

A RETROSPECTIVE STUDY OF CANINE TESTICULAR TUMOURS IN SLOVENIA

Tanja Švara^{1*}, Mitja Gombač¹, Estera Pogorevc², Tanja Plavec², Petra Zrimšek³, Milan Pogačnik¹

¹Institute of Pathology, Forensic and Administrative Veterinary Medicine, ²Clinic for Small Animal Medicine and Surgery, ³Clinic for Reproduction and Horses, Veterinary Faculty, University of Ljubljana, Gerbičeva 60, 1000 Ljubljana, Slovenia

*Corresponding author, E-mail: tanja.svara@vf.uni-lj.si

Summary: The aim of this study was to provide up-to-date information on the incidence of and some epidemiological data on the testicular tumours of dogs in Slovenia. Amongst the 1975 tumours of male dogs submitted to the Institute of Pathology, Forensic and Administrative Veterinary Medicine at the Veterinary Faculty of the University of Ljubljana between January 1995 and January 2012, testicular tumours were diagnosed in 206 dogs (the mean age 9.9 ± 2.7 years). The detection rate of testicular tumours was 10.4% (206/1975) in all tumours in male dogs.

Altogether, 301 testicular tumours were diagnosed in our study: 144 seminomas (SEMs) (47.8%), 86 interstitial cell tumours (ICTs) (28.6%), 59 Sertoli cell tumours (SCTs) (19.6%) and 12 mixed germ cell-sex cord stromal tumours (MGCSTs) (4%). Single unilateral testicular tumours were detected in 141 dogs (68.4%), whereas 37 dogs (18%) exhibited multiple unilateral tumours. Twenty-eight dogs (13.6%) had bilateral tumours: 12 dogs (5.8%) had one tumour in each testicle, and 16 dogs (7.8%) had multiple bilateral tumours. Foci of neoplastic cells were found in the lymph or/and blood vessels of six (50%) MGCSTs, 20 (40.8%) SCTs and 34 (28.1%) SEMs. The frequency of blood/lymphatic vessel invasion was higher in SEMs with a diffuse growth pattern ($P < 0.05$) and in SCTs with diffuse/tubular growth, but the difference was near the limit of significance ($P = 0.07$). No metastases were noted in ICTs.

The highest prevalence of testicular tumours was detected in mixed breed dogs (20.4%), followed by German Shepherds, Collies, Poodles, Golden Retrievers, Cocker Spaniels, German Boxers, Labrador Retrievers and Samoyeds.

Key words: pathology; testicular tumours; dog; Slovenia

Introduction

According to the World Health Organization's (WHO) classification of tumours of domestic animals (1), the major types of testicular tumours are sex cord-stromal (gonadostromal) tumours, germ cell tumours and mixed germ cell-sex cord stromal tumours. Interstitial (Leydig) cell tumours (ICT) and Sertoli (sustentacular) cell tumours (SCT) are the most common types of testicular tumours, derived from the sex cord-stromal

tumours, whereas seminoma (SEM) is the most common type is derived from the germ cells (1).

Testicular tumours are common in dogs, and their prevalence is increasing: from 1960 to 1992 the prevalence ranged from 0.91 to 16% (2, 3, 4, 5), and from 2000 to 2009 was from 5.4% to 27% (6, 7, 8, 9). In men, the worldwide incidence of testicular cancer has doubled since 1970s (10, 11).

This paper reports on the first retrospective study on testicular tumours of dogs in Slovenia since 1995, providing information on their incidence, as well as their histopathological, clinical and epidemiological characteristics.

Materials in methods

A retrospective study was done on the paraffin-embedded archive samples of testicular tumours collected at the Institute of Pathology, Forensic and Administrative Veterinary Medicine at the Veterinary Faculty of the University of Ljubljana. The largest proportion of samples is represented by surgical biopsy samples sent from veterinary clinics, while the rest were samples taken during necropsies performed at the institute.

