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Original Article

HISTOPATHOLOGICAL DIAGNOSIS OF MAMMARY GLAND NEOPLASMS IN DOGS

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ABSTRACT

The objective of this study was to describe and identify the cases of mammary gland neoplasms in dogs, and to classify them within the types of tumors established by the World Health Organization, based on the data from the samples received in the Pathology Laboratory. of the Faculty of Veterinary Medicine and Zootechnics of the Meritorious Autonomous University of Puebla, located in El Salado, Tecamachalco, Puebla, during the period from January 2011 to June 2013. A retrospective investigation of the histopathological characteristics of mammary gland neoplasms in female dogs and predisposing factors was performed. Samples of mammary gland neoplasms in dogs, preserved in paraffin blocks or microscope slides, were used. Seven cases were found which were re-examined to reconfirm the diagnosis. Of the seven samples examined, 86% of them were obtained from purebred animals, with the Pit bull breed (2) being the most affected; the remaining 14% corresponded to mestizo canines (1). All the samples came from canine females, which had an average age of 7 years. Malignant neoplasms (71%) were more frequent than benign ones (29%).
Key words: mammary gland, neoplasms, dogs.

INTRODUCTION

In today's society, dogs and cats are considered one more member of the family and extremely strong affective ties are established; therefore, cancer is not currently synonymous with immediate euthanasia (Martínez et al., 2011). Neoplasms are pathological processes that occur in all species of domestic animals (Cárdenas, 2012), these are highly prevalent in canines and felines, compared to other domestic species (Ferreira et al., 1997; Bravo et al., 2010); Torres and Fajardo, 2005); The exact figures about the incidence of neoplasms in canines and felines are unknown, but it is estimated that one in 10 dogs or cats will develop a neoplasm in their life (Limón, 2009). In most homes there are pets, which have a better quality of life thanks to the veterinary medical services provided to them and as a result their life tends to be longer and with this the risk of developing neoplasms of mammary gland (CMTs) (Limón, 2009). However, from our veterinary point of view, the approach to the canine species is in itself of great

interest as CMTs is one of the most frequent causes of death in companion animals (Pérez, 1994).

Neoplasia is defined as a pathological process characterized by excessive cell proliferation, indefinite and independent of normal inhibitory control mechanisms (Ziller, 2004) and persists even when the originating agent ceases (Calderón, 2007). Canine CMTs are complex pathologies of multifactorial origin with various forms of presentation (Torres and Fajardo, 2005), their biological behavior and histogenesis in canines are similar to those of humans (Ferreira et al., 1997) in such a way that, Canine CMTs have been proposed as a comparative model for the study of breast cancer in women by numerous authors (Pérez, 1994). It is important to differentiate the concepts of benign neoplasm and malignant neoplasm, since their classification will have a marked influence on the appropriate treatment and prognosis of the disease (Ziller, 2004). For the classification of these neoplasms, clinical and histopathological parameters have been used: within the former are growth rate, size and postsurgical recurrence and in the latter, cell lineage, cellular and nuclear morphology, growth form, mitotic index, blood invasion and lymphatic, distant metastasis (Torres and Fajardo, 2005; Limón, 2009), biological behavior and degree of differentiation (Limón, 2009). On the other hand, the nomenclature of neoplasms depends on whether their origin is epithelial or mesenchymal (Ziller, 2004).

It is worth mentioning that it is often difficult to differentiate between benign and malignant mammary nodules by clinical criteria, even in their early stages, benign and malignant neoplasms do not differ at all, therefore, the histopathological study continues to be the diagnostic method of choice. (Croosley et al., 2010).

Epidemiological studies in Veterinary Medicine allow the identification of risk factors in the presentation of diseases that affect animals (Ziller, 2004). The objective of the present study was to carry out the histopathological diagnosis of mammary neoplasms in dogs, of the cases received in the pathology laboratory of the Faculty of Veterinary Medicine and Zootechnics of the Benemérita Universidad Autónoma de Puebla, and to classify them histologically according to the criteria proposed by the World Organization Health (WHO) (Hampe and Misdorp, 1974; Ziller, 2004).

MATERIALS AND METHODS

This is a retrospective study that was carried out with data from the Pathology Laboratory of the Faculty of Veterinary Medicine and Zootechnics of the Meritorious Autonomous University of Puebla, located in El Salado, in the Municipality of Tecamachalco, Puebla, during the period from January 2011 to June 2013. This laboratory routinely performs histopathological diagnosis of different samples sent from other institutions, including samples or biopsies of canine mammary gland neoplasms included in formaldehyde. A retrospective investigation of the general aspects related to mammary gland neoplasms in female dogs was carried out.

Samples of mammary gland neoplasms in dogs, preserved in paraffin blocks or in histological sections, were used. Seven cases of mammary gland neoplasms were

found in dogs, received in the pathology laboratory that were admitted during the study period. In the seven cases, the tissues were processed following the traditional histotechnic protocols for inclusion in paraffin, section and hematoxylin-eosin staining, the corresponding original histological sections were made on slides and re-examined to reconfirm the diagnosis (Bravo et al. , 2010). Each case of mammary gland neoplasia in dogs was histologically characterized and classified according to the criteria proposed by the World Health Organization (WHO) (Hampe and Misdorp, 1974). Information corresponding to age (years), race (including mestizo) and histopathological diagnosis were recorded.

For the digitization of images, a Leyca® brand microscope was used with a camera and image measurement and digitization software. Microsoft Office Excel and Word 2007 were used for data processing.

RESULTS AND DISCUSSION

The cases corresponded to female dogs since mammary gland neoplasms occur more frequently in females (99%) than in males (1%) (Ochoa et al., 2009). Malignant neoplasms were the most prevalent (71%), while benign ones corresponded to 29% of the total samples (Table 1), coinciding with the studies by Ziller (2004) and Chau et al., (2013).

Table 1. Number of benign and malignant neoplasms and their percentage of presentation in the 7 CMTs samples examined.

