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Clinical, morphological and diagnostic characteristics of malignant mammary tumor in bitches

Características clínicas, morfológicas e diagnósticas de tumor de mama maligno em cadelas

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ABSTRACT

Mammary tumor is the most frequent neoplasia in bitches in Brazil, and most of the mammary tumors in female dogs in the country, are malignant. This study aimed to evaluate clinical, morphological and diagnostic characteristics of malignant mammary tumors in 32 bitches. The average age of the bitches was 10.1 years, demonstrating that older bitches are more predisposed. Most bitches weren't neutered. Tumor size in most animals was greater than 5 cm. and showed rapid growth in most cases. In all bitches, no signs of metastases in the lungs were observed. The results of the cytological exams showed a mixed malignant tumor and adenocarcinoma, and about 81.5% of adenocarcinomas were confirmed by histopathological exam. It was concluded that non-castrated elderly female dogs were the majority. Malignant tumors larger than 5 cm with fast growth and firm consistency were the most frequent

Keywords: Adenocarcinoma; Canine; Mammary neoplasia; Cytology

RESUMO

O tumor de mama é a neoplasia mais frequente em cadelas no Brasil, sendo que a maior parte dos tumores mamários em cadelas no país é maligna. No presente estudo, objetivou-se avaliar características clínicas, morfológicas e diagnósticas de tumores de mama malignos em 32 cadelas. A idade média das cadelas foi de 10,1 anos, demonstrando que cadelas idosas são mais predispostas. A maioria das cadelas não eram castradas; O tamanho tumoral na maioria dos animais era maior do que 5 cm. e apresentaram crescimento rápido na maior parte dos casos. Em todas as cadelas não foram observados sinais de metástases nos pulmões. Os resultados dos exames citológicos demonstraram tumor misto maligno e adenocarcinoma, sendo que cerca de 81,5% dos adenocarcinomas foram confirmados pelo exame histopatológico. Concluiu-se que as cadelas idosas não castradas foram maioria. Os tumores malignos maiores de 5 cm com crescimento rápido e consistência firme foram os mais frequentes

PALAVRAS-CHAVE: Adenocarcinoma; Canino; Neoplasias mamárias; Citologia

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INTRODUCTION

Among the various existing areas in the clinic of dogs, the veterinary oncology has excelled in the search for improvements in health, prevention, diagnosis and treatment of neoplasias, (ANTUNES et al. 2008), since these diseases are frequent affections in dogs. A Brazilian study showed that 62% of the diagnoses of biopsies of dogs and cats, refers to neoplasias (ANDRADE et al 2012).

Mammary tumors (MT) are the most frequent neoplasias in dogs in Brazil (RIBAS et al., 2012; BIONDI et al., 2014) and most of these tumors are malignant (BIONDI et al., 2014; DIAS et al., 2016; NUNES et al., 2018; TORÍBIO et al., 2012). Approximately 90% of malignancy was detected in breast tumors of bitches in the country (BIONDI et al., 2014; NUNES et al., 2018; TORÍBIO et al., 2012).

In studies on the incidence of mammary tumors it was observed that age, overweight and not ovariohysterectomy (castration) are risk factors for the development of mammary tumors in bitches (SANTOS et a., 2020; VARMA et al., 2021). Therefore, the etiology of MT can be related to dietary, genetic, environmental, infectious and, mainly, hormonal factors (REYS et al., 2020). Thus, MT in bitches are considered hormone-dependent (KRISTIANSEN et al. 2016; SANTOS et al., 2020). Due to this, castration early is recognized as the main way to prevent the disease in bitches. In canine females already affected by the disease, but with benign tumors, castration prevents the formation of new tumors in 50% of the bitches castrated after diagnosis (KRISTIANSEN et al. 2016). These data reinforce that the hormonal exposure during the life increases the predisposition to develop MT and that castration early (before the first estrus) shows good results in the reduction of the risk of developing such tumors (KAMIGUCHI et al. 2016).

