Orchitis and epididymitis

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Abstract

Inflammation of the male testis and/or epididymis produces canine and feline subfertility and infertility. Causative agents include bacteria, trauma, non-infectious immune-mediated response, prostatitis, urinary tract infection, or an accompanying endocrine disorder. Each possible etiology should be evaluated to both determine the reason for the abnormal reproductive function and to justify its treatment.

Keywords: Orchitis, epididymitis, dog, cat, *Brucella*

Introduction

In the male, loss of reproductive performance is sometimes first observed as failure of conception in the female to whom the male had been bred, or as a painful attempt during a natural breeding. This change in behavior may be the most apparent sign in an otherwise asymptomatic male. A male who historically exhibited normal breeding behavior may become unwilling to mount and gain intromission. An affected male may start scrotal licking to the extent of hair loss and scrotal dermatitis. Multiple etiological agents are possible for such behavior. Only after obtaining a good history, performing a thorough physical examination, and choosing the appropriate diagnostic tests can the underlying reason for a behavioral change, pregnancy failure in bred females, or purulent preputial discharge be determined. Subsequent therapy can then begin which may or may not maintain the male's potential to be a satisfactory breeder.

Orchitis and epididymitis can occur separately or in concert since each organ has close anatomical positioning and connection to a common excurrent duct system. Inflammation of one structure can lead to inflammatory response of the other and thus the term orchiepididymitis or epididymo-orchitis is used in veterinary literature.[1-4] This condition is rarely found or perhaps diagnosed among tom cats.

Anatomy

Body weight and breed dimensions should correlate with testicular weight, volume, width and, therefore, quantity of ejaculate. Each testicle is positioned obliquely within the scrotum of the stud dog and tom cat. The head of the epididymis is attached to the cranial aspect of the testis, the body lying on the dorsolateral surface, and the tail fixed to the caudal end by the ligament of the tail of the epididymis or former gubernaculum testis.[5] The epididymis continues as the ductus deferens within the spermatic cord, which also encloses the testicular artery and vein, pampiniform plexus, cremaster muscle, and lymphatics. The cord is wrapped on the outside by the visceral vaginal tunic and overlaid by the parietal vaginal tunic as it passes through the inguinal canal. Deep to these two tunics, the testis is also covered by a thick, white, fibrous, tightly adherent capsule called the tunica albuginea.

The body of the testis or testicular parenchyma is subdivided into compartments of seminiferous tubules by connective tissue septae. Spermatogenesis occurs within these seminiferous tubules. The sections of tubules feed sperm into a collection of spaces and ducts called the rete testis. A band of connective tissue called the mediastinum testis splits the testicle longitudinally and serves as the entry and exit point for testicular blood

vessels and lymphatics. From the rete testis, sperm cells then move into and through the head, body and tail of the epididymis where spermatozoal maturation and storage occur.

Descent of the testicles into the scrotum occurs in a similar pattern for the dog and tom cat. As the gubernaculum shortens, each testis passes through its respective inguinal canal and ring. When this passage occurs, the testes is already covered by the visceral tunic and then overlaid with the outer or superficial parietal tunic. Completion of this process usually occurs prior to birth in the normal male. However, male cats have been noted to have testicular movement back and forth through the inguinal canal after birth and prior to puberty.[6]

Each testis is partitioned into three sections. The interstitial portion contains the Leydig or interstitial cells, blood vessels and some support tissue. This section functions to provide hormones and nutrition to its respective area. The second or basal compartment is comprised of Sertoli cells and undifferentiated germ cells called spermatogonia. The third and innermost adluminal compartment houses the developing stages of spermatozoa and is separated from the basal section by the immunologically sensitive blood-testis barrier.