Type of neoplasm	No. of samples	% of samples
Benign	2	29
Malignant	5	71
Total	7	100

Regarding age, it was observed that although there are few cases described, the average age of presentation was 7 years, and the 3 years (29%) and 7 years (29%) ages with the highest tendency of neoplastic growth in this study, where the youngest were 3 years old and the oldest were 12 years old (Table 2). Two cases with an age of 3 years were found, coinciding with Chau et al., (2013) and Ferreira et al., (1997) who reported that the presentation of CMts in female dogs under 6 years of age is infrequent, however the majority of CMTs occur in the range of 7 to 11 years (Ziller, 2004; Ferreira et al., 1997) where most of the cases in this study are included.

Regarding the breed, breeds such as the Cocker Spaniel (1), Poodle (1) and Mestiza (1) were mentioned as the breeds most affected by CMTs (Ferreira et al., 1997; Ziller, 2004; Torres and Botero, 2008). ; Chau, et al., 2013) and other breeds with less frequency of presentation such as the Pit bull (2) (Morales, 2014; Gómez et al., 2012), Schnauzer (1) (Morales, 2014), and the Bull Terrier (1) (Salazar and Lucatero, 2005) (Table 2).
In relation to other risk factors associated with CMTs, no clinical history was

obtained that would allow us to clearly approximate any other risk factor.

Table 2. Neoplasms of the Mammary Gland in Dogs received in the Pathology Laboratory of the Faculty of Veterinary Medicine and Zootechnics of the BUAP, during the period from January 2011 to June 2013.

Núm.	Case	Sex	Age (años)	Raza	Result is compatible with:
1	BP 310111	Female	8	Cocker Spaniel	Fibroadenoma (Hampe y Misdorp, 1974; Ziller, 2004; Chau, *et al*., 2013).
2	HP 280911	Female	7	Poodle	Carcinosarcoma (Ferreira, *et al*., 1997; Ziller, 2004; Chau, *et al*., 2013; Hampe y Misdorp, 1974; Bravo, *et al*., 2010
3	BP 140911	Female	7	Bull Terrier	Simple solid carcinoma (Hampe y Misdorp, 1974; Ziller, 2004; Santin, *et al*., 2009; Guajardo, 1988; Torres y Botero, 2008)
4	BP 010612	Female	3	Pitbull	Squamous cell carcinoma (Hampe y Misdorp, 1974; Ziller, 2004; Echeverry y Buriticá, 2007; Berrocal, 2012; Chandrashekaraiah *et al*., 2011; Silva, *et al*., 2015)
5	HP-220513-1	Female	3	Pitbull	Simple tubular adenocarcinoma (Hampe y Misdorp, 1974; Ziller, 2004; Baba y Câtoi, 2007; Citopatvet, 2011).
6	HP-220513-2	Female	9	Mestiza	Complex tubular adenocarcinoma (Hampe y Misdorp, 1974; Ziller, 2004; Baba y Câtoi, 2007)
7	BP 040613	Female	12	Schnauzer	Complex adenoma (Hampe y Misdorp, 1974; Ziller, 2004; Gómez *et al*., 2012; Chau, *et al*., 2013)

Table 2 shows us the mammary gland neoplasms found, where fibroadenoma (1) and complex adenoma (1) are benign neoplasms and carcinosarcoma (1), simple solid carcinoma (1), squamous cell carcinoma (1), Complex tubular adenocarcinoma (1) and simple tubular adenocarcinoma (1) are malignant neoplasms. Each of which is described below in its respective case.

Case 1. Fibroadenoma. BP 310111

Canine female, Cocker Spaniel breed, age 8 years. Marked desmoplasia was observed due to stromal hypercellularity of fibrous connective tissue in the midst of an extracellular matrix containing scant collagen. Sectors of fibrous proliferation were found showing a pericanalicular growth pattern of moderate cellularity, where ductal structures and lobes delimited by dense fibrous tissue are observed, while cystic dilations show papillary projections and some calcifications in their lumen (Figure 1A). The lobules showed epithelial hyperplasia and apocrine metaplasia, with acidophilic content in their lumen (Figure 1B). In another area, the fibrous proliferation

shows a highly cellular intracanalicular pattern (Figure 1C). The stromal proliferation showed areas of myxoid tissue, with fibrocytes and areas with fibroblastic activity (Figure 1D). According to what was observed, the findings are compatible with fibroadenoma both in a pericanalicular and intracanalicular pattern (Hampe and Misdorp, 1974) different from mixed benign neoplasia. This neoplasm is of low presentation and it is necessary to differentiate it from mixed neoplasms (Ziller, 2004).

For Ziller (2004) and for Chau, et al., (2013), fibroadenoma was the third most common benign CTMs in canines. Ziller (2004) reports in his study that the average age of presentation of fibroadenomas was 10 years, being 11 years the oldest age of presentation and 9 years the youngest age of presentation, finding similarity with this case.

Regarding the breed, Torres and Botero (2008) found that the Cocker Spaniel breed is the breed most affected by CMTs, while for Chau, et al., (2013) it is the second; however, for Ziller (2004) it is the third most affected, with an age range of 8 to 16 years similar to this case.

Case 2. Carcinosarcoma. HP 280911

Canine female, Poodle breed, 7 years old. Histologically, numerous areas of bone and cartilage metaplasia were observed (Figure 2A). Note the chondroid matrix where the neoplastic cells form pink acellular osteoid, together with a sector of malignant fatty tissue, also note the hemorrhagic areas and cystic hemorrhagic foci, the abundant blood vessels contained neoplastic cells in their lumen (Figure 2B). An area with cells with a fusiform cell morphology with a hyperchromatic nucleus was found (Figure 2C). An area of dense connective tissue metaplasia to cartilage was found (Figure 2D).

