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Urinary Tract Disease Mini Series

Session Three: Below the Kidney: Lower Urinary Tract Diseases of Cats and Dogs

Mayank Seth BSc(Hons) BVetMed(Hons) DACVIM(SAIM) DipECVIM-CA MRCVS
American, European and Royal College Specialist in Small Animal Internal Medicine

Feline Urethral Obstruction

Feline lower urinary tract disease (FLUTD) is considered to be one of the most common diagnoses in feline patients, affecting 1% of cats annually in the UK and is the commonest cause of urethral obstruction seen in small animal patients. While FLUTD may occur in any cat, obstruction is seen almost exclusively in male cats due to the long, narrow, tortuous nature of their urethra.

Initial Stabilisation

In the early stages of obstruction, the condition is painful and distressing to the patient. Once it has been present for any length of time, the pressure build-up in the bladder and ureters leads to post-renal obstructive AKI and this becomes a medical emergency. Similar to any other form of AKI, cats with urethral obstruction may experience circulatory collapse. Recognition of this critical state is vital and so cats should be properly assessed, considering cardiovascular status and emergency bloodwork (particularly urea, creatinine and potassium). A recent study correlated a low rectal temperature upon presentation with worse azotaemia and in turn, azotaemia was associated with length of hospitalisation required, providing the owners with useful prognostic information to help in their decision making.

An episode of obstructive FLUTD should be treated as a medical emergency. The affected cat may have life-threatening acidosis, dehydration, hyperkalaemia, or hypocalcaemia and may be anaemic due to blood loss in the urinary tract. Stabilisation is required prior to further diagnostic work-up or procedures. Initial stabilisation should focus on restoring perfusion through fluid boluses. Evidence suggests that the use of a buffered isotonic crystalloid solution (eg Hartmann's Solution) is preferable as it is associated with better correction of acid-base imbalance and faster renal recovery. While this solution contains potassium and affected patients may be hyperkalaemic, the effect of this small amount of potassium is negligible.

If hyperkalaemia is present and associated with cardiac changes (bradycardia with flattening of the p-waves and tall t-waves) then it should be addressed as outlined in the AKI notes.

Anaesthetic Considerations

Once the patient is stabilised, abdominal radiographs can be performed to look for calculi and urethral patency restored by catheterisation under sedation or general anaesthesia. Opioids and benzodiazepines are the sedative agents of choice. Buprenorphine (20 µg/kg IV) is a safe, effective opioid and provides mild sedation, analgesia and anaesthetic-sparing effects. Benzodiazepines (e.g. midazolam 0.1 – 0.2 mg/kg IV) cause muscle relaxation with little effect on the cardiovascular system and can be combined with an opioid to provide sedation or co-administered at induction to reduce the amount of induction agent required. Benzodiazepines are most effective in patients that are very young, old or sick as otherwise they may cause excitation. Propofol is a useful induction agent as small amounts can be administered slowly IV to effect. Alpha-2-agonists are contraindicated due to their cardiovascular effects and suppression of endogenous insulin production (therefore permitting hyperglycaemia). A recent study described the use of a lidocaine coccygeal nerve block in following sedation as detailed above to provide analgesia and allow urinary catheterization without the need for general anaesthesia.

Relief of Obstruction

Once sedated or anaesthetised, catheterisation can be performed to relieve urethral obstruction. My preferred technique is briefly described below:

1. Position the patient in dorsal recumbency.
2. Gently massage the urethral tip between a thumb and forefinger to encourage dislodgement of urethral plugs from the distal urethral lumen.
3. Connect a well lubricated urinary catheter (preferably open-ended e.g. Slippery Sam™ or Mila EZGO™) to an intravenous extension set and 10 ml syringe filled with sterile saline.
4. Flush through the extension set and urinary catheter with sterile saline to evacuate air.
5. Exteriorise the penis caudally and dorsally to eliminate the distal urethral flexure.

6. Carefully introduce the tip of the urinary catheter into the urethral opening.
7. Slowly and gently advance the urinary catheter along the urethra whilst flushing with sterile saline. NB. Walpole's solution should never be used for this purpose as it is highly irritant to the urethra and bladder and causes severe inflammation.
8. Once the catheter has been advanced approximately 1-2cm into the urethra, if resistance is felt then the penis should be released and the prepuce pulled forward to adjust the position of the urethra and aid advancement.
9. As the urethral plug is disrupted the catheter should be advanced until its tip is in the bladder.
10. The syringe can then be used to remove urine from the bladder. I prefer to copiously lavage the bladder using Hartmann's solution until the solution that is recovered is clear of debris but this is of no proven benefit. Any solid material recovered should be sent for analysis.

