

Cancer Diagnostics and the Essentials of Compassionate Oncologic Care: From the Basics to the Cutting Edge

Several exciting advances have been made in recent years with regard to diagnostic testing for various tumor types. The evolution of molecular diagnostics, sophisticated predictive models to anticipate individual patient response to therapy, and the advent of cutting-edge techniques involving liquid biopsy and next-generation sequencing for tumor mutation analysis, have revolutionized the approach to both the diagnosis and management of these patients. This presentation reviews the basics of working up the veterinary patient with suspected or known cancer, and introduces new diagnostic modalities that may detect cancer at an earlier stage and allow for more nuanced monitoring of these patients.

Veterinary cancer patients have a myriad of potential clinical presentations, and thorough physical examination and staging are vital to securing a correct diagnosis and informing treatment options and prognosis going forward. Baseline bloodwork (complete blood count, chemistry panel), urinalysis, thoracic and abdominal +/- additional imaging, and fine needle aspiration or biopsy of enlarged peripheral and/or internal lymph nodes and abnormal organs, in addition to sampling of effusions and skin lesions if present, should all be considered as part of a standard workup in patients with suspected cancer.

When planning for biopsy of solid tumors, punch, tru-cut, or incisional (blade) biopsy of lesions may initially be preferable to excisional biopsy, particularly if complete staging including advanced imaging has not already been performed. Care must be taken to ensure that pre-treatment biopsies are performed with eventual tumor excision in mind, ie, the biopsy tract should ideally not extend into normal tissue to avoid seeding or tracking of tumor cells along the tract, and should be positioned such that the tract can be removed en bloc with a follow-up procedure. It is strongly recommended to thoroughly evaluate local tumor extent and to complete staging of patients prior to excisional biopsy, particularly for larger, ill-defined, or aggressive tumors that are deemed to be of high risk for recurrence or metastasis. Cautery should not be used for tumor excision, as this removal method renders margin analysis impossible, and may damage tumor cells beyond recognition.

The advent of molecular diagnostics such as flow cytometry, PARR (PCR for antigen receptor rearrangements), and very recently liquid biopsy (OncoK9TM), has further facilitated the accurate diagnosis and classification of various cancers. Flow cytometry detects the expression of multiple antigens on the surface of lymphocytes. It can determine phenotype (B- versus T-cell origin) of lymphomas and leukemias, and discern neoplastic lymphocyte populations – typically characterized by a homogeneous expansion of cells with a single phenotype – from reactive/benign populations, which are phenotypically heterogeneous. Flow cytometry can be performed on a variety of samples, including peripheral blood, effusions, and needle aspirate samples of lymph nodes or organs, with results generally available within 4-7 days. PARR provides limited information compared to flow cytometry, however it is a highly sensitive and specific test to detect the presence of lymphoma in low-cellularity or ‘aged’ samples (flow cytometry, by contrast, should be performed within 24 hours of sample collection). Liquid biopsy is a blood-based early detection test using Next-Generation Sequencing technology, which can be employed as a screening test and diagnostic aid, and has the potential for use in monitoring of treatment response, monitoring for early disease relapse, and for the detection of minimal residual disease in patients with lymphoma and other cancers.

Newer predictive models driven by artificial intelligence (eg, ImprimedTM) have been developed that anticipate response to various anti-neoplastic agents in dogs with hematopoietic cancers and enable more nuanced decision-making with regard to chemotherapy selection. As these models continue to be refined, we may begin to see improved outcomes in chemotherapy-treated patients.

Various diagnostic and prognostic panels have also more recently come into vogue. Panels that have been more rigorously validated are those tailored to the diagnosis and/or prognostication of mast cell tumors and melanomas in the dog.

A new urine assay detecting a common mutation in the BRAF gene in dogs with urinary tract and prostatic carcinomas (CADET BRAF) has revolutionized the diagnosis of these cancers in this species, which hitherto required typically low-yield or increasingly invasive diagnostics with correspondingly higher risks of tumor seeding to achieve a definitive diagnosis.

Finally, the dawn of attempts at ‘precision medicine’ in the veterinary realm, informed by achievements in the human medical field, has spawned a growing number of companies offering high-tech methods of tumor mutation analysis to allow veterinarians, in theory, the ability to identify actionable therapeutic targets and tailor anti-cancer treatment to the individual patient, rather than broadly treating based on tumor type alone. Precision medicine is an

imperfect science at best, and one which bears continual refining. Nevertheless, while still in its infancy, the promise of precision medicine has brought forth some exciting developments in this regard which herald an ever-increasing sophistication within veterinary oncologic practice (and, we hope, improvement in patient outcomes) in the coming years.

