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Tumors of the Eye and Ocular Adnexa in Cats and Dogs

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ABSTRACT

Objective: The present study aimed to determine the frequency of canine and feline ophthalmic tumors, as well as to characterize the affected population, based on 287 cases of ophthalmic tumors from the Lisbon region, Portugal.

Procedures: A retrospective study (2001-2013) involving 214 canine and 73 feline ophthalmic tumors was conducted. Clinical data including species, breed, age, gender, affected ophthalmic structures, surgical treatment and histopathological diagnosis were analysed. Statistical analysis was performed using R-Statistics® and Microsoft Office Excel 2007®.

Results: Considering the canine population, 69.6% of the ophthalmic tumors were benign while 84.9% of feline ophthalmic tumors were malignant. In both species, the eyelids were the ocular adnexal structure most affected by neoplasms, which represented 65.4% of canine adnexal tumors and 34.2% of feline adnexal tumors. Regarding dogs, 64.3% of the eyelid neoplasms corresponded to meibomian gland tumors. Concerning the ocular globe, the structure most affected by neoplasms was the uvea for both dogs (45.5%) and cats (48.4%). In cats, iridal tumors comprised 80% of the uveal tumors. Epithelioma (22.4%) and adenoma (15.4%) of the meibomian glands were the most frequent ophthalmic tumors in dogs, while diffuse iris melanoma (11.0%) and squamous cell carcinoma of the eyelids (13.7%) were the most common in cats.

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Conclusion: In this study, a high frequency of eyelid and uveal neoplasms was seen in both the canine and feline populations. Moreover, a considerably high frequency of ocular globe neoplasms was present in cats when compared to dogs. The majority of canine ophthalmic tumors were benign whereas in cats they were malignant. Knowing the frequency, location and histological classification of ophthalmic tumors in cats and dogs from Portugal will help us to better understand their biological behavior.

Key words: Ophthalmic Tumors; Histological Diagnosis; Prevalence; Dogs; Cats

INTRODUCTION

The average life expectancy of companion animals has been increasing, which may be the reason for a higher incidence of neoplasms occurring in cats and dogs throughout the past few decades.

According to some authors, tumors are the most frequent cause of death in dogs (47%) and cats (32%) [1]. As stated by Miller and Dubielzig, 0.87% of canine tumors and 0.34% of feline tumors affect the ophthalmic area. They also believed that these results could be underestimated because many excised tumors were considered benign and would not be submitted for histological evaluation [2]. A study using data from the Comparative Ocular Pathology Laboratory of Wisconsin **(COPLOW)** analyzed 20219 cats and dogs with ocular diseases and concluded that 39% of the feline and canine ophthalmic diseases were neoplastic [3], which reveals the importance of neoplasms in veterinary ophthalmology. Another study refers that 47% of canine ophthalmic tumors was located in the ocular globe, being 64.6% melanocytic tumors and 29.3% iridociliary epithelium tumors [4]. About 25.3% of the canine ophthalmic tumors are located in the conjunctival tissue, 23.1% in the eyelids and 4,6% in the orbit [5]. No gender predisposition was found in any of the canine ocular neoplasms [4]. The majority of neoplasms had a typical age distribution, affecting middle-age to old dogs (mean 9.2 y/o and median 9.5 y/o) [4]. A breed predisposition was found in some studies, being more relevant the next examples: spindle cell carcinoma in blue-eyed breeds like Siberian Husky and Australian Shepard; squamous cell carcinoma in the Pug; conjunctival hemangiosarcoma in the Border Collie, Australian Shepard, English Setter, Basset Hound, Beagle and Boxer; eyelid melanoma in the Vizsla and Doberman Pinscher [5].

