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Canine Perineal Tumours

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With 6 figures and one table

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Summary

One hundred and thirty nine canine perineal tumours were histologically evaluated. The vast majority (134 tumours = 96.4 %) appeared to originate from the characteristic glandular structures of this region. They were classified as well differentiated perianal gland tumours (58.3 %), as moderately or poorly differentiated perianal gland tumours (21.6 %) and as carcinomas without perianal gland differentiation (16.5 %). Only 5 tumours (3.6 %) appeared to originate from non-characteristic perineal structures. A prominent male predominance was found with respect to the perianal gland tumours, whereas the carcinomas showed a distinct female predisposition. Tumours showing perianal gland differentiation almost invariably will have a benign behaviour. The carcinomas lacking any perianal gland differentiation often show a distinct malignant behaviour with metastases to regional lymph nodes and internal organs. These malignant neoplasms showed morphological and clinical features comparable to canine anal sac gland adenocarcinomas and carcinoids in man and animals.

Key words: Perianal gland tumours, perineal carcinomas, anal sac gland adenocarcinomas, carcinoids, dog

Introduction

Tumours located in the canine perineum may originate from various glandular structures characteristic for this region viz. the perianal or circumanal (hepatoid) glands, the anal sac glands and the anal glands (2, 25). The perianal glands are non-secretory abortive sebaceous glands situated around the anus (2, 31). The anal sac glands are apocrine, tubular mural glands of the anal sacs (2, 12). The anal glands are modified tubulo-alveolar sweat glands located in the submucosa of the anal canal (2). Moreover, perineal tumours also can originate from the non-characteristic epithelial and mesenchymal structures in this region, e. g. epidermis, sebaceous glands, hair follicles, fibrous tissue and smooth musculature.

Tumours in the perineal region are quite common (5, 8, 9, 12, 13, 27). The vast majority arises from the perianal glands (14, 15, 25) and is known to have a benign course (5, 9, 14, 17, 27). These perianal gland adenomas constitute one of the most common canine skin tumours (14, 25, 26, 32, 37). The tumours predominantly occur in male dogs

attributable to the androgenic dependency of the perianal glands (9, 19) and their tumours (9, 14, 17, 27). Consequently these tumours are only occasionally encountered in females (17, 27) and rarely in castrated males (14, 17, 27). A breed predisposition has been reported for the cocker spaniel (9, 14, 27).

Malignant tumours originating from the perianal glands are incidental findings (9, 17, 26, 27, 32), and these carcinomas infrequently metastasize (9, 14, 27). Furthermore, also malignant tumours with an evident aggressive behaviour are known to occur in the perineal region (3, 12, 23, 31). These tumours are assumed to originate from the anal sac glands (12, 21, 23, 31) and occur much less frequently than perianal gland adenomas (12, 17, 22). Contrary to the latter these adenocarcinomas are almost exclusively found in females (3, 12, 14, 23, 31), although also a few cases in males have been reported (12, 23, 33). Furthermore, tumours originating from other perineal structures can be encountered (15).

Perineal tumours mostly are manifested clinically as bulging masses (4, 12, 23, 31). The apocrine adenocarcinomas often also are accompanied by systemic symptoms mostly characterized by polyuria and polydipsia (PU/PD), correlated with hypercalcaemia and hypophosphataemia (3, 12, 13, 23, 31).

In this paper the histomorphological characterization of perineal tumours is presented with special emphasis on differences in morphology and biological behaviour. In addition, the morphology is discussed in relation to the tumour histogenesis.

Material and Methods

One hundred and thirty nine perineal tumours received from private practitioners and the Department of Clinical Sciences of Companion Animals, University of Utrecht, in the period 1985—1987 were used for a histomorphological study. Almost all were received as surgical specimens; in 6 dogs they were observed during post mortem examination.

