Head and Neck Tumours

Pathology, Pathophysiology, Clinical Presentation and Treatment

David J. Argyle BVMS PhD DECVIM-CA (Oncology) FRSE MRCVS
William Dick Professor of Veterinary Clinical Studies and Head of School.
Royal (Dick) School of Veterinary Studies and Roslin Institute
The University of Edinburgh
Easter Bush, Midlothian
EH25 9RG

Introduction

Head and neck cancers in cats represent a diverse group of tumour types that can affect a diverse range of structures. Complicating this, is the fact that a tumour of a particular histiotype can sometimes behave different biologically depending on location (the classical example being Squamous carcinoma). For simplicity, I will divide this synopsis by anatomical location.

Oropharyngeal Tumours

Introduction

Oral cancer is frequently encountered in the feline and canine patient. Dogs are more frequently affected than cats with oral tumours accounting for 6% of canine cancer and 3% of feline cancer. The most common oral tumours in dogs are malignant melanoma, squamous cell carcinoma, fibrosarcoma and acanthomatous ameloblastoma. In cats squamous cell carcinoma is by far the most commonly diagnosed oral tumour, followed by oral fibrosarcoma.

Diagnostic Approach And Staging

The majority of cases will present with a noted oral mass, however oral lesions can often be missed by owners, especially those located caudally. Typical clinical signs include halitosis, increased salivation, dysphagia, loose teeth, weight loss, pain on opening the mouth and less commonly exophthalmos or facial asymmetry. No specific paraneoplastic conditions are associated with oral tumours.

The diagnostic work up of any dog or cat presenting with an oral mass should include a through history and physical examination followed by determination of the diagnosis and staging. A diagnosis in the case of oral tumours is typically via histopathology requiring a wide incisional biopsy of the lesion under general anaesthesia. Initially cytology samples can be undertaken however given the common secondary inflammation, infection and necrosis of oral lesions these can often be non-diagnostic. Oral lesions typically have a vast blood supply and preparation for adequate haemostasis should be considered prior to biopsy. The use of electrocaudery can distort the specimen and should only be used for haemostasis following blade incision or punch biopsy. Biopsies should always be taken from within the oral cavity and not via overlying dermis to avoid seeding of tumour cells to normal skin. Curative-intent resection for small lesions (especially those of the labial mucosa) may be considered at the time of initial work up, however excisional biopsy of more extensive disease is not recommended.

The general anaesthesia will apart from facilitating a biopsy, firstly allow a through oral examination. Close inspection of the pharynx, tonsils and hard palate should be undertaken as well as the gross margins of the lesion itself. Secondarily the opportunity to undertake oral radiographs or a Computed Tomography (CT) scan of

the head should be undertaken to assess for microscopic disease extent. A CT scan allows for greater detail and can serve to analyse more precisely the location and extent of the mass as well as underlying bone lysis. Following advanced imaging surgical resectibility and discussion of best surgical approach as well as likelihood of obtaining wide surgical margins can be interpreted. Additionally contrast uptake in the draining lymph nodes can be assessed. Another advantage of a CT scan in the initial work up is the use of the images for radiotherapy treatment field planning for cases where surgical resection is not appropriate or is declined by the owner.
Further staging should routinely include aspiration of the draining mandibular lymph node if palpable (even if considered normal on palpation) and aspiration of the tonsils should they appear grossly abnormal. Regional lymph nodes include the mandibular, parotid and medial retropharyngeal, however generally only the mandibular nodes are palpable. Thoracic cavity imaging is essential to assess for distant metastasis via either three view thoracic radiographs or extension of the CT through the thoracic cavity. The World Health Organisation's (WHO) clinical staging system for oral tumours in dogs as outlined in table 1, should be considered in each case as the clinical stage of disease can be prognostic for oral tumours (especially in the case of malignant melanoma).
Oral malignancies are typically locally aggressive with a low to intermediate metastatic potential (apart from malignant melanoma). They typically occur in older animals >8 years old and all commonly cause bone lysis. Dogs previously documented as being at an increased risk of developing oral tumours include the cocker spaniel, German shepherd dog, German shorthaired pointer, weimaraner, golden retriever, Gordon setter, miniature poodle, chow chow and the boxer.
Surgery and radiotherapy are the mainstays of therapy for any oral tumour. The extent of the surgical approach will be dictated by the location and size of the lesion. The expectation that in most cases bone resection will be necessary should be outlined to the owners to allow for increased local tumour control. The functional and cosmetic outcome for most patients following mandibuletomy (segmental or hemi), maxillectectomy (segmental) or orbitectomy is generally very good and owners satisfaction deemed to be high. With most oral tumours 2cm margins are required for consideration of reasonable local control. This can be very challenging in the case of caudally located tumours or tumours which breach the midline of the palate.
Radiotherapy can be instigated as a primary therapy, as a curative intent protocol or a palliative therapy, or as an adjunct to incomplete or marginal surgical excision of an oral tumour. Here consideration of the biological activity of the tumour type and estimation of the responsiveness of the tumour either in the gross disease or microscopic disease setting should be considered in order to determine an appropriate treatment protocol for each patient.

