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Canine mast cell tumors current advances in diagnosis management and prognosis

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Abstract

Canine mast cell tumors (MCTs) are among the most common and biologically aggressive cutaneous neoplasms in dogs, accounting for approximately 11-21% of all skin tumors and presenting significant challenges in veterinary oncology due to their highly variable clinical behavior, invasive growth, and metastatic potential. The present study evaluated the clinical presentation, diagnostic findings, treatment outcomes, and survival of six dogs diagnosed with mast cell tumors affecting different anatomical locations. Comprehensive clinical evaluation included hematological and biochemical analyses performed pre-operatively and on the 14th post-operative day. Fine needle aspiration cytology (FNAC), thoracic radiography, abdominal ultrasonography, and computed tomography (CT) were employed for diagnosis, staging, assessment of tumor extent, and detection of metastatic disease. All dogs underwent wide-margin surgical excision under general anaesthesia followed by routine post-operative management. Excised tissues were subjected to histopathological examination and graded using both Patnaik and Kiupel grading systems. The affected dogs ranged from 3.5 to 12 years of age (mean 7.2 years), with most being intact males. Histopathological grading identified both low-grade and high-grade tumors, with high-grade lesions demonstrating aggressive clinical behavior and poor prognosis. Four of six dogs died within three months following surgery, resulting in an overall mean survival period of three months. The dogs were subjected for hematological and blood biochemical evaluation. The findings indicate that high-grade mast cell tumors remain a devastating canine malignancy characterized by rapid progression, frequent metastasis, and limited survival despite surgical intervention. Early diagnosis, accurate staging, histopathological grading, and implementation of comprehensive treatment strategies are essential for improving clinical outcomes and prolonging survival in affected dogs.

Keywords: Canine mast cell tumor, high-grade mast cell tumor, Patnaik and Kiupel grading system, prognosis, veterinary oncology

Introduction

Cancer is a major health challenge in veterinary medicine, affecting a large number of animals across different species. In dogs older than ten years, cancer is recognized as the leading cause of mortality, accounting for approximately 23% of all canine deaths (Gardner *et al.*, 2016) [2]. Canine mast cell tumors (MCTs) are among the most frequently diagnosed cutaneous neoplasms in dogs and represent one of the most significant challenges in veterinary oncology. Canine MCTs account for approximately 11-21% of all skin tumors in dogs and are considered the most common malignant skin tumor in this species. Predisposed breeds include Boxers, Boston Terriers, Labrador Retrievers, Golden Retrievers, Pugs, Staffordshire Bull Terriers, and Shar-Peis. Although the precise etiology remains unclear, genetic alterations involving the c-kit proto-oncogene play a central role in tumor development and progression. Canine mast cell tumors (MCTs) are among the most frequently diagnosed and biologically aggressive neoplasms, characterized by their invasive growth and potential for metastasis. These tumors are of considerable clinical importance in veterinary oncology and comprise approximately 16-21% of all cutaneous tumors in dogs (Blackwood *et al.*, 2012) [1]. Mast cell tumors originate from the neoplastic transformation of mast cells, which are immune cells that play a crucial role in allergic and inflammatory responses (Misdorp, 2004 and Warland and Dobson, 2013) [5, 7]. The marked variation in the biological behavior of these tumors creates challenges in accurately determining prognosis

and selecting the most effective treatment approach for affected dogs (Welle *et al.*, 2008 and Tamlin *et al.*, 2020) [8, 6]. The biological behavior of canine MCTs ranges from benign lesions with excellent long-term prognosis to highly malignant tumors associated with widespread metastasis and early mortality. Given the heterogeneous nature of mast cell tumors, comprehensive clinical evaluation, accurate staging, and assessment of prognostic factors are critical for predicting disease progression and formulating appropriate therapeutic plans (Knight *et al.*, 2022) [4]. The introduction of the Kiupel two-tier histological grading system has significantly improved prognostic assessment by categorizing tumors as either low-grade or high-grade. High-grade mast cell tumors are characterized by marked cellular atypia, increased mitotic activity, multi-nucleation, bizarre nuclei, and extensive tissue invasion. These tumors exhibit metastatic rates exceeding 50% and frequently result in death within the first year following diagnosis if not aggressively managed. Early recognition and implementation of comprehensive treatment strategies are therefore critical for improving survival and quality of life.

