

INCIDENCE OF CANINE NEOPLASMS - A RETROSPECTIVE HISTOPATHOLOGICAL STUDY.

I. MAMMARY NEOPLASMS IN THE BITCH

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Summary

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A histopathological study on 124 samples of mammary neoplastic material collected from bitches within the period 1991–2000 was performed at the Faculty of Veterinary Medicine, Stara Zagora. The tumours were classified according to the World Health Organization Classification (1974).

According to the histogenesis, the tumours were divided into three principal groups: epithelial (20.15 % benign and 32.26% malignant), mesenchymal (4.86 % benign and 12.14% malignant) and mixed (12.09% benign and 14.50% malignant). The ratio of malignant and benign tumours was 62.9:37.1. The average age when mammary tumours were detected was 8.55 years and the most predisposed breed were Bolognese dogs (20.16% of all cases).

Key words: bitch, incidence of mammary tumours, mammary tumours

INTRODUCTION

Mammary neoplasms are among the commonest tumours encountered in the bitch. According to Lagadic and Cohn-Bendit (1995) their incidence was 25–50% from all neoplasms and the annual incidence rate – 198.8–203.4 per 100 000 dogs. The incidence reported by Tsvetkov (1998) was 40.9%. One percent of mammary neoplasms were encountered in male dogs (Rostami et al., 1994; Tsvetkov, 1998).

The mean age of dogs with histologically diagnosed mammary tumours was 8–10 years (Priester, 1979; Bastianello, 1983; Boidizsar et al., 1992). The cases at an age younger than 2 years are rare (Warner, 1976). It is considered that the incidence was lower under the age of 5–7

years and in older animals (14–15 years) (Moulton et al., 1970; Taylor et al., 1976). Recently, a tendency towards progressive increase in malignant tumour incidence on the account of benign ones was noticed, as well as towards a relatively younger age of dogs affected by benign neoplasms (Perez Alenza et al., 1998; 2000; Benjamin et al., 1999; Gourley, 2000).

The results of studies performed in different countries vary considerably with regard to the breed predisposition. Some authors reported a predisposition in Pointers, English and Irish Setters, Labradors, Foxterriers, Bologneses and Cockers (MacVean et al., 1978; Else and Hannant, 1979). According to others however, small canine breeds as Dachshunds, York-

shire Terriers, Pintchers, Bologneses were more susceptible (Schneider et al., 1969; Sartin et al., 1992, 1995; Selman et al., 1994). Tsvetkov (1998) observed the highest predisposition towards malignant epithelial tumours in Poodles, while benign neoplasms were more frequent in Bologneses and mixed neoplasms – in German Shepherds. The opinion that purebred dogs were more predisposed towards mammary neoplasms compared to crossbreeds prevails (Taylor et al., 1976; Sonnenschein et al., 1991; Lagadic and Cohn-Bendit, 1995).

The origin of the most commonly encountered mammary neoplasms is epithelial. Then followed mixed mesenchymal-epithelial mammary tumours and at the end, those with mesenchymal origin, both benign and malignant (Bastianelo, 1983; Helmen et al., 1993; Rostami et al., 1994).

Numerous studies have shown that the metastases of those tumours in dogs exhibit most frequently a pulmonary (60-80%) followed by the subcutaneous tissue and the regional lymph nodes distribution (Braund et al., 1987; Ogilvie et al., 1989).

The development and the aggressiveness of mammary tumours could be predicted via clinical prognostic criteria but the histological ones are the most reliable (Helmen et al., 1993; Yamagami et al., 1996b; Gourley, 2000). Such studies in Bulgaria have been performed only on the territory of Sofia and the Sofia district (Zhelev et al., 1996; Tsvetkov, 1998). The present study was carried out to determine the age- and breed-related type and incidence of mammary neoplasms in bitches using histopathological methods and the samples of tumour material referred for analysis at the Trakia University – Stara Zagora in 1991-2000, aiming to use the data as prognostic criteria in the diagnostics of tumours.

MATERIALS AND METHODS

The studies were performed in 1991-2000 at the Department of General and Clinical Animal Pathology, Faculty of Veterinary Medicine, Trakia University – Stara Zagora. A total of 468 samples of spontaneous neoplastic growths in dogs originating from all over the country were studied. The material was collected via biopsy, excision or necropsy (commonly following euthanasia). The histological samples were fixed in 10% neutral formaldehyde and processed by routine histological techniques. The cross-sections were stained with hematoxylin-eosin (H/E). Histologically, mammary neoplasms were determined according to the criteria for World Health Organization Classification (Hampe and Misdorp, 1974).