Canine Oral Tumours

- **Malignant Melanoma**

Malignant melanoma is the most common oral tumour affecting dogs, accounting for 30-40% of oral malignancies. Typically occurring in dogs over 10 years old and small dog breeds especially the cocker spaniel, are over represented, as well as dogs with darkly pigmented mucosa. The mass can occur at any oral location, however in order of decreasing frequency they are found on the gingiva, lips, tongue and hard palate. Approximately 2/3 are said to be pigmented and 1/3 amelanotic, they are commonly ulcerated and frequently have bone involvement. The histopathology of an oral melanoma can be confusing and they can often be misdiagnosed as poorly differentiated sarcomas or carcinomas. Melan A is an immunohistochemical marker used as a melanoma specific marker, however its sensitivity drops with increasing degrees of differentiation.

These tumours are locally aggressive and have a high metastatic potential. The typical sites of metastasis include the regional lymph nodes (up to 74%) and then the lungs (up to 67%). The WHO staging system for canine malignant melanoma is prognostic with tumour size being of most relevance. The metastatic rate is size, site and stage dependent. Other poor prognostic factors include incomplete surgical margins, location (caudal mandible and rostral maxilla), mitotic index >3, bone lysis, and more recently documented the ki67 value.

- **Squamous Cell Carcinoma**

Squamous cell carcinoma (SCC) is the second most common oral tumour in dogs, accounting for 17-25% of cases. Two separate disease entities should be considered, tonsillar SCC and non tonsillar SCC. The overall prognosis for non tonsillar SCC is good especially for small and rostrally located lesions. These tumours are typically locally aggressive frequently causing bone lysis, but considered to have a low metastatic potential. Regional lymph node metastatic disease is reported as up to 10% and distant metastatic disease to the lungs reported in 3 to 36% of cases (1). Tonsillar SCC has a much higher metastatic potential; up to 77% of cases will have regional metastatic development and 42-63% distant metastasis. Here frequent local tumour recurrence following surgical or radiation therapy is common.

- **Fibrosarcoma**

Oral fibrosarcoma (FSA) is the third most common oral tumour in dogs. This tumour will in many cases have a very benign histopathology and can be sometimes misdiagnosed as non-neoplastic. However it will commonly show an extremely aggressive biological behaviour growing rapidly and causing severe bone destruction and facial deformity. This subset of oral fibrosarcomas is often referred to as biologically high grade, histologically low grade. These tumours have a predilection for the hard palate and maxilla and while typically being very locally aggressive metastasize to the regional lymph nodes and lungs in less than 30% of cases. Once again the size and location of the tumour are prognostic. Multimodality therapy utilising both surgery and radiation therapy is considered standard of care for these patients. Historically when surgery is utilised alone the one year survival rates have been said to typically not exceed 1 year, however a more recent publication has outlined more favourable local control and survival times (Overall survival 24.8 months) than previous reports. This may be due to advancing surgical techniques as well as the increased use of CT imaging prior to surgical resection. The goal of surgical excision when planning resection of an oral FSA should be to obtain the widest margins possible, however surgical excision should still be considered even when 2cm margins are not expected. Radiation therapy to a large tumour volume is considered less ideal and this tumour is considered in the gross disease setting to be relatively radiation resistant. Outcomes are improved where surgery and radiotherapy are used in combination. With a generally recognised low metastatic rate the role of chemotherapy here has not been fully identified, the focus should remain on local disease control.