According to the findings found, the result is compatible with mammary gland carsinosarcoma (Hampe and Misdorp, 1974), finding both cells resembling malignant epithelial cells (luminal epithelial and/or myoepithelial) and malignant connective tissue cells, as well as the mixture of carcinomatous components (bone, cartilage and fat (Hampe and Misdorp, 1974; Bravo, et al., 2010). However, the diagnosis of this neoplasm is difficult due to its morphological similarity with mixed neoplasms and complex-type carcinomas (Ziller, 2004).

Carcionosarcomas have a rare presentation, corresponding to less than 5% of all malignant tumors (Ziller, 2004). Ferreira, et al., (1997) found that a higher percentage for these (9.3%). While for Chau, et al., (2013) it was the second malignant CMTs with the highest presentation. The Poodle breed is the second breed most affected by CMTs as reported by Bravo, et al., (2010) and Ziller (2004), being the most frequent malignant neoplasms, while in other studies it was the sixth most frequent (Ferreira, et al., 1997; Chau, et al., 2013) and the third breed most affected by carcinosarcomas (Ferreira, et al., 1997).

For Ferreira, et al., (1997) the average age of CMTs presentation was 7 and 11 years, similar to Ziller (2004) where the age range in the Poodle breed was 5 to 16 years, where this case would be included. While the age of presentation of carcinosarcomas was 12 years, differing with this case (Ziller, 2004).

Case 3. Simple Solid Carcinoma. BP 140911

This case corresponded to a female of the Bull Terrier breed, 7 years old, white. Microscopic examination of the neoplastic mass revealed proliferation of myoepithelial cells forming masses or cords on a matrix of collagen fibers. A moderate amount of fibrous tissue was also observed (Figure 3A). Detail of the proliferation of pleomorphic myoepithelial cells showing intense nuclear pleomorphism and scant mitotic activity. Note also the intense polynuclear inflammatory infiltrate as well as abundant blood vessels of variable caliber (Figure 3B). Areas of myxoid tissue with proliferating spindle-shaped myoepithelial cells arranged in a reticular pattern were observed (Figure 3C). Proliferation of blood vessels surrounded by neoplastic tissue and polynuclear inflammatory cells (Figure 3D). When evaluating the changes found as a whole, it was possible to conclude that they correspond to a simple solid carcinoma as described by Hampe and Misdorp (1974) where myoepithelial-type cells could be observed forming cords or masses (Ziller, 2004; Santin, et al., 2009).

Differentiation between this type of neoplasm and complex adenomas is difficult (Ziller, 2004). Areas of angiogenesis could be observed, which is fundamental in the development of metastases, just as the marked neovascularization in the histological images of neoplasms is considered of prognostic value in human medicine, as well as in veterinary medicine (Salas and Romero, 2011).

Ziller (2004) found that simple solid carcinoma was the second most common malignant CMTs; and an age range between 5 and 16 years where this case can be included. While in previous studies Guajardo (1988) was the third, with a presentation age of 10 years, differing from this case. However, for Torres and Botero (2008) it was the neoplasm with the least presentation.

Regarding the Bull Terrier breed, Salazar and Lucatero (2005) mention it as one of the breeds predisposed to mammary gland carcinomas, with ages of 6 and 8 years, this case being in the range.

Case 4. Squamous Cell Carcinoma (SCC). BP 010612

Female, Pit-bull breed, age 3 years old, white color. Microscopic examination revealed islands of squamous cells with central dyskeratosis. In other areas, the squamous cells are generally organized in the form of solid sheets and cords, the nucleus is round-oval, pale, with one or two nucleoli (Figure 4A). Proliferation of polygonal neoplastic squamous cells was observed, arranged in solid groups with a tendency to keratinization, with nuclear hyperchromasia, pleomorphism, vesicular chromatin and prominent nucleolus, and the presence of some eosinophilic giant cells with a clear nucleus and hyperchromatic nucleolus (Figure 4B). According to what was observed, the findings are compatible with squamous cell carcinoma of the mammary gland (Hampe and Misdorp, 1974; Ziller, 2004; Echeverry and Buriticá, 2007; Filgueira and Júnior, 2012; Berrocal, 2012).

It is usually uncommon in dogs (Ziller, 2004) and is a malignant neoplasm of epithelial cells (Filgueira and Júnior, 2012). It is a fatal neoplasm in dogs with rapid metastatic spread (Chandrashekaraiah et al., 2011). The literature indicates two different origins,

one is that the tumor originates from a major duct (nipple), which histologically is lined by squamous epithelial cells, while the second is that first, the epithelial cells of the ducts undergo metaplasia, and later they become neoplastic that occurs in other glandular organs (Berrocal, 2012).

Ziller (2004) reported that SCC corresponded to 5.4% of malignant tumors, with 12 years being the age of presentation of the 2 samples observed. Torres and Botero (2008) mention that only 1% of malignant CMTs are SCC, with an age of presentation of 15 years and an age of 16 years for Berrocal (2012), ages older than the presentation of this case.

Silva, et al., (2015) in their study mention the mammary gland as the third frequent anatomical place of SCC, and mentions an age of greater presentation of 2 to 4 years, a range where this case would enter, it is important to highlight that it mentions that white-mantled animals are the most affected by SCC. However Chandrashekaraiah et al., (2011) reports the mammary gland as the site most frequently affected by SCC with three cases. Morales, (2014) and Gómez et al., (2012) mention the Pit Bull breed as one of the breeds affected by CMTs.

