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Clinico-pathological Studies on Canine Mammary Tumors in Dachshund Dog

Anindita Sarkar[1], Kalyani Ray[1], Siddhartha Basu[1], Ajeet Kumar Jha[2], Anirban Mandal[3], Durgadas Mandal[1], Pradip Sarkar[1], Keshav Kumar[1], Sanjoy Datta[4]

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ABSTRACT

Background: The study was aimed to find out the epidemiological data of canine mammary tumor in Dachshund breed in relation to age, growth rate, lymph node status, histological type of tumor and to compare hematological alterations of any within the tumor to compare hematological alterations due to different types of tumor.

Methods: Mammary neoplasms were clinically evaluated. The measurement of total erythrocyte count (TEC), total leukocyte count (TLC), platelet count and packed cell volume (PCV %) was carried out as per standard methods. Histological observation was performed by staining with Hematoxylin and Eosin stain. Benign and malignant mammary tumors were found highest in the younger age group of 8 to 12 years and lowest thereafter.

Result: 79.16% cases of the mammary tumors located in the inguinal region were found. The fast growth rate was observed in 45.83% of tumors. The hematological profile showed no difference. However, the platelet count in the malignant mammary gland tumor dogs showed significant ($P<0.01$) decrease than the normal and benign tumor dogs. Distant metastasis to lung was found only in 8.33% of the total mammary tumor dogs. Mammary tumors with stage I, stage II and stage III were restricted to benign mammary tumors whereas, those with stage IV and stage V were of malignant mammary tumors.

Key words: Benign, Canine, Dachshund breed, Malignant, Mammary tumor.

INTRODUCTION

Mammary neoplasms in dogs are the second most common neoplasms after skin tumors (Rezia *et al.,* 2009; Benjamin *et al.,* 1999) occupying about 52% of all tumors (Egenvall *et al.,* 2005). Nearly 41% to 53% of the mammary tumors that occur in the bitch are malignant (Misdorp 2002). Malignant mammary tumors are most nonresponsive if the treatment is not started earliest (Shoji *et al.,* 2016). Female spayed dogs have low risk of developing mammary tumors before their first oestrus (0.5% incidence compared to intact female dogs) and between first and second oestrus this rate is 8% (Salas *et al.,* 2015). World Health Organization International classification of mammary tumor of the dogs and cat combines histogenic and descriptive morphologic classification, incorporating histologic prognostic features that have been associated with increasing malignancy (Patel *et al.,* 2019). Dog has not only a tremendous mental healing power but also the guarding ability and is also becoming one of the biggest income-generating animals (Ray *et al.,* 2019). But, there are a lot of clinical problem which affects their commercialization. A number of breeds such as Airedale terrier, Brittany spaniel, Boston terrier, Cocker spaniel, English setter, English springer spaniel, Fox terrier, German shorthaired pointer, Great pyrenees, Irish setter, Keeshond, Labrador retriever, Pointer, Dachshund, Poodle and Samoyed have already been reported to be predisposed to mammary tumor (Mitchell *et al.,* 1974; Moe, 2001). Palta (2000) reported that white spitz breed most commonly suffered from canine mammary tumours (34.10%) followed by Doberman (19.65%), German Shepherd (9.83%), non-descript (8.10%), Labrador Retriever (7.57%), Pointer (5.78%), Crossbred (5.20%), Dachshund (2.89%), Boxer (2.31%), Cocker Spaniel (1.73%) and Lhasa (1.16%). Dachshunds and Cocker Spaniels bitches had an increased risk of developing mammary tumours, while Chihuahuas had reduced risk. Beagles had a risk slightly higher than mean risk for all dog breeds (Gupta, 2012).

[1]Department of Veterinary Gynaecology and Obstetrics, West Bengal University of Animal and Fishery Sciences, Belgachia-700 037, Kolkota, West Bengal, India.

[2]Regional Agricultural Research Station, NARC, Parwanipur, Bara, Nepal.

[3]Department of Microbiology, Mrinalini Datta Mahavidyapith, Birati-700 051, Kolkata, West Bengal, India.