RESULTS

The tumour growths of the mammary gland (124 cases or 26.5%) were dominating among all 468 studied spontaneous neoplastic growths in dogs. The number of samples referred for analysis along the years showed a tendency towards gradual increase in mammary neoplasms incidence during the period of the study (Fig. 1). The cases in bitches originating from South-eastern Bulgaria were the most common (about 70%).

Table 1 presents the data for mammary tumour incidence depending on the breed of the host and the mean age at which the tumour was detected. The highest percentage of detected tumours was encountered in Bologneses (20.16%), followed by German Shepherds (9.7%) and Dobermans (8.87%). A predisposition towards development of mammary neoplasms was observed in Cocker Spaniels (4.83%), Boxers (4.03%), Dachshunds, Pekigneses, Poodles and Rottweilers

(3.22% each). A relatively rare prevalence was found out in frequently encountered breeds as Pintschers (1.61%) and Setters (1.61%).

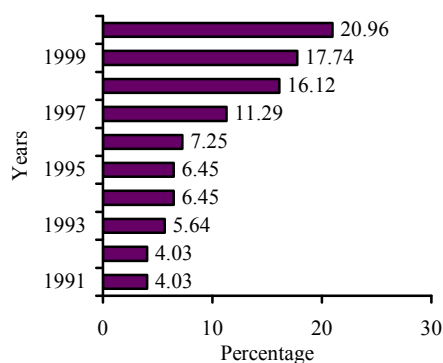


Fig. 1. Percentage of canine mammary neoplastic samples, referred for histological analysis at the Trakia University – Stara Zagora in the period 1991-2000.

The mean age of dogs with diagnosed mammary tumours was 8.55 and it varied from 5.75 years in Kurzhaars to 14 years

in Pintschers. The mean age in the most commonly affected breeds - Bolognese, German Shepherd and Doberman was 9.2; 9 and 7.4 years respectively (Table 1).

A tumour or a tumour-like growth in the mammary gland of male dogs was not observed during the period of the study.

The incidence of neoplastic types depending on the histological diagnosis is given in Table 2. The malignant growths dominated with 62.9% while the overall percentage of benign neoplasms was 37.1%. In both malignant and benign tumours, the mixed mammary tumours were the commonest (14.5% and 12.09% respectively). The malignant mixed tumours consisted 33.3% of mammary neoplasms in Bologneses, 22.2% of those in German Shepherds and mixed-breed dogs and 5.5% in the other breeds. The benign variant was encountered in 26% of affected Bologneses and mixed-breed bitches, 13.3% of Dachshunds and Pekigneses and 6.6% in the other breeds.

The second position of tumour inci-

Table 1. Incidence of mammary neoplasms in bitches depending on the breed and age

No.	Breed	Average age, years	Bitches with mammary neoplasms	
			Number	Percentage
1	Boxer	9.20	5	4.03
2	Bolognese	9.20	25	20.16
3	Dackel	9.00	4	3.22
4	Doberman	7.40	11	8.87
5	Cocker Spaniel	8.20	6	4.83
6	Kurzhaar	5.75	2	1.61
7	German Shepherd	9.00	12	9.74
8	Pekignese	9.00	4	3.22
9	Pintcher	14.00	2	1.61
10	Pointer	6.00	1	0.80
11	Poodle	10.00	4	3.22
12	Rottweiler	6.50	4	3.22
13	Setter	7.00	2	1.61
14	Fox Terrier	9.00	1	0.80
15	Mixed-breed	9.10	41	33.06
	Total	8.55	124	100.00

Table 2. Incidence of mammary neoplasms in bitches according to the histological diagnosis