Tumour tissue specimens and eventually metastatic tumour tissue were routinely fixed in 10 per cent neutral buffered formalin, dehydrated and embedded in paraffin. Sections 6 µm thick were stained with haematoxylin and eosin (H. E.), periodic acid-Schiff (P. A. S.), toluidine blue and according to Grimelius and Masson-Fontana.

Post-operative follow-up was performed with respect to tumours classified in group II and III (see Results).

Results

Based on differences in histological features the tumours were classified into four groups.

Group I

In the dermis and subcutis a well-circumscribed tumour nodule was observed consisting of lobes separated by massive connective tissue. The lobes were composed of solid lobules mainly consisting of large and medium-sized, rounded or polyhedral cells with eosinophilic and sometimes granular cytoplasm, and a relatively large vesicular nucleus with one or incidentally two small, but prominent nucleoli. At the periphery of the lobules a rim of cells with small elongated or rounded nuclei and scanty cytoplasm was observed (Fig. 1). Within the lobules and in between the lobes regularly structures were seen with a concentric, lamellar, duct-like arrangement of the cells and central keratinization. The cells did not show any malignant features such as mitotic figures, and cellular or nuclear pleomorphism. The interlobar septae sometimes exhibited oedema and haemorrhages or dilated thin walled veins. Additional inconsistent findings were inflammation, apoptotic necrosis of tumour cells and cholesterol granulomas.

Special stains were negative except for the P. A. S. stain which incidentally showed some P. A. S. positive granules in the tumour cells, which were diastase-digestable (probably glycogen).

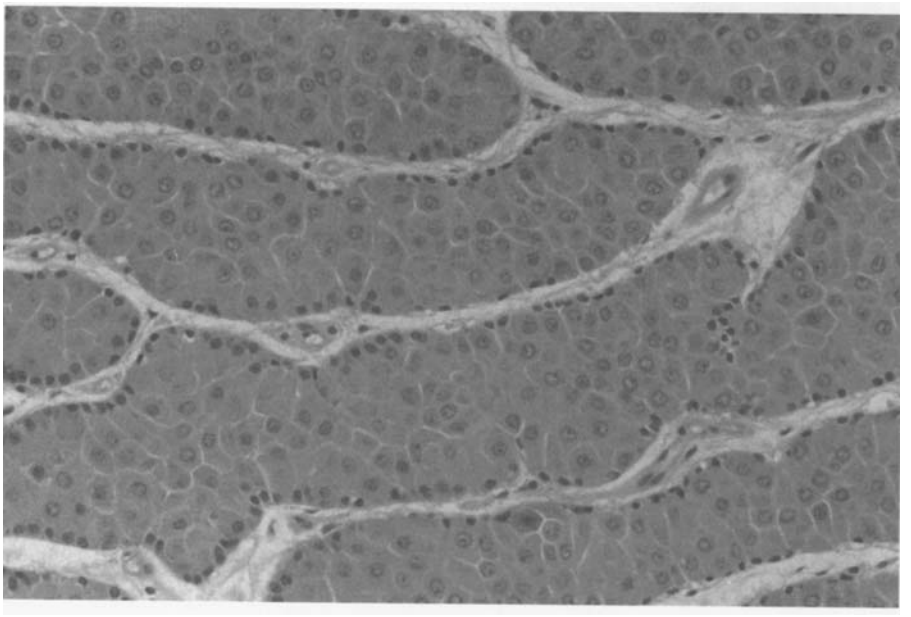

Fig. 1. Well differentiated perianal gland adenoma (group I) with lobules composed of large and medium-sized, rounded or polyhedral cells with vesicular nuclei surrounded by small cells with hyperchromatic rounded or elongated nuclei (reserve cells). H. E. 200×

As the histological aspects of these tumours corresponded with the histological characteristics of normal perianal glands and as the tumours did not show any indication of malignancy, they were classified as well differentiated perianal gland adenomas. The majority of the tumours, comprising 81 cases (58.3 %) was classified into this group.

