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Everything You Need to Know about Cancer Management Mini Series

Session Three: Everything You Need To Know About....Cancer Management in Cats

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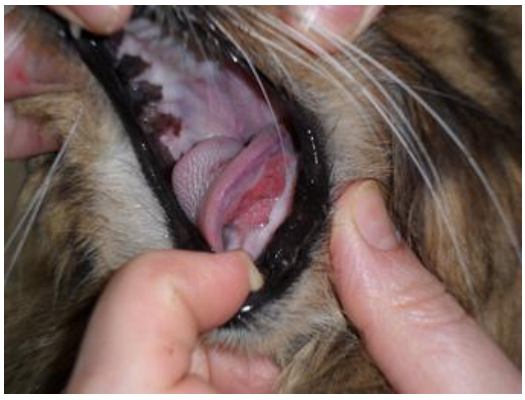

Lymphoma (and Leukaemia)
Feline lymphoma has long been compared to canine lymphoma but the first and most important message to convey is that these two diagnoses should not be considered similar. Of course there are similarities but the differences are more marked. We are in the habit, as veterinary surgeons trained in omnicompetence, to extrapolate interspecies differences. That is dangerous for lymphoma.
The principal differences between cats and dogs are anatomic distribution, response to therapy, prognosis and importance of immunophenotype. You could say, pretty much everything.

The most common presenting form of feline lymphoma is the alimentary form. This presents no difficulty of interpretation. Everybody is familiar with the notion of a cat with lethargy, inappetence, weight loss and a palpable abdominal mass. The overwhelming majority of cases presenting with these signs have intermediate to high-grade alimentary lymphoma. Further reading may take you on a journey of explanation of the various other anatomic forms of feline lymphoma and quite honestly from that point forward, the whole thing is a mess. Different authors try to a greater or lesser extent to use similar terms as we use for canine lymphoma. As soon as they do we end up with classifications of disease which have cases shoehorned into them rather than a classification mechanism which accurately defines particular disease presentations.

Realisation that lymphoma classification between investigators is variable immediately challenges any prospect of drawing legitimate comparisons between published case series, something we like to do to develop a sense of whether one treatment might be superior to another. This is then further compounded by the fact that there are geographic variations in the prevalence of Feline Leukaemia Virus which has probably, but not definitely, had a significant impact on the anatomic classification of diagnoses of feline lymphoma and the response to therapy and therefore prognosis in different parts of the world.

FeLV Prevalence
There are data from the University of California reporting the prevalence of FeLV and FIV among cats diagnosed with lymphoma from 1984 to 2003. Remarkably, 56% of feline lymphoma cases diagnosed with ‘retrovirus-positive’ lymphoma were diagnosed between 1984 and1990. Over the following fourteen years there were only 35 retrovirus positive cases. This epidemiological change reflects the advent of commercially available testing kits for FeLV and FIV and the implementation of prevention strategies by vaccination for FeLV specifically and by ‘test and remove’ management for both. Unexpectedly, the prevalence of lymphoma has increased despite a marked reduction in the prevalence of retrovirus-associated lymphoma. The cause is unknown but it appears that the change seen can be attributed more or less entirely to an increase in the diagnosis of alimentary lymphoma. Speculation abounds but not surprisingly, much speculation surrounds the possibility that the change in prevalence may somehow reflect a change in cat food or cat-feeding habits.

Specific Lymphoma Subtypes
Despite my previously gloomy assessment of the state of our knowledge of feline lymphoma, there are certain specific lymphoma subtypes which are recognised entities and which merit discussion.

Small Cell Lymphoma
Approximately 5% of intestinal lymphoma cases in cats are described as small cell or lymphocytic lymphoma. These are thought to arise as an epitheliotropic lymphoma. Diagnosis is notoriously difficult because of the histological similarity between these cases and those with inflammatory bowel disease. Many cases have only very limited structural change in the bowel wall.

