ISSN: 1220-3173; E-ISSN: 2457-7618

EPIDEMIOLOGICAL STUDY OF THE CANINE CUTANEOUS MAST CELL TUMOR

STUDIU EPIDEMIOLOGIC AL MASTOCITOMULUI CUTANAT CANIN

M. NEGRU[1),*)], C. TOMA[1)], R. POPA[1)], R. MARICA[1)], A. BIRIȘ[1)], C. CĂTOI[1)], M. TAULESCU[1)], F. TĂBĂRAN[1)], A. FOTEA[1)]

ABSTRACT | REZUMAT

This paper aimed to study canine cutaneous mastocytomas (MCTs), diagnosed in the Department of Pathological Anatomy, Necropsic Diagnosis and Veterinary Forensic Medicine of the Faculty of Veterinary Medicine, Cluj-Napoca, Romania, by conducting a retrospective study over a period of 15 years (2005-2020). We evaluated all of the cases that were identified from the database, which consisted of histopathological samples from dogs, sent in for diagnosis, subsequently determined to be cutaneous MCTs. In this regard, a number of 161 cases of MCT were obtained from dogs of different breeds, both males and females, aged between 9 months and 18 years. The vast majority of cases consisted of tissue fragments sent in by clinics within the faculty or private practices throughout the country, but there were also situations in which whole cadavers were admitted in our department, being subjected to a complete necropsy examination. After evaluating the data we obtained, we found that the highest number of cases was recorded in the Mixed-breed (n = 26, 15.5%), followed by Boxer (n =17, 10.5%),Labrador Retriever (n=11, 6.8%), Golden Retriever (n=10, 6.2%) and Shar-Pei (n=9, 5.5%). Canine MCT was identified in patients aged between 9 months and 18 years, the largest share of cases (n = 41, 25.4%) belonging to the age group 7-8 years. There is a significant positive relationship between animal age and MCT incidence (r=0.8913; p <0.01). The gender differences were not remarkable, having identified a number of 91 cases in males (56.5%) and 70 cases in females (43.4%). MCTs presented mainly as single tumors (n=141, 88.6%) and less as multicentric tumours (n=18, 11.3%),and the most frequently affected anatomical region was the trunk (n=63, 52.9%), followed by limbs (n=38, 31.9%) and head or neck (n=18, 15.1%). The average period recorded from the onset of the lesion until the diagnosis was established 10.7 months (with limits of 2 weeks - 24 months) and the average diameter of the MCTs 5.4 cm (with limits of 0.3-30 cm).

Keywords: MCT, dog, epidemiological, cutaneous, diagnosis

Scopul acestei lucrări a fost reprezentat de studierea mastocitoamelor (MCT) cutanate canine, diagnosticate în cadrul disciplinei de Anatomie Patologică, Diagnostic Necropsic și Medicină Legală Veterinară a Facultății de Medicină Veterinară, Cluj-Napoca, România, prin efectuarea un studiu retrospectiv pe o perioadă de 15 ani (2005-2020).

Am evaluat toate cazurile identificate din registre, care au constat în probe histopatologice provenite de la câine, trimise în vederea stabilirii unui diagnostic, ulterior stabilite ca fiind MCT cutanate. În acest sens, a fost obținut un număr de 161 de cazuri de MCT provenite de la câini din rase diferite, atât masculi cât și femele, cu vârste cuprinse între 9 luni și 18 ani. După evaluarea datelor obținute am constatat că numărul cel mai mare de cazuri a fost înregistrat la rasa Metis (n =26, 15.5%), urmată de Boxer (n=17, 10.5%), Labrador Retriever (n=11, 6.8%), Golden Retriever (n=10, 6.2%) și Shar-Pei (n=9, 5.5%). MCT canin a fost identificat la pacienți cu vârsta cuprinsă între 9 luni și 18 ani, cea mai mare pondere a cazurilor (n=41, 25.4%) aparținând grupei de vârstă 7-8 ani. Între vârsta animalelor și incidența MCT există o relație pozitivă semnificativă (r=0.8913; p<0.01).

Diferențele de sex nu au fost remarcabile, fiind identificat un număr de 91 cazuri la masculi (56.5%) și 70 la femele (43.4%). MCT s-au prezentat îndeosebi ca formațiuni unice (n=141, 88.6%) și mai puțin ca tumori multicentrice (n=18, 11.3%), iar regiunea anatomică cea mai frecvent afectată a fost trunchiul (n=63, 52.9%), urmată de membre (n=38, 31.9%) și cap sau gât (n=18, 15.1%). Perioada medie de timp înregistrată de la debutul leziunii până la stabilirea diagnosticului a fost de 10.7 luni (cu limite de 2 săptămâni – 24 luni), iar diametrul mediu al MCT a fost de 5.4 cm (cu limite de 0.3–30 cm).