Group II

These tumours were mostly well demarcated, but in several specimens with much inflammation and/or necrosis, the border of the tumour was irregular or not well discernable anymore. The tumours were composed of solid lobules separated by delicate to massive stroma. The lobules consisted predominantly, and occasionally almost entirely, of reserve cells characterized by medium-sized, round or oval rather hyperchromatic nuclei, a small amount of eosinophilic cytoplasm and indistinct cell borders (Figs. 2 and 3). Incidentally the cells and nuclei became elongated and these lobules presented with streaming fusiform cells (Fig. 3). A small to moderate number of mitotic figures was present. Between the reserve cells invariably solitary or groups of well differentiated neoplastic perianal gland cells with a moderate to large amount of eosinophilic cytoplasm were observed (Figs. 2 and 3). Also duct-like structures with central keratinization were regularly seen (Fig. 3). The proportion of reserve cells and well differentiated cells varied among the tumours and among the individual lobules within a tumour. Single cell necrosis and lytic necrosis of tumour cells with secondary cyst formation were regularly observed. Although the tumours showed malignant features (irregular border, moderate number of mitotic figures, necrosis), invasion of lymph or blood vessels was not observed. The interlobular septae often showed local oedema and haemorrhages or dilated thin walled veins. Inflammation was an inconsistent finding.

Specific stains were negative except for the P. A. S. stain, which sometimes showed the presence of P. A. S., diastase digestable positive granules (probably glycogen) in the tumour cells.

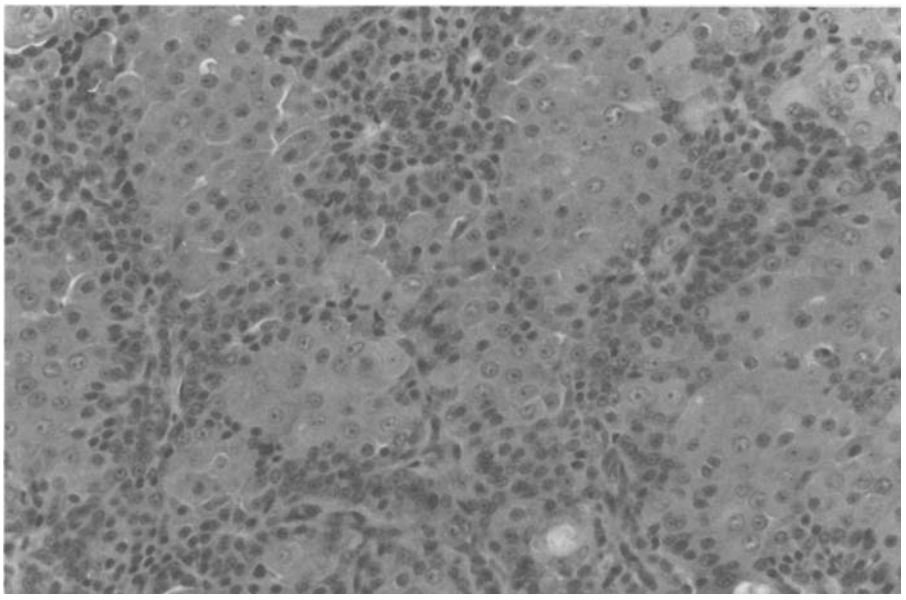

Fig. 2. Moderately differentiated perianal gland tumour (group II) with many reserve cells surrounding groups of well differentiated perianal gland cells. H. E. 200×

According to the histological characteristics these tumours were classified as moderately or poorly differentiated perianal gland tumours. Thirty tumours (21.6 %) were assigned to this group.

