Introduction of Veterinary Oncology and Diagnostic Approach to the Cancer Patient

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In setting out to treat a cancer patient, the clinician must answer 3 important questions:

1) What is the cancer?
2) Where is the cancer?
3) How do we expect the cancer to behave biologically?

The first question is answered by biopsy or cytology. The second question is answered by performing a standard staging work up. The third question is answered by acquiring an understanding of the biology of the tumor type in question. Once these 3 questions are answered, it is then possible to design an optimum treatment plan, and to discuss the options for treatment with the owner of the animal.

Diagnosis

The starting point in dealing with the cancer patient is establishing the diagnosis of malignancy. The probability that the problems seen in a patient are attributable to malignancy can be estimated from a thorough history and physical examination. For example, the presence of a mammary mass in an intact older female dog carries a 30-40% probability of malignancy, while the same mass in a cat carries an approximately 80% chance of malignancy. Overall, approximately 75% of tumors in cats are malignant, as estimated from epidemiological studies, while in dogs one third of tumors are malignant. Young animals are less likely to have malignancies than are older animals. A careful history can reveal subtle clues that alert the clinician to the possibility of malignant disease, such as melena, profound unexplained weight loss, chronic cough, and other signs of chronic disease.

Cytology - It is extremely helpful to perform needle aspirations for cytology on patients with mass lesions. Differentiation of benign versus malignant lesions can generally be accomplished, and this may aid the surgeon in treatment planning. A more radical surgical approach is necessary to achieve surgical cure of a malignant tumor than for a benign one. Prior cytologic confirmation of the presence of a malignancy allows the surgeon adequate warning to plan for a more difficult surgery.

Fine needle aspirations are typically performed with a 22-gauge needle and 6 cc syringe, or in some cases a 22 GA needle without a syringe attached (fenestration technique). Some tumor cells are very fragile, and applying suction results in rupture of cells. This is especially true for lymphomas. However, other solid masses require suction to obtain cells, as is the case in sarcomas, which are firmly adherent and exfoliate poorly. For tumor types likely to exfoliate well, it is preferable to perform a fenestration technique wherein a hypodermic needle is inserted into the mass several times but not aspirated. Cells obtained are blown onto microscope slides, squash preps are made, and staining with a modified Wright's stain such as Diff-Quik is carried out.

Biopsy - In many instances it is wise to perform a biopsy for histologic diagnosis prior to definitive therapy. Some tumor types, such as the soft tissue sarcomas, exfoliate poorly in needle aspirations, and also require radical surgical approaches to achieve a cure. In the case of hemangiopericytoma, for example, primary tumors behave in a highly invasive fashion and are prone to frequent local recurrence if not resected adequately. These tumors may be difficult to diagnose cytologically and may therefore be better addressed with a two-stage procedure, first for diagnosis and then for definitive therapy. Another concern necessitating biopsy prior to definitive surgical excision is the case of high-grade tumors with significant metastatic potential. The client should be informed of the potential for occult metastasis of a high grade lesion, particularly if an aggressive, disfiguring surgery would be required to eradicate the primary lesion.

Obviously, small tumors are best handled by excisional biopsy. In the case of large masses, incisional biopsy for diagnosis is helpful. When excisional biopsies are obtained, it is important to send the entire excised lesion to the pathologist so that evaluation of normal tissue margins can be performed. Evidence of incomplete resection indicates the need for additional therapy, such as more radical surgical excision, radiation therapy, or chemotherapy.

Staging

Once a patient has been found to have cancer, staging is performed. The objectives of determining the stage of disease are to aid in treatment planning, to help with prognostication, assist in evaluation of results of therapy, and to facilitate the exchange of information between treatment centers and investigators. An anatomic staging system is used, and is patterned after the World Health Organization staging criteria for human tumors. For most tumors, the TNM system of classification is used. In this system, evaluation of the Tumor, regional and
Histologic grading of tumors is established for some tumor types and can be provided by the pathologist. Grading reflects the degree of invasiveness into the surrounding normal tissue, the extent of the body’s response to the tumor, the mitotic index and degree of anaplasia of tumor cells, and the presence of lymphatic or vascular invasion of tumor. Tumor grading can be helpful in prognosis also, as more aggressive tumors of higher malignant grade could be expected to have poorer long term survival times than those associated with well differentiated, low grade malignancies. Tumors with published grading criteria in veterinary medicine include mast cell tumors, lymphomas, mammary carcinomas, and soft tissue sarcomas.

Cancer Patient Assessment

In addition to the evaluation of the tumor with regard to histology, size, ocation, and dissemination, it is important to assess the general health of the patient. Most of the patients we see are geriatric at the onset of their malignancy, so the likelihood of chronic unrelated diseases (such as mitral valve insufficiency, arthritis, dental disease, or renal insufficiency) is high. This may affect the client’s willingness to treat and the types of therapy that are likely to be safe for the patient. Laboratory evaluation with complete blood counts, serum chemistry, and urinalysis are mandatory baseline panels if chemotherapy is being considered. Drugs that require hepatic activation (such as cyclophosphamide), or hepatic or renal excretion (such as doxorubicin or cisplatin, respectively), may prove inappropriate for certain patients based on laboratory evaluation. Most chemotherapeutic drugs cause myelosuppression, so pre-existing anemias or marrow disorders must be carefully explored prior to undertaking therapy and the risk verses benefit ratio must be carefully weighed.

Tumors are capable of inducing paraneoplastic syndromes, which are defined as distant effects of the tumor unrelated to the physical presence of a mass lesion. Examples of paraneoplastic syndromes recognized in animals include cancer cachexia, hypercalcemia, hypoglycemia, hyperestrogenism, hyperthyroidism, monoclonal gamopathy, fever, leukocytosis, glomerulonephritis, hypertrophic osteopathy, and others. Paraneoplastic syndromes are the result of the release of hormones, hormone-like substances, or cytokines from the tumor, or from the immune system’s attempt to combat the malignant cells. Evaluation of these paraneoplastic syndromes allows an assessment of the causes of symptoms seen the patient and can serve as a marker of the efficacy of therapy. For example, the level of total plasma protein can be used to evaluate the response of multiple myeloma to chemotherapy.

In summary, the approach to the veterinary cancer patient involves careful assessment of the patient, the type and extent of malignancy, and full

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Tumor Staging

- **T** – Tumor (Size, degree of invasion, ulceration)
- **N** – Node (Number and size of involved nodes)
- **M** – Metastasis (Presence or absence of distant metastasis)

For some tumor types, a staging category exists in which combinations of the TNM status are used to assess the patient overall. An example of such a staging system in veterinary medicine is that used for lymphoma staging. Lymphomas are classified as Stage I through V based on the number and location of involved lymph nodes, involvement of non-lymphoid tissue, and bone marrow involvement. For diseases in which such staging categories have not been developed, the TNM system usually gives categories for the primary tumor, T, ranging from 1 to 4 based on characteristics such as size, local invasion and ulceration. The N or node staging is also usually listed as 1 to 4 based on the number and size of lymph nodes involved in the malignant process, and the M or metastasis category is generally given as 0 (no distant metastatic lesions) or 1 (presence of distant metastasis).

Staging involves a careful and thorough physical examination, and also radiographs, abdominal ultrasound, and certain laboratory tests such as bone marrow cytology for selected tumor types. It is important that 3 dimensional measurements of tumors be obtained prior to therapy, so that response to therapy can be accurately assessed. A careful search for distant metastasis is important when considering local forms of therapy, such as surgery or radiation.

Understanding of the anticipated biologic behavior of the tumor type is helpful in efficient staging. For example, Grade 3 mast cell tumors may originate in the spleen or bone marrow and be present as multiple disseminated foci in the skin. Therefore, bone marrow aspiration and abdominal radiographs or ultrasound with splenic aspiration may be helpful in staging, whereas thoracic radiographs are less helpful, as mast cell tumors are highly unlikely to cause metastatic foci in the pulmonary parenchyma (except as a terminal event, when a diffuse interstitial pattern may occur). For other types of tumors, such as mammary carcinomas, osteosarcomas, and hemangiosarcomas, the very high likelihood of pulmonary metastasis make thoracic radiographs absolutely essential in treatment planning. Small pulmonary metastases are best detected radiographically on three views of the chest (dorsoventral or ventrodorsal, right and left lateral). In many cases, abdominal radiographs or ultrasound are also important for clinical staging to detect abdominal dissemination.
communication with the pet owner to allow for the most successful therapeutic outcome.

1. Is the sample adequately cellular? Is the preparation and staining adequate?
2. Is the population of cells seen inflammatory or neoplastic?
   a. Inflammatory - Neutrophils, macrophages, eosinophils, lymphocytes, plasma cells, microorganisms, proteinaceous background. Cells may appear toxic or degenerate.
   b. Neoplastic - A relatively uniform population of cells of some type.
3. If neoplastic, is this condition benign or malignant?
   a. Benign lesions are a uniform population of very similar appearing cells (ie. no pleomorphism).
   b. Neoplastic lesions contain criteria of malignancy:
      Cytoplasmic criteria: Vacuolization, basophilia, irregular and indistinct cytoplasmic boundaries, variable cytoplasm quantity from cell to cell.
4. If malignant, is this condition a round cell, epithelial, or connective tissue tumor?
   a. Round cell tumors: Round to oval cells, easily exfoliated, well-defined cytoplasmic margins.
   b. Epithelial tumors – Carcinomas:
      Abundant exfoliation in clusters, oval to round cells, possible ductal or acinal pattern, secretory products may be seen in cytoplasm.
   c. Connective tissue tumors - Sarcomas:
      Exfoliate poorly, individual cells, spindle or flame shaped cells, cytoplasmic extensions with ill-defined borders.