A 12-Year Retrospective Study of Canine Testicular Tumors

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ABSTRACT. To provide up-to-date information on the incidence and risk factors of canine testicular tumors, 476 pathological reports of male canine tumors from two institutes of veterinary medicine in Taiwan over a period of 12 years were reviewed. The detection rate of testicular tumors was 16.8% (80/476) in male canine tumors, and 94.1% (80/85) in male genital tumors. Ninety-six testicular tumors from 80 dogs were identified in this study, including 33 (34.4%) seminomas (SEMs), 25 (26%) interstitial cell tumors (ICTs), 22 (22.9%) mixed germ cell-stromal cell tumors (MGCSTs), and 16 (16.6%) Sertoli cell tumors (SCTs). Of the 96 testicular tumors, 52 (54.2%) tumors developed from cryptorchid testes in 45 dogs (56.3%), and 44 (45.8%) tumors developed from scrotal testes in 35 dogs (44.7%). Cryptorchidism was significantly associated with development of MGCSTs, SCTs, and SEMs, but not ICTs ($p < 0.01$). The detection rate of testicular tumors in the dog younger than 10-years-old was significantly associated with cryptorchidism ($p < 0.01$). Except for mixed breed dogs, the Maltese breed had high detection rate of testicular tumors, and may have high risk in cryptorchidism in this study. In conclusion, our results indicate that cryptorchidism alone or in addition to age will significantly affect the incidence and type of canine testicular tumors, and a high detection rate of testicular tumors in Maltese dogs is documented for the first time.

KEY WORDS: canine, cryptorchidism, testicular tumor.

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Primary testicular tumors are the prevailing tumor in male dogs, accounting for about 90% of all tumors affecting the male genitalia [1, 6, 20]. According to the World Health Organization (WHO) classification of tumors of domestic animals, the major types of testicular tumor in dogs are sex-cord stromal tumors, germ cell tumors, and mixed germ cell sex-cord stromal tumors [9]. The most common types of testicular tumors in dogs are Sertoli cell tumors (SCTs) and interstitial cell tumors (ICTs) in sex cord-stromal tumors, as well as seminomas (SEMs) in germ cell tumors [3, 10], which probably occur with approximately equal frequency [6]. Mixed germ cell-sex stromal cell tumors (MGCSTs; two or more different tumor types from germ cell or sex cord stromal cell in one testis) consist of intimately associated germ cells and Sertoli cells, but not interstitial cells [12, 19]. However, a previous study on 110 tumors from 62 tumor-affected dogs demonstrated that ICTs and SEMs share equally over 90% of testicular tumors and the prevalence of SCTs is extremely low (8%) [2]. It is rarely reported that testicular tumors arising from other cell lineages and giving raise to tumors, including hemangiomas, granulose cell tumors, teratomas, sarcomas, embryonal carcinomas, gonadoblastomas, lymphomas, and rete testis mucinous adenocarcinomas [12, 15, 19].

Several factors may influence the development of dog testicular tumors, including age, breed, cryptorchidism, and exposure to environmental carcinogens. One study com-

pared the incidence of testicular tumors in cryptorchid and normal dogs. Cryptorchid testes were approximately 13.6 times more likely to develop a tumor than scrotal testes [6]. Thirty years later, a similar result at 14.3 times the previous rate was reported from a study of 308 stray dogs [11]. The occurrence rate of SCTs and SEMs in the cryptorchid testis of dogs was much higher than in scrotal testis [16]. Another study demonstrated that cryptorchid dogs older than 10 years were more likely to develop tumors than younger dogs under 6 years [17]. Certain breeds seemed to have an increased risk of developing primary testicular tumors, including the Boxer, German Shepherd, Afghan Hound, Weimaraner, and Shetland Sheepdog [2, 10, 14, 16, 21]. Epidemiological studies on military working dogs serving in the Vietnam War implied that exposure to phenoxy herbicide, dioxin, or tetracycline may have promoted the development of testicular tumors [4, 5].

To provide up-to-date information on incidence and risk factors in canine testicular tumors, past 12 years pathological reports diagnosed by routine pathology service from two veterinary medicine research institutes in Taiwan were collected and reviewed. The result of this study also represented the first epidemiological analysis of canine testicular tumors in Taiwan.

