Bringing Up the Rear: Anal Sac Adenocarcinoma Lili Duda, MBE, VMD, DACVR (Radiation Oncology) <u>dudal@vet.upenn.edu</u> Jennifer Mahoney, DVM, DACVIM (Oncology) <u>jamah@vet.upenn.edu</u> Michael Mison, DVM, DACVS <u>mmison@vet.upenn.edu</u> University of Pennsylvania, Philadelphia, PA, USA

Introduction

Apocrine gland anal sac adenocarcinoma (AGASACA) is a relatively uncommon tumor in dogs, representing approximately 17% of perianal tumors and 2% of all skin and subcutaneous tumors. These tumors form from the apocrine sweat glands in the connective tissue surrounding the anal sacs. The average age of dogs at diagnosis is 9 to 11 years, but dogs as young as 5 years of age have been reported. Males and females are affected equally, and spaniels, particularly English Cocker Spaniels, have been reported to be at increased risk. Usually only one anal sac is affected, but bilateral tumors have been reported. Apocrine gland anal sac adenocarcinoma has a metastatic rate of about 50% at the time of diagnosis, most commonly to the regional draining lymph nodes (sublumbar and sacral nodes). Distant metastasis to the lungs is less common, and metastasis to the liver and spleen occurs infrequently. Approximately 27% of dogs have a paraneoplastic hypercalcemia of malignancy associated with this tumor.

History and Clinical Signs

Dogs may present with clinical signs related to the primary mass, such as discomfort, swelling, or scooting. Larger masses or enlarged regional lymph nodes may cause obstruction of the pelvic canal, leading to tenesmus. Some dogs may present with clinical signs referable to hypercalcemia, such as polyuria, polydipsia, anorexia, lethargy, and vomiting. In many cases, the primary tumor is an incidental finding on routine physical examination.

Diagnostic Work-Up

A rectal exam should be a routine part of the physical examination in all adult dogs, particularly in dogs with hypercalcemia. If an anal gland mass is palpated, the diagnosis of apocrine gland adenocarcinoma can often be made on fine-needle aspiration cytology, with characteristic polyhedral cells, uniform round nuclei, and many naked nuclei. Patients should be staged with a CBC, serum chemistries, urinalysis, thoracic radiographs, and abdominal ultrasound or abdominal CT scan.

Treatment

Surgery

The treatment of choice for AGASACA is complete surgical excision. Wide and aggressive removal is not feasible due to the adjacent rectum and anus. With large tumors, additional tissue attached to the tumor may need to be removed. This may result in some postoperative complications such as wound breakdown (dehiscence) and fecal incontinence. Fecal incontinence can occur in up to 33% of dogs especially with removal of larger masses. This is usually temporary but owners need to be aware of this risk. If the tumor is unilateral, fecal incontinence is typically partial--the dog can have difficulty controlling bowel movements but will not continuously drop stools. If the sublumbar lymph nodes are enlarged, they should be removed as well (through an abdominal approach) because enlarged lymph nodes typically indicate metastatic spread. Hypercalcemia, if present, will usually resolve on its own within 24 to 48 hours of surgical excision of the tumor.

Radiation therapy

Radiation therapy is the recommended treatment for dogs that are not surgical candidates. Palliative radiation can be very effective in decreasing tumor size and alleviating symptoms in dogs that are symptomatic from large primary tumors and/or regional lymph nodes. This approach to radiation is typically given once weekly for 4 to 6 doses. Radiation therapy can also decrease hypercalcemia in some affected dogs, but is not nearly as effective as surgery for this purpose. Radiation therapy is also recommended for dogs that have residual tumor postoperatively at either the primary site and/or regional lymph nodes. In these cases, radiation is administered 5 days a week for about 1 month.

Systemic therapy

The role of chemotherapy in the treatment of AGASACA is not well understood, although its use makes biologic sense given the relatively high metastatic incidence of this tumor. Many of the studies in the literature involve patients treated with a variety of treatment modalities, and therefore prospective, controlled clinical trials are needed to determine the ideal treatment combination for apocrine gland anal sac adenocarcinoma.

Chemotherapy is indicated in dogs with negative prognostic factors including large tumor size, presence of lymph node metastasis, or presence of distant metastasis. Tumors with a high mitotic index may also be at greater risk for metastasis, although this has not been evaluated in the literature. There are conflicting reports of hypercalcemia as a negative prognostic factor, with two studies demonstrating shorter survival times in dogs with hypercalcemia, but other studies do not support this.

Chemotherapy drugs that have demonstrated efficacy in treating AGASACA include carboplatin, mitoxantrone, and melphalan. Median survival times in the range of 1 ½ to 2 ½ years have been reported using various combinations of surgery, radiation therapy, and these chemotherapy drugs. Toceranib (Palladia) is a tyrosine kinase inhibitor that has shown some clinical benefit in dogs with AGASACA, including dogs that had failed prior therapy and dogs with metastatic disease.