

Transitional Cell Carcinoma in Dogs

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Transitional cell carcinoma (TCC) is the most common malignancy of the bladder and urethra. There are many treatment options for this disease and, as with any disease with many options, there is no perfect treatment. The pros and cons of each approach must be weighed for each case. The clinical signs associated with TCC include pollakuria, stranguria, hematuria, dysuria, chronic urinary tract infections and signs of partial or total obstruction of the urethra. Patients with chronic urinary tract infections that do not resolve with an appropriate course of antibiotics should have further investigation of their lower urinary tract with ultrasound or cystoscopy.

If a TCC is suspected, both ultrasound and cystoscopy are useful for local staging. In general, ultrasound-guided aspirate is not recommended if it can be avoided because of the high risk of tumor seeding with TCC. Cystoscopy or traumatic catheterization (with or without ultrasound guidance) are recommended to obtain a diagnosis. Abdominal ultrasound can also be used to evaluate the local lymph nodes (iliac) for evidence of metastasis. Three-view thoracic radiographs should be taken to evaluate for pulmonary metastasis. TCC is both aggressive locally and systemically, so therapy should be directed at both local and distant disease, even in cases with no gross metastasis.

Treatment with medical therapy, such as chemotherapy (mitoxantrone or doxorubicin) and a nonsteroidal anti-inflammatory is often the first line treatment. The type of NSAID used is somewhat controversial. Piroxicam, a nonselective NSAID, is the NSAID that is reported for this disease and has been specifically evaluated and shown to have an effect. The concern is that this medication can cause gastrointestinal side effects. Further, because of the effect of this medication on platelets, this medication should not be used preoperatively if surgery is being considered. I prefer to use a selective NSAID, such as meloxicam. In my opinion, this will result in a similar local effect with a decreased risk of side effects. However, this has not been proven and is anecdotal.

Palliative treatment of transitional carcinoma of the bladder neck and urethra that is causing obstruction has been treated with a cystostomy tube. This can be used as a short-term palliative measure alone or as a means of relieving urinary tract obstruction until definitive therapy such as radiation and chemotherapy can be initiated to relieve the urinary tract obstruction. Techniques for placing a cystostomy tube include an open approach to the caudal abdomen, a minimally invasive approach to the abdomen, a laparoscopic approach or by using fluoroscopy and a self-retaining, pig-tail catheter. A full understanding of the owner's intent to treat is important before placing a cystostomy tube, as manipulation of the bladder with the cystostomy tube could lead to seeding of the tumor in the abdomen. A more sophisticated way to manage malignant urethral obstruction is urethral stenting, developed and reported by Weisse et al. With this method, a self-retaining nitinol stent spans the urethral mass and relieves the obstruction. Urethral stenting is a palliative procedure and should not be used when the treatment goal is curative-intent. For neoplasia confined to the urethra, vaginourethroplasty has been reported. Liptak et al reported management of urethral

tumors with transurethral resection. This method had some promise in male dogs with prostatic carcinoma, but had a high intraoperative urethral perforation rate in female dogs with urethral tumors, and was not recommended in these cases. Transurethral resection also requires specialized equipment and training. A further evolution of this approach in veterinary medicine is the use of urethroscopy and a laser to ablate tumors of the urethra. This technique is new and also requires specialized equip, but holds promise as a palliative technique for urethral tumors. Another technique for resection of invasive tumors of the bladder neck and trigone has been described by Saulnier-Troff et al. The bladder neck and trigone region is removed while sparing the dorsal neurovascular structures. I have not used this technique personally and I believe that more work is needed in this area in order to evaluate its utility as a technique for TCC of the bladder neck.

Partial cystectomy for the treatment of TCC should be considered when it is technically feasible. Unfortunately, TCC is most often found in the trigone region in dogs. This is possibly due to the fact that the carcinogens that may lead to this tumor will contact this region first. Partial cystectomy in this area is challenging and may not be feasible. Preoperative evaluation with cystoscopy will help to assess this. However, sometimes a cystotomy is necessary to assess the resectability of a tumor. reimplantation of one or both ureters may be necessary. Even in cases where the tumor can be successfully removed, recurrence is common. This may be due to incomplete margins of excision, or to the so-called “field effect”, where the genetics of the patient and the carcinogen exposure will cause transformation of cells adjacent to the primary tumor and the development of de novo tumors.

Full course radiation or palliative radiation are also treatment options that should be considered for local control, especially in cases that are not resectable. Stereotactic radiosurgery (SRS), the administration of a highly conformal dose of radiation to a select target, has created the possibility of treating TCC with curative intent radiation therapy, with a much lower risk of damage to surrounding tissues. Bacon et al explored feasibility of SRS treatment in 9 dogs; 7 dogs died of tumor related disease and 2 dogs were alive at time of reporting, with survival times ranging from 88-460 days. Local control of disease within the radiation field was good, with no side effects of SRS were reported.

Total cystectomy is an uncommon procedure for treatment of bladder neoplasia in dogs. The technique is rarely used because of complications associated with ureteral reimplantation. Ureterocolonic anastomosis and cystectomy was reported in 1988 by Stone et al; however, complications like hyperchloremic metabolic acidosis, hyperammonemia, pyelonephritis, hydroureteronephrosis, and death from metastatic disease were reported. Although this technique has the advantage of anal continence, the other complications have precluded its widespread use. Kadosawa et al reported 14 cases of total cystectomy for treatment of cancer. The method used was creation of a single lumen with the remaining ureters and anastomosis of the distal ureteral lumen with the distal urethra, vaginal, or preputial mucosa. The results of Kadosawa were

promising, with long term survival in some cases and an overall median survival time of 6 months without adjunctive chemotherapy.

Although distant metastatic disease is common, in most dogs with TCC the primary tumor is the most common cause of death. This highlights the need for aggressive local therapy. All cases managed with total cystectomy and ureteral reimplantation into the urethra, prepuce or vagina will obviously be incontinent and will need to be managed with a diaper and considerable care on the part of the owners to ensure that these dogs do not develop urine scald. The acceptance of incontinence and a diaper by an owner will vary. However, many of these dogs are partially or completely incontinent and the owners are already managing this at home.

Total cystectomy is a technically feasible procedure that serves 2 important purposes in the treatment of lower urinary tract TCC: to remove the source of pain due to the tumor, inflammation and urinary tract obstruction and to remove the primary tumor, which may limit or prevent metastatic spread of disease. Major disadvantages of this procedure are incontinence and the potential for ascending infection. Often a total cystectomy is not offered during original consultation for a bladder TCC because it is considered too radical, because it is assumed that the owners will not manage urinary incontinence, or simply because it is below our collective consciousness as a treatment option.

Until a perfect treatment for this disease is developed, all options should be on the table and discussed with the owners so that a treatment plan can be tailored to the patient and the owner.