

Oral Tumours in Dogs: A Retrospective Study of 110 cases (2002 to 2014)



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Date: February - April 2015

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Summary

Biopsy files of 110 canine oral neoplasms submitted to the Veterinary Pathology Department of Utrecht University between 2002 and 2014 were reviewed. These biopsies were submitted by the Small Animal Clinic, Utrecht University where the animals were presented after being referred by veterinarians throughout the Netherlands. The purpose of this study was to report the prevalence of different types of tumours, sex, breed, location, lymph node swelling, bone infiltration or lysis, metastasis to other organs and recurrence.

Acanthomatous ameloblastoma, fibrosarcoma, squamous cell carcinoma and melanoma were most frequently found. Together, these tumours made up 62,9% of all tumours found in 110 patients. The breeds that were overrepresented included the Golden Retriever, Labrador Retriever, German Shepherd, Flatcoated Retriever, Berner Sennen, Rottweiler, Jack Russell, Schapendoes and Boxer. In these breeds, 3 or more tumours were found.

Acanthomatous ameloblastoma made up 19,1% of all tumours. A male predisposition was found, with 17 males and 4 females diagnosed. The mean age of presentation was 6,5 years and the tumour was mainly located in the mandible. Of these cases, 3 were presented at the Small Animal Clinic with a recurrent tumour after primary surgery by the referring veterinarian. Two cases showed regional lymph node swelling and 1 case showed signs of osteolysis.

Fibrosarcoma made up 16,4% of all tumours. A female predisposition was found, with 7 males and 11 females diagnosed. The mean age of presentation was 7,1 years and the tumour was mainly located in the maxilla. Of these cases, 6 were referred to the Small Animal Clinic with a recurrent tumour after primary surgery by the referring veterinarian. Two cases showed a local recurrence of the tumour after surgery at the Small Animal Clinic.

Squamous cell carcinoma made up 15,6% of all tumours. A male predisposition was found, with 12 males and 5 females diagnosed. The mean age of presentation was 8,2 years and the tumour was mainly located in the mandible. Of these cases, 9 were presented with a recurrent tumour after primary surgery by the referring veterinarian. Two cases showed signs of bone infiltration and 1 case showed angiogenesis in the tumour.

Melanoma made up 11,8% of all tumours. No sex predisposition was found, with 6 males and 7 females diagnosed. The mean age of presentation was 9,0 years and the tumour was mainly located in the mandible. Of these cases, 5 were presented with a recurrent tumour after primary surgery by the referring veterinarian and 5 cases showed signs of regional lymph node swelling.

Introduction

Oral tumours are not uncommon in dogs as 7% of all tumours are located in the oral cavity¹. Oral neoplasms are the fourth most common cancer overall in dogs². The literature about oral neoplasms dates back several decades and the purpose of this study was to shed some light on the recent prevalence of oral tumours among dogs that were presented at the Small Animal Clinic, Utrecht University, the Netherlands. Other subjects that will be discussed in this study are the prevalence of tumours among sex and breeds, location of the tumours, lymph node swelling, bone infiltration or lysis, metastasis to other organs and recurrence.

Oral tumours are frequently found in a late stage of the disease, when the prognosis for the patient will be less positive. Most patients are presented at the veterinary clinic when the tumour is classified as stage 3 (84%), stage 1 and 2 make up 8% of the patients and stage 4 also makes up 8%³. Staging is necessary to give an indication of the extent of tumour growth and spread. Staging of a tumour helps the veterinarian in developing a therapeutic plan and makes it easier to estimate the prognosis. The TNM system is a widely used scheme, which is based on the size of the primary tumour (T), degree of lymph node involvement (N), and extent of metastasis (M). Within each category, a number is assigned based on clinical, diagnostic and histopathologic evaluation. Below, the TNM system is explained according to WHO standards.

Figure 1. Classification of T according to WHO⁴

T (size of primary tumour)	Meaning
T ₀	No evidence of primary tumor
T ₁	<2 centimeters in greatest dimension
T ₂	2-4 centimeters in greatest dimension
T ₃	>4 centimeters in greatest dimension
T _{4a}	Invades through cortical bone into extrinsic muscle of tongue, maxillary sinus or face of skin
T _{4b}	Invades masticator space, pterygoid plates or skull base; or encases internal carotid artery

Figure 2. Classification of N according to WHO⁴

N (degree of lymph node involvement)	Meaning
N ₀	No regional lymph node metastasis
N ₁	Metastasis in a single ipsilateral lymph node, <3 centimeters
N _{2a}	Metastasis in a single ipsilateral lymph node, 3-6 centimeters
N _{2b}	Metastasis in multiple ipsilateral lymph nodes, <6 centimeters
N _{2c}	Metastasis in bilateral or contralateral lymph nodes, <6 centimeters
N ₃	Metastasis in a lymph node, >6 centimeters

Figure 3. Classification of M according to WHO⁴

M (extent of metastasis)	Meaning
M ₀	No distant metastasis
M ₁	Distant metastasis

Figure 4. WHO classification of oral tumours⁴

Tumour stage	Characteristics
1	T ₁ N ₀ M ₀
2	T ₂ N ₀ M ₀
3	T ₁ , T ₂ N ₁ M ₀
	T ₃ N ₀ , N ₁ M ₀
4A	T ₁ , T ₂ , T ₃ N ₂ M ₀
	T _{4a} N ₀ , N ₁ , N ₂ M ₀
4B	Any T N ₃ M ₀
	T _{4b} Any N M ₀
4C	Any T Any N M ₁

Oral tumours are usually discovered in a late stage because the mouth is not regularly checked by the owner or veterinarian. When the following symptoms occur, the tumour is usually in an advanced state. The most common symptoms of tumours in the oral cavity are halitosis, increased salivation, exophthalmos or facial swelling, weight loss, epistaxis, bloody oral discharge, dysphagia or pain on opening the mouth. Loose teeth in a dog with generally good dentition could also be a sign of underlying neoplastic bone lysis⁵.