[4]Department of Animal Genetics and Breeding, West Bengal University of Animal and Fishery Sciences, Belgachia-700 037, Kolkota, West Bengal, India.

Corresponding Author: Kalyani Ray, Department of Veterinary Gynaecology and Obstetrics, West Bengal University of Animal and Fishery Sciences, Belgachia-700 037, Kolkota, West Bengal, India. Email: kalyaniray2@gmail.com

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Dachshund breed is prone to developing certain types of tumors such as mammary tumor, oral melanoma, mast cell. However, osteosarcoma, testicular tumor, bladder cancer and lymphoma are also found in Dachshund breed. Mammary gland tumor is the most common type of tumor in the dachshund breed (Moulton *et al.,* 1970). The present study was undertaken to find out the epidemiological data of canine mammary tumor in relation to age, growth rate, lymph node status, type of tumor Besides focusing on their TNM (T means the degree of the primary tumor, N is the condition of the regional lymph nodes, and M means the absence/presence of distant metastases) grading in the Dachshund breed.

MATERIALS AND METHODS

This study was performed at the Department of Veterinary Gynecology and Obstetrics, West Bengal University of Animal and Fishery Sciences, Kolkata and different clinics of Kolkata, India. During this period of study, a total of 59 cases of canine mammary neoplasm were detected and out of these 24 cases were in dachshund breed. Also, 6 normal dachshund bitches were included in this study as control animals.

Stages of tumors were classified using TNM with slight modification as descried earlier by Owen (1980). The tumor size were classified as T1 (<3 cm), T2 (3-5 cm), or T3 (>5 cm), N indicates the condition of the regional lymph nodes and M for presence of distant metastases. With this system, animal were classified into five clinical stages namely stage I, stage II, stage III, stage IV and stage V. In Stage I, II and III tumor size is ≤3 cm, 3-5 cm and ≥ 5 cm without lymph node metastasis and absence of distant metastases. Where as in stage IV tumor size varies with metastasis in lymph node present and absence of distant metstases. Stage V tumor size varies with or without lymphnode metastasis and presence of distant metastases (Gundim *et al.,* 2016).

The total erythrocyte count (TEC), total leukocyte count (TLC), platelet count and packed cell volume (PCV %) was carried out as per standard methods described by Schalm *et al.,* (1975). The hemoglobin was estimated by using photoelectric colorimeter by cyanomethemoglobin method as described by Cannan (1958).

Pre-operated mammary tumor patients were stabilized by giving balanced electrolyte fluid and vitamins. The mammary tumor patients were operated upon a combination of injectable anesthesia. The bitches were injected with Atropine Sulphate @ 0.04 mg/kg sub-cutaneously. and later Xylazine HCL @ 0.8 mg/kg was injected. Injection of Ketamine HCL @ 7 mg/kg body weight and diazepam @ 0.05 mg/kg body weight was given with Ringer's lactate drip to maintain the surgical stage of anesthesia.

Histological examination was performed by staining with H&E stains and observed under microscope according to the World Health Organizations (WHO) diagnostic criteria (Sharma *et al.,* 2018).

Data generated were analyzed using procedure described by Snedecor and Cochran (1968). Data were analyzed by using IBM SPSS version 23.0 statistical software.

RESULTS AND DISCUSSION

All animals in this study were intact. Highest number of benign and malignant mammary tumor was observed in the age group of 8 to 12 years but benign tumor was found lowest below 12 years and malignant before 8 years of age. (Table 1). The specific occurrence of mammary tumors in this study showed a trend of increasing the percentage of malignant and benign neoplasia with advancing age till 12 years and reduces thereafter. Our result also indicates that chances of malignant neoplasia is more than Benign after 12 years of age. The growing age results in the accumulation of thrombogenesis factors leading to malignant tumors (Witsch *et al.,* 2010). Findings of the study matches with those of Egenvall *et al.,* (2005), who reported that mammary tumours were extremely rare in dogs younger than five years of age and the incidence increased sharply at approximately six years of age and incidence peaked at about 8-12 years of age. Similar result was also obtained by Taylor *et al.,* (1976).

Maximum number of mammary tumors were recorded in the inguinal region (Table 2). We observed more involvement of Caudal 4th and 5th mammary glands than that of cranial glands. this result is also supported by Misdrop and Hart, (1976); Hellmén *et al.,* (1993). Multiple involvements were recorded in 5 mammary tumor patients.

Table 1: Distribution of 24 mammary tumors according to the age affected Dachshund breed.

Age	Total		Benign		Malignant	
	Number	%	Number	%	Number	%
<8 years	3	12.5	2	18.18	1	7.92
8-12 years	17	70.83	8	72.72	9	69.23
<12 years	4	16.67	1	9.09	3	23.07

Table 2: Distribution of mammary tumors (n=24) according to their location.

Location	Total		Benign		Malignant	
	Number	%	Number	%	Number	%
Thoracic	5	20.84	3	27.28	2	15.39
Inguinal	19	79.16	8	72.72	11	84.61

These findings corroborated with the earlier observation made by Moulton *et al.,* (1970). Multiple mammary gland involvement occurs possibly due to the infiltration of tumor cells to the adjacent mammary gland (Else and Hannant, 1979; Rosychuk, 1988).

Maximum benign mammary tumor showed a slow growth rate while malignant mammary tumors had a faster growth rate (Table 3). The slow growth rate in benign mammary tumors might be due to less angiogenesis in tumor mass compared to malignant tumors.

Maximum (79.16%) tumors were found >5 cm in diameter. A high percentage of large size tumors may be due to the result of the owner's improper attention for slowly growing mammary neoplasm. All the small-sized tumors were benign type and among the large-sized tumors 63.63% were benign type and 92.3% were malignant type (Table 4). Perez-Alenza and Tbarena (2001) reported that 10 to 50% of dogs with mammary tumors have an enlarged lymph node. A similar finding is also reported by Misdrop and Hart (1976).

Regional lymph node enlargement were observed in 6 out of 24 cases. All cases of regional lymph node enlargement except one were associated with malignant tumor (Table 5). Only 9.10% of benign tumors showed an enlarged lymph node presumably because of local inflammatory reactions.

Thoracic radiography revealed lung metastasis only in two dogs (8.33%) suffering malignant mammary tumors (Table 6). Cotchin (1958) reported that 10% of the histologically malignant neoplasms had distant metastasis. However, Krook (1954) found metastasis in 50% of dogs with carcinoma. This lower percentage of distant metastasis in this study might be due to early diagnosis and quick excision of tumor mass in mammary tumor patients.

Malignant mammary tumors were of clinical stage III (46.15%), 38.46% were of clinical stage IV, 15.38% patient showed stage V and 7.69% patient shows clinical stage II but no malignant of stage I was observed (Table 7). Benign tumors were hardly associated with lymph node or distant

Table 3: Distribution of mammary tumor (n=24) according to their rate of growth.

Growth rate	Total		Benign		Malignant	
	Number	%	Number	%	Number	%
Slow	8	33.33	8	72.72	0	0
Medium	5	20.84	2	18.18	3	23.08
Fast	11	45.84	1	9.10	10	76.92

Table 4: Distribution of mammary tumor (n=24) according to their size.

Tumor size	Total		Benign		Malignant	
(cm)	Number	%	Number	%	Number	%
0-3	1	4.16	1	9.10	0	0
3-5	4	16.68	3	27.27	1	7.7
>5	19	79.16	7	63.63	12	92.3

Table 5: Distribution of mammary tumors (n=24) according to lymph node involvement.

Lymph node status	Total		Benign		Malignant	
	Number	%	Number	%	Number	%
Enlarge	6	25	1	9.10	5	38.47
Normal	18	75	10	90.90	8	61.53

Table 6: Distribution of mammary tumors (n=24) according to distance metastasis.

Distant metastasis	Total		Benign		Malignant	
	Number	%	Number	%	Number	%
Present	2	8.33	0	0	2	15.38
Absent	22	91.67	11	100	11	64.61

Table 7: Distribution of mammary tumors (n=24) according to clinical stage.