The first approach to a canine patient with mammary nodules should consist of a thorough physical examination, not only of the mammary glands, but also of general characteristics that enable the assessment of the animal's general condition. The physical examination of the breast chain should record the following aspects of the lesions: number, location, consistency and size, as well as any signs of adherence to adjacent tissues, breast deformations and skin ulceration (LANA et al., 2007).

To diagnose the disease, laboratory tests (cytology and histopathology) are used (MAGALHÃES et al., 2020). Differential diagnosis is possible through microscopic evaluation, cytology or histopathology. Differential diagnoses that should be considered in the clinical presentation of mammary nodules are: 1) malignant mammary tumors; 2)

benign mammary tumors; 3) skin and subcutaneou tumors; 4) mastitis; and 5) mammary hyperplasia or dysplasia (MISDORP et al., 1999).

The cytological examination through FNAC (fine needle aspiration cytology) is easy to apply, minimally invasive, cheap and practical. However, it must be performed with caution so as not to facilitate the infiltration and dissemination of neoplastic cells. Some authors emphasize its definitive importance only in differentiating neoplastic processes from other non-neoplastic ones, but question the effectiveness regarding the distinction between benign and malignant ones. However, many authors value the technique, demonstrating a correlation above 63% with the histopathological diagnosis through excisional biopsy or surgical specimen evaluation (CASSALI et al., 2011; MISDORP et al., 1999; SORENMO et al., 2013).

After diagnosis, an early therapeutic approach is necessary for the treatment to be effective and promote quality of life for the animals (CASSALI et al., 2020).

Regarding the malignancy of mammary neoplasia, there is variation among authors, but among Brazilian researchers all agree that most mammary tumors in female dogs in Brazil are malignant, with rates ranging from 52% to 90% (BIONDI et al., 2014; DALECK et al., 2009; OLIVEIRA et al., 2009; OLIVEIRA and PANDOLFI, 2020; TORÍBIO et al., 2012).

In canine malignant mammary tumors metastases should be investigated using imaging tests (CASSALI et al., 2020). In 25% of cases of malignant neoplasias in bitches, metastases occur at the time of diagnosis, in regional lymph nodes and, in some cases, in the lung parenchyma. Thoracic radiographic examination should be performed before any surgical indication, as metastases in the lung parenchyma and regional lymph nodes are common. However, in most patients, there are micrometastases, which are not visualized by radiographic examination (DALECK et al., 2009),

This study aimed to evaluate clinical, morphological and diagnostic characteristics of malignant mammary tumors in bitches.

MATERIAL AND METHODS

The study was approved by the Ethics and Animal Welfare Committee of the institution of origin (protocol nº 005/15).

Thirty-two bitches with cytological diagnosis of malignant mammary tumor were submitted to the study, which were submitted to mastectomy. These bitches came from

routine care at a Teaching Veterinary Hospital (TVH). For the cytological examination, three smears were performed on slides for microscopy of the material obtained through the puncture of each tumor. Subsequently, they were stained with Panotype and visualized under an optical light microscope using 40X and 100X objectives with the aid of immersion oil for determination of cytological diagnosis.

All bitches underwent clinical examination, where data such as: age, race, reproductive history (castrated or not), presence of regular or not estrus and history of contraceptive use were collected. During the physical examination of the masses, their macroscopic characteristics were analyzed according to tumor evolution (slow or fast), tumor appearance (regular or irregular), tumor consistency (firm or floating), measurement of the nodules and anatomical location of the masses.

The macroscopic aspect of each neoplasia was evaluated and the fragments collected after mastectomy were fixed in a 10% formalin solution, buffered with phosphates (pH 7.4) and routinely processed until inclusion in paraffin. 5μm sections were made in a microtome and later stained with hematoxylin and eosin. In light microscopy analysis, the neoplasia was classified according to the criteria of the World Health Organization (MISDORP et al., 1999). All bitches were submitted to chest X-rays in three positions (ventrodorsal, right lateral and left lateral), to verify the presence or not of pulmonary metastases.