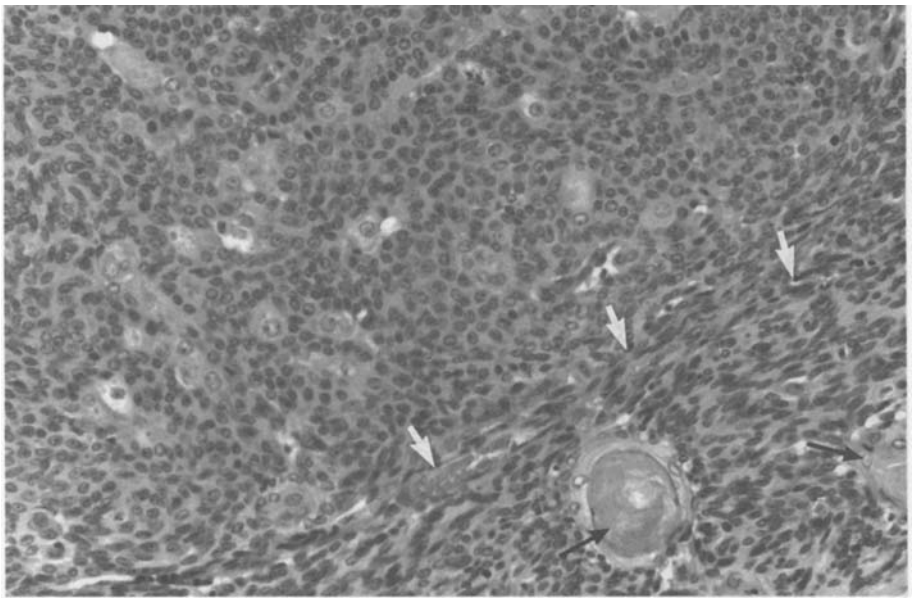

Fig. 3. Poorly differentiated perianal gland tumour (group II), predominantly composed of reserve cells with locally elongation of cells and nuclei (white arrows). Differentiated perianal gland cells are present as scattered solitary cells or small groups of cells. Local concentric arrangement of cells forming a duct-like structures with central keratinization (black arrows). H. E. 200×

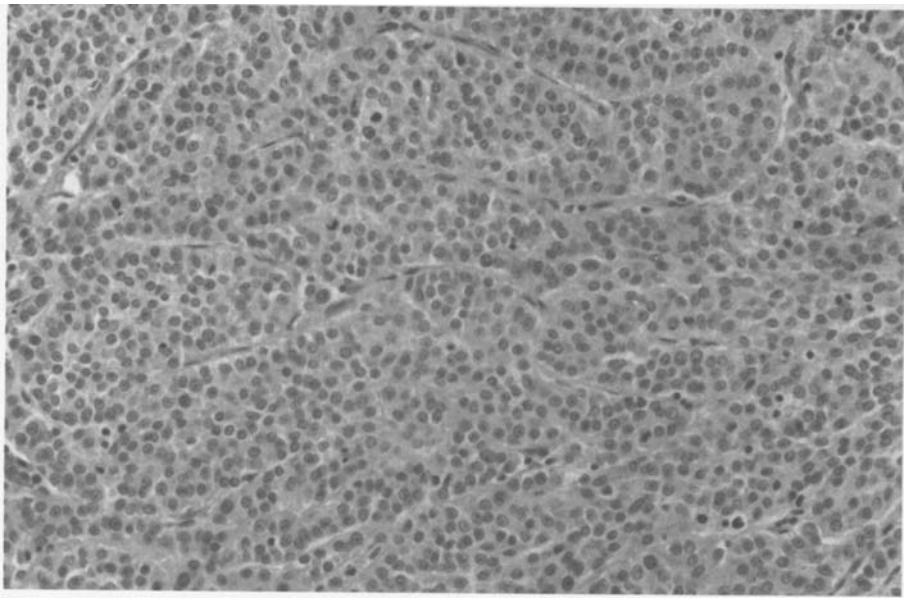

Fig. 4. Carcinoma without perianal gland differentiation (group III) consisting of solid groups of neoplastic cells separated by fine connective tissue strands with capillaries. H. E. 200×

