Cancer Cachexia as a Manifestation of Malignancy*

Gregory K. Ogilvie, DVM, DACVIM (Internal Medicine and Oncology)
Director, Angel Care Cancer Center
California Veterinary Specialists
Carlsbad, California

President, Special Care Foundation for Companion Animals
San Marcos, California

Antony S. Moore, BVSc, MVSc, DACVIM (Oncology)
Co-Director, Veterinary Oncology Consultants Ltd
Wauchope, New South Wales, Australia
Adjunct Professor, Faculty of Veterinary Science
University of Sydney
Consulting Oncologist, Animal Referral Hospital
Sydney, Australia

Cancer cachexia is a syndrome that affects many cancer patients. If not treated, it results in involuntary weight loss even when caloric intake is adequate. As with all other paraneoplastic syndromes, this condition is a remote effect of cancer. Cancer cachexia has been shown to result in dramatic alterations in carbohydrate, lipid, and protein metabolism before clinical evidence of cachexia is detectable. This syndrome is encountered by every practitioner who treats dogs with cancer but is often suspected only in patients with unexpected weight loss.

Dogs with cancer do not commonly have weight loss, although many have dramatic alterations in metabolism regardless of the type, size, or stage of the cancer. These effects impair quality of life, response to therapy, and overall survival. The actual cause of cancer cachexia is the subject of a great deal of research.

MECHANISM

The mechanisms of cancer cachexia are complex and include:

• Starvation and malnutrition.
• Impaired oral intake.
• Stomatitis, taste aversions, zinc deficiency.
• Dehydration.
• Nausea.
• Constipation.
• Bowel obstruction.
• Pain.
• Impaired gastrointestinal absorption.
• Maldigestion.
• Exocrine pancreatic insufficiency.

• Diarrhea.
• Development of ascites, pleural effusion.
• Infections.
• Heart, lung, kidney failure.
• Prolonged deconditioning.
• Growth hormone deficiency.

In addition to these items, profound alterations in carbohydrate metabolism are seen in dogs and humans with cancer cachexia. In dogs, elevated serum insulin and lactate concentrations associated with lymphoma and other malignancies rise higher still, compared with those in control dogs, in response to glucose-tolerance tests. Increased lactate and insulin levels in dogs with cancer do not normalize even when complete remission is obtained after doxorubicin chemotherapy or surgery. Dogs with lymphoma have even higher lactate and insulin levels on reevaluation after relapse and show signs of cachexia. Additional studies suggest that dogs with lymphoma may have a postreceptor defect, indicating that dietary therapy may be effective in combating the problem. Hyperlactatemia becomes more pronounced on administration of lactate-containing parenteral fluids (e.g., lactated Ringer’s solution) in dogs with lymphoma compared with control dogs.

Dogs with untreated lymphoma have significantly higher free fatty acid, total triglyceride, and very-low-density lipoprotein and triglyceride serum concentrations compared with untreated control dogs. High-density lipoprotein cholesterol levels in dogs with lymphoma are significantly lower than those in control dogs. After doxorubicin treatment, dogs with lymphoma develop significantly elevated total cholesterol levels, as is noted in humans with cancer.

Indirect calorimetry has been used in clinical cancer patients to quantify nutritional and water requirements. It demonstrates that energy expenditure and caloric needs in dogs with lymphoma and other malignancies are equal to or lower than those in normal dogs. Furthermore, it demonstrates that major or minor surgery fails to significantly increase the energy expenditure of normal or cancer-bearing dogs. This is opposite of the common belief that animals and humans with cancer have elevated energy metabolism.

The above-mentioned alterations in carbohydrate, protein, and lipid metabolism are important to practitioners because they affect a diverse population of dogs with a wide variety of cancers. Therapies to improve these changes must begin early and continue even after surgery or other treatment eliminates the malignancy.

**DIAGNOSTIC CRITERIA**

**Clinical Presentation**
Dogs with cancer cachexia show few clinical signs of the paraneoplastic syndrome in the early stages. As the syndrome progresses, weight loss is noted despite a good appetite (Figure 1). Later, weight loss, anorexia, lethargy, and depression predominate. Anorexia, fatigue, chronic nausea or vomiting, decreased activity level, and weight loss are a few of the obvious clinical signs and clinical parameters associated with this condition.

**Diagnosis**
The changes in metabolism noted above can be documented early in the course of malignant disease. Dogs in the early phase of cancer cachexia may only show exercise intolerance, lethargy, and anorexia. Later in the course of the disease, there is overt wasting and loss of body condition despite adequate nutritional intake. Hypoalbuminemia is a notable finding in the later stages of the disease. The later stages are followed by death owing to failure of one or more organ systems.

**TREATMENT RECOMMENDATIONS**
• The patient should consume an adequate quantity of highly bioavailable nutrients presented in a palatable form.
• A diet composed of modest amounts of complex carbohydrates, minimal quantities of rapidly absorbed simple carbohydrates, relatively modest amounts of high-quality bioavailable proteins, and a modest amount of fats of the omega-3 (n-3)
series may be ideal for supporting cancer patients without enhancing tumor growth.
— Supplementing the diet with oils containing omega-3 or with purified omega-3 fatty acids has been shown to slow the growth of various types of cancers in animals.
— The efficacy of chemotherapeutic drugs, such as doxorubicin, epirubicin, irinotecan, 5-fluorouracil, and tamoxifen, and of radiation therapy has been improved when the diet included omega-3 fatty acids.
— Omega-3 fatty acids induce beneficial effects in cancer patients, such as modulation of eicosanoid production and inflammation, angiogenesis, proliferation, and susceptibility for apoptosis.
— Omega-3 fatty acids have been used to suppress cancer-associated cachexia and to improve the quality of life.

- Dogs should be fed enterally when possible. If appropriate, methods such as warming the food, increasing palatability, and using pharmacologic agents (e.g., megestrol acetate, benzodiazepine derivatives, cyproheptadine) to enhance appetite and stimulate oral feeding should be used before considering nasogastric, gastrostomy, or jejunostomy tube feeding.
- When enteral feeding is not feasible, parenteral feeding using minimal simple carbohydrates should be used.
- When possible, lactate- and glucose-containing fluids should be avoided because they may produce lactate and stimulate release of insulin. An exception is in cases of septic shock or during an insulin overdose, when glucose-containing fluids may be required specifically to treat hypoglycemia.
- Adequate calories should be provided; however, it may not be necessary to provide more nutrients than needed by disease-free dogs. The following formula is a general approximation of the amount of metabolizable food to feed (kcal/day): 2(30 × body weight [kg]) + 70. A more accurate formula is 70(body weight in kg).75.
- Frequent, small, energy-dense meals should be provided.
- Metoclopramide should be given when possible to reduce nausea. Ondansetron may also be of value.
- The dog should be exercised regularly to maintain lean body mass and to keep the attitude positive.

RECOMMENDED READING