

A four year retrospective study of the prevalence of canine follicular tumours in Croatia

Ana Beck^{1*}, Doroteja Huber¹, Valentina Šćuric², Miroslav Benić³,
Marko Hohšteter¹, and Snježana Kužir⁴

¹Department of Veterinary Pathology, Faculty of Veterinary Medicine, University of Zagreb, Zagreb, Croatia

²Graduate, Faculty of Veterinary Medicine, University of Zagreb, Zagreb, Croatia

³Department for Bacteriology and Parasitology, Croatian Veterinary Institute Zagreb, Croatia

⁴Department of Anatomy, Histology and Embryology, Faculty of Veterinary Medicine,
University of Zagreb, Zagreb, Croatia

BECK, A., D. HUBER, V. ŠĆURIC, M. BENIĆ, M. HOHŠTETER, S. KUŽIR:
A four year retrospective study of the prevalence of canine follicular tumours in Croatia. Vet. arhiv 86, 453-466, 2016.

ABSTRACT

Canine follicular tumours (CFT) are an uncommon type of keratin-producing tumours in dogs that develop from different structures of the hair follicle. CFT are classified as infundibular keratinizing acanthoma (IKA), tricholemmoma, trichoepithelioma, pilomatricoma and trichoblastoma. Studies on CFT are rare and most descriptions of these tumours are presented as case reports. Thus, we performed a retrospective study to investigate the prevalence and types of CFT within the Croatian canine population. The study included all CFTs presented to the Department of Veterinary Pathology in a 4 year period (2009 to 2012). In the investigated period, 714 skin tumours were diagnosed, from which only 69 presented as CFT: 10 IKA, 21 pilomatricoma, 1 malignant pilomatricoma, 12 trichoepithelioma, 4 malignant trichoepithelioma and 21 trichoblastoma. No breed or gender predisposition was found. However, pilomatricoma was mostly diagnosed in breeds with continuous hair growth, while IKAs were mostly found in breeds without continuous phase hair growth coats. Tumours were mostly presented as nodules and rarely as warts or plaques, growing in the dorsal aspect of the skin on the head, back and hind legs. CFT still represent a small number of tumours compared to other types of neoplasia diagnosed in Croatian canine patients. In the majority of cases, these tumours consist of a benign proliferation. However, in 7.2 % of CFT an infiltrative malignant form was diagnosed. Keratin-filled skin nodules are therefore required for histopathological evaluation to avoid the unfavorable consequences of malignant spread.

Key words: dog, pilomatricoma, trichoepithelioma, trichoblastoma, IKA, prevalence in Croatia

*Corresponding author:

Assist. Prof. Ana Beck, DVM, Department for Veterinary Pathology, Faculty of Veterinary Medicine, University of Zagreb, Heinzelova 55, 10000 Zagreb, Croatia, Phone: +385 1 2390 310; E-mail: abeck@vef.hr

Introduction

Hair follicles are unique structures found only in mammalian skin. They also represent the starting point for skin follicular tumour development, described so far exclusively in humans and domesticated animals (HENDRICK et al., 1998; ROSAI and ACKERMAN, 2010; MYERS, 2014). Compared to felines, equids and ruminants, domesticated canines seem to be the species with the highest occurrence and diversity of hair follicle origin neoplasms reported (HENDRICK et al., 1998; GROSS et al., 2005; MAULDIN and PETERS-KENNEDY, 2016). Canine follicular tumours (CFT) are a diverse group of mostly benign common, uncommon to extremely rare skin tumours (GROSS et al., 2005).

According to the World Health Organization, CFTs are classified into the five types based on the follicular epithelial type, as: infundibular keratinizing acanthoma (IKA), tricholemmoma, trichoepithelioma, pilomatricoma and trichoblastoma. IKA consists of adnexal keratinocytes of the infundibular and isthmic regions of the hair, that keratinize through a sparse granular layer.

Bulb type tricholemmoma is built from small polyhedral glycogen-rich keratinocytes which poorly keratinize without the presence of keratohyalin granules. Isthmic type tricholemmoma consists of small keratinocytes with pink glassy cytoplasm without keratohyalin or trichohyalin granules. Trichoepithelioma consists of a mixture of three cell types: small basaloid epithelial cells of the hair bulb type, keratinocytes exhibiting transition to squamous epithelium containing glycogen, and keratinocytes with trichohyalin granules. Pilomatricoma grows from the germinative cells of the follicular matrix which are small basaloid epithelial cells. Trichoblastomas are composed of small basaloid epithelial cells which recapitulate primitive hair germ. Very rarely primitive hair germ cells may have a polyhedral shape and markedly glycogenated cytoplasm (HENDRICK et al., 1998; GROSS et al., 2005).