Origin	Histological diagnosis	Neoplasms	
		Number	Percentage
Benign or benign-like neoplasms			
Epithelial (20.15 %)	Adenoma	9	7.25
	Cystadenoma	11	8.87
	Fibroadenoma	5	4.03
Mesenchymal (4.86%)	Fibroma	1	0.80
	Myxoma	2	1.61
	Osteochondroma	3	2.45
Mixed (12.09%)	Mixed benign mammary neoplasm	15	12.09
Total of benign neoplasms		46	37.10
Malignant neoplasms			
Epithelial (36.26 %)	Adenocarcinoma		
	- tubular	12	9.67
	- papillary	8	6.45
	- papillary cystic	12	9.67
	Solid carcinoma	4	3.22
	Squamous cell carcinoma	9	7.25
Mesenchymal (12.14%)	Fibrosarcoma	4	3.22
	Liposarcoma	4	3.22
	Leiomyosarcoma	1	0.80
	Chondrosarcoma	3	2.45
	Myxosarcoma	3	2.45
Mixed (14.50%)	Malignant mixed mammary neoplasm – carcinosarcoma	18	14.50
Total of malignant neoplasms		78	62.90
Total of observed neoplasms		124	100.00

dence was that of the epithelial type. The commonest malignant growths were tubular and papillary cystic adenocarcinomas (9.67% each) followed by squamous cell carcinomas (7.25%) and solid carcinomas (3.22%). The incidence of adenocarcinomas in Bologneses was 31.25%, in Dobermans, Cocker Spaniels and Poodles – 12.5% and in the other breeds including mixed-breed bitches – 6.25%. The benign epithelial tumours were represented by cystadenomas (8.89%), adenomas

(7.25%) and fibroadenomas (4.03%).

The mammary tumours from a mesenchymal origin were relatively rarely found out. The highest percentages among malignant mesenchymal neoplasms was those of fibrosarcomas and liposarcomas (3.22%), followed by chondrosarcomas and myxosarcomas (2.45%) and a single case of leiomyosarcoma (0.8%). Fibrosarcomas were observed in Boxers, Rottweilers and Kurzhaars. Liposarcomas and myxosarcomas were diagnosed as single

cases in a Bolognese, a German Shepherd and a Pointer. Benign mesenchymal tumours were represented by osteochondromas (2.45%), myxomas (1.61%) and fibroma (0.8%).

The localisation of neoplasms in 75% of cases was in IV (abdominal posterior) and V (inguinal) mammary complexes, with almost equal location on the left and on the right side. In 14% of cases the neoplasms were found out in left II (thoracic posterior) and III (abdominal anterior) mammary complexes and in 7% - in the corresponding right ones. Generalized neoplastic growths affecting almost all mammary complexes were observed in about 3% of all cases.

Macroscopically, both benign and malignant neoplasms affected a single or multiple mammary complexes at a time. Their size was various – from 2-3 mm to 1– 10-15 cm in diameter. In some cases they were observed like mobile, confined nodes with a various density. In others, they appeared as irregular masses with various size and restrained motility (Fig. 2). Sometimes, the neoplasms were pendulating. In larger tumours, the upper skin was frequently ulcerated because of mechanical irritation. The colour of the

cross-section varied from greyish-white to cream or reddish-brown. Often, tumour growths were embraced by necrotic foci with various size with haemorrhages within. Their cross-section was with a various density. In some neoplasms there were cystic lacunae filled with fluid and in others – dense areas containing cartilage or bone (Fig. 3). In 30% of bitches with benign and 45% of patients with malignant tumours, a different degree of inguinal lymph node enlargement was seen.

Histologically, benign mammary tumours showed the characteristic structural features according to the histological type. The histostructure of the most commonly encountered mixed benign mammary tumours varied greatly, but their features were usually more or less uniform. Those tumours were always limited, surrounded by a thin fibrous capsule and with parenchyma consisting from both epithelial and mesenchymal elements, usually well differentiated. The epithelial component was composed by glandular structures lined by a single layer of cubic epithelial cells, occasionally containing an eosinophilic discharge. The mesenchymal component was usually myxomatous tissue, in fewer cases cartilaginous and osseous tissues



Fig. 2. Mixed benign mammary neoplasm of the 5th inguinal right mammary complex in an 10-year-old female Cocker Spaniel.



Fig. 3. Cystic lacunae and necrotic foci on the cross section of adenocarcinoma from the cystic papilliferous type in an 11-year old female Bolognese.

