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Canine Mast Cell Tumors: Clinical Signs, Laboratory Diagnosis, Treatment, and Prognosis

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ABSTRACT

Canine mast cell tumors, a tumor originating from mast cells involved in allergic reactions and inflammation, are among the most common skin tumors in dogs. The present study aimed to explore the clinical features, diagnostic approaches, and prognosis of canine mastocytomas through a case study. A 5-year-old male Akita, weighing 35.8 kg, was brought to the Doctor VET veterinary clinic in Kamianets-Podilskyi, Ukraine, for evaluation. Upon initial examination, the dog had a body temperature of 38.5°C, a heart rate of 74 beats per minute (bpm), and a respiratory rate of 28 breaths per minute, all of which were within normal physiological limits. The animal was alert and responsive and displayed no signs of systemic distress. A detailed physical examination revealed a tumor located 35.2 mm below the plantar surface of the tarsal joint (art. tarsi). The tumor was round, mobile, and surrounded by a thin fibrous capsule, with no signs of pain or discomfort during palpation. Cytological analysis showed a high-cellularity smear with numerous mast cells scattered throughout the field. These cells were round to oval in shape with abundant cytoplasm containing dense, basophilic to metachromatic granules. The hematological evaluation indicated a systemic inflammatory or immune response triggered by the tumor, as evidenced by neutrophilic leukocytosis (73.1%; 8.89×10⁹/L). Biochemical analysis revealed an elevated alkaline phosphatase activity level (4.45 µmol/L), suggesting systemic involvement. The tumor was surgically excised, ensuring complete removal with wide margins to minimize the risk of recurrence. Histological examination of the excised tissues confirmed a densely cellular neoplastic infiltrate composed predominantly of mast cells arranged in sheets and clusters. The mast cells displayed significant cellular and nuclear pleomorphism, characterized by moderate to marked anisocytosis and anisokaryosis. While no significant necrosis was observed, scattered apoptotic bodies were present, indicating ongoing cellular turnover. This case highlighted the critical importance of early diagnosis and comprehensive management of canine mastocytomas. Low-grade tumors often carry a favorable prognosis when treated promptly and appropriately. However, higher-grade or poorly differentiated tumors may require multimodal therapeutic approaches to achieve better outcomes.

Keywords: Canine, Diagnosis, Mast cell tumor, Mastocytoma, Skin tumor

INTRODUCTION

Mast cell tumors (MCTs) are among the most prevalent cutaneous neoplasms in dogs, arising from mast cells, which play a key role in allergic responses and inflammatory processes (Blackwood et al., 2012; Gerasimos et al., 2023; Zhelavskyi et al., 2024a). These tumors exhibit a wide range of clinical behaviors and morphological features, complicating diagnosis and therapeutic management. MCTs represent approximately 7-21% of all cutaneous malignancies in canines (Gómez et al., 2020). MCTs are frequently diagnosed in middle-aged to older dogs, with certain breeds, such as Boxers, Labrador Retrievers, Boston Terriers, and Pugs, showing a higher predisposition (Warland and Dobson, 2013). Despite ongoing research, the exact mechanisms underlying the development of mast cell tumors remain unclear. However, mutations in the *c-KIT* gene have been identified as a significant factor contributing to their pathogenesis (MacDonald et al., 2023), which encodes the tyrosine kinase receptor, and plays a key role in the development of mastocytomas (Watson et al., 2020; Coelho et al., 2023; Zmorzynski et al., 2024). Mast cells grow and multiply uncontrollably as a result of these mutations. Clinical signs of mastocytoma can range from small nodules on the skin to large, ulcerated, and infiltrative masses (Cino et al., 2023). Tumors often appear on the trunk, limbs, or head. Symptoms may include itching, ulcers, swelling, and systemic reactions, such as vomiting and anorexia due to histamine release from tumor cells (Kimura et al., 2021; Bhanpattanakul et al., 2025). Cytological examination reveals characteristic mast cells with granules (Berlato et al., 2021; Oberholtzer et al., 2024). Histological analysis allows for the

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determination of the tumor's grade according to Patnaik (Grade I-III), which is crucial for prognosis (Rassnick et al., 2010; Horta et al., 2018; Roberts et al., 2022).

The excision should include sufficient healthy tissue around the tumor to minimize the risk of recurrence (Hoshino et al., 2020). The primary treatment method for mastocytomas is surgical removal with wide margins. Chemotherapy serves as an adjuvant therapy in cases with a high risk of recurrence or metastasis (London et al., 2009; Korbelik et al., 2021). Medications, such as vincristine, cyclophosphamide, and prednisolone, help reduce residual tumor cells (Wilson et al., 2020; Roberts et al., 2022).