IKA is uncommon in dogs. It originates from the infundibular portion of the hair follicle. Canines may develop two types of tricholemmomas which are both very rare: the bulb types arise from the inferior segment of the external root sheath, while the isthmic types arise from the isthmic segment of the external root sheath. Trichoepitheliomas are fairly common in dogs, as tumours which arise from germinative cells and exhibit rudimentary differentiation towards all three segments of the follicle. Pilomatricomas are uncommon in dogs, and are derived from the germinative cells line of the hair bulb (hair matrix) cells (HENDRICK et al., 1998; GROSS et al., 2005). Trichoblastomas are common neoplasms in dogs, derived from the remnants of the primitive hair germ of embryonic follicular development. They are divided into four primary histological subtypes: ribbon, trabecular, granular and spindle cell. Ribbon type trichoblastomas occasionally develop an outer root sheath differentiation pattern (MAULDIN and PETERS-KENNEDY, 2016). Within all of the listed tumours, despite the level of hair follicle epithelial differentiation,

accumulation of keratinocytes and/or keratin is mandatory because neoplastic cells unavoidably undergo gradual-indirect and abrupt-direct cornification (GROSS et al., 2005). Trichoepitheliomas, pilomatricomas and advanced stages of IKA are composed of simple or multiloculated cysts, filled with lamellar or matrixal keratin (GOLDSCHMIDT and HENDRICK, 2002; GROSS et al., 2005). Tricholemmomas may contain small foci of tricholemmal keratinization, while trichoblastomas are a single variant of CFT composed of primitive hair germ epithelial cells without prominent keratin accumulations (GOLDSCHMIDT and HENDRICK, 2002; GROSS et al., 2005). The vast majority of listed trichogenic adnexal tumours are benign. Although extremely rare malignant forms of trichoepithelioma and pilomatricoma are encountered in dogs (ABRAMO et al., 1999; HARDISSON et al., 2001). Clinical presentation on the skin of dogs affected with benign or malignant CFT is unspecific, presenting mostly as well demarcated dermal or subcutaneous solitary or multiple proliferations, which may affect all regions of the skin (GROSS et al., 2005). CFT lesions may appear as dome-shaped, oval, nodular or plaque-like structures, with or without epidermal involvement, and, in cases of IKA, accompanied with pore or keratin horn formation (GOLDSCHMIDT and HENDRICK, 2002; GROSS et al., 2005).

In order to investigate the prevalence and types of CFT within the population of Croatian dogs, we provide a retrospective study using the available quota of domesticated canine skin tumours collected over a period of four years. All available clinical data related to collection of CFTs found were analyzed to expand the knowledge about these uncommon skin tumours.

Materials and methods

The Department of Veterinary Pathology, Zagreb is the main national veterinary service which provides histopathological analysis of tumours in domestic animals. The vast majority of biopsies and necropsies originating from Croatian dogs are processed there, resulting in the formation of a national referral canine neoplasm database (ŠOŠTARIĆ-ZUCKERMANN et al., 2013). We searched this database for the presence of samples of canine skin nodules primarily diagnosed as IKAs, tricholemmomas, trichoepitheliomas, pilomatricomas and trichoblastomas. The selected samples consisted of biopsy request forms accompanied by histology and/or necropsy reports. In this survey, we focused on canine skin tumour samples received between January 2009 and December 2012. Data on the breed, gender and age of all dogs diagnosed with CFT were collected and classified. In order to estimate the possibility of higher mitotic potential of epithelial cell types in the investigated CFT, we classified affected dog breeds into two groups, according to coat growing characteristics: (a) breeds with continuously-growing coats, with larger cell pools for neoplastic transformation, and (b) breeds with phase-growing coats (hair grows to a specific length and then stops growing), with lower neoplastic transformation potential (GROSS et al., 2005). We searched the archival database for clinical information

on nodule growth location (head, neck, chest, abdomen, back, front legs, hind legs and the tail) and for the presence of single and multiple synchronous or asynchronous CFT lesions. We also recorded and analyzed tumour dimensions expressed in millimeters, growth distribution pattern (solitary or multicentric), the presence of alopecia, ulcerations and pore formation within adjacent skin.

Results

Over a period of four years, a total of 714 canine skin neoplasms of different origins were diagnosed. Only 69 out of 714 neoplasms (9.7 %) were classified as canine tumours of follicular origin. These could be sub-classified into: 10/69 IKA, 21/69 pilomatricomas, 1/69 malignant pilomatricoma, 12/69 trichoepitheliomas, 4/69 malignant trichoepitheliomas and 21/69 trichoblastomas. No single feature of tricholemmal morphology was detected within the pool of investigated CFTs, meaning that tricholemmoma was the single follicular tumour type not found in this survey. CFT were mostly diagnosed in different pure-breed dogs (48/65), and in 17 mixed-breed dogs (Table 1). From 65 dogs found to suffer from CFT in this survey, both genders were almost equally represented: 32 males and 33 females. The youngest animal in this survey was a one year old Cairn Terrier with pilomatricoma, while the oldest dog diagnosed with trichoepithelioma was a 14 year old Yorkshire Terrier. The distribution of age of the investigated dogs is presented in Fig. 1. A detailed presentation of the signalment of the investigated dogs, with information on the diagnosed tumour in each case, is presented in Table 1. The vast majority of tumours were present as a solitary lesion (61 dogs). Only four dogs were diagnosed with multiple CFTs. A German Shepherd was diagnosed with double lesions: IKA on the back and pilomatricoma on the hind leg. One Yorkshire Terrier and a Labrador Retriever were found to have two synchronous trichoepitheliomas. The Yorkshire Terrier had one trichoepithelioma located on the head and one on the abdomen, while the Labrador Retriever presented with a trichoepithelioma growing in the skin on the neck and one on the back of the animal. A cross breed dog had trichoepithelioma on the front leg and a malignant trichoepithelioma on the back. The skin of the dorsal aspect of the head (21.1 %), the back (31 %) and hind legs (22.5 %) were found to be the most common sites of CFT growth location. An overview of all anatomical locations of CFT growth, from all analyzed cases, is presented in Fig. 2.

