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PREVALENCE OF CANINE EPITHELIAL, MELANOCYTIC AND MESENCHYMAL TUMOURS OF THE SKIN AND SOFT TISSUES: A 10-YEAR STUDY

R. SIMEONOV¹, I. DINEV¹, G. SIMEONOVA², N. GORANOV², M. PASKALEV², S. KRASTEV², I. TODOROVA², T. CHAPRAZOV², R. ROIDEV², I. BORISSOV², H. HUBENOV² & D. DINEV²

¹Department of General and Clinical Pathology, ²Department of Veterinary Surgery, Faculty of Veterinary Medicine, Stara Zagora, Bulgaria

Summary

Simeonov, R., I. Dinev, G. Simeonova, N. Goranov, M. Paskalev, S. Krastev, I. Todorova, Ts. Chaprazov, R. Roidev, I. Borissov, H. Hubenov & D. Dinev, 2011. Prevalence of canine epithelial, melanocytic and mesenchymal tumours of the skin and soft tissues: A 10-year study. *Bulg. J. Vet. Med.*, **14**, No 3, 171–178.

A histopathological analysis of 430 specimens of canine skin tumours obtained in the period 2000–2010, was performed at the Department of General and Clinical Pathology, Faculty of Veterinary Medicine, Trakia University, Bulgaria. The tumours were classified according to the last World Health Organization classification. The incidence of benign and malignant neoplasms was 48.14% and 51.86% respectively. Among the total number of skin tumours, 250 cutaneous growths were diagnosed as epithelial and melanocytic tumours and another 78 - as mesenchymal skin and soft tissue tumours. The most frequently diagnosed tumours from the skin epithelial and melanocytic group were hepatoid gland adenoma (9.3 %), squamous cell carcinoma (8.6 %), hepatoid gland carcinoma (5.34 %) and basalioma (5.11 %). The most frequently diagnosed canine mesenchymal skin and soft tissue tumours were lipoma (5.58 %), fibrosarcoma (4.41 %), haemangiopericytoma (2.32 %) and haemangioma (2.09 %).

Key words: dogs, incidence, melanocytic, mesenchymal, skin epithelial, tumours

INTRODUCTION

The skin is continuously exposed to a wide variety of chemical and physical insult and other environmental factors, and therefore, is prone to neoplastic proliferation. Tumours of the skin and subcutaneous tissues are the commonest tumours affecting dogs, accounting for approximately one third of all tumours encountered in the species (Brodey, 1970; Finnie & Bostock, 1979; Bostock, 1986; Rothwell *et al.*, 1987). The incidence of cutaneous tumours in dogs is estimated to

be 450 cases every years per 100,000 dogs (Priester, 1979; Bostock, 1986). Approximately 20 % to 40 % of primary tumours of the skin and subcutaneous tissues are histologically malignant in the dog, compared to 50–65% in the cat (Brodey, 1970; Bostock, 1986; Carpenter *et al.*, 1987; Kaldrymidou *et al.*, 2002; Mucuratirwa *et al.*, 2005). Epithelial and melanocytic skin tumours appeared in approximately 38% of cases, while mesenchymal skin tumours – in 30% of Prevalence of canine epithelial, melanocytic and mesenchymal tumours of the skin and soft tissues...

cases (Chalita *et al.*, 2001). The age of the dogs with diagnosed skin tumours is reported to range widely between 4 months and 16 years, although the average age is approximately 9 years (Tzvetkov, 1998; Kaldrymidou *et al.*, 2002). One report calculated the odds ratio of the development of malignant cutaneous tumours in dogs based on age and breed (Kaldrymidou, 2002). The researcher found that the risk increased linearly by a factor of 1.1 per year of increasing age and that purebred dogs were twice as likely to develop a malignancy as crossbred dogs.

Information on the prevalence and distribution of individual cutaneous tumours helps veterinary practitioners to diagnose them in time, determine an appropriate therapy, and anticipate an adequate prognosis (Vail & Withrow, 2001).

The study aims to determine the relative prevalence and distribution of canine skin epithelial, melanocytic and mesenchymal tumours in bioptic samples, received and analyzed between 2000–2010 at the Department of General and Clinical Pathology, Faculty of Veterinary Medicine, Trakia University, Bulgaria.

MATERIALS AND METHODS

Animals and tumours

The study was performed between 2000–2010 at the Department of General and Clinical Pathology, Faculty of Veterinary Medicine, Trakia University, Bulgaria. Four hundred and thirty samples of spontaneous skin tumour growths in dogs were studied. The study included dogs of all breeds and both sexes (216 male dogs and 214 bitches), aged between 3 months and 15 years.