Targeted therapies, particularly tyrosine kinase inhibitors (imatinib, toceranib), show promising results in treating mastocytomas with *c-KIT* mutations (Cilloni et al., 2021; Bertola et al., 2024). The prognosis depends on the tumor grade, the presence of metastasis, and treatment effectiveness. Well-differentiated tumors (Grade I) have a favorable prognosis with high survival rates after surgical removal (Kiupel et al., 2011; Ribatti, 2025). Tumors of intermediate and low differentiation (Grade II-III) have a poor prognosis and require comprehensive treatment (Horta et al., 2018; Roberts et al., 2022; Larsen et al., 2023). The present study aimed to investigate canine mastocytoma, including its clinical features, diagnosis, treatment, and prognosis.

MATERIALS AND METHODS

Ethical approval

The clinical investigations were carried out in compliance with the Law of Ukraine "On Protection of Animals from Cruel Treatment" (21/02/2006, 3447-IV) and followed the European Commission's guidelines on the treatment of vertebrates, ensuring protection from thirst, hunger, malnutrition, discomfort, fear, pain, and suffering.

Study design

A 5-year-old male Akita weighing 35.8 kg was brought to the Doctor VET veterinary clinic in Kamianets-Podilskyi, Ukraine, for evaluation. Upon initial examination, the dog had a body temperature of 38.5°C, a heart rate of 74 beats per minute (bpm), and a respiratory rate of 28 breaths per minute, all of which were within normal physiological limits. The animal was alert and responsive and displayed no signs of systemic distress. The owner's primary concern was the presence of a well-defined, palpable mass on the left hind limb, which had gradually increased in size over time. A detailed physical examination revealed the location of the tumor: 35.2 mm below the tarsal joint (art. tarsi) in the plantar surface (Figure 1). The tumor had smooth borders, was round, 35.2 mm in diameter, hard to palpation, and surrounded by a thin fibrous capsule. The surface was hilly, pink in color, without hair and damage (ulcer, exudation). The tumor was mobile and not attached to deep tissue structures. During palpation, no pain reaction or discomfort was noted in the animal. External examination and palpation revealed no changes in the regional lymph nodes. During ultrasonography of the internal organs of the abdominal cavity (SonoSite 180 Plus FUJIFILM, Sonosite, USA), C60/5-2 Transducer (5-2 MHz), Ultrasound gels (Parker Laboratories, USA) and X-ray (Vet Ray Digital DR [Vet Ray Technology, IDEXX, USA]) of the chest, no signs of metastasis were found.

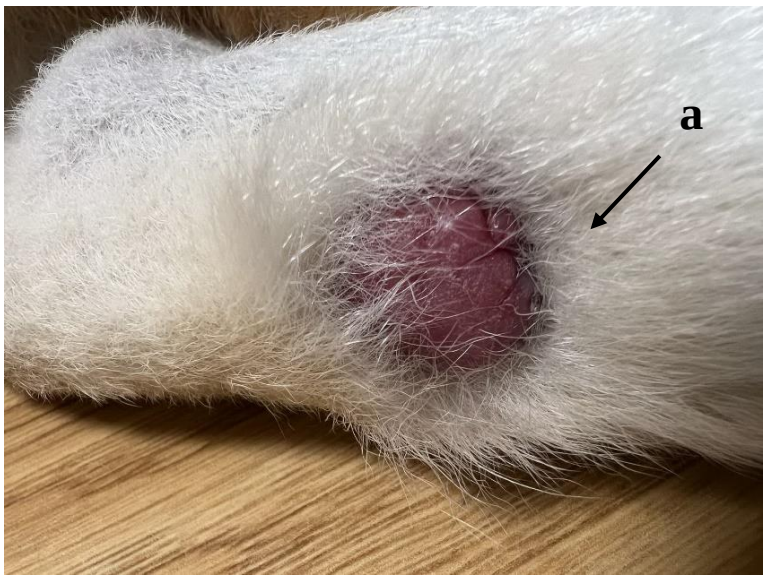

Figure 1. Mastocytoma in in a 5-year-old male Akita dog. The tumor (35.2 mm) is located below the tarsal joint (art. tarsi) on the plantar surface of the left hind leg (**a**).

Anesthetic protocol and surgical procedure

In the beginning, a preoperative clinical examination was performed. The fur around the tumor was shaved, and the skin was cleaned with a 5% alcohol solution of iodine (B. Braun Medical Inc., USA). Methadone hydrochloride (Lannett Company, Inc., USA) was used for premedication at a dose of 0.2 mg/kg intravenously (vena cephalica). The use of propofol for general anesthesia ensures rapid induction of anesthesia, smooth awakening, and minimal side effects with proper monitoring (Johnson et al., 2022).

Anesthesia was induced with propofol (Propofol 200mg/20ml emulsion for injection vials, Baxter International Inc., USA). The basic dose was 4 mg/kg intravenously (vena cephalica). The drug was administered slowly until the required level of anesthesia was reached (within 30-60 seconds). Anesthesia was maintained using propofol at a dose of 0.5 mg/kg, administered intravenously to ensure a stable anesthetic state and minimize discomfort during the procedure. Continuous monitoring of vital signs was performed throughout anesthesia (temperature of 38.3°C, a heart rate of 71 beats per minute (bpm), respiratory rate of 31 breaths per minute; the arterial blood pressure: systolic pressure of approximately 131 mmHg and a diastolic pressure of 95 mmHg: Dawei HD10-VET (Dawei Veterinary Medical, China)) to maintain patient safety and optimal physiological conditions. For local anesthesia, 2% lidocaine hydrochloride (Lidocaine, Mylan Pharmaceuticals, Italy) was utilized to ensure adequate pain management during the procedure (Kudnig and Séguin, 2022; Duffee et al., 2023).