Case 5. Simple tubular adenocarcinoma. HP-220513-1

Pitbull female, 3 years old. Microscopically, the proliferation of tubular structures with an angular pattern or forming islets and trabeculae was found, these infiltrate the stroma in a disorderly manner in focal or multifocal extension, both continuously or discontinuously, desmoplastic stroma and in some areas loose tissue with inflammatory infiltrate and erythrocytes showing degenerative and regenerative tissue changes (Figure 5A). The neoplastic proliferation is surrounded by a variable inflammatory infiltrate (Figure 5B). Another important finding was the intense accumulation of polymorphs infiltrating the stroma of loose tissue around the blood vessels (Figure 5C), foci of necrosis of fat and fibrous tissue with intense mononuclear inflammatory infiltrate (Figure 5D). Observing in more detail the tubular formations, atypical epithelial intraductal hyperplasia and squamous metaplasia of the ducts were observed, where the proliferation of neoplastic cells fills the duct, others with or without the formation of secondary lumens, where cellular debris was observed grouping together forming syncytia, central microcalcifications, the cells that line the tubules show hyperchromatic and overlapping nuclei, mitotic figures (Figure 6A), in some ducts the neoplastic epithelium shows considerable atypia, loss of cohesion and polarity between the neoplastic cells and presence of inflammatory and necrotic material in the light (Figure 6B). As observed, it is compatible with simple tubular carcinoma of the mammary gland (Hampe and Misdorp, 1974), and corresponds to the most common type of mammary gland carcinoma in canines (Ziller, 2004; Baba and Câtoi, 2007). Histologic differentiation between some tubular adenocarcinomas and some benign adenomatous lesions can be very difficult (Ziller, 2004; Baba and Câtoi, 2007).

Few authors mention the Pitbull breed as one of those affected by CMTs, however Morales (2014) and Gómez et al., (2012) include it as one of the breeds affected by these neoplasms. Regarding age, Ziller (2004) found an age range of presentation between 7 and 10 years for simple tubular adenocarcinoma, disagreeing with this case, which is younger than this. The

finding of tubular formations with atypical epithelial ductal hyperplasia or ductal carcinoma in situ (DCIS) is associated in humans with tubular adenocarcinoma (Citopatvet, 2011), however in this work canine neoplasms are classified according to the histological criteria of the World Organization (WHO) (Hampe and Misdorp, 1974), the classification does not establish differences between adenocarcinomas (originating in the glandular epithelium) and ductal carcinomas (originating in the epithelium of mammary ducts, intra or extralobular) (Citopatvet, 2011; opinion of experts). On the other hand, some studies of premalignant lesions with new names directly derived from human pathology are beginning to emerge (Mouser, 2010), so for this case this distinction would be fundamental as it is in human pathology, since there are marked differences in biological behavior (Karayannopoulou et al. 2005).

Case 6. Complex tubular adenocarcinoma. HP220513-2

Female, 9 years old, mixed race. Histologically, extensive proliferation of tubular structures was found, some with atypical ductal epithelial hyperplasia of a papillary and/or cribriform pattern, lined with cuboidal or cylindrical cells (some showed squamous changes) and surrounded by masses or solid sheets of spindle-shaped cells. arranged in a reticular pattern (Figure 7A). Duct with atypical epithelial hyperplasia with detachment of neoplastic cells forming syncytia, inflammatory infiltrate and necrotic material in its lumen (Figure 7B). Detail of the polyhedral or spindle-shaped neoplastic cells, showing vacuolated cytoplasm, nuclear hyperchromasia, vesicular chromatin, and evident nucleoli (Figure 7C). Nest of polyhedral neoplastic cells similar to keratinocytes, area of necrosis and blood vessels (Figure 7D). As observed, it is compatible with complex tubular adenocarcinoma of the mammary gland (Hampe and Misdorp, 1974), and corresponds to the most common type of mammary gland carcinoma in canines (Ziller, 2004; Baba and Câtoi, 2007). Histologic differentiation between highly differentiated carcinomas of this type and complex adenomas can be difficult (Ziller, 2004; Baba and Câtoi, 2007). The mestizo race is one of the most affected by CMTs (Chau, et al., 2013; Ziller, 2004), with benign neoplasms being more prevalent. Ziller (2004) reports an average age of presentation of CMTs in mongrel bitches of 9.7 years.

Case 7. Complex adenoma. BP 040613

Non-ovariectomized female, Schnauzer breed, 12 years old. The proliferation of cellular fibrous connective tissue stroma was observed, separating numerous tubular-alveolar secretory areas and cystic spaces, with secretory material in its lumen (Figure 8A). In detail, lobular hyperplasia is apparently benign, I present multiple proliferated tubular formations, with intraluminal eosinophilic content lined with single-layer pleomorphic epithelium, surrounded by myoepithelial cells with hyperchromatic nuclei and few collagen fibers (Figure 8B), while in other lobes Apocrine metaplasia and epithelial cells were observed in its lumen (Figure 8C), another important finding was mononuclear inflammatory infiltrate in the stroma and peritumoral lymphocytic inflammatory infiltrate (Figure 8D).
According to the findings found, the structure is compatible with: complex adenoma (Hampe and Misdorp, 1974). Overlap of this neoplasm can occur with fibroadenomas, benign mixed neoplasms, and complex lobular hyperplasias (Ziller,

2004). Complex adenoma is quite common in female dogs (Ziller, 2004; Gómez et al., 2012; Chau, et al., 2013). The differential diagnosis between complex adenoma and complex adenocarcinoma is difficult (Hampe and Misdorp, 1974; Ziller, 2004; Baba and Câtoi, 2007).

Ziller (2004) reports an age range of presentation from 5 to 12 years for complex adenomas, where this case with 12 years can be included. Morales (2014) include the Schnauzer breed as one of the breeds with the lowest NGM presentation.