Histopathologic examination

For histopathologic examination, the tissues were fixed in 10% phosphate-buffered neutral formalin, routinely processed, parafin embedded, and stained with hematoxyllin and eosin (H&E). Replicate sections of particular cases were also stained with special stains such Giemsa, periodic acid-Schiff and toluidine blue whenewer needed to confirm the diagnosis. All tumour diagnoses were histopathologically confirmed according WHO International Histological to Classification of Tumours of Domestic Animals (Goldschmidt et al., 1998). The criteria for histopathological classification of investigated tumours included cellular and nuclear pleomorphism, number of nucleoli, frequency of mitosis, discreteness of cellular borders, presence of necrosis and stromal tissue.

RESULTS

Based on the final diagnosis, 223 (51.86%) out of 430 cutaneous neoplasms were malignant, while 207 (48.14 %) were benign. Among the biopsy specimens, 250 cases were diagnosed as skin epithelial and melanocytic tumours and 78 cases – as mesenchymal tumours of skin and soft tissues (Table 1).

The most frequently diagnosed epithelial and melanocytic tumours were hepatoid adenoma (9.3%), squamous cell carcinoma (8.6%), hepatoid carcinoma (5.34%) and basal cell tumour (5.11%). The other neoplastic types varied between 0.23 % and 4.18 %.

Hepatoid gland adenoma is a benign tumour of the modified sebaceous gland developing on the skin of the anal and paranal region, as well as on the tail, hind limbs, laterally on the preputium, on the back and other locations. Of all 40 cases, **Table 1.** Incidence of canine skin epithelial,
melanocytic and mesencymal tumours
diagnosed at the Department of General and
Clinical Pathology, Faculty of Veterinary
Medicine – Stara Zagora from 2000 to 2010.

Tumour diagnosis	Number (%)*
Skin epithelial and melanocytic tumours	
Hepatoid gland adenoma	40 (9.30)
Squamous cell carcinoma	37 (8.60)
Hepatoid carcinoma	23 (5.34)
Basalioma	22 (5.11)
Malignant melanoma	18 (4.18)
Anal sac carcinoma	12 (2.79)
Apocrine adenoma	12 (2.79)
Anal sac adenoma	10 (2.32)
Apocrine carcinoma	10 (2.32)
Sebaceous adenoma	8 (1.86)
Sebaceous carcinoma	8 (1.86)
Ceruminous adenoma	8 (1.86)
Ceruminous carcinoma	8 (1.86)
Benign melanoma	7 (1.62)
Papilloma	6 (1.39)
Meibomian adenoma	6 (1.39)
Trichoepithelioma	2 (0.46)
Meibomian carcinoma	1 (0.23)
Pilomatricoma	1 (0.23)
Total	250 (58.13)
Total	230 (38.13)
Mesenchymal tumours of skin	
and soft tissues	
Lipoma	24 (5.58)
Fibrosarcoma	19 (4.41)
Haemangioma	9 (2.09)
Liposarcoma	8 (1.86)
Canine	10 (2.32)
haemangipericytoma	
Fibroma	4 (0.93)
Myxoma	2 (0.46)
Myxosarcoma	1 (0.23)
Schvannoma	1 (0.23)
Total	78 (18.14)

* of all cutaneous tumours.

28 were observed in male dogs aged approximately 11 years. Histologically,

the neoplastic parenchyma was composed of cells with well-defined borders and pale eosinophilic cytoplasm, whose structure looked like liver trabeculae. The cells were polyhedral and had centrally located large, ovoid nuclei with a central small nucleolus, abundant eosinophilic cytoplasm and distinct cell borders. Basaloid reserve cells, usually one layer thick, with small hyperchromatic nuclei and little cytoplasm were observed at the periphery of the lobules (Fig. 1).

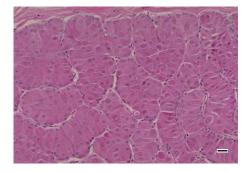


Fig. 1. Hepatoid gland adenoma. Note the "hepatoid" appearance of neoplastic tissue. H/E, bar=20 $\mu m.$

Squamous cell carcinoma is a malignant tumour which most frequently develops on the skin of limbs, trunk, head and neck, as well as on poorly pigmented skin areas. The average age of affected dogs was 8 years, varying from 6 to 10 years. No sex predilection was noted. Histologically, extending to the dermis, associated or not to the overlying epidermis, were islands, strands, and trabeculae of neoplastic epithelial cells showing a variable degree of squamous differentiation. The amount of keratin, seen as intracytoplasmic, eosinophilic fibrillar material (keratin tonofibres), produced by the neoplastic cells was quite variable: there was an extensive keratinization, and in well-differentiated tumours - formation of distinct keratin "pearls" (Fig. 2).

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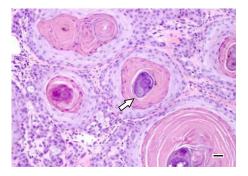


Fig. 2. Squamous cell carcinoma. Formation of a distinct keratin "pearl" (arrow). H/E, bar= 20 μm.