IKAs represented 1.4 % of investigated skin tumours and 14.5 % of investigated CFTs. They were mostly detected in pure-breed dogs (80 %). Some affected dogs had continuous growth of their coat (37.5 %). Sixty percent of the animals with IKAs were males. The mean age of affected dogs was 7.6 years (range 4-10 years). IKAs were mostly located on the back (6 cases, Fig. 2). All IKAs presented as nodules. The mean diameter of investigated IKAs was 19.3 mm (range 5 to 50 mm). The epidermis above the lesion was alopecic in 80 %, alopecic and ulcerated in 10 %, and unremarkable in 10 %. Pores were present in 70 % of cases. A cutaneous horn emerging from the pore was found in one third of cases with pore formation. There was well demarcation in 90 % of cases, while

the case of a poorly demarcated IKA was recorded in a German Shepherd, with double lesions.

Table 1. Breed, gender and age of animals diagnosed with follicular tumours. M- male gender; F- female gender; ? - data not available

Diagnosis	Breed	Gender	Age (years)
Infundibular keratinizing acanthoma	German Shepherd	M	10
	Scottish Terrier	F	6
	German Shepherd	F	11
	German Shepherd	F	8
	Tibetan Terrier	F	7
	Mixed-breed	F	4
	German Shepherd ¹	M	8
	Mixed-breed	F	7
	Airedale Terrier	M	7
Pilomatricoma	Miniature Poodle	M	8
	Maltese	M	3
	Cane Corso	F	5
	Mixed-breed	M	2
	Yorkshire Terrier	M	7
	West Highland White Terrier	F	3
	Cairn Terrier	F	9
	Cairn Terrier	M	4
	Mixed-breed	M	5
	Golden Retriever	M	9
	Cairn Terrier	M	1
	Terrier	M	3
	Miniature Poodle	M	2
	Mixed-breed	M	5
	Briard	F	8
	Kerry Blue Terrier	M	2
	Mixed-breed	F	9
	Standard Poodle	F	?
	Mixed-breed	F	10
	German Shepherd ¹	M	8
Kerry Blue Terrier	M	2	
Standard Poodle	F	10	
Malignant pilomatricoma	German Shepherd	M	7

Table 1. Breed, gender and age of animals diagnosed with follicular tumours. M- male gender; F- female gender; ? - data not available

Diagnosis	Breed	Gender	Age (years)
Trichoblastoma	Samoyed	F	5
	Miniature Poodle	F	6
	West Highland White Terrier	M	9
	Miniature Poodle	F	11
	West Highland White Terrier	M	6
	Mixed-breed	M	9
	Cocker Spaniel	F	4
	Mixed-breed	F	12
	Mixed-breed	F	5
	Mixed-breed	M	8
	Miniature Poodle	F	2
	Standard Poodle	M	13
	English Cocker Spaniel	M	9
	Anatolian Shepherd	M	4
	Mixed-breed	F	4
	Sarplaninac	F	8
	Bernese Mountain Dog	F	4
	Golden Retriever	M	8
	Brittany	F	7
	Newfoundland	F	4
Mixed-breed ²	M	9	
Trichoepithelioma	Mixed-breed	F	8
	Mixed-breed ³	F	10
	American Staffordshire Terrier	M	5
	Golden Retriever	M	9
	German Pointer	M	10
	Yorkshire Terrier ⁴	M	14
	Labrador Retriever ⁴	F	11
	Mixed-breed	F	12
	Mixed-breed	F	5
	Old English sheepdog	M	10
Malignant trichoepithelioma	Mixed-breed ³	F	10
	Pit bull terrier	F	2
	Rottweiler	M	6
	Cavalier King Charles Spaniel	F	6