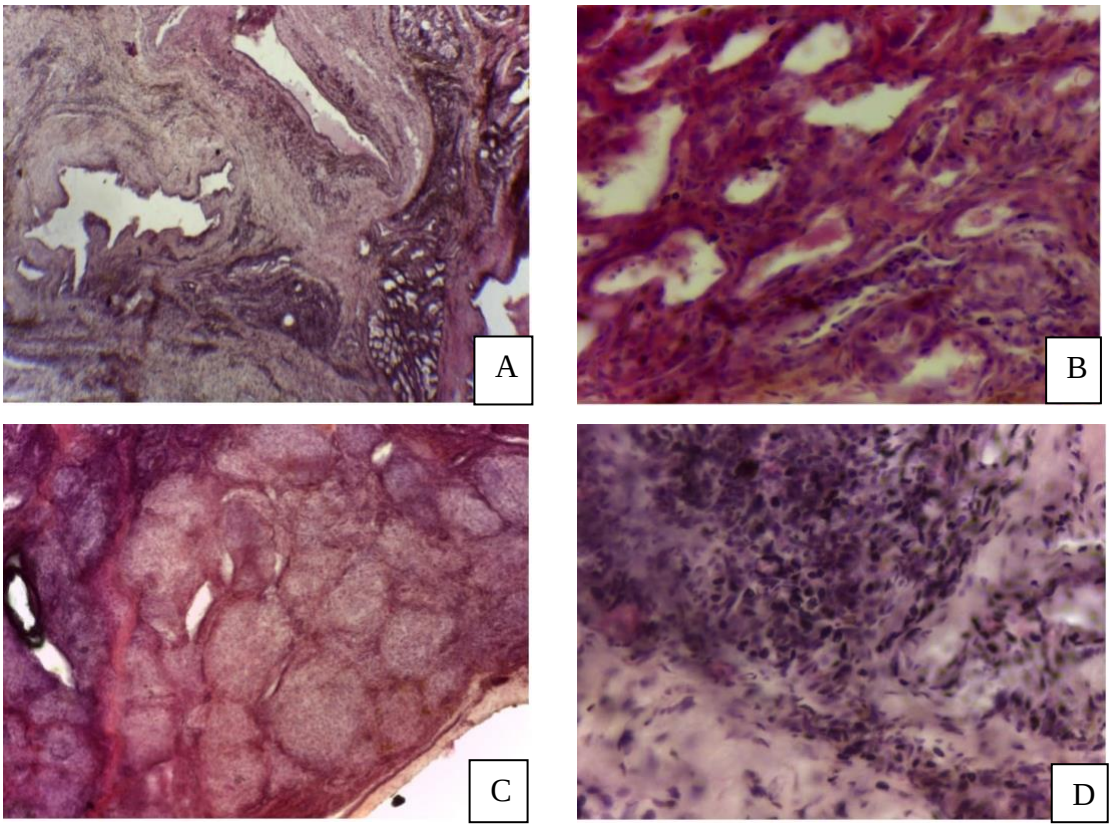

Figure 1. Fibroadenoma. A) Ductal structures surrounded by fibrous proliferation and lobes delimited by dense fibrous tissue (pericanalicular fibroadenoma) are observed. The ductal and cystic spaces show papillary formations (HE, 4X). B) Lobe with epithelial hyperplasia and apocrine metaplasia (HE, 40X). Fibroadenoma with intracanalicular growth pattern, the borders are delimited from the adjacent tissue (HE, 10X). Fibrous tissue, with myxoid characteristics and areas with high fibroblastic cellularity (HE, 40X).

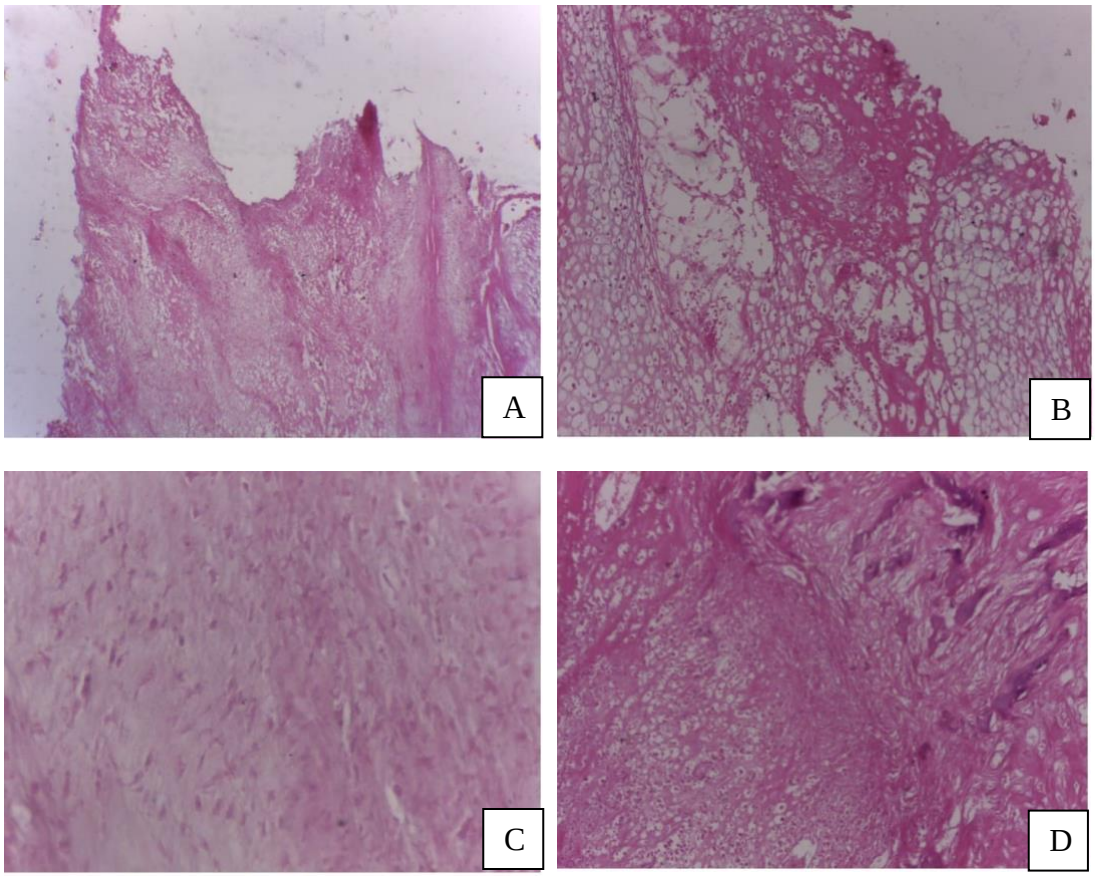

Figure 2. Carcinosarcoma of the canine mammary gland. A) Area of bone and cartilage metaplasia (HE, 4X). B) Note the formation of pink osteoid, malignant fatty tissue, areas of cartilage and hemorrhagic cysts (HE, 10X). C) Myxomatous tissue (sarcomatous portion) (HE, 40X). D) Focus of metaplastic transformation of connective tissue to cartilage (HE, 40X).