Cuvinte cheie: MCT, câine, epidemiologic, cutanat, diagnostic

Mast cells are immune cells derived from the bone marrow, their maturation from CD34 mast cell precursor cells taking place in peripheral tissues. During haematopoiesis, the development of precursors is closely

1) University of Agricultural Sciences and Veterinary Medicine, Faculty of Veterinary Medicine, Cluj-Napoca, Romania
*) *Corresponding author: mihaingr@yahoo.com*

coordinated by transcription factors. Mast cell precursor cells migrate into tissues in an immature state. They express the c-kit stem cell factor (SCF) receptor and the high-affinity IgE receptor FcεRI, just like mature cells. Migration of precursors at the tissue level is a process stimulated by inflammation and leads to an increase in the number of mast cells in those tissues, as well as their maturation through the coordinated effects of integrins, chemokines, adhesion molecules, cytokines and growth factors. Mastocytomas (MCTs) are neoplastic proliferations of mast cells. Their etiology is not fully known, but, as with most tumours, it is most likely multifactorial (1). According to studies conducted in recent years, the KIT protein appears to have some importance in the pathogenesis and biological behaviour of mast cells (14). KIT protein is a tyrosine kinase receptor, which is a product of the c-kit proto-oncogene (23). It is expressed in many tissues or cells, of which we can list: glioblastoma, placenta, brain, melanocytes, erythroid precursors, basophils, and last but not least, mast cells (5; 16; 23). The KIT receptor ligand, called stem cell factor (SCF) or mast cell growth factor, induces several effects on them, including proliferation, maturation, migration, degranulation, apoptosis suppression, and fibronectin adhesion (8; 15; 21; 24). More recent research has shown the presence of mutations in the canine MCTs of the c-KIT gene, located in the juxta-membrane region, mainly in exon 11. These consist of internal tandem duplications and deletions (13). This suggests that mutations in this gene may be associated with the development or evolution of MCTs, but there is a very high probability that certain gene mutations that presently remain unidentified are involved in the initiation and progression of the vast majority of these tumours (22). Dogs with cutaneous MCTs present to a specialist consultation most often to evaluate a skin formation identified by the owner. Rarely, the main cause for which they present for consultation is the clinical signs produced by the release of chemical mediators following the degranulation of tumour mast cells (20).

MATERIALS AND METHODS

The epidemiological study was conducted over 15 years (2005-2020), using data obtained from the database of the Department of Pathological Anatomy, Necropsic Diagnosis and Forensic Veterinary Medicine within the Faculty of Veterinary Medicine, Cluj-Napoca. We evaluated all of the cases identified from the database, which consisted of histopathological samples from dogs, sent in for a diagnosis, later determined to be cutaneous mastocytomas. In this regard, 161 cases of mastocytoma were obtained from dogs of different breeds, both males and females, with ages covering the entire usual lifespan of dogs.

The vast majority of cases consisted of tissue fragments submitted by clinics within the faculty or private practices throughout the country, but there were also situations in which the entire corpse was admitted to our department, being subjected to a complete necropsy examination. The cases that were diagnosed cytologically preoperatively, with the diagnosis being confirmed by subsequent histopathological examination, were recorded only once. In the case of multiple tumours, with different diagnoses, the tumours were registered with the same registration number but evaluated and diagnosed individually. The locations of the tumours were determined to be the head, trunk, limbs, or multiple locations. A separate category was represented by cases where the anatomical location was not specified in the anamnesis. An Olympus BX41 optical microscope with an Olympus UC-30 digital camera and StreamBasic image acquisition and editing software were used to examine and diagnose the tumours. Data and graphs were processed and generated using MS-Excel (Microsoft, Redmont, WA). For the statistical analysis of the data, the correlation coefficient linear regression and the equation of the regression line were used (MiniTab 19, Minitab 2020 LLC).

RESULTS AND DISCUSSIONS

The literature names the following breeds as predisposed to develop MCTs: Boxer, Boston Terrier, Bull Terrier, Bull Mastiff, Cocker Spaniel, American Staffordshire Terrier, Fox Terrier, English Bulldog, Dachshund, Labrador Retriever, Golden Retriever, Beagle, Pug, Schnauzer, Shar-Pei, Rhodesian Ridgeback, Weimaraner, and Australian cattle dog (3; 18; 2; 19).