An incision was made in the skin and tissues above the mastocytoma during the operation. An incision was performed at an adequate margin, maintaining a distance of 0.5 cm (not mm, which is typically insufficient in surgical oncology) from the visible tumor borders to ensure the removal of all potentially affected tissues and minimize the risk of residual disease.

After the removal of the tumor, a thorough examination of the operating area was carried out to detect possible remnants of tumor cells. The excised mastocytoma, measuring 38.2 mm in diameter, was immediately placed in a sterile container and transported to the laboratory for histopathological evaluation to verify the diagnosis and assess the tumor's malignancy grade. Intraoperatively, the surgical site was extensively irrigated with 0.9% sodium chloride solution (B. Braun Melsungen AG, USA) to reduce the risk of infection and remove cellular debris. Hemostasis was carefully managed to prevent excessive bleeding, and the wound was closed in multiple layers using an atraumatic suturing technique to enhance tissue recovery and minimize postoperative complications. The deeper layers of tissues were closed using absorbable sutures, followed by the closure of the skin with non-absorbable sutures to ensure wound strength and minimize the risk of dehiscence. Appropriate aseptic techniques were employed throughout the procedure to prevent postoperative infections. For this, absorbable (size: 3-0, Ethicon, Johnson and Johnson, USA) and non-absorbable suture material (size: 3-0, Surgipro II, Medtronic, USA) were used (Johnson et al., 2022). During the operation, physical indicators were monitored on the patient's monitor (Digicare Animal Health DigiVet, Life Window Lite Series, USA). After the operation, the dog was transferred to the postoperative ward for condition monitoring and recovery from anesthesia. Postoperative care included the use of the antibiotic 15% amoxicillin (Amoxicillin Bioveta 150 mg/ml LA injectable suspension) at a dose of 1.0 ml per 15 kg of body weight, intramuscularly, and painkillers meloxicam (0.5% Metacam, Boehringer Ingelheim Vetmedica GmbH, Boehringer Ingelheim, Germany), on the first day-0.4 ml/10 kg of body weight, subcutaneously, then in the dose on the first day-0.2 ml /10 kg of body weight, subcutaneously. Regular examinations were also carried out to monitor wound healing and detect possible complications (Wustefeld-Janssens et al., 2021). Pain assessment and infection monitoring were conducted using a multimodal approach beyond routine medication administration. The Glasgow Composite Measure Pain Scale (CMPS; Kudnig and Séguin, 2022) was utilized to evaluate the dog's discomfort postoperatively, while wound inspection was performed daily to check for signs of infection, such as erythema, swelling, discharge, or increased local temperature. The follow-up period lasted 14 days, during which the wound healing process was monitored, and the sutures were removed at the appropriate time. No significant postoperative complications were observed.

Conducting a biopsy for cytological examination

During the clinical examination, a cytological diagnosis was established: mastocytoma. For this, the field of operation was prepared (Berlato et al., 2021; Bellamy and Berlato, 2022). The skin at the biopsy site was treated with 80% ethyl alcohol (Decon Laboratories, Inc., USA). An aspiration fine needle (ABTG, Argon Chiba Biopsy Needle, USA) was used for the biopsy (Valenciano and Cowell, 2019).

The collected material was carefully placed onto a clean glass slide. It was then evenly smeared to create a thin, uniform layer suitable for microscopic examination. The smear was immediately fixed using 70% methyl spirit (BASF SE, Germany) to preserve cellular morphology and prevent artifacts. This preparation ensured the sample's integrity for subsequent staining and analysis. Staining was performed using Quik-Diff (Siemens Healthineers, Germany). The puncture site was treated with 80% ethyl sprite (Decon Laboratories, Inc., USA).

The sample was stained using the Romanowsky method (Raskin and Meyer, 2016). Initially, the sample was fixed in 70% methanol (BASF SE, Germany). Then, it was immersed in a mixture of dyes containing azure II and eosin (Merck, MilliporeSigma, Germany). After staining, the sample was washed with water to remove excess dye and dried before microscopic examination (Axioscope 5 Zesis, Germany).

Sample selection and drug preparation

The biopsies were promptly immersed in a container with 10% aqueous formaldehyde (Sigma-Aldrich, Merck KGaA, Germany), appropriately labeled, and dispatched to the histology laboratory (Kamianets-Podilskyi, Ukraine). A sterile adhesive plaster was applied over the biopsy site (Berlato et al., 2021; Bellamy and Berlato, 2022). The skin biopsy was fixed in 10% formaldehyde for at least 24-48 hours. The samples were then processed using the hematoxylin and eosin (H&E) staining protocol provided (Leica Biosystems, Germany).

