Canine Urothelial Carcinoma

WHAT IS UROTHELIAL CARCINOMA?
Urothelial carcinoma (also called transitional cell carcinoma (TCC)) is the most commonly diagnosed cancer of the urinary tract of dogs. Transitional cells make up the epithelial lining of the urinary tract. The areas most frequently affected include the bladder, the urethra (the tract along which urine exits the body), and the region of the trigone (the region where the bladder connects to the urethra). All regions of the urinary tract can be affected given the infiltrative nature of this cancer.

Breeds at risk for developing urothelial carcinoma include Scottish Terriers, West Highland White Terriers, beagles, and Shetland sheepdogs. In male dogs, the prostate may be secondarily affected.

WHAT ARE THE CLINICAL SIGNS?
Clinical signs are associated with the extent of disease and the location. The most common signs include straining to urinate, painful urination, increased frequency of urination or incontinence, decreased urine stream and blood in the urine. As tumors grow, clinical signs worsen. End stage progression includes urinary obstruction or extreme difficulty urinating. This is a life-threatening emergency and immediate evaluation is necessary. The majority of dogs succumb to consequences of the local tumor within the bladder, however metastasis (spread) to local lymph nodes, lungs, and bones can occur, particularly later in the course of disease.

WHAT DIAGNOSTICS ARE PERFORMED?
Staging and monitoring are important in cases of urothelial carcinoma. Staging includes a complete physical exam, blood tests (CBC/Chemistry), and abdominal ultrasound. Chest x-rays are recommended to examine for metastases to the lungs and for age related monitoring. The physical examination allows identification of disease and establishes a baseline for future monitoring, while blood tests can reveal changes that affect prognosis (renal disease) in addition to assessing a patient’s overall health for therapy. An abdominal ultrasound is recommended for accurate diagnosis and measurement of a primary tumor, to examine for any intra-abdominal metastases, and for monitoring response once therapy is initiated.

Urinalysis, with culture, is important, as the clinical signs seen with urothelial carcinoma are similar to those seen with urinary tract infections. Diagnosis is typically achieved with cytologic or tissue biopsy (cystoscopy or cystotomy), a urine sample through a catheter (“traumatic catheterization”), or fine needle aspirate. These diagnostics are necessary to differentiate a cancerous cause of a mass within the urinary tract from benign inflammatory lesions or infections.

A commercially available BRAF mutation test can be done on a urine sample in cases of suspicious lesions or for breeds predisposed to urothelial carcinoma who show urinary signs as this test provides additional supportive evidence for a diagnosis of cancer.
TREATMENT OPTIONS AVAILABLE AND PROGNOSIS:
The complicating factors for the treatment of urothelial carcinoma are the location and extent of disease. Clinical signs may not develop until disease has extensively progressed or has metastasized, contributing to a guarded prognosis. Tumors located nearest the trigone, the urethra, or prostate are more difficult to treat due to their likelihood of causing obstruction of the flow of urine.

Due to potential development of obstruction, dogs may succumb to the disease within a few months. While treatment of urothelial carcinoma is not curable, there are several options that can prolong quality of life including surgery, non-steroidal anti-inflammatory drugs (NSAIDs), chemotherapy, and radiation therapy.

For tumors located away from the bladder entrance (at the apex), surgery may be an option. For tumors causing an obstruction of the ureters or urethra, stents can be placed to help temporarily improve urine flow.

NSAIDs can prolong and improve quality of life by reducing tumor size and reducing regional inflammation. NSAIDs are given orally, at home. Regular bloodwork is recommended to monitor for side effects including gastrointestinal (upset or bleeding) and systemic compromise (liver and kidneys). Chemotherapy is recommended to limit the progression of local and metastatic disease, and works best when combined with an NSAID. With the addition of chemotherapy to NSAID therapy, the average survival time is approximately 1 year for dogs with bladder involvement, and 6 months if there is prostate or urethral involvement.

There are several forms of radiation therapy used to treat urothelial carcinomas that vary in number of treatments, success in disease control, side effects, and cost. In general, radiation therapy is most often used to limit the progression or reduce obstructive disease and as pain relief in cases of bony metastatic disease. Anesthesia is required for treatments.