RESULTS AND DISCUSSION

The age range of these bitches with malignant mammary tumor ranged from six to 14 years and the mean age was 10.1 years. Such results are similar to those found by other authors in Brazil (BIONDI et al., 2014; OLIVEIRA FILHO et al., 2010; OLIVEIRA and PANDOLFI, 2020; SILVA et al., 2014; TORÍBIO et al., 2021; TORÍBIO et al., al., 2012; VITAL et al., 2015;) and demonstrates that older bitches are more predisposed to mammary cancer (OLIVEIRA FILHO et al., 2010; SANTOS et al., 2020; VARMA et al., 2021).

Regarding breed, in the present study 56.25% (18/32) were bitches of no defined breed, 18.75% (6/32) were Poodle breed, 6.25% (2/32) were Maltese breed and 6.25% (2/32) Cocker Spaniel breed, 6.25% (2/32) Pinscher breed and 6.25% (2/32) German Shepherd breed. Other Brazilian studies have results similar to those found here (BIONDI et al., 2014; OLIVEIRA and PANDOLFI, 2020; TORÍBIO et al., 2012). There are

controversies about the fact that the poodle breed is more affected than other breeds, but some authors claim that there is no racial predisposition (CAVALCANTI and CASSALI, 2006; PELETEIRO, 1994;). However, taking into account that the results found in this study in relation to the poodle breed are similar to studies carried out in several Brazilian municipalities (BIONDI et al., 2014; OLIVEIRA FILHO et al., 2010; OLIVEIRA and PANDOLFI, 2020; RIBAS et al., 2012; SANTOS et al., 2020; TORÍBIO et al., 2012) it is likely that poodle dogs have a genetic predisposition to the development of mammary cancer (MISDORP, 2002).

Of the studied bitches, 87.5% (28/32) were not castrated, while four 12.5% bitches had a history of ovariohysterectomy (OH) (Table 1). Most bitches affected by mammary tumor are not castrated (BIONDI et al., 2014; KAMIGUCHI et al., 2016; FELICIANO et al., 2012; OLIVEIRA and PANDOLFI, 2020; RIBAS et al., 2012; SANTOS et al., 2012; SANTOS et al., 2020; TORÍBIO et al., 2012; VARMA et al., 2021), which may denote the lack of knowledge of owners about the protection provided by the early castration of females (MAGALHÃES et al., 2016). Four female dogs were neutered, but they were neutered after three years of age. This fact is in agreement with the literature that states that late castration does not reduce the risk of malignant tumors (DALECK, et al., 2009).

Tumor size is one of the most important parameters in the prognosis of mammary tumors in bitches (CASSALI et al., 2011; CAVALCANTI and CASSALI, 2006; ESTRELA-LIMA et al., 2010; MISDORP et al. 1999; PELETEIRO, 1994; TORÍBIO et al., 2012), and malignant tumors are rarely smaller than 3 cm. (DALECK et al., 2009; TORÍBIO et al., 2012). Confirming these facts, in the studied bitches, most tumors presented more than 5 cm. in diameter (62.5%; 20/32). No bitch had a tumor smaller than 3 cm. (Table 2). One of the factors that contributes to tumor size is the fact that most owners take the animal late for consultation and many are even unaware that bitches may have mammary tumors

One of the factors that contributes to tumor size is the fact that most tutors take the animal late for consultation and many are even unaware that bitches may have mammary tumors, which has already been detected in Teresina (PI, Brazil) (MAGALHÃES et al., 2016).

As to location, 50% (16/32) of the tumors were in the caudal abdominal mammary glands, 25% (8/32) in the inguinal mammary glands and 25% (8/32) in the caudal thoracic

mammary glands. The detected anatomical locations of tumor masses are similar to studies by other authors (DALECK et al., 2009; OLIVEIRA and PANDOLFI, 2020; RIBAS et al., 2012; SANTOS et al., 2020; TORÍBIO et al., 2012), and the inguinal and caudal abdominal mammary gland are more affected, because of the greater amount of mammary parenchyma, thus suffering a greater proliferative change in response to hormones (MISDORP, 2002).

Table 1. Clinical aspects of bitches with mammary tumors attended at a Teaching Veterinary Hospital (n=32).

BITCH	AGE (YEARS)	BREED	CASTRADE		TUMOR SIZE		
			YES	NO	<3 cm (S1)	Between 3 and 5 cm in diameter (S2)	Greater than 5cm of diameter (S3)
1	9	Mixed breed		X			X
2	9	Mixed breed		X			X
3	7	Mixed breed		X			X
4	10	Mixed breed		X		X	
5	14	Poodle		X		X	
6	11	Poodle		X		X	
7	7	Maltese	X			X	
8	9	Cocker spaniel		X			X
9	6	Mixed breed		X			X
10	12	Mixed breed		X			X
11	10	Poodle		X			X
12	9	Pastor		X			X
13	9	Cocker		X			X
14	9	Poodle		X			X
15	12	Mixed breed		X			X
16	12	Mixed breed	X				X
17	9	Mixed breed		X			X
18	10	Mixed breed		X			X
19	11	Pinscher		X			X
20	11	Mixed breed		X			X
21	12	Maltese		X		X	
22	7	Mixed breed		X		X	
23	8	Mixed breed		X			X
24	10	German Shepherd		X			X
25	10	Mixed breed	X				X
26	11	Mixed breed		X			X
27	13	Poodle		X			X
28	11	Pinscher		X			X
29	11	Mixed breed		X			X
30	10	Mixed breed	X				X
31	12	Mixed breed		X			X
32	12	Poodle		X			X

Média	10,1					
		Total	4	28	0	7	25

Source: The authors, 2023

Table 2. Tumor size of primary malignant neoplasms in the breast of bitches treated at a Teaching Veterinary Hospital (n=32). (S1: <3cm in diameter; S2: 3-5cm in diameter; S3: >5cm in diameter).

Primary tumor	Number	Percentage (%)
S1	0	
S2	12	37,5%
S3	20	62,5%
Total	32	100%

Source: The authors, 2023.

Table 3. Characteristics of growth and tumor consistency of bitches with malignant mammary tumor treated at a Teaching Veterinary Hospital (N=32).

BITCH	FEATURES OF GROWTH			CONSISTENCY		
	SLOW	FAST	STABLE	SOFT	FIRM	MIXED
1	x				x	
2	x				x	
3		x			x	
4		x				x
5	x					x
6	x			x		
7	x					x
8		x				x
9			x			x
10		x				x
11		x		x		
12		x		x		
13		x			x	
14			x			x
15		x				x
16		x				x
17		x				x
18		x		x		
19		x				x
20		x			x	
21		x			x	
22		x			x	
23		x			x	
24		x			x	
25		x			x	
26	x				x	
27		x				x
28	x			x		
29		x		x		
30		x				x
31		x				x
32		x				x

Total	10	20	2	6	11	15
%	31,25	62,5	6,25	18,75	34,37	46,87

Source: The authors, 2023.

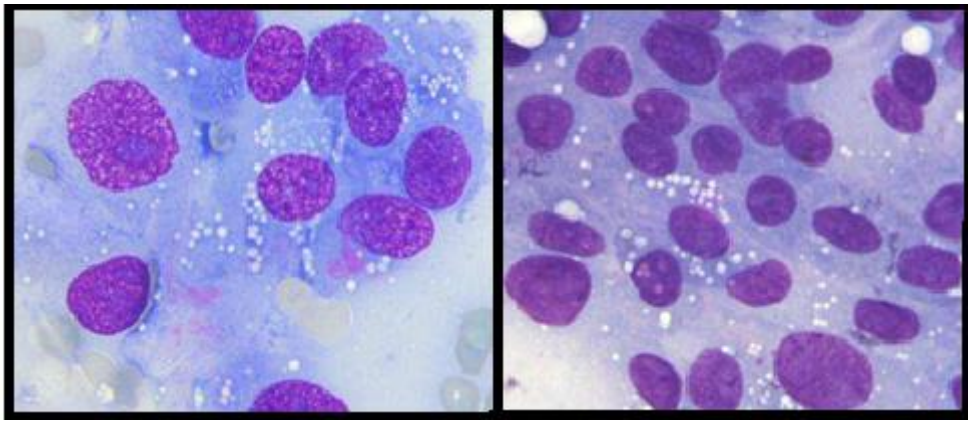
Regarding tumor consistency, only six bitches had a tumor with soft consistency (6/32; 18.75%), 11 with firm consistency (11/32; 34.37%) and 15 with mixed consistency (Table 3). However, the authors state that tumor consistency is not directly related to the type of mammary tumor found. However, it is suggested that the presence of firm or soft structures may be correlated with the presence or not of cystic areas in the neoplasia. However, authors report that there was no difference ($p>0.05$) between tumor tissues evaluated with the type of tumor consistency (FELICIANO et al., 2012).

As for the growth characteristics, 31.25% (10/32) showed slow growth, 62.25% fast growth (20/32) and 6.25% (2/32) stable (Table 3). The rapid growth, which was more frequent in the study, is characteristic of malignant neoplasias (VASCONCELOS, 2000) and can be used as a prognostic factor and as an aid in the diagnosis and tumor differentiation.

In the radiographs taken in all bitches, no signs of metastases in the lungs were observed. However, in other studies involving the disease in bitches, metastases were detected (BIONDI et al., 2014: OLIVEIRA and PANDOLFI, 2020; TORÍBIO et al., 2012). This discrepancy is probably related to differences in sample sizes, although in the studies cited the incidence of pulmonary metastases was low. In most patients, there are micrometastases, which are not visualized by radiographic examination (DALECK et al., 2009), which may be the case in the present study.

The results obtained by FNAC were malignant mixed tumor and mammary adenocarcinoma (Figures 1 and 2), and about 81.5% of adenocarcinomas were confirmed by histopathological examination (Figure 3; Table 4). Similar results were obtained by other authors (CASSALI, 2000; OLIVEIRA et al. 2013) and confirm the value of cytological examination. Evidently, the histopathological examination must be performed and it is considered the gold standard. However, cytological examination is more accessible, easier and cheaper. These characteristics make the cytological exam ideal to be used in low-income settings, where the incidence of malignant neoplasms is high (TORÍBIO et al., 2012).

Figure. 1. Photomicrograph of fine-needle aspiration cytology performed in a female dog with an adenocarcinoma-type mammary tumor. There is presence of pleomorphism, evident nucleoli and coarse chromatin. 100x. Panotic.