Formalin-fixed, paraffin embedded, 4 µm-thick tissue sections stained with haematoxylin and eosin, collected over 17 years, from January 1995 to January 2012, were reviewed. Tumours were classified according to the latest WHO classification of tumours of the genital system of domestic animals (1). If more than one tumour was diagnosed in one testicle, the tumour was classified in the category of multiple testicular tumours. If tumours were found in both testicles, they were classified as bilateral testicular tumours.

Furthermore, data regarding age and breed of the dogs and the location of the tumours were obtained from the necropsy records.

A Chi-square test was used to evaluate the relationship between the tumour type and the age of dogs, tumour type and tumours with metastases, between tumour types and tumour location, and between the age of dogs and the number of tumours.

Results

Detection rate of testicular tumours

From January 1995 to January 2012, different tumour types were histopathologically diagnosed in 1975 samples of various tissues and organs of male dogs. Amongst them, testicular tumours were diagnosed in 206 dogs. The detection rate of testicular tumours was 10.4% (206/1975) of all tumours in male dogs.

The tumour types and their characteristics

In total, 301 testicular tumours were diagnosed in 206 dogs involved in this study.

Unilateral tumours were detected in 178 dogs (86.4%); in 141 dogs (68.4%) only single testicular tumours were detected, and 37 dogs (18%)

exhibited multiple unilateral tumours. The most common multiple unilateral testicular tumours were SEM-ICT (12/37 dogs=32.4%) and multiple SEMs (12/37 dogs=32.4%). Combination SEM-SCT tumours were found in nine dogs (24.3%) and SCT-ICT in two (5.4%). In two dogs (5.4%), three tumour types: SEM, SCT and ICT were detected in one testicle.

Bilateral tumours were found in 28 dogs (13.6%). Twelve dogs (5.8%) with bilateral tumours had one tumour in each testicle, but 16 dogs (7.8%) had multiple tumours in one or both testicles. The most common amongst the first group were bilateral SEMs (5 dogs= 2.4%), followed by bilateral SCTs (3 dogs= 1.5%). Bilateral ICT, SEM-ICT, SEM-MGCSCCT and SCT-MGCSCCT were found in one dog each.

Data regarding the group with multiple bilateral tumours are shown in Table 1.

Amongst 301 testicular tumours, there were 144 SEMs (47.8%), 86 ICTs (28.6%), 59 SCT (19.6%) and 12 mixed germ cell-sex cord stromal tumours (MGCSCCT) (3.99%).

Seminomas

The total number of SEMs was 144 (47.8%); 121 tumours were available for histopathological re-evaluation. Histologically, 47 tumours (38.8%) had a diffuse growth, 62 tumours (51.2%) showed intratubular growth, whereas both types of growth were observed in 12 tumours (9.9%).

Blood/lymphatic vessel invasion was found in 34 (28.1%) of 121 SEMs. A significant relationship was found between the tumour type and the frequency of blood/lymphatic vessel invasion ($P<0.05$). The frequency of blood/lymphatic vessel invasion was the highest in SEMs with a diffuse growth pattern (57.5%) and much lower in a combination of diffuse and intratubular and intratubular growth patterns (Table 2) ($P<0.05$).

In only two of 1043 dissected male dogs (0.19% of dissected dogs) were metastases of SEM found; in both cases, they were in the iliac lymph nodes, and distant metastases were found in the lungs of one dog.

Interstitial cell tumours

The total number of ICTs was 86 (28.6%), and 81 tumours were available for histopathological

Table 1: Combinations of testicular tumour types in 16 dogs with multiple bilateral tumours. Legend: SEM, seminoma; SCT, Sertoli cell tumour; ICT, interstitial cell tumour; MGCSCT, mixed germ cell-sex cord stromal tumour

Tumour combination	Number of dogs	%
SEM/ICT-SEM/ICT	4	25
multiple SEMs-multiple SEMs	4	25
ICT-ICT/SEM	4	25
multiple ICT-multiple ICT	2	12.5
SEM-SEM/ICT	2	12.5
Together	16	25

Table 2: The frequency of blood/lymphatic vessel invasion in different growth patterns of seminomas