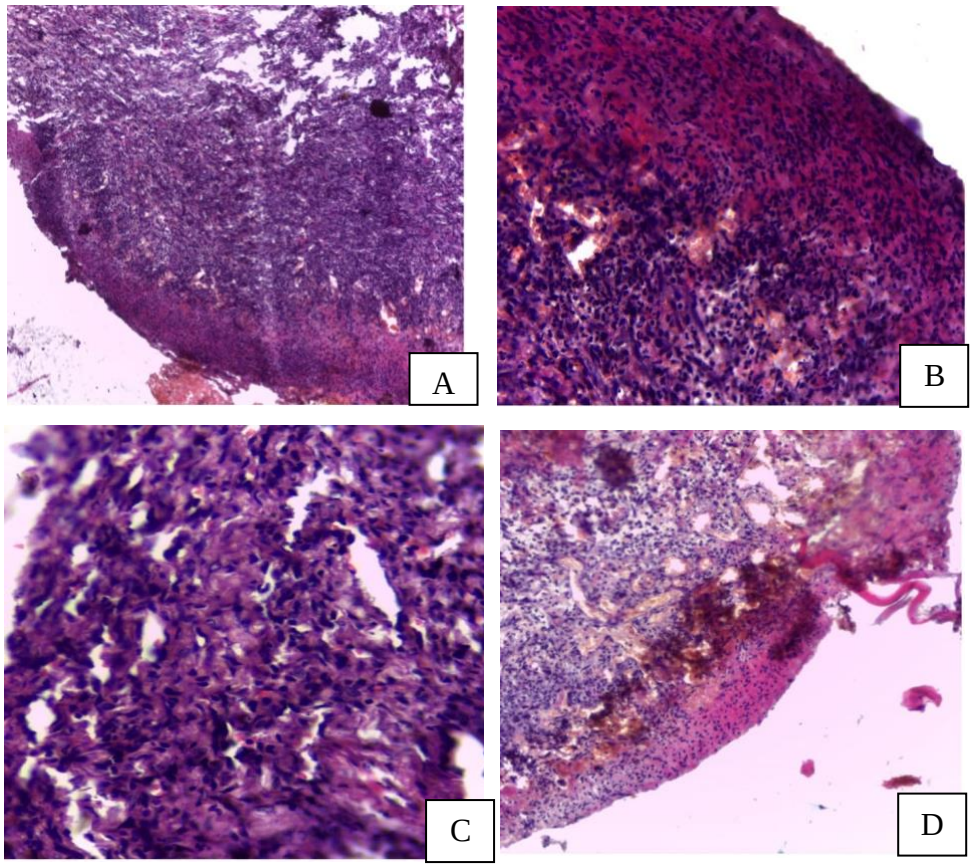

Figure 3. Simple solid carcinoma. A) Proliferation of pleomorphic myoepithelial neoplastic cells on a matrix of few collagen fibers (HE, 10X). B) Proliferation of pleomorphic myoepithelial cells, intense polynuclear inflammatory infiltrate (HE, 40X). C) Area of myxoid tissue (HE, 40X). D) Angiogenic sector surrounded by polynuclear inflammatory cells (HE, 10X).

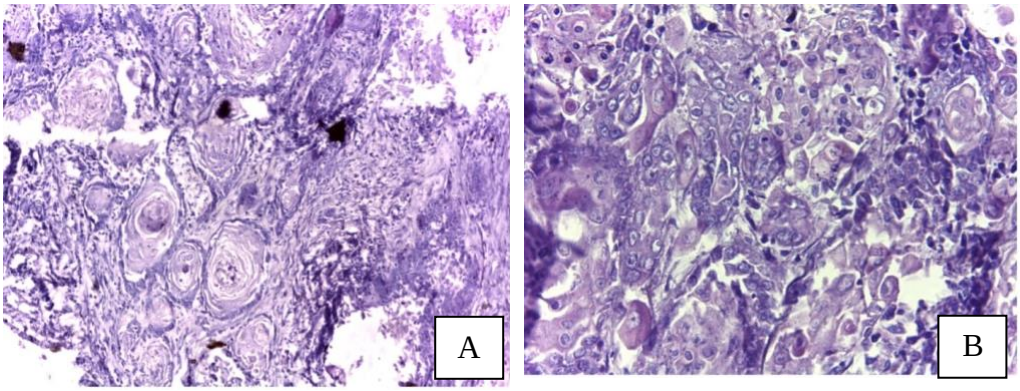

Figure 4. Squamous cell carcinoma of the mammary gland. A) Islets of squamous cells with central dyskeratosis are observed, in other areas the squamous cells are organized in the form of solid sheets and cords. (HE, 10X). B) Detail of the proliferation of polygonal neoplastic squamous cells, with eosinophilic cytoplasm, nuclear hyperchromasia, pleomorphism, vesicular chromatin and prominent nucleolus, presence of some eosinophilic giant cells with a clear nucleus and hyperchromatic nucleolus (HE, 40X).