Endoscopic biopsies are unlikely to yield an accurate diagnosis as it is often the presence of infiltrating T lymphocytes passing into the muscularis layer of the bowel which assists the pathologist in making the diagnosis. Cases of small cell lymphoma are managed very differently from cases of intermediate or high-grade lymphoma and the prognosis is very different. Treatment comprises chlorambucil and prednisolone. Dose recommendations vary, I use chlorambucil at 20mg/m2 once every two weeks and prednisolone at 5mg once daily for week then once every second day. Some oncologists use up to 5mg/m^2 every second day. Higher doses of chlorambucil in the long term confer a higher risk of toxicity, in particular myelophthisis, which can be lethal if left unrecognised.

Hodgkin's Like Lymphoma

This is a relatively unusual form of lymphoma which typically manifests as firm enlarged (3-4cm) paired submandibular lymph nodes without evidence of disease affecting other sites. Over the course of a few months, the disease appears to extend caudally as though flowing along a lymph node chain so that caudal cervical and prescapular lymph nodes become affected. The disease does spread to visceral lymph nodes if patients live long enough. There are no recognised treatments for this. There are investigations ongoing at present to examine the possible use of radiotherapy in the management of these cases. To date they have not been successful. I suspect that cases would still succumb to systemic disease at the same rate even if locoregional radiotherapy appeared successful. Diagnosis can be challenging because up to 98% of the cells present in the grossly enlarged lymph nodes can be non-neoplastic reactive lymph node components. A diagnosis is therefore often not possible using cytology alone.

Large Granular Lymphocyte (LGL) Lymphoma/Leukaemia

Under normal circumstances approximately 1/1000 nucleated cells in the peripheral blood is a large granular lymphocyte. These cells are natural killer cells or specialised cytotoxic T cells and in fact are adapted to recognise tumour cells (and virally infected cells). Lymphoma can arise due to proliferation of these cells. It can be aggressive or it can be very indolent. The classic aggressive form arises as a gastric lymphoma. Median life expectancy with chemotherapy is less than two months. The classic indolent form is chronic LGL leukaemia, which can remain stable for eighteen months or more without any therapy. Importantly, on routine H&E histology, eosinophilic cytoplasmic inclusions are not consistently detectable.

For the majority of the remaining lymphoma and leukaemia patients, we treat them as though they were all the same.

Chemotherapy

There remains an ongoing debate about best therapy for (intermediate to high grade) feline lymphoma. As alluded to above, as soon as we start to open our minds to the reality that feline lymphoma is not a single entity, we might start to make some progress here. Although I do not believe that there is a single optimal treatment plan for feline lymphoma, personally, I prefer COP in cats. As far as I can see there is no compelling study published which clearly demonstrates a superior survival time for cats treated with one over the other (COP or CHOP) and therefore I prefer a treatment strategy that is simple and therefore does not require cats to be taxied for hundreds of miles for therapy which they undoubtedly will not enjoy which incurs a significant risk of treatment-induced side effects.

An interesting publication (Milner 2005) about feline lymphoma reports the outcome for a retrospective cohort of 38 cats treated with what is described as 'The Madison-Wisconsin Protocol'. The treatment comprises a two-year plan with the option to restart at any time if relapse is identified.

The median survival time was no different from every other feline lymphoma protocol I recall reading about (210 days) but the moderately interesting thing is that the cats that demonstrated a complete remission, of which there were 18, did apparently go on to enjoy a prolonged survival time, median survival time was quoted to be 654 days. This may indicate a superior treatment has been found but close scrutiny of the data does reveal that by day 655, there were only three cats left alive. It is therefore quite conceivable that this apparently exciting outcome is simply a statistical phenomenon rather than a true advantage. For those cases achieving partial remission the survival profile was almost identical with other published protocols.

A more recent publication described a prospective cohort of cats receiving a short (12 week) CHOP protocol. 46% of cases achieved complete remission and for those cats the median survival time was 454 days. When the group was evaluated as a whole, median survival time was only 78 days.