Tumour types	Number of tumours	Number of tumours with blood/lymphatic vessel invasion	Frequency of blood/lymphatic vessel invasion (%)
Diffuse growth pattern	47	27	57.4
Intratubular growth pattern	62	6	9.7
Diffuse and intratubular growth pattern	12	1	8.3
SEM – together	121	34	28.1

Table 3: The frequency of blood/lymphatic vessel invasion in different growth patterns of Sertoli cell tumours. Legend: SCT, Sertoli cell tumour

Tumour types	Number of tumours	Number of tumours with blood/lymphatic vessel invasion	Frequency of blood/lymphatic vessel invasion (%)
Diffuse/tubular SCT	22	12	54.5
Tubular SCT	27	8	29.6
SCT – together	49	20	40.8

Table 4: Location of testicular tumour types. Legend: SEM, seminoma; SCT, Sertoli cell tumour; ICT, interstitial cell tumour; MGCSCT, mixed germ cell-sex cord stromal tumour.

Tumour type	N	Left testicle	Right testicle	Unknown location
SEM	144	39	31	74
ICT	86	22	23	41
SCT	59	12	11	36
MGCSCT	12	0	3	9
Total	301 (100.0%)	73 (24.2%)	68 (22.6%)	160 (53.2%)

re-examination. Histologically, two growth patterns were observed: a solid-diffuse pattern and a cystic-vascular growth one. No metastases were noted in ICTs.

Furthermore, in nine dogs, microscopic proliferations of interstitial cells, considered to be nodular hyperplasia of interstitial cells, were detected.

Sertoli cell tumours

The total number of SCTs was 59 (19.6%). Paraffin tissue blocks of 49 tumours were available for histopathological examination. Histologically, two growth patterns were found: diffuse/tubular and tubular. Both had a similar frequency, while SCTs with pure diffuse growth were not detected.

Blood/lymphatic vessel invasion was found in 20 of 49 SCTs (40.8%). The frequency of blood/lymphatic vessel invasion was 54.6% in SCTs with diffuse/tubular growth patterns; however, in SCTs with the tubular pattern, the frequency of invasion was almost two times lower (29.6%), but the difference was near the limit of significance ($P=0.07$) (Table 3).

In only one out of 1043 dissected male dogs (0.10% of dissected dogs) were metastases found in the iliac lymph nodes and the liver.

Mixed germ cell-sex cord stromal tumours

The total number of detected MGCSTs was 12 (4%), in which a combination of neoplastic germ and Sertoli cells was found. Foci of neoplastic cells were found in lymph and/or blood vessels in six tumours (50%).

Tumour locations

The data on the tumour locations were available only for 141 tumours. Seventy-three tumours (24.2%) developed in the left testicle and 68 (22.6%) in the right (Table 4). The tumour location was unknown in 160 (53.2%) cases. There was no relationship between tumour type and tumour location ($P=0.283$).

The age of dogs

Data about the age of dogs with testicular tumours was available for 191 dogs. Their age varied from 2 to 17 years. Most of the testicular tumours were diagnosed between 9 and 12 years (38.8%), less frequently between 6 and 9 years (22.3%) and between 12 and 15 years (21.4%). The mean age of dogs with testicular tumours was 9.9 ± 2.7 years (Fig. 1). A significant relationship was found between the tumour type and the age of dogs ($P<0.05$).