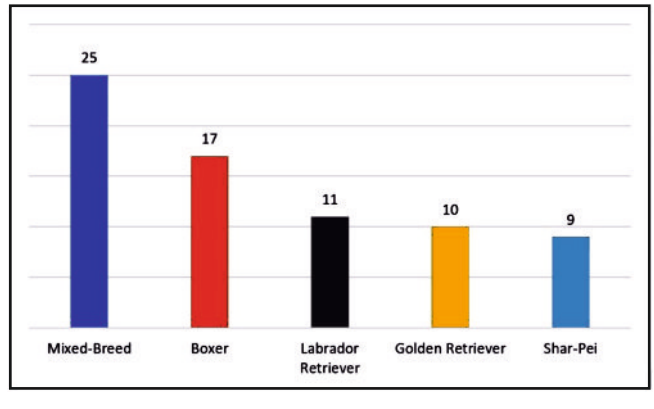

Fig. 1. The distribution of canine cutaneous mastocytoma cases according to the most affected breeds included in the study

Another study ranks the Boxer and Boston Terrier first, with an incidence of over 50% of MCT cases (4). In the present study, 40 dog breeds with MCTs were identified, with either cutaneous and subcutaneous subtypes. Of these, the highest number of cases was

Table 1

The breeds of the 161 dogs with cutaneous mastocytomas

Breed	Number of cases	Percentage (%)
Mixed-Breed	25	15.5
Boxer	17	10.5
Labrador Retriever	11	6.8
Golden Retriever	10	6.2
Shar-Pei	9	5.5
Pug	8	4.9
Poodle	7	4.3
Beagle	6	3.7
German Shepherd	6	3.7
American Staffordshire Terrier	5	3.1
Pitbull	5	3.1
Great Dane	4	2.4
Siberian Husky	4	2.4
Bichon	3	1.8
English Bulldog	3	1.8
Rottweiller	3	1.8
Daschund	3	1.8
Yorkshire Terrier	3	1.8
German Shorthaired Pointer	2	1.2
Bullmastiff	2	1.2
French Bulldog	2	1.2
Bernese Mountain Dog	2	1.2
Hungarian Puli	2	1.2
English Setter	2	1.2
American Bully	1	0.6
Bobtail	1	0.6
American Bulldog	1	0.6
Chihuahua	1	0.6
Chow-Chow	1	0.6
Central Asian Shepherd	1	0.6
Caucasian Shepherd	1	0.6
Border Collie	1	0.6
Cocker Spaniel	1	0.6
Dogo Argentino	1	0.6
Fox Terrier	1	0.6
Lagotto Romagnolo	1	0.6
Pekingese	1	0.6
Schnauzer	1	0.6
Viszla	1	0.6
West Highland White Terrier	1	0.6

recorded in the Mixed-breed (n=25), followed by Boxer (n=17), Labrador Retriever (n=11), Golden Retriever (n=10) and Shar-Pei (n=9) (Fig. 1). This result can be explained, on one hand, by the uncontrolled breeding of dogs and, on the other hand, by the large population of stray dogs belonging to the mixed-breed in this country. The percentages of the breeds included in the study are found in Table 1.

The average age of dogs when they usually develop MCTs is between 7.5 and 9 years old (y.o.), but cases have also been reported in which patients were 4-6 months old (6). Other studies claim that this tumour is specific to geriatrics (mean age 9 y.o.), but this time the youngest age was found to be 3 weeks (9).

An epidemiological study conducted in 2014 separates the number of cases by age categories so that patients aged 6.1 to 8 y.o. were the most numerous, followed by those with 4.1 and 8 years, respectively 8.1 and 10 years. The mean age was 8.6 y.o. (12). In this study, canine MCT was identified in patients aged 9 months to 18 years. We identified the highest number of cases (n=41, 25.4%) belonging to the age group 7-8 y.o. The following age groups, in descending order of the number of cases, are 5-6 y.o. (36 cases, 22.3%), over 10 y.o. (34 cases, 21.1%), 9-10 y.o. (26 cases, 16.1 %), 3-4 y.o. (13 cases, 8%), 1-2 y.o. (10 cases, 6.2%) and under 1 y.o. (1 case, 0.6%) (Fig. 2).

The average age at which individuals develop MCTs in this study is 7.7 years old, similar to the data found in the literature. Thus, we can say that dogs over 5 years of age are more affected, without excluding the appearance of tumours at younger ages.