Etiology

Infectious

Bacteria enter the testis or epididymis through several routes: from an ascending source through the penile urethra, from descending flora within the adjacent bladder or prostate, and hematogenously. The primary bacterium associated with canine infertility is *Brucella canis,*[7] however other *Brucella* spp. (eg. *Brucella abortus)* have been cultured from the epididymis in the canine.[8] Additional bacteria are hemolytic *E. coli*, *Proteus*

vulgaris, *Staphylococcus* spp. as a natural skin contaminant, and *Mycoplasma* spp.[3-9] Also the canine distemper virus[10] with its cytoplasmic and intranuclear inclusions, granulomatous epididymitis from mycotic *Rhodotorula glutinis*,[11] *Blastomyces*,[12] human tuberculosis,[3] Rocky Mountain spotted fever,[4] and canine ehrlichiosis (Lyme disease) have been reported as potential causes. The distemper virus is spread venereally to susceptible bitches which acquire an endometritis.[3] *Mycoplasma canis* is a natural component of urogenital and respiratory mucosal surfaces in the dog and cat[13] and can cause purulent prostatitis and epididymitis. A bacterial urinary tract infection can incite orchiepididymitis since there is potential for retrograde or reverse urethral pressure through the ductus deferens. Bacterial infections can occur following injuries from pelvic fracture and surgical resection of ileum.[3] Unusual reports occur when certain stud dogs still sire litters despite heavy bacterial growth of *Klebsiella pneumoniae* and *Streptococcus* after antibiotic treatment for a preliminary diagnosis of epididymitis.[14]

A stray cat that was positive for feline immunodeficiency virus (FIV) and feline leukemia virus (FeLV) had chronic necrotic and fibrinous orchitis.[15] Tuberculosis was reported as the cause for a reproductive infection of tom cats in foreign countries.[16] *Brucella* spp.[7,17,18] and periorchitis from feline infectious peritonitis (FIP) were noted as well. Cats are resistant to infection with *Brucella canis*.[19]

Testicular injury from a bite wound or puncture results in injection of bacteria or viral particles into the animal, followed by entry into the venous blood and initiation of an inflammatory response. The cellular influx causes swelling and edema of the immediate area. White blood cells are attracted to the site and begin phagocytosis. The increased blood supply soon spreads a local infection systemically. If the animal

becomes septicemic with bacteria such as hemolytic *E. coli*, effects of endotoxemia on the kidney impair glomerular filtration rates. As endotoxemia ensues, the animal becomes febrile. A local thermal effect on the ipsilateral testis diminishes spermatogenesis and promotes agglutination of sperm which turns into oligospermia, anesthospermia, or azoospermia. As the condition becomes chronic, testicular atrophy results. Bacterial ascension from proximal prostatic secretions or a urinary tract infection can initiate orchitis and epididymitis**.**

Non-infectious

Non-infectious, atraumatic orchitis or epididimytis occurs with the entry of sterile urine through the ductus deferens into the testicle. Blunt force injury to the abdomen, such as happens from an animal being hit by a car, can cause urine to abnormally flow from a full bladder to the testicles.[3]

In humans, even temporary duct blockage secondary to prostatitis can lead to immune-mediated infertility.[20] The blood-testis barrier was described in detail by Amann in 1989.[21] The blood-testis barrier is comprised of tight junctions between adjacent Sertoli cells resting on the basement membrane. Any breakdown of this barrier, from trauma, infection or an inflammatory response, breaches the immunologically protected status of the testis. This affront allows the immune system to react to the antigenic insult. Sometimes the reaction produces a sperm granuloma at the puncture point. The attraction of plasma cells and lymphocytes into the testicle does produce a residue of immunoglobulins within the seminiferous tubules. The loss of testicular function by the tubules, Leydig cells and impaired vascular flow results in reduced sperm development. Clinically, immune-mediated infertility will be manifested by

oligospermia or azoospermia. Immune-mediated orchitis can be temporary or permanent.[20]

Similar to that observed in humans, immune-mediated disease has been associated with infertility in the dog. The incidence of lymphocytic orchitis in dogs is correlated with lymphocytic thyroiditis, a heritable trait in Beagles.[22,23] Males with this autoimmune disorder had lesions of tubular degeneration, atrophy and lymphocytic orchitis. Therefore, a history of reproductive failure in a stud dog that has been diagnosed with other endocrine diseases should prompt further analysis.