- **Acanthomatous Ameloblastoma**

Canine acanthomatous ameloblastoma (CAA) is characterised as a benign odotogenic tumour or epulis. The term epulis is a descriptive term applied to expansile gingival lesions. Odontogenic tumours are generally considered rare and there has been much confusion regarding their nomenclature and origin as well as other reactive lesions of the gingiva. The acanthomatous epulis has microscopic

features in common with human ameloblastoma. However its clinically invasive nature with common destruction of underlying bone (unlike other odontogenic tumours) is similar to the human intraosseous ameloblastoma. The tumour is now termed CAA because it is considered its own entity with no precise human equivalent. CAA most commonly affects the rostral mandible and a golden retrievers, akitas, cocker spaniels and Shetland sheepdogs are overrepresented breeds (1, 10). The typical appearance is cauliflower like, red and ulcerated. While considered locally aggressive the tumours have not been known to metastasize and hence local tumour control is the mainstay of therapy.

FELINE ORAL TUMOURS

Squamous Cell Carcinoma

SCC is the most common oral tumour of cats accounting for approximately 65% of tumours seen. It can arise from any oral mucosal surface including the sublingual region the tonsils and the pharynx. The tumour is very locally aggressive and commonly causes underlying bone lysis. The regional lymph node and distant metastatic rate is low and estimated at 10%. Cats that wear a flea collar are at 5 times the risk, additional risk factors include a high canned food intake, canned fish and tobacco smoke within the environment may have a role in the pathogenesis of the disease. The average age of cats affected is 10-12 years, any oral lesion in an older cat should be biopsied promptly as early diagnosis of may improve the prognosis. Many cats will present because the owners have noted an oral mass and the most common clinical signs include ptyalism, halitosis and in some cases dysphagia. Staging should include as for canine oral tumour cytology of the regional mandibular lymph node and three view thoracic radiographs. While oral radiographs can be helpful and may be reasonable to determine underlying bone lysis, CT imaging allows for greater accuracy of bone involvement and should be undertaken in all cases where aggressive therapy is being considered.
While surgery and radiation therapy can be undertaken the median survival time is short with survival times over 3 months uncommon and a one year survival rate of less than 10%. However the prognosis is potentially improved for those patients with small and rostrally located lesion where wide surgical excision can be undertaken and/or adjuvant radiotherapy employed. Resection of the mandible plus curative intent radiotherapy gives a median survival of 14 months. In the majority of cases surgery alone does not offer a significantly extended survival time to untreated cats due to the fact that the disease is so locally invasive and wide margins are typically unachievable. Likewise palliative radiotherapy is not proven to improve survival significantly over untreated cases. No chemotherapy to date has been shown to be effective in the treatment of these cases. Historically results were improved with the combination of radiotherapy and radiation sensitizers, however rapid recurrence was documented. A recently published paper has described an accelerated radiation protocol with concurrent chemotherapy. Here cats received 14 fractions of 3.5 Gy for a total of 49 Gy in a nine day period while receiving concurrent intravenous Carboplatin. The protocol was intense but well tolerated with a median survival time of 169 days. Cats with disease of the tonsils or cheek had an increased survival time.