Group III

These tumours displayed evidently infiltrative growth into adjacent tissues and showed a solid, rosette, tubular or mixed growth pattern. In the solid parts a trabecular or

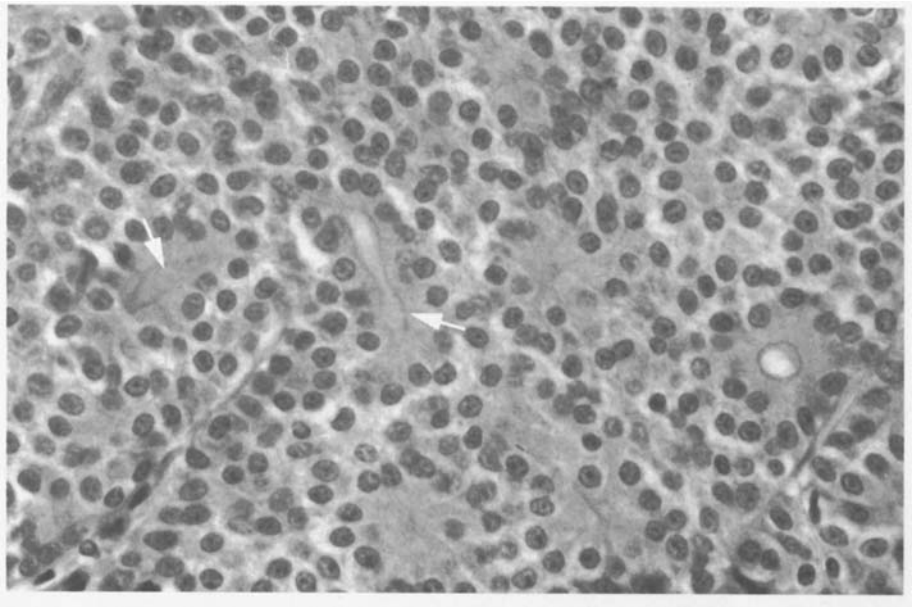

Fig. 5. Carcinoma without perianal gland differentiation (group III) showing a rosette-tubular pattern with intraluminal protein accous material (arrows). The tumour cells are medium-sized with only slight nuclear pleomorphism. H. E. 400×

ribbon pattern could be observed with pallisading of tumour cells. The cellularity varied with cellular size. The cells were small or medium-sized with pale eosinophilic, slightly granular cytoplasm and mostly indistinct cell borders. The nuclei were medium-sized and rounded with slight anisokaryosis and one or more small nucleoli (Fig. 4). Sometimes also spindle shaped cells with elongated nuclei were present. Mitotic figures were often seen. Within the solid areas fine connective tissue strands and capillaries were observed (Fig. 4).

The rosette-tubular pattern was characterized by cubic to cylindrical cells with basally located round or oval nuclei and ample pale cytoplasm, arranged around a small, often inconspicious lumen. The lumen regularly contained some proteinaceous material (Fig. 5). The nuclei were medium-sized with slight anisokaryosis and had one or several small nucleoli. Mitotic figures were often seen. Also in these areas delicate stroma was present often surrounding rosettes and tubular structures.

In both solid and rosette-tubular areas pseudo-rosettes i. e. rosette formation around a central capillary or venule were observed (Fig. 6). Oedema surrounding these vessels locally resulted in "adenocystic" structures. Additionally lytic necrosis of tumour cells also resulted in cyst formation. In none of the tumours, cells with characteristics of differentiated perianal gland cells or duct-like structures were observed.

In the P. A. S. stain the proteinaceous material in the rosette-tubular structures was often strongly positive. The tumour cells irregularly showed P. A. S. positive granules, which disappeared after diastase treatment suggesting glycogen. The other specific stains were negative.

According to these histological findings the tumours were classified as carcinomas without perianal gland differentiation. Twenty-three cases (16.5 %), including all autopsies, were categorized in this group.