Pathophysiology

The blood supply to the testes and epididymides comes from the testicular artery and the artery of the ductus deferens, respectively. Both structures are influenced by hormones, both play an important role in spermatogenesis, and both tissues are altered by inflammation and antibody formation. Existing infections within the bladder or prostate gain entry into the ductus deferens by retrograde route. Inflammation from regional lymph nodes reaches the testis or epididymis by lymphatic drainage and then into the blood stream. Epididymal occlusion may appear secondary to an infection. The more proximal the blockage to the adjacent testis, the worse the damage to that testicle.[24]

Viral agents such as feline coronavirus are engulfed by and replicate in macrophages. These macrophages then travel to target organs and mix with lymphocytes to form a fibrin layer on the tunica albuginea (i.e., periorchitis), a finding consistent with FIP.[15] Since the parietal and vaginal tunics are continuations of the peritoneal cavity, seeding from a contaminated surgical site or traumatic injury can extend infections into these reproductive organs. Small abscesses within the lumen or testicular parenchyma

increase in size and extend fistulous tracts through the scrotal wall. Adhesions develop and block tubular patency. Gangrenous inflammation occurs within the unyielding tunics, which inhibit testicular mobility and increase scrotal temperature. Inflammation of the spermatic cord results in vascular compromise, tissue necrosis and eventually testicular atrophy.[3]

The interstitial compartment houses immune cells that maintain the testis in an immunologically secure location. Spermatogonia within this compartment are protected from an autoimmune attack. In addition to the blood-testis barrier, a multitude of factors establish this privileged immune status. Androgens influence the inhibition of proinflammatory cytokines.[25] Pro- and anti-inflammatory cytokines regulate testicular function relative to both spermatogenesis and steroidogenesis.[26] Pro-inflammatory cytokines such as interleukin and anti-inflammatory cytokines are linked to testicular development.[27] Therefore, an insult from infection or trauma induces production of these respective regulatory proteins and likewise disrupts testicular function. Timed progression of focal or diffuse inflammation in testicular tissue eventually results in loss of seminiferous tubules by replacement with connective tissue fibrosis. The clinical outcome of this sequence is manifested as infertility.

Another source of immune protection in the testis is the resident population of macrophages. Macrophages assert cytotoxic and phagocytic activity against infection through the cellular inflammatory response.[28] For example, *Brucella canis* embeds itself within macrophages that ultimately seek steroid-dependent organs such as the testis and epididymis.[7] These immune and inflammatory components combat and modify normal

internal testicular functions that correspond to owners' complaints of nonpregnant matings, scrotal swelling or pain.

Clinical signs

Historical information provided from the breeder client often supplies the first clue to the diagnosis of orchiepididimytis. Breeder clients are conscientious and notice conception failures. Owners or handlers observe stud dogs not wanting to ejaculate, or an enlarged scrotum while grooming for a show or field trial. The client may report previous urinary or reproductive tract infections, an increased licking of the scrotum, an obscure hindleg lameness, stiff or altered gait, purulent preputial discharge, or palpable unilateral testicular atrophy. All prior medical problems, treatments, hormonal adjuvants and products should be chronologically recorded for review.[29] As one source commented, a client's conclusion may be 'infertility in an otherwise asymptomatic dog'.[2] Additional signs include lethargy, anorexia, fever of unknown origin, inappetance, and vomition. Physical findings indicate a swollen scrotum and testicle or epididymis, primarily unilateral enlargement, but it can be bilateral. The testis is asymmetrical; the scrotum is reddened or hyperemic and hyperthermic. The dog licks the area causing a 'lick' granuloma or scrotal dermatitis and exhibits a level of discomfort and pain during palpation of the testicles. If the dog resists or is reluctant for digital examination, tranquilization might be necessary. The expression of pain can be acute, episodic and increase with intensity during a natural cover or manual collection. A decrease or loss of libido is evident. One older male had a progressive bilateral alopecia and feminization syndrome associated with acute and chronic epididymitis.[30]

Digital palpation may distinguish swelling of the head, body and/or tail of the epididymis and testes. The swollen area often has a soft, doughy texture in acute cases, and a firm, fibrotic consistency in chronic cases. A small puncture wound may be discovered with or without draining purulent exudate or concurrent orchitis. A spermatocoele, sperm granuloma, or hematoma within the tunic linings or in the vaginal cavity may be found. A serosanguineous or purulent discharge from the dog's preputial orifice may be present.