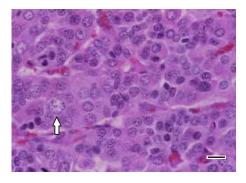


Fig. 3. Hepatoid gland carcinoma. The "hepatoid" cells have a vacuolated cytoplasm and large nuclei with several prominent nucleoli. The neoplastic cells show nuclear pleomorphism (arrow). H/E, bar=20 μ m.

Hepatoid gland carcinomas generally appear as nodular lesions affecting the perianal region. The average age of affected dogs was 11 years, varying from 7 to 15 years. Histologically, the tumour could consist of a single cell type; these cells were undifferentiated, with hyperchromatic nuclei, prominent nucleoli, and little cytoplasm. Only individual cells within the sheets and lobules of tumour cells showed differentiation to hepatoid cells. Other tumours may consist of reserve cells and hepatoid cells: the reserve cells showed pleomorphism of their nuclei and abundant mitotic figures. The hepatoid cells had a vacuolated cytoplasm and large nuclei with several prominent nucleoli (Fig. 3).

The basal cell tumour is an epithelial tumour without epithelial or adnexal differentiation. The neoplasms were mainly localized on the skin of the head and neck. Affected dogs were 7.8-years old on the average. The individual tumour cells were small and round to polyhedral in morphology (Fig. 4). The nuclei were ovoid, nucleoli were inconspicuous, and few mitotic figures were found. A small amount of cytoplasm was present. Melanocytes could be found interspersed between the basal cells, with transfer of melanin to the neoplastic cells.

The most frequently diagnosed canine skin mesenchymal tumours were lipoma (5.58%), fibrosarcoma (4.41%), haemangiopericytoma (2.32%) and haemangioma (2.09%). The incidence of the other neoplastic types varied between 0.23% and 1.86%.

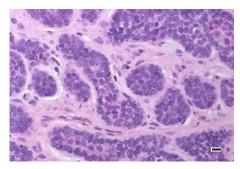


Fig. 4. Basal cell tumour. The nuclei of the neoplastic cells are ovoid, nucleoli are inconspicuous, and few mitotic figures are found. A small amount of cytoplasm is present. H/E, bar=40 μ m.

Lipomas were well circumscribed, unencapsulated, soft to yellow masses, indistinguishable from normal fat. Most were freely moveable over the underlyning deeper tissues and could be easily shelled out. The average age of affected dogs was 6.5 years, varying from 3 to 11 years. Out of all 24 cases, 17 (70.84%) were observed in female dogs. Histologically, the cells of lipomas were identical to those of normal adipose tissue. Large clear vacuoles replaced the cytoplasm, with peripheralization and compression of nuclei (Fig. 5). Some tumours had regions of necrosis, inflammation, and/or fibrosis.

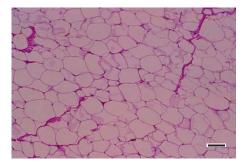


Fig. 5. Lipoma. H/E, bar=20 µm.

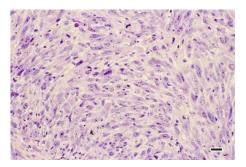


Fig. 6. Fibrosarcoma. Cellular and nuclear pleomorphism. H/E, bar=20 µm.

Fibrosarcomas were most commonly seen in adult dogs (mean age of 10 years). No breed or sex predisposition has been noted. The tumour could be circumscribed or infiltrative. Capsules were usually not seen. Histologically, the neoplastic cells were arranged in interwoven or herringbone patterns (Fig. 6). Cytoplasm was scant, and nuclei were elongated to oval with inconspicuous nucleoli. The more anaplastic tumours were with marked cellular pleomorphism.

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The number of mitotic figures varied widely. Peripheral aggregates of lymphocytes were occasionally seen.

Hemangiopericytomas had variable gross appearances: white/gray to red, soft to firm, rubbery to "fatty". The average age of affected dogs was 7 years, varying from 5 to 10 years. No breed or sex predisposition was observed. Histologically, the hallmark of this neoplasm was the presence of perivascular whorls of fusiform cells (Fig. 7). Although this feature could be present in other sarcomas, it is usually dominant in hemangiopericytomas. The neoplastic cells could range, sometimes within the same tumour, from thin to thick, spindle shaped to almost piriform, and they were separated by variable amounts of collagenous stroma.

Hemangiomas are benign tumours of the vascular endothelium. They appeared as well demarcated, encapsulated masses which range from bright red to dark brown. The average age of affected dogs was 6 years, varying from 4 to 8 years, without breed or sex predisposition. Histologically, most growths were well circumscribed and composed of variably sized vascular spaces filled with erythrocytes and lined by a single layer of uniform endothelial cells (Fig. 8). Organized thrombi were often found in tumours, with foci of haemosiderosis.