By way of contrast, other publications describing outcome for cats with lymphoma receiving COP chemotherapy report overall median survival times of 266 days (Teske 2002) 388 days (Teske 2012) and 171 days (Taylor 2009). The Taylor paper reports a superior outcome with COP compared to so-called Madison Wisconsin protocols (171 vs 112 days). The cases reported by Taylor have 'extranodal' lymphoma; it is not clear whether this is relevant to the apparently different survival times.

The most recent study by Teske and others (2012) described the intraperitoneal administration of vincristine and cyclophosphamide with no apparent reduction in survival prospects compared to intravenous administration.

What is clear from all chemotherapy studies concerning cats with (intermediate or high-grade) lymphoma is that acquisition of complete remission is critical to their chances of achieving a durable remission.

My presumption that one day feline lymphoma will catch up with human lymphoma. By this I mean that we will stop publishing studies and talking about feline lymphoma as though it were a single entity. We are beginning to recognise specific forms of feline lymphoma as indicated above. Until we can reliably separate feline lymphoma cases on the basis of something more than the part of the body they inhabit there will always be scope for someone to publish their superior management protocol which is only apparently superior due to the collection of cases reported.

Leukaemia

It is worth writing a few words on leukaemia specifically. Leukaemia is no longer considered a distinct entity in human haemato-oncology. We should aim to adopt a similar appreciation of the nature of disease in our patients. The distinction between lymphoma and leukaemia is one of tropism. In lymphoma the cancer cells naturally accumulate in tissues; in leukaemia the cells naturally accumulate in the blood. In all other respects the cancer cells can exhibit the same sensitivity to treatment as each other. Once we can satisfactorily categorise lymphoma and leukaemia on a clinically meaningful basis this anatomic distinction will become considerably less relevant. However, it will always be true that leukaemia could be associated with other changes in the bone marrow which result in the patient being at higher risk of chemotherapy induced bone marrow complications. Practitioners must be aware of this and must manage patients accordingly. It is also true that there are changes in the dynamics of blood flow and this results in an increased risk of coagulopathy and ischaemia.

Oral Squamous Cell Carcinoma

Feline oral squamous cell carcinoma (FOSCC) is a troubling disease. It rarely presents at a sufficiently early stage in disease progression for surgical intervention to be a rational proposition. This means that all therapeutic options are essentially palliative. For decades oncologists have grappled with this tumour, trying to squeeze a few extra days or weeks out of a moribund patient. Historically the treatment options have been surgical: there is one paper that describes really quite radical surgical excisions for FOSCC. Even with predominantly small tumours, lasting remission is unusual. Furthermore there are significant complications associated with oral surgery including permanent ptyalism, inability to groom properly and death due to anorexia. Only 9/42 cats undergoing mandibulectomy for oral neoplasia were reported to experience no long-term complications of their surgery. Although nearly half of the FOSCC cases were reported to have survived to one year from surgery, the statistical methods used may artificially inflate the apparent success of the treatment. Median survival time was quoted to be 217 days. However, 15/21 cases were no longer alive by seven months from the time of surgery.

Other options for FOSCC management include radiotherapy and chemotherapy. The expected survival time with these treatments are 3 months for radiotherapy and 2 months for chemotherapy. In that same study, life expectancy for surgical cases was only 1.5 months. It is clear to see why oncologists struggle to define best management for these cases. Typically cases are seen at a late stage of progression. Bone invasion is already established and there is significant gingival or mucosal involvement.

The trick with FOSCC therefore is to diagnose early. Cats are frequently presented for dental attention and asymmetry of the gingival inflammation should ALWAYS prompt a biopsy and histological evaluation. It is vital for any prospect of a successful surgical outcome that only the abnormal mucosal tissue is biopsied. Cats have precious little slack tissue in their oral cavities with which to repair any possible surgical deficit.