In summary, the typical clinical signs exhibited with prostatitis include a blood-tinged ejaculate, hematuria, and difficulty in defecation. Massage of the prostate per rectum may aid in detection of a purulent discharge from the urethra.[3] However, like prostatitis, orchioepididymitis can present with similar signs: altered hindlimb gait, lethargy or pain. To help differentiate prostatitis from orchioepididymitis, digital examination would reveal symmetrical or asymmetrical distension of the inflamed prostate.

Diagnosis

A thorough anamnesis should be recorded. Historical information should include details of prior reproductive attempts, onset and duration of signs and subtle changes in behavior or clinical signs. A chronologically ordered medical history is beneficial. Notations are made of diet, supplements, deworming program, schedule of vaccinations and past medications or surgical therapy. Potentially confounding effects of age, temperament and conformation on behavior or locomotion need to be noted. A physical examination, beginning with a TPR, should conclude with a digital evaluation per rectum of the prostate for size, symmetry, consistency, and pain response. Palpation of each

testis for size, shape and consistency can often discern a soft, acute onset condition from a firm, nodular chronic problem. Likewise, palpation of the epididimydes can aid in the identification of unilateral or bilateral testicular atrophy based upon the relative prominence of epididymal structures. If severe, acute pain is shown during examination, the primary differential diagnosis is torsion of the spermatic cord. If the scrotum itself is swollen, the examiner then must determine whether it is an intratesticular enlargement or an extratesticular disorder. Ultrasonography would assist in differentiation of the location and tissues involved.[31] A swollen scrotum should be distinguished from swollen testes.[32] Symmetrical scrotal enlargement occurs in orchitis, hydrocele, and torsion of the spermatic cord. Asymmetrical scrotal shape results from neoplasia, varicocele, epididymitis, abscess, or hematoma. An ultrasound-guided cystocentesis can be performed and urine submitted for cytology and culture.

In all cases of orchioepididymitis, a screening test for *Brucella canis* should be submitted with other samples for clinical pathology. A caution should be issued at that time to client and clinic regarding minimization of potential for human exposure to this zoonotic disease until the results are confirmed.

For the breeding soundness evaluation, testicular measurements with a caliper document any change in size or shape. The semen collection should be fractionated into separate samples for determination of sperm motility, morphology, concentration, cytology, culture and sensitivity, and pH. Sperm can also be placed in extender for computerized analysis. In azoospermic samples, an alkaline phosphatase value from seminal plasma of the second fraction would confirm epididymal patency or blockage. In cases of oligospermia or azoospermia, retrograde ejaculation of sperm into the urinary

bladder can be diagnosed by the presence of spermatozoa in urine obtained post-collection.[9,23] A stained cytology slide of the third fraction containing ample bacteria and greater than three to five neutrophils per high power field (100X) is diagnostic for prostatitis. Further imaging or follow-up evaluation is indicated. The semen evaluation yields a decreased number of sperm and an increased amount of abnormal morphology from increased agglutination. Bacterial epididymitis causes sperm acrosomal degeneration with subsequent loss of the plasma membrane. Affected sperm cells cannot penetrate the zona pellucida of the oocyte. Infertility results.[34]