Pain management and the consideration of NSAID therapy, antibiotic therapy as well as frequent quality of life assessment are crucial in the medical management of

Feline Cutaneous SCC

- Accounts for 15% of feline cutaneous tumours

- Often associated with poorly pigmented skin and UV exposure
- In cats, the most common areas for SCC development are the nasal planum, the eyelids and the pinnae.
- Tumours are locally invasive but slow to metastasize.
- The tumour may be 'productive' forming a papillary growth with a cauliflower like appearance, or 'erosive' forming a shallow ulcer with raised edges. In both instances the lesion is frequently ulcerated, infected and associated with a chronic inflammatory infiltrate. It is not uncommon for these tumours to be dismissed as infective/inflammatory lesions on initial presentation.
- Multifocal distribution of superficial lesions has been reported in cats. This is referred to as "multicentric SCC *in situ*" or **Bowen's disease**. Bowen's disease is an unusual feline skin condition of unknown origin. Recently, papillomavirus antigen has been demonstrated in 45% of the feline skin lesions using immunohistochemical methods. Unlike solar induced SCC, Bowen's disease is found in haired, pigmented areas of the skin and is unrelated to sunlight exposure. Lesions are confined to the epithelium with no breachment of the basement membrane. Lesions are crusty, easily epilated, painful and hemorrhagic. When excision is possible, recurrence has not been reported, however similar lesions often develop at other sites.

Surgery:
- For tumours of the pinnae, surgery (pinnectomy) offers tumor control for >1.5 years
- For nasal planum tumours, surgery can offer good local control, but recommend referral to a specialist, board certified surgeon for best results.
- En bloc resection of lower eyelid tumours also offers good control, but advise referral to a board certified surgeon.

Cryotherapy
- Aggressive cryotherapy can offer good local control for tumours of the pinnae and eyelid.
- Tumours of the nasal planum appear to have a poorer response.

Radiotherapy
- External beam radiotherapy has demonstrated good local control for lower stage tumours.
- Strontium-90 Plesiotherapy has shown efficacy for superficial lesions

Chemotherapy
- Intratumoral administration of carboplatin in a sesame oil suspension appears safe, practical and effective for SCC of the nasal planum in cats

Photodynamic Therapy
- Benefit has been demonstrated only in superficial tumours of low stage

Nasosinal tumours in dogs

Key Points:
- Tumours arise from the nasal cavity and/or paranasal sinuses and are almost always malignant. Most are adenocartcinomas
- Older dogs are most commonly affected, although dogs as young as one year have been reported
- Medium and large breed dogs are predisposed

- The most common malignant tumour types are carcinoma, including adenocarcinoma, and sarcoma, including fibrosarcoma, chondrosarcoma and osteosarcoma
- Less common malignant tumours include lymphoma, mast cell tumour, olfactory neuroblastoma and others.
- Benign tumours rarely occur but can include polyps and fibromas.
- Malignant tumours are locally aggressive, often causing destruction of bone. Tumours can extend beyond the cribiform plate into the calvarium.
- The rate of regional and distant metastasis is low at the time of diagnosis. Most common sites of metastasis include lymph node and lungs.
- Therapy is aimed at local tumour control or palliation of clinical signs
- Paraneoplastic syndromes associated with nasal tumours are rare. Erythrocytosis and hypercalcemia have been reported.
- Environmental factors including tabacco smoke and indoor exposure to fossil fuel combustion products may be related to tumour development.

Clinical Signs of Nasosinal Tumors
○ Unilateral or bilateral nasal discharge: mucoid, purulent, hemorrhagic, or any combination thereof ○ Epistaxis ○ Nasal congestion or stertorous breathing ○ Sneezing ○ Facial deformity due to subcutaneous extension of tumour ○ Epiphora ○ Exophthalmous ○ Neurologic signs including seizures, behavior change, and obtundation due to direct tumour extension into the calvarium ○ Halitosis ○ Oral mass due to tumor extension into the oral cavity

Differential Diagnosis For Dogs With Clinical Signs Relating To The Nasal Cavity And Nasal Sinuses:

Neoplasia (see Histologic Classification below)
Fungal rhinitis (Aspergillosis, Blastomycosis or Sporotrichosis)
Bacterial rhinitis
Immune-mediated lymphoplasmacytic rhinitis
Coagulopathies
Hypertension
Foreign body
Trauma
Embroyonic vestige (Rathke's clefts cyst)

Diagnosis:

- If epistaxis is the only nasal sign, coagulation parameters (PT, PTT) and platelet count should be evaluated to rule out a primary coagulopathy.
- In almost all cases of nasosinal neoplasia, a mass lesion is present in the nasal cavity

- Imaging is necessary to localize the lesion and determine its extent
    - Advanced imaging including computed tomography (CT) or magnetic resonance imaging (MRI) is more sensitive than radiography
- Histopathology is required for definitive diagnosis
- Nasal biopsy techniques include non-invasive and invasive methods (see table below).
- To avoid misdiagnosis, it is important to keep in mind that nasal signs caused by a tumour may improve temporarily with the use of antibiotics, non-steroidal anti-inflammatory drugs or steroids.

Non-invasive Nasal Biopsy Techniques	Invasive Nasal Biopsy Techniques
Nasal flushing Blind transnostril biopsy[1,2] Endoscopy-guided fiberoptic biopsy[1] Fine needle aspiration or biopsy of facial deformities	Surgical biopsy via rhinotomy

[1]Coagulation parameters should be assessed prior to transnostril biopsy as bleeding from the biopsy site is expected
[2]Blind transnostril biopsy instruments should not be introduced further than the medial canthus of the eye to avoid penetration of the cribiform plate

Treatment and Prognosis:

- Since the rate of metastasis is low at the time of diagnosis, local therapy is indicated.
- Radiation therapy is the treatment of choice.
- Surgery (rhinotomy) alone results in rapid tumour re-growth
- Palliative therapy: NSAIDS

Feline Nasosinal Tumours

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<u>Nasosinal tumours in cats:</u> Key Points:

- Less common than in the dog
- Older cats are most often affected
- Malignant tumors are more common than benign tumors

- Tumours are **locally aggressive**, often causing destruction of bone. Tumours can extend beyond the cribiform plate into the calvarium.
- Most common tumour type is **lymphoma**, followed by **carcinoma and adenocarcinoma**
- Rhinitis can mimic neoplasia in clinical signs and imaging findings
- Risk of metastasis is moderate to high for lymphoma, but low for carcinoma
- Lack of clinical data regarding efficacy of treatment
- Cats with nasosinal lymphoma should be tested for FeLV and FIV

Thyroid Tumours in Dogs

Key Points

- Account for 1-4% of all tumours in dogs
- 30-50% are benign, non-functional adenomas
- Adenomas are very small and are usually not detected clinically (incidental finding at necropsy)
- Most clinically detected tumours are classified as malignant.
- Age range of 9-11 years
- In rare cases, ectopic thyroid tissue can be affected
- 35-40% of dogs have visibly detectable metastatic disease at presentation (lymph nodes and lungs)

- **The treatment of choice is dictated by:**
  - Size of the mass
  - Degree of invasion
  - Concurrent metastatic disease
  - Evidence of thyrotoxicosis

- **For freely moveable, non-invasive tumours,** surgical excision is the treatment of choice, giving a median survival time of around 3 years.

- **Non-resectable tumours** are managed with external beam radiation.
  - May be used in the neoadjuvant setting to improve a definitive surgery
  - Can be used post-operatively to treat minimal residual disease
  - Used alone: shrink tumours over a 6-month period giving very good local control.

- **Dogs with gross metastatic disease**
  - Metastasis (even when detected visually), takes a long time to become clinical (sometimes 1-2 years)
  - Surgery for freely mobile tumours or palliative radiotherapy for non-mobile tumours is therefore still a reasonable option without compromising patient quality of life.

Is radioactive Iodine ever indicated in canine thyroid tumours?