New Chemoradiotherapy Protocol

Janean Fidel and colleagues from Washington State University have recently published information about an experimental radiotherapy and chemotherapy approach to the management of FOSCC. The study was based upon perceived gold standard management for human patients with head and neck cancer, the human equivalent of FOSCC. Treatment comprises multiple radiotherapy doses delivered twice daily over nine days (with two days off for the weekend) and with a low dose of carboplatin chemotherapy given on days one and four, theoretically as a radiosensitiser. The team at Washington have now reported treating 31 cases. They have shown that tonsillar and buccal mucosal FOSCC may respond better to therapy, however, median survival time remains poor at 163 days. This does exceed the previously published results with conventional radiotherapy alone. However, it is also true to say that there are no data published reporting the outcomes for cases treated with great hope for a miraculous result that actually only receive analgesia or even a placebo. Late effects of radiotherapy including bone necrosis, lip or tongue fibrosis and aphonia were reported but the true incidence of these side effects cannot be evaluated since so few cases live sufficiently long.

This protocol certainly holds interest for cases with tonsillar or buccal mucosal FOSCC. Outcomes for bone invasive or lingual FOSCC remain disappointing.

Surface Radiotherapy

Very recently, two cases of FOSCC, one affecting two sites on the palate and a third site on the mandible and a second case affecting the lingual frenulum, were reported. Both were treated with high total doses of electron radiotherapy (beta particles) from a radioactive strontium probe. In both cases a response was seen.

Complete remission was achieved in the first case and a partial remission in the second. It is too early to comment on whether this treatment might have greater application but it is certainly an appealing treatment option.

Metronomic Chemotherapy

In the absence of superior treatment strategies, the currently in vogue 'metronomic chemotherapy' protocol pushes to the foreground. This treatment plan should still be regarded as theoretically useful, but nonetheless, many oncologists can now cite one or two cases of cats or dogs with a presumed-to-be intractable tumour that has appeared to respond to therapy. Treatment comprises a combination of the NSAID meloxicam and cyclophosphamide in low doses. There is no question that FOSCC is a very inflammatory lesion so it is reasonable to assume that there would be some symptomatic response to therapy. My own experience is that cases that receive this treatment significantly outlive expectation. However, I cannot guarantee that they would not have done so for other reasons such as the nature of the owner/pet relationship in these particular cases.

Mammary Tumours

Mammary tumours are reported to be the third most common tumour diagnosed in cats. An annual incidence rate of 25/100,000 has been reported (compared to approximately 200/100,000 in bitches). Peak age incidence occurs at 10-12 years. There is some evidence to suggest that Siamese cats are predisposed to mammary tumours. Neutering practices markedly reduce the tumour risk. Mammary tumours in cats are also seen with greater frequency in cats who have received exogenous progestins, typically for the management of pruritic skin disease. The risk of the development of mammary neoplasia is reduced by 91% in queens speyed before the age of six months. Considering all cats speyed before twelve months of age, there was an 86% reduction in risk compared to intact females; speying between 13 and 24 months conferred only a (statistically non-significant) 11% reduction in mammary tumour risk. Parity appears to have no effect on mammary tumour risk.

Presenting Signs

Mammary tumours in cats are reported to typically manifest as a solitary well-defined subcutaneous nodule. My experience is different from this; the majority of cases that I see present with flattened plaque-like lesions, typically with a multilobular nature. The physical appearance of these tumours gives some indication of the readiness with which these tumours infiltrate into surrounding mammary tissue and this capacity for infiltration underpins some of the treatment recommendations. Cats will rarely exhibit clinical evidence of metastasis at the time of diagnosis. However, approximately 85% of feline mammary tumours are reported to be metastatic. Approximately 55-60% of cases will present with multiple independent primary mammary tumours. Some of these can be very small and therefore the clinician should be very detailed in their examination of the remaining mammary tissues when a primary mammary tumour is diagnosed or suspected. In one study the majority of cases of subsequent mammary neoplasia arose in the same mammary chain as the original tumour.

