There's Some Leaking in This House

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Introduction:

In the urogenital system, the ureters carry urine from the kidneys to the trigone of the bladder. The bladder then stores the urine until it is voluntarily voided. Ectopic ureters are a congenital malformation that results in one, or both, of the ureteral openings not being at the trigone of the bladder. This results in urinary incontinence. Though they are uncommon, ectopic ureters, or EU, are the most frequent cause of urinary incontinence in young dogs[2]. Females are more commonly affected than males, and usually diagnosed at a younger age[6]. Often there are multiple internal urinary anatomical abnormalities along with EU. High risk breeds include Golden retriever, Labrador retriever, Siberian husky, Newfoundland, and English bulldog[2]. This condition is heritable and those patients that are diagnosed should not be used to breed. Clinical signs vary with different severities of urinary incontinence, nocturia, and urinary tract infections. Novel surgical techniques and adjunctive medical management have improved the prognosis for dogs with EU. EU should always be considered as a differential in any incontinent dog with an unknown history[2].

History and Presentation:

Lulu, a 1-year old female spayed English bulldog, presented to MSU-CVM Internal Medicine Department on 7/7/2020 for a history of frequent urination, recurrent urinary tract infections, and a recessed vulva. Lulu was originally surrendered due to incontinence and had been adopted her owners approximately 6 months prior to her initial visit at MSU. Lulu's owners stated that Lulu had always scooted at home and urinated when excited. She had never strained to urinate, never had blood in her urine, or had accidents in the house. Lulu's owner noted that in the mornings Lulu's kennel sometimes smelt of urine, however there was never any evidence of urine in the kennel. Approximately 3-4 weeks prior to Lulu's initial visit at MSU-CVM, Lulu was having white discharge that was malodorous around her vulva. Lulu previously had been treated for UTI's at her primary veterinarian with antibiotics for extended amounts of time, initially getting better only for the scooting to return after discontinuing treatment. She had previously been diagnosed with a recessed vulva by her primary veterinarian. On 5/20/2020 a free catch culture and

sensitivity at Lulu's rDVM yielded a Methicillin-Resistant Staphylococcus Pseudintermedius (MRSP) infection. On 6/15/2020 a cystocentesis was preformed at the same time as an abdominal ultrasound. Abdominal ultrasound had no significant findings with no evidence of congenital defects noted. The cystocentesis was sent out for a repeat culture and sensitivity. This yielded no growth in 48 hours. At this time, it was suspected that the MRSP infection was colonized in the vaginal tract. Lulu was referred to MSU-CVM for further workup for her recurring UTIs, scooting, and vulvar discharge.

Upon initial presentation, Lulu was bright, alert, and responsive. She squatted to urinate various times on the way into the building, leaving multiple urine spots. Lulu weighed 15.6 kg and had a body condition score of 5/9. She appeared hydrated with pink, moist mucous membranes and a capillary refill time of 2 seconds. She had increased respiratory effort with stertor and a panting respiration rate. She had a heart rate of 126 beats per minute and a temperature of 103.9 F. Her increased temperature as most likely due to excitement or due to infection. There was a clear discharge on her vulva and her vulva was recessed. The rest of the physical exam was within normal limits.

Diagnostics:

For initial work-up, a CBC and chemistry panel were sent out. There were no significant findings on the CBC besides a mild leukocytosis of 15.97 10^3/ul (5.00-14.20), most likely due to UTI or chronic vaginitis. Chemistry revealed an increased BUN of 33mg/dl (8-24) which could be due to kidney damage, kidney disease, a kidney anomaly, or due to the patient's diet. Since an abdominal ultrasound had just been completed at Lulu's primary veterinarian with no significant findings, it was not repeated at this time.

On 7/7/2020 under general anesthesia, a vaginoscopy and urethrocystoscopy were performed for further diagnostics on Lulu. Urethrocystoscopy revealed a left ectopic ureter, with a normally positioned right ureter. The left ectopic ureter was approximately 1-1.5cm distal to the right ureteral opening. Contrast-

enhanced computed tomography has also been used as well to diagnose ectopic ureters. Retrograde cystography, pneumocystography, and vaginoscopy may also help correctly define ectopic ureter morphology[5].

Since Lulu's case had been referred from her primary veterinarian, the complete work up was not done at MSU. With diagnosing ectopic ureters, abdominal radiographs should ideally be taken. This allows assessment of the size and shape of the kidneys, bladder, and prostate (if male). Bloodwork should be completed to assess renal function, as well as a urinalysis with culture. The majority of patients with ectopic ureters (up to 83%) have been reported to have concurrent urinary tract infections[9]. These are most commonly due to *Escherichia coli*[9]. To avoid complications in further work up, patients urinary tract infections must be treated and resolved. Ultrasound can be diagnostic if the ureter is distended or if there is presence of ureteral jets in the bladder[5]. However, the normal ureter is too small to typically be visible on ultrasound. Ultrasound is typically used more as a screening modality[9].

Intravenous pyelogram, or excretory urography, has historically been the most commonly used method for confirming ectopic ureters[5]. This allows visualization of the ectopic ureter emptying into the urethra, the uterus, or the vagina. Other urogenital abnormalities can also be seen such as hydronephrosis, hydroureter, hypoplastic bladder, and ureteroceles[5]. Hydronephrosis and hydroureter occur due to increased resistance of urine flow at the ureteral exit[1]. Contrast radiography is widely available technique that is relatively low cost[9]. However, it cannot differentiation intramural from extramural lesions and does not diagnose all ectopic ureters. Intravenous pyelography is associated with 60-70 percent accuracy[3]. Fluoroscopy has the added benefit of seeing ureteral peristalsis, however it is less widely available[9]. Computed tomography allows visualization of the ureters in multiple planes and takes away issues of the ureter being obscured by surrounding tissues[3].

Endoscopy can be very helpful in pre-operative planning for surgery. The exact location of the ectopic ureter can be found, and in some cases of intramural ectopic ureters, laser ablation can be performed under the same anesthetic event. As in Lulu's case, urethrocystoscopy and vaginoscopy allowed diagnosis to be confirmed. A combination of any of these diagnostic procedures can be used[3]. New studies show that when using cystoscopy, bilateral EU appear more often than older studies once documented[2]. This is most likely due to the new technology and visualization of the trigone area. Cystoscopy allows better visualization of the vestibule and genitourinary mucosa for other abnormalities to be identified as well[2]. The use of CT and cystoscopy are reported to be the most sensitive and specific method for diagnosing ectopic ureters[2].

Pathophysiology:

As stated above, ectopic ureter, or ureteral ectopia, is a congenital anomaly in dogs in which one or both ureters do not enter the urinary bladder in the correct anatomic position[2]. It is the result from an abnormal development of the metanephric ducts in utero[2]. Ureters should naturally open into the bladder at the trigone after a brief intramural course[7]. Instead of connecting to the bladder, with ectopic ureters the ureters connect to the urethra, the vagina, colon, or even the uterus. The ureters are thus bringing urine to an area unequipped for urine storage, and this results in urine leaking out.

Ectopic ureters are classified according to the point of termination of their orifice as either intraluminal or extraluminal. Extraluminal ectopic ureters completely bypass the trigone and enter somewhere in the distal genitourinary tract. Intraluminal ectopic ureters enter the bladder at the correct anatomic position, but then course submucosally in the bladder to open distal to the trigone[5]. More than 95% of EU are intramural, and approximately 70-80% of all ectopic ureters are unilateral[5]. Other abnormalities include double ureteral openings, where the ureter opens to the bladder and more distally, and urethral troughs, or elongations[5]. It is extremely rare for cats to have ectopic ureters, however when they do, cats are usually bilateral and extraluminal[5].

The most common clinical sign of ectopic ureters is urinary incontinence at a young age, consequent urine dribbling, and urinary infection. In some cases, nocturia is the only clinical sign[2]. Females are more commonly diagnosed than males, however males can still be affected. Due to anatomical urinary structure, males' ureteral entrance into the urethra with an ectopic ureter may be closer to the bladder than to the tip of the penis[2]. Urine in the urethra will flow in the direction of least resistance, which in males will be towards the bladder. This allows males to be less clinical than females, who will dripple out urine when it is in their urethra as that is the direction of least resistance anatomically[1]. Therefore, ectopic ureters in male dogs are likely underestimated due to the lack of clinical signs[2]. Many animals that are affected unilaterally are able to urinate normally[2].

Often there are multiple urogenital anatomical abnormalities in animals with ectopic ureters such as, urethral sphincter incompetence, bladder hypoplasia, vestibulovaginal abnormalities, ureteroceles, renal agenesis, intrapelvic bladders, pyelitis, pyelonephritis, hydroureter, and hydronephrosis[10]. These abnormalities occur in embryogenesis of the urinary system or as a secondary result of obstruction or infection. Approximately 90% of cases in females have a persistent paramesonephric remnant that may result in a vaginal septum or dual vagina[6]. 86% of females reportedly have a persistent vestibulovaginal septal remnant. This is a band or wall of tissue in the vagina that is present between the cervix and vestibule, starting at the vaginal opening[9]. When a persistent vestibulovaginal septal remnant is present it can also be laser ablated, although the significance of this intervention is unknown[9]. It is hypothesized that a persistent vestibulovaginal septal remnant may contribute either to persistent UTIs or urinary incontinence by anchoring the urethral orifice in an open position or pooling of urine in the vagina[9].

The following breeds have been found to be at an increased risk of ectopic ureters; English bulldog, Fox terrier, golden retriever, Labrador retriever, Newfoundland, Pembroke Welsh corgi, Poodle, Siberian

Husky, Skye terrier, and West Highland white terrier[4]. It should be considered heritable in these breeds, and they should not be bred if an ectopic ureter is diagnosed.

Treatment:

Traditionally, treatment for dogs with ureteral ectopia is with surgical correction. Techniques used to correct EU depend on the location of the ureteral opening, the functional condition of the ipsilateral kidney, and the presence of other malformations[8].

Neoureterocystostomy is used when the ureter is extraluminal, bypassing the urinary bladder. With this technique, the ureter is ligated and a new opening in the bladder is made. The ureter is then replaced into this new opening[8]. Complications due to swelling at the attachment site can interrupt the urine flow and cause damage to the kidneys[8]. Nephroureterectomy is the complete removal of the kidney and the ureter. This is done when the kidney is too diseased and no long working[8]. This can only be performed if the other kidney is healthy.

When the EU is intraluminal, a neoureterostomy with ligation of the distal ureteral segment or intravesicular ureteral transplantation technique, neoureterostomy with resection of the distal ureteral segment, extravesicular ureteral transplantation technique and most recently, cystoscopic guided laser ablation have been described[8]. In a neoureterostomy, an opening into the bladder is made where the ureter attaches but has failed to penetrate[3]. The part of the ureter that extends distally to this point is resected. Cystoscopic guided laser ablation is a less invasive procedure that incises the tissue separating the ectopic lumen from the lumen of the urethra or bladder with a cystoscopic guided laser[3]. It is thought to have a more successful outcome with better continence in the post-surgical patient, however there is still not much data on the long-term outcome of these patients.

Affected dogs with ectopic ureters opening near the sphincter, or proximal urethra, may have some response to medical management, mimicking dogs with acquired urinary incontinence[3]. However, surgery is the treatment of choice for EU[8]. Post-operative persistent incontinence can be managed medically with phenylpropanolamine, an a-adrenergic stimulant, and estrogen compounds that increase sensitivity of a-adrenergic receptors in the urethra, such as diethylstilbesterol. Medical management helps to increase urethral sphincter tone if incontinence persists post-surgery. In a small case series of 12 female dogs, continence was achieved in 47% of dogs without additional medical management. When pharmacologic intervention (eg, phenylpropanolamine or estrogen compounds) were added, continence increased to 77% of dogs[2]. If incontinence persists even with medical management, placement of an artificial urethral sphincter or colposuspension can be offered[9]. The placement of an artificial urethral sphincter after laser ablation in dogs that are still incontinent has shown to be effective in 80% of case[9].

Antibiotics and pain medication should be supplied to the patient during post-operative recovery. A urinary catheter is typically placed to prevent urinary distention post-surgery during the first few days of healing. Follow up serial urinalysis and cultures are advised for patients getting surgical correction. The main post-operative complications include incontinence, leakage of urine into the abdomen, stricture of the surgical site, and urinary tract infections[3]. Persistent incontinence is likely caused by the trough effect of the remaining intraurethral ureteral remnant left behind because of surgical inaccessibility[2]. Postoperative success rates vary between 50% and 75%. For laser ablation, the reported long-term continence rate is 31% to 47% without additional medication and 69% to 77% with medication[9]. Long term outcomes between different procedures used are broadly similar. This suggests that one technique is not superior to another in the long-term effectiveness of treatment for EU[9]. Dogs weighing less than 20 kg have been reported to have a better outcome postoperatively as well as male dogs[2]. In another study, 55% of dog's incontinence improved post-surgery and 33-58% became free of their incontinence post surgery[8].

Case Outcome:

Lulu returned to MSU-CVM 8/5/2020 for corrective surgery. A urinalysis with culture and sensitivity was submitted prior to going to surgery. This came back negative with no growth over 48 hours. On 8/6/2020 under general anesthesia, Lulu's left intramural ectopic ureter was corrected using laser ablation via cystoscopy. The vaginal vestibule, urethra, and bladder were explored during cystoscopy to check for other anatomical abnormalities. The openings of the normal right ureter and the left ectopic ureter were located. A hydrophilic "weasel" guide wire was advanced through the scope and threaded into the ectopic ureter on the left side. Non-iodinated contrast media was injected via the catheter into the kidney, ureter, and bladder. The C-arm with fluoroscopy was used to identify the ectopic ureter as intramural. A catheter was then placed over the guide wire into the ureter and the scope was advanced, beside the catheter, up to the trigone. A fiber laser was passed through the scope and used to ablate the membrane of the ectopic ureter, enlarging the opening to the level of the other, normal ureteral opening.

The guide wire, catheter, and scope were removed, and then threaded into the normal right ureter using the same procedure outlined above. Contrast was instilled, and the renal pelvis, ureter, and bladder were visualized in fluoroscopy.

Lulu recovered from her surgery without any complications and was able to go home the following day. She returned to MSU-CVM 9/8/2020 for a recheck examination, urine culture, and ultrasound of her kidneys, ureters, and bladder. At this time Lulu's examination had no abnormal findings, with no evidence of stricture or obstruction.

As of 2/20/2021 Lulu's owner reports that she is doing great. She no longer is dribbling urine, scooting, or having any urinary issues since her surgery. Her owner is thankful for her success and says she is a spunky healthy puppy!

Conclusion:

Ectopic ureters should not be excluded as a possible diagnosis even if urinary incontinence is intermittent or if the animal seems to urinate normal volumes[2]. Ectopic ureters have been diagnosed in older animals that have no evidence of incontinence[2]. Thus, congenital ectopic ureters should be considered a differential diagnosis in animals with hydronephrosis, even if there is no urinary incontinence[7]. Ectopic ureters can be diagnosed with excretory urography, fluoroscopic urethrography or ureterography, abdominal ultrasonography, cystoscopy, computed tomography, or a combination of these diagnostic procedures[7]. Other congenital abnormalities can also occur in dogs with ectopic ureters, including renal agenesis or dysplasia, hydronephrosis, and/or hydroureter and vestibulovaginal anomalies; therefore, the entire urinary system must be evaluated with ultrasonography if cystoscopy is the only other diagnostic tool used before surgery[2]. Novel surgical techniques and adjunctive medical management have improved the prognosis for dogs with urinary ectopia[2]. Resolution of incontinence post-surgical repair ranges from 22-59% and another 7-28% become continent with adding phenylpropanolamine[8]. Continued incontinence is likely due to functional abnormalities of the bladder neck and urethra[8]. Prognosis with laser ablation is similar to surgical intervention with less post-operative pain and hospitalization time[8]. Success rates with surgical correction in males is reported to be higher than with females likely because of male's longer urethra[8].

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