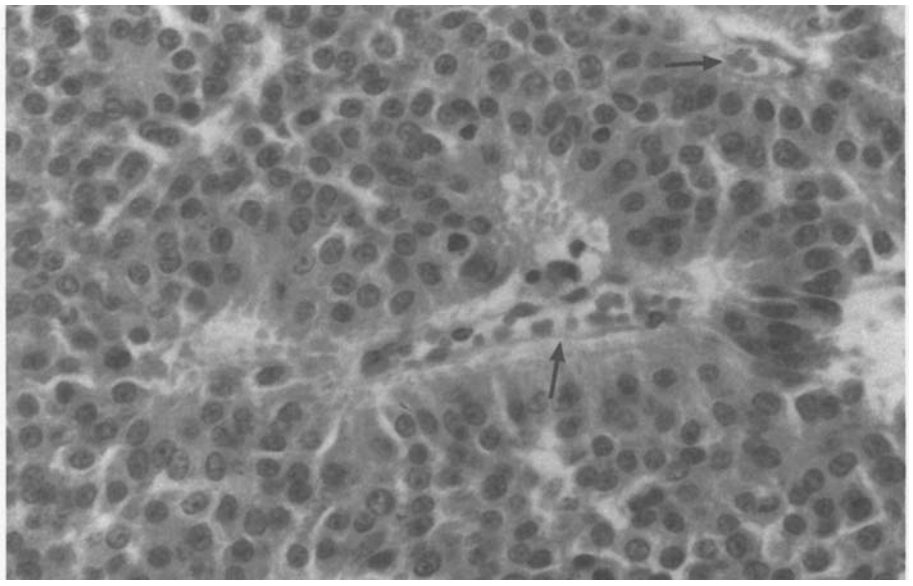

Fig. 6. Carcinoma without perianal gland differentiation (group III) showing pseudo-rosettes, i. e. cuboidal or cylindrical cells surrounding vascular structures (arrows). H. E. 400×

Group IV

Tumours evidently not originating from the characteristic glandular structures were classified in this group. Only 5 tumours (3.6 %) were designated to this group, comprising a leiomyoma, a leiomyosarcoma, a basalioma, a squamous cell carcinoma and an unclassifiable tumour.

The most important clinical data of the tumours classified in group I, II and III are summarized in table 1. With respect to group II tumours, follow-up was available in 23 cases. In 6 animals post operative recurrence was reported by the veterinary surgeons. However, they did not report the presence of metastases in any of the 23 cases. Post operative follow-up with respect to group III tumours was available in 13 cases. In 4 of these tumour recurrence was reported; one dog was euthanized clinically suspected of pulmonary metastases. In the 6 autopsies the tumours appeared to have metastasized all to lumbar lymph nodes and additionally to the liver (4 ×), the lungs (4 ×), the spleen (2 ×), the adrenal glands (1 ×), the kidneys (1 ×) and the mediastinum (1 ×).

Discussion

The histomorphological features of the tumours classified as well differentiated perianal gland adenomas (group I) are unconditionally compatible with the features of similar tumours reported previously (25, 27, 37). The benign behaviour of these tumours is incontestable (9, 14, 26, 27). Contrary to previous reports (9, 14, 26, 27) no breed predisposition could be established. The male predilection regarding this tumour type was once again explicitly demonstrated.

Table 1. The most important data of well differentiated perianal gland tumours (group I), moderately and poorly differentiated perianal gland tumours (group II) and carcinomas without perianal gland differentiation (group III)

	Tumour Classification		
	I	II	III
M/F ratio	3.9	4.0	0.5
age range (years)	5–14*	7–14	7–14
mean age (years)	10	11	10
breed predisposition	–	–	–
notable clinical signs			
tenesmus	4	1	8
pruritus	4	2	2
tumour bleedings	9	7	3
PU/PD	1	1	9
tumour duration range before presentation (months)	0.5–12	2–12	0.25–3
range tumour size (cms)	0.2–7.0	0.4–5.0	0.3–8.5
mean tumour size (cms)	2.4	2.1	4.0
tumour ulceration	55.9 %	69.0 %	57.1 %
tumour localization			
dorsal to anus	16	4	0
lateral to anus	14	6	6
ventral to anus	9	1	1
anal sac region	0	2	8
not reported	42	17	8

M = male; F = female; PU/PD = polyuria/polydipsia; cms = centimeters; * = additionally one tumour was seen in a one-year-old dog.