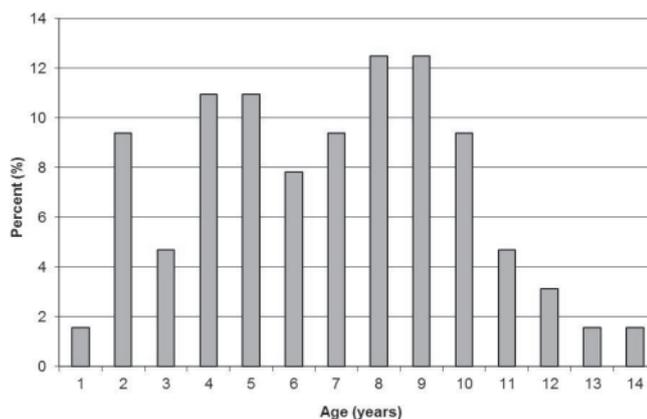


Fig. 1. Distribution of ages in the investigated dogs

Trichoepitheliomas represented 1.7 % of diagnosed skin tumours and 17.4 % of investigated CFTs. In 66.7 % of cases, trichoepitheliomas were detected in pure-breed dogs. In 33.3 %, continuous coat growth was present. The male to female ratio was 1:1. The mean age of affected dogs was 9.9 years (range 5-14 years). The most common location of growth was the back (7 cases, Fig. 2). Diagnosed lesions had average diameter of 37.5 mm (range 8 to 100 mm). These tumours were presented as nodules (83.4 %), plaques (8.3 %) or warts (8.3 %). The skin was alopecic (33.3 %), alopecic and ulcerated (41.7 %) or unremarkable (25 %). The tumours were mostly well demarcated (75 %), while only 25 % showed poor demarcation from the surrounding tissue.

Malignant trichoepitheliomas represented 0.6 % of skin tumours and 5.8 % of investigated CFTs. In 75 % of cases, they were detected in pure-breed dogs, but also in one female. All cases were from dogs with a phase-growing coat. The mean age of affected dogs was 6 years (range 2-10 years). These tumours were mostly found on the back (2 cases, Fig. 2). The majority of these tumours presented as nodules, with only one dog presenting with a wart. In 50 % of cases, alopecia and ulcers were present in the epidermis above, in 25 % only alopecia was present, and in another 25 % the epidermis was unremarkable. All malignant trichoepitheliomas were poorly demarcated and showed infiltrative growth into the adjacent, surrounding tissue.

Pilomatricomas represented 2.9 % of the investigated skin tumours and 30.4 % of the investigated CFTs. They were mostly detected in pure-breed dogs (76.2 %). In 80 % of dogs continuous hair growth was present. These tumours were mostly found in males (62 %). The mean age of affected dogs was 5.1 years (range 1-10 years). Pilomatricomas were

mostly found on the back and hind legs (8 cases each, Fig. 2). They were presented as skin nodules and as a wart in a single case. The mean diameter of investigated pilomatricomas was 22.3 mm (range 2 to 70 mm). In nearly half of the cases (47.6 %), the epidermis was unremarkable. Otherwise, the epidermis was alopecic (38.1 %) and/or ulcerated (14.3 %). In 76.2 % of pilomatricomas, sharp demarcation was recorded.

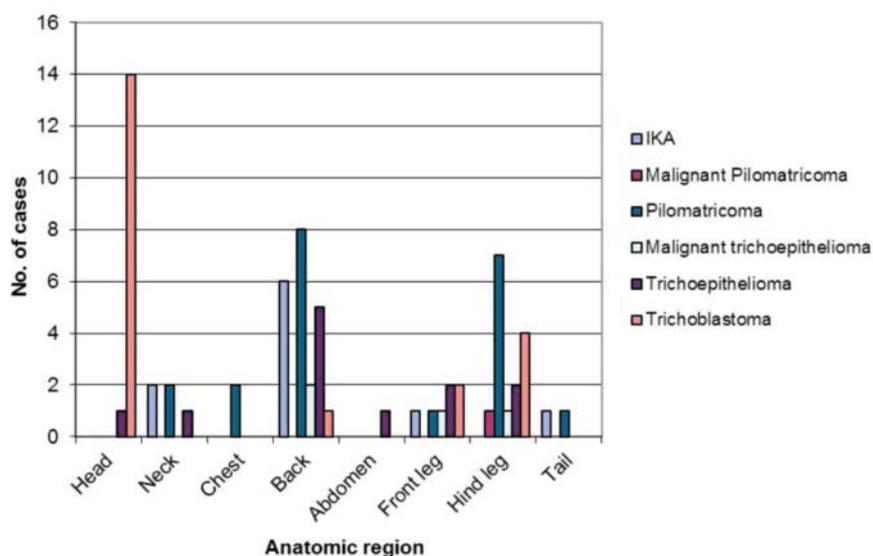


Fig. 2. Detailed view on the anatomical location of diagnosed tumours. IKA - infundibular keratinizing acanthoma.

The one malignant pilomatricoma was a solitary infiltrative nodule, located in the dermis of the hind leg of a 7-year old, male German Shepherd. The diameter of the ulcerated and alopecic nodule was 60 mm.

