



# Retrospective study of melanocytic neoplasms in dogs and cats

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Submitted August 24<sup>th</sup> 2010, Accepted September 27<sup>th</sup> 2010

## Abstract

Melanoma is one of the most lethal skin neoplasms among dogs and cats, and its incidence is increasing worldwide in the last years. The relation between the study of tumor biology and epidemiologic data from melanocytic tumors (melanomas and melanocytomas) can help in the achievement of an earlier and safer clinical diagnosis. However, epidemiologic data for these neoplasms are still rare in Brazil. Thus, we performed a retrospective study of melanocytic neoplasms in dogs and cats registered at the Animal Pathology Service of the School of Veterinary Medicine and Animal Science (SVMAS), University of São Paulo (USP), between January of 2000 and December of 2006. The epidemiological data extracted from pathology records regarded affected population (age, gender, hair color) and tumor characteristics (anatomic location and histological type). Of 2154 histopathological reports analyzed 193 (8.9%) were melanocytic neoplasms, of which 186 cases in dogs (96.4%) and only 7 in cats (3.6%). Male dogs, of mixed breed, among 8 and 11 years of age and black hair were most affected by melanocytic neoplasms. Histological types most often found were epithelioid cell melanoma mainly located in the buccal cavity, and melanocytomas, located on the skin. Among cats, females between 8 and 11 years of age of mixed breed and black hair were most often affected. Epithelioid melanoma again presented as the most common histological type, located, however, on the skin. In conclusion, this casuistic demonstrated that melanocytic neoplasms develop mostly in middle age dogs with dark hair, in the oral cavity or skin, with histological type of epithelioid cells. Melanocytic tumors are rare in cats when compared to dogs; in our cases, they were diagnosed in middle aged female cats, mostly located in skin, and with epithelioid histological type. Epidemiological data strengthen the importance of early diagnosis of melanocytic tumors in Veterinary Medicine, promoting initiation of the most appropriate therapeutical process, improving diagnosis and promoting animal welfare.

**Key Words:** Epidemiology, dog, cat, melanocytic neoplasm, tumor biology

## Introduction

Melanocytic neoplasms have a high incidence in canines and humans, occurring less often in felines. They originate in melanocytes, the cells responsible for melanine production and derived from neurectodermal melanoblasts, which migrate to the epidermis, dermis, mucosa and eyes during embryogenesis. Melanocytes do not establish intercellular contact among themselves, but form adherent and regulatory junctions with keratinocytes through adhesion molecules known as E-cadherins (10). Any unbalance in the interaction between melanocytes and keratinocytes can lead to

initiation of the tumoral process, resulting in uncontrolled growth and development of a neoplasm (9; 12). Several etiological factors can be related, including consanguinity, trauma, chemical exposure, hormones and genetic susceptibility (22). However, there is no consensus regarding its etiology. (24).

Macroscopically, melanocytic neoplasms are characterized by dark, single lesions shaped as plaques or lobulated, affecting any region of the body and reaching from 1 to 10 cm in diameter (17;28). Microscopically, melanocytic neoplasms can be classified according to histological types, behavior, tissue location and presence of pigment (6;7). Benign

neoplasms are named melanocytomas and subclassified according to cell type; melanoacantoma, a rare subtype with characteristics similar to melanocytomas; compound melanocytoma; dermic or junctional (18). These tumors originate from melanocytes from epidermis, dermis or hair follicles. Malignant neoplasms are named melanoma (24) and are characterized by increased mitotic activity, nuclear pleomorphism and metastatic potential, affecting regional lymph nodes, lungs and other organs (28). Melanomas are classified according to the predominant cell type, as spindle, epithelioid or mixed. Additionally, the presence of melanin is a differential characteristic in this cancer, subdividing melanomas in melanotic or amelanotic (25). A rare form of melanoma is the one composed of giant epithelioid cells (balloon cells).