A recent study correlated the darkness of the initially recovered urine with the severity of the patient's azotaemia, but not with the presence of infections, which are very uncommon in cats less than 7 years old. Another small study suggested that intra-urethral instillation of atracurium besylate to relax the urethral musculature has been associated with decreased time to dislodge any obstructive material. In some instances, obstructive material cannot readily be dislodged and in these cases retrograde hydropulsion can be attempted to help dislodge material (see notes on canine urethral calculi below). It is often reported that cystocentesis is contraindicated in the face of urethral obstruction as bladder rupture may occur. Several studies indicate that this is unlikely to occur and reduction of intravesicular pressure may be associated with improved analgesia and ease of dislodging any urethral obstruction. If cystocentesis is performed then it is probably important to make sure that significant bladder distension does not occur again immediately afterwards as this may heighten the risk of leakage or rupture.

Urethral rupture may occasionally occur with particularly traumatic catheterization attempts. If this is suspected then positive contrast urethography should be performed to assess the extent of any damage and leakage. In minor cases then this may heal of its own accord with a urinary catheter left in place but in more severe situations surgical expertise may be required to debride away damaged tissue and close the defect. In cases where rupture or obstruction prevent passage of a catheter, anterograde catheterization has been described where a wire is inserted percutaneously into the bladder and then down the urethra. This wire may then be used to guide a catheter back into the bladder without it causing further urethral damage.

Hospitalisation Following Relief of Obstruction

Much concern has previously been raised about catheterization and urethral irritation leading to re-obstruction from spasm. Recent studies indicate that a smaller urinary catheter (3.5Fr) is associated with a lower rate of re-obstruction. Similarly, suturing a catheter in place and leaving it indwelling for a period following relief of obstruction is likely to be associated with a lower rate of re-obstruction compared to immediate removal of the catheter. Use of a closed collection system is strongly recommended so that fluid balance can be properly assessed (see below) and to minimise the risk of ascending infections.

Following removal of the obstruction, monitoring of fluid input and output is important as post-obstructive diuresis occurs in nearly half of patients and may be marked (resulting in hypovolaemia/dehydration). Fluid therapy with a balanced electrolyte solution is usually adequate for rehydration. Analgesia (e.g. buprenorphine 20 µg/kg IV every 6-8 hours) and anti-spasmodics such as the α1-antagoinsts prazosin (0.2-1 mg/cat PO every 12 hours) or phenoxybenzamine (0.5-1 mg/kg PO every 12 hours) may be used in an attempt to relieve urethral spasm. One study indicates that prazosin use may be associated with a decreased rate of re-obstruction in the 30 days following treatment. In rare cases, significant post-obstructive blood loss can occur in the urinary tract resulting in profound anaemia which may require a blood transfusion.

I tend to maintain the urinary catheter in place until any significant diuresis (>4ml/kg/hr) has subsided, the patient appears comfortable and the urine appearance is relatively normal. This typically takes in the region of 48 hours. Following removal of the urinary catheter, a cystocentesis sample should be taken to look for evidence of a urinary tract infection. Urine samples should not be from the catheter or bag as this may identify colonizing bacteria rather than a true infection.

Alternative Treatments

Although urethral catheterisation is typically required to relieve obstruction, a recent small scale study described a protocol without catheterisation. It consisted of sedation and analgesia (acepromazine 0.25 mg IM or 2.5 mg PO every 8 hours, buprenorphine 0.075 mg PO every 8 hours, and medetomidine 0.1 mg IM every 24 hours) and decompressive cystocentesis and SC administration of fluids as needed. Cats were also placed in a quiet, dark environment to minimize stress. This protocol may be an option for cases with a functional blockage only (no evidence of urolithiasis or urethral plugs) and financial constraints which preclude catheterisation. However ACP and medetomidine should only be used once the patient is stable (neither hypovolaemic nor dehydrated) and the complication rate in a larger cohort of patients is yet to be determined.

Long-term Treatment

Following discharge from the hospitalization the due consideration needs to be given to the causes of the urethral obstruction and attempts to prevent it. If calculi were identified then treatment recommendations depend in part on the nature of these. In may instance, calculi are not identified and a diagnosis of idiopathic cystitits is made. In such cases preventative treatment is largely focussed on environmental enrichment and removal of stressors combined with a diet that promotes diuresis and prevents calculus formation. Various drugs have been advocated for long term control of idiopathic cystitis but evidence for their use is lacking.

If obstructive episodes are recurrent then perineal urethrostomy (PU) can be considered to prevent these from occurring, although it should be noted that these do not prevent ongoing problems of cystitis. Re-occurrence is reported in upto half of cats that have had an obstructive event and so many surgeons advocate a 3-strike rule, whereby PU is recommended after the 3rd obstructive event.