Finally, trichoblastomas accounted for 2.9 % of skin tumours and nearly a third (30.4 %) of the investigated CFTs. Pure-breed dogs were more prevalent (71.4 %) than cross breed dogs (28.6 %). In 40 % of dogs with diagnosed trichoblastoma, a continuous coat growth was present. The male to female ratio was almost equal (43:57 %). The mean age of affected dogs was 7 years (range 2-13 years). The most common location of growth was the head, more precisely at the base of the ears (14 cases, Fig. 2). The mean diameter of the lesions were 32.2 mm (range 6 to 70 mm). They presented as nodules (90.5 %) or warts (9.5 %), with a solitary pattern of distribution. Alopecia was present in 71.4 % of cases while alopecia and ulcers were found in 23.8 % of cases. In 4.8 % of cases,

the epidermis was unremarkable. They were mostly well demarcated (76.2 %). Poor demarcation was seen in a minority of cases (23.8 %).

Discussion

CFTs display the complexity of hair follicle structure through hyperproduction of cells from one of three different epithelial segments (the infundibular segment-outer root sheath, isthmic segment- outer root sheath and inferior segment-outer root sheath, inner root sheath, hair bulb).

Microscopic recognition of one of nine possible follicle epithelial types (1. adnexal keratinocytes of infundibular and isthmic region, 2. small polyhedral glycogen-rich keratinocytes which poorly keratinizes, without the presence of keratohyalin granules, 3. small keratinocytes with pink glassy cytoplasm, without keratohyalin or trichohyalin granules, 4. small basaloid epithelial cells of hair bulb type, 5. keratinocytes exhibiting transition to squamous epithelium containing glycogen, 6. keratinocytes with trichohyalin granules, 7. germinative cells of the follicular matrix, 8. basaloid epithelial cells which recapitulate primitive hair germ, 9. primitive hair germ polyhedral cells, with markedly glycogenated cytoplasm) as the dominant pattern within CFTs is crucial for diagnosis selection within the five established canine follicular tumour types (HENDRICK et al., 1998; GROSS et al., 2005). Criteria certain for histomorphological determination of CFT were proposed by the World Health Organization (WHO) International Histological Classification of Tumors of Domestic Animals (HENDRICK et al., 1998) and later detailed by GROSS et al. (2005). Created to help distinguish between CFTs types and also to discriminate CFTs from other skin basal and squamous cell tumours, characterized by similar morphological pattern (HENDRICK et al., 1998; GROSS et al., 2005), these criteria are crucial for slide readers in veterinary pathology.

Using these WHO tumour classification criteria, we found CFTs in this four year period survey to be a rare skin tumour in Croatian dogs, with an prevalence of 9.7 % amongst all diagnosed skin tumours. The low prevalence was expected on the basis of a survey on CFTs carried out in central Italy by ABRAMO et al. (1999) where, in a period of 12 years, 10.4 % of CFT and follicular tumour-like lesions were found from a total of 4005 skin biopsies.

The most prevalent CFT in Italy was trichoblastoma, followed by IKA, pilomatricoma, trichoepithelioma and tricholemmoma (ABRAMO et al., 1999). In the Croatian dog population investigated, the most prevalent tumours were both trichoblastoma and pilomatricoma, followed by trichoepithelioma and IKA. In our survey, tricholemmomas were not found, in contrast to the Italian study, where this rare CFT type was recorded, but with the lowest prevalence rate of all tumour types investigated (ABRAMO et al 1999). Due to the low number of cases, the true prevalence/incidence of CFTs is unknown, but

published estimates are based on the studies of ABRAMO et al. (1999) and GOLDSCHMIDT and HENDRICK (2002). The problem in prevalence/incidence estimations in all published studies, as well as in dermatopathology texts which cite those studies, is the fact that the terms “prevalence” and “incidence” are intermingled and differently calculated. Namely, prevalence is defined as the number of affected animals, by disease within the investigated population (THRUSFIELD, 2007). Incidence is calculated differently, by dividing the number of new cases of disease by the number of animals within the population in a defined period of time (THRUSFIELD, 2007). The study published by ABRAMO et al. (1999) used the prevalence calculation for presenting the results, but the dermatopathology texts by GOLDSCHMIDT and HENDRICK (2002) and GROSS et al. (2005), citing the Italian study, used incidence to present what was originally prevalence in the study. This intermingled use of prevalence-incidence is confusing for scientists and complicates estimation of the real prevalence and incidence. Despite the confusing terminology, from both the Italian study (ABRAMO et al., 1999) and our survey, the conclusion that trichoblastoma, as well as pilomatricoma and IKA, are the most common forms of CFT can be drawn.

Regarding the data on the clinical manifestation and lesion distribution of the CFTs described in Croatian dogs, they were very similar to that previously described in the relevant dermatopathology literature (GROSS et al., 2005). In comparison to the Italian study (ABRAMO et al., 1999), where IKA was mostly found on the trunk, trichoblastoma and tricholemmoma on the head, and pilomatricoma on the neck, in our survey, trichoblastoma was similarly most prevalent on the head, while IKA, pilomatricoma and trichoepithelioma were most prevalent on the skin covering the lumbosacral region. Generally, we confirmed in this survey that epithelial follicular cells located within the dermis of the dorsal aspects of the canine skin (head and back) have a pronounced tendency for mutation and CFT development. A predilection for trichoblastoma growth on the head, more precisely at the base of the ears, was also found in 14 of 21 cases in our survey (GROSS et al., 2005). However, they may also be present within the skin covering the dorsal aspects of the front legs, hind legs and the back, as presented in our survey (GROSS et al., 2005).

