Improve
Veterinary Education

Summary of **'Urologic Oncology - Kristine Elaine Burgess, DVM, Carol J. DeRegis, DVM, PhD.**

Abstract

PRIMARY RENAL TUMOURS

Urologic tumours involving the kidneys, bladder, or urethra are infrequently encountered in domestic animals and represent fewer than one percent of all diagnosed neoplastic conditions and approximately two percent of malignant tumours.1–3 Among these, primary renal neoplasms are particularly rare, comprising an estimated 0.3 percent of all canine tumours. Secondary involvement of the kidneys due to metastatic spread from other primary sites is substantially more common.1–3

Renal cell carcinoma (RCC), which originates from epithelial cells of the nephron, is the most frequently diagnosed primary renal malignancy in dogs, accounting for approximately 49 percent to 65 percent of cases. Additional primary renal tumour types include a variety of sarcomas and, less commonly, nephroblastoma.1–4

Available literature indicates that outcome is strongly influenced by histologic subtype and the therapeutic approach selected. Dogs presenting with extensive metastatic disease at the time of diagnosis have significantly reduced survival compared with animals lacking evidence of metastasis, whereas dogs treated surgically prior to dissemination may survive for several years following nephrectomy.1–8

Renal Cell Carcinoma

Because renal cell carcinoma is uncommon in dogs, information regarding its biological behaviour and metastatic tendencies is limited primarily to retrospective analyses.3,4 Clinical signs at presentation are often vague and may include lethargy, decreased appetite, increased thirst and urination, abdominal discomfort, or progressive weight loss. In advanced disease, a palpable abdominal mass may be detected during physical examination. Haematuria is the most frequently reported presenting abnormality, occurring in approximately 32 percent of affected dogs. Azotemia typically develops later in the disease course and represents the most common biochemical abnormality, while other laboratory changes are uncommon. Rarely, dogs may develop paraneoplastic polycythemia associated with RCC.3

Renal cell carcinoma often progresses silently, allowing tumours to reach substantial size before clinical signs become apparent. As a result, diagnosis frequently occurs at an advanced stage.3,4 Metastatic disease is identified in approximately 16 percent to 34 percent

of dogs at the time of diagnosis, with rates increasing to 70 percent to 75 percent in later stages. Common metastatic locations include the contralateral kidney, abdominal organs, omentum or peritoneum, and lungs. Bilateral renal involvement is reported in approximately five percent of cases.1–4

Histologic characterization of renal cell carcinoma has provided insight into prognostic factors. In one study evaluating kidneys from 70 dogs following nephrectomy, tumours were classified into four histologic subtypes based on morphologic features and histochemical and immunohistochemical staining patterns: clear cell, chromophobe, papillary, and multilocular cystic RCC.4 Clear cell carcinoma, representing nine percent of tumours, was associated with a markedly reduced median survival time of 87 days. The mitotic index, defined as the number of mitotic figures observed in ten high-power fields at 400× magnification, emerged as the only independent prognostic indicator. Dogs with a mitotic index exceeding 30 had a median survival of 187 days, whereas those with fewer than ten mitotic figures survived a median of 1184 days. Intermediate values between ten and 30 were associated with a median survival of 452 days.

Nephroblastoma

Nephroblastoma is an embryonal tumour reported primarily in young dogs younger than two years of age. It may arise as a primary renal mass or develop within the thoracolumbar spinal cord.1,6,7 This neoplasm is analogous to Wilms tumour in humans.6–8 Tumour development is believed to result from malignant transformation during nephrogenesis or from residual nephrogenic tissue persisting after birth.1–3,6–8

Information regarding prognosis and treatment is limited due to the rarity of the condition. A small case series involving five dogs with primary renal nephroblastoma reported a median survival time of six months.8 However, individual case reports describe prolonged survival following combined surgical excision and chemotherapy.

Renal Cystadenocarcinomas

A hereditary syndrome characterized by bilateral, multifocal renal cystadenocarcinomas accompanied by nodular dermatofibrosis has been documented in German shepherd dogs.1–3 Affected animals commonly develop multiple subcutaneous fibrous nodules, uterine leiomyomas, and numerous renal adenomas or adenocarcinomas.1–3 This condition is inherited in an autosomal-dominant pattern and has been linked to a mutation in the folliculin gene located on chromosome 53.9

An analogous disorder in humans, known as Birt–Hogg–Dubé syndrome, is similarly associated with folliculin gene mutations and is characterized by benign cutaneous tumours.9

Renal Sarcomas

An earlier investigation of primary renal tumours in dogs identified 28 cases of renal sarcomas, including hemangiosarcoma, renal sarcoma, leiomyosarcoma, malignant fibrous histiocytoma, spindle cell sarcoma, and fibroleiomyosarcoma.3 All dogs underwent nephrectomy followed by chemotherapy. Median survival for dogs with sarcomas was nine months, compared with 16 months for dogs with renal carcinomas, although this difference did not achieve statistical significance. Metastatic disease was present in 14 percent of dogs at diagnosis and in 88 percent at the time of death.3

Primary renal hemangiosarcoma has also been described.10 As with hemangiosarcoma in other organs, treatment typically includes surgical excision followed by chemotherapy. However, the benefit of adjuvant chemotherapy for this specific tumour type remains uncertain.