- In humans ^{131}I is often used post-surgically to treat microscopic disease. Experience in dogs is limited.
- The major limiting factor in dogs is the high dose of ^{131}I required, as these tumours do not accumulate iodine in the same way as functional adenomas. Most centres do not have the facilities required (health and safety) to handle such doses.

Is chemotherapy indicated in the management of canine thyroid tumours?

- Where surgery of radiotherapy is not a viable option, chemotherapy with either doxorubicin or carboplatin could be considered. However, only partial responses should be expected and it must be considered palliative only.
- Where radiation is not available, chemotherapy may be considered where surgical resection has been performed, but surgical margins demonstrate microscopic disease.
- Chemotherapy can be considered where there is gross metastatic disease. However, disease progression in these cases is often slow anyway. The beneficial effects of adding in chemotherapy are unproven.
- Large tumours and bilateral tumours have been shown to have a greater metastatic potential. Consequently adjunctive chemotherapy may be considered for tumours above 20-30cm^3

Feline Thyroid Tumours

Key Points

- Hyperthyroidism is the most common endocrinopathy in cats
- 70-75% of cases are caused by multinodular adenomatous hyperplasia
- 20-25% are caused by solitary adenomas
- 1-3% are caused by malignant carcinomas

Clinical Signs:

- Older cats > 8years
- Weight loss with polyphagia
- PUPD
- Vomiting and diarrhoea
- Hyperactivity
- Tachycardia, heart murmur, gallop rhythm
- Poor coat
- Palpable goitre

Diagnosis

- Clinical signs and history
- Elevated serum total T4 (tT4)
- free T4 by equilibrium dialysis if tT4 in mid to high range but highly suspicious
- Dynamic testing rarely indicated

Staging

- CBC, serum chemistry and urinalysis
- Thoracic radiography, ECG, Echocardiography
- Blood pressure measurement
- +/- technetium scintigraphy to determine the extents of disease (uni or bilateral, ectopic)

Medical Management:

- Thiamazole (licensed in UK) or carbimazole
- Inhibit thyroid hormone synthesis
- Used as:
    - Sole treatment
    - To stabilize a patient prior to thyroidectomy
    - During ^{131}I treatment
- Cats are monitored using tT4 levels
- Side effects include vomiting and anorexia
- Not effective for carcinomas

Surgical Management:

- Cats are managed medically (see above) prior to surgery (for around 2 weeks).
- Intracapsular and extracapsular techniques are described
- Intracapsular method preserves the adjacent parathyroid tissue, but the extracapsular technique is superior for achieving adequate surgical excision.
- Post-operative complications include
    - Laryngeal paralysis
    - Horner's syndrome
    - Hypocalcaemia
    - Hypothyroidism
- For cats where surgery does not resolve clinical signs consider:
    - Long-term medical management
    - ^{131}I treatment

^{131}I Treatment

- Treatment of choice, especially where:
    - Bilateral disease
    - Ectopic thyroid tissue is affected
    - Thyroid carcinoma (higher dose often required)
- Specialist facilities required
- Refer

Ear Canal Tumours of Dogs and Cats

Key points

- These are not uncommon tumours in both species, and may be associated with chronic inflammation from otitis externa
- Clinical signs include chronic irritation, presence of a mass lesion, aural discharge, pain and an odor. In severe cases with middle or inner involvement, patients may present with vestibular signs or Horner's syndrome.
- The most common benign tumours in both species are:
    - Inflammatory polyps
    - Ceruminous adenomas
    - Papillomas
    - Basal cell tumours
- The most common malignant tumours are:
    - Dogs
        - Ceruminous gland adenocarcinoma
        - Squamous cell carcinoma
        - Carcinoma of undetermined origin

- Cats
  - Ceruminous gland adenocarcinoma
  - Squamous cell carcinoma

Therapy:

- For benign lesions, conservative surgical resection in both species offers a good prognosis.
- For malignant lesions, ear canal ablation and lateral bulla osteotomy should be considered the treatment of choice.
  - Prognosis for dogs is better than for cats
  - Local radiotherapy may be considered where incomplete resection is achieved.