Most of the case reports of CFT, especially of malignant forms, were published between 1960 and 2000 (SELLS and CONROY, 1976; JOHNSON et al., 1983; VAN HAM et al., 1990; RODRIGUEZ et al., 1995; HENDRICK et al., 1998; ABRAMO et al., 1999). Nowadays, reports of CFT are mostly based on the clinical picture of malignant CFT, with treatment options and outcome, and survey studies are rarer (ABRAMO et al., 1999).

Although malignant forms of CFT are especially rare, they must be still considered if a skin proliferation filled with keratin is found. In the veterinary literature so far, few malignant trichoepitheliomas have been reported (GOLDSCHMIDT and HENDRICK, 2002; SHIDA et al., 2008; HOSHINO et al., 2012), in contrast to about 15 cases of malignant

pilomatricomas (SELLS and CONROY, 1976; JOHNSON et al., 1983; VAN HAM et al., 1990; RODRIGUEZ et al., 1995; HARDISSON et al., 2001; DE GALVEZ-ARANDA et al., 2002; CARROLL et al., 2010; NOIVA et al., 2012; BARROT et al., 2013; MARTANO et al., 2013). It is important to note that most cases of pilomatricoma were diagnosed in breeds with continuous hair growth. The explanation is that those breeds have a greater number of mitotically active cells which provide a larger pool for neoplastic transformation than in breeds without these coat characteristics (GOLDSCHMIDT and HENDRICK, 2002; GROSS et al., 2005; HAUCK, 2012). Interestingly, in the Croatian dogs examined all four malignant trichoepithelioma and one malignant pilomatricoma were found in breeds that do not show continuous coat growth. However, differentiation between malignant forms of pilomatricoma and trichoepithelioma may pose a challenge, because of the similar histologic picture. In four cases of malignant trichoepithelioma, diagnosis was based on the higher amount of squamous epithelium, with features of inner and outer root sheath within infiltrative plates of basaloid epithelium (GROSS et al., 2005). In the single case of malignant pilomatricoma, the basaloid cell population was the only cell type present, and regions of calcification and bone metaplasia were also found (GROSS et al., 2005). Additionally, all CFTs, except trichoblastomas, were over-represented in pure-breed dogs in comparison with mixed-breed dogs. A unique, yet unknown sensitivity in pure-breed dogs for these tumours might be the cause, as it is in cutaneous malignant melanoma (DORN et al., 1968). Also, in humans, mutations in the gene CTNNB1, a gene encoding β -catenin, that are important in malignancies as well as inherited disease, have been found in pilomatricomas (KRAFT and GRANTER, 2014).

The mean age of affected dogs corresponds to the mean age reported in other countries (GOLDSCHMIDT and HENDRICK, 2002; GROSS et al., 2005; HAUCK, 2012). We found that pilomatricomas were more frequent in males, while malignant trichoepitheliomas, IKAs and trichoblastomas were found more frequently in females. However, due to the small number of cases, no gender association or breed predisposition could be proven in any of the investigated tumours.

The mean diameters of the investigated tumours were 10 to 30 mm in benign tumours. The range in diameter of these tumours was not wide, probably reflecting the care and will of the owner to remove the lesion. Malignant tumours were generally larger (60 mm for malignant pilomatricoma and 57.5 mm for malignant trichoepithelioma), probably due to the faster growth that characterizes malignant tumours (GOLDSCHMIDT and HENDRICK 2002; GROSS et al., 2005). The vast majority of examined tumours grew mostly as single nodular dermal lesions causing mild disruptions within the surrounding subcutaneous tissue. In cases of superficially oriented growth, mild to advanced adnexal displacement or epidermal atrophy was found. Synchronous or asynchronous multifocal tumours were found only in three dogs: a Yorkshire Terrier, a Labrador Retriever and a cross breed dog

with trichoepitheliomas. Interestingly, the single case of asynchronous trichoepithelioma consisted of both a benign and a malignant trichoepithelioma in the same animal. This finding stresses the obligation for submission of tumours for histopathology after excision. An accurate diagnosis with prognosis can be made, even in cases when lesions macroscopically suggest a benign cystic lesion filled with keratin, as in the case of a trichoepithelioma.

We conclude that follicular tumours are rare tumours in canine patients, which are mostly benign. The exceptions are trichoepithelioma and pilomatricoma, where a malignant growth pathway is possible, posing a disadvantage to the animal. In the last two decades, a single survey describing the prevalence of CFT has been published. This survey was carried out in central Italy and represents the sole reference for epidemiological information published in chapters dedicated to CFT in influential veterinary pathology and dermatopathology text books (ABRAMO et al., 1999; GROSS et al. 2005; MAULDIN and PETERS-KENNEDY, 2016). The very limited data base on CFT prevalence, histomorphology and clinical features, available from the last 45 years consists only of this publication and fewer than 20 case reports. In order to understand these specific tumours better and to estimate their real prevalence, biological behavior and morphological patterns on a global level, further basic investigations of the prevalence from different diagnostic centers worldwide are needed.