Canine Urethral Obstruction

Similar to cats, urethral obstruction is much more common in male dogs compared to females but it is generally less common. The causes of urethral obstruction in dogs tend to be more varied than commonly seen in cats, although it should be noted that most of the causes described below have also been seen in cats. Considerations of post-renal obstruction, AKI and its stabilisation are similar to those as noted above but in my experience, renal problems are less common in obstructed dogs. This is likely as they present at an earlier stage of the disease as dysuria is usually evident to dog owners relatively quickly.

Calculi

Urinary calculi of any sort can get lodged in the urethra leading to obstruction. The commonest sites of obstruction in the male dog are just proximal to the os penis and at the curvature caudal to the ischium. Obstruction is usually preceded by a variable period of dysuria due to cystic calculi. The diagnosis is usually easily made from survey radiographs but it is important to include the entire perineum so that the ischial urethra is visualised and to remember that cysteine and urate stones may be radiolucent. In such cases contrast urethrography, CT or urethroscopy may be required to identify the obstruction.

Once identified, the first attempted method to relieve the obstruction is usually retrograde hydropulsion. This involves placing a catheter into the distal penis and a gloved finger per rectum to occlude the intrapelvic urethra. The catheter is then flushed with saline to distend the urethra and once this is achieved the finger in the rectum is moved to relieve the obstruction and hopefully displace the calculus into a more proximal location (and eventually the bladder).

In most instances, if this is not possible then some form of urethrostomy is recommended to allow urination to occur proximal to the level of obstruction. Readers are directed to appropriate surgical texts for further information.

An alternative treatment that can be considered in select cases is laser lithotripsy to break up a calculus that is causing obstruction. This may allow the stone fragments to pass or it may allow them to be more readily hydropulsed back into the bladder but this procedure is not widely available in the UK.

Benign Prostatic Hyperplasia

Benign prostatic hyperplasia (BPH) is a common problem of male intact dogs that may lead to urethral compression and obstruction. The treatment of choice is castration and surgical is preferred over chemical as it is permanent and not associated with late problems such as testicular neoplasia. The progestogen osaterone acetate is licensed for the treatment of BPH in dogs and may be useful in the early management as it can lead to a faster reduction in prostatic size than castration alone.

Urethral Dyssynergia

Whilst not truly a cause of urethral obstruction, dyssynergia may be confused with urethral obstruction (or incontinence) as it is characterized by difficulty urinating, bladder distention and dribbling of urine. The cause of this condition is poorly understood and likely to be multi-factorial but the result is a neurologic incoordination. The problem may be self-perpetuating as bladder distention may lead to detrusor atony. Diagnosis is based on exclusion of other causes of bladder/uretheral dysfunction (neurologic examination, urine culture and contrast radiography of the lower urinary tract). Treatment mainly focusses on reduction of resistance to bladder outflow using the alpha-antagonists prazosin or phenoxybenzamine and skeletal muscle relaxants such as diazepam. Bethanechol use may also be considered to encourage bladder contraction.

Stricture or Stenosis

Urethral strictures and stenoses are occasionally described. These may be idiopathic or associated with previous trauma (eg catheterization or passage of a small calculus). Diagnosis is generally by contrast urethrography and treatment is by balloon dilation, stent placement (see below) or urethrostomy. Permanent cystostomy tubes have also been placed for the treatment of these and other causes of obstruction listed in this section, but these require a significant long-term owner commitment and are associated with chronic or recurrent urinary tract infections, amongst other complications.

Neoplasia

A variety of neoplasia have been described affecting the urethra but far the most common is transitional cell carcinoma (TCC). In the first instance, obstruction may be relieved by catheterization, alpha antagonists (see above) and NSAIDs. NSAIDs may reduce spasm, reduce inflammation around a tumour and may also be directly cytotoxic in approximately a third of TCC cases. If these strategies +/- chemotherapy do not relieve urethral obstruction then a urethral stent may be placed to alleviate the obstruction and relieve urethral patency. Stents have been reported to be very successful for this purpose and have greatly improved survival times reported in TCC as they change the cause of death from urethral obstruction to other complications (eg tenesmus or distant metastasis). Varying degrees of incontinence are seen following stent placement and this seems to be independent of the stent length/location (but related to the duration of dysuria prior to placement) and so owners must be prepared to accept this potential side effect. Stents have also been used to treat a variety of benign causes of urethral obstruction (see above). More recently, radiotherapy protocols have been described for the treatment of urethral neoplasias. These can be used to achieve cytoreduction and relieve an obstruction but they also (partially) treat the underlying neoplasia. Relief of an obstruction is generally slower and less predictable by this method and so it is often combined with stenting and the medical management outlined above.

