Diagnosis and Treatment of Bladder Tumors

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Bladder tumors are relatively common tumors of dogs accounting for about 2% of all canine malignancies. Bladder tumors are rarely seen in cats. Female dogs have 1.5 to 2 times the rate of tumor development that male dogs have. Scottish Terriers, Shelties, Airedales and Beagles are over-represented. Tumor development occurs in middle age to older dogs. When tumors occur in younger dogs they may be more aggressive. It is unclear why bladder tumors occur in dogs but exposure to insecticides and herbicides may influence the development of tumors. Overweight dogs seem at greater risk of developing bladder tumors.

The clinical signs of bladder tumors are similar to urinary tract infections or bladder stones. Hematuria, pollakiuria and stranguria are commonly seen. Abnormalities are not commonly found on physical examination but a bladder mass or thickening of the bladder may be found on palpation. A rectal examination can be helpful in identifying thickening of the urethra or enlargement of the iliac lymph nodes. There are usually no signs of systemic disease and the complete blood count and chemistry panels are usually normal. It is not unusual for bladder tumors to be accompanied by urinary tract infections. If there is pyuria noted on the urinalysis, a urine culture is advisable. Antibiotic treatment should resolve a simple bladder infection and is likely to improve a dog with bladder tumor and urinary tract infection. If signs of straining and blood in the urine persist in spite of antibiotic therapy, the urinalysis should be repeated. If the sediment is principally red blood cells, then further diagnostics are needed. The identification of malignant cells on cytology of the urine sediment can make the diagnosis of transitional cell carcinoma in about a third of dogs with bladder tumor. In the face of a bladder infection, it may be difficult to make a diagnosis of bladder cancer because inflammation causes reactive changes in the bladder epithelial cells making a diagnosis of malignancy difficult. There is a urine assay that identifies tumor antigens that has a 90% sensitivity but hematuria will produce a false positive test. Unfortunately, most dogs with transitional cell carcinoma will have hematuria making interpretation of the assay difficult.

Imaging with radiographs or ultrasound is helpful in identifying a bladder mass and defining the extent of disease. The local disease is usually advanced at time of diagnosis. The tumor is typically located in the area of the trigone making surgical removal of the tumor impossible. There is usually invasion into the bladder wall and metastasis is evident in 40% of the cases at time of diagnosis. On radiographs, positive contrast with iodine based contrast agents help visualize a filling defect in the dorsal neck of the bladder. Air contrast or double contrast radiographs provide better definition of the lesion. Ultrasound examination is very helpful because it can identify hydronephrosis and hydrouretters that occur commonly in advanced disease. Obstruction of the ureters causing renal failure is a common cause for euthanasia of dogs with transitional cell carcinoma. Ultrasound is also very useful in identifying enlargement of the iliac lymph nodes due to metastasis. Radiographs of the abdomen may identify metastatic lesions in the vertebrae and pelvis especially in dogs that show signs of hindleg lameness. Three views of the chest looking for metastases is important in staging the extent of disease.
Catheterization of the bladder and palpation of the bladder will often dislodge a number of tumor cells making cytologic evaluation of the urine more likely to identify tumor cells. When a bladder tumor is suspected, it is better to avoid doing a cystocentesis because transitional cell carcinomas have been known to establish tumor metastatic sites along the path of the needle. Catheterization of the bladder must be done carefully to avoid puncturing the weakened area of the bladder.

Surgical treatment of transitional cell carcinoma is rarely curative in dogs because of infiltrative disease into the bladder wall and the tumor's location in the trigone area where the ureters enter the bladder. Bladder tumors in cats are more localized and more likely to be cured with surgery. The feline bladder tumors are more likely to be leiomyomas and leiomyosarcomas than transitional cell carcinomas. Techniques for complete removal of the bladder with diversion of the ureters to the colon have been tried but they result in ascending infection and renal failure. The complications associated with cystectomy and the high likelihood of recurrence of tumor make this technique unacceptable. Surgery may be helpful in surgically reducing a tumor mass that is obstructing outflow of urine from the bladder and making a histologic diagnosis. Surgical placement of a prepubic cystotomy tube will provide relief in dogs that have urethral obstruction.

Radiation therapy has been attempted but radiation injury results in severe fibrosis and reduced bladder volume leading to incontinence.

Most transitional cell carcinomas express cyclo-oxygenase enzyme 2 (COX-2) on immunohistochemistry and a number will respond to non-steroidal antiinflammatory drugs. COX-1 is a normal component of the mucosa and produces prostaglandins necessary for protection of the gastric mucosa. COX-2 occurs in tumors and in areas of tissue damage. COX-2 appears to play a significant role in the development and progression of certain tumors. Over-expression of COX-2 inhibits apoptosis allowing damaged tumor cells to survive. COX-2 reduces immune system attack on tumor cells and may increase angiogenesis to improve tumor blood supply. Most non-steroidal antiinflammatory drugs inhibit both COX-1 and COX-2 activity but newer drugs such as carprofen, deracoxib, meloxicam and firocoxib are more COX-2 specific. Unfortunately, the newer non-steroidal antiinflammatory drugs have not been evaluated for their antitumor effects. Piroxicam is the best studied non-steroidal antiinflammatory drug used in the treatment of bladder tumors.

Piroxicam at doses of 0.3 mg/kg/day have shown reduction in size of the tumor in about 20% of the dogs. In a study of 65 dogs with transitional cell carcinoma treated with piroxicam alone, 2 dogs had complete responses with no evidence of disease at necropsy 2 years later. Another 9 dogs had a partial response and 35 dogs had stable disease. There was a median survival time of 195 days and 20% of dogs were alive at a year. Even in dogs that do not have objective responses, the discomfort and straining is reduced greatly improving quality of life. The constant straining and the frequent need to urinate seen in some dogs affects quality of life and results in euthanasia.

As with any of the non-steroidal drugs piroxicam inhibits the COX-1 activity and gastrointestinal signs of vomiting and anorexia can occur. Gastric ulceration is a complication of non-steroidal antiinflammatory drugs and stools should be checked for melena. COX-1 enzymes also protect the kidneys. Nephrotoxic drugs such as amphotericin B and aminoglycosides should be avoided in dogs on non-steroidal anti-inflammatory drugs. If vomiting occurs discontinuation of the drug until adverse effects are eliminated and start misoprostol as a gastric protectant. Response to treatment should be evaluated 4 and 8 weeks after starting therapy by measuring changes in
tumor size and evaluating iliac lymph nodes with ultrasound. Inflating the bladder with saline will improve visualization of the tumor. The best response of transitional cell carcinomas has been with a combination of mitoxantrone chemotherapy with piroxicam. Mitoxantrone is given at a dose of 5 mg per meter square body surface area intravenously over 20 minutes every 3 weeks for a total of 5 doses. As with any chemotherapy, blood counts need to be monitored to be sure there are adequate neutrophils and platelets before treatment. The combination of piroxicam and mitoxantrone will give a complete or partial response in 35% of the dogs and provide a median survival time of 291 days.

With therapy some dogs will be controlled for an extended period of time. Recurrent bladder infections are often seen secondary to the tumor and straining is a persistent problem. Renal failure secondary to obstruction of the ureters is the usual cause of death.

References: