

Neoplasia of the reproductive tract of the male dog

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Abstract

A brief review of tumors of the male reproductive tract is provided. Diagnosis is straightforward in most cases, with resolution of disease easily achieved. The exception to the latter is prostatic neoplasia, a high morbidity, high mortality form of cancer to which we may predispose dogs by castration.

Keywords: Neoplasia, penis, prostate, testes, transmissible venereal tumor

Introduction

Neoplasia of the male canine reproductive tract is uncommon and often easily diagnosed. The most common reproductive tract tumor of male dogs worldwide is testicular neoplasia, with transmissible venereal tumor also very common. The most devastating cancer of the reproductive tract of male dogs is prostatic neoplasia. Less common tumors include those of the soft tissues of the penis and prepuce, those of the os penis, and those of the scrotal skin and mammary tissues. Excellent published reviews of this topic exist.^{1,2} This manuscript will provide brief reviews of cancer biology and updated information.

Testicular tumors

The three most common tumor types are seminomas, Leydig (interstitial) cell tumors, and Sertoli cell tumors. In humans, testicular neoplasia is common in young men and is aggressively malignant. In dogs, testicular neoplasia occurs in older individuals

and is malignant in 10% of cases at most. It is not uncommon for there to be more than one tumor type in a given testes or between testes concurrently.^{3,4}

Incidence of testicular neoplasia is higher in retained than in descended testes. There is no research documenting increased risk of neoplasia in the descended testis of unilateral cryptorchids.⁵ Controversy exists regarding whether or not the predisposition to neoplasia in retained testes remains if the cryptorchid testis is surgically pulled down and tacked into the scrotum. In human medicine, studies suggest increased incidence in tumor incidence if orchiopexy is delayed until puberty or beyond.^{5,6} This may suggest that medical therapies to induce testicular descent are beneficial in prepubertal dogs, both by potentially decreasing tumor incidence and making castration of those dogs easier.

Dogs with testicular neoplasia may present with enlargement of one or both testes. If neoplasia is unilateral, oftentimes there will be atrophy of the contralateral testis due to increased intrascrotal temperature and possibly to hormone secretion by the affected testis. Components of an associated paraneoplastic syndrome, most commonly associated with estrogen secretion, include gynecomastia, attraction of male dogs, and bilaterally symmetrical alopecia. Malignant tumors metastasize locally and to the regional lymph nodes and lungs, with occasional reports of hypertrophic osteoarthropathy.⁷ A fair proportion of dogs (28.3% in one study) have inapparent testicular neoplasia; these dogs may present for testicular atrophy, poor semen quality, or infertility.³

Diagnosis is by inspection. For dogs with no overt change in testicular size or consistency, testicular ultrasound is the preferred diagnostic technique. Fine-needle aspirate (FNA) of the testes also may be used to identify abnormal cells. The dog is

sedated and the scrotal skin cleaned. A 20 ga needle is attached to a 12 cc or larger syringe. The needle is introduced on or just lateral to the midline and redirected several times, with suction at each location. Negative pressure is released and the needle withdrawn. The sample is expelled onto a glass slide and submitted to a cytologist for interpretation.⁸⁻¹⁰

Treatment is surgical. Bilateral castration is recommended. Caution during surgery is recommended; there are reports of neoplastic tissue (n = 11 Sertoli cell tumors, n = 1 Leydig cell tumor) arising in the spermatic cord, at the incision site, on the scrotal skin, and in the inguinal canal, presumably due to transplantation of cells during castration.¹¹ In valuable breeding animals, one may consider removing only the affected testis but the owners must be cautioned that spermatogenesis may be altered by inapparent changes in the remaining testis.

In humans, incidence of testicular neoplasia is increasing. This same trend appears to be true in veterinary medicine, with incidence of testicular tumors increased in one study from that described in 1962.¹² The primary theory explaining this in human medicine is increase in exposure to environmental toxins.

Transmissible venereal tumor

Transmissible venereal tumor (TVT) is a cellular transplant containing an average of 59 chromosomes, rather than a transformed canine cell, which would contain 78 chromosomes. Analysis of TVTs from five continents showed that all are genetically similar, suggesting that all arose from a single mutation. That mutation is believed to have arisen 250 to 2500 years ago in a wolf or east-Asian breed of dog.¹³

Incidence of TVT in one study was 5.4%; this incidence varies greatly by region.⁴ TVT is most common in young, sexually intact, free-roaming dogs, and so is primarily a problem in sub-tropical and tropical areas of the world.

Most TVTs invade only locally and so usually are not considered malignant. The tumor is a meaty and irregular, and is easily ulcerated. Lesions may be noted on the mouth and nose; this is from transplantation of cells by licking of the genitalia. Occasionally tumor will spread to regional lymph nodes and the internal organs.¹⁴ Metastasis is more common in very young animals and immunosuppressed animals.¹⁵

Diagnosis is by cytology. TVT is easily identified as round cells with abundant cytoplasm and an eccentrically placed round to oval nucleus.