The less differentiated perianal gland tumours of group II were characterized by the predominance of reserve cells, which is considered to be indicative for malignancy (4, 16, 17, 37). However, the group II tumours did not display evident stromal invasion or the intravascular presence of neoplastic cells. Moreover, no indications of tumour metastases were reported in those cases in which follow-up information was available. The reported occurrence of post operative tumour recurrence in 6 out of 23 cases is difficult to evaluate in view of malignancy as newly arised tumours from neighbouring perianal glands cannot be unequivocally ruled out (4, 26, 27). Perianal gland carcinomas are only concisely described in literature (4, 5, 17, 25, 26, 27, 37). Nevertheless, from the reported descriptions and figures it seems that also tumours without perianal gland differentiation have been included. In our material tumours without perianal gland differentiation were designed to group III. So, our findings indicate that moderately or poorly differentiated perianal gland tumours do not show evident stromal or vessel invasion and will behave like the well differentiated perianal gland tumours. These less differentiated tumours also showed a male predominance as did the well differentiated perianal gland adenomas.

The histomorphology of the tumours classified as carcinomas without perianal gland differentiation (group III) is compatible with the histological features revealed by adenocarcinomas of the anal sac glands, which show a characteristic bimorphic solid and acinar growth pattern with rosette and pseudo-rosette formation (8, 12, 14, 21, 22, 23, 31, 33), and eosinophilia of tumour cell cytoplasm (12, 14, 23). These tumours are often associated with a distinct clinical syndrome (22) characterized by hypercalcaemia and hypophosphataemia and secondary polyuria/polydipsia (PU/PD), muscular weakness, lethargy, weight loss, anorexia and vomiting (4, 12, 14, 23, 31, 33). These clinical signs are due to the systemic effect of the electrolyte imbalance on the central nervous system, and on the gastrointestinal and urinary tract (38). Furthermore, there is an explicit female predominance (4, 12, 23, 31), although also a few cases in male dogs have been reported (12, 23, 33), and the tumours are almost invariably malignant (22). Surprisingly only one perineal apocrine adenoma has been reported (20). In our group III tumours also a female predisposition exists and PU/PD and a localization near the anal sac are relatively often mentioned in the clinical history. In addition they showed malignant features with stromal invasion, and often were metastasized. Also, the average tumour size appeared to be larger and the duration of tumour presence before presentation appeared to be shorter compared to the other groups, both indicative for a faster growth rate and potential malignancy. So, both the histomorphological features and the clinical findings indicate that these carcinomas without perianal gland differentiation (group III) are identical to the adenocarcinomas of the anal sac glands as described in literature.

The growth pattern of the tumours classified as carcinomas without perianal gland differentiation viz. solid and/or tubular pattern with formation of rosettes, pseudo-rosettes, trabeculae or ribbons of quite uniform cells with often granular eosinophilic cytoplasm and medium-sized nuclei with slight anisokaryosis and small nucleoli are additionally accordant with the characteristic features of carcinoid tumours in man (1, 35) and in animals (15, 17). The identification of carcinoids is based on its microscopic appearances (1, 10, 35). A characteristic silver affinity of tumours cells is often present and may help to establish its identification (6). In our cases both argentaffin and argyrophylic staining reactions were negative, which also has been previously reported with respect to canine hindgut carcinoids (7, 36) and also with respect to anal sac gland adenocarcinomas (21, 23). Also in man non-silver affinity reactive intestinal carcinoids have been described (34). However, rapid deterioration of granules resulting in false negative argentaffin reaction has to be taken into consideration (36) as the presence of argentaffin (10) and argyrophilic granules (10, 20) have been reported in canine intestinal carcinoids. In man, the production of neurohormonal peptides by carcinoids is well-known (6) e.g. insulin, adrenocorticotropic hormone, prostaglandins and parathormone (18). Particularly hindgut carcinoids are able to produce a wide range of hormonal peptides (6). The hypercalcaemia often found in dogs with adenocarcinomas of the anal sac glands is considered to be