Male dogs have a 2,4 times greater risk compared to female dogs⁶. Some breeds have a higher risk of developing oral tumours, the breeds include the Cocker Spaniel, German Shepherd, German shorthaired Pointer, Weimaraner, Golden Retriever, Gordon Setter, miniature Poodle, Chow Chow, and Boxer⁷. Oral tumours can arise from the mucosa (including lips), dental root, periodontium, bone of maxilla or mandible, incisive bone and palate bone. Because of these diverse locations, different types of histological tumours are identified³.

The majority of tumours that were diagnosed by the Veterinary Pathology Department of Utrecht University are described below, to give an overview of possible tumours.

Odontogenic tumour

Acanthomatous ameloblastoma

Acanthomatous ameloblastoma is a fairly common tumour. In the past, there has been confusion about naming this tumour. In older literature and classification schemes, it was called acanthomatous epulis and was differentiated from other epulides by their habit of infiltrating surrounding tissue^{8,9}. The acanthomatous epulis was later recognized as a type of ameloblastoma and was named a peripheral ameloblastoma¹⁰. However, this term was later replaced by canine acanthomatous ameloblastoma to distinguish it from the peripheral ameloblastoma in humans, which does not invade surrounding tissue¹¹.

Acanthomatous ameloblastoma arises from remains of odontogenic epithelium in the gingiva, where the teeth develop⁹. The tumour can also arise intraosseously and then break out of bone¹¹.

The tumour invades bone and has the tendency to recur after incomplete surgery⁹. Macroscopically, the ameloblastoma looks like a gingival enlargement, with a papillary surface, that sometimes displaces the adjacent teeth. The tumour is mostly found in the region of the mandibular incisor to premolar region⁹. A predisposition is described for Shetland and Old English Sheepdogs¹². The mean age at presentation is 7-10 years. Mandibulectomy or maxillectomy is necessary in this type of tumour because of frequent bone infiltration without distant metastasis. The prognosis is good if the tumour is completely removed and local recurrence rates after surgery are less than 5%⁵. After complete excision, one study described a 1 year survival rate of 100% among 25 dogs¹² while another

study reported a 1 year survival rate of 97%⁵. In the last study, excision was incomplete in one dog, leading to recurrence of the tumour.

Odontoma

Odontoma is a rare type of tumour^{8,13-15}. It is a benign tumour arising from the dental follicle during the early stages of odontogenesis. This is why odontomas are mainly found in young dogs^{8,16}.

Odontomas are actually not considered to be neoplasms, but they are thought to be hamartomas⁹. A hamartoma is a malformation that looks like a tumour. It arises from local cellular hyperactivity and is made up of excessive cells and tissues which arise during development¹⁷.

Odontomas are very much alike ameloblastomas. The difference between an odontoma and ameloblastoma consists of the fact that a neoplasm, which contains only odontogenic epithelial elements is named an ameloblastoma, while a tumour which also contains dental matrix components is termed an odontoma¹⁸. It is important to diagnose the tumour correctly because ameloblastomas are locally invasive and generally require a drastic approach, as mentioned before.

Odontomas can be subdivided into complex and compound tumours¹⁹. Complex odontomas contain all odontogenic tissues, which are disorderly organized. Compound odontomas consist of tooth-like structures that are normally present in a tooth^{15,19}. Compound odontomas are very uncommon and are reported in dogs in a few cases appearing in literature^{16,18,20-23}. Compound odontomas can be localised in the mandible or maxilla and they cause swelling and distortion²⁴. Surgery is the best treatment and the prognosis is usually good. Mandibulectomy has been used successfully in a few cases^{16,18,20,23}.

Other

Odontogenic fibroma is a slowly growing, benign neoplasm that is quite common in the dog^{9,10,14}. The tumour is characterized by a proliferation of fibroblastic connective tissue in which several structures can be present such as bone, osteoid, dentinoid or cementum-like material^{9,10}. The best treatment for this tumour is complete resection of the mass and underlying bone to prevent recurrence. In a study were 17 dogs were treated using marginal excision (without including underlying bone) 3 of the tumours recurred²⁵.

Amyloid producing odontogenic tumour is rare in dogs and appears as an epulis on the jaw, usually develops in patients between 8 to 13 years of age⁹. The tumour looks like a gingival enlargement which grows by expansion. It is locally invasive but not metastatic²⁶. Any epithelial tumour of the jaw that contains amyloid should be suspected of being odontogenic in origin⁸. The best treatment is surgery with a wide margin to completely excise the tumour, which is needed for a good prognosis without recurrence^{14,27}.

Non-odontogenic tumour

Melanoma

Melanoma is reported to be the most common tumour in dogs²⁸. It is a solitary, ulcerated, sometimes pigmented tumour that can lead to loose teeth²⁹⁻³². Smaller body weight dogs tend to develop melanoma easier. Breeds that might have a predisposition include the Cocker Spaniel, miniature Poodle, Anatolian Sheepdog, Gordon Setter, Chow Chow and Golden Retriever³³. The mean age at presentation is 11,4 years³³. Melanomas can have a confusing histologic picture if the tumour does not contain melanin. Amelanotic melanomas are also a common tumour in the dog, making up one third of all cases. Melanomas are highly malignant with frequent metastasis to the regional lymph nodes and the lungs. Metastasis was reported in 80% of dogs³⁴.

Most dogs diagnosed with melanoma die due to metastasis to the lungs, reported in 14% to 67% of dogs^{5,35}. The treatment used for local management of the tumour is surgery, with a local tumour recurrence rate that varies from 22% following mandibulectomy to 48% after maxillectomy^{5,35}. The mean survival time after surgery alone ranges from 150 to 318 days. Less than 35% of dogs are alive 1 year after surgery^{5,35}. In comparison, the mean survival time for untreated dogs is 65 days³⁶. Some

characteristics of the tumour have a positive effect on the prognosis when treated with surgery including tumour size, clinical stage and achieving local control after the first treatment³⁶. Dogs with tumours smaller than 2 centimeters in diameter have a mean survival time of 511 days compared to 164 days for dogs with tumours larger than 2 centimeters³⁷. Dogs with recurrent tumours have a shorter survival time compared to dogs with previously untreated melanomas³⁶. If the tumour is located in the region of the rostral mandible, the prognosis is better than in other sites³⁸. Age, sex, degree of pigmentation, microscopic appearance and breed are not of prognostic importance.

