Neoplasms of the urinary tract are a rare overall tumor type in dogs and cats, but create significant morbidity and mortality when encountered. Like most neoplastic disease, urinary tract tumors usually develop in older dogs and cats. An exception to this generalization is renal lymphoma, which can affect any age. Most urinary tract tumors are aggressive, usually malignant (>90%) and often metastasized at diagnosis (>50%). The typical metastatic pattern for renal tumors is to peritoneal or serosal surfaces, liver, and lungs. The pattern of dissemination for prostatic, urinary bladder or urethral tumors is to lumbar vertebra, regional lymph nodes, liver, kidney and (most commonly) lungs. Three-view thoracic radiographs for metastases are essential for prognostic purposes. With the exception of some transitional cell carcinomas, most urinary tract tumors are poorly responsive to chemotherapy.

Prostatic neoplasia (dogs)
Prostatic neoplasia is an uncommon but devastating disease in older male dogs. The disease differs from the common human counterpart in stage at detection, clinical signs, and treatment options, but shares a similar pathogenesis. Tumor types include adenocarcinoma and transitional cell carcinoma, depending on the tissue origin. From a practical viewpoint, differentiation of urethral origin versus glandular origin is not necessary.

Clinical signs
Prostatic carcinoma is encountered most commonly in older (>8 yrs) medium to large breed dogs. Intact OR neutered dogs can be affected; in fact, the relative risk for disease is higher for neutered males. Most dogs will have a history of typical urogenital signs: hematuria, urethral discharge and prostatic enlargement. In addition to these signs, several “ominous” signs point to the possibility of neoplastic disease:

- Pain, weakness, or trembling in hind limbs
- Tenesmus
- Weight loss and anorexia
- Urinary incontinence or urinary obstruction
- Regional lymph node enlargement or bone pain
- Systemic illness and inflammatory leukogram

Diagnosis
A presumptive diagnosis can be made based on rectal palpation findings, imaging results and cytology. Definitive diagnosis requires biopsy but often is not needed.

- Rectal examination: enlarged firm, irregular or nodular prostate; often the prostate or surrounding nodes, bones are painful
- Survey Radiographs: Asymmetric or nodular prostatic enlargement, mineralization, enlarged sublumbar nodes, vertebral bone lesions
- Ultrasonography: Irregular, mixed echogenicity with multifocal hyperechoic areas, some cysts
- Cytology of prostatic samples: Suspicious or neoplastic cells usually observed, with or without secondary inflammation
- Prostatic biopsy: definitive if appropriate area is sampled; usually perabdominal or transrectal approach
- Serum markers such as Prostate –specific antigen, used widely in men, do not detect canine PSA and are not helpful in dogs

Treatment
Although many options are available for men with early, non-aggressive, disease, most dogs have aggressive, advanced disease at diagnosis. The morbidity associated with prostatectomy (major surgery, incontinence) has prevented its application as well, although some newer, subtotal techniques are promising for palliative treatment. Chemotherapy may reduce clinical signs and prolong survival in some cases. Piroxicam (NSAID inhibiting COX- 2 expression) is most commonly recommended (see further discussion in bladder neoplasia section).

Palliative care is needed for advanced cases. Urinary diversion (with a stent or cystostomy device) may be considered for short term extension of survival when the urethra is obstructed. Pain management may be needed, especially for bone pain (consider bisphosphonates or analgesics).

Prognosis
The prognosis for prostatic neoplasia in dogs is poor. The disease is usually advanced by the time of diagnosis and quickly obstructs the urethra. Euthanasia is usually considered when voiding impairment or systemic clinical signs interfere with an acceptable quality of life.
Urinary bladder and urethral neoplasia

The most common tumor type in the urinary bladder or urethra is the transitional cell carcinoma. Squamous cell carcinoma of the urethra is also observed. Other tumor types less frequently encountered include adenocarcinoma, leiomyosarcoma, rhabdomyosarcoma, and hemangiosarcoma. Note that a non-neoplastic inflammatory condition of the urethra (granulomatous urethritis) in dogs can look very much like neoplasia but is benign, usually related to chronic urinary tract infection. Risk Factors for urinary bladder neoplasia are known for dogs and people. In dogs, obesity, breed (older small breed dogs), sex (females) and exposure to urban environments, organophosphate dips and cyclophosphamide increase the risk for bladder cancer. High risk breeds include the Scottish Terrier, Sheltie, other Terriers and Beagles. In cats, the tumor is slightly more common in male cats than female cats and often arises in the bladder apex or fundus, as opposed to the trigone—the most common location in dogs. Environmental and other risk factors are unknown for cats.

Clinical signs

Clinical signs are similar to other lower tract disorders, including chronic hematuria, dysuria, or pollakiuria, recurrent or unresponsive urinary tract infections, or urinary incontinence. Transitional cell carcinoma is most often diagnosed in dogs or cats presented after multiple suspected urinary tract infections that no longer respond to antimicrobial treatments. Urinary obstruction is possible with bladder neck or urethral tumors; hydroureter and azotemia are possible if both ureteral orifices become obstructed. Additionally, polyuria and polydipsia (probably psychogenic) are seen in some affected dogs. Respiratory signs or lameness may be seen with metastatic disease.

