Hydraulic Artificial Urethral Sphincter for Treatment of Urethral Sphincter Mechanism Incompetence

A Case Report

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Introduction

Urinary incontinence can be an incredibly frustrating problem for pet owners and may ultimately hinder the unique human-animal bond. Unresolved urinary incontinence often leads to relinquishment or unnecessary euthanasia of otherwise healthy, happy pets. Therefore, it is imperative to correctly identify the specific cause of the urinary incontinence to properly treat the patient.

Urinary incontinence is defined by the involuntary leakage of urine during the storage phase. Urinary incontinence is often broken down into two major categories, but the most common etiology is urethral sphincter mechanism incompetence (USMI). Urethral sphincter mechanism incompetence occurs in approximately 20% of female dogs after ovariohysterectomy but may surprisingly also occur in male dogs [1]. Due to its association in ovariohysterectomized female patients, it is often called spay-induced incontinence. At this time there are several theories behind this frustrating disorder, but the exact mechanism is unclear.

There are several pharmaceutical treatments available such as alpha adrenergic antagonists and estrogens that provide relief in approximately 75-90% of dogs [1]. However, despite a relatively high success rate with medical management, 27% of patients are refractory to treatment [2]. With failure to traditional medical therapies, pet owners are desperate for resolution of this long-term condition. Fortunately, through the advent of newer treatments such as the hydraulic artificial urinary sphincter, urinary continence is a reality for many patients.

History and Presentation

On May 4, 2016, Brin, a 9-year-old, spayed female Mountain Cur, was presented to the Small Animal Internal Medicine Service on referral for a 3-year history of leaking urine and urinating in her sleep that began after her ovariohysterectomy. Prior to presentation to MSU-

CVM, the referring veterinarian diagnosed Brin with urinary incontinence and initiated single-agent medical therapy including phenylpropanolamine, diethylstilbestrol, and estriol, with no improvement in clinical signs.

Upon initial presentation to the Internal Medicine service, Brin was bright, alert, and responsive. Her mucus membranes were pink and moist with a capillary refill time of less than 2 seconds. She had a normal body condition score of 5/9, weighing 22.5 kg. Her heart rate was 132 beats per minute and her respiratory rate was 28 breaths per minute, with normal bronchovesicular sounds. Her temperature was normal at 101.4ºF. A minimum database of a complete blood count, chemistry, and urinalysis were performed. The complete blood count and chemistry were unremarkable. The urinalysis revealed no significant findings and a normal specific gravity of 1.030. A urine culture, performed to rule out a potential urinary tract infection, revealed no growth of bacteria. Abdominal radiographs were performed which revealed no abnormities and a normally positioned bladder.

At this time it was suspected that Brin had urethral sphincter mechanism incompetence, and combination medical therapy was implemented using phenylpropanolamine HCL (Proin 50 mg PO q12 hours) and estriol (Incurin1 mg PO q24 hours) to create a synergistic effect by increasing alpha receptors and stimulation of smooth muscle at the same time. This combination therapy had not been administered prior to this trial. At the time of discharge, surgical options were discussed in the event that Brin was refractory to medical treatment within 1 month.

On July 6, 2017, Brin was presented to the MSU-CVM Small Animal Surgery Service for urinary incontinence that was nonresponsive to combination medical management. A repeat complete blood count, chemistry, urinalysis, and culture were repeated which revealed no significant findings. Brin was then anesthetized, and a retrograde vaginocystourethrogram and

urethrocystoscopy were performed. The vaginal vault, urethra, and bladder all appeared to be within normal limits, ruling out any structural abnormalities such as ectopic ureters, pelvic bladder, vestibulovaginal abnormalities, or other disorders. Through exclusion, urethral sphincter mechanism incompetence was diagnosed. Surgical options were discussed with the owners, and placement of an artificial urethral sphincter was ultimately recommended by the surgical service for the best resolution for Brin's clinical signs. The following day, on July 7, 2016, the artificial urethral sphincter was implanted. The urethra was dissected circumferentially, and the AUS was placed around the urethra 1 cm caudal to the neck of the bladder and was sutured in place. The tubing was tunneled through the body wall and the subcutaneous port was secured to the fascia of the body wall at the level of the inguinal skin fold. The cuff was left uninflated for 6 weeks after surgery to allow for urethral healing and revascularization. Brin was discharged to go home on July 8th 2017.