The melanoma is one of the most lethal cutaneous neoplasms and its incidence worldwide is increasing in the last years, probably due to its rapid evolution and low response to chemotherapy (5; 8; 14). Treatment most often indicated is the radical surgery, however, local recurrence rate varies from 22 to 48% and survival from 9 to 10 months. Notwithstanding, conservative surgery presents recurrence rates up to 70% and mean survival of 3 to 4 months. (21). Thus, the poor prognosis of melanocytic neoplasms augments the importance of epidemiological and tumor biology studies as an aid to the practice of preventive and curative oncology, contributing to the development of new therapeutical procedures.

Epidemiological studies of melanocytic neoplasms concentrate on the USA on the decade of the 1990s. According to data obtained in different US States, dogs are most often affected, mainly in the oral cavity (1; 19; 22; 23, 24; 25). In Brazil, epidemiologic information on animal tumors is scarce. According to Camargo et al., 2008 (3), the oral region was most affected in 19 cases of canine melanomas; however, analysis was only based on macroscopic aspects. Another Brazilian study registered only one case of melanoma in canine skin, in a Poodle, consulted at the University of Espírito Santo do Pinhal (13).

The shortage of epidemiological studies of melanocytic neoplasms in Brazil deprives knowledge about these diseases, as incidence, recurrence and lethality, restricting diagnostic, clinical and therapeutical advances. Therefore, this study aimed to complement epidemiological information regarding melanocytic neoplasms in cats and dogs. Thus, we analyzed histopathological records from the Animal Pathology Service, of the School of Veterinary Medicine and Animal Science, University of São Paulo, from January of 2000 to December of 2006. Main epidemiological data extracted from records regarded the affected population (age, gender and hair color) and tumor characteristics (anatomic location and histological type). Our study found that melanocytic neoplasms develop mostly in middle age canines with dark hair, are located mainly in the buccal cavity, with histological type of epithelioid cells. In cats, melanocytic neoplasms occur more often in middle

aged animals, with dark hair, located mainly in skin, with histological type of epithelioid cells.

## Material and Methods

### *Casuistic*

We analyzed histopathological records of canine and feline melanocytic neoplasms registered in the Animal Pathology Service of the Department of Pathology, School of Veterinary Medicine and Animal Science (SVMA), University of São Paulo, Brazil, between January of 2000 and December of 2006. Epidemiological data extracted were affected population (age, gender, breed and hair color) and tumor characteristics (anatomic location and histological type).

### *Histopathological Analysis*

Nomenclature of melanocytic neoplasms was adopted in conformity with the World Health Organization in 1998 (7). Morphological classification of tumors was revised by two veterinary pathologists in slides stained with hematoxylin-eosin (H&E). All neoplasms were reevaluated according to its behavior (melanocytoma vs melanoma), their histological type and the presence or absence of melanin (melanotic vs. amelanotic).

### *HMB-45 Immunohistochemistry*

Anti-melanosome HMB-45 antibody is a specific marker of immature melanocytes and was employed in order to confirm the diagnosis in amelanotic melanomas. Immunostaining was performed as previously described by Hsu et al., 1981(11), with modifications. Briefly, histological samples in silanized slides were deparaffinized, hydrated and endogenous peroxidase was blocked with a methanolic solution of hydrogen peroxide (6%) for 30 minutes. Potassium permanganate and oxalic acid were employed in order to remove melanin, as described by Sulaimon (26). Slides were incubated with monoclonal antibody anti-melanosome HMB45 clone (*DakoCytomation*), 1:50, overnight in humidified chamber at a 4 °C. Then, slides were incubated with reagents from the kit LSAB+System HRP (*DakoCytomation*) as per manufacturer specifications. Slides were developed in a solution containing diaminobenzidine (DAB) and hydrogen peroxide and counter-stained with hematoxylin.

## Results and Discussion

In the period between January of 2000 and December of 2006 the Animal Pathology Service of the University of São Paulo School of Veterinary Medicine and Animal Science registered 2154 reports, of which 193 (8.9%) corresponded to melanocytic neoplasms in cats and dogs. Initial analysis showed that the incidence of melanocytic neoplasms was significantly higher in canines (186; 96.4%) when compared to felines (7; 3.6%). According to Smith et al., 2002 (24), melanoma is a relatively common disease in dogs,

responsible for 7% of all malignant tumors. Nevertheless, cats rarely develop these neoplasms.