The most common cause of enucleation in cats is the ophthalmic neoplasm [6]. Some studies identified the iris melanoma as the most common tumor in the feline ocular globe. However, these studies did not include recently characterized neoplasms such as the feline restrictive orbital myofibroblastic sarcoma and the conjunctival adenocarcinoma, and did not discriminate the several subtypes of feline ocular post-traumatic sarcoma [6]. A study using data from the COPLOW concluded that 81.7% of the feline ophthalmic tumors was in the ocular globe, of which 82.1% corresponded to melanocytic tumors [6]. Conjunctival neoplasms represented 12.2% of the feline ophthalmic neoplasms. On the other hand, eyelid and orbital neoplasms corresponded

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to, respectively, 4.2% and 1.8% of the feline ophthalmic neoplasms [6]. Intraocular tumors were most commonly seen in middle-age to old cats, being the mean age 10.6 y/o and the median 11 y/o [6]. Feline ocular post-traumatic sarcoma showed a higher prevalence in male, rather than female cats [6]. Older cats with a mean age of 11.8 y/o presented with a considerably higher prevalence of squamous cell carcinoma, comparing to other ophthalmic neoplasms. Concerning breeds, Persians are one of the most predisposed to the development of ocular globe melanocytic tumors [6].

It is important for a veterinary clinician to have some knowledge about the epidemiology of ocular tumors because macroscopic similarities could mean very different clinical courses depending on the species, breed, age and tumor's location, stage and histopathologic characteristics. Therefore, the present study aimed to determine the frequency of canine and feline ophthalmic tumors, as well as to characterize the affected population, based on 287 cases of ophthalmic tumors from the Lisbon region Portugal.

MATERIAL AND METHODS

Population Studied

All data was retrieved from the archives of the Pathology Laboratory of the Faculty of Veterinary Medicine - University of Lisbon **(FMV-UL)**, from 2001 till 2013. Data consisted of pathology reports which provided information concerning species, breed, age, gender (intact and neutered), affected ophthalmic structure, surgical treatment performed and histological diagnosis. Unavailable data is presented as "NA".

Tumor Location and Histological Classification

The neoplasms were organized according to (i) location and (ii) histological classification. Regarding the location, five main categories were considered: orbit, conjunctiva, eyelids, nictitating membrane **(nictitans)** and globe. The orbit section included all retrobulbar and periocular tumors and those from the lacrimal duct. The eyelids and the globe were divided into specific structures. Concerning eyelids, Meibomian glands and Moll glands were analyzed separately. The category "globe" was further divided into:

- Fibrous tunic – sclera and cornea
- Vascular tunic – iris, ciliary body and choroid
- Nervous tunic – retina and optic nerve

Results presented as "eyelid", "uvea" or "globe" only correspond to those where the neoplasm affected the entire structure.

Regarding histological classification, tumors were organized according to their embryonic origin and malignancy and grouped, to simplify statistical analysis. Histological classification was adapted from the World Health Organization's Histological Classification of Ophthalmic Tumors of Domestic Animals [7].

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Surgical Treatment

Three surgical approaches were performed: local excision, enucleation, or exenteration of the globe and orbital contents.

Statistical Analysis

Data were stored in Microsoft Office Excel 2007® and statistical analysis was done using R-Statistics®. The statistical unit was the ophthalmic tumor. The population was characterized using descriptive statistic methods, such as mean and standard deviation.

RESULTS

Studied Population

From 2001 to 2013, the Pathology Laboratory of the FMV-UL classified 13597 tissue samples as neoplasms, of which 76.4% (n=10388) belonged to dogs and 23.6% (n=3209) to cats. Our sample was composed of 287 cases of ophthalmic tumors, being 214 canine and 73 feline tumors. Therefore, the ophthalmic neoplasms analyzed in this studied corresponded to approximately 2.1% of the total of canine neoplasms and to 2.3% of the total of feline neoplasms.

Gender

Considering the canine population, gender distribution was as follows: 50.9% (109/214) were intact males, 4.7% (10/214) corresponded to neutered males, 34.6% (74/214) were intact females and 8.4% (18/214) corresponded to neutered females. In 1.4% (3/214) of the cases, gender information was not available. In cats, 37.0% (27/73) of the studied population were intact males, 15.1% (11/73) neutered males, 32.9% (24/73) intact females and 8.2% (6/73) neutered females. Data about gender was not available in 6.8% (5/73) of the cases.

Age

The mean age of both species corresponded to 10.0 ± 3.6 years old. 84.1% (180/214) of dogs and 78.1% (57/73) of cats were older than 6 years old.