Squamous cell carcinoma

Squamous cell carcinoma is the second most common oral tumour in dogs². It is a solitary grey-white to pink nodular tumour with an irregular and ulcerated surface^{29,32,39}. The tumour frequently invades bone, with a metastatic rate of 20%. The metastatic risk depends on the location of the primary tumour: the rostral oral cavity has a low metastatic rate and the caudal tongue and tonsils region having a high metastatic risk⁴⁰.

The prognosis is good, particularly for rostral locations. Metastasis to the regional lymph nodes is reported in up to 10% of dogs, metastasis to the lungs has been reported in 3% to 36% of dogs⁴⁰. Local tumour control is usually the most challenging. The local recurrence rate after mandibulectomy is 10% and the mean survival time lies between 19 to 26 months with 91% of the dogs still alive after 1 year⁵. In comparison, the local recurrence rate is 29% after maxillectomy with a mean survival time of 10 to 19 months and a 1 year survival time of 57%³⁵.

Fibrosarcoma

Fibrosarcoma is the third most common tumour in dogs². It is a solitary, nodular, non-pigmented tumour, localised in the gingiva^{31,41-43}. The tumour tends to occur in large breeds such as the Golden and Labrador Retriever. The mean age of presentation is 7,3 to 8,6 years and possibly with a male predisposition. This type of tumour can look benign histologically and this usually leads to a diagnosis such as fibroma or low-grade fibrosarcoma. This syndrome is called a histologically low-grade but biologically high-grade fibrosarcoma. The tumour is usually located on the hard palate and maxillary arcade between the canine and carnassial teeth⁴⁴. The treatment should always be aggressive, even if the biopsy suggests fibroma or low-grade fibrosarcoma because of this syndrome that was mentioned before. This drastic approach should be used if the tumour is rapidly growing, a recurrent tumour or if it is invading bone. Metastasis to the regional lymph nodes is reported in 19% to 22% of dogs and to the lungs in up to 27% of dogs^{5,35}. Local recurrence is reported in 59% of dogs with a mean survival time of 12 months after mandibulectomy. When the dog is only treated with surgery, the 1 year survival rates rarely exceed 50%^{5,35}.

Osteosarcoma

Osteosarcoma of axial sites is less common than appendicular osteosarcoma and represents approximately 25% of all cases⁴⁵. Of the axial osteosarcomas, the mandible is involved in 27% of the cases and the maxilla in 16 to 22% of the cases⁴⁵. The prognosis for dogs with oral osteosarcoma is better than dogs with appendicular osteosarcoma because oral osteosarcoma tends to metastasize less often.

Mean survival times after mandibulectomy alone is variable with mean survival times of 14 to 18 months and 1 year survival rates of 35% to 71%. Two studies have shown that the majority of dogs with osteosarcoma located in the maxilla died as a result of local tumour recurrence without metastasis^{45,46}. Some factors that have a positive effect on the prognosis are complete surgical excision, mandibular location and dogs with smaller body weight⁴⁶.

Other

Osteomas are very rare in dogs. It is a smooth, protruding mass of abnormally dense but normal bone originating from the periosteal surface of bone. In structure, osteomas have the appearance of exostoses and cannot be differentiated from them on a histopathologic basis. Their incidence by age, breed and sex is unknown⁴⁷. These slow growing tumours will cause clinical signs when they affect adjacent structures. It has been suggested that osteomas are hamartomas rather than true neoplasms, while others think osteomas are the end stage of fibrous dysplasia⁴⁸. Neoplastic transformation is unreported and is unlikely to happen. One study⁴⁹ described 6 cases of osteoma, all masses had radiographic signs of bone proliferation without bone lysis. One case showed signs of root resorption of adjacent teeth. Of these 6 cases, 3 masses were excised with a wide margin and 2 were treated with marginal excisions. No recurrence was reported in the cases with wide margin excision and minimal progression was seen in the cases that had marginal excision at 5,5 months after surgery.

Multilobular tumour of bone is a relatively uncommon tumour in dogs^{50,51}. There has been some confusion in the veterinary literature about this tumour because it is so rare, has a varying biological behaviour and it produces fluctuating levels of matrix. Different names have been used in the literature as a synonym to multilobular tumour of bone including chondroma rodens, cartilage analogue of fibromatosis, calcifying or juvenile aponeurotic fibroma, multilobular osteoma, multilobular chondroma, multilobular osteosarcoma and multilobular osteochondrosarcoma. The tumour is now called multilobular tumour of bone, the term covers the characteristic histologic features of the tumour and does not refer to being benign or malignant⁵². In a report of 39 dogs with multilobular tumour of bone, locations where the tumour was found included the maxilla (11 cases), mandible (14 cases) and skull (14 cases)⁵¹. In this report, there were 20 males and 19 females diagnosed. The ages of presentation ranged between 4 to 17 years with a mean age of 8 years. Body weight of these dogs ranged from 8,2 to 69,4 kilograms with a mean weight of 29 kilograms. Of the dogs treated with surgery, 47% experienced local tumour recurrence and 56% showed signs of metastasis⁵¹. The mean time to recurrence was 797 days, the mean time to metastasis was 542 days, and the mean survival time was 797 days with a range from 28 to 1670 days⁵¹. At presentation, 4 dogs already had metastasis. The mean time to local recurrence in dogs where the tumour was removed completely was not reached at 1332 days with 8 out of 19 dogs having recurrence. Dogs with incomplete excision had a mean time to local recurrence of 320 days with 10 out 13 dogs experiencing recurrence⁵¹.

Spindle cell carcinoma and verrucous squamous cell carcinoma are a subtype of squamous cell carcinoma. The diagnosis spindle cell carcinoma is made when a tumour is composed of squamous cells and has a malignant spindle cell component of epithelial origin. In a survey⁵³ in animal hospitals, there was no significant difference in age and sex between the different subtypes of squamous cell carcinoma being verrucous carcinoma, basaloid squamous cell carcinoma, spindle cell carcinoma, papillary squamous cell carcinoma and adenosquamous carcinoma. Whether there is a difference in biological behavior between these subtypes and the well-differentiated squamous cell carcinoma is not certain and will be subject of new studies⁵³.