Blood collection and analysis

At the start of the study, a 50.0 µL blood sample was collected from the cephalic vein. A thorough hematological assessment was performed to analyze several key parameters. These included the erythrocyte count ($\times 10^{12}$/L), which measures the number of red blood cells; the leukocyte counts ($\times 10^{9}$/L), indicating the total white blood cell count; and the leucogram values ($\times 10^{9}$/L, %), which detail the distribution of different white blood cell types. The analysis also evaluated hemoglobin concentration (µmol/L), a critical measure of the blood's oxygen-carrying capacity; hematocrit (L/L), representing the proportion of blood volume occupied by red blood cells; mean corpuscular volume (MCV, fl); mean corpuscular hemoglobin (MCH, fmol); mean corpuscular hemoglobin concentration (MCHC, mmol/L); and thrombocyte count ($\times 10^{9}$/L), which quantifies platelets essential for blood clotting. The analysis was performed using the Abaxis Vetscan HM5 Hematology Analyzer (USA), a device known for its precision in evaluating blood components. In addition to hematological analysis, blood chemistry was assessed using the VetScan VS2 Biochemistry Analyzer (USA). This instrument was employed for the in vitro quantitative measurement of various biochemical markers, such as albumin (ALB, mmol/L), alkaline phosphatase (ALP, µmol/L), alanine aminotransferase (ALT, µmol/L), amylase (AMY, µmol/L), total bilirubin (TBIL, µmol/L), blood urea nitrogen (BUN, mmol/L), calcium (Ca, mmol/L), phosphorus (P, mmol/L), creatinine (CRE, µmol/L), glucose (GLU, mmol/L), sodium (Na^+, mmol/L), potassium (K^+, mmol/L), total protein (TP, g/L), and globulin (GLOB, g/L). These parameters provide critical insights into metabolic, renal, hepatic, and electrolyte status, ensuring a comprehensive evaluation of the subject's physiological condition.

Statistical analysis

Statistical analysis was performed to evaluate the data collected during the study. All computations and analyses were conducted using the Statistica® 12.6 software (StatSoft, USA), a comprehensive tool for statistical and data visualization tasks.

RESULTS

Hematological findings

The RBC count (8.22×10^{12}/L) had remained within the reference range (Table 1). A mild leukocytosis had been observed, with WBC values (12.17×10^{9}/L) slightly exceeding the upper reference limit, which could have been attributed to a systemic inflammatory or immune response triggered by the tumor. Neutrophil levels (NEU, 73.1%; 8.89×10^{9}/L) had fallen within the normal range for both percentage (52.0-81.0%) and absolute count ($3.0\text{-}12.0 \times 10^{9}$/L), indicating a well-regulated inflammatory response without excessive neutrophil activation. The lymphocyte percentage and absolute count had also been within normal limits, suggesting an appropriate immune response without signs of lymphopenia or lymphocytosis. Monocyte levels had remained within the expected range. Basophils (BAS, 0.1%) had been at the upper limit of the normal range (0-0.1%), while the absolute count had stayed within acceptable limits ($0\text{-}1.0 \times 10^{9}$/L), suggesting no significant basophilia despite potential mast cell involvement. Hemoglobin levels had exceeded the reference range, indicating possible hemoconcentration, likely due to tumor-associated metabolic changes. The hematocrit value (HCT, 0.44 L/L) had been at the upper limit of normal (0.35-0.45 L/L). The mean corpuscular volume (MCV) had been below the normal range (60.0-76.0 fl), indicating microcytosis, while the mean corpuscular hemoglobin concentration (MCHC) had been elevated above the reference range (18.61-23.58 mmol/L), suggesting hyperchromasia. The platelet count (PLT, 134.0×10^{9}/L) had been at the lower end of the normal range. These hematological findings highlighted a mild systemic response to mastocytoma, characterized by leukocytosis and specific alterations in red blood cell and platelet parameters.

Table 1. Hematological parameters in a 5-year-old Akita male dog with mastocytoma

Parameter	Units	Measured values*	Results
Erythrocytes (RBS)	$\times 10^{12}$/L	5.4-8.50	8.22
Leukocytes (WBS)	$\times 10^{9}$/L	6.0-12.0	12.17
Neutrophil (NEU)	%	52.0-81.0	73.1
	$\times 10^{9}$/L	3.0-12.0	8.89
Lymphocyte (LYM)	%	15.0-25.0	21.3
	$\times 10^{9}$/L	1.0-4.80	2.59
Eosinophils (EOS)	%	0.5-3.0	2.1
	$\times 10^{9}$/L	0-1.0	0.2
Monocytes (MON)	%	0-6.0	3.4
	$\times 10^{9}$/L	0.2-1.50	0.4
Basophils (BAS)	%	0-0.1	0.1
	$\times 10^{9}$/L	0-1.0	0
Hemoglobin (HGB)	G/L	95.0-150.0	178
Hematocrit (HCT)	L/L	0.35-0.45	0.44
MCV	fl	60.0-76.0	53.6
MCH	fmol	1.24-1.67	1.34
MCHC	mmol/L	18.61-23.58	25.0
Thrombocyte (PLT)	$\times 10^{9}$/L	117.0-490.0	134.0