Acknowledgements

This study was supported by: FP7-ERA Chairs-Pilot Call-2013 project, acronym: VetMedZg (Grant agreement No: 621394).

References

- ABRAMO, F., F. PRATESI, C. CANTILE, S. SOZZI, A. POLI (1999): Survey of canine and feline follicular tumours and tumour-like lesions in central Italy. *J. Small. Anim. Pract.* 40, 479-481.
- BARROT, A.-C., L. CARIOTO, M. GAINS, M.-E. NADEAU (2013): Metastatic malignant pilomatricoma, acanthomatous ameloblastoma, and liver tumor in a dog with polyphagia, polyuria, polydipsia, and weight loss. *Can. Vet. J.* 54, 387-391.
- CARROLL, E. E., S. L. FOSSEY, L. M. MANGUS, M. E. CARSILLO, L. J. RUSH, C. G. McLEOD, T. O. JOHNSON (2010): Malignant pilomatricoma in 3 dogs. *Vet. Pathol.* 47, 937-943.
- DE GALVEZ-ARANDA, M. V., E. HURRERA-CEBALLOS, P. SANCHEZ-SANCHEZ, R. J. BOSCH-GARCIA, A. MATILLA-VICENTE (2002): Pilomatric carcinoma with lymph node and pulmonary metastasis. *Am. J. Dermatopathol.* 24, 139-143.
- DORN, C. R., D. O. N. TAYLOR, R. SCHNEIDER, H. H. HIBBARD, M. R. KLAUBER (1968): Survey of animal neoplasms in Alameda and Contra Costa Counties, California. II. Cancer Morbidity in Dogs and Cats From Alameda County. *J. Natl. Cancer.* 1. 40, 307-318.

- GOLDSCHMIDT, M. H., M. J. HENDRICK (2002): Tumors with adnexal differentiation. In: Tumors in Domestic Animals. 4th ed. (Meuten, D. J., Ed.), Iowa State Press, Iowa, pp. 55-78.
- GROSS, T. L., P. J. IHRKE, E. J. WALDER, V. K. AFFOLTER (2005): Follicular tumors. In: Skin diseases of the Dog and Cat: Clinical and Histopathologic Diagnoses, 2nd ed. (Gross, T. L., P. J. Ihrke, E. J. Walder, V. K. Affolter, Eds.), Blackwell Science Ltd., UK, USA, Australia, pp. 604-640.
- HARDISSON, D., M. D. LINARES, J. CUEVAS-SANTOS, F. CONTRERAS (2001): Pilomatrix carcinoma: a clinicopathologic study of six cases and review of literature. *Am. J. Dermatopathol.* 23, 394-401.
- HAUCK, M. L. (2012): Tumors of the skin and subcutaneous tissues. In: Small Animal Clinical Oncology, 5th ed. (Withrow, S. J., D. M. Vail, R. L. Page, Eds.), Elsevier Saunders, Missouri, USA, pp. 305-320.
- HENDRICK, M. J., E. A. MAHAFFEY, F. M. MOORE, J. H. VOS, E. J. WALDER (1998): Histological Classification of Mesenchymal Tumors of Skin and Soft Tissues of Domestic Animals (WHO International Classification of Tumors of Domestic Animals). American Registry of Pathology, USA, pp. 1-64.
- HOSHINO, Y., T. MORI, H. SAKAI, M. MURAKAMI, K. MARUO (2012): Palliative radiation therapy in a dog with malignant trichoepithelioma. *Aust. Vet. J.* 90, 210-213.
- JOHNSON, R. P., J. A. JOHNSON, S. C. GROOM, L. BURGESS (1983): Malignant Pilomatrixoma in an Old English Sheepdog. *Can. Vet. J.* 24, 392-394.
- KRAFT, S., S. R. GRANTER (2014): Molecular Pathology of Skin Neoplasms of the Head and Neck. *Arch. Pathol. Lab. Med.* 138, 759-787.
- MARTANO, M., L. NAVAS, L. MEOMARTINO, F. ABRAMO, B. RESTUCCI, P. MAILOLINO, L. L. MUZIO (2013): Malignant pilomatricoma with multiple bone metastases in a dog: Histological and immunohistochemical study. *Exp. Ther. Med.* 5, 1005-1008.
- MAULDIN, E. A., J. PETERS-KENNEDY (2016): Integumentary System. In: Jubb, Kennedy & Palmer's Pathology of Domestic Animals, Volume 1, 6th ed. (Grant Maxie M., Ed.), Elsevier Inc., Missouri, USA, pp. 714-717.
- MYERS, P. (2014): Animal diversity web-hair-mammals. http://animaldiversity.org/collections/mammal_anatomy/hair/.
- NOIVA R. M., F. B. COSTA, R. PRATAS, M. C. PELETIERO (2012): Metastatic malignant pilomatricoma with bone and lung metastasis in a Portuguese Water Dog. *Rev. Port. Cien. V.* 107, 101-104.
- RODRIGUEZ, F., P. HARRAEZ, E. RODRIGUEZ, J. C. GOMEZ-VILLAMANDOS, A. ESPINOSA DE LOS MONTEROS (1995): Metastatic pilomatricoma associated with neurologic signs in a dog. *Vet. Rec.* 137, 247-248.
- ROSAI, J. (2010): Skin. In: Rosai and Ackerman's Surgical Pathology Ninth Edition, Volume 1. (Rosai, J., Ed.). Mosby Elsevier, USA, pp. 93-236.
- SELLS, D. M., J. D. CONROY (1976): Malignant epithelial neoplasia with hair follicle differentiation in dogs (malignant pilomatricoma). *J. Comp. Pathol.* 86, 121-129.