Adenocarcinoma is extremely rare in the dog and not all types have been recognized. It is a malignant tumour of the salivary gland and they usually arise from the mandibular and parotid glands⁵⁴. In a study that included 87392 biopsies, there was a total of 245 cases in which salivary gland tissue was examined from 160 dogs and 30,2% of these biopsies were malignant neoplasms⁵⁵. In another study where 35609 biopsies were examined, there were 140 submissions of salivary gland tissue. Of these submissions, 23 were adenocarcinomas⁵⁶. The mean age of presentation was 10 years with a range from 2 to 16 years⁵⁷. No specific breed predisposition has been reported⁵⁸. Metastasis to the lymph

nodes, lungs, bone, eyes and kidneys has been reported^{59,60}. Surgery is the best treatment but removal with wide margins is difficult due to the location.

Plasmacytoma is usually located in a mucocutaneous area and occur mostly in the mouth, feet or in the ears^{61,62}. In a study of 75 dogs with plasmacytomas, 17 of the tumours were located in the mouth⁶¹. Plasmacytomas are usually small with a diameter of 8 millimeter and are spherical or dome-shaped⁶³. The first choice of treatment is surgery and for most dogs this means long local control^{61,62}. The chance of local recurrence and distant metastasis is low⁶². Gingival tumours have the highest chance of recurrence (4 tumours out of 17), this may be due to difficulty in excising the tumour completely with a wide margin⁶².

Materials & Methods

Data was obtained from the biopsy files of the Department of Veterinary Pathology of University Utrecht, the Netherlands, covering the period from 2002 to 2014.

The patients were only included in this study if the tumour was located in the oral cavity. Epulides were excluded, because of this type of tumour being benign and usually not locally invasive. All dogs have had surgery at the Small Animal Clinic and the tumours were sent to the Department of Veterinary Pathology to determine the type of tumour and if the tumour was completely removed. These reports from the Department of Veterinary Pathology were reviewed to collect information about the patients. The age, breed, sex, location of the tumour, regional lymph node swelling, metastasis and recurrence were reported. The results were compared to information in veterinary literature.

Results

Prevalence and sex

During the period of 2002 to 2014, 110 dogs were diagnosed with oral tumours. The frequency of the tumours is shown in table 1. Acanthomatous ameloblastoma, fibrosarcoma, squamous cell carcinoma and melanoma were most frequently diagnosed. Other tumours that were found included plasmacytoma (1), multilobular tumour of bone (1), chondrosarcoma (1), verrucous squamous cell carcinoma (1), odontogenic fibroma (1), malignant roundcell tumour (2), epithelial respiratory carcinoma (1), carcinoma of dental origin (2), amyloid producing odontogenic tumour (2), plasmacell tumour (1), undifferentiated sarcoma (3), osteoma (1).

The sex distribution is also shown in table 1. Squamous cell carcinoma, acanthomatous ameloblastoma and amelanotic melanoma were mostly found in male dogs. The number of the remaining tumours is too small to draw any reliable conclusions about sex predisposition.

Table 1. Types of tumours and their sex distribution.

Tumour type	Number	%	Male	Female	M:F
Ameloblastoma	21	19,1	17	4	4,3 : 1
Fibrosarcoma	18	16,4	7	11	0,6 : 1
Squamous cell carcinoma	17	15,6	12	5	2,4 : 1
Melanoma	13	11,8	6	7	0,9 : 1
Amelanotic melanoma	5	4,5	4	1	4,0 : 1
Spindle cell carcinoma	5	4,5	3	2	1,5 : 1
Osteosarcoma	6	5,5	3	3	1 : 1
Odontoma	6	5,5	4	2	2 : 1
Adenocarcinoma	2	1,8	2	0	2,0 : 0
Others	17	15,5	11	6	1,8 : 1
Total	110	100	69	41	1,7 : 1

Breeds

Only breeds in which 3 or more tumours were found, were included in table 2. The tumours were distributed over 49 breeds of which 9 breeds in table 2 accounted for 42,5% of all tumours. Labrador and Golden Retrievers seem to be diagnosed with malignant oral tumours more often than other breeds.

Table 2. Distribution of the various tumour types in breeds with 3 or more tumours.

Breed	Tumour type										
	OD	SCC	AA	FS	OS	SA	M	AM	AD	CS	Others
Golden retriever	1	1	2	-	-	2	-	1	-	-	-
Labrador retriever	2	2	5	3	3	-	2	1	-	-	-
German shepherd	-	1	2	-	1	-	-	1	-	-	-
Flatcoated retriever	-	-	1	2	-	-	-	-	-	-	-
Berner Sennen	-	-	1	2	-	-	-	-	1	-	-
Rottweiler	-	-	-	-	-	1	1	-	-	1	-
Jack Russell	-	1	-	-	-	1	1	-	-	-	1
Schapendoes	-	-	1	-	-	-	-	-	-	-	2
Boxer	1	-	-	-	-	-	-	-	-	-	-

OD: odontoma. SCC: squamous cell carcinoma. AA: acanthomatous ameloblastoma. FS: fibrosarcoma. OS: osteosarcoma. SA: sarcoma. M: melanoma. AM: amelanotic melanoma. AD: adenocarcinoma. SC: spindle cell carcinoma. CS: chondrosarcoma.

Age

The mean age and age range are shown in table 3. The neoplasms occur in dogs of all ages but most of the animals were around 7 to 8 years of age at diagnosis. However, in each group of tumour type there were very young and very old dogs which is shown in the age range.

Table 3. Mean age and age range in years.

Tumour type	Mean age (years)	Age range (years)
Ameloblastoma	6,5	0,6 - 13
Fibrosarcoma	7,1	3 - 11
Squamous cell carcinoma	8,2	0,8 - 16
Melanoma	9,0	3 - 13
Amelanotic melanoma	9,6	8 - 11
Spindle cell carcinoma	8,2	5 - 12
Osteosarcoma	7,8	2 - 12
Odontoma	1,3	0,6 - 2,5
Adenocarcinoma	6,0	6 - 6
Other	8,6	0,6 - 16

Location

Locations of every oral tumour were recorded as shown in table 4. Most of the tumours were found in the gingiva of the mandible, with different specific locations.

Table 4. Location of 110 oral tumours.