MCV: Mean corpuscular volume, MCH: Mean corpuscular hemoglobin, MCHC: Mean corpuscular hemoglobin concentration, Source of control data: Harvey (2012)

Biochemical findings

Amylase levels were 20.48 µmol/L, within the normal range, showing no pancreatic dysfunction (Table 2). Total bilirubin remained low (at 0.71 µmol/L), excluding hyperbilirubinemia. Blood urea nitrogen was 5.58 mmol/L, indicating normal renal function. Calcium levels were 2.54 mmol/L. Phosphorus was slightly below the normal range at 1.46 mmol/L (1.50-2.50 mmol/L), suggesting potential dietary or metabolic factors affecting phosphorus balance. Creatinine was 98.08 µmol/L (53.0-125.0 µmol/L), confirming preserved kidney filtration. Glucose levels were slightly elevated at 6.20 mmol/L (3.9-6.7 mmol/L), possibly reflecting stress hyperglycemia. Sodium and potassium levels were 147.0 mmol/L (143.0-150.0 mmol/L) and 4.80 mmol/L (4.1-5.4 mmol/L), respectively, indicating normal electrolyte balance. Total protein was at a normal range of 66.87 g/L (54.0-75.0 g/L), with globulin levels at 3.21 g/L (1.9-3.7 g/L), suggesting no significant protein loss or immune abnormalities. These results highlighted minor deviations in alkaline phosphatase and glucose levels, which may reflect the systemic impact of mastocytoma, while most parameters indicated stable metabolic and organ functions.

Table 2. Biochemistry parameters in a 5-year-old Akita male dog with mastocytoma

Parameter	Units	Measured values*	Results
Albumin	mmol/L	0.36-0.67	0.56
Alkaline phosphatase	µmol/L	0.2-2.01	4.45
Alanine aminotransferase	µmol/L	0.31-1.16	0.35
Amylase	µmol/L	5.0-25.0	20.48
Total bilirubin	µmol/L	0-3.42	0.71
Blood urea nitrogen	mmol/L	3.5-10.4	5.58
Ca	mmol/L	2.34-2.76	2.54
P	mmol/L	1.50–2.50	1.46
Creatinine	µmol/L	53.0-125.0	98.08
Glucose	mmol/L	3.9-6.7	6.20
Na^+	mmol/L	143.0–150.0	147.0
K^+	mmol/L	4.1-5.4	4.80
Total protein	g/L	54.0–75.0	66.87
Globulin	g/L	1.9–3.7	3.21

Source of control data: Bonagura and Twedt (2013)

Cytological findings

The cytological smear obtained from the fine-needle aspiration of a mastocytoma in a 5-year-old Akita dog showed numerous round to oval cells with distinct cytoplasmic granules (Figure 2). These cells exhibited moderate to high cellularity with round nuclei, some of which are eccentrically located, and a finely granular chromatin pattern. Occasional binucleated cells and anisokaryosis (variation in nuclear size) were observed, indicating mild nuclear atypia. The cytoplasm was abundant and filled with metachromatic granules, staining prominently purple with the cytological dye. The basis background was scattered mast cell degranulation, contributing to a granular extracellular appearance. Few eosinophils and scattered inflammatory cells were present, consistent with a reactive or inflammatory component associated with mast cell tumors. Overall, the findings supported a diagnosis of mastocytoma, with cytological features suggesting a well-differentiated to moderately differentiated grade.

The cytological preparation demonstrated a high cellularity smear with numerous mast cells dispersed throughout the field (Figure 3). The mast cells were round to oval in shape, with moderate to abundant cytoplasm filled with dense, basophilic to metachromatic granules. The nuclei were round to oval and centrally to eccentrically located, with a fine to moderately coarse chromatin pattern. Occasional cells exhibited binucleation, and mild anisokaryosis was observed, reflecting nuclear pleomorphism. The cytoplasmic granules are uniformly distributed, although some areas show evidence of degranulation in the background, producing a granular extracellular matrix. Additionally, small clusters of eosinophils and rare lymphocytes were present, indicating a mild inflammatory response. The smear background appeared clean, with minimal proteinaceous material and a lack of significant necrosis. No evidence of mitotic figures or overtly malignant characteristics, such as marked pleomorphism or nuclear atypia, was noted, which was consistent with a low-to intermediate-grade mast cell tumor.