Except during the active process of ejaculation and urination, seminal fluid normally moves from the ductus deferens into the bladder.[21] The prostatic fluid travels cranially into the bladder by normal urethra pressure.[35] Therefore, bacteria from the ductus can produce an ascending prostatic or urinary tract infection (UTI). Culture of a urine sample obtained by cystocentesis would identify the causative bacteria, including the opportunist, *Mycoplasma canis,* if the specimen is cultured on appropriate media.[13]

Careful manipulation of the scrotum and its contents is useful in the identification of a puncture wound or laceration, a draining tract, a change in skin thickness, altered sensitivity, differentiation of intratesticular or extratesticular origin, or the soft core of an abscess as one sequela of orchioepididymitis. Fibrosis and scrotal adhesions restrict testicular mobility, and with degeneration, the consistency changes from soft, edematous tissue to a firm, hard, smaller and fibrotic testis.

Ultrasonography (US) provides a rapid, non-invasive imaging tool beneficial for diagnosis, prognosis and a therapeutic plan.[31,36] With US, abnormal testicular architecture can be differentiated from the diffuse, hypoechoic pattern imaged in normal

testicular parenchyma.[37] Fluid in testicular cysts, a spermatocele, or an abscess can also be detected.[37] In humans, the most common diagnosis for a swollen, painful scrotum is epididimytis, and it is most commonly diagnosed on ultrasound examination when viewed as increased vascularity in a testis of otherwise normal architecture.[38] When a dog presents with an acute onset of scrotal pain and swelling, color flow or power Doppler US imaging can distinguish between the lack of arterial and venous perfusion caused by torsion of the spermatic cord and the hyperemic blood flow from an infectious agent.[39,40] Following an incident of testicular torsion, Doppler can visualize disrupted blood flow within the cord and altered echogenicity from testicular infarction. Doppler US is helpful in the localization of a lesion in either the tail of the epididymis, the spermatic cord or tunics, or the testis proper. Neoplasia, either Leydig or Sertoli cell tumors, may have hypoechoic and hyperechoic areas that are usually well-defined.[4] Testicular tumors have an irregular, lobulated contour versus orchitis with a moderately enlarged, oval shaped, smooth textured testicle.[4,39] Tumors of the epididymis are rare.[41] However, documentation in human cases is more widely reported.

One author suggested using fine-needle aspiration (FNA) from the caudae epididymides to collect diagnostic samples under sterile conditions from infertile males for cytology, histopathology, culture (aerobic, anaerobic, and *Mycoplasma*).[42] Fine-needle aspiration has been used to confirm obstructive lesion or maturation arrest for oligospermia and azoospermia.[43] Ultrasonography can select which patient would benefit from this procedure and avoid inherent risk or immunological consequences.[36] The accuracy and placement of the needle can be improved through ultrasound guidance as well. While a FNA sample for a cytology smear is presumptive for diseases such as

lymphocytic orchitis, a testicular slice biopsy will confirm the diagnosis. It may be advisable to weigh the short-term benefit versus the long-term risk since adverse effects may develop later. Focal hemorrhage, interstitial fibrosis and tubular atrophy can occur at a biopsy site, but adjacent tissue and semen quality may remain within normal limits.[44,45] With either method, there is risk for sperm granuloma formation or antisperm antibody production as a result of 'foreign' protein leaking from the point of surgical extraction through tunics, cavity, parenchyma and blood-testis barrier. One would obviously not perform a testicular biopsy or risk anesthesia in the presence of inflammation.[2]

Prostatic disease can be verified by anamnesis, digital examination, culture and sensitivity, cytology of the third fraction or prostatic wash, ultrasonography, and ultrasound-guided aspirate or biopsy.

If an orchidectomy of a diseased testis is performed, samples obtained at surgery should be cultured for aerobic bacteria, *Mycoplasma spp*. and fungi, and tissues should be sent for histopathology.