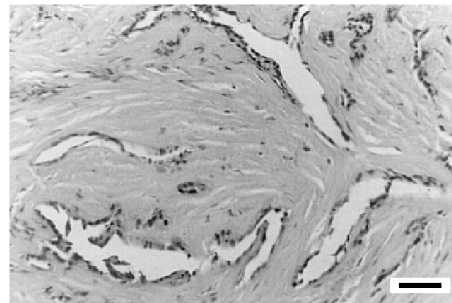
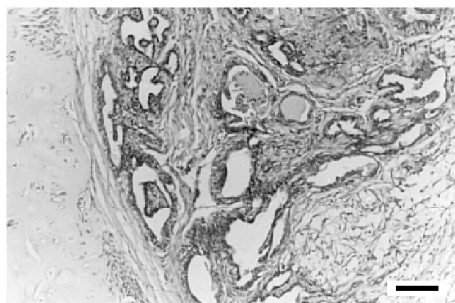


Fig. 5. Fibroadenoma in an 11-years-old female Dachshund, H/E, bar $\approx 4 \mu\text{m}$.

with a various degree of differentiation (Fig. 4). They were generally detected as foci – the myxomatous and cartilaginous tissue being most frequently well capsulated by fibrous tissue. In single cases (2.45%), the mesenchymal components were predominating among the parenchyma and epithelial ones could be found only as single acini.

All other benign neoplasms – adenomas, fibroadenomas, fibromas, myxomas, osteochondromas – showed the characteristic features for the respective histological type (Fig. 5).

Malignant neoplasms were mainly malignant mixed mammary neoplasms – carcinosarcomas. Their parenchyma was composed of epithelial and mesenchymal component with various ratio. In all cases, the epithelial components, forming tubular or acinous structures dominated, but foci of squamous cell formations (cancroid) could also be observed (Fig. 6). The mesenchymal component was tending to differentiate into fibro-, myxosarcomatous or chondrosarcomatous elements, but most commonly, areas of fibroblast-like cell dominated. Among those cells, collagen fibres forming bundles were sometimes found out. Cysts with a various size filled

with acidophil secretion and lined by single-layer epithelium were occasionally seen. The parenchyma was frequently embraced by miscellaneous degrees of haemorrhages and necroses. Despite the positive signs of malignancy in the individual neoplasms, the parenchyma was separated from the surrounding tissue by a fibrous capsule.

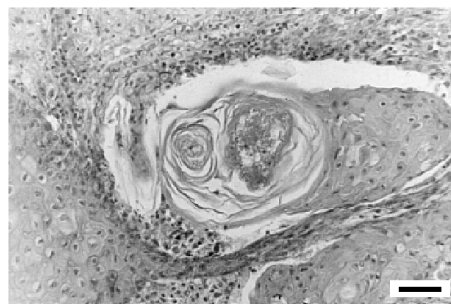


Fig. 6. Component of a squamous-cell tumour (cancroid) among the parenchyma of a mixed malignant mammary tumour in a 9-years-old female German Shepherd, H/E, bar $\approx 4 \mu\text{m}$.

In 4 cases (22.2%), after the operative excision of a mixed malignant mammary tumour (carcinosarcoma), we observed recurrences in adjacent mammary complexes within 6-10 months. In 7 cases

(8.97%) the primary tumour was accompanied by metastases in the lungs and the regional lymph nodes. The recurrences and the metastases usually showed the structure of a low-differentiated sarcoma.

The second place among malignant neoplasms belonged to adenocarcinomas. Histologically, the papillary cystic and tubular types dominated (12 cases each or 9.67%) followed by the papillary type (8 cases, 6.45%). The papillary tumours showed the characteristic parenchymal prominences towards the lumen, lined by multilayer epithelium and containing eosinophilic secretion. The parenchyma of tubular adenocarcinomas was composed by epithelial cells with various size. Some tubules were covered by one or several rows of cells and the lumen of other tubules was filled by grown epithelium.

The adenocarcinomas were accompanied by metastases in 8 bitches (10.25%). In 7 animals they were pulmonary and in single cases – the lungs, kidneys and the axillary lymph nodes were simultaneously affected. Pulmonary metastases in papillary cystic adenocarcinomas and papillary adenocarcinomas were observed in 7 (8.97%) and 4 (5.12%) dogs respectively.

The other malignant neoplasms of epithelial origin that were encountered were squamous cell and solid carcinomas while those of mesenchymal origin – fibro-, lipo-, myxo- and leiomyosarcomas. Their growth was characterized by infiltration and their histological appearance was classical. Metastases of one fibrosarcoma and one liposarcoma were observed in the inguinal lymph nodes.