Materials and Methods

The present study was conducted on six clinical cases of canine mast cell tumors (MCTs) presented with tumors at various anatomical locations. A comprehensive clinical evaluation was performed in all dogs. Hematological parameters, including hemoglobin (Hb), total erythrocyte count (TEC), total leukocyte count (TLC), differential leukocyte count (DLC), platelet count, and packed cell volume (PCV), were assessed pre-operatively and on the 14th post-operative day. Blood biochemical parameters, namely serum creatinine and serum glutamate pyruvate transaminase (SGPT), were also evaluated at the same time points. Fine-needle aspiration cytology (FNAC) was performed as an initial diagnostic screening procedure. Thoracic radiography was carried out to assess pulmonary metastasis and thoracic lymphadenopathy. Although pulmonary metastasis is relatively uncommon in canine MCTs, thoracic imaging was included as part of the staging protocol. Abdominal ultrasonography was performed to evaluate the liver, spleen, abdominal lymph nodes, and other abdominal organs for evidence of metastatic disease. Computed tomography (CT) examination was conducted to

determine tumor extent, assess deep tissue involvement, identify regional lymph node metastasis, and facilitate surgical planning. To minimize mast cell degranulation and associated complications, all dogs received pre-operative antihistamine and gastroprotective therapy consisting of Benadryl syrup, chlorpheniramine maleate tablets, and famotidine tablets. These medications were administered to reduce histamine-mediated gastrointestinal effects and improve patient comfort. All dogs underwent wide-margin surgical excision of the tumor with lateral margins of 2-3 cm and a minimum of one fascial plane deep margin wherever anatomically feasible. Premedication consisted of atropine sulphate (0.045 mg/kg, SC), followed 15 minutes later by dexmedetomidine hydrochloride (10 µg/kg), butorphanol tartrate (0.20 mg/kg), and midazolam hydrochloride (0.20 mg/kg) administered intramuscularly in a single syringe. Anesthesia was induced using ketamine hydrochloride (2-3 mg/kg, IV) and maintained with isoflurane at a concentration ranging from 1.50% to 3%. Excised tissue samples were submitted for histopathological examination. Tumors were graded according to both the Patnaik and Kiupel grading systems. Post-operative management included ceftriaxone-tazobactam (25 mg/kg, IV) for five days, tramadol hydrochloride (2 mg/kg) on the day of surgery, followed by piroxicam (0.30 mg/kg, PO) for 14 days and pantoprazole (1 mg/kg, PO) for seven days. Routine antiseptic wound dressing was performed throughout the post-operative period. Post-operative survival time was recorded and monitored in all cases.

Results and Discussion

The clinical appearance of high grade MCTs was highly variable. Dogs were presented with different tumors which were either solitary or multiple cutaneous masses with varying size, consistency, and ulceration. The dogs were presented with the age group ranging from 3.50 years to 11 years with mean age 7.20 years. Common clinical signs in presented dogs included rapid enlargement of cutaneous masses, erythema and edema, notable darier's reaction, ulceration and bleeding, pruritus and inflammation, gastrointestinal signs secondary to histamine release, vomiting, melena, anorexia and weight loss. One dog was presented with history of recurrence within a month of surgery and size was increasing day by day very rapidly.

Table 1: Details of the dogs with their respective grading

S. No.	Age in years	Sex	Breed	Post operative survival duration and status	Grade	
					Patnaik	Kiupel
1	9	Intact male	Labrador	8 months-alive and metastasis	II	Low
2	12	Intact male	Mongrel	3 months-dead	III	High
3	4	Intact male	Mongrel	1 month-dead and metastasis	III	High
4	3.5	Intact female	Pitbull	2 month-dead	III	High
5	7	Neutered female	Mongrel	1.5 month-dead	II	Low
6	8	Intact male	Doberman	3 months-alive	I	Low

The affected dogs were between the age group of 3.50 to 12 years with a mean age of 7.20 years. Most of the affected dogs were intact except one female and were all males except two. Four out of six dogs died within three months of

operation, the average survival period for all the dogs was three months, the longest survivor being 8 months has developed metastasis into lungs and other organs like liver.

Table 2: Haematological parameters

Parameter	Day 0	Day 14
Haemoglobin	12.75±0.70	12.37±0.70
TEC	5.58±0.45	5.29±0.32
TLC	21.5±5.07	17.7±0.81
Neutrophils	70.73±2.05	71.43±1.52
Lymphocytes	23.18±2.89	21.53±1.89
Eosinophils	2.83±0.82	2.73±0.26
Monocytes	1.62±0.37	2.23±0.19
Basophils	1.55±0.20	2.58±0.15
Platelets	250.66±27.77	257.17±26.39
PCV	36.33±2.07	36.37±2.02

A significant reduction in total leucocyte count was noticed that could be due to recovery from ulcerated tumour and infected tumor masses. Slight variations in Monocytes, Basophils and platelets count was noticed, however all the values were within the normal physiological range.