Introduction

Over the past 20 years, ureteral obstruction in cats and dogs has evolved from a rare condition to one of the most commonly recognised causes of acute kidney injury. This in undoubtedly in part due to improved diagnostic imaging and awareness of the problem but the incidence appears to be genuinely increasing, as does the geographic distribution of cases. Over that same time period, many therapeutic strategies have been attempted and these continue to be developed, with decreasing mortality rates and improved long term survival being reported in recent years.

Pathophysiology

The ureter is composed of a layer of transitional epithelial cells and connective tissue, surrounded by a thick wall of smooth muscle. In dogs the ureter measures 1-3mm whereas in cats the luminal diameter is approximately 0.4mm. The ureter is normally collapsed and is opened by intermittent of boluses of urine, stripped though by peristaltic waves. Ureters are surrounded by renal parenchyma at the proximal end. They pass caudally through the retroperitoneal space, with the left ureter passing lateral to the aorta and the right ureter passing lateral to the caudal vena cava. In some cats the right ureter passes dorsal to the vena cava, a variant known as circumcaval ureter that may be associated with idiopathic ureteral stricture formation. As the ureters pass caudally, the distal end curves, resulting in a J-shaped hook before they then enter the bladder at the dorsocaudolateral aspect of the trigone.

Experimental data from healthy dogs indicates that after complete occlusion of the ureter, hydrostatic pressure proximal to the occlusion rapidly rises and this occurs throughout the nephron. Subsequently there is a marked decrease in glomerular filtration rate (GFR) within that kidney and an influx of inflammatory cells and the development of oedema, followed later by fibrosis. The blood flow, GFR and urine output of the contralateral kidney increases in a compensatory fashion if it is able to do so. Relief of the obstruction after 7 days results in a permanent 35% decrease in GFR in the affected kidney, whereas obstruction for 14 days leads to a 54% reduction in GFR. This is in contrast to partial ureteral obstruction, where function can return to 100% if normal ureteral flow is restored after 4 weeks. Given that partial obstructions have the potential to progress to complete ones and from the above data it should be clear that ureteral obstructions require rapid recognition and treatment in order to maximise outcome.

Many causes of ureteral obstruction have been reported in the literature, including idiopathic strictures, accidental surgical ligation, blood clots, neoplasias of the bladder trigone and other forms of neoplasia. The commonest cause by far is urolithiasis, with calcium oxalate stones accounting for 98% of ureteroliths in cats and >50% in dogs. These stones often form in association with chronic kidney disease and this has important implications for management of these cases as expectations for contralateral kidney function and the ability of the affected kidney to repair are diminished.

Diagnosis and Further Investigation

Ureteral obstruction cases can present in a variety of ways. In cases of unilateral kidney disease serum biochemistry may be unremarkable as 75%of renal function must be lost before azotaemia is seen. Ureteral obstructions not associated with lower urinary tract infections or neoplasias are unlikely to have signs of stranguria or hematuria. Such cases are likely to present simply for abdominal pain, perhaps with associated vomiting, or they may go completely unnoticed. If the other kidney is in some way compromised then azotaemia is likely to be seen and such animals typically present with signs of acute uraemia, similar to other acute kidney injury cases. The affected kidney is often palpably enlarged. This can lead to bilateral renomegaly in bilateral obstruction cases or so called “Big Kidney, Little Kidney” if the contralateral kidney has suffered previous insult (such as a previous, clinically silent, ureteral obstruction).

Survey abdominal radiographs can be used to identify renomegaly or renal asymmetry, Mineralised ureteroliths may be identified on plain radiographs but can easily be missed due to their small size or material in overlying structures such as the colon. Renal mineralisation or nephroliths are commonly seen in association with ureteroliths and these are easily identified on radiographs.

Abdominal ultrasonography can be used to reliably detect ureteral obstruction. Pyelectasia and proximal ureteral dilation are the most notable features, particularly if the distal ureter is visualised to be of normal diameter. With patience, a cooperative patient and suitable expertise, the obstruction itself can usually be identified although it can be challenging to determine if it is a complete or partial obstruction and data suggests that the position of stones within the ureter can vary over time.

Iodinated contrast agents can be used to highlight the ureters, making it easier to identify obstructions and determine if they are complete. Intravenous contrast studies can be performed but are often unrewarding as the decreased GFR of the affected kidney results in poor ureteral filling. Computed tomography allows better visualisation of the ureters but intravenous studies must still be conducted with great caution as iodinated contrast media are potentially nephrotoxic and renal excretion of these drugs will be impaired in such cases.