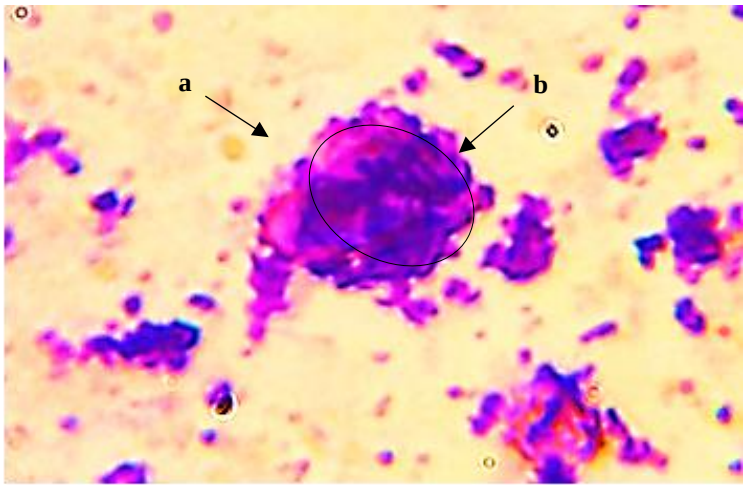

Figure 2. Mastocytoma in a 5-year-old male Akita dog. **a**: Mast cell, **b**: Intracellular granules stained dark blue. Magnification x2000, stained with Quik-Diff.

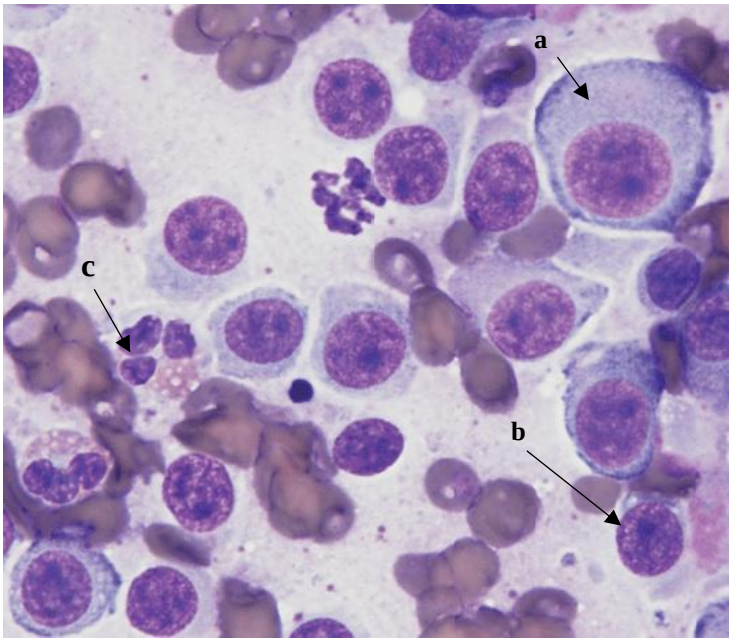

Figure 3. Mastocytoma in a 5-year-old male Akita dog. **a**: Mast cell, **b**: lymphocytes, and neutrophils (**c**). Magnification x3000, stained with aqueous Romanowsky.

Histological findings

The tissue showed a densely cellular neoplastic infiltrate composed predominantly of mast cells arranged in sheets and clusters. The mast cells display cytoplasm was abundant, containing numerous metachromatic granules typical of mast cells (Figure 4). Notable cellular and nuclear pleomorphism was observed, characterized by moderate to significant anisocytosis and anisokaryosis. The surrounding stroma was moderately fibrous, with evidence of infiltration by small numbers of eosinophils and occasional lymphocytes, suggesting a reactive inflammatory response. The presence of mast cells extending into deeper dermal layers was observed, and the margins of the tumor appeared infiltrative, consistent with locally invasive behavior. There was no significant necrosis within the examined field, although scattered apoptotic bodies were visible.

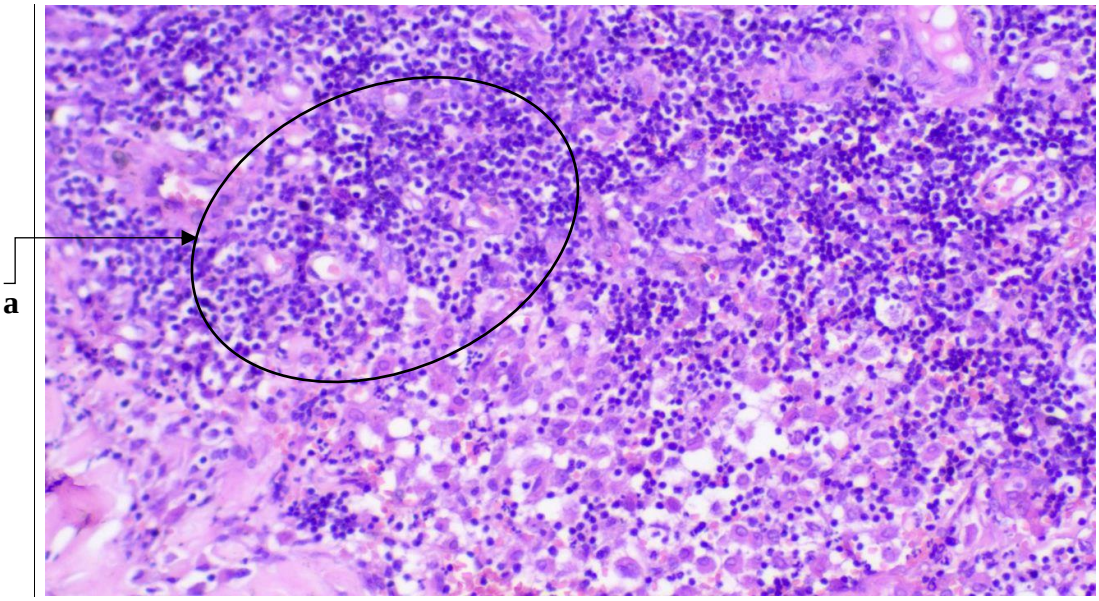

Figure 4. Mastocytoma in a 5-year-old male Akita dog. Active cellular (**a**): Infiltration (lymphocytes, plasma cells, neutrophils) is visualized in the histological preparations, magnification x160, stained with H and E.