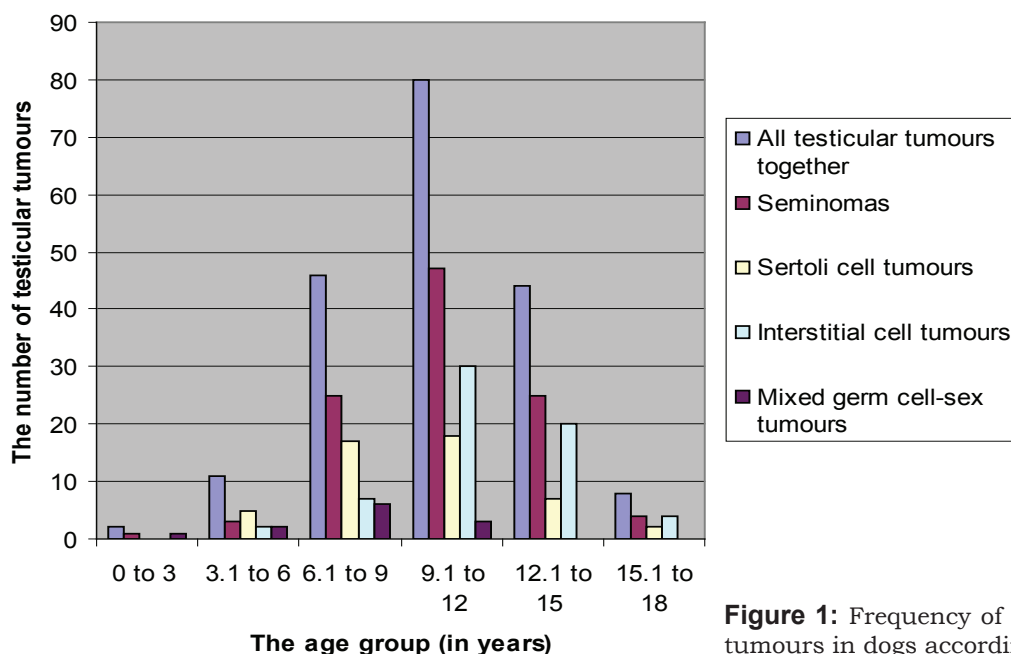
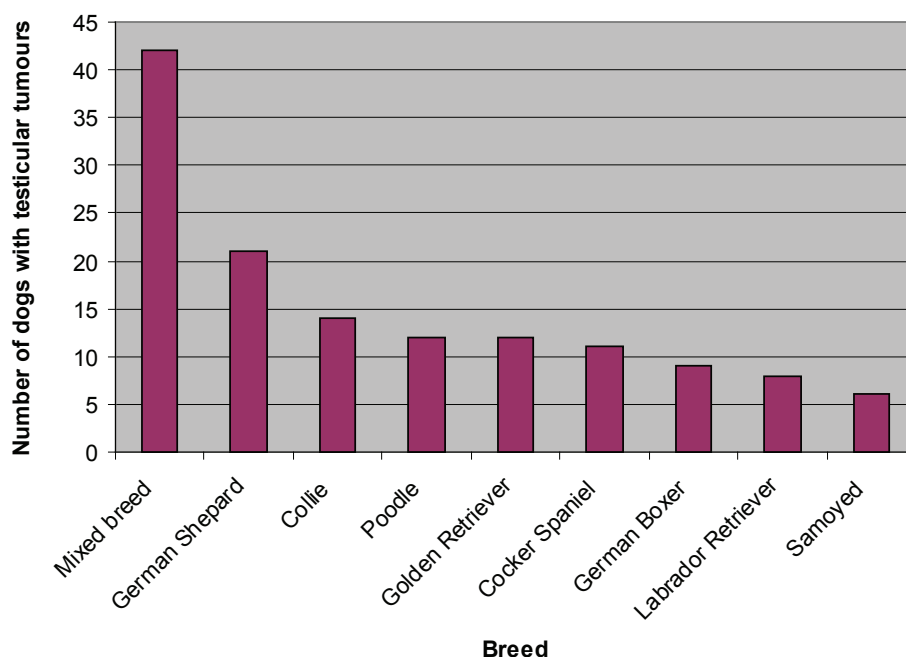


Figure 1: Frequency of different types of testicular tumours in dogs according to age.

Figure 2: Frequency of different types of testicular tumours in dogs according to breed



The age distribution of dogs with SEMs, SCTs and ICTs was similar to the one listed above; they were most often diagnosed between 9 and 12 years.

Mixed germ cell-sex cord stromal tumours were diagnosed in dogs younger than 12 years, with the highest frequency between 6 and 9 years of age (50%) (Fig.1 and 2).