	AA	FS	SCC	M	AM	SC	OS	OD	AD	Other
Lip	-	-	-	-	-	1	-	-	-	-
Palate	-	1	-	1	-	-	-	-	-	-
Buccal mucosa	-	1	-	-	-	-	-	-	-	-
Mandible	12	3	12	8	3	1	3	3	1	10
Maxilla	9	13	5	4	2	3	3	3	1	7

AA: acanthomatous ameloblastom. FS: fibrosarcoma. SCC: squamous cell carcinoma. M: melanoma. AM: amelanotic melanoma. SC: spindle cell carcinoma. OS: osteosarcoma. OD: odontoma. AD: adenocarcinoma.

Regional lymph node swelling, metastasis and recurrence

Regional lymph node swelling was identified in 5 cases which were diagnosed with malignant melanoma (4 cases) and respiratory epithelial carcinoma. There was bone infiltration in 8 cases and the different tumours were squamous cell carcinoma (2 cases), fibrosarcoma (2 cases), osteosarcoma, acanthomatous ameloblastoma (2 cases) and sarcoma. Osteolysis was found in 3 cases with osteosarcoma, adenocarcinoma and acanthomatous ameloblastoma. Metastasis to other places than the regional lymph nodes was determined in 2 cases. A patient with squamous cell carcinoma was suspected of having metastasis to other organs because the tumour showed angiogenesis. The other patient was diagnosed with osteosarcoma and showed signs of micro-metastasis to the lungs.

Of 110 cases, 30 patients were presented at the Small Animal Clinic in Utrecht with a recurrent tumour after being treated by the referring veterinarian. The types of tumours included squamous cell carcinoma (9 cases), fibrosarcoma (6 cases), verrucous squamous cell carcinoma, melanoma (5 cases), osteosarcoma (2 cases), acanthomatous ameloblastoma (3 cases), sarcoma, amelanotic melanoma (2 cases) and adenocarcinoma. After surgery at the Small Animal Clinic, only 3 patients experienced recurrence of their tumours, being sarcoma with regrowth in the nasal cavity, fibrosarcoma with infiltration of bone and regrowth in the sinus. The last patient was presented at

the clinic with recurrent fibrosarcoma after being treated by the referring veterinarian and experienced another recurrent fibrosarcoma in the same location after surgery at the Small Animal Clinic.

Discussion

Of all types of tumours, 5 types were more prevalent than others in patients presented at the Small Animal Clinic, University Utrecht. These types of tumours were acanthomatous ameloblastoma, fibrosarcoma, squamous cell carcinoma and melanoma, which were also the most common types in other studies^{6,30,32,41,42,64-66}. These results were also found in another research conducted at Utrecht University with the same research method as in this study⁶⁷. Together, these tumours made up 62,9% of all tumours found in 110 patients. Breeds in which 3 or more tumours were found, were included in this study. These breeds were the Golden and Labrador Retriever, German Shepherd, Flatcoated Retriever, Berner Sennen, Rottweiler, Jack Russell, Boxer and Schapendoes. Breeds in which most malignant tumours are found in other studies were the Boxer, Cocker Spaniel, German shorthaired Pointer, Weimaraner and Golden retriever^{64,68}. These breeds were not found in this study and the difference in representation can be explained by a difference in popularity of breeds in countries where these studies were conducted.

Acanthomatous ameloblastoma

Acanthomatous ameloblastoma was mostly located in the gingiva of the mandible, with 12 cases located in the mandible and 9 in the maxilla. This predilection for the mandible was also the result in another study⁶⁹. Acanthomatous ameloblastoma was mostly diagnosed in the Golden Retriever, Labrador Retriever, German Shepherd, Flatcoated Retriever, Berner Sennen and Schapendoes. The Labrador Retriever might be predispositioned with 5 dogs out of a total of 21 patients. However, the fact that the Labrador Retriever is a popular breed in the Netherlands can make it seem as a predisposition (www.hondencentrum.com). There might be a male predisposition with 17 males and 4 females being diagnosed. However, a study by Dubielzig et al. found no breed or sex predisposition⁷⁰.

The mean age was 7,1 years old which is a lot younger than the results of another study where a mean age of 8 to 9 years old was found⁷⁰. This result can be explained because a younger animal (8 months old) and a few older dogs (13 years old) were among the cases.

Osteolysis and bone infiltration was found in 3 cases out of 21 cases in total, while another study noted that this type of tumour infiltrates into underlying bone with loose teeth as a result⁴². This is a strange outcome, since acanthomatous ameloblastoma is known for infiltrating into surrounding tissue in almost every case. This low number of cases with signs of bone infiltration might be explained by the fact that bone infiltration was not described in every pathology report made by the Department of Veterinary Pathology.

Fibrosarcoma

Fibrosarcoma was mostly found in the gingiva of the maxilla, with 13 cases being located there out of a total of 18 cases. On the contrary, other studies found that the most frequent location was the gingiva of the mandible^{31,41,42,71}. Fibrosarcoma was diagnosed in the Labrador Retriever, Flatcoated Retriever and Berner Sennen dogs which are large breeds. Two studies found a predisposition for large breeds^{42,71} and males^{41,64,68}. There was no male predisposition found in this study with 7 males and 11 females diagnosed. This contradiction is possibly explained by the small group of patients in this study. The mean age of presentation was 7,3 years, which was also a result in two other studies where the mean age was around 7 to 8 years^{42,71}. At the Small Animal Clinic, 6 cases of a total of 18 cases were presented with recurrent fibrosarcoma after being treated by the referring veterinarian. One case experienced a recurrent tumour after surgery at the Small Animal Clinic. Fibrosarcoma is almost always invasive into surrounding bone tissue and this results in large numbers of recurrent tumours after surgery^{29,32,41,71,72} which is also seen in this study.