MATERIALS AND METHODS

Samples: The dogs in this study were admitted for routine castration or for orchiectomy because of cryptorchidism or an obvious testicular tumor. The tissues collected from National Taiwan University Veterinary Hospital and numerous private clinics around Taiwan were fixed in 10% neutral

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Table 1. Testicular tumors identified in 80 dogs

Tumor type	Left side	Right side	Unknown	Total	%
All Testes (80 dogs)					
SEM	6	20	7	33	34.4%
ICT	13	9	3	25	26.0%
MGCSCCT	7	14	1	22	22.9%
SCT	5	7	4	16	16.6%
Total	31	50	15	96	
Cryptorchid Testes (45 dogs)					
SEM	2	15	2	19	36.5%
MGCSCCT	5	11	0	16	30.7%
SCT	4	6	1	11	21.3%
ICT	5	1	0	6	11.5%
Total	16	33	3	52	
Scrotal Testes (35 dogs)					
ICT	8	8	3	19	43.2%
SEM	4	5	5	14	31.8%
MGCSCCT	2	3	1	6	13.6%
SCT	1	1	3	5	11.4%
Total	15	17	12	44	

ICT: Interstitial cell tumor; SEM: Seminoma; SCT: Sertoli cell tumor; MGCSCCT: Mixed germ cell-sex cord stromal cell tumor.

buffered formalin. The fixed tissues were then submitted to either Division of Animal Medicine, Animal Technology Institute Taiwan (from 1997 to July 1999) or Department of Veterinary Medicine, School of Veterinary Medicine, National Taiwan University (each April, August, and December, from Aug. 1999 to the Aug. of 2008) for pathologic evaluation. Representative samples from each tissue submitted were dehydrated in alcohol, clarified in xylene, and embedded in paraffin. Sections were taken and stained with hematoxylin and eosin (HE) for routine histological examination. Tumors were classified according to the latest histological classification of tumors of the genital system of domestic animals from the WHO.

Statistics: The *t*-test was used to evaluate the relationship between cryptorchidism and tumor type, and the Chi-square test was used to evaluate between age and tumor type or tumor development. The relationship between cryptorchidism and tumor development or type in different age groups was also evaluated using Chi-square. The level of significance used was $p < 0.05$.

RESULTS

Detection rate of testicular tumors: Over the past 12 years, 1706 submitted canine tissues were reviewed in this study and 476 samples from male dogs were pathologically diagnosed with various tumors. Of 476 tumor samples, 80 cases were located in either unilateral or bilateral testes. The detection rate of testicular tumors was 16.8% (80/476) in all male tumors and 94.11% (80/85) in male genital tumors. Since dogs frequently had more than one testis sub-

Table 2. Neoplastic cells identified in the 22 mixed germ cell-sex cord stromal cell tumors

Tumor type	Left side	Right side	Unknown	Total
MGCSCCT				
-SCT/SEM	4	8	0	12
-SEM/ICT	1	3	1	5
-SCT/ICT	1	3	0	4
-SCT/SEM/ICT	1	0	0	1
Total	7	14	1	22

ICT: Interstitial cell tumor; SEM: Seminoma; SCT: Sertoli cell tumor; MGCSCCT: Mixed germ cell-sex cord stromal cell tumor.

mitted, 96 testicular tumors from 80 dogs were identified in this study. They were 33 (34.4%) SEMs, 25 (26%) ICTs, 22 (22.9%) MGCSCCTs, and 16 (16.6%) SCTs. (Table 1) Of 22 MGCSCCTs, the SCT-SEM combination was diagnosed in 12 tissue samples, five tissue samples had both SEM and ICT, four tissue samples had a SCT-ICT combination, and one tissue sample had all three tumor types (ICT, SEM, & SCT) (Table 2). SCTs (16.6%) were infrequently identified in single type testicular tumors, while they appeared in over 70% (17/22) of MGCSCCTs.