Treatment of Primary Renal Tumours

Across tumour types, effective management of primary renal neoplasia relies on complete surgical removal of the affected kidney.1,3–10 Given the high likelihood of metastatic disease, adjuvant chemotherapy is commonly advised. Chemotherapy protocols are tailored to tumour histology, though standardized treatment guidelines are lacking, and therapeutic decisions are often extrapolated from clinician experience and human oncology literature.

In humans, RCC exhibits poor responsiveness to traditional cytotoxic chemotherapy, suggesting intrinsic resistance.5 Advances in treatment have been achieved through targeted therapies, angiogenesis inhibitors, and immunomodulatory agents. Interleukin-2 and interferon are widely used in human patients.5 Comparable data supporting these approaches in dogs are unavailable, although anecdotal reports suggest that the tyrosine kinase inhibitor toceranib phosphate may provide some disease control.

In a study involving 14 dogs with renal hemangiosarcoma, median survival was approximately nine months following nephrectomy combined with a doxorubicin-based chemotherapy protocol, with a one-year survival rate of 29 percent.10 Dogs presenting with haemoabdomen had significantly shorter survival times than those without this complication.

Because nephroblastoma is rare, a superior adjuvant therapy protocol has not been established, and treatment approaches remain largely anecdotal.

RENAL LYMPHOMA

Renal lymphoma is infrequently diagnosed in cats and typically manifests as bilateral renal enlargement detectable on physical examination. Clinical signs are primarily attributable to renal failure.1,11 Confirmation of the diagnosis is achieved through ultrasound-guided renal biopsy or fine-needle aspiration.

Treatment consists of multiagent chemotherapy. Given the high risk of central nervous system involvement, protocols incorporating agents with central nervous system penetration, such as lomustine (CCNU), are recommended.

TUMOURS OF THE URINARY BLADDER AND URETHRA

Neoplasms affecting the urinary bladder and urethra represent approximately 0.5 percent to 1.0 percent of canine tumours. The majority are malignant, and transitional cell carcinoma accounts for 75 percent to 90 percent of primary epithelial bladder tumours. Other less common tumour types include squamous cell carcinoma, adenocarcinoma, rhabdomyosarcoma, leiomyoma, and leiomyosarcoma.1–3,12

TRANSITIONAL CELL CARCINOMA

Transitional cell carcinoma most often arises from the bladder trigone, urethra, or prostate. Tumours are typically solitary but may be locally invasive and involve extensive regions of the bladder mucosa.1–3,12–17

Incidence and Risk Factors

Female dogs are affected approximately twice as often as males, and neutered animals of either sex have a fourfold increased risk compared with intact dogs.1,2,12–15 Certain breeds, including Scottish Terriers, West Highland White Terriers, Shetland Sheepdogs, Beagles, and other terrier breeds, are at increased risk.1,2,12–15

Environmental exposure to pesticides has been identified as a significant risk factor.18–21 Obesity is associated with a threefold increased risk, whereas regular consumption of vegetables in Scottish Terriers has been shown to reduce risk to approximately one-third of that observed in dogs not consuming vegetables.20,22

Although cyclophosphamide exposure and environmental tobacco smoke are established risk factors in humans, a definitive causal relationship has not been demonstrated in dogs. Nevertheless, transitional cell carcinoma has been reported in dogs previously treated with cyclophosphamide.23

Clinical Signs and Physical Examination Findings

Because transitional cell carcinoma frequently involves the bladder trigone, affected dogs commonly present with lower urinary tract signs indistinguishable from urolithiasis or infection, including stranguria, haematuria, pollakiuria, and tenesmus.1–3,12–15 Temporary improvement with empiric antimicrobial or anti-inflammatory therapy often delays diagnosis.

Physical examination findings may include bladder distension, palpable masses or thickening involving the bladder, urethra, or vagina, prostatomegaly, and enlargement of regional lymph nodes. Digital rectal examination is essential, as portions of the urethra are not adequately visualized with routine imaging modalities.

Diagnostic Tests

Non-invasive diagnostic evaluation includes urinalysis, urine culture, urine cytology, bladder tumour antigen testing, and molecular testing for BRAF mutations.24–27 Cystocentesis is contraindicated in high-risk breeds and in dogs with known bladder masses because of the risk of tumour implantation along the needle tract.28,29

Voided urine cytology alone is insufficient for definitive diagnosis, as reactive transitional epithelial cells may resemble malignant cells.

Bladder tumour antigen testing may support a diagnosis but yields false-positive results in the presence of proteinuria, glucosuria, pyuria, or haematuria.24–26 The test is most useful as a screening tool in high-risk populations due to its high negative predictive value and low positive predictive value.24,25

A commercially available molecular assay detects the cBRAF V595E mutation in urine samples.27 This mutation is present in approximately 80 percent of dogs with bladder or prostate cancer. The test offers a highly sensitive, non-invasive diagnostic option for tumours harbouring this mutation.