Squamous cell carcinoma

Squamous cell carcinoma was mostly located in the gingiva of the mandible with 12 cases out of a total of 17 cases. This was also noticed by others^{30,42,71,73}. Squamous cell carcinoma was mostly diagnosed in the Golden and Labrador Retriever, German Shepherd and Jack Russell. Todoroff et al.⁷¹ found a predisposition for large breeds and the majority of dogs diagnosed with squamous cell carcinoma in this study were also large breeds. A male predisposition could be associated with a male:female ratio of 2,4:1. The mean age of presentation was 8,2 years old while other studies found the same male predisposition and mean age as in this study^{29-31,41,71}. Bone infiltration was found in 1 case and distant metastasis in only 1 case, out of 17 cases in total. This type of tumour is locally invasive in bone or tissue with few and late metastasis^{30,42,71}.

Melanoma

Melanoma was mostly found in the gingiva of the mandible with 8 cases out of 13 cases in total. This result is in accord with other reports^{29-31,41,43,72,74}. Multiple studies^{31,32,41,43,68,71-73} suggest one of the most common locations being the lips, but there was no melanoma found on the lips in this study. Studies report unanimously that melanoma is the most common type of tumour in dogs^{1,30,32,43,64,68,72} which is not the case in this study. Melanoma reached the fourth place with only 13 cases out of 110 cases of oral neoplasms in total. Melanoma was mostly diagnosed in the Labrador Retriever, Rottweiler and Jack Russell. Esplin et al. state that melanoma was found mostly in Golden and Labrador Retrievers⁷⁵. Breed popularity may have some influence on the seemingly increased representation of Labrador and Golden retrievers ([www.hondacentrum.com](http://www.hondencentrum.com)). Other studies found a predisposition for small breeds^{71,76}, dark haired breeds^{31,43,77,78} and animals with pigmented oral mucosa^{30,72,79}. That was not the case in this study, the breeds with melanomas are large breeds (except the Jack Russell) and only the Rottweiler has a dark coat. A predisposition is also likely for the breeds Cocker Spaniel^{7,30,31,41,43}, Airdale, Scottish and Boston Terrier and English Springer Spaniel⁸⁰. Studies show a male predisposition^{7,29-31,43,68} however, the results of this study show no male predisposition with 6 males and 7 females diagnosed. The mean age of presentation is 10 to 11 years of age^{7,29,68} while the patients in this study had a mean age of 9 years. Metastasis to the regional lymph nodes was stated in 4 cases out of 13 cases in total, with no known metastasis to other organs or signs of bone infiltration. Other studies found invasive behaviour^{29-32,41,71,72} with metastasis within weeks to regional lymph nodes and internal organs^{30,42,71} especially to the lungs^{32,42,72}. The results of this study are very contradictory to the findings in other studies, because very few cases showed metastasis and none showed distant metastasis to other organs.

Conclusion

The prevalence of oral tumours in dogs presented at the Small Animal Clinic, Utrecht University has been surprising. Multiple articles state that melanoma is the most common type of tumour, but the results of this study tell differently. Acanthomatous ameloblastoma was the most common tumour, with a prevalence of 19,1%. The second most common tumour was fibrosarcoma, being 16,4% of all oral tumours. Squamous cell carcinoma came in third place with a prevalence of 15,6%. Melanoma was the fourth most common tumour in study with a prevalence of 11,8%. Mostly males were diagnosed with a tumour in the oral cavity, but this seemingly male predisposition can be explained by the fact that there were more males presented at the Small Animal Clinic compared to female dogs. The breeds Golden Retriever, Labrador Retriever, German Shepherd, Flatcoated Retriever, Berner Sennen, Rottweiler, Jack Russell, Schapendoes and Boxer were overrepresented. This can be explained by the fact that these breeds are very popular in the Netherlands.

This study has some limitations, for example the fact that it is a retrospective study, where not all information that needed to be registered was available. Statistics were not used and this makes it difficult to be sure of a predisposition for breeds or sex. Also, the group was too small to draw any reliable conclusions. The literature with which the results were compared, dates back several decades making it difficult to draw correct conclusions. There has been such a great development in the veterinary medicine, but most of the articles about oral tumours date before the 1980's.

More new studies should be set up to get to know more about oral tumours in dogs to find the true prevalence and possible predispositions for breeds, age and location. More research has to be done to clarify the biological behaviour of the different types of tumours that can develop in the oral cavity. This will be useful to make it easier to determine what type of tumour the veterinarian is dealing with and how to successfully treat the tumour with or without surgery or alternative medication. Veterinarians underestimate the importance of a good clinical exam which would make it easier to find oral tumours in an early stage and increases the prognosis positively for the patient. With new studies, this information should become available to inform people about this underestimated type of cancer in dogs. This way, dogs will have a better prognosis and tumours that are now discovered when it's too late, will become better treatable in the future.

References

1. Priester WA & McKay FW. The occurrence of tumors in domestic animals. *Natl. Cancer Inst. Monogr.* 1–210 (1980).
2. Hoyt FR, Withrow SJ. Oral malignancy in the dog. *J Am Anim Hosp Assoc* **20**, 83–92 (1984).
3. Vos JH & van der Gaag I. Canine and feline oral-pharyngeal tumours. *Zentralbl. Veterinarmed. A* **34**, 420–427 (1987).
4. TNM classification of carcinomas of the oral cavity. *IARC scientific publications* (2013). at <http://screening.iarc.fr/atlasoralclassiftnm.php?lang=1>
5. Kosovsky JK, Matthiesen D. Results of partial mandibulectomy for the treatment of oral tumors in 142 dogs. *Vet Sur* **20**, 397–401 (1991).
6. Dorn CR, Taylor DON, Frye FL. et al. Survey of animal neoplasms in Alameda and Contra Costa Counties, California. 1. Methodology and description of cases. *J Natl Cancer Inst* **40**, 307–318 (1968).
7. Cohen D, Brodey RS, Chen SM. Epidemiologic aspects of oral and pharyngeal neoplasms in the dog. *Am J Vet Res* **25**, 1776–1779 (1964).
8. Gardner DG. An orderly approach to the study of odontogenic tumours in animals. *J. Comp. Pathol.* **107**, 427–438 (1992).
9. Gardner, DG. Epulides in the dog: a review. *J. Oral Pathol. Med.* **25**, 32–37 (1996).
10. Verstraete FJ, Ligthelm AJ, Weber A. The histological nature of epulides in dogs. *J Comp Path* **106**, 169–182 (1992).
11. Gardner DG, Baker DC. The relationship of the canine acanthomatous epulis to ameloblastoma. *J Comp Path* **108**, 47–55 (1993).
12. White RA & Gorman NT. Wide local excision of acanthomatous epulides in the dog. *Vet. Surg. VS Off. J. Am. Coll. Vet. Surg.* **18**, 12–14 (1989).
13. Walsh KM, Benholm LJ, Cooper BJ. Epithelial odontogenic tumors in domestic animals. *J. Comp. Oncol.* **97**, 503–521 (1987).
14. Poulet FM, Valentine BA, Summers BA. A survey of epithelial odontogenic tumors and cysts in dogs and cats. *Vet Pathol* **29**, 369–380 (1992).
15. Cawson RA, Odell EW. in *Essentials of Oral Pathology and Oral Medicine* 117–131 (Churchill Livingstone, 1998).
16. Eickhoff M, Seeliger F, Simon D, Fehr M. Erupted bilateral compound odontoma in a dog. *J. Vet. Dent.* **19**, 137–143 (2002).