In canine, 43 melanocytomas (23.1%) and 143 melanomas (76.9%) were found. In feline, only one melanocytoma (14.3%) and six melanomas (85.7%) were found. Corroborating our epidemiological results, Schultheiss (2006) presented a casuistic of 46 melanocytic neoplasms in dogs, also finding a higher prevalence of melanomas (69.5%). Camargo et al., 2008 (3) presented contradictory results when compared to our findings, stating a higher prevalence of melanocytomas (67.2%) in canine species. However, that study was performed only with melanocytic neoplasms located on the skin and digits, disregarding the main site of melanoma development, which is located in the oral mucosa.

Cats and dogs of mixed breed were most often affected by melanocytic neoplasms, including small, medium and large dogs (Table 1). These results are in disagreement with the findings of Camargo et al., 2008 (3), where a higher prevalence of melanocytomas in Schnauzer dogs was observed. Generally, the difference between breed profiles can simply reflect changes in popularity of a breed in a certain moment or reflect local population and its cultural aspects (23). According to Modiano et al., 1999 (16), the reason for breed predilection is not yet clear. Canine and feline with dark hair were most often affected by melanomas,

yet the development of this neoplasm is not reportedly associated with sun or skin pigmentation in animals.

Melanocytic neoplasms were more prevalent in male animals (Table-1), what was also observed in a casuistic by Camargo et al., 2008 (3). In addition, Perrone, 2001 (20) and Muller et al., 2001 (18) found a higher prevalence in females, while other authors disagree with gender predisposition in melanocytic neoplasms (2; 22; 23; 24). Our results demonstrated that canine and feline between 7 and 11 years of age were most often affected, as reported by Spangler and Kass, 2006 (25). Of 143 cases of melanoma described in canines, buccal cavity was the main site (57 cases – 39.86%), followed by the skin (44 cases - 30.77%), eye (21 cases – 14.69%), digits (17 cases – 11.88%) and scrotum (4 cases – 2.78%) (Table 2). The location of melanoma in the oral cavity of dogs is associated with decreased survival when compared to dermic location (15). Spangler and Kass, 2006 (25) found mortality of 68% in dogs with melanoma in buccal cavity versus 7% in dogs with skin melanoma. The reason for this difference in mortality is still unknown, but it is believed that some factors can have a negative influence on survival, such as difficult surgical resection with adequate margins, decreased immunologic response, alterations of tumor biology and abundant vascularization in the region (15).

Table 1 – Features of breeds, gender and age of animals affected by melanocytic neoplasms.

Species	Dogs		Cats		Dogs		Cats	
	Melanomas	143 (76.9%)	6 (23,1%)	Melanocytomas	43 (85,7%)	1(14,3%)		
Breeds	Without defined breed (WDB)	55 (38,46%)	4(66,7%)	Without defined breed (WDB)	8 (18,6%)	1 (100%)		
	Rottweiler	18 (12,59%)	-----	Boxer	5 (11,63%)	-----		
	Poodle	12 (8,39%)	-----	Cocker	5 (11,63%)	-----		
	Cocker	11 (7,69%)	-----	Doberman	5 (11,63%)	-----		
	Boxer	10 (6,99%)	-----	Poodle	3 (6,97%)	-----		
	German Shepherd	8 (5,59%)	-----	Schanauzer	2 (4,65%)	-----		
	Daschund	5 (3,49%)	-----	Others	15(34,88%)	-----		
	Labrador	5 (3,49%)	-----					
	Siamese	-----	2(33,3%)					
	Others	19(13,29%)	-----					
Gender	Males	80 (55,94%)	2 (33,3%)	Males	27(62,79%)	1(100%)		
	Females	63 (44,06%)	4 (66,7%)	Females	16(37,2%)	-----		
Age	0-3 years	12 (8,39%)	-----	0-3 years	-----	-----		
	4-7 years	33 (23,07%)	-----	4-7 years	10(23,26%)	1(100%)		
	8-11 years	72 (50,35%)	6 (100%)	8-11 years	23(53,49%)	-----		
	12-15 years	26 (18,2%)	-----	12-15 years	10(23,26%)	-----		