Table 3: Biochemical parameters

Parameter	Day 0	Day 14
Serum creatinine	1.16±0.13	1.19±0.11
SGPT	46.54±6.78	44.2±5.44

There was a significant reduction in SGPT values, suggesting that the muscles damage and hepatocellular damage due to tumour has been reduced.

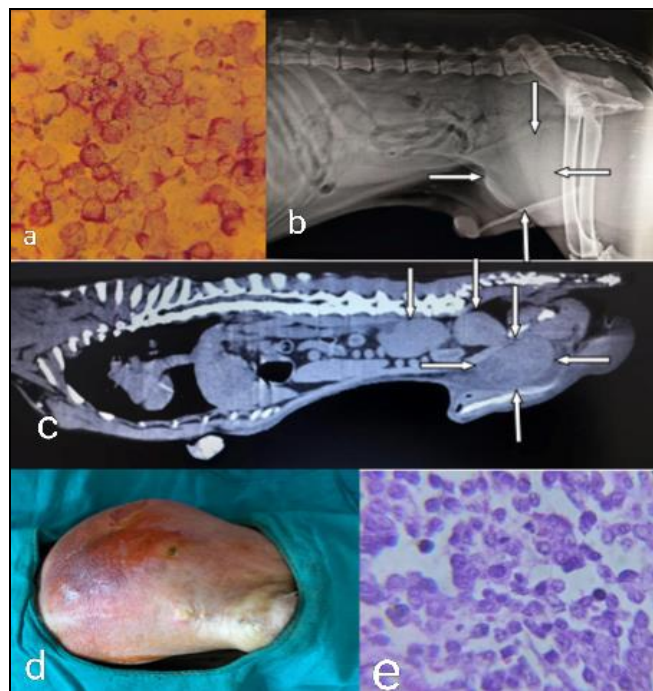


Fig 1: Images showing a. Cytology, b. X-ray abdomen, c. Computed tomography of abdomen, d. Gross tumour image and e. Histopathology.

- a. **Cytological features:** Cytology smear revealed diffuse population moderately granulated mast cells arranged in loose sheets. Cytoplasmic borders were distinct with granules obscuring the nuclear morphology. Eosinophils are also present. Mitotic figures and binucleation are rare. Features are suggestive of mast cells tumor.
- b. **X ray image of abdomen:** Large extra abdominal tumour mass at inguinal region adjacent to penis.

- c. **Computed tomography image of abdomen:** Large mass at inguinal region with both enlarged iliac lymph nodes, as shown by arrow heads.
- d. **Gross tumour image:** Enlarged tumour mass with inflamed and edematous skin.
- e. **Histopathology features:** The histopathology image revealed moderate to poorly differentiated neoplastic round cells arranged in loose sheets, with scant population of Eosinophils separated by thin collagen fibers. These tumour cells are moderately cellular, and the neoplastic cells infiltrated or replaced the lower dermal and subcutaneous tissue focally. Cells were round and pleomorphic with ample cytoplasm, most had distinct cytoplasmic borders and fine intracytoplasmic granules were noticed occasionally. Nuclei were round with coarse chromatin, binucleated cells with mitotic figures were observed (2-3/high power field).the impression is suggestive of mast cell tumour.

Grading

- 2-Tier grading (Kiupel grading., 2011): High grade
 - a. Mitotic figures->7 in 10 hpf
 - b. Multinucleated cells: >3 in 10 hpf
 - c. Bizarre nuclei: >3 in 10hpf
 - d. D. Karyomegaly: Mild.
- Patnaik grading: Grade III

Conclusions

Clinical outcomes in dogs with high grade mast cell tumours remain guarded despite advances in treatment. The median recorded survival times in the present study range from 1.5 to 8 months with a mean duration of 3 months. Dogs undergoing complete surgical excision and lacking metastatic disease at diagnosis experience significantly longer survival compared with patients presenting with advanced stage disease. High-grade mast cell tumors represent one of the most devastating forms of canine cutaneous cancer owing to their aggressive biological behavior, high metastatic potential and significant impact on survival. Early diagnosis, comprehensive staging, accurate histopathological grading, and implementation of multimodal treatment strategies are essential for optimizing clinical outcomes. Advances in diagnostic imaging, molecular diagnostics, and targeted therapies continue to improve disease management; however, prognosis remains guarded in many affected dogs. Continued research into tumor biology and precision oncology approaches is expected to enhance future therapeutic success and improve survival rates in canine patients with high-grade mast cell tumors.

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