The location and nature of an obstruction can be determined by performing an antegrade pyelogram. This technique involves placing an ultrasound guided needle into the renal pelvis of an anesthetised patient and directly administering an iodinated contrast agent. This can be combined with pyelocentesis to obtain a sample for urine culture as concurrent pyelonephritis is common. If a complete obstruction is identified then pyelocentesis can lead to retroperitoneal urine leakage as urine will flow through the path of least resistance (the puncture site). Consequently this procedure should not be performed without a strategy for decompression of the kidney being in place (see below).

Scintigraphy is sometimes used in the investigation of ureteral obstruction cases as it allows assessment of the GFR in each kidney individually. This is not useful for assessing the prognosis of the affected kidney as GFR is markedly decreased in the face of obstruction, but the return of function following relief of the obstruction cannot be assessed by scintigraphy beforehand. Scintigraphy may be useful in assessing the function of the unaffected kidney, which can help to choose the most appropriate therapeutic options for some patients.

Treatment options

Treatment of ureteral obstruction should initially mimic treatment for other forms of acute kidney injury, ensuring that the patient is cardiovascularly stable with adequate renal perfusion and is adequately analgised (see other course notes). Ureteral obstruction cases can be particularly challenging to manage with respect to fluid balance as they have decreased urine output from the affected kidney and urine output from the contralateral kidney can be highly unpredictable. Patients are often part of a geriatric population and may have pre-existing chronic kidney disease in addition to other potential co-morbidities such as cardiac disease or hypertension. Careful monitoring of fluid balance is required and so consideration should be given to early placement of urinary and central venous catheters. The patient's weight, respiratory status and electrolytes should also be carefully monitored to look for signs of fluid imbalance.

Cats with ureteral obstructions frequently have poor nutritional intake prior to diagnosis and whilst in hospital. Placement of a feeding tube (naso-oesopahgeal or oesophageal) should be considered early in the treatment of such patients which also provides the advantage of managing fluid balance with enteral water rather than intravenous fluids.

Antibiotics are usually indicated in patients with ureteral obstruction at the time of diagnosis as concurrent urinary tract infections are common (>75% of dogs) and if an obstruction is not definitively diagnosed, pyelonephritis is another possible diagnosis for acute kidney injury with renal pelvis dilation.

Although ureterolithiasis is the commonest cause of ureteral obstruction, medical dissolution is not a useful treatment strategy as calcium oxalate are the commonest stones identified and the stones are only intermittently bathed in urine due to peristalsis within the ureter. “Benign neglect” was a frequently recommended treatment option at one time, owing to the poor success rate and high morbidity/mortality associated with treatment procedures. Given that chronic kidney disease is one of the commonest diseases of elderly cats, the affected kidney can be painful and potentially filled with infected urine, sacrificing a kidney in this manner cannot be recommended.

Various medical strategies have been advocated in the treatment of ureterolithiais with the aim of allowing the stone to pass into the bladder, increasing its chances of being voided spontaneously. These strategies are certainly worth attempting as they can be combined with the initial period of patient stabilisation but it should be noted that none of the suggested treatments have a strong evidence base and in 1 study only 17% of cats with ureteroliths showed significant movement of the stone with aggressive medical management. They are more likely to be successful if the obstruction is a single ureterolith located in the distal ureter, close to the ureterovesicular junction. These strategies have the potential to cause significant cardiovascular instability and so they should be immediately discontinued if signs of fluid overload or hypotension develop. Similarly patients should be carefully monitored by repeat imaging and if passage of stones is not noted over 48 hours then these treatments should be discontinued as they are unlikely to work, may be detrimental to the patient and delay further intervention, worsening renal damage.

Aggressive diuresis can be used to encourage stone movement. Intravenous fluid therapy should be planned to replace volume depletion and dehydration and to exceed ongoing maintenance requirements if the patient can tolerate this without developing signs of fluid overload. Mannitol can also be used as an osmotic diuretic (0.5g/kg as a slow IV bolus followed by 1mg/kg/min CRI) to increase pressure in the proximal ureter and encourage stone passage.

In addition to diuresis, antispasmodics are frequently used to encourage stone passage, although data regarding their success is sparse and not encouraging. Prazosin, an alpha-1 receptor blocker has been used to encourage passage of urethral plugs (0.5mg/cat or 1mg/15kg q8hrs) but it has not been investigated in clinical cases of ureteral obstruction and while low doses have an anti-spasmodic effect, higher doses can cause ureteral spasm and any dose may cause systemic hypotension. Amitryptiline can be used to relax urinary smooth muscle (1mg/kg/day) but again it has not been investigated in this context. Glucagon (0.1mg/cat IV q 12) causes ureteral smooth muscle relaxation and has been studied in feline ureteral obstruction. It was found to increase urine output in oliguric cats but not to improve outcome with respect to obstructions. It can cause severe gastrointestinal signs and dyspnoea making its value in these cases questionable. Many additional anti-spasmodic drugs have been investigated in an experimental setting and several show promise but the lack of data regarding their safety and clinical effectiveness mean they cannot be recommended at this time.