Pathology

Epididymitis is one of the more common inflammatory diseases of the reproductive tract. The usual route of entry for pathogens into the epididymis is via an ascending or retrograde mechanism. Trauma to the scrotum combined with endotoxin-producing bacteria such *E. coli* results in septicemia. The epididymis lacks a natural local immune system. Lymphocytes or plasma cells are recruited after the initial insult from infection occurs. Edema progresses to an abscess or sperm granuloma formation. Fibrous bands appear between the tunics, which are extensions of the peritoneal cavity,[3]

and the epididymis. In time, these adhesions lead to testicular atrophy and firm, nodular ducts. Scrotal swelling is caused by the accumulation of fibrinopurulent exudate in the tunic cavity. This cellular response includes lymphocytes, neutrophils and macrophages. Extensive luminal fibrosis and spermatocele can occlude the ducts even after successful treatment and decreased signs of inflammation. Disruption of the blood-testis barrier initiates an immune-mediated reaction and results in lymphocytic infiltration. Inflammation of the seminiferous tubules causes degeneration. The inflammatory response within the testicular parenchyma is suppurative, with abscessation and possible fistula formation to the exterior scrotum.[17] Lesions in a cat with orchitis were consistent with vasculitis, increased fibrinogen and infarction from simultaneous viral infections.[15] Multifocal necrotic granulomatous inflammation of the pleura, lung, eye and lip were found.

Treatment

Similar treatment protocols are suggested for both orchitis and/or epididymitis. Once the cause is known, an appropriate regimen can be instituted. Antimicrobial therapy is started based upon results of the culture and sensitivity. A minimum duration of treatment is three to four weeks. Concurrent sexual rest is implied. Another culture should be obtained one to two weeks after the antibiotic has been discontinued. Resolution of epididymitis requires the correct antimicrobial choice, dosage and length of administration. Too often, failure of client compliance alters the outcome when treatment is stopped prematurely. Within days, owners may supplement with their choice of medication in addition to or in place of the one prescribed. Immunosuppressive drugs have been used on a short-term basis to treat immune-mediated disease. However,

continued use of immuosuppressive agents may adversely affect spermatogenesis and lead to infertility.

Owners should be apprised of possible outcomes and expense. Serial monitoring can document changes in semen parameters and allow for alteration of therapy if necessary. Brucellosis management requires immediate quarantine and testing of dogs having had contact with the confirmed case. Positive dogs are removed from the premises and are either euthanized or retested until two negative results have been obtained. Antibiotics will decrease bacteremic signs and neutering does eliminate the target organs, but the chance for relapse is probable. Since brucellosis is zoonotic, exposure to pregnant women, children and immunosuppressed people, in particular, should be avoided. Treatment for unilateral epididymitis offers a better recovery rate; bilateral infection has a poorer prognosis for a return to satisfactory reproductive performance.[23]

The treatment of choice may be surgical excision of the infected tissue. Relief is immediate and the potential for fertility may be salvaged. Hemicastration or orchidectomy of the diseased testis not only removes the source of inflammation or benign neoplasia but also decreases the potential for thermal insult on the unaffected, contralateral testis. Following unilateral orchidectomy, an immediate reduction in sperm output was followed by increased spermatogenesis and compensatory hypertrophy by the remaining testis.[46] If the preliminary histopathology confirms malignancy or an irreversible condition, complete castration may be recommended for the animal's welfare. If the cause can be reversed, then the male may recoup fertility. If the primary problem is torsion of the spermatic cord, an infectious disease or immune-mediated

disorder which resulted in secondary damage, any resolution of pre-existing orchioepididymitis may be irrelevant. The progressive fibrosis within the tubular compartments would gradually prevent spermatogenesis and steroidogenesis. An epididymotomy has been suggested as a treatment for bacterial epididymitis in men.[47]

Prevention

To control exposure and transmission of disease, screen new arrivals to a kennel, test animals at least annually for *Brucella canis*, disinfect facilities regularly especially the whelping environment, reduce fomite contamination during breeding, and employ artificial insemination when possible. Judicious use of antibiotics in the female during her estrous cycle and breeding is important to avoid bacterial resistance and birth defects. Good management includes periodic monitoring for urinary tract infections and early detection of subfertility or infertility, followed by an accurate diagnosis and prompt treatment.

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