The age of the dogs taken into study has a direct influence on the incidence of tumours (Fig. 3). The determined correlation coefficient is significantly positive, between age and tumour incidence establishing a linear regression; so that the transition to a higher age category influences an increase of almost 3-fold in the number of individuals with tumours.

The literature claims that there is no predisposition to sex when it comes to the incidence of canine MCTs. In our study, the gender differences are not remarkable, identifying 91 males (56.5%) and 70 females (43.4%) (Fig. 4). We can observe, thus, that there is no significant predisposition of one sex or another for the appearance of MCTs.

According to several authors, the main anatomical regions in which mastocytomas can occur are the trunk, in more than half of the cases, the hind limbs in 25-40% of cases and, to a lesser extent, the head and neck (17; 19). In another study, conducted in Austria by LEIDINGER et al. in 2014, they identified the limbs as the most affected location of the tumor, followed by the trunk, head, and neck and cases with multiple locations. By examining the total number of MCTs (n = 159) of which we obtained data on tumor distribution, we observed that they presented mainly as single masses (n=141, 88.6%) and less as multicentric tumors (n=18, 11.3%) (Fig. 5). Multicentric MCTs were noted in the Pitbull breed (n = 2, 11.1%), Labrador Retriever (n=2, 11.1%), Mixed-breed (n=2, 11.1%), Dachshund (n = 2, 11.1%), and Hungarian Puli, Bullmastiff, Boxer, German Shepherd, American Bulldog, Pug, Dogo Argentino, American Bully, Shar-Pei, Rottweiller with only one case each (5.5%).

In the present study, the most frequently affected anatomical region was the trunk, with 63 unique tumours (53%) showing this location.

The localization on the limbs was second in the number of identified cases (n=38, 32%), followed by the head and neck (n = 18, 15%) (Fig.6).