attributable to the production of a humoral substance by the tumour cells (4, 12, 23, 31, 38) inducing increased osteolysis (24). This increased osteolytic activity has appeared not to be due to the production of immunoreactive parathormone or prostaglandin E_2 (24). However, ultrastructurally membrane-bound electron-dense granules were observed both in tumour cells and in anal sac gland cells (21), from which these adenocarcinomas are thought to be derived (12, 23, 31). These granules resemble secretory granules in polypeptide-secreting endocrine cells (21), and similar granules have been found in canine carcinoids (36) and canine neuroendocrine tumours (11, 39). In contrast to the female predisposition with respect to the described carcinomas (group III) and to the adenocarcinomas of the anal sac glands, no sex predilection seems to be present in canine carcinoids/neuroendocrine carcinomas (7, 10, 11, 29, 30, 36, 39). In man a female predisposition has been established for carcinoids localized in the appendix (32). In man, carcinoids are potentially malignant (34) with a varying behaviour dependent of tumour localization, e. g. the major part of appendiceal tumours is benign, whereas a large number of ileal neoplasms metastasizes (6). Almost all canine carcinoids were found to have local (7, 30) or distant metastases (10, 28, 29, 30), indicative for high malignancy or late stage of disease (30). Occasionally only infiltrative growth without metastasis has been observed (36). Also canine neuroendocrine carcinomas can show widespread metastasis (11).

In conclusion, the major part of canine perineal tumours apparently originates from the specific glandular structures of this region. The tumours originating from these glands can be histologically differentiated in benign well, moderately or poorly differentiated perianal gland tumours, and carcinomas with a characteristic histomorphology. These carcinomas, probably identical to adenocarcinomas of the anal sac glands, lack perianal gland differentiation and display striking characteristics of carcinoids and neuroendocrine tumours. Further research is needed to elucidate the exact nature of these carcinomas.

Zusammenfassung

Tumore des Perineums beim Hund

Einhundertneununddreißig Tumore des Perineums wurden beim Hund histologisch ausgewertet. Die große Mehrheit (134 Tumoren = 96,4 %) schien sich von den Drüsenstrukturen dieses Areals abzuleiten. Sie wurden als gut differenzierte Tumore der Perianaldrüsen (58,3 %), mäßig oder wenig differenzierte Tumore der Perianaldrüsen (21,6 %) und als Carcinome ohne Perianaldrüsen-Differenzierung (16,5 %) klassifiziert. Nur 5 Tumore (3,6 %) schienen sich von nicht charakteristischen perinealen Strukturen herzuleiten. Für die Perianaldrüsen-Tumore ergab sich beim männlichen Geschlecht eindeutig eine Dominanz, während sich für die Carcinome beim weiblichen Geschlecht eine Prädisposition zeigte. Tumore mit einer Perianaldrüsen-Differenzierung erweisen sich im allgemeinen als gutartig. Die Carcinome ohne Perianaldrüsen-Differenzierung zeigen oft ein ausgeprägtes bösartiges Verhalten mit Metastasen in den regionalen Lymphknoten und inneren Organen. Diese malignen Neoplasmen wiesen Merkmale auf, die mit denjenigen von Adenocarcinomen der Analbeuteldrüsen beim Hund und der Carcinoide beim Menschen und bei Tieren vergleichbar sind.

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