Chemotherapy with vincristine is the recommended treatment. Surgical debulking may be required in some cases. Vincristine treatment has been demonstrated to cause resolution of clinical signs with minimal side-effects within 4 treatments in most dogs, and to decrease semen quality in breeding dogs for only up to 15 days after treatment is completed.^{16,17} Treatment failure is more likely if tumors are large, the affected animal is old or immunosuppressed, and if the treatment is performed during hot or rainy months.¹⁸

Prostatic neoplasia

The most common prostatic neoplasm reported is adenocarcinoma. It is considered to have metastasized by the time of diagnosis in the majority of cases. It is a disorder of older male dogs and may occur in either intact or castrated dogs. It is the only prostatic disorder commonly seen in castrated dogs. Overall incidence of prostatic neoplasia is reported as 0.4 to 0.7%.^{19,20} It is a high mortality disorder; in one survey of

72 affected dogs, 58 were euthanized at the time of diagnosis and mean survival for those who survived more than one week from diagnosis was 30 days.²¹

In humans, prostatic neoplasia is hormone-dependent. That is not true in dogs. In fact, castration, and subsequent removal of testosterone, appears to predispose dogs to prostatic neoplasia, with increased risk of 2.8 to 4.3 times reported.^{22,23} Castrated dogs tend to develop more poorly differentiated tumors than intact dogs, suggesting that testosterone has a protective effect.²⁴ Number of androgen receptors is decreased in the prostates of dogs with neoplasia compared to dogs with normal prostates or benign prostatic hypertrophy, again suggesting loss of a protective effect of testosterone.²⁵ In one survey of 56 affected dogs, time from castration to onset was variable and there was no difference in mean age at time of diagnosis between intact and castrated dogs, suggesting that castration does not favor tumor initiation but may favor tumor progression.²⁰

It has been shown in dogs that castration leads to an increase in number of receptors for endothelin on the prostate; endothelin increases mitogenic responses and uncontrolled cell growth.²⁶ Endothelin also supports osteoblastic function and stimulates bony growth at areas of metastasis from prostatic neoplasia in dogs.²⁷

Dogs may present with signs of prostate disease, such as dripping of bloody fluid from the penis unassociated with urination, hematuria, and passage of ribbon-shaped stools. Commonly, dogs also present with stranguria and signs referable to sites of metastasis including stiff gait or ataxia, coughing, and cachexia.

Because prognosis is grave, definitive diagnostics are required. Definitive diagnosis requires collection of a sample directly from the prostate, either as FNA or

biopsy. Ultrasound guidance is recommended with either technique. For FNA, sedation usually is not required. A 20 ga needle is attached to a 12 cc syringe. The needle is passed into the prostatic parenchyma and negative pressure applied. Pressure is released and the needle withdrawn. The sample is expelled onto a glass slide and submitted to a cytologist for interpretation. For biopsy, sedation is required. Prepare the area over the prostate as for sterile surgery and place a sterile sleeve over the ultrasound probe. Viewing the prostate by ultrasound, trigger the biopsy instrument to see it pass within the prostatic parenchyma. Withdraw the biopsy instrument and retrieve the sample; make sure you have an adequate sample before reversing sedation. Samples should be submitted to a pathologist for interpretation. A diagnostic sample is more commonly retrieved by biopsy than by FNA. Side-effects include hematuria and hemospermia.^{28,29} In humans, seeding of the abdomen with tumor cells and subsequent growth of transplanted cells is reported to occur in 0.009% of cases after these techniques.³⁰ This is less of a concern in dogs, who rarely live long enough after diagnosis for significant secondary tumor development to occur.

Treatment is palliative. Most dogs are treated with anti-inflammatory medications (meloxicam, piroxicam) and antibiotics to control secondary infection. Prostatectomy rarely is performed because it cannot cure disease and often causes urinary or fecal incontinence. There are reports of transurethral resection of the prostate using electrocautery, with or without associated radiation and chemotherapy,³¹ and subcapsular prostatectomy using a laser.³² Some of the dogs in these studies showed a resolution of clinical signs and had longer mean survival times than is commonly reported but other dogs in those studies did not respond to treatment or died from complications of therapy.

That, coupled with the technical skill required to perform this work, makes them unsuitable alternatives for most veterinarians and their patients.

Tumors of the penis, prepuce, scrotum, and mammary tissue

Tumors of the soft tissue of the penis and of the os penis are described in the literature. Tumors of the soft tissue of the penis often are associated with preputial extension and, along with tumors of the scrotum, are the common skin tumors seen elsewhere including papillomas, squamous cell carcinoma, lymphosarcoma, and mast cell tumors.^{33,34} Tumors of the os penis are less common and may be either benign or malignant. Stranguria is a common presenting complaint with tumors of the os penis, which may be confused with fracture of the os penis.³⁴⁻³⁸ Mammary neoplasia rarely is reported in male dogs; one institution reported that male dogs at that institution were 62 times less likely to develop mammary neoplasia than female dogs in that population.³⁹ Mammary tumors usually are benign and easily surgically removed.

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