Pathophysiology

To understand urethral sphincter mechanism incontinence, it is important to review the physiology of the lower urinary tract system. The basic musculature of the lower urinary tract includes the detrusor muscle of the urinary bladder, the smooth muscle of the internal urethral sphincter, and the skeletal muscle of the external urethral sphincter. Urine retention and micturition is dependent on the musculature receiving specific signals from the nervous system instructing specific muscles to contract or relax [4].

Urine retention is controlled by the sympathetic nervous system through the hypogastric nerve. The hypogastric nerve provides stimulation of the ß-receptors in the bladder allowing it to fill and acts as a reservoir. Concurrently, the hypogastric nerve also provides stimulation of the α-receptors in the trigone and urethra causing constriction of the internal sphincter, acting as a

closed valve. The pudendal nerve supplies somatic input to the external sphincter causing contraction resulting in voluntary storage. Micturition is under parasympathetic nervous system control through the pelvic nerve. Voiding occurs during contraction of the detrusor muscle and concurrent sphincter relaxation [4].

Urinary incontinence is defined by the involuntary leakage of urine during the storage phase, and is categorized into neurogenic and non-neurogenic etiologies. Neurogenic causes include lower-motor neuron, upper motor neuron, detrusor-urethral dyssynergy, or primary bladder atony. These causes may be ruled out with a thorough neurological examination and work-up. Non-neurogenic causes can be further divided into functional and anatomic etiologies. Functional causes may include sphincter mechanism incompetence, secondary bladder atony, or detrusor instability. Anatomic causes may include ectopic ureters, vaginal pooling secondary to vestibulovaginal abnormalities (vaginal stricture, persistent paramesonephric remnant, vestibulovaginal stenosis, vaginal septum, or dual vagina), short urethra syndrome, or pelvic bladder. Another type of incontinence is overflow incontinence, in which the urethral sphincter mechanism is normal but urine is forced out of the bladder because of increased pressure in the bladder associated with over filling. Urethral obstruction, functional (reflex dyssynergia) or structural causes may cause overflow incontinence [4].

Despite the lengthy list of disorders causing urinary incontinence, urethral sphincter mechanism incompetence represents an overwhelming number of cases. USMI represents 60% of all cases of acquired urinary incontinence [4]. The pathophysiology of USMI is not fully understood but it is thought to be multifactorial.

Estrogen plays one of the most essential roles affecting urethral tone by exerting a permissive effect on the alpha receptors in the internal urethral sphincter [5]. Estrogen also has a

trophic effect on periurethral tissue and vasculature vital for urinary continence [7]. It is said that there is a likelihood of reduced urethral tone in select female dogs following an ovariohysterectomy, due to decreased levels of estrogen. However, some studies demonstrate estrogen measurements to be similar between spayed dogs with urinary incontinence and to those that are intact [4]. A majority of spayed females remain continent, so therefore it is unclear why a select few develop USMI. In addition, 35% of dogs with spay-induced urinary incontinence do not respond to just estrogen supplementation, proving USMI to be a complex disease [5]. Alternatively, it is theorized that decrease testosterone may influence USMI in male neutered dogs.

A second theory involves structural causes including altered collagen and smooth muscle and intrapelvic bladder due to ovariohysterectomy surgery. In spayed females the bladder may be positioned more caudally lessening the intrabdominal pressures on the urethra that helps maintain urethral closure. In addition, there is decreased urethral pressure theorized due to the altered smooth muscle post-ovariohysterectomy, causing decrease in urethral closure [7].

Urethral sphincter mechanism incompetence has also been reported in patients with concurrent ectopic ureters. Patients are incidentally diagnosed with USMI when the urinary continence persists despite surgical correction of the ectopic ureters [8]. This correlation may suggest that there is a congenital factor associated with USMI.

Risk factors may include a short urethra, obesity, and being a medium to large breed dog. Predisposed breeds include Doberman pinschers, Old English sheepdogs, Springer Spaniels, Boxers, Rottweilers, Weimaraners, Giant schnauzers, and Irish setters [4]. There are conflicted data related to the age of ovariohysterectomy. Some suggest spaying dogs before 3 months of age may cause an increase in urinary incontinence [9].

Diagnostic Approach/Considerations

For animals exhibiting inappropriate urination, it is important to distinguish between urinary incontinence, polyuria, pollakuria, or behavioral issues. A detailed history is an important first step and allows the veterinarian to determine whether the patient is truly incontinent. It is vital for owners to observe the timing of the accidents, volume of urine, evidence of stranguria, and events surrounding the urination [5]. USMI patients have a history of involuntarily leaking urine and of leaving urine puddles after sleeping. This is due to the increase in abdominal pressure when the dog is lying on its side and increase in parasympathetic activity during sleep. An important aspect of USMI is the dog's ability to have episodes of normal voiding.