A. Beck et al.: Retrospective study of canine follicular tumours in Croatia in a period of 4 years

- SHIDA, T., T. MARUO, Y. HAGIWARA, H. TAKEDA, K. KANAKUBO, H. SUGIYAMA, T. ISHIKAWA, A. INOUE, H. MADARAME, H. KAYANUMA, T. SUGANUMA (2008): A canine case of malignant trichoepithelioma with bone metastasis. *J. Anim. Clin. Med.* 17, 117-122.
- ŠOŠTARIĆ-ZUCKERMANN, I.-C., K. SEVERIN, M. HOHŠTETER, B. ARTUKOVIĆ, A. BECK, A. GUDAN KURILJ, R. SABOČANEC, P. DŽAJA, Ž. GRABAREVIĆ (2013): Incidence and types of canine tumours in Croatia. *Vet. arhiv.* 83, 31-45.
- THRUSFIELD, M. (2007): *Veterinary Epidemiology*, 3rd ed., Blackwell Science, USA.
- VAN HAM, L., H. VAN BREE, T. MAENHOUT, M. TSHAMALA, D. BROEKAERTT, J. HOORENS, D. MATTHEEUWS (1990): Metastatic pilomatricoma presenting as paraplegia in a dog. *J. Small. Anim. Pract.* 32, 27-30.

Received: 21 December 2015

Accepted: 24 April 2016

BECK, A., D. HUBER, V. ŠĆURIC, M. BENIĆ, M. HOHŠTETER, S. KUŽIR:
Četverogodišnje retrospektivno istraživanje pojave folikularnih tumora pasa u Hrvatskoj. *Vet. arhiv* 86, 453-466, 2016.

SAŽETAK

Folikularni tumori pasa (FTP) pripadaju skupini rijetkih tumora kože koji stvaraju keratin, a razvijaju se iz različitih dijelova dlačnog folikula. Skupina psećih folikularnih tumora sastoji se od infundibularnog keratinizirajućeg akantoma (IKA), triholemoma, trihoepitelioma, pilomatrikoma i trihoblastoma. Sustavna istraživanja FTP-a su rijetka, a većina publiciranih opisa ovih tumora odnosi se na prikaze kliničke i histološke slike pojedinačnih slučajeva. S ciljem da odredimo prevalenciju i tipove FTP-a u populaciji pasa u Hrvatskoj proveli smo četverogodišnje retrospektivno istraživanje na uzorcima FTP-e koji su obrađeni u Zavodu za veterinarsku patologiju od 2009. do 2012. godine. U istraživanom razdoblju dijagnosticirano je 714 tumora kože, od kojih je samo 69 tumora svrstano u FTP: 10 IKA, 21 pilomatrikom, 1 maligni pilomatrikom, 12 trihoepitelioma, 4 maligna trihoepitelioma i 21 trihoblastom. Pasmenska i spolna predispozicija nisu utvrđene, ali je uočeno da pilomatrikomi u najvećem broju slučajeva nastaju u pasmina pasa s kontinuiranim rastom dlake, dok je IKA-e većinom dokazana u pasmina koji nemaju tu karakteristiku rasta dlačnog pokrova. FTP se najčešće očituju kao noduli, rijetko kao bradavice ili plakovi, te su većinom zahvaćali dorzalno područje kože na glavi i leđima te proksimalno područje na stražnjim nogama. Usporedno s ostalim tipovima neoplazija dijagnosticiranih u hrvatskih pasa FTP predstavljaju rijetkost. Iako dominantno pokazuju biološko ponašanje tipično za benigne proliferacije, u ovom istraživanju je u 7,2% slučajeva FTP-a dijagnosticirana infiltrativna, maligna varijanta. Kako bi se izbjegle neželjene posljedice širenja malignog procesa, sve kožne nodule ispunjene keratinom potrebno je histološki klasificirati.

Ključne riječi: pas, pilomatrikom, trihoepiteliom, trihoblastom, akantom, prevalencija, Hrvatska