Histopathologic examination of biopsy specimens remains the diagnostic gold standard.13–17 Biopsy samples may be obtained through traumatic catheterization, cystoscopy, or open surgery.30 Disruption of tumour tissue carries a risk of abdominal seeding.31 Tumour grade, invasiveness, and surgical margins are assessed following biopsy or excision. Most canine transitional cell carcinomas are classified as grade II or III.1,12–17 Higher grade tumours are associated with increased vascular invasion and reduced survival.16,17

Imaging Options

Initial diagnosis often relies on identification of a mass on abdominal ultrasonography or other imaging studies, although inflammatory and alternative neoplastic conditions must be considered.

Plain radiography is of limited value for detecting transitional cell carcinoma, though secondary findings such as lymphadenopathy, prostatic mineralization, or skeletal metastases may be observed. Contrast urography improves visualisation of the lower urinary tract and reveals filling defects or urethral irregularities in the majority of cases.32,33

Ultrasonography is the most frequently used imaging modality but cannot reliably distinguish transitional cell carcinoma from other conditions based solely on appearance.32,33 Measurement variability limits its utility for monitoring treatment response, with reported correlation coefficients ranging from 0.4 to 0.7.34

Cystoscopy permits direct visualisation of the urethra and bladder and allows biopsy collection.30,34,35 However, lesion appearance alone is not diagnostic, as benign and inflammatory processes may appear similar.

Staging

Staging evaluation includes routine laboratory testing, urinalysis, urine culture, thoracic radiographs, and abdominal ultrasonography. Lung metastases may appear as subtle interstitial patterns on radiographs and may be misinterpreted as age-related changes.36 Abdominal imaging assesses involvement of regional lymph nodes and other organs.

Staging follows the TNM classification system.41 Common metastatic sites include medial iliac lymph nodes, lungs, liver, and vertebrae.1,12–17 Because most dogs succumb to complications related to the primary tumour, the full metastatic potential remains incompletely defined.1

Prognosis

Prognostic indicators are largely related to tumour stage. Lymph node involvement, distant metastasis, and T3 classification are consistently associated with decreased survival.1,13–17

Treatment Options

Cyclooxygenase-2 inhibitory nonsteroidal anti-inflammatory drugs form the foundation of treatment for canine transitional cell carcinoma.42–45 Treatment with piroxicam has

resulted in disease stabilization, partial responses, and occasional complete responses. Similar efficacy has been observed with deracoxib and meloxicam.46,47

Chemotherapy

Multiple chemotherapeutic agents have been evaluated in combination with COX-2 inhibitors, including doxorubicin, cisplatin, carboplatin, mitoxantrone, vinblastine, and chlorambucil.37–39,48–61 Combination therapy with chemotherapy and a COX-2 inhibitor is considered the preferred initial approach.54

Sequential administration strategies have shown promise. In one study, dogs receiving vinblastine followed by piroxicam had significantly longer survival than those receiving both agents concurrently.60 Potential explanations include delayed resistance development or tumour sensitization.

Surgery

Complete surgical excision is generally not feasible due to the trigonal location and invasive nature of transitional cell carcinoma.62,63 Multifocal disease and tumour implantation at surgical sites further limit surgical options.31,64,65 As a result, surgery is typically reserved for palliative interventions such as cystostomy catheter placement to relieve obstruction.66,67

Palliative Therapies

Laser ablation may provide rapid symptomatic improvement but carries risks including haematuria, urethral stenosis, infection, tumour seeding, and perforation.68,69

Urethral and ureteral stenting can alleviate obstruction, though complications such as incontinence are common and survival times are generally short.70–73 These techniques are best performed by clinicians with specialized experience.

Radiation Therapy

Radiation therapy has limited efficacy due to moderate radioresistance and efficient DNA repair mechanisms.74 Combined approaches involving surgical debulking and radiation have resulted in median survival times of approximately three to four months.15,74–77

FELINE TRANSITIONAL CELL CARCINOMA

Urinary tract tumours are uncommon in cats aside from renal lymphoma. Transitional cell carcinoma accounts for approximately 60 percent of feline bladder tumours and may also

involve the kidneys.1,2,11 Unlike dogs, cats more frequently develop tumours in nontrigonal regions of the bladder, making surgical intervention more feasible.11,78

Urethral stenting has been successfully performed in select cases.79 Overall tumour behaviour and survival outcomes are similar to those observed in dogs.78,80

COMPARATIVE ASPECTS OF TRANSITIONAL CELL CARCINOMA

Canine transitional cell carcinoma serves as a valuable comparative model for muscle-invasive bladder cancer in humans, sharing molecular features, metastatic patterns, and therapeutic responses.81 Studies demonstrate the utility of dogs in predicting outcomes of immunotherapies, targeted agents, and novel chemotherapeutic combinations.81–85

The identification of BRAF mutations has facilitated development of targeted therapies effective in both human and canine cancers.81,82,85 Continued research is required to establish mutation-guided personalized treatment strategies for genitourinary tumours across species.27,85

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