The gross appearance of liposarcoma, the malignant counterpart to the lipoma, varied depending of the amount of produced lipid. The average age of affected dogs was 9 years, varying from 7 to 11 years. No breed or sex predisposition was present. Histologically, most tumours were composed of round to polygonal cells arranged in sheets, with little or no collagenous stroma. In the well-differentiated variant, the majority of cells resembled normal adipocytes, with a single clear fat vacuole and a peripheral Prevalence of canine epithelial, melanocytic and mesenchymal tumours of the skin and soft tissues...

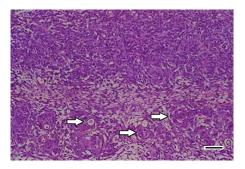


Fig. 7. Hemangiopericytoma. Its hallmark is the presence of perivascular whorls of fusiform cells (arrows). H/E, bar=20 μm.

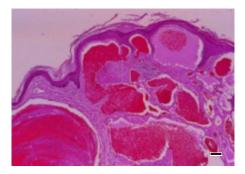


Fig. 8. Haemangioma. Variably sized vascular spaces filled with erythrocytes and lined by a single layer of uniform endothelial cells. H/E, bar=20 μ m.

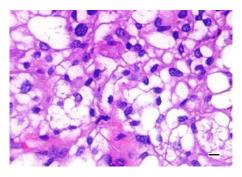


Fig. 9. Liposarcoma. Cellular and nuclear pleomorphism. H/E, bar=10 μm.

nucleus (Fig. 9). Other cells had variably sized round to oval nuclei and abundant cytoplasm that contains variably sized lipid droplets. The diagnosis could be difficult in anaplastic and myxoid variants.

The other canine epithelial, melanocytic and mesenchymal tumours of skin and soft tissues observed in this survey did not differ from the classical appearance.

DISCUSSION

The skin is permanently exposed to the influence of physical, chemical and other environmental factors and is readily accessible to clinical examinations. These are some reasons for more frequent diagnostics of cutaneous neoplasms (Bostock, 1986; Sanja *et al.*, 2005).

Out of the total number of tumours examinated for the period 2000–2010, skin tumours are the second most frequent group of neoplasms with an incidence of 33%, coming after mammary gland tumours (35%), which is consistent with the findings of others authors (Finnie & Bostock, 1979; Benjamin *et al.*, 1999; Moulton, 1990; Dinev, 2002; Sanja *et al.*, 2005).

According to the final diagnosis, out of all 430 canine cutaneous tumours 223 were malignant, while 207 were benign. This is in agreement with the finding of Sanja *et al.* (2005). However, based on the findings of Kaldrymidou *et al.* (2002) malignant cutaneous neoplasms accounted for 46.6% vs 53.4% for benign. Bostock *et al.* (1975) reported an incidence of malignant cutaneous neoplasms of approximately 40%. The results of Pakhrin *et al.* (2007) are similar.

There was not any significant sex predilection of investigated tumours, but males were more affected by hepatoid gland adenoma. Hepatoid gland tumours are associated with androgen sex hormones; hence, are reported more frequently in male dogs (Kaldrymidou *et al.*, 2002; Sanja et al., 2007).

The age-related incidence in our survev is very close to that reported from most researchers (Finnie & Bostock, 1979: Benjamin et al.. 1999: Kaldrymidou et al., 2002; Dinev, 2002; Pakhrin et al., 2007; Sanja et al., 2007). They confirmed the fact that the highest incidence of canine skin tumours is observed by the age of 10 years. The localization of tumour growth in the regions of the head, neck and limbs is also analogous to what is already reported (Finnie & Bostock, 1979; Benjamin et al., 1999; Kaldrymidou et al., 2002; Dinev, 2002; Pakhrin et al., 2007; Sanja et al., 2007).

Our study revealed that canine skin tumours that are prevalent in other parts of the world are also found among dogs in Bulgaria.

It is important to provide detailed information as well as proper bioptic specimens when submitting samples for diagnosis (Pakhrin *et al.*, 2007). Clinical history and gross morphology are important and integral components of diagnosis. This should include the duration and rate of tumour growth, change in appearance over time, size shape, colour, consistency, tissue of origin, and the presence or absence of attachment with the underlying tissues (Vail & Withrow, 2001).

According to our investigation it may be concluded that canine cutaneous tumours are increasingly frequent and are an important problem in the pathology of this animal species. Information on frequency and appearance of individual cutaneous tumours helps the clinicians to recognize them in time, to perform appropriate sampling and on the basis of histopathological analysis to provide a correct prognosis and a therapy as effective as possible.

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Correspondence:

Dr. Radostin Simeonov Department of General and Clinical Pathology, Faculty of Veterinary Medicine, Student's Campus, 6000 Stara Zagora, Bulgaria e-mail: rsimeonov@uni-sz.bg