Histology

At the present time, there is a coordinated international movement to better classify canine mammary tumours on histologically and prognostically relevant bases. With improved collaboration and coordination, additional histological tumour entities are being discovered which may prove to have distinct clinical characteristics. Histological type and grade are shown to be of true prognostic significance.

In feline mammary tumours the body of knowledge is more limited because mammary neoplasia is less common and because it is less commonly reported or investigated. Furthermore, there is a much higher proportion of malignant and metastatic tumours in cats than in dogs, with the result that there is less overall variability. Without variability there is less impetus behind efforts to better categorise patients as treatment decisions would not alter with this improved knowledge.

However, similar histological tumour types do exist. Adenocarcinomas, tubular carcinomas, papillary carcinomas and solid carcinomas are most common. Many cases are described to have combinations of these tumours. Other specific histological types reported include cystic papillary carcinoma, cribriform carcinoma, micropapillary invasive carcinoma, comedocarcinoma, squamous cell carcinoma, mucinous carcinoma, and lipid-rich carcinoma. While it would not be unreasonable to make broad assumptions that behaviour in the individual tumour types would be likely to reflect the behaviour of similar tumour types in dogs, there is a lack of data at present to really substantiate any such assumptions.

Histological grade has been shown to act as a broad predictor of prognosis in feline mammary tumours (it has also been shown to be non-predictive in other studies). Grade is defined according to degree of differentiation (tubule formation), cellular and nuclear pleomorphism and mitotic index. In one study all patients with high-grade tumours and no patients with low-grade tumours had died within twelve months of surgery. Approximately 50% of intermediate-grade tumours had died within the twelve-month study period. A more recent study showed similar prognostic value to discriminating low-grade and high-grade tumours. Another histological factor noted is the presence or absence of extensive myoepithelial cell differentiation. There is a hypothesis that myoepithelial cell proliferation somehow limits the possible acquisition of characteristics of malignancy classically associated with the more malignant mammary tumour types.

Immunohistochemistry

There are countless reports of hormone receptor staining. In feline mammary tumours, there is a relatively high prevalence of hormone negative tumours and this may correlate with the fact that feline mammary tumours are more consistently malignant than other species' or it may be irrelevant. For the patient in front of you at any one time, I do not believe that hormone status in the tumour is of importance to decision-making. The proliferation marker, Ki-67, has been shown to have prognostic value. I would not be surprised if I was lecturing in five years time that Ki-67 assessment was an important part of feline mammary tumour evaluation, but at present I think Ki-67 assessment is just a good way of corroborating histological grade information. COX-2 immunohistochemistry in my opinion is highly variable, highly unreliable and to date, of no clinical value because use of COX-2 inhibitors in feline mammary tumour management has not been shown to improve prognosis. In fact, by comparison with historical controls, it would be reasonable to conclude that use of meloxicam actually worsens prognosis.

Clinical Stage

Most feline mammary tumours are invasive carcinomas which extend beyond the limit of the physically detectable mass and most are metastatic at the time of diagnosis. Size of the primary tumour has consistently been shown to be of prognostic significance. This is of relevance in lesions that do present as large solitary masses but less applicable for the more diffuse multilobular plaque lesions. Tumours less than 2cm in diameter are reported to have a better prognosis. Presence of lymph node metastasis or distant metastasis has not been consistently evaluated and is therefore sometimes reported as being of no prognostic significance. However, lymph node metastasis has been shown, in at least two separate studies, to be of prognostic significance. Furthermore, any absence of evidence of prognostic significance is likely to reflect the fact that patients with overt metastases are not referred for specialist care and those without overt metastasis may be misclassified as non-metastatic cases.