Physical examination is usually normal in patients with urethral sphincter mechanism incompetence, but sometimes perineal urine staining may be observed. A full physical exam includes a rectal examination, visualizing urination, observing vulva positioning, and a digital vestibulovaginal exam [6]. A complete neurological exam should be conducted to rule out neurogenic incontinence. It is important to complete a minimum data base of a complete blood count and biochemistry profile to rule out any other health concerns. In cases of USMI, the CBC and chemistry are normal systemic disease that may be causing polyuria or worsening signs must be ruled out. A urinalysis and culture may reveal evidence of a secondary urinary tract infection.

Imaging including abdominal radiographs, abdominal ultrasound, and combination urethrocystoscopy and retrograde vaginocystourethrogram under fluoroscopy are recommended to rule out any other functional or structural causes. A retrograde vaginocystourethrogram may be performed preoperatively if intraoperative fluoroscopy is unavailable. It is important to check for other abnormalities including: prostate size in males, bladder location, lumbosacral region tumor, fractures, hydroureters/hydronephrosis, and masses [8].

The only definitive method for diagnosing urethral sphincter mechanism incompetence is with urethral pressure profilometry. To perform a urethral pressure profile a specialized catheter is inserted within the bladder and urethra and pressures are measured [5]. USMI is diagnosed by a low maximal urethral closure pressure and decreased functional profile length [9]. However, due to its false values and little indication clinically it has fallen out of favor. In addition, the ability to perform the urethral pressure profile is in limited specialty centers and academic institution.

Treatment and Management

Medical treatment should be recommended as the first line of therapy for USMI, as it has a high efficacy and is typically easy to implement. The goal of medical treatment is to improve urethral resistance and bladder holding capacity.

The most common class of drugs used for urinary incontinence is the alpha agonist sympathomimetics. The sympathetic nervous system involves mediators of smooth muscle contraction and relaxation in a variety of muscles [7]. Stimulation in the smooth muscle of the urethra and bladder neck leads to increased urethral closure pressures. Phenylproanolamine (PPA), is a common alpha agonist that increases internal urethral sphincter tone. This treatment is approximately 74-90% effective in females with USMI [9]. Side effects may include inappetence, gastrointestinal upset, lethargy, or restlessness. Hypertension is the most common adverse effect. Therefore, systolic blood pressure on any patient should be measured prior to treatment and 1-2 weeks after starting therapy.

A second option for medical management is estrogen available as estriol and synthetic nonsteroidal estrogen (diethylstibersterol - DES). Estrogen is used to strengthen pelvic and periurethral tissues as it enhances collagen strength and increases the number and sensitivity of

alpha receptors [7]. Estriol (Incurin) is the only commercially available FDA approved estrogen for the treatment of urinary incontinence. This line of therapy should not use in male dogs because of possible prostatic squamous metaplasia [7]. Diethylstilbesterol (DES), a synthetic estrogen, increases sensitivity of internal urethral sphincter to catecholamines. It is effective in 40-65% in female dogs [9]. Excessive doses may be associated with bone marrow suppression, and therefore, CBCs are recommended to monitor values [7].

Testosterone cypionate may be used in castrated male dogs with USMI, but the mechanism of action and efficiency is unclear. It is theorized that testosterone acts on the prostate which sits at neck of the bladder and incorporates the sphincter [7].

Gonadotropin releasing hormone (GnRH) analog can be used in place of DES but is less effective than PPA. In spayed dogs, the removal of the negative feedback of estrogen system leads to increases in follicle stimulating hormone and luteinzing hormone [7]. This may decrease bladder function or have a negative impact on the urethral closure pressure.

Bulking agents, such as collagen can be injected into the periurethral submucosa through cystoscopy. The bulking agents are used to increase the stretch in the sphincter muscle, leading to an increased closure pressure in urethra [7]. It may also narrow the diameter of the urethral lumen allowing the urinary sphincter to close more effectively [7]. However, the collagen injections are effective for short term, and repeated injections are needed to maintain satisfactory results. Collagen injections have a 68% success rate with a mean duration of full continence of 17 months [9]. However, there is an 80-90% success rate when used in conjunction with medical management [9].