Clinical stage	Total		Benign		Malignant	
	Number	%	Number	%	Number	%
Stage I	1	4.17	1	9.10	0	0
Stage II	4	16.67	3	27.27	1	7.69
Stage III	12	50	6	54.54	6	46.15
Stage IV	5	20.8	0	0	5	38.46
Stage V	2	8.33	0	0	2	15.38

metastasis, so clinical stage IV and V were not found. Contrarily in malignant tumor lymph node and distance metastasis was involved, therefore stage IV and stage V found. This finding also supported by those of Gundim *et al.* (2016). During this study more than 50% tumors were of malignant type. Varallo *et al.* (2019) reported similar findings of benign and malignant mammary gland tumors with a range from 41-53%. Benjamin *et al.,* (1999) and Sorenmo (2003) reported approximately 40-50% of canine mammary tumors are malignant. Comparatively benign mammary tumors were restricted to stage I, stage II and stage III while malignant mammary tumors were having the stages of III, stage IV and Stage V. Highest incidence of benign and malignant tumor was recorded with Stage III.

Histopathological examination (Table 8 and Fig 2 A-D) revealed that out of 24 mammary tumors, 11 (45.83%) were benign tumors and 13 were malignant tumors (54.17%). Among the benign tumors, the maximum percentage having fibroadenoma and lower percentages were with duct papilloma. Moulton *et al.* (1970) and Bostock (1975) also reported the same. In case of malignant tumors, highest percentage (38.46) of papillary adenocarcinoma and lowest percentage (7.69) of solid adenocarcinoma were observed. This finding also collaborates with Moulton *et al.* (1970) who also concluded that Benign mixed tumors comprising 45.1% consisting of an adenomatous epithelial component and proliferative fibrous connective tissue and Malignant mixed tumors accounted for only 8.5%.

Hematological analysis of 24 dachshund bitches and 6 normal bitches are presented below (Table 9). No significant change in any of the hematological parameters were observed in any of the group, Benign and malignant group as compared to normal group. However malignant group showed significant had significantly (P<0.01%) lower platelet count than the normal and benign group. The hematological findings were in contrast to our previous research which showed significant value of Hb, WBC, Eosinophil, BUN and SGOT from day 0 to day 28 during before and after treatment (Kumar *et al.,* 2020) and corroborated with the findings of Sorenmo (2003) who stated that Blood parameters are

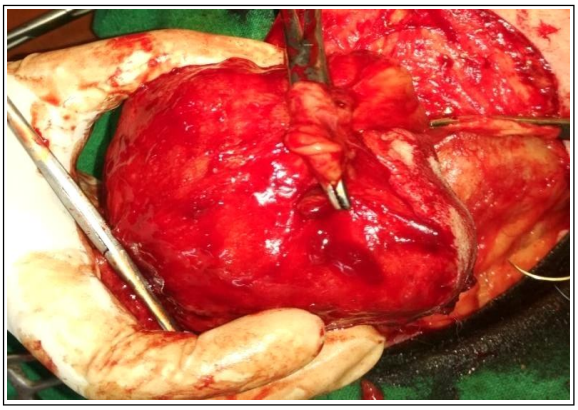

Fig 1: The gross picture of canine mammary tumor during surgical operation in Dachshund bitches.

Table 8: Distribution of mammary tumor (n=24) according to different types and classification of tumors.

Tumor type	Total		Benign		Malignant	
	No.	%	No.	%	No.	%
Benign	11	45.83				
Simple adenoma			4	36.36		
Complax adenoma			2	18.18		
Duct papilloma			1	9.10		
Fibroadenima			4	36.36		
Malignant	13	54.17				
Papillary adenocarcina					5	38.46
Tubular adenocarcinoma					5	30.71
Solid adenocaecinoma					1	7.69
Malignant mixed tumor					2	15.38

Table 9: Mean (±) SE of hematological parameter in different groups of dogs, normal (n=6) and 24 mammary tumors (n=24) patients.