Breeds of dogs

Data on dog breeds were available for 200 dogs. The highest prevalence of testicular tumours was found in mixed breed dogs (41 dogs=20.4%), followed by German Shepherds (21 dogs= 11%), Collies (14 dogs=7.3%), Poodles and Golden Retrievers (12 dogs=6.3%), Cocker Spaniels (11 dogs=5.8%), Boxers (9 dogs=4.7%), Labrador Retrievers (8 dogs=4.2%) and Samoyeds (6 dogs=3.1%). Cases of testicular tumours were found in single dogs of other breeds (Fig. 2).

Discussion

In this study, the detection rate of testicular tumours was 10.4% of all tumours of male dogs. The incidence reported in the literature since 2000 varied from 9.45% to 27% (6, 7, 8, 9). Differences in the reported prevalence are partly due to different methodologies used; some authors (7, 8)

determined the relative incidence after histological examination of both testes collected at the necropsy of each dog, although macroscopically testes were without visible alterations, while others (6, 9) determined the detection rate on biopsy and necropsy samples collected due to visible testicular tumours or other gross pathological testicular lesions. Earlier studies were based mostly on biopsy samples (2, 4, 5) or tumours detected at routine necropsies (3). The real prevalence of testicular tumours in dogs from Slovenia is presumably higher than calculated in this study, since many samples of testicular tumours are not sent for histopathological examination (personal communication with clinicians). In the year 2010, when clinicians were encouraged to submit all detected testicular tumours, the detection rate rose to 18.8%.

Almost a third of the dogs (65 dogs=31.6%) included in this study had more than one testicular tumour, either multiple uni- or bilateral or one tumour in each testicle. This frequency is similar to the 31% incidence reported by Grieco et al. (2008), and slightly lower than the 38.29% incidence reported by Santos et al. (2000). An earlier study (12) stated that 8.45% of dogs had more than one testicular tumour. In dogs from Slovenia, the most common tumour type detected in animals with more than one testicular tumour was SEM. Solely or in other combinations, it was found in 56 dogs (86.2%) with more than one testicular tumour.

SEMs were also the most common tumours found in this study (47.8%). SEMs were also reported as the most frequent tumour type by authors of recent studies (7, 9, 13), while some other authors described ICTs as the most common tumours (6, 8) or reported that both tumour types occur at equal frequencies (12, 14, 15). However, the highest prevalence of SEMs in the most recent studies is interesting, as SEMs in men are the prevailing testicular type and their incidence is on the increase (10, 11).

Twelve MGCSTs (3.99%) were also diagnosed; this is a group of tumours in which Sertoli and germ cell elements are intimately combined within a single tumour (16). This type of testicular tumour was first described in 1981 (17) and was later detected with a prevalence from 4.76% (7) to 22.9% (9).

Blood/lymphatic vessel invasion was found in 28.1% of SEMs, 40.8% of SCTs and 50% of MGCSTs. In SEMs, foci of neoplastic cells in lymph/blood vessels were significantly related to diffuse type of growth. In SCTs in which the pure diffuse type was not detected, blood/lymphatic vessel invasion was connected with diffuse/tubular growth. According to the literature, in SEMs and SCTs the diffuse histological pattern is more likely to be associated with malignant behaviour (1, 16). Regional and distant metastases were reported in less than 15% of dogs diagnosed with either SCTs or SEMs (18). Metastasis occurs in the adjacent lymph nodes of the sublumbar and pelvic region and to internal organs (16). The metastatic rate was assessed mainly in older retrospective studies (3, 12, 19). Single case reports of metastatic disease are described in newer references (20, 21, 22, 23).

The data on the location were available for less than half of the tumours. Statistical analysis did not show any relationship between tumour type and tumour location ($P=0.283$). According to the literature, in the descended testes there is no predilection for cancer development in either the right or the left testis (18). However, the abdominal and inguinal location of the testis is known to be one of several predisposing factors for the development of testicular tumours, with the right testis more often being retained (18) and, therefore, predisposed to tumorigenesis (7, 14, 18, 24). The occurrence of SCTs and SEMs in cryptorchid testes is much higher than in scrotal testes (1, 18, 24). In the records of this study, the data regarding cryptorchidism were sparse and

were, therefore, not included in our study.