WHAT ARE THE SIDE EFFECTS?
Side effects are associated with the treatment selected and the extent of disease and clinical signs. The most common side effects from NSAID therapy include gastrointestinal upset (vomiting, diarrhea, dark or reddened stool associated with gastrointestinal bleeding) and systemic effects on the liver and kidneys. Bloodwork is used for monitoring and gastrointestinal supportive medications can be provided to assist in the development of these side effects.

Radiation therapy includes the use of anesthesia during treatments and side effects include gastrointestinal upset (vomiting, diarrhea), acute increase of urinary clinical signs including increased frequency and increased blood in the urine due to secondary inflammation. Less common side effects include stricture or inability to reduce progressive/obstructive disease rapidly. Side effects of chemotherapy are infrequent and can include temporary mild gastrointestinal upset such as vomiting or diarrhea. Decreased appetite and lethargy may also occur.

Your pet will be prescribed supportive medications for nausea (should decreased appetite, or increased salivation, or drooling occur) and diarrhea for you to have on hand at home to use if necessary. It is best to be proactive with these medications and provide these as soon as signs are noted. Should you have any questions, your oncology team is available to assist.
CONCERNS OF CHEMOTHERAPY FOR MY PET:
Chemotherapy often carries a negative impression, especially with our understanding of chemotherapy in human medicine. Our approach to chemotherapy in veterinary medicine is focused on limiting severe side effects and providing increased quality of life. Chemotherapy in human medicine is provided with intent to cure by using very high doses and increased side effects. As quality of life is imperative for our pets, doses are adjusted and your pet is monitored to limit severe side effects. Hair loss is rare except in certain breeds such as poodles. Though there is a slight risk of hospitalization in our pet population and mild gastrointestinal upset, the majority of pets tolerate therapy well. Should you have concerns during therapy, speak with your oncologist in order to develop a tailored plan for your pet.

HOW DO I PREPARE?
We understand this is a difficult time and we are here to support you and your pet by providing the options and care necessary. Selecting a therapy is not binding and can be adjusted to you and your pet’s needs. During treatment sessions, you will be provided with updates and any recommendations depending on your pet’s response. Should any concerns arise, your oncology team will provide answers and help to guide you.

NAVIGATING THROUGH MY OPTIONS:

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Prognosis- (median)</th>
<th>Treatment schedule</th>
<th>Approximate cost*</th>
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</thead>
<tbody>
<tr>
<td>NSAIDs</td>
<td>3 - 6 months</td>
<td>Scheduled procedure.</td>
<td>~$50 - 100 per month (variable depending on drug choice and pet’s size)</td>
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<tr>
<td>Chemotherapy:</td>
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<tr>
<td>• Mitoxantrone</td>
<td>6 - 12 months (with concurrent NSAID therapy)- dependent on extent of disease and progression</td>
<td>IV chemotherapy every 1-3 weeks.</td>
<td>$350 - $450 per treatment.</td>
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<tr>
<td>• Vinblastine</td>
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<tr>
<td>• Carboplatin</td>
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<td>Radiation Therapy</td>
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<tr>
<td>• IM/IGRT Stereotactic</td>
<td>6 - 20+ months (depending on extent of disease and type of radiation)</td>
<td>CT, Radiation treatments, follow-up IV chemotherapy once every three weeks.</td>
<td>$1500 - $6500 depending on protocol.</td>
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<tr>
<td>• Palliative</td>
<td></td>
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<td>Surgical</td>
<td>Pending tumor behavior and extent of disease</td>
<td>Pending further diagnostics including CT and follow-up</td>
<td>Pending recommendations.</td>
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</table>

*Cost estimates are based on individual appointments and overall cost is dependent on patient response, which does not include additional supportive care or hospitalization, if required.
GETTING STARTED
Once you have determined the best therapeutic option for your pet, you may work with our oncology team to develop an appointment plan.

Scheduling: Appointments for patients undergoing treatments and rechecks should be scheduled in advanced. You are responsible for making this appointment with the front desk:

- Schedule your appointments at reception upon check out
- Drop offs are requested between 7:30-8:30am
- Pick ups are requested by 4:30pm