Session 2:

True Incontinence or Detrusor Urethral Dyssynergia in the Male Dog: Are we mis-diagnosing them?

Introduction

For the veterinary practitioner, the presentation of a male dog with urinary incontinence can be perplexing. The first inclination may be to use phenylpropanolamine to address urethral sphincter mechanism incompetence (USMI). However, response to treatment for USMI has been frustratingly poor and this may be due to misdiagnosis of a disorder of voiding with overflow incontinence rather than a disorder of storage as in classic USMI. Male dogs presenting for incontinence must be evaluated through history, physical examination, and observation of voiding in order to determine if outlet obstruction is the primary problem.

Functional urethral or bladder outlet obstruction has been recognized in people from a variety of causes including benign prostatic hyperplasia, pediatric voiding dysfunction, and detrusor hypocontractility, as well as a primary functional urethral obstruction in women. These disorders are treated with a variety of alpha-antagonists, PDE-5 inhibitors, skeletal muscle relaxants and biofeedback systems. Since the majority of veterinary patients with functional obstruction are males, and often neutered, direct extrapolation of underlying pathophysiology and treatment effect cannot be made from human medicine. This has complicated our ability to predict the efficacy or treatment response to various therapies in our patients and has led to challenges in diagnosis and management.

In veterinary patients, functional urethral obstruction, or detrusor-urethral dyssynergy (DUD), is suspected to arise from an abnormality in the reflex arc which allows the urethral sphincter to relax at the initiation of detrusor contraction and urination. The lesion is thought to be in the reticulospinal tract, Onuf's nucleus, or the caudal mesenteric ganglion, and it is possible that the lesion involves the loss of inhibitory signals to the pudendal and hypogastric nerves[1]. It is unknown if there is a more local lesion to the nerves, the neuromuscular junction, or the smooth or striated urethral sphincters[2] or if there is a dynamic outflow obstruction at the bladder neck, as has been described in people[3]. Unlike the 'upper motor neuron bladder' seen in animals with thoracolumbar intervertebral disc disease and other spinal cord lesions, these animals typically have an otherwise normal neurologic examination and have the ability to consciously initiate a detrusor contraction.

Diagnosis

The disorder affects primarily middle-aged, large and giant breed male dogs, although female dogs and cats can be affected. One case series of 22 dogs reported a mean age of 4.9 years[4]. Clinical signs are similar to those of mechanical obstruction. The animal often postures to urinate and is able to produce a urine stream that quickly becomes attenuated or stops completely. The animal may continue to posture to urinate or make several attempts without fully emptying the bladder. The presence of large amounts of residual urine typically leads to overflow incontinence and may be mistaken for USMI. This leakage can occur because the hypertonicity of the involved sphincter is likely dynamic and is triggered by the act of voiding. In

chronic cases, bladder over-distension and subsequent dertrusor hypofunction may develop. Unlike animals with mechanical obstruction, these dogs are typically easy to catheterize.

Presumptive diagnosis of DUD is often made by observing the dog urinate with a typical interrupted pattern, documentation of a large residual urine volume, easy passage of a urinary catheter, and ruling out of a mechanical obstruction. Normal residual urine volumes in 48 normal dogs were reported to be 0.1 – 3.4 ml/kg body weight with a mean of 0.2 ml/kg[5]. The author uses < 1.0 ml/kg as a general guideline. Ultrasonography is recommended to assess the ureters and renal pelves for dilation secondary to chronic obstruction and ureterorenal reflux of urine. Additional diagnostics, including contrast urethrography, urethroscopy may be necessary to verify the diagnosis and rule out anatomic abnormalities in patients who fail to respond to medical therapy.

In people, voiding videofloroscopy and measurement of bladder pressures with urine flow rates are considered standard diagnostic testing for bladder outlet obstruction. This can assist in determining if the obstruction is located at the bladder neck, internal, or external urethral sphincter. Due to the need for sedation in our patients when performing urodynamic studies, the utility of these studies has not been evaluated in dogs with signs of functional obstruction. In addition, the dynamic nature of this obstruction may lead to normal cystourethrography and normal urethral pressure profiles on urodynamic evaluation unless the animal is actively voiding during the study. Contrast urethrography may be normal or reveal areas of narrowing of the urethra (urethrospasm). Further investigation of the use of EMG studies and uroflow parameters needs to be performed to determine the feasibility and practicality of these measures in veterinary patients.