Once a cancer diagnosis and appropriate baseline have been established, compassionate support of the veterinary cancer patient from diagnosis through treatment and end-of-life transition is essential. The enhancement and maintenance of quality of life is of paramount concern, and care must be tailored to address the specific needs of the individual, with consideration given to pain management, nutritional support, and relief of other distressing tumor- and treatment-related symptoms. This presentation examines the various ways in which we can deliver compassionate oncologic care through the use of supportive medications, acupuncture, chemotherapy, and radiation. The progressive stages of nutritional support, as well as palliative procedures such as the removal of tumor-related effusions or obstructions, are also reviewed.

The WHO definition of palliative care is care which provides relief from pain and other distressing symptoms; intends neither to hasten or postpone death; enhances quality of life, and may also positively influence the course of illness; and is applicable early in the course of illness, in conjunction with other therapies that are intended to prolong life, such as chemotherapy or radiation therapy. Palliative care is appropriate for those patients with advanced-stage cancer that do not stand to benefit from, or are not good candidates for, definitive therapies, and for general relief of tumor- or treatment-related symptoms. Some pet owners may elect not to pursue definitive treatment of their companion's cancer, whereby the focus shifts to alleviating suffering as the cancer progresses. Palliative care should not be viewed as 'prolonging the inevitable' – if quality of life is sub-optimal and cannot be restored, humane euthanasia should be considered.

Many veterinary cancer patients experience some degree of pain with their disease process, which can often be difficult to assess in those patients presenting with more subtle signs. Social withdrawal, aversion to petting, decreased grooming, decreased appetite and activity level, changes in urinary and defecation habits, self-trauma, and vocalization are common indicators of pain in the cancer patient. Chronic pain can produce changes in the peripheral and central nervous systems that make pain control challenging due to the 'wind-up' phenomenon, thereby early intervention is critical once signs of pain are recognized. Anti-inflammatory medications, such as NSAIDs or steroids, pain medications such as opioids and NMDA antagonists, gabapentin, and bisphosphonates are effective in treating tumor-related discomfort. A multi-modal approach is typically used to achieve an appropriate level of pain control.

Palliative surgical resection and palliative radiation can also be employed to alleviate tumor-related discomfort. Acupuncture constitutes an important complementary therapy for addressing pain in many cancer patients, and while contraindications exist to using this treatment in a small subset of cancer patients, this therapy can be administered safely and with good effect in many dogs and cats.

Nutritional support of the cancer patient is vital to maintaining body weight and organ function. Cancer anorexia and cachexia can result when there is inadequate food intake (anorexia), or in the face of adequate food intake (cachexia), resulting in significant weight loss, muscle wasting, and poor quality of life. Coaxing, pharmacologic interventions such as anti-emetics, appetite stimulants, and gastroprotectants, as well as assisted enteral support, can be used to nutritionally support cancer patients throughout their disease process.

Malignant cavitory effusions can occur with many types of cancer, and develop secondary to metastatic or infiltrative lesions that can affect vascular permeability and impair lymphatic

drainage. Inflammation is also a key factor in the development and persistence of malignant effusions. Removal of effusions via centesis +/- infusion of chemotherapy in an intracavitary fashion or the use of oral tyrosine kinase inhibitor (TKI) therapy may help to decrease fluid production, however unless the primary tumor source is addressed – and sometimes even despite surgical removal or irradiation of the primary tumor – effusions often persist, and contribute to a significant decline in quality of life.

Finally, malignant obstructions – typically a mechanical obstruction of an organ or vessel/duct by the tumor causing serious or life-threatening sequelae – can be relieved with the aid of surgery, radiation, or mechanical stenting. Because of the typically dire consequences of malignant obstructions in cancer patients, these scenarios must be promptly identified and addressed to prevent grave outcomes.

Holistic support of the veterinary cancer patient involves the consideration of the ‘whole’ patient in one’s clinical decision-making process. It recognizes the uniqueness of each individual, and addresses the constellation of factors that may contribute to or detract from quality of life during the course of their disease. The tumor type and location, the patient’s clinical status, and the pet owner’s goals and constraints (eg, financial) must all be considered when developing a palliative care plan for each patient. Care plans are dynamic in nature, and should be periodically reassessed to ensure that a patient is receiving appropriate and adequate support. In addition, regular and clear communication with the pet owner is vital in ensuring treatment compliance and empowering owners to be active participants in their companion’s care **plan**.