17. Gardner DG. The concept of hamartomas: its relevance to the pathogenesis of odontogenic laesions. *Oral Surgery, Oral Med. Oral Pathol.* **45**, 884–886 (1978).
18. Smith KC, Brearly MH, Jeffery N. Odontoma in a juvenile Boxer: clinical, radiographic and pathological findings. *J Small Anim Pr.* **34**, 142–145 (1993).
19. Kramer IRH, Pindborg JJ, Shear M. in *Histological Typing of Odontogenic Tumours* 16–21 (Springer-Verlag, 1992).
20. Brodey RS, Morris AC. Odontoma associated with an undifferentiated carcinoma in the maxilla of a dog. *J Am Vet Med Assoc* **137**, 553–559 (1960).
21. Valentine BA, Lynch MJ, May JC. Compound odontoma in a dog. *J Am Vet Med Assoc* **186**, 177–179 (1985).
22. Hale FA, Wilcock BP. Compound odontoma in a dog. *Vet. Dent.* **13**, 93–95 (1996).
23. Marti JM, Nalley WS, Wallace DR. Guided bone regeneration in the treatment of a compound odontoma in a dog. *Vet. Comp. Orthop. Traumatol.* **13**, 204–207 (2000).
24. Papadimitriou S. *et al.* Compound maxillary odontoma in a young German shepherd dog. *J. Small Anim. Pract.* **46**, 146–150 (2005).
25. Bostock DE, White RAS. Classification and behaviour after surgery of canine epulides. *J Comp Path* **97**, 197–206 (1987).
26. Ohmachi T, Taniyama H, Nakade T. Calcifying epithelial odontogenic tumours in small domesticated carnivores: histological, immunohistochemical and electron microscopical studies. *J Comp Path* **114**, 305–314 (1996).
27. Gardner DG, Dubielzig RR & McGee EV. The so-called calcifying epithelial odontogenic tumour in dogs and cats (Amyloid-producing odontogenic tumour). *J. Comp. Pathol.* **111**, 221–230 (1994).
28. Bergman PJ. Canine oral melanoma. *Clin. Tech. Small Anim. Pract.* **22**, 55–60 (2007).
29. Borthwick R, Else RW, Head K. Neoplasia and allied conditions of the canine oropharynx. *Vet Annu.* **22**, 248–269 (1982).
30. Brodey RS. A clinical and pathologic study of 130 neoplasms of the mouth and pharynx in the dog. *Am J Vet Res* **21**, 787–812 (1960).
31. Gorlin RJ, Peterson WC. Oral disease in man and animals. *Arch Derm* **96**, 380–403 (1967).
32. Richardson RC, Jones MA, Elliot GS. Oral neoplasms in the dog: a diagnostic and therapeutic dilemma. *Comp Cont Educ Vet Pr.* **5**, 441–446 (1985).
33. Ramos-Vara JA, Beissenherz ME & Miller MA. Retrospective Study of 338 Canine Oral Melanomas with Clinical, Histologic, and Immunohistochemical Review of 129 Cases. **37**, 597–608

34. Kudnig ST, Ehrhart N. Survival analysis of oral melanoma in dogs. *Vet Cancer Soc Proc* **23**, 39–45 (2003).
35. Wallace J, Matthiesen DT, Patnaik A. Hemimaxillectomy for the treatment of oral tumors in 69 dogs. *Vet Surg* **21**, 337–341 (1992).
36. Harvey HJ, MacEwen GE, Braun D. Prognostic criteria for dogs with oral melanoma. *J Am Vet Med Assoc* **178**, 580–582 (1981).
37. MacEwen EG, Patnaik AK, Harvey HJ. Canine oral melanoma: comparison of surgery versus surgery plus *Corynebacterium parvum*. *Cancer Invest* **4**, 397–402 (1986).
38. Hahn KA, DeNicola DB, Richardson RC. Canine oral malignant melanoma: prognostic utility of an alternative staging system. *J Small Anim Pr*. **35**, 251–256 (1994).
39. Quigley PJ, Leedale A, Dawson IMP. Carcinoma of mandible of cat and dog simulating osteosarcoma. *J Comp Path* **82**, 15–18 (1972).
40. Théon AP, Rodrieuz C. Analysis of prognostic factors and patterns of failure in dogs with malignant oral tumors treated with megavoltage irradiation. *J Am Vet Med Assoc* **210**, 785–788 (1997).
41. Brodey RS. Biological behaviour of canine oral and pharyngeal neoplasms. *J Small Anim Pr*. **11**, 45–53 (1970).
42. Dubielzig RR. Proliferative dental and gingival diseases of cats and dogs. *J Am Anim Hosp Assoc* **18**, 577–584 (1982).
43. Gorlin RJ, Barron CN, Chaudry AP, Clark JJ. The oral and pharyngeal pathology of domestic animals. A study of 487 cases. *Am J Vet Res* **20**, 1032–1061 (1959).
44. Ciekot PA, Powers BE. Histologically low grade yet biologically high grade fibrosarcomas of the mandible and maxilla of 25 dogs (1982-1991). *J Am Vet Med Assoc* **204**, 610–615 (1994).
45. Heyman SJ, Diefenderfer DL, Goldschmidt MH & Newton CD. Canine axial skeletal osteosarcoma. A retrospective study of 116 cases (1986 to 1989). *Vet. Surg. VS Off. J. Am. Coll. Vet. Surg.* **21**, 304–310 (1992).
46. Hammer AS, Weeren FR, Withrow SJ. Prognostic factors in dogs with osteosarcomas of the flat and irregular bones. *J Am Anim Hosp Assoc* **31**, 321–326 (1995).
47. Goldschmidt MH, Thrall DE. in *Textbook of Small Animal Orthopaedics* Chapter 75 (1985).
48. Resnick D, Niwayama G. in *Diagnosis of Bone and Joint Disorders* 4396–4466 (1994).
49. Volker MK & Luskin IR. Oral osteoma in 6 dogs. *J. Vet. Dent.* **31**, 88–91 (2014).
50. Straw RC, LeCouteur RA, Powers BE. Multilobular osteochondrosarcoma of the canine skull: 16 cases (1987-1988). *J Am Vet Med Assoc* **195**, 1764–1769 (1989).