Diagnosis

The diagnostic approach for suspected lower urinary tract neoplasia may include:

- Urinalysis: inflammatory or neoplastic cells may be observed
- Abdominal Radiographs: soft tissue densities, enlarged lymph nodes or a distended urinary bladder may suggest neoplastic disease. Carefully evaluate the bladder neck area.
- Abdominal ultrasound is a good tool for detecting tumors > 0.5 cm
- Contrast cystourethrogram or cystoscopy further delineates suspicious lesions
- Cystoscopy: Very sensitize for detecting subtle urethral lesions, taking biopsy samples, doing laser treatments or placing stents
- Thoracic radiographs to screen for metastasis
- Urinary antigen tests: These detect tumor antigen in urine; work well in people, but many false positives seen in dogs with other causes of hematuria. Tumor antigen tests may be useful in high risk breeds. Other tests for bladder cancer include flow cytometry and measurement of fibroblastic growth factor.

Cytologic or histopathologic confirmation is required. TCC cells usually exfoliate readily and a reasonably sound diagnosis can be made by combining the imaging findings and cytology findings. A fine needle aspirate, forceps or catheter biopsy, bladder washing, urethral brush, traumatic catheterization or surgical biopsy can be used to gain cells or tissue. Many oncologists strongly discourage any perabdominal aspirates, including cystocentesis, in suspect patients because of the high possibility of neoplastic cells seeding the abdomen.

Treatment options for transitional cell carcinoma

Surgical resection may be considered for an isolated mass in apex of bladder or a benign tumor. Most bladder tumors in dogs develop in the trigone area and are not completely resectable, but many cat bladder tumors develop elsewhere in the bladder and may be more amenable to resection. Margins of approximately 2 cm are suggested; fortunately up to 74% of the bladder can be removed with little impact on urine storage. It is important to recognize that microscopic spread or metastasis may have already occurred, despite the gross appearance of a resectable mass. Additionally, there is some evidence that the entire bladder may be transformed when an isolated tumor develops, leading to the possibility of spontaneous cancerous transformation in other areas at any time. For this reason, some oncologic surgeons are performing total cystectomy with ureteral diversion in severely affected patients.

In most cases, chemotherapy with piroxicam or mitoxantrone/piroxicam is used to reduce clinical signs and modestly prolong survival. Piroxicam (0.3 mg/kg/day PO) is a NSAID with additional antineoplastic activity. The anti-tumor effect may be due to immunomodulation (blocked COX 2 expression) or direct activity on tumor receptors. It is most effective against urinary bladder transitional cell carcinomas. Concurrent antacids (H2 blockers or omeprazole) or misoprostol are administered to protect the gastrointestinal tract. Complete or partial remission is seen in some dogs (about 30%), with survival times of approximately 6 months. Many treated dogs do well for a year or more. Similar results have been observed with Deracoxib (Deramaxx 3 mg/kg PO q 24 hrs)

Adjuvant chemotherapy (mitoxantrone, chlorambucil, vinblastine), may be started initially or after NSAID treatment fails to maintain stable disease. The best outcomes have been reported with a mitoxantrone/piroxicam combination protocol. In this report, 17 of 48 dogs (35% had at least partial response) whereas 9 more dogs had stable disease and the median survival time was extended to 10 months. Cisplatin and carboplatin has also been advocated for TCC; cisplatin combinations are more nephrotoxic, however.
Palliative or debulking procedures

The effect of chemotherapy is enhanced when tumor volume can be decreased by debulking procedures. Additionally, debulking may be necessary to temporarily open the trigone and urethral outflow in obstructed dogs. Minimally invasive options for debulking use cystoscopic approaches to reach neoplastic tissue. Using a diode laser, surface tumor can be steadily “burned” off in thin layers. Ultrasound guided endoscopic laser ablation (UGE LAB) can be used to debulk TCC if an expert team is available. The sonographer works with the cystoscopist to provide a sonographic view of the bladder, mass, scope and laser tip and guide the overall procedure. Tissue rupture and tumor seeding are potential serious complications. These procedures are easiest to perform in female dogs but can be done in male dogs via a urethrostomy.

Other palliative options for obstructed dogs include urethral stent placement or cystostomy tubes for urinary diversion. Many dogs with bladder or urethral neoplasia require antimicrobial treatment for secondary infections as well.

Prognosis

TCC of the urinary bladder is usually slowly progressive; affected patients are usually euthanized when disease causes obstruction of ureters or urethra or when metastases cause clinical debilitation. Depending on the stage of disease at diagnosis, dogs and cats can live months to approximately one year with palliative treatment.

Key points

- Urinary tract neoplasms are usually malignant, readily metastasize and respond poorly to chemotherapy.
- Neutered males can be affected with prostatic neoplasia. An enlarged prostate gland in a neutered dog is almost always neoplastic.
- Prostatic neoplasia is diagnosed by the appearance of key “ominous” clinical signs, gross prostatic gland findings and cytological or histopathological confirmation. The main differential diagnosis is chronic prostatitis or atypical BPH. Prostatic tumors will not shrink following castration.
- Lower urinary tract signs that are accompanied by a negative urine culture, or that do not have a sustained response to antimicrobial therapy, should increase your suspicion of neoplasia, especially in older, female dogs.
- Instrumentation during sampling or surgery of transitional cell carcinomas creates a risk of seeding tumor cells in the abdomen or urethra. Clinician opinion varies regarding the probability and significance of this complication, however.
- Piroxicam is a valuable and usually well tolerated option for long term palliative treatment of TCC and prostatic carcinoma in dogs and cats, with remarkable results in some patients. Gastrointestinal protectants are usually given concurrently.