If medical management is unsuccessful, as it is in most cases, the surgical intervention is required. These interventions require a great deal of technical ability and specialist equipment and should not be attempted without specific training but are briefly described to allow a complete understanding of available treatment options.

Many patients with ureteral obstruction benefit from the placement of nephrostomy tubes which allow drainage of urine from the obstructed kidney. These can be placed percuteneously in dogs by ultrasound or fluoroscopic guidance but should be placed via a brief surgical procedure in cats. Nephrostomy tubes decompress the kidney, preventing further renal damage, allowing restoration of urine output and decreasing inflammation in the kidney and ureter. They can be beneficial for management of a patient prior to more definitive procedures by buying time and restoring urine output and allowing post-obstructive diuresis to be handled prior to longer surgical procedures which carry a higher morbidity rate. They allow assessment of individual kidney urine output and can be used to obtain urine for culture samples and provide a route for conducting anterograde pyelograms. They are most commonly used for a few days/weeks prior to another procedure but their long term placement is described for management of malignant ureteral obstruction with owners managing patients at home for several months as a palliative procedure.

Experimental data in dogs indicates that the relief of ureteral inflammation/oedema can be significant enough to allow subsequent passage of an obstruction.

In patients with low urine output that cannot be stabilised for anaesthesia (required for nephrostomy tube placement) then dialysis (intermittent of continuous renal replacement) can be used to manage fluid balance and uraemia. This still requires some sedation for placement of a dialysis catheter but this is usually well tolerated. Dialysis is not the preferred method of stabilisation, however, as it does not address renal pressures in the same manner as a nephrostomy tube.

Many different surgical techniques have been described for treatment of ureteroliths. Ureterotomy has fallen out of favour as a treatment option as microvascular equipment and skills are needed for surgery on such fine structures and complications such as stricture, leakage and recurrence were common. Ureteroneocystomy is the resection of the distal ureter followed by re-implantation of the more proximal ureter into the bladder. This can be used to successfully manage distal ureteral obstructions but this technique also has complications including a high rate of re-obstruction. Nephrectomy remains a valid treatment choice in patients with abdominal pain or an infected kidney if the other kidney is functioning well and the owners do not wish to pursue more advanced attempts at salvaging renal function.

In recent years many more advanced treatment strategies have become available for dealing with urteroliths and other ureteral obstructions. These techniques must still be considered investigational in nature as long term follow-up is limited but they are being performed with increasing frequency around the globe as short term success rates seem significantly higher.

Extracorporeal shockwave lithotripsy involves applying shockwaves through the body wall to the area of a urolith to fragment it and ease its passage. The technique has limited use in cats as their kidneys are very prone to damage from this modality and their ureters are so small that it is difficult to fragment stones to a small enough degree. The technique has been successfully used in in dogs with stones <5mm diameter if they are not embedded in the ureteral mucosa.

In larger dogs urteroscopy or percutaneous nephroeteroscopy (inserting an endoscope into the ureter via a nephrostomy tube) can be performed to directly visualize the obstructed ureter in a non-invasive fashion. Large stones can be broken down by laser lithotripsy and smaller stones/fragments can be removed using a wire basket. Ureteral strictures can also be treated by balloon dilation if identified.

One of the commonest treatments now used for ureteral obstruction is ureteral stent placement. These are devices that are passed through the ureter, with curled ends keeping them in place in the kidney and bladder. They can be placed surgically (most common in cats) or they may be placed non-invasively using fluoroscopic, ultrasonographic and endoscopic guidance. They maintain a patent lumen allowing passage of urine and stone fragments and promote gradual dilation of the ureter. In people they are commonly placed temporarily but they have been left in long term in cats/dogs with minimal complications reported to date. They have the advantage of aiding not just with current obstructions but also with problems that may arise in the future due to new stone formation or movement of other existing stones.

Placement of stents can be challenging in cats with complete occlusions and damage can easily occur when attempting to pass a stent beyond an obstruction in such a delicate, inflamed tissue, leading to failure of the procedure. This has led to the development of a new prosthesis known as a SUB (Norfolk Veterinary Products), which can be used to divert urine around the ureter rather than through it. These are a combination of a nephrostomy tube and cystostomy tube, connecting in the subcutaneous space, accomplishing restored urine flow in much the same way as a ureteral stent does. These devices are rapidly becoming the treatment of choice for cats with ureteral obstruction

Aftercare and prognosis

Using a combination of the techniques listed above, experienced groups are able to relieve ureteral obstruction successfully in >90% of cases, although there is certainly a steep learning curve involved in attaining such success rates.

As discussed above, ureteral obstruction is most commonly identified in cats with chronic kidney disease and as with any other 'acute on chronic' episode, chronic kidney disease is an ongoing concern after successful treatment and the kidneys are likely to be in worse condition after the acute incident than before. Thankfully, the majority of cats with ureteral obstruction end up with IRIS stage 1 or 2 kidney disease following treatment and recent data suggests that these cats can go on to live for many years after their obstruction episodes. The degree of azotaemia seen in these cats pre-operatively was somewhat predictive of the degree of chronic kidney disease identified post-operatively, which is in turn predictive of survival. It should be noted that in that same study, imaging findings were not reported to be predictive of outcome. When ureteral obstruction was originally due to a malignancy then understandably survival times are lower, but most commonly animals in this situation go on to die from disease associated with metastatic spread rather than urinary complications and this may not be for many months.

Diets aimed a calcium oxalate prevention are not suitable for use in most patients with ureterolithiasis as the high sodium content of these diets is a potential problem with respect to chronic kidney disease and risk of hypertension. If chronic kidney disease is identified or suspected then a renal diet, combined with strategies to encourage water intake is the preferred method of reducing further stone formation.

Animals with stents and SUBS require regularly ongoing monitoring after their discharge from hospital. Stent placement can be associated with the development of lower urinary tract signs due to bladder irritation. Such signs are usually transient but occasionally warrant removal of the stent after ureteral dilation has occurred. Renal repair can take several weeks and so the degree of chronic kidney disease cannot be accurately assessed until bloodwork 3 months after placement. Repeated imaging should be performed at 3 monthly intervals to check that prostheses are appropriately positioned and that pyelectasia has not worsened, suggesting infection or obstruction. Urine cultures should also be regularly checked. If a problem is identified that stents may require removal and/or replacement, which can usually be achieved via a quick procedure. Thankfully, ureteral dilation means that replacement is often not needed in such situations.

Animals with SUBS in place require delicate handling, particularly with respect to injection administration, restraint and obtaining cystocentesis samples to ensure that damage/displacement leading to urine leakage does not occur. These devices have only been in use for a couple of years and so long term complications are uncertain, but infection is certainly a risk and blockage of the tube with fibrinous material is occasionally seen. Thankfully, a subcutaneous port on these devices allows for easy aspiration of urine from the renal pelvis for culture samples and similarly allows obstructions to be flushed.

Other Ureteral Disease

Ureteral obstruction is by far the most common ureteral disease seen in cats and dogs. Ureteral rupture is occasionally seen secondary to trauma or iatrogenic surgical injury. Treatment of rupture is generally similar to that for obstruction, with stabilisation of the patient followed by surgical repair or re-implanation. Stent placement is often advised following any form of ureteral surgery to minimise the chance of stenosis formation. If primary closure of a rupture or re-implantation is not possible then stent placement and placement of abdominal drains will allow time for the ureter to heal without the formation of strictures or uro-abdomen.

Another disease that is occasionally grouped with ureteral diseases is **"idiopathic renal haematuria"** (IRH), which is particularly common in Boxer dogs. As the name suggests, this is a disease characterized by haematuria of no apparent cause. The aetiology of this condition is not well characterised in dogs. In people, haematuria may be due to "nephritic syndrome" where glomerular defects lead to loss of RBCs into the tubules and subsequently into urine. In dogs it has been suggested that vascular lesions in the renal pelvis or ureter are commonly to blame. Diagnosis of the condition is based on identifying haematuria (not haemoglobinuria) and excluding other common causes (cystitis, neoplasia, calculi etc). Ideally, cystoscopy is performed to identify blood coming from the ureter and to determine which side is affected (although this can vary over time).

Many treatments have been suggested for IRH but it is unclear how successful these are as all reports have small case numbers and the problem can be intermittent, making assessment of success challenging. One study reported success using ACE inhibitors (benazepril – 0.5mg/kg SID) but if it is not a glomerular problem, it is unclear how these would be beneficial. The Chinese herbal medicine Yunnan Baiyo (1-2 capsule per dog q8-12 hours) is used by many internists to treat the condition as it appears to reduce bleeding and promote clot formation. In severe cases, iron deficiency anaemia may develop over time and if this is detected, ferrous sulphate should be initiated. More recently, endoscopic sclerotherapy has been described, where silver nitrate is infused into the affected ureter to cauterize any bleeding lesion. This procedure is technically challenging but has a good reported outcome. As an option of last resort, nephrectomy can be considered in severe cases but this is avoided where possible as the same problem may occur in the contralateral kidney at a later date.