51. Dernell WS, Straw RC, Cooper MF. Multilobular osteochondrosarcoma in 39 dogs: 1979-1993. *J Am Anim Hosp Assoc* **34**, 11–18 (1998).
52. Hanley CS, Gieger T, Franck P. What is your diagnosis? Multilobular osteoma. *J Am Vet Med Assoc* **225**, 1665–1666 (2004).
53. Nemec A, Murphy B, Kass PH & Verstraete FJM. Histological subtypes of oral non-tonsillar squamous cell carcinoma in dogs. *J. Comp. Pathol.* **147**, 111–20 (2012).
54. Carberry CA, Flanders JA, Anderson WI. Mast cell tumor in the mandibular salivary gland in a dog. *Corn Vet* **77**, 362–366 (1987).
55. Spangler WI, Culbertson MR. Salivary gland disease in dogs and cats: 245 cases (1985-1988). *J Am Vet Med Assoc* **198**, 465–469 (1991).
56. Thomsen BV, Meyers RK. Extraskeletal osteosarcoma of the mandibular salivary gland in a dog. *Vet Pathol* **36**, 71–73 (1999).
57. Carberry FA, Flanders JA, Harvey HJ. Salivary gland tumors in dogs and cats: a literature review and case review. *J Am Anim Hosp Assoc* **24**, 561–567 (1988).
58. Hammer A, Getzy D. Salivary gland neoplasia in the dog and cat: survival time and prognostic factors. *J Am Vet Med Assoc* **37**, 478–482 (2001).
59. Grevel V, Schmidt S, Mettler F. Multiple bone metastases of a salivary gland carcinoma in a dog. Roentgenologic, angiographic and pathologic anatomy. *Schweiz. Arch. Tierheilkd.* **120**, 13–22 (1978).
60. Habin DJ, Else RW. Parotid salivary gland adenocarcinoma with bilateral ocular and osseous metastases in a dog. *J Small Anim Pr.* **36**, 445–449 (1995).
61. Rackich PM, Latimer KS, Weiss R. Mucocutaneous plasmacytomas in dogs: 75 cases (1980-1987). *J Am Vet Med Assoc* **194**, 803–810 (1989).
62. Clark GN, Berg J, Engler S. Extramedullary plasmacytomas in dogs: results of surgical excision in 131 cases. *J Am Anim Hosp Assoc* **28**, 105–111 (1992).
63. Baer KE, Patnaik AK. Cutaneous plasmacytomas in dogs: a morphologic and immunohistochemical study. *Vet Pathol* **26**, 216–221 (1989).
64. Dorn CR. Epidemiology of canine and feline tumors. *J Am Anim Hosp Assoc* **12**, 307–312 (1976).
65. Langham RF, Keahley KK, Mostosky UV, Schirmer RG. Oral adamantinomas in the dog. *J Am Vet Med Assoc* **146**, 474–480 (1965).
66. Werner RE. Canine oral neoplasia: a review of 19 cases. *J Am Anim Hosp Assoc* **17**, 67–69 (1981).
67. Vos JH, Gaag I. Canine and feline oro-pharyngeal tumors. *J Vet Med* **34**, 420–427 (1987).

68. Dorn CR, Priester WA. Epidemiologic analysis of oral and pharyngeal cancer in dogs, cats, horses and cattle. *J Am Vet Med Assoc* **169**, 1202–1206 (1976).
69. Mills JHL, Lewis RJ. Adamantinoma - histogenesis and differentiation from the periodontal fibromatous epulis and squamous cell carcinoma. *Can Vet J* **22**, 126–129 (1981).
70. Dubielzig RR, Goldschmidt MH, Brodey RS. The nomenclature of periodontal epulides in dogs. *Vet Path* **16**, 209–214 (1979).
71. Todoroff RJ, Brodey RS. Oral and pharyngeal neoplasia in the dog: a retrospective survey of 361 cases. *J Am Vet Med Assoc* **175**, 567–571 (1979).
72. Nielsen SW. Classification of tumors in dogs and cats. *J Am Anim Hosp Assoc* **19**, 13–52 (1983).
73. Head KW. Tumors of the upper alimentary tract. *Bull WHO* **53**, 145–167 (1976).
74. Liptak JM, Withrow SJ. in *Small Animal Clinical Oncology* 455–475 (2007).
75. Esplin DG. Survival of dogs following surgical excision of histologically well-differentiated melanocytic neoplasms of the mucous membranes of the lips and oral cavity. *Vet. Pathol.* **45**, 889–896 (2008).
76. Bradley RL, MacEwen EG, Loar AS. Mandibular resection for removal of oral tumors in 30 dogs and 6 cats. *J Am Vet Med Assoc* **184**, 460–463 (1984).
77. Cotchin E. Neoplasia in the dog. *Vet Rec* **66**, 879–884 (1954).
78. Cotchin E. Melanotic tumors in the dog. *J Comp Path* **29**, 115–129 (1955).
79. Schlumberger HG. Comparative pathology of oral neoplasms. *Oral Surg* **6**, 1078–1094 (1953).
80. Mulligan RM. Neoplastic diseases of the dog. Neoplasms of melanin-forming cells. *Am J Path* **25**, 339–355 (1949).