There is an array of surgical options including colposuspension, cystourethropexy, and transpelvic slings in order to increase pressure on the urethra by compression or by advancement of the bladder and proximal urethra into the abdomen. However, with these types of surgical therapies recurrence of incontinent does occur over time.

An adjustable hydraulic urethral sphincter can be placed which supplies a more permanent solution. The artificial urethral sphincter provides more than 2 years of urinary continence in one study using 4 dogs with USMI [6]. It is an inflatable silicone hydraulic vascular occluder that is placed around the urethra that provides urethral resistance, with the port placed subcutaneously for saline administration to allow inflation of the sphincter. In one study 39% of patients become incontinence even without inflating the cuff [9].

To begin surgery, a caudal celiotomy incision is performed to gain access to the abdominal cavity. One to two stay sutures are placed in the bladder in order to properly retract the bladder for better visualization of the proximal urethra. A portion of the urethra equal to the width of the AUS cuff is dissected from the surrounding soft tissue, 1 cm caudal to the neck of the bladder. In the female dog, the AUS is placed 1 cm caudal to the neck of the bladder and is secured with suture through the cuff's eyelets. In the male dog the AUS may be placed 1 cm caudal to the prostate due to the thickness of the urethra at this portion. An alternative placement location in the male dog is between the neck of the bladder and prostrate. Before applying the AUS, the urethral circumference is measured using a piece of suture. Then a silicone AUS of equal or larger diameter to the pelvic urethra is selected. The AUS is primed with sterile saline and tested for leaks. The total filling volume of the cuff is recorded before emptying the AUS. The primed AUS cuff is placed around the pelvic urethra. The tubing is then tunneled through the abdominal wall. It is then connected to the subcutaneous infusion port that is anchored to the

fascia of the abdominal wall just cranial to the flank fold. At this time excess tubing is trimmed. The connection of the tubing to the male adaptor on the port is secured with a silicone boot after flushing all air from the port [6].

In dogs with persistent urinary continence post AUS placement, 0.1-0.2 ml of sterile saline (or an amount equal to 10% of the total fill volume) can be injected into the subcutaneous port using a Huber needle and a 1 ml syringe [6]. After inflation of the cuff, it is important to observe the animal urinating to ensure a patent urethra. AUS inflation may be repeated every 2 weeks to improve signs of incontinence. In one study 15 of the 27 dogs required inflation of the cuff with an average of 0.4 ml [6].

Case Outcome

On August 24, 2016, Brin returned to the surgery service for her 6-week recheck post surgery. The owner expressed that they were quite satisfied with the results, but reported that Brin did dribble urine in her sleep. At this time the subcutaneous vascular access port was aspectically prepared and 0.1 ml of sterile saline was injected into the AUS. Brin was then taken outside to urinate and the bladder was empty on ultrasound. On October 27, 2016, Brin returned to the surgery service for continuing to urinate in her sleep. Therefore, another 0.1 ml of saline was added to the device, resulting in a total volume of 0.2 ml. On May 11, 2017, Brin presented for a third time for continuing to urinate in her sleep, and 0.1 ml of sterile saline was added**.** Brin was brought outside to urinate but struggled to produce a normal urine stream. Brin was able to urinate once a small amount of saline was removed, making the final total volume of 0.22 ml.

Complications may occur with AUS placement including worsening of incontinence, stranguria, adhesions, stricture formation, implant infection, and acute postoperative obstruction

caused by urethral kinking. It is judicious to wait at least 2 weeks between performing an urethrocystocopy and placing an artificial sphincter to decrease the risk of stricture formation. In one study, urethral obstruction occurred in 2 female dogs 5 and 9 months after surgery and removal of the AUS device was recommended [6]. Necropsies were performed, and adhesions were noted between the small intestines and tubing in 1 dog. One possible cause of urethral obstruction is inappropriately selecting a small AUS size. Patients with pre-existing conditions such as hydronephrosis, hydroureters, recurrent UTIs and ectopic ureters may decrease surgical success.

On average, patients require 3 inflations of the AUS device to achieve maximum effectiveness [9]. However, 39% of female dogs with primary USMI do not require any inflation. In one study over 2 ½ years there was 89% improvement reported in greater than 75% of female patients with USMI [9]. With its high success rate of resolution of clinical signs, hydraulic urethral sphincters make an excellent treatment choice for patients refractory to medical management.

Approximately 2 years after Brin's artificial urethral sphincter placement, no known complications have been reported. A total of 0.22 ml of saline was injected into the cuff over three total visits achieving maximum results without complications. The owner expressed that they were quite satisfied with Brin's improvement.

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