Lymph node metastasis is common. Rigorous assessments for detectable metastasis should be performed prior to undertaking surgery. Cats have paired caudal abdominal lymph nodes, in contrast to dogs, and both pairs should be evaluated. This can be performed ultrasonographically or by advanced co-axial imaging. Any detectably enlarged lymph nodes should undergo fine needle aspirate prior to undertaking surgery. All ipsilateral lymph node tissue should be removed if unilateral mammary excision is performed.

Distant metastasis does not only affect the pulmonary tissues. In mammary neoplasia, metastases are also noted in the pleura, peritoneum and liver. These sites are not evaluated by radiography and that is a significant shortcoming of the 'routine met check' in this particular cancer. I prefer to perform thoracic and abdominal CT imaging prior to embarking upon surgery.

Treatment

The mainstay of treatment is unilateral or bilateral mastectomy. Unilateral surgery is appropriate for solitary mass lesions. Bilateral mastectomy is appropriate for bilateral disease. Outcome reports for cases that did not undergo full chain mastectomy are consistently poorer than for those that did. For infiltrative tumours that extend out with the mammary tissue into the abdominal musculature, deep muscle layers must be taken in the en bloc excision for any chance of a curative excision. Lymph node evaluation prior to surgery is mandatory. The regional lymph nodes must be removed along with the mammary tissue at the time of surgery and must undergo histological evaluation.

Given the high incidence of metastasis in these tumours, a case can be made for the administration of adjuvant chemotherapy. A retrospective case series examined the impact of adjuvant doxorubicin and reported a significant difference in outcome for all cats receiving doxorubicin compared to all cats who did not. The difference was even greater when only cats undergoing full chain mastectomy were considered. Other chemotherapies have been reported including mitoxantrone and more recently, carboplatin.

Co-administration of meloxicam and doxorubicin following mammary tumour excision has been shown to achieve survival times broadly comparable with studies which did not incorporate meloxicam. As noted above, one could infer that the addition of meloxicam actually worsened prognosis. I do believe that this may be true for some but not all cases. Doxorubicin is nephrotoxic in cats and it is easy to believe that the combination with meloxicam would prove intolerable for a proportion of patients that were not shown to be azotaemic before treatment.

Prognosis

There are a number of studies describing outcomes for cats with mammary neoplasia spanning many decades. The relative paucity of reports leads to inappropriate comparisons being made between studies which were performed at very different times. It is inappropriate to extrapolate too much from studies which may no longer really reflect normal practice. It has been shown that primary tumour size is of prognostic significance, with three tumour diameter categories being of importance: <2cm, 2-3cm and >3cm diameter. However, this distinction was not supported in a recent large retrospective study and our improving understanding of the variety of mammary tumour types in veterinary species undermines the case for tumour size being an overarching prognostic factor. For patients undergoing unilateral mammary chain removal and adjuvant chemotherapy a median survival time of 1998 days has been reported compared with a survival time of 414 days in cats in the same study that only underwent comparable mammary surgery. Interestingly, in this study, only 49% of cases developed metastases or local recurrence.

Soft Tissue Sarcoma Including Feline Injection Site Sarcoma

Most feline sarcomas diagnosed in veterinary practice would fit under the soft tissue sarcoma banner. There are notable exceptions such as haemangiosarcoma and osteosarcoma. Soft tissue sarcomas can arise in a variety of sites but are most definitely found most frequently at sites of chronic inflammation or irritation, including sites classically used for injection of medicines, vaccines or microchips.

The term soft tissue sarcoma is deliberately vague. The precise presumed histogenesis of these tumours appears unimportant as the natural behaviour of these tumours is defined by other matters.It is notable that feline soft tissue sarcomas, in particular higher-grade sarcomas, can exhibit a remarkably mixed histological picture. It is not unusual to receive reports describing areas of osseous or chondroid differentiation within a tumour. There is no prognostic significance to this, except to reiterate that this mixed appearance appears to be associated with higher-grade tumours.