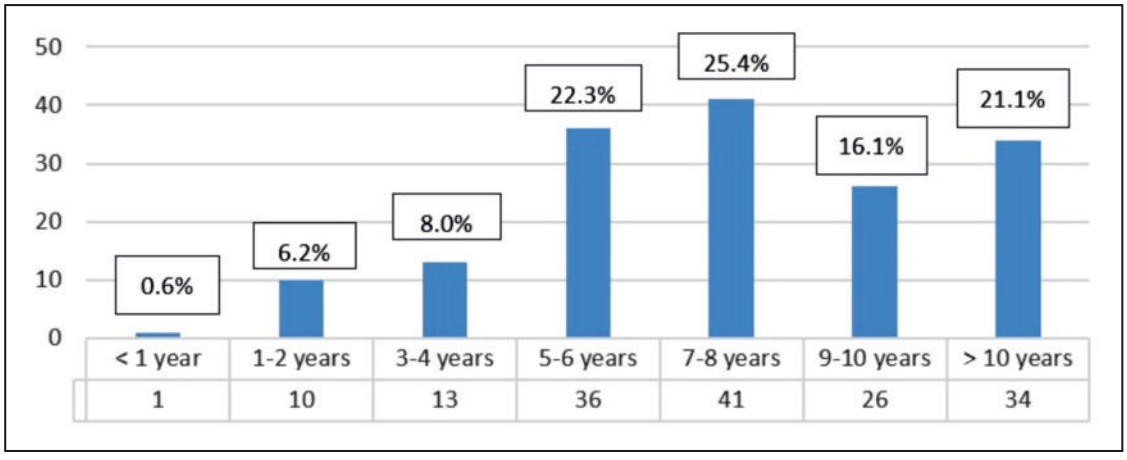

Fig. 2. Incidence of canine cutaneous MCTs according to the age categories

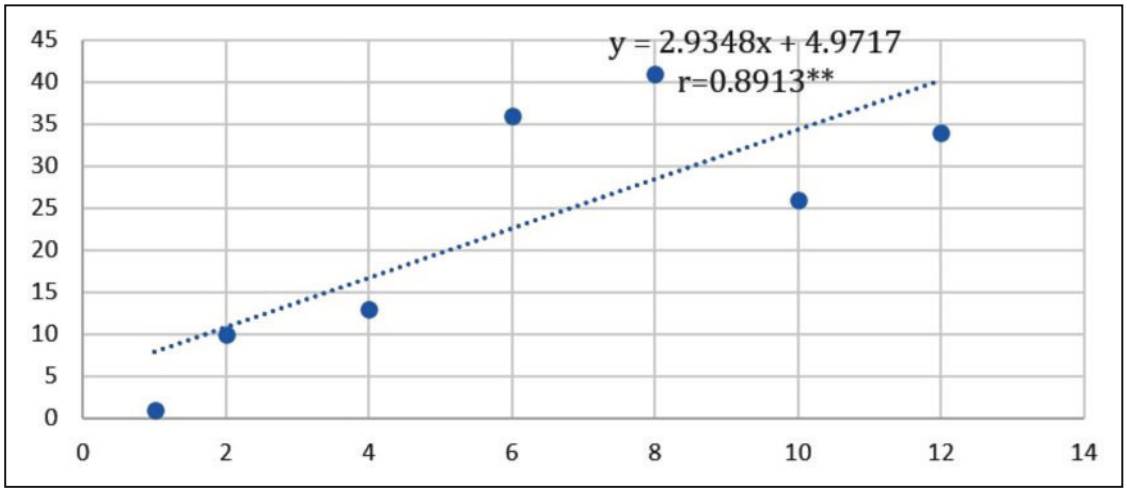

Fig. 3. Statistical relation between the age groups and tumour incidence

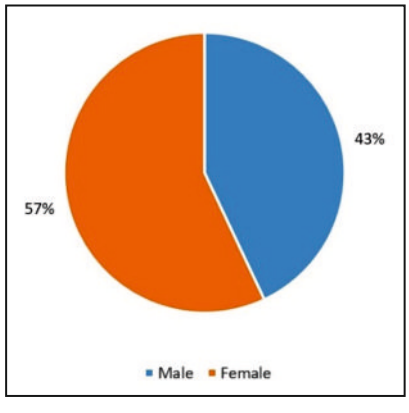

Fig. 4. Incidence of MCTs according to gender

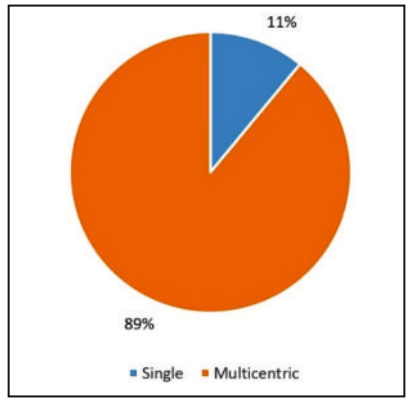

Fig. 5. Incidence of MCTs according to the number of tumors

The data regarding the tumour-location/tumours was not complete, having identified 39 cases in which the affected anatomical region was not specified, this information being missing from the anamnesis sent by the owners or veterinary clinics. The period from the onset of the lesion to the establishment of the anatomopathological diagnosis was recorded in 34 cases (21%). We managed to calculate the average period recorded from the onset of the lesion until the diagnosis, which is 10.7 months (with limits of 2 weeks - 24 months). The size of the tumours was recorded in 84 cases, the average diameter of MCTs being 5.4 cm (with limits of 0.3 - 30 cm).

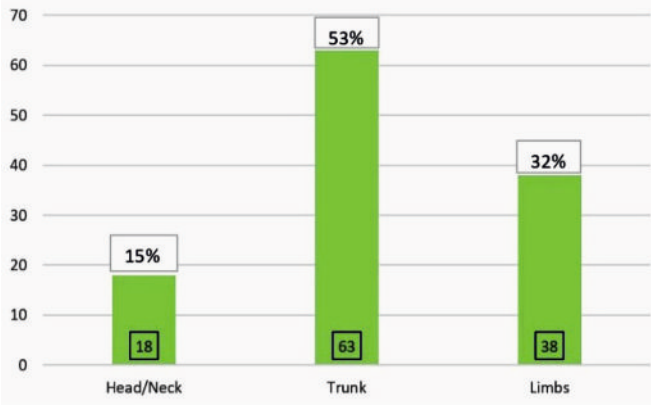

Fig. 6. Incidence of MCTs based on the anatomical localization

CONCLUSIONS

In the period 2005-2020, within the Department of Pathological Anatomy, a very large number of canine MCTs were registered and diagnosed (n=161).

A higher number of cases was recorded in the Mixed-breed compared to other predisposed breeds like the Boxer, Labrador Retriever, Golden Retriever, or Shar-Pei. There is a significant positive relationship between animal age and MCT incidence, the largest share of cases belonging to the age group 7-8 years. No significant gender predisposition has been identified in this study. Most of the MCTs develop as single masses and less as multicentric tumours. The most frequently affected anatomical region was the trunk, followed by the limbs and then head and neck. The average period recorded from the onset of the lesion until diagnosis was relatively high (10.7 months), with the average tumour size being 5.4 cm. This suggests that many tumours have gone undiagnosed for large periods, leading to significant tumour growth.

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