DISCUSSION

According to previous studies, mast cell tumors account for approximately 20-25% of all skin neoplasms in dogs. They are most frequently observed in dogs over the age of 5, with an average age of onset around 9 years. It is noted that MCTs can present as solitary lesions, but in 11-14% of cases, multiple tumors may occur (Blackwood et al., 2012; Harshbarger and Meinkoth, 2017; Bellamy and Berlato, 2022). Certain breeds exhibited a higher predisposition to developing mast cell tumors, including Boston Terriers, Boxers, Labradors, and Shar Peis. There was no significant evidence of gender predisposition for MCTs (Berlato et al., 2021; Gerasimos et al., 2023).

Classification is primarily determined by the histological zone exhibiting the highest number of mitotic or nuclear variations. A study by Kiupel (2020) demonstrated a principled approach and correlation between tumor grade and clinical outcome (Kiupel et al., 2021). The 2013 Oncology and Pathology Working Group (OPWG) consensus statement recommended the use of both the Kiupel (2011) classification schemes for cutaneous MCTs (Kiupel et al., 2011). In 2021, the OPWG suggested incorporating two classification systems to better predict tumor behavior and study survival rates. Therefore, MCTs are classified into several categories (grades), including low grade (I), medium grade (II), and high grade (III, Berlato et al., 2021).

New data have emerged on the association of histological nodule grades with clinical outcomes in dogs with MCT exposed to radiopharmaceuticals (Stefanello et al., 2024). It is possible for mast cell tumors in dogs to be differentiated at a low to a high grade.

A significant factor is the presence of mutations in the *c-KIT* gene, which are found in approximately 13.6% of cases (Bellamy and Berlato, 2022; Song et al., 2025). The studies indicate that *c-KIT* mutations are more frequently associated with low-grade tumors (66.7%) and rarely found in high-grade tumors (Camus et al., 2016; De Ridder et al., 2021). Activating mutations in the *c-KIT* gene lead to constitutive activation of the *KIT receptor*, promoting uncontrolled cell proliferation and survival of mast cells. These mutations are commonly found in exon 11, but can also occur in exons 8, 9, and 17. *c-KIT* mutations are often associated with higher-grade MCTs and more aggressive tumor behavior (Korbelik

et al., 2021; De Nardi et al., 2022). Detection of *c-KIT* mutations can aid in the diagnosis and prognostication of MCTs. Molecular testing for these mutations is increasingly used to guide treatment decisions (Roberts et al., 2022). The presence of *c-KIT* mutations makes MCTs potential candidates for targeted therapy with tyrosine kinase inhibitors (*TKIs*), such as toceranib or masitinib, which specifically inhibit the *KIT receptor* and can improve outcomes in affected animals (Larsen et al., 2023). This finding suggested that histological classification may influence the prognosis of the disease (Iamone et al., 2024).

Cytology is a quick and cost-effective method commonly used for diagnosing MCT. These tumors typically exfoliate numerous cells containing many small, round, purple granules, facilitating diagnosis (Shaw et al., 2018; Zhelavskyi, 2024). Cellular features central to Kiupel's classification system can be evaluated using cytological preparations. Several recent studies have explored the correlation between cytologic characteristics and histologic grade.

Cytology is a rapid and cost-effective diagnostic method widely used for detecting mast cell tumors (MCT) in animals. Due to the high exfoliation rate of tumor cells, this technique provides valuable material for analysis (Paes et al., 2021). A key characteristic of mast cells is the presence of numerous small, round, purple-stained granules in the cytoplasm, which significantly facilitates their identification (Shaw et al., 2018). One of the main advantages of cytological examination is the ability to assess key morphological features used in Kiupel's classification system to predict the biological behavior of the tumor (Sabattini et al., 2018). Recent studies have identified a correlation between cytological features and histological grading of mast cell tumors (Del Río-Sancho and Christen-Zaech, 2025). Parameters, such as the number and characteristics of intracellular granules, nuclear atypia, mitotic count, and the presence of inflammatory infiltrates have been recognized as predictive markers of tumor malignancy (Cilloni et al., 2024). Moreover, cytological analysis allows for the rapid determination of the need for further histopathological evaluation, which is crucial for developing an effective therapeutic strategy. Current research focuses on improving cytological assessment methods, particularly through the use of immunohistochemical markers and molecular approaches, to enhance diagnostic accuracy and prognosis of MCTs (Larsen et al., 2023).