Expected Behaviour

One of the most significant determinants of outcome with feline soft tissue sarcomas is tumour grade. This term can be taken to mean the histologist's view of the degree of malignancy. It could be taken to mean the aggressiveness of the clinical manifestation of the tumour. To limit confusion, I will try to refer to these as histological grade and clinical grade, respectively. Low-grade sarcomas almost never spread. Therefore prognosis is defined by matters relating to the primary tumour alone. High-grade soft tissue sarcomas spread in approximately 30% of cases. Therefore prognosis is similarly defined by primary tumour matters in most cases. Metastasis really only threatens these cases if the primary tumour has been successfully managed.

Histological grade is defined by microscopic characteristics of the tumour specimen which have been shown to bear a relationship to prognosis. It is important to state that a defined tumour-grade scheme has never been validated for feline (or canine) sarcomas. However, schemes have been borrowed and modified from human sarcoma medicine and are used to good effect. The three most significant features of sarcomas are the degree of differentiation, proportion of tumour that has undergone necrosis, and mitotic index. Schemes are used which score these criteria and then descriptors, such as low-grade and high-grade are applied according to score thresholds. However, I prefer users to understand the criteria and how they are scored, and to consider each of these criteria in turn to gain an impression of whether a tumour should be considered bad, not so bad, or somewhere in between.

Microscopic Characteristic	Interpretation
Degree of differentiation	Cells that uniformly resemble a single tissue of origin are well-differentiated, grade is lower. Cells exhibiting no clear differentiation indicate higher grade.
Proportion of necrosis	None is good. <50% is intermediate. >50% indicates high grade
Mitotic index	0-10 mitoses per 10 x400 fields is low. 11-20 mitoses per 10x400 fields is intermediate. More than 20 is high.

Clinical grade is my term used to describe the physical characteristics of the tumour. Low-grade tumours are slow-growing and tend not to be fixed to the deeper tissues. Ulceration is less common. Lesions tend to have distinct boundaries. High-grade clinical characteristics include rapid growth, ulceration, diffuse infiltration, fixity to deeper tissues and larger size. There are no schemes for classification of clinical grade. Nevertheless these factors can be extremely instructive in the initial assessment of one of these patients.

Low-Grade Tumours

Soft tissue sarcomas in cats are rarely reported to be low-grade. Classically, the term fibrosarcoma is used in these cases. It should be expected that these tumours will have grown slowly and are likely to cause minimal challenge to the patient. Despite the low-grade nature of the tumour, they can still be difficult to treat. While I am not aware of a specific predilection site for these tumours, I do see them most frequently arising in the distal limb and around the head and neck. These sites present great challenges for the complete removal of locally infiltrative tumours. Since low-grade tumours have a very low incidence of metastasis, complete excision is regarded to be the treatment of choice. However, complete excision is likely to require 2-3cm measured lateral margins and an intact clean deep fascial plane to permit en bloc tumour removal. This will be a significant challenge in most cases.

Given the difficulty of achieving a complete wide local excision in many of these cases, consideration may be given to alternative management strategies. Options include: deliberate incomplete excision and observation for planned further intervention when relapse is detected; marginal excision followed by adjuvant (after surgery) radiotherapy; definitive (many doses) radiotherapy; radical surgery (amputation for distal limb tumours), and incomplete excision followed by metronomic chemotherapy (more on this later).

Since these tumours are relatively uncommon, they progress slowly and since there are so many potential strategies for dealing with them, there are no robust data that really demonstrate superiority of one treatment over another. For this reason choices are driven by owners' intuitive comfort with each of the various strategies that apply in their cat's case. In my experience, the radiotherapy options are rarely chosen, as there is a perception that there is too much risk and aggravation for the patient, which is not sufficiently counterbalanced by the expected improvement in length or quality of life that results.