Treatment

At this time, very few studies have been performed evaluating the efficacy of any treatment for DUD in dogs. Treatment of the dyssynergic urethral sphincter mechanism (since we are unsure if it is the smooth muscle or striated muscle component that is a fault) generally consists of α-adrenergic blockade. Prazosin, an α_1-specific antagonist with demonstrated effects on both the internal and external urethral sphincter[6] and tamsulosin, which is specific for the α_{1A} subtype found in the internal urethral sphincter, have been successful in these dogs. Alpha blockade carries with it the side effect of systemic hypotension, particularly with the less subtype specific prazosin. Based on this risk, as well as the convenience of once a day vs. three times a day dosing, and a large safety margin, the author has begun to use tamsulosin as first-line treatment in these patients. Many dogs will require additional therapy to address striated muscle involvement. Benzodiazepines, such as diazepam, or other skeletal muscle relaxants, including acepromazine and methocarbemol, may be more effective if the external urethral sphincter is involved. Diazapam is typically administered 30 minutes before voiding to decrease external urethral sphincter pressure. Dantrolene and baclofen have been used in the past as skeletal muscle relaxants; however, the potential for adverse effects has decreased their use in veterinary patients[6,7]. In severe and refractory cases, intermittent sterile catheterization by the owner at home may be necessary. Medical therapy of associated bladder atony should only be started after adequate relief of the functional urethral obstruction has been reached (**Table 1**).

Close monitoring of these patients for residual urine volume and UTI is needed to assess efficacy of treatment and prevent complications.

Anecdotally, some dogs have shown worsening of signs or relapse of previous response when stressed. The relationship of stress and voiding complications has not been investigated in these dogs, and may provide some assistance for sever cases.For these patients, the addition of an anxiolytic may be necessary to maintain normal voiding.

Prognosis for recovery of normal voiding is good, based on the limited available information, but most dogs will require life-long therapy for DUD. Attempts to taper medications to the lowest effective dose may be hampered by relapse of clinical signs after months of normal voiding[4]. Prognosis appears to be worse in patients with bladder atony or UTI secondary to urine retention. Anecdotally, urethral stenting may improve clinical signs, however, this is considered a salvage procedure with several potential complications, and indicated only in the most refractory of cases.

References

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Table 1: Drugs frequently used to treat disorders of emptying[8].

Drug	Mechanism	Dose	Side Effects/Caution
Prazosin	α_1-antagonism, smooth muscle relaxant	1 mg/animal < 15 kg 2 mg/animal > 15 kg q 8 – 12 h PO	Hypotension, weakness, syncope, GI upset/ renal disease, cardiac disease
Tamsulosin*	α_{1A}-antagonism, smooth muscle relaxant	0.01-0.2 mg/kg PO q 24 h	Hypotension
Phenoxybenzamine	Non-specific α-antagonism, smooth muscle relaxant	Dog: 0.25 mg/kg q 8 – 12 h Cat: 1.25 – 7.5 mg/cat q 8 – 12 h PO	Hypotension, tachycardia, miosis/ first dose hypotension
Acepromazine	Non-specific α-antagonism Skeletal muscle relaxant Anxiolytic	0.5-2.2 mg/kg q 6- 8 h PO	Sedation, hypotension
Diazepam	Skeletal muscle relaxant Anxiolytic	Dog: 0.5 – 2 mg/kg q 8 h PO or 30 min prior to voiding	Sedation, ataxia/ liver dysfunction Do not use oral in cats
Methocarbamol	Skeletal muscle relaxant	22-44 mg/kg q 8 h PO	CNS sedation, weakness, hypersalivation
Baclofen*	Skeletal muscle relaxant	Dog: 1-2 mg/kg q 8 h PO	Weakness, GI upset/Do not use in cats

Dantrolene	Skeletal muscle relaxant	Dog: 1-5 mg/kg q 8 h PO Cat: 1-2 mg/kg q 8 h PO	Weakness/ liver disease
Bethanechol	Parasympathomimmetic	Dog: 2.5-15 mg/dog q 8 h PO Cat: 1.25-5 mg/cat q 8 h PO	Diarrhea/GI or urethral obstruction
Cisapride	Prokinetic	Dog:0.1-0.5 mg/kg q 8 – 12 h PO Cat: 2.5-5 mg/cat q 8 – 12 h PO	Ataxia, GI upset/ GI obstruction

*From Lane IF, Westropp JL, Urinary incontinence and micturition disorders: pharmacologic management, *Kirk's Current Veterinary Therapy*, 14th ed., Elsevier, St. Louis, MO, 2009, pp 955-959.