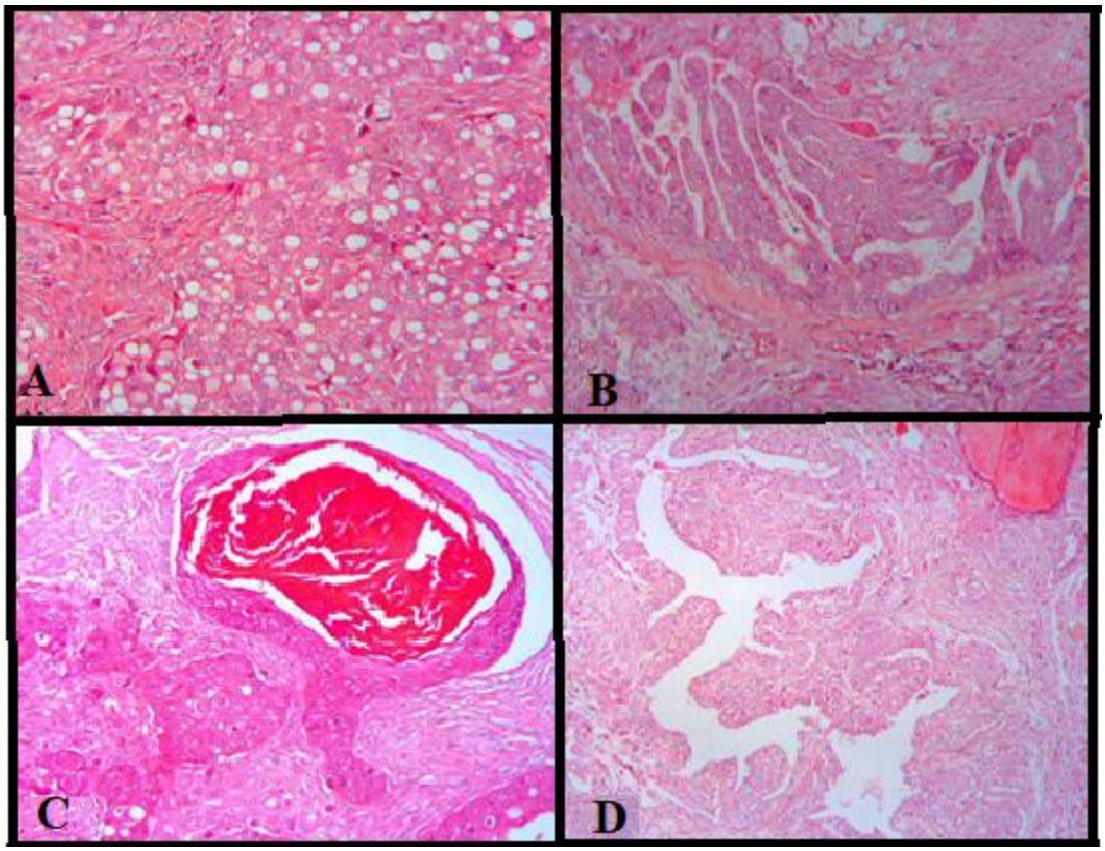
Source: the authors, 2023.

Table 4. Cytological and Histopathological Diagnoses of 32 bitches with malignant mammary tumor.

Histopathological Diagnosis			Cytological Diagnosis		
Types	Number	Percentage	Types	Number	Percentage
Invasive ductal carcinoma	7	21,87%	Adenocarcinoma	26	81,25%
Tubular carcinoma	7	21,87%	Malignant mixed tumor	6	18,75%)
Solid carcinoma	5	15,62%			
Carcinoma in mixed tumor	3	9,37%			
secretory carcinoma	2	6,25%			
Malignant myoepithelioma	1	3,12%			
Carcinoma in situ	1	3,12%			
Solid secretory carcinoma	1	3,12%			
Micropapillary Carcinoma	1	3,12%			
Carcinosarcoma	1	3,12%			
Inflammatory anaplastic carcinoma	1	3,12%			
Intraductal carcinoma	1	3,12%			
Carcinoma Spinocellular	1	3,12%			

Source: the authors, 2023.

Figure 2. Photomicrograph of mammary tumors in bitches. A: Solid secretory carcinoma (HE, 200x). B: Micropapillary Carcinoma (HE, 200x). C: Squamous cell carcinoma (HE, 100x). D: Tubulopapillary Carcinoma (HE, 100x).



Source: The authors, 2023.

CONCLUSION

After analyzing 32 cases of malignant mammary tumor in bitches, it was concluded that older bitches were the majority, as well as non-castrated ones. Regarding the tumor mass, tumors larger than 5 cm were the most frequent, with fast growth and firm consistency on palpation. Cytological examination was considered important for diagnosis.

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