High-Grade Tumours

It appears that high-grade soft tissues sarcomas in cats are becoming more prevalent. This may simply be a function of the fact that owners and vets are more ready to consider treatment in these cases than they were in the past. It could be that there is a genuine increase in case numbers. (In some regions of the world a genuine increase in injection site associated tumours has been very clearly demonstrated). These tumours are characterised by rapid progression, infiltration and fixity into underlying tissues and large tumour size relative to the patient.

The most notorious specific context in which we consider these tumours is the so-called injection site sarcoma. In my opinion it is correct that the profession is anxious about the risk that our efforts to protect from infectious disease might be inducing a lethal side effect. The management of these tumours is not unique to injection site sarcomas. The relative uniformity of the injection site tumours makes comparison of data possible so these are used as the model by which we can judge how to manage high-grade sarcomas in all sites.

Diagnosis is made by biopsy. Be warned; these tumours will frequently develop so fast that the central part of the tumour simply undergoes liquefactive necrosis. A palpable fluid centre can be palpated leading the unwary practitioner to suspect a simple fluid-filled cyst. This misconception is supported by fine needle aspirate which simply yields a colourless liquid and even by cytological evaluation of the resulting fluid in some cases. By contrast, histological or cytological evaluation of viable cells from the tumour periphery demonstrates extremely aggressive neoplasia. A further consideration here is the fact that the liquid necrosis within the tumour will conduct viable cancer cells instantly to the whole reach of the surgical field during attempted excision or biopsy if the tumour body is incised.

Therefore, incisional biopsy, which does not introduce the liquid cancer vehicle to unaffected tissue planes, must be the technique of choice when seeking to make a diagnosis of a possible high-grade sarcoma. Your decision-making at this time can determine whether this becomes a curable complaint or a terminal one.

High-grade sarcomas are reported to metastasise in approximately 30% of cases. Thoracic imaging and evaluation of the regional lymph node(s) are appropriate when a diagnosis is suspected or indeed known.

The surgeons' mantra that a chance to cut is a chance to cure certainly applies with these tumours but it should also be noted that that same first chance to cut is also a chance to royally foul up any chances you ever had of curing the patient if the surgery performed is inappropriate. Surgery needs to be radical and it needs to be planned. Ideally co-axial imaging would be performed to ensure that the anatomic extent of the tumour is known so that surgery can be planned appropriately. The surgeon then needs to be competent enough to execute the plan that has been made.

It is true that improved survival times have been reported when radiotherapy and/or chemotherapy are given in addition to surgery, but that is when those treatments are given as part of planned multimodality intervention, not when they are given after injudiciously performed surgery.

My own clinical research into feline injection site sarcomas has investigated a combination of chemotherapy and surgery. With some quite stringent case selection, we recorded an 84% six-year survival rate, which is unprecedented with this particular tumour.

Other treatment strategies which merit further investigation include the immunotherapeutic strategies, metronomic chemotherapy and interleukin-2 treatment. Merial recently launched an exciting new synthetic interleukin-2 product, Oncept IL-2. This is licensed as part of a multimodal therapy for feline injection site sarcomas for use in combination with surgery and radiotherapy.

Vaccination Practice

It is impossible to discuss the management of injection site sarcomas without considering the wisdom of vaccination practice. Most practitioners will be aware of the work of the VAFSTF, the Vaccine Associated Fibrosarcoma Task Force, a cross-disciplinary specialist group that were convened following recognition of injection site sarcomas as a distinct pathological entity in the early 1990's. One of their recommendations was that cats undergoing vaccination should receive their vaccination injections in the distal limbs, the better to perform radical surgery if a tumour should arise. It seems legitimate to me that the profession asks questions of its own vaccination practice. However, we do not yet have all of the answers. Work has been done to establish whether certain vaccine formulations are more or less likely to induce an injection site tumour. It would appear that recombinant vaccines pose less threat than inactivated vaccines and that injection of depot steroid administrations poses a significant threat. Epidemiological work in the UK and the US has led to the conclusion that vaccine associated tumours arise with a frequency of approximately one per 10 000 vaccine injections.