Currently, there are promising opportunities for diagnosticians to refine methods for selecting cytological samples and optimizing staining techniques, as well as in the development of specific tumor markers (Vicente et al., 2024). Advances in cytological techniques aim to enhance the accuracy of mast cell tumor (MCT) diagnosis, improve the differentiation between low- and high-grade tumors, and facilitate early detection, which is crucial for effective treatment planning (Vicente et al., 2024). Immunobiological aspects of oncogenesis are being increasingly studied, providing deeper insights into the mechanisms driving tumor progression, including the role of inflammatory mediators, immune evasion, and genetic mutations contributing to malignancy. Researchers are focusing on identifying molecular markers that could serve as reliable prognostic indicators, guiding personalized treatment approaches (Wilson et al., 2020; Gianni et al., 2024). Additionally, new data are emerging on the use of effective pharmacological treatments for cutaneous mastocytosis, contributing to the advancement of targeted therapeutic approaches (Oberholtzer et al., 2024). Recent studies have highlighted the potential of tyrosine kinase inhibitors, monoclonal antibodies, and other novel pharmacological agents in managing mast cell-related disorders. These therapeutic advancements not only improve patient outcomes but also provide a foundation for further exploration of combination therapies that could enhance treatment efficacy and minimize adverse effects (Green et al., 2023).

The ongoing integration of cytology, molecular diagnostics, and targeted therapies underscores the importance of a multidisciplinary approach in the diagnosis and management of mast cell tumors. Future research will likely focus on various criteria, developing non-invasive biomarkers, and expanding treatment options to improve the prognosis and quality of life for affected animals and humans (Oberholtzer et al., 2024). The drug cyclosporine is commonly used in the treatment of autoimmune disorders in dogs and to prevent the rejection of transplants (Wustefeld-Janssens et al., 2021). While effective, cyclosporine use can lead to a range of side effects, including an increased risk of neoplastic conditions, such as mastocytoma (Kudnig and Séguin, 2022). The immunosuppressive effects of cyclosporine help to manage autoimmune diseases but can also impair immune surveillance, increasing the risk of tumor development (Gómez et al., 2020; Kimura et al., 2021; Zhelavskyi et al., 2024b). Common side effects include vomiting, diarrhea, and anorexia, which are often dose-dependent and may decrease with dose adjustment (Walker et al., 2025). Long-term use of cyclosporine can cause gingival overgrowth, which may require dental care or surgical intervention (London et al., 2009). Though less common in dogs than in humans, nephrotoxicity remains a concern, particularly with prolonged use at high doses (Roberts et al., 2022; Brown et al., 2023). Increased incidence of different cancers, including mast cell tumors, has been observed in dogs receiving long-term cyclosporine therapy (De Ridder et al., 2021; Deng et al., 2024). Specific cases document the development of mastocytomas in dogs treated with cyclosporine, suggesting a potential causative relationship (De Andrade et al., 2023). Analyses of veterinary records indicate a higher frequency of mastocytomas in dogs that received cyclosporine compared to those not receiving the drug (Radia, 2025). Routine veterinary check-ups, including blood evaluation and physical examinations, are crucial for early detection of potential

side effects or neoplastic developments (De Ridder et al., 2021). Combining cyclosporine with other immunosuppressive drugs may allow for lower dosages and reduced side effects (Wustefeld-Janssens et al., 2021).

CONCLUSION

Canine mast cell tumors are among the most prevalent skin tumors in dogs, arising from mast cells involved in allergic and inflammatory responses. The current study underscores the importance of early detection and a comprehensive management approach. Cytological and histological analyses revealed characteristic mast cell features and moderate pleomorphism. Surgical removal was successful, with histology showing no significant necrosis, suggesting a favorable prognosis. However, advanced cases with metastasis or high-grade malignancies require a multidisciplinary approach, including surgery, chemotherapy, and targeted therapy. Regular veterinary check-ups are crucial for early detection, timely intervention, and improved quality of life for dogs.

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Availability of data and materials

Data generated from this research are available for readers upon a well-founded request to ensure transparency and reproducibility.

Authors' contributions

Mykola Zhelavsky developed the study concept, reviewed the clinical records, collected the data, and performed the experimental procedures. Serhii Kernychnyi and Tatiana Zakharova led the development of the research base and supervised clinical studies. Tamara Betlinska and Maksym Luchka performed laboratory analyses and related research work. All authors actively participated in the critical evaluation and revision of the manuscript, ensuring its scientific rigor and consistency. They jointly revised and improved the final version of the manuscript, confirming that it accurately reflected the study's findings and their shared opinions. All authors approved the manuscript for submission, affirming their agreement with her findings and their commitment to the accuracy and integrity of the entire work.

Ethical considerations

Authors check and admit to ensure originality, maintain high ethical standards, and avoid fabrication of data, falsification, plagiarism, or improper publication.

Competing interests

The authors declare that they have no financial, professional, or personal conflicts of interest that could influence the content, outcomes, or interpretation of this research.

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