Parameters	Normal (Mean±SE)	Benign (Mean±SE)	Malignant (Mean±SE)
RBC ($X10^6$ cmm)	4.80^a±0.07	4.58^a±0.08	4.54^a±0.08
WBC ($X10^3$ cmm)	11.8^a±0.61	13.50^a±0.62	14.41^a±0.69
PCV (%)	42.49^a±0.92	43.2^a±0.74	41.50^a±0.68
Hb (%)	12.60^a±0.32	13.54^a±0.34	13.05^a±0.41
Nutrophil (%)	77.90^a±1.20	77.60^a±1.50	78.05^a±1.61
Lymphocyte (%)	18.00^a±1.12	17.74^a±1.25	16.55^a±1.72
Monocyte (%)	1.3^a±0.25	1.41^a±0.15	1.23^a±0.11
Eosinophil (%)	1.80^a±0.34	3.32^a±0.64	2.29^a±0.32
Platelate ($X10^5$ cmm)	2.4^a±0.03	2.45^a±0.04	2.14^b±0.06

NB: Row-wise similar superscripts does not differ significantly (P<0.01%).

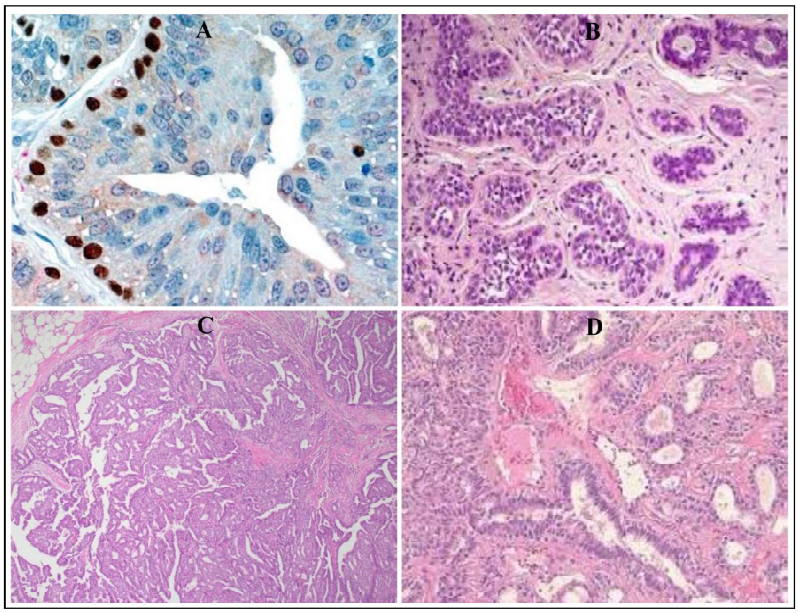

Fig 2: Histopathology of mammary gland tumor in Dachshund breed (H&E stain) A. Simple adenoma B. Fibroadenoma C. Papillary adenocarcinoma and D. Tibular adenocarcinoma.

normal in most dogs with mammary gland tumors but changes may occur in case of some other medical problems and tumoural bleeding. Perez Alenza and Tabanera (2001) reported that thrombocytopenia may be observed in some cases of malignant mammary tumors. Several factors such as polymorphism and mutation in some TFs and cytokines and effects of treatment could be associated with the incidence of thrombocytopenia in solid tumors. In spite of the importance of serious bleeding complication in solid tumors, few studies have yet analyzed the exact mechanisms of the impact of SNPs and mutation in the incidence of thrombocytopenia in solid tumors (Ghanavat *et al*., 2019).

CONCLUSION

Mammary tumors in Dachshund breeds are heterogeneous in nature. Hematological data is not significant as a prognostic factor for mammary tumor in Dachshund breed. Biochemical and Molecular study may be carried out to find the exact genetic factor if there responsible to cause the canine mammary tumour in some breeds of dog so as to draw effective breeding strategy to preclude the disease from the population.

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Author's contribution

Anindita Sarkar and Ajeet Kumar Jha conducted lab work and prepared manuscript, Kalyani Ray designed the work and guided throughout the period. Siddhartha Basu, Anirban Mandal, Durgadas Mandal, Pradip Sarkar and Sanjoy Datta guided throughout the study and analysis of result. Keshav Kumar involved during correction of manuscript. All authors read and approved the final manuscript.

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