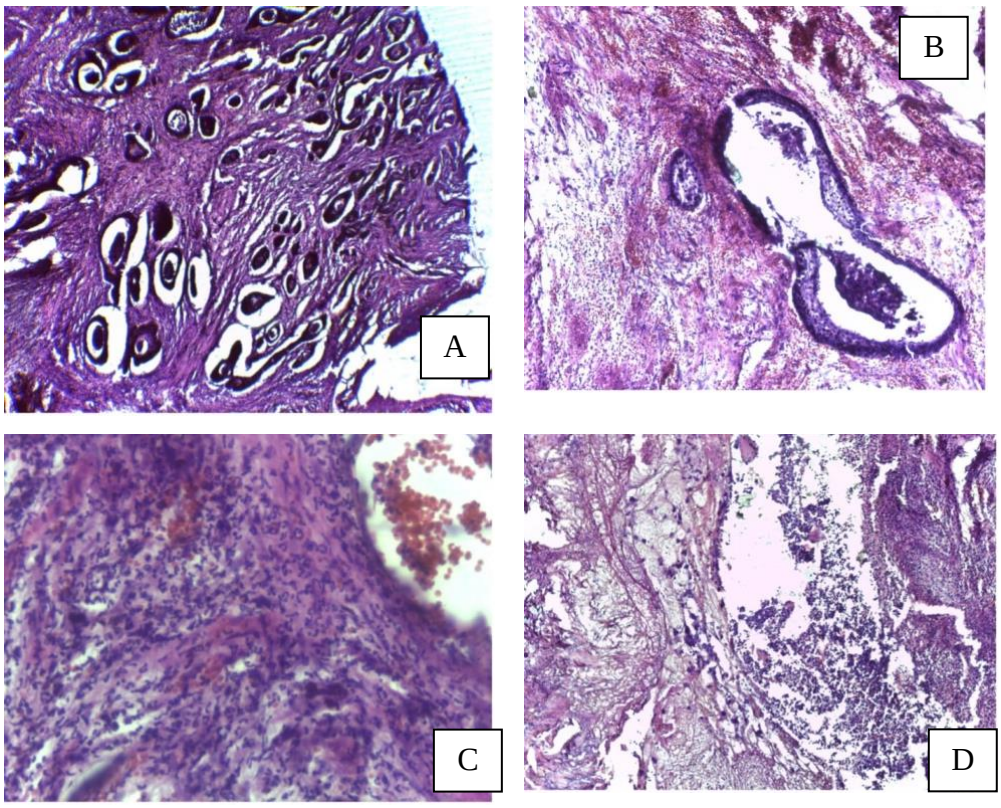

Figure 5. Simple tubular adenocarcinoma A) Proliferation of tubular structures with an angular pattern or forming islets and trabeculae, infiltrating the desmoplastic stroma (HE, 4X). B) Neoplastic proliferation surrounded by variable inflammatory infiltrate (HE, 10X). C) Accumulations of polymorphs infiltrating the stroma of loose tissue and around the blood vessels (HE, 40X). D) Foci of necrosis, is fat and fibrous tissue with intense mononuclear tissue inflammatory infiltrate (HE, 40X).

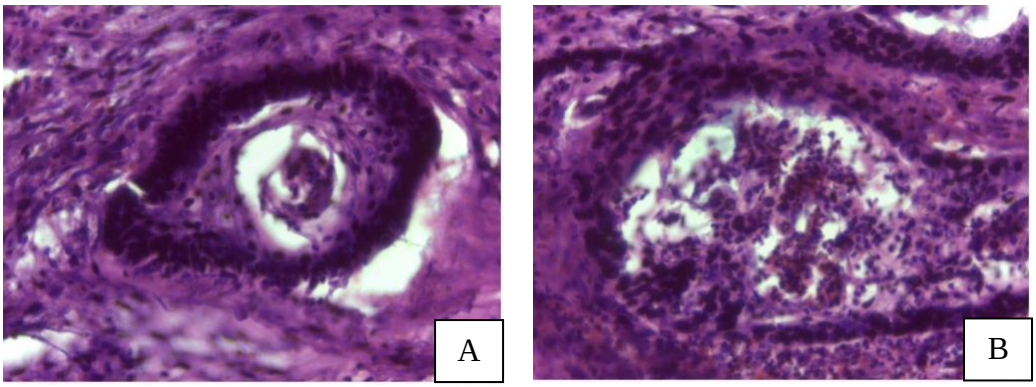

Figure 6. Simple tubular adenocarcinoma. A) Detail of a duct with intraductal hyperplasia of atypical malignant epithelial cells, overlapping nuclei, few mitoses (HE, 40X). B) Duct with neoplastic epithelium shows considerable atypia and loss of cohesion between neoplastic cells, loss of polarity and overlapping nuclei, and presence of inflammatory material, giant cells, and erythrocytes in the lumen (HE, 10X).

