dogs and less often in cattle, horses and man [2, 3]. Mast cell tumors usually occur on the skin but they can also grow in the intestines, liver, spleen and elsewhere [6]. Cutaneous MCTs comprise 7-25% of the skin tumors in dogs [7, 8, 9]. The behavior of cutaneous MCTs is unpredictable and their gross appearance can frequently mimic that of other tumors [1]. Mast cell tumors may produce clinical signs as a result of histamine and heparin release from the mast cell granules. These paraneoplastic syndromes include gastric and duodenal ulceration, delayed healing, impaired blood coagulation, and anaphylactoid reactions [1, 4, 5]. Mast cell tumors can also result in an animal’s death because of the consequences of paraneoplastic disorders such as anaphylaxis or gastro-duodenal ulceration and perforation, which are caused by biological substances released by degranulating tumor cells. Most neoplastic mast cells in the dog resemble their normal counterparts, except those in undifferentiated (grade 3) tumors [19]. The cells are round to polygonal with round central nuclei and pink cytoplasm containing granules, which stain purple with metachromatic stains (toluidine blue). Cytological examination appeared to be a successful technique to discriminate between MCT and other round cell tumors [10, 11]. Cytology may be even superior to histologic examination of very anaplastic MCTs [10]. On the other hand, histological evaluation allows the pathologist to evaluate completeness of surgical removal [20]. Anyhow, MCTs having a variegated gross appearance should be examined either by cytology or (preferably) by histology, also with a view on prognosis and eventually additional therapy. Although surgery is the mainstay of therapy for MCTs, and is curative in a large percentage of cases, there is still much controversy over surgical margins. Removing the tumor with gross margins of 2–3 cm lateral margins and a deep margin one-tissue plane beyond the tumor has been recommended. The treatment of choice is wide (3 cm. free margin) excision eventually followed by other treatment modalities such as irradiation, cortisone and/or chemotherapy [22,24].
2. Material and methods

2.1. Case history

A ten-year-old male Bhotia dog was presented to Animal Birth Control Centre (ABCC) Nagar Nigam Dehradun Utrakhand India, with a huge firm irregular superficial hairless mass, 7 inches in diameter present in the axillary region near left forelimb (Fig. 1A & B).

Since one year, when it looked a small growth and was left unattended. Further, pre-scapular lymph nodes were greatly enlarged suggesting the occurrence of grade II mast cell tumor. The dog was unable to eat and stand on its own. The section of the mass was subjected to histopathological examination after fixing in neutral buffered formal saline (NBFS) and it was concluded that it is a case of a mast cell tumor based on certain resemblance of round cells, which were identical to mast cells. Further, aspirate from the pre-scapular as well as parotid lymph nodes were subjected to fine needle aspiration cytology (FNAC) and stained with Wrights Giemsa before observing them at 10 and 100X magnification, which clearly showed the mast cells containing typical abundant cytoplasmic granules, diagnostic of mast cell tumor.

3. Results

On physical examination, the dog was found to be moderately obese. The mass on the axillary region of left fore limb had dimensions of 20.0 x 10.0 x 4.5 cm. This mass was firm, slightly painful, and had invaded the muscles of the limb with no fixation to the deep tissues was evident. Histological examination of the mass near fore limb was performed which revealed presence of round cells which were identical to mast cells (Fig. 2A) along with moderate eosinophilic and lymphocytic infiltration. In addition, most of the round cells were showing high nucleo-cytoplasmic ratio, mild to moderate nuclear pleomorphism and hyperchromasia with cytoplasm containing few grey to blue granules (Fig. 2A) apart from few mitotic figures and nuclear binucleation confirming the evidence of mast cell tumor-Grade II. Fine needle aspiration from the tumor mass revealed masts cells containing numerous metachromatic cytoplasmic granules (Fig. 2B & C) with purple shades (Wrights Giemsa, 10X & 100X respectively)\textsuperscript{12}, thus strengthening the possibility of occurrence of the grade II mast cells tumor, which is a single tumor growth along with involvement of superficial pre-scapular lymph node. Further, pre-scapular lymph nodes were greatly enlarged, thus further characterizing grade II mast cell tumor. The thoracic radiography of the affected dog was taken before surgical intervention, which did not reveal any sign of metastasis of the tumor to any visceral organ, thus excluding metastatic property of the tumor.

