

Urothelial Carcinomas in Dogs

Tumors of the urinary tract comprise less than 2% of all canine cancer, with urothelial carcinomas (previously known as transitional cell carcinoma being the most common tumor diagnosed in the urinary bladder of dogs. Other tumors that can occur in the bladder include adenocarcinoma, squamous cell carcinoma, fibroma or rhabdomyosarcoma. TCC is usually found in the trigone region of the bladder which is where the ureters empty into the bladder and the urethra leaves the bladder.

The exact cause of these tumors is unknown although there are several factors that increase the risk of developing a bladder tumor. Risk factors include certain over-the-counter topical insecticides for flea and tick control (this does not include Frontline or Advantix), obesity and gender - females appear to be more commonly affected than males. Scottish terriers, Beagles, shelties and mixed breed dogs are the most common breeds affected.

Clinical signs

Most owners notice their pet has had some urinary accidents in the house, they are straining to urinate, they are urinating more frequently, or, they have an increased sense of urgency without producing more urine. Signs may be present for weeks to months and may have temporarily resolved with symptomatic therapy such as antibiotics and/or anti-inflammatories, however, the signs quickly recur once the medications are discontinued.



Diagnostics/staging

Several diagnostic tests are recommended for making a diagnosis and determining the extent of the cancer (staging) including:

- Blood work, which consists of a complete blood count (CBC) to assess red and white blood cells and platelets, a chemistry panel to assess organ function, and a urinalysis.
- A rectal examination to feel for an enlarged or thickened urethra, enlarged lymph nodes, or an enlarged prostate. Note: 30% of physical examinations will be normal without any external evidence of disease.
- An abdominal ultrasound is recommended to obtain a better view of the bladder, urethra and kidneys as well as the regional lymph nodes and other abdominal organs. Measurements of any lesions can be obtained for future reference.
- Chest radiographs (X-rays) or CT scan due to the potential for spread (metastasis) and are recommended prior to initiating any therapy. Note: This disease can spread to the regional lymph nodes, prostate, bones and lung.
- The new gold standard for diagnosis is the CADET Braf urine test. This test entails collecting 30-40mls of urine (can be done over a few days) and assessing the urine for a

specific mutation called B-raf. If this mutation is detected, a diagnosis of urothelial carcinoma is made. If negative, it does not rule out the diagnosis, and cystoscopy may be warranted. This involves inserting a flexible tube (scope) through the urethra then into the bladder. It is possible to look at both the urethra and the bladder through the scope and also to retrieve samples for biopsy.

A fine needle aspirate, via ultrasound guidance, is not advised in most patients since this tumor has a high tendency to seed tumor cells along the aspirate channel. This means that the tumor could be seeded along the body wall where the needle entered the patient trying to get to the urinary bladder.

Treatments

Several treatment options have been evaluated and include:

- Piroxicam, which is an oral anti-inflammatory that has been shown to help decrease the inflammation around the tumor and improve or resolve clinical signs. It also has some anti-cancer activity as it can slow the progression of new blood vessel formation which in turn slows the tumor growth. Around 20% of patients will have a benefit from Piroxicam by slowing the tumor growth but a much higher percentage will experience improvement in their clinical signs. Side effects can include GI upset (vomiting, diarrhea, anorexia, GI ulceration), but when given with food, this is rarely seen. Piroxicam may also, albeit less likely, cause toxicity to the kidneys so periodic blood work is recommended to ensure that the kidney function is not affected. Note: when Piroxicam is used alone, the average survival time is 6 months.
- Chemotherapy is also another option for the treatment of urothelial carcinomas. Chemotherapy can be used either alone or in combination with Piroxicam. The most commonly used chemotherapy agents include mitoxantrone and vinblastine. Mitoxantrone is administered intravenously once every 3 weeks. Vinblastine is administered intravenously once every 14 days. Side effects are not common but may include nausea, vomiting, diarrhea, anorexia and bone marrow suppression. We will typically treat with 2-3 doses and then repeat an abdominal ultrasound of the urinary system to evaluate the patient's response. If a benefit is noted, therapy is continued. Most patients receive chemotherapy until their tumor progresses or they are no longer tolerating the treatment. Note: when Piroxicam is used in combination with Mitoxantrone approximately 40% of patients will have a benefit with a median survival time of 8-12 months, but this depends on the patient's disease level. Lapatinib is an oral targeted chemotherapy agent that has also shown some promise in treating urothelial carcinomas. This chemotherapy agent is administered at home on a daily basis with similar side effects to mitoxantrone and vinblastine. We typically treat for 4 weeks and then assess response. If a benefit is noted, then therapy is continued.
- Surgery is rarely recommended because complete surgical excision is not usually an option due to the location of the tumor. Even if surgery is an option, unfortunately, most tumors recur within a year which is likely because the entire bladder mucosa is thought to be diseased (known as field carcinogenesis), so adjuvant chemotherapy is recommended to try and slow tumor recurrence and metastatic disease.
- Radiation therapy can be considered, however there is debate as to whether or not it helps to increase the survival time for urothelial tumors of the bladder, but there are a few studies that have shown benefit for tumors confined to the urethra. In addition radiation can be used as a palliative treatment to help alleviate the signs/discomfort secondary to the tumor.

- There are also some procedures that are performed to help improve a patient's ability to urinate, but are not directed at treating the tumor. These include urethral stents (placing a tube in the urethra to hold it open) and laser ablation (using a laser to destroy tissue) of a mass or masses that are obstructing the bladder and urethra. These procedures are not benign and can lead to additional side effects (urinary incontinence, urethral perforation); however, the goals of these procedures are to help open the urethra and alleviate the difficulty of urinating. These are short-term fixes because the tumor continues to progress since these procedures are not treating the cancer.

Once the tumor becomes resistant to chemotherapy, the clinical signs will recur as a result of tumor progression. As the tumor starts to progress, it can lead to obstruction of both the urethra and ureter/kidneys. The most common cause for euthanasia is locally progressive disease that causes obstruction so that the patient cannot urinate and/or their kidneys fail.

Our goal for both you and your pet is to provide a good quality of life. Treatment is dependent on several factors, and we want to make sure you take all of these into consideration. We want to be able to give you the best quality time with your pet and will work to the best of our ability to accomplish that.