Breed

Mongrel dogs were the most represented accounting for 26.6% of the cases (57/214), followed by Labrador Retrievers with 16.4% (35/214), Poodles with 11.2% (24/214) and English Cocker Spaniels with 5.6% (12/214) of the cases. 36 different canine breeds were identified in this study.

Among feline breeds, 78.1% (57/73) of the affected animals were Domestic Shorthair and the two pure breeds identified corresponded to Persian (8.2%; 6/73) and Siamese (5.5%; 4/73). In 8.2% (6/73) of the cases, breed information was not available.

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Tumor Location

Regarding canine ocular adnexal tumors (n=170), the most affected structure was the eyelid (82.4%; 140/170), more specifically the meibomian glands, representing 67.1% (94/140) of the eyelid tumors. The meibomian gland tumors represented 43.9% of the total of ophthalmic neoplasms in dogs (figure 1, table 1). Considering the ocular globe tumors in dogs (n=44), the uvea was the most affected structure, representing 45.5% (20/44) of the globe tumors.

Regarding adnexal tumors in cats (n=42), the most affected structure was the eyelid with 59.5% (25/42) of the cases (figure 1, table 1). Concerning ocular globe neoplasms (n=31), uveal neoplasms were the most common (48.4%; 15/31), more specifically iridal neoplasms that corresponded to 80.0% (12/15) of the feline uveal tumors (figure 1, table 1).

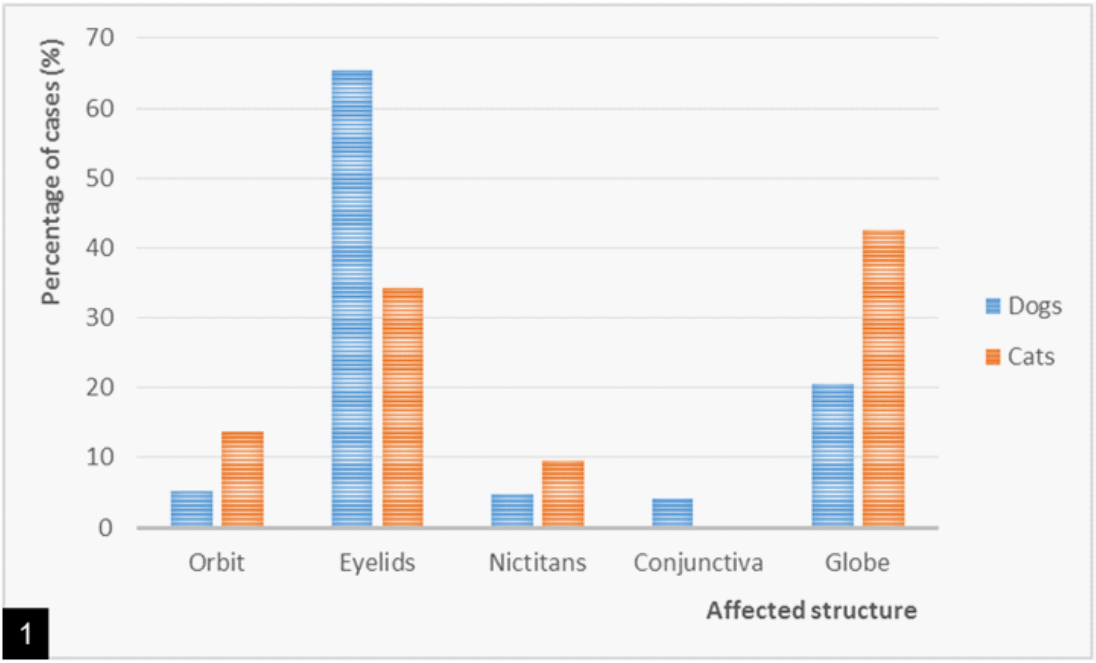

Figure 1: Chart showing the distribution of the neoplasms (%) by ophthalmic structure (orbit, eyelids, nictitans, conjunctiva and globe) in both cats and dogs.