DISCUSSION

The results of our studies within 1991–2000 showed a considerable increase in the number of mammary tumours since

1996 with peaks in 1998 and 1999. Those data are in accordance with the existing tendency towards progressive increase in this neoplastic kind in the bitch and the neoplastic incidence in general (Benjamin et al., 1999; Perez Alenza et al., 2000; Restucci et al., 2000). The prevalence of malignant tumours, observed in our study (62.9% vs 37.1% benign) also correlates with the tendency towards a progressive increase in the number of malignant tumours during the last years.

The highest incidence of both malignant and benign neoplasms was observed in mixed-breed dogs. Then followed the pure-bred dogs from the breeds Bolognese (20.16%), German Shepherd (9.74%) and Doberman (8.87%). The results of other investigators are various, showing that separate breeds are predisposed to mammary tumours. According to Tsvetkov (1998) Poodles are predisposed to malignant epithelial tumours (54.5%), Bolognese – to formation of benign epithelial tumours (46.6%), and the German Shepherd - mixed malignant tumours (carcinomas) – 37%. According to some authors (Schneider et al., 1969; Selman et al., 1994; Sartin et al., 1995; Lagadic and Cohn-Bendit, 1995) small canine breeds as Dachshund, Yorkshire Terrier, Pintscher, Bolognese) are more susceptible but others reported a higher susceptibility in larger breeds as Pointer, Setter as well as in some smaller races like Foxterriers, Cockers and Bolognese (MacVean et al., 1978; Else and Hannant, 1979).

Thus, the existence of any breed predisposition to mammary neoplasms could hardly be established. According to Selman et al. (1994) and Yamagami et al. (1996a), the frequent hormonal treatment in smaller breeds could be involved, but we cannot support this statement because we are lacking such data. The incidence

could be however related to the predominating breed in a given region (Taylor et al., 1976; Priester, 1979; Boidizar et al., 1992). The prevalence of cases from South-eastern Bulgaria could be explained by the location of the Trakia University that enables the performance of histological studies. In our cases we observed increased percentage of malignant tumours with a type similar to those encountered at the territory of the Sofia district (Zhelev et al., 1966; Tzvetkov, 1998).

The mean age of the host and the location of mammary growths evidenced a highest incidence in dogs at the age of 8-10 years (8.55 years). Our data are very similar to most of the reported ones (Bastianello, 1983; Boidizar et al., 1992; Tzvetkov, 1998). In 75% of our cases the tumours affected the IV and V caudal mammary complexes. The anatomical topographic location of neoplasms is similar to that observed by Moulton et al., (1970), Priester (1977), Schafer et al. (1998). We accept the suggestions of Sonnenschein et al. (1991) and Tzvetkov (1998) that the more frequent traumatism in this area could be predisposing to a neoplastic transformation.

The high incidence of mixed mammary tumours with malignant (14.5%) and benign (12.09%) character and the dynamics of spreading of those neoplastic types during the period of the study permits to conclude that there is a tendency towards increase in the percentage of malignant growths. Our results correspond with those of other authors (Zhelev 1969; MacVean et al., 1978; Priester, 1979; Bastianello, 1983). Zhelev et al. (1969) reported a 6% incidence of benign tumours, Lagadic and Cohn-Bendit (1995) – 21% benign and 10% malignant mixed tumours and Tzvetkov (1998) – 20.93% carcinomas. The significant difference in

the ratio between benign and malignant mixed tumours is most probably related to the problematic definition of objective criteria for determination of the benign character of a mammary tumour (Lagadic and Cohn-Bendit, 1995).

Our results, as those of many authors show that lungs are a predilection site for mammary neoplasms (33.3%) followed by inguinal lymph nodes (16.6%) (Braund et al., 1987; Ogilvie et al., 1989). Many studies revealed that from a clinical point of view malignancy is associated with recurrence and metastases (Taylor et al., 1976; Braund et al., 1987). According to Helmen et al. (1993), there are relapses in 25% of dogs with carcinosarcoma within 2 years following mastectomy.

The analysis of our results confirms the importance of the histological study for both mammary neoplasms diagnosis and prognosis (Helmen et al., 1993; Yamagami et al., 1996b; Gourley, 2000; Perez Alenza et al., 2000).

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