Concerning histological types, our results showed a higher prevalence of melanocytoma (20 canines and 1 feline) and of epithelioid melanoma (52 canines and 6 felines) (Table 2). Similar data were found by Millanta et al., 2002 (15), with prevalence of epithelioid melanomas (31%) in canine and by Spangler and Kass, 2006 (25), with prevalence of 65.7% of the same histological type. However, some

authors suggest that mixed melanomas are more common in dogs (4; 22; 27). Although preliminary studies indicate that histological type can correlate to prognosis in ocular melanocytic neoplasms, the same is not valid for other sites as oral cavity, skin and digits (16). Thus, aggressiveness can not yet be attributed to tumor histological type (15).

Table 2 - Morphologic diagnosis, anatomical localization and color of animals affected by melanocytic neoplasms.

Species	Melanomas	Dogs	Cats	Melanocytomas	Dogs	Cats
		143 (76,9%)	6 (23,1%)		43 (85,7%)	1 (14,3%)
Histological Subtypes	Epithelioid	52 (36,6%)	6 (100%)	Melanocytomas	20 (46,51%)	1 (100%)
	Spindle	37 (25,87%)	-----	Compounds	11 (25,58%)	-----
	Miscellaneous	13 (9,09%)	-----	Junctional	2 (46,51%)	-----
Melanin Production	Amelanotic	21 (14,67%)	-----	Dermic	6 (13,95%)	-----
	Melanotic	15(10,49%)	-----	Cel. of Balloon	4 (9,3%)	-----
Location Tumor	Buccal Cavity	57 (39,86%)	2(33,3%)	Skin	25 (58,14%)	1 (100%)
	Skin	44 (30,77%)	3 (50%)	Eyelid	8 (18,6%)	-----
	Ocular Globe	21(14,69%)	1(16,7%)	Perianal Region	4 (9,3%)	-----
	Digits	17(11,88%)	-----	Buccal Cav.	4 (9,3%)	-----
	Scrotum	4 (2,78%)	-----	Digits	2 (4,65%)	-----
	Cilliary Body	5 (3,49%)	-----			
Hair Colour	Black	75 (52,45%)	2(33,3%)	Black	22 (51,16%)	1 (100%)
	Golden	38 (26,57%)	2(33,3%)	Gray	11 (25,58%)	-----
	Gray	20 (13,98%)	-----	Golden	9 (20,93%)	-----
	White	10 (6,9%)	2(33,3%)	White	1(2,32%)	-----

In conclusion, this casuistic demonstrated that according to the record of the Service of Animal Pathology of the SVMAS, USP, melanocytic neoplasms were found more often in middle aged canines with dark hair, without defined breed, with location in oral cavity, and histological type of epithelioid cells. Melanocytomas were also found in dogs, located only in skin. In cats, melanomas were more common than melanocytomas. They were seen, in middle aged cats with dark hair, without defined breed, and located in skin, with histological type of epithelioid cells.

Epidemiological data here presented have shown up that dark haired and dark skinned animals (both dogs and cats) may present a predisposition to the development of melanocytic neoplasms. This information, however, merits further investigation.

The aim of any study focusing animal cancers is to call the attention of veterinarians to these diseases, in an attempt to promote early diagnosis and the initiation of the most proper therapeutical procedure, improving prognostic and promoting animal welfare.

#### Acknowledgements

This study is part of the thesis of Tarso Felipe Teixeira at the Experimental and Comparative

Pathology Program of the School of Veterinary Medicine and Animal Science of the University of São Paulo, Brazil. Tarso was the recipient of a fellowship from Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq).

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