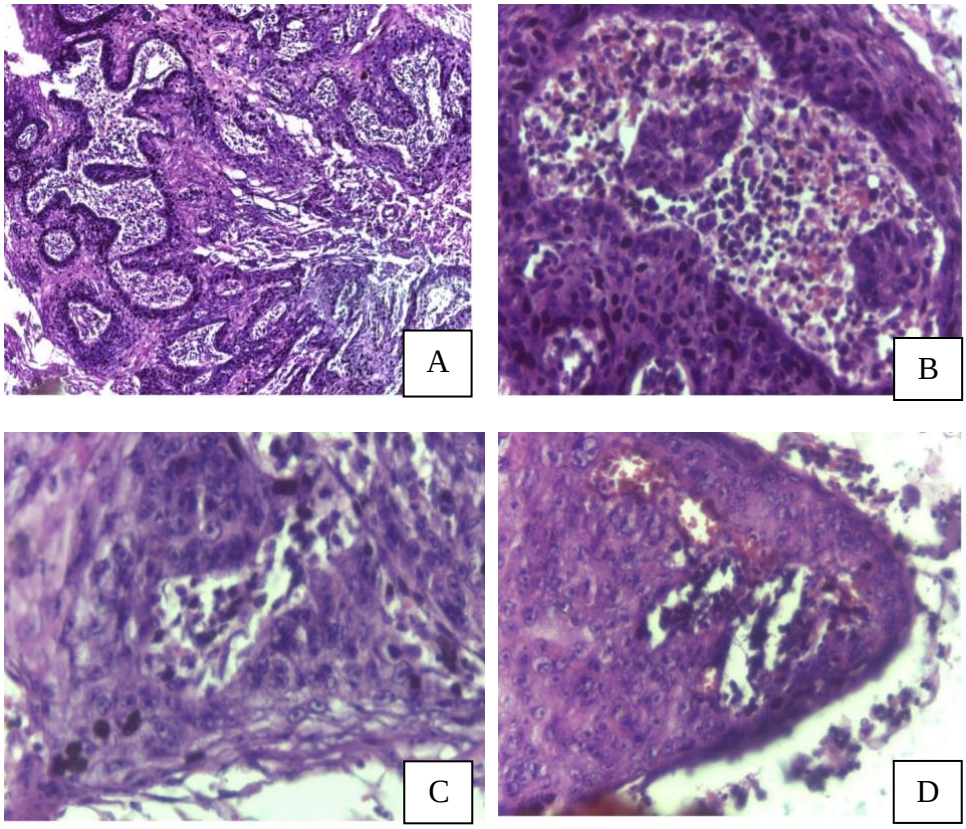

Figure 7. Complex tubular adenocarcinoma. A) Proliferation of tubular structures surrounded by solid masses of spindle-shaped cells arranged in a reticular pattern (HE, 10X). B) Duct with atypical epithelial hyperplasia with detachment of neoplastic cells forming syncytia, inflammatory infiltrate and necrotic material in its lumen (HE, 40X). C) Detail of the stroma of polyhedral or spindle-shaped neoplastic cells, with vacuolated cytoplasm, nuclear hyperchromasia, pleomorphism, vesicular chromatin and evident nucleolus (HE, 40X). D) Nest of polyhedral neoplastic cells similar to keratinocytes, area of necrosis and blood vessels (HE, 40X).

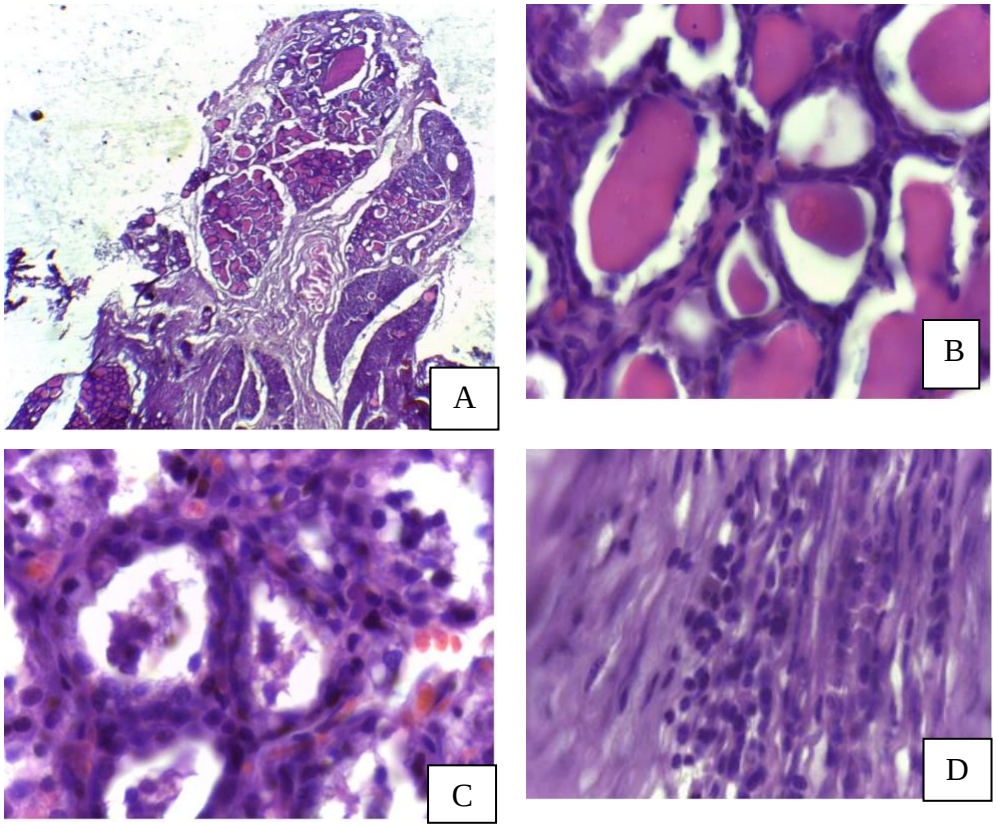

Figure 8. Complex adenoma. A) Abundant lobes with multiple tubular formations and large cystic formations, surrounded by fibrous connective tissue stroma (HE, 4X). B) Detail of the lobular hyperplasia (HE, 40X). C) Apocrine metaplasia with epithelial cell detachment grouping together forming syncytia in its lumen (HE, 40X). D) Mononuclear-type inflammatory infiltrate (HE, 40X).

CONCLUSIONS

The follow-up of mammary gland neoplasms in canines is of great importance due to the emotional attachment of the owner to his pet, which seeks to prolong the life of his pet affected by these pathologies. It is important to know more about the risk factors involved in canine CMTs. Although the histological diagnosis of CMTs in canines is essential, it is not enough to establish more precise prognoses. The rise of veterinary oncology, the development of diagnostic techniques and the use of molecular markers, implies a substantial benefit both in animal patients and in human patients.

CONFLICT OF INTEREST

The authors declare that they have no potential conflict of interest with respect to the authorship and/or publication of this article.

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AUTHORS' CONTRIBUTION

AVC conceived the study and wrote the manuscript. ECA contributed with the practical performance of the study and supervised all the stages of the study. AVC,RSMM, RAB, CFPR, FRA, JAGD contributed to the practical performances of this research. AVC and ECA contributed in giving critical revisions to the final version and performance of the manuscript.

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