![Fig 2: H&E stained histopathological slides showing presence of round cells, identical to mast cells along with moderate eosinophilic and lymphocytic infiltration (A). In addition, most of the round cells were showing high nucleo-cytoplasmic ratio, mild to moderate nuclear pleomorphism and hyperchromasia with cytoplasm containing few grey to blue granules (A). Cytology of fine needle aspirate from mass showing easily identified mast cells and their abundant cytoplasmic granules (arrow) (B, C) with purple shades when stained with Wright's Giemsa, 10X &100X respectively.](image)
4. Surgical management
The mass was surgically removed successfully under general anaesthesia by 8ml Ketamine @10mg/kg body weight Intramuscular and 2ml Diazepam @0.5mg/kg body weight Intravenous after proper sedation by 2.8ml Atropine @0.04mg/kg body weight Intramuscular and 1.3ml Xylazine @1mg/kg body weight Intramuscular. The mass on the left axillary region was removed with wide excisional margins. Garrett [13] has recommended removing the tumor with gross margins of 2–3 cm lateral margins and a deep margin one-tissue plane beyond the tumor. The dog was sent home two days after surgery and the owners were instructed to continue Intacef 0.5 gm BID for 7days, Melonex 3ml OD for 3 days, Avilin 3ml OD for 5 days intramuscularly and Himex cream applied locally on the surgical incision site for 10 days. Further, it was advised to monitor the dog closely for any evidence of tumor regrowth or signs of paraneoplastic syndromes.

5. Discussion
Mast cell tumors are common neoplasms, representing 7 to 21% of all skin tumors and 11 to 27% of all malignant skin tumors in the dog [13], however in the present case there was no sign of metastasis to any visceral organ as conformed by thoracic radiographs taken. A recent retrospective study evaluating the prevalence of gross lung metastasis on three view thoracic radiographs in 115 dogs with mast cell tumors yielded 1/115 (0.87%) dog that was positive for gross metastasis. (Fung & Boston, unpublished data). Cutaneous MCTs generally present with one of two gross appearances. The most common is a raised, firm, and well-circumscribed mass, usually less than 3.0 cm in diameter. The surface may be erythematous or ulcerated. A less common form is a soft, poorly circumscribed, raised lesion that is usually haired and lacks ulceration or erythematous changes. This second form may be easily mistaken for a lipoma on physical examination [16]. The most common sites of occurrence of MCTs in the dog are the skin of the trunk and perineal region (50%) as in accordance with our case and the skin of the extremities (40%). Those arising from the perineal, preputial and nailbed regions unlike in our study are more often malignant than those arising from other regions of the body [3, 17]. Malignant MCTs metastasize early to local lymph nodes and hematogenously to other organ systems which, in our case is supported by the involvement of the pre-scapular, parotid and mandibular lymph nodes. Histopathological examination of the tumor mass and FNAC of the associated enlarged lymph nodes hold promise as an important laboratory tool for diagnosing mast cell tumors and in the present case, it was a grade-II mast cell tumor in accordance with the WHO classification scheme for canine mast cell tumours which is as: Stage I – One tumour confined to the dermis without regional lymph node involvement (Ia – Without systemic signs, Ib – With systemic signs); Stage II – One tumour confined to the dermis with regional lymph node involvement (Iia – Without systemic signs, Iib – With systemic signs); Stage III – Multiple dermal tumours or one large infiltrating tumour with or without regional lymph node involvement (IIa – Without systemic signs, IIb – With systemic signs); and Stage IV – Any tumour with distant metastasis or a recurrence with meta- stasis (including blood and/or bone marrow involvement). Treatment options for mast cell tumors include surgery, radiation therapy, chemotherapy, or a combination of these modalities. Surgery remains the mainstay of treatment for canine mast cell tumors. Surgical excision alone has been found to be most useful for tumours of histological grade I [20] and grade II [21] in which a single tumour is confined to the skin and subcutaneous tissues and metastases are absent as in accordance with our case. The completeness of surgical excision has shown a significant effect on prognosis of mast cell tumors [18, 22]. Although the dogma has been that malignant tumors should be removed with 3cm margins and one fascial plane deep, this has recently been critically evaluated [14].

6. Conclusion
The results of the present study indicate that the Histopathological examination of the H&E stained slides is an important laboratory tool for diagnosing mast cell tumors which is supplemented by Fine needle aspiration cytological (FNAC) study of the Wrights Giemsa stained slides prepared from the enlarged pre-scapular and parotid lymph node aspirate. Mast cell tumors in the dogs can be successfully managed by surgical excision under general anaesthesia with prior sedation by pre-anæsthetics including Atropine and Diazepam. The Mast cell tumors recurrence rate is high, but the chances of its resurgence were absent in our case.

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8. References