Management of Urinary Tract Bacteria

Introduction

Urinary tract infections (UTIs) are commonly encountered in small animal practice and in many cases they are easily resolved with a short course of empirically selected antibiotics. In many other cases, however, UTIs can present a significant challenge, either failing to respond to antibiotics or repeatedly occurring in patients following cessation of treatment, despite good initial response. This can lead to client and vet frustration, escalation of antibiotics and development of antibiotic resistance problems.

Infection and Colonization

Vets tend to think of the urinary tract as a sterile site and in many instances this is true, but it is not necessarily the case. Benign bacterial colonization is well recognised in human medicine and is increasingly recognised in veterinary medicine, whereby bacteria are identified on urine culture but they are of no apparent clinical consequence.

In many instances, infection is clear. If there is evidence of dysuria, pyuria, and/or haematuria and bacteria are identified in the urinary tract then the presence of bacteria is likely to be pathologic and this should be appropriately tackled.

If bacteria are identified on urine culture and there is no dysuria and no active sediment, then the decision to treat is less clear. The first consideration in such instances should be in vitro contamination of the sample and so repeat culture is warranted if treatment is a consideration. If the bacteria are genuine then their presence must be put in context. For instance, if the patient is diabetic with evidence of insulin resistance then the bacteria must be considered significant and should be treated. Similarly, if the patient has hyperadrenocorticism or renal disease, where the normal inflammatory response may be muted, then one should always err towards treatment.

If the bacteria are picked up on a routine health screening or other such instances and there is no evidence of a problem then treatment of the bacteria may simply lad to colonization with more pathogenic or more resistant organisms and so benign neglect may be recommended. This is particularly true as enterococcus species are often implicated in bacterial colonization of the urinary tract and these species tend to develop antibiotic resistance profiles more readily.

Similarly, colonization of indwelling urinary tract devices (eg catheters) is very common and may be associated with the development of biofilm, making them difficult to eradicate. Often, these bacteria are associated only with the device and not with the urinary tract itself and so evaluation for the presence and nature of any UTI is best done either before placement or after removal of a catheter.

Bacterial Culture

Whenever a UTI is suspected or possible, culture is the gold standard method of investigating this. Microscopy or dipsticks, which look for the presence of bacteria or active sediment, should not be relied upon as haematuria may occur for many other reasons, leukocyte dipstick squares are not meaningful in cats and dogs and infection can occur with minimal active sediment.

If pyelonephritis is suspected then a single negative culture does not exclude this possibility as only intermittent seeding from the renal pelvis to the bladder may occur. A total of 3 cultures is often recommend to investigate this possibility.

Urine cultures are usually a straight forward test but it important to note that contamination of samples may occur and for this reason, cystocentesis is the preferred method of collection. If collection is via another method then quantitative cultures can help to guide the significance of any bacteria identified. It is often recommended that samples are shipped in tubes containing boric acid as this prevents overgrowth of contaminants during shipping. One recent study indicated that boric acid inhibited growth of some significant bacteria following shipping whereas it made minimal difference to the specificity of urine culture. This study concluded that plain tubes are almost always preferable to those containing boric acid for canine urine culture.

If a UTI is strongly suspected but cultures are negative then possible explanations include:

- An incorrect suspicion and the clinical signs are due to another cause.
- A false negative urine culture due to a fastidious organism or the presence of antibiotics in the urine, inhibiting in vitro growth. In this instance repeated culture is advised, with discussion with the laboratory about ensuring freshness of the sample and perhaps extended opportunity to grow. Some labs now offer a urine antibiotic activity test but to my knowledge this assay has not been validated in cats or dogs. Specific cultures or PCR of mycoplasma or ureaplasmas may need to be considered in some cases but these assays are challenging to get reliable results from and the infections are rare.
- Localisation of the bacteria within the mucosa but not the bladder. In this instance biopsy of the bladder wall can be considered to obtain a meaningful culture. This can be done by transurethral passage of flexible biopsy forceps, with cystoscopic, fluoroscopic or ultrasonographic guidance.

Causes of Urinary Tract Infections

UTIs are often classified as simple or complicated. Simple UTIs refer to those for which there is not an underlying cause but the UTI is considered primary, such as seen in young bitches. Simple UTIs generally respond well to short (1 week) courses of an empirically selected broad spectrum antibiotic. Typically involved organisms include staphylococcal species or E.Coli and so potentiated penecillins, cephalosporins or potentiated sulphonamides are often used. A recent study investigated a 3 day course of TMS compared to a 10 day course of cephalexin and in both instances documented a similar instance of cure, with resolution of clinical signs in ~90% of patients at 1 week. Interestingly, that study also documented that microbiologic cure only occurred in ~50% with either treatment and that clinical signs recurred within 30 days in the other dogs, suggesting many apparently simple UTIs are in fact more complicated.

Complex UTIs refer to any UTI where an