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Table 1: Distribution of the tumors by ophthalmic structure (location) in cats and dogs. Results are presented in units (n) and percentage (%) of the total amount of adnexa and globe tumors in dogs and cats.

Location			Dogs			Cats		
			n	%	total	n	%	total
Adnexa	Orbit		11	6.5	170	10	23.8	42
	Eyelid*	Meibomian gland	94	52.9		6	14.3	
		Moll gland	3	1.8		0	0.0	
		Eyelid**	43	27.6		19	45.2	
	Nictitans		10	5.9		7	16.7	
	Conjunctiva		9	5.3		0	0.0	
Globe	Fibrous tunic	Cornea	4	9.1	44	0	0.0	31
		Sclera	8	18.2		1	3.1	
	Vascular tunic (Uvea)*	Iris	4	9.1		12	38.7	
		Ciliary body	3	6.8		2	6.5	
		Choroid	2	4.5		0	0.0	
		Uvea**	11	25.0		1	3.2	
	Nervous tunic	Retina	1	2.3		1	3.2	
		Optic nerve	2	4.5		0	0.0	
	Globe**		9	20.5		14	45.2	

*∑ Eyelid Dogs = 140; ∑ Uvea Dogs = 20; ∑ Eyelid Cats = 25; ∑ Uvea Cats = 15.

**structure entirely affected by the neoplasm.

Surgical Treatment

On what concerns surgical approaches in canine adnexal tumors, local excision with preservation of the globe was the most frequently used technique (88.2%; 150/170), while enucleation (81.8%; 36/44) was the most common procedure for ocular globe tumors. No exenteration of the ocular globe and orbital contents was performed in dogs with globe tumors. In fact, 7% (15/214) of canine tumors and 21,9% (16/73) of feline tumors were only diagnosed after necropsy.

Similarly to dogs, the most frequent surgical approach in feline adnexal tumors was local excision with preservation of the globe (64.3%; 27/42), while enucleation (61.3%; 19/31) was the most common procedure applied to ocular globe tumors. There were 5 cases (16.1%) in which exenteration of the ocular globe and orbital contents was used to treat feline globe tumors.

Histopathological Diagnosis and Tumor Location

Tumors were grouped according to their histological characteristics, in order to simplify statistical analysis (tables 2 and 3).

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Table 2: Histological distribution of the eye and ocular adnexa neoplasms in dogs. Data are presented in units (n) and percentage (%) of the total amount of neoplasms.

Neoplasm	n	%	Neoplasm	n	%
Adenocarcinoma	4	1.9	Lymphoma	13	6.0
Adenoma	40	18.7	Mast cell tumors	3	1.4
Epithelioma	57	26.6	Melanocytoma	9	4.2
Fibroma	1	0.5	Melanoma	31	14.5
Fibrosarcoma	5	2.3	Meningioma	1	0.5
Hemangioma	1	0.5	Neuroblastoma	1	0.5
Hemangiosarcoma	5	2.3	Neurofibroma	2	0.9
Histiocytic sarcoma	1	0.5	Nodular fasciitis	8	3.7
Histiocytoma	1	0.5	Papilloma	27	12.6
Lipoma	1	0.5	Squamous cell carcinoma	3	1.4

*∑ Adenoma = 40; ∑ Epithelioma = 57; ∑ Melanocytoma = 9; ∑ Melanoma = 31; ∑ Papilloma = 27.

Table 3: Histological classification of the eye and ocular adnexa neoplasms in cats. Data are presented in units (n) and percentage (%) of the total amount of tumors.

Neoplasm	n	%	Neoplasm	n	%
Adenocarcinoma	1	1.4	Mast cell tumors	3	4.1
Adenoma	6	8.2	Melanocytoma	1	1.4
Carcinoma	4	5.5	Melanoma	14	19.2
Ependymoma	1	1.4	Osteosarcoma	3	4.1
Fibrosarcoma	4	5.5	Papilloma	3	4.1
Histiocytic sarcoma	2	2.7	Squamous cell carcinoma	20	27.4
Lymphoma	11	15.1			

*∑ Adenoma = 7; ∑ Melanoma = 14; ∑ Papilloma = 3.

Regarding canine patients, epithelioma, adenoma and melanoma (figure 2) were the most common ophthalmic tumors, representing respectively 26.6% (57/214), 18.7% (40/214) and 14.5% (31/214) from the total of canine ophthalmic tumors (table 2). The majority of ophthalmic neoplasms in dogs were benign (69.6%; 149/214). Concerning the ocular adnexa, the most commonly affected structure was the meibomian gland (n=94), and both the epithelioma (53.3%; 52/94) and the adenoma (35.1%; 33/94) were the most common tumors in this location. Likewise, epithelioma (24.3%; 52/214) (figure 3) and adenoma (15.4%; 33/214) of the meibomian glands were the most frequent canine ophthalmic tumors identified in this study. Regarding canine ocular globe, the uvea (n=20) was the ocular tunic most commonly affected by neoplasms and the melanoma (50.0%; 10/20) was the most frequent neoplasm in this location.

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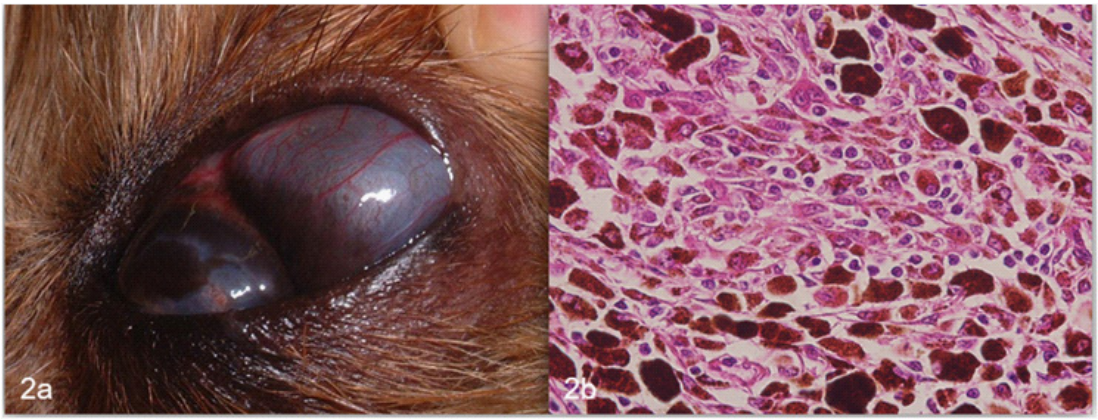

Figure 2: Male dog, Yorkshire terrier, 10 years old, intraocular melanoma of the left eye. 2-A Macroscopic appearance. Note the extensive intraocular pigmented mass that deforms the sclera dorsally between the two white arrows. The cornea has pigment and fibrosis. 2-B Photomicrograph (H & E, x 400).

Figure 3: Mongrel female dog, 12 years old, eyelid papilloma of the left eye. 3-A Macroscopic appearance. Note the large friable ulcerated mass that occupies2/3 of the upper eyelid. 3-B Photomicrograph (H & E, x 40).

Considering feline patients, squamous cells carcinoma (27.4%; 20/73), lymphoma (15.1%; 11/73) and melanoma (19.2%; 14/73) were the most frequent ophthalmic neoplasms (table 3). About 84.9% (62/73) of feline ophthalmic neoplasms were malignant. Regarding ocular adnexal tumors, the eyelid (n=25) was the most affected structure and squamous cell carcinoma (40.0%; 10/25) was the most common tumor in this location. Concerning the ocular globe, the iris (n=12) was the most affected structure and melanoma was the most frequent neoplasm in this site, (91.7%; 11/12) specially the diffuse iris melanoma (72.7%; 8/11). In conclusion, diffuse iris melanoma (11.0%; 8/73) and squamous cell carcinoma of the eyelid (13.7%; 10/73) were the most frequent feline ophthalmic neoplasms identified in this study.

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DISCUSSION

The present study aimed to characterize the population and to determine the frequency of feline and canine ophthalmic neoplasms considering 287 cases from the Lisbon region, Portugal, from 2001 till 2013.