The largest number of testicular tumours (38.8%) was diagnosed at the age between 9 and 12 years (the mean age was 9.9 ± 2.7 years). The mean age of dogs with testicular tumours in other studies was between 9.5 years (25) and 11.9 years (13). Dogs older than six years had a 21.5 times higher risk of developing testicular tumours than dogs under two years of age and 4.2 times higher risk than 3- to 5-year-old dogs (7).

Of the studied dogs with testicular tumours, 20.4 % were mixed breeds, followed by German Shepherds, Collies, Poodles, Golden Retrievers, Cocker Spaniels, Boxers, Labrador Retrievers and Samoyeds. Testicular tumours in other breeds were found only sporadically. Several authors wrote about increased risk of the development of primary testicular tumours in Boxers (12, 25), German Shepherds (8), Afghan Hounds (26), Weimaraners (26), Shetland Sheepdogs (15, 24), cairn terriers (25), border and Shetland collies (15, 25), Pekingese (25) and Maltese dogs (9). According to statistical data, German Shepherds and mixed breeds are most common amongst dogs in Slovenia, together constituting 55% of the canine population (27). Similarly, other authors state that some of the breeds with a high incidence of testicular tumours are also dominant in the population of dogs in their countries (8, 9) and, therefore, this may not represent the true breed predisposition.

This study provides the first information on the incidence, histopathological, and some clinical and epidemiological characteristics of testicular tumours of dogs in Slovenia from 1995 to 2012. Further studies would be required to elucidate the role of other risk factors, such as body condition, diet, physical activity, testicular trauma, etc., in the pathogenesis of canine testicular tumours.

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RETROSPEKTIVNA ŠTUDIJA TUMORJEV MOD PRI PSIH V SLOVENIJI

T. Švara, M. Gombač, E. Pogorevc, T. Plavec, P. Zrimšek, M. Pogačnik

Povzetek: Retrospektivno študijo tumorjev mod pri psih v Sloveniji smo opravili, da bi pridobili najnovejše podatke o njihovi incidenci in nekaterih epidemioloških značilnostih. Med 1975 tumorji, ki smo jih na Inštitutu za patologijo, sodno in upravno veterinarstvo Veterinarske fakultete Univerze v Ljubljani diagnosticirali pri psih med leti 1995 in 2012, smo tumorje mod ugotovili pri 206 psih, kar predstavlja 10,4% pojavnost (206/1975). Skupno smo diagnosticirali 301 tumor mod: 144 seminomov (SEM) (47,8%), 86 tumorjev intersticijskih celic (ICT) (28,6%), 59 tumorjev sertolijevih celic (SCT) (19,6%) in 12 mešanih tumorjev semenskih trakov in germinalnih celic (angl. mixed germ cell-sex cord stromal tumours, MGCSCT) (4%). Po en tumor na enem od mod smo ugotovili pri 141 psih (68,4%), 37 psov (18%) pa je imelo na enem modu multiple tumorje. Osemindvajset psov (13,6%) je imelo bilateralne tumorje mod, od teh jih je 12 (5,8%) imelo po en tumor na vsakem modu, 16 (7,8%) pa multiple tumorje na obeh modih. Skupine tumorskih celic smo v limfnih in/ali krvnih žilah ugotovili pri 6 (50%) MGCSCT, 20 SCT (40,8%) in 34 (28,1%) SEM. Metastaziranje je bilo bolj pogosto pri SEM z difuzno obliko rasti ($P < 0,05$) in SCT z difuzno/tubularno rastjo. Pri slednjih je bila razlika blizu meje signifikance ($P = 0,07$). Pri ICT nismo ugotovili metastaziranja.

Povprečna starost psov s tumorji mod je bila $9,9 \pm 2,7$ let. Tumorje smo najpogosteje ugotovili pri mešancih (20,4%) in nemških ovčarjih (11%), škotskih ovčarjih (7,3%), manj pogosti pa so bili pri kodrih in zlatih prinašalcih (6,3%), koker španjelih (5,8%), nemških bokserjih (4,7%), labradorcih (4,2%) in samojedih (3,1%).

Ključne besede: patologija; tumorji mod; psi; Slovenija