Cryptorchidism and testicular tumors: In our study, 52 of 96 testicular tumors (54.2%) developed from cryptorchid testes in 45 dogs (Table 1). SEMs (19) plus MGCSCCTs (16) accounted for 67.2% (35/52) of cryptorchid testicular tumors, while ICTs (19) and SEMs (14) were specified in 75% (33/44) of scrotal testicular tumors. Most of the cryptorchid testicular tumors were MGCSCCTs (16/52), SCTs (11/52), and SEMs (19/52), while ICTs were rarely identi-

Table 3. The percentage of testicular tumors developed from cryptorchid over total testicular tumors in each tumor type

Tumor Type	Scrotal	Cryptorchid				
		Ab	In	Un	Sub	% of tumors
MGCST (22)	6	6	9	1	16	72.7%
SCT (16)	5	1	9	1	11	68.8%
SEM (33)	14	4	13	2	19	57.6%
ICT (25)	19	0	4	2	6	24.0%
Total (96)	44	11	35	6	52	54.2%

Ab: Abdominal, In: Inguinal, Un: Unknown, Sub: Subtotal.

Table 4. Age distribution of tumor type in 93 testicular tumors from 78 dogs

Age	ICT	SEM	SCT	MGCST	Subtotal
Young (< 6yrs)	1	1	3	2	7
Middle (6 - 10yrs)	8	19	7	9	43
Older (> 10yrs)	16	13	3	11	43
Total	25	33	13	22	93

The age information was not available on 3 testicular tumors from 2 dogs.

Table 5. Age distribution of testicular tumors developed from either scrotal or cryptorchid testes

Age	Scrotal testes		Cryptorchid testes				
	Sum	Group %	Ab	In	Un	Sub	Group %
Young (< 6yrs)	3	7.1% (3/42)	2	2	0	4	7.8% (4/51)
Middle (6 - 10yrs)	15	35.7% (15/42)	9	15	4	28	55% (28/51)
Older (> 10yrs)	24	57.2% (24/42)	0	17	2	19	37.2% (19/51)
Total	42		11	34	6	51	

The age information was not available on 3 testicular tumors from 2 dogs.

Ab: Abdominal, In: Inguinal, Un: Unknown, Sub: Subtotal.

fied in cryptorchidism ($p < 0.01$). ICTs (19/44) and SEMs (14/44) were the most common tumor types identified in scrotal testes (Table 3). Of 52 tumors developed from cryptorchid testes, 11 tumors developed from abdominal cryptorchidism, 35 tumors developed from inguinal cryptorchidism, and the information for the rest of the tumors was unavailable. Most of the testicular tumors developed from abdominal cryptorchidism were SEMs (4/11) and MGCSTs (6/11).

Age and testicular tumors: In this study, age information was available for 78 dogs with 93 testicular tumors, and the age distribution is listed in Table 4. Dogs ranged in age from 3 to 16 years old with a mean age of 10.1 years old and were divided into three age groups, young (< 6 years old), middle (from 6 to 10 years old), and older (>10 years old). Most of the testicular tumors were identified in middle (43/96) or older (43/96) aged dogs, and testicular tumors were rarely reported before the age of six years old (7/96) (Table 4). Most of the testicular tumors developed during middle age were SEMs (19/43), while ICTs (16/43), SEMs (13/43), and MGCSTs (11/43) were reported frequently in older age. However, there is no significant correlation between age and tumor development or type. We also evaluated the relationship between cryptorchidism and tumor develop-

ment or type in different age groups (Table 5). The detection rate of testicular tumors in dogs younger than 10 years old was significantly associated with cryptorchidism ($p < 0.01$). There was no significant association between cryptorchidism and tumor development or type in dogs older than 10 years old, and over 60% of the cryptorchid testicular tumors were identified earlier, during young or middle age ($p < 0.01$). Interestingly, all of the testicular tumors developed from abdominal cryptorchid testes were reported within young or middle age (younger than 10 years old) dogs, and none of them was observed in the older age group.

Other factors may affect the development of testicular tumors: In addition to the cryptorchidism and age, dog breed and testicular position might also affect the development of testicular tumors. The location information of the affected testis was available on 81 of 96 testicular tumors. Of 81 testicular tumors, 50 developed on the right side, and 31 developed on the left side (31) (Table 1). The detection rate of testicular tumors developed from both sides of the scrotal testes was about same (15 versus 17), whereas the detection rate of testicular tumors developed from the right cryptorchid testes (33) was twice that of tumors developed from the left side (16). Testes located in right cryptorchidism seemed to have increased risk of developing tumors than the

Table 6. Breeds association with testicular tumors in this study

Breeds	Dogs	Cryptorchid	Scrotal
Mongrel	25	12	13
Maltese	13	8	5
Poodle	6	4	2
Shihtzu	6	3	3
Pomeranian	6	3	3
YT	5	4	1
Others	19	11	8
Total	80	45	35

YT: Yorkshire Terrier; Others including Old England Sheepdog(3), Schnauzer (3), Chihuahua (2), German Shepherd Dog (2), Bichon (1), Golden Retriever (1), Dalmatian (1), Labrador Retriever (1), Husky (1), Mastiff (1) and no data (3).

testes located in any other place. Additionally, breed information was available on 77 of 80 dogs in Table 6. Except for 25 mongrel dogs, the Maltese (17 tumors from 13 dogs) breed had the highest prevalence of testicular tumors in this study, following the Poodle (6), Shihtzu (6), Pomeranian (6), and Yorkshire Terrier (5). Moreover, cryptorchid testes (8/13) in the Maltese seemed more prone to developing a testicular tumor than scrotal testes (5/13).

DISCUSSION

ICTs, SEMs, and SCTs were the most common tumor types observed in canine testicular tumors. These were equally represented in the earlier retrospective study of testicular tumors collected from databases of university hospitals and clinics [6]. Similar results were presented in the present study with slightly higher values of SEMs and lower values for SCTs. Interestingly, most of SEMs and SCTs were specified before the age of 10 years old, while over 60% of ICTs were identified in the older ages with tumor appearance. In addition, ICTs were the most common tumors (> 50%) identified in clinically normal testes (no signs of testicular tumor, feminization, or cryptorchidism) in the earlier reports [2, 10]. This implies that the tumorigenesis of ICTs may appear more slowly than other tumor types, and will therefore not be identified until tumors have grown large enough to draw attention during older age.

Cryptorchidism had been reported as a definitive risk factor for primary testicular tumors [16, 17] and this was reconfirmed in the present study. In comparison with scrotal testicular tumors, cryptorchid testicular tumors in this study were most likely to be identified in middle and young ages. Particularly, all of the testicular tumors developed from abdominal cryptorchidism were identified before the age of 10 years old. This means that cryptorchidism may contribute to and/or speed up the tumorigenesis of testicular tumors. Heat shock protein 70, superoxide dismutase, and inhibin- α are thought to affect the tumor cell proliferation in canine cryptorchid testes [8]. Future work on those factors may clarify the effect of age and cryptorchidism on tumorigenesis of testicular tumors.

Several breeds had been reported to have an increased risk of developing primary testicular tumors, including the Boxer, Afghan Hound, German Shepherd, and Shetland Sheepdog [10, 16, 21], which are all large breed dogs. In Taiwan, most residents live in a city and their companion animals are small or toy size. Numerous small or toy size breeds were mentioned as high risk in regards to cryptorchid testes, including the Miniature, Toy and Standard Poodles, Chihuahua, Yorkshire Terrier, and Miniature Schnauzer [7, 13, 17]. Moreover, since cryptorchidism is associated with testicular tumors, these small size dogs should be at high risk for testicular tumors [17]. Surprisingly, our study indicated that Maltese dogs, in addition to mongrels, have a high risk of developing testicular tumors from either cryptorchid or scrotal testes (Table 6). They also have similar detection rate of cryptorchidism to most of small breed mentioned above, therefore Maltese may have high risk for cryptorchidism, too. This is the first time that the Maltese breed was mentioned as high risk for development of testicular tumors. According to a non-official report from Taipei Pets Appliances Association in 2006, the Maltese is the second most popular dog in Taiwan (the Toy Poodle is most popular breed, rest of them is Dachshund, Chihuahua, YT, Pomeranian, Shiba, Shihtzu, and Beagle). This fact might explain why Maltese have such a high detection rate of testicular tumors in the present study.

In conclusion, the distribution of tumor types in our retrospective study is similar to previous reports. The risk factors of cryptorchidism alone or plus age were identified as affecting the development of testicular tumors. A high detection rate of testicular tumors was also identified in Maltese dogs.

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