The obtained results concerning ophthalmic tumor frequency in dogs (2.1%) and cats (2.3%) were near to those reported by others which corresponded to 2.5% for dogs and 1.8% for cats [8]. Therefore, our results support the hypothesis that both cats and dogs have approximately the same probability of developing ophthalmic tumors.

There was no significant difference between genders in either species, which is in agreement with the literature [4]. Although Dubielzig et al. have reported a higher prevalence of feline ocular post-traumatic sarcoma in males [3], such tumor was not identified in our study.

Considering the age of the affected animals, it seems that cats and dogs over 6 years old have a higher probability of developing ophthalmic tumors, which is consistent with other studies [4,6,2], although the mean age can vary between authors.

In this study, the most commonly affected canine breeds (Labrador Retriever, Poodle and English Cocker Spaniel) were the same described by Salvado as the most frequent breeds affected by neoplasms, although not specifically ophthalmic [8]. However, according to the Portuguese Kennel Club, the most common breeds in the past 13 years in Portugal [9] nearly match the ones identified in this study, so no conclusion can be drawn regarding the breed predisposition already described in other studies [2,4,6].

Regarding feline breed predisposition, Salvado described Persian and Siamese as the feline breeds more frequently affected by neoplasms, not specifically ophthalmic [8]. However, such statement could not be supported by this study due to the few cases of pure breeds identified.

Regarding tumors' malignancy, our results suggest a tendency for cats to have malignant ophthalmic neoplasms (84.9%) while dogs tend to have benign ones (69.6%), which is in agreement with the literature [6].

Considering histologic classification, the most common tumors identified in dogs were the epithelioma, the adenoma and the melanoma, while in cats it was the squamous cell carcinoma **(SCC)**, the lymphoma and the melanoma, which is in accordance with other authors [4-6,8,10-12].

In our study, epithelioma and adenoma were the most frequently diagnosed canine ophthalmic tumors, which is consistent with Maggs' studies [10,11]. Moreover, they were the most frequent meibomian glands' neoplasms, which is also in agreement with the literature [12-14]. Regarding cats, diffuse melanoma and squamous cell carcinoma were the most common neoplasms found in the iris and in the eyelids, respectively. In addition, both neoplasms were the most frequent in cats, being these results consistent with the literature [3, 6,13,15].

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According to some authors, the eyelids, more specifically the meibomian glands, are the canine ophthalmic structures most affected by tumors, which is consistent with our results [11, 16]. Regarding cats, the most affected locations were the ocular globe, more specifically the uvea, and the eyelids. Some studies are in agreement with these results, except for the high incidence of feline eyelid neoplasms found in this study (34.2%; 25/73) [8, 12]. Mould stated that eyelid tumors were not common in cats and Dubielzig mentioned a prevalence of 4.2% [6, 17]. Considering the portuguese weather conditions with high intensity of solar radiation, the large number of feline eyelid tumors identified could be due to a more frequent and extended exposure to actinic radiation. This information should be subject to further investigation. On the other hand, some possible explanations for a lack of SCC reported in feline eyelids by other authors could be failure to submit these masses to an ophthalmic biopsy service due to presumptive gross diagnosis, or submission without specification of the exact site.

In our studied population, local excision with preservation of the globe was the most common surgical therapy for adnexal tumor in both species, which is consistent with previous studies [18-20]. The higher percentage of exenteration procedures (16.1%) in cats when compared to dogs (0.0%) was probably due to the feline´s higher incidence of intraocular and orbital tumors with a malignant behavior, needing a more aggressive surgical approach.

One limitation of the present study was the lack of information concerning some parameters like macroscopic appearance of the lesions, medical treatment and follow up. In future studies it would be of value to add data concerning immunohistochemical characterization of tumor cells through the use of immunomarkers such as Melan A in melanomas and Ki67 and p53 in malignant tumors. These data, together with follow up studies, could help establish degrees of malignancy with prognostic value.

Early diagnosis and appropriate treatment are essential to restore quality of life and maintaining patient's vision, whenever possible. Improving the knowledge of the biological behavior of ophthalmic tumors in cats and dogs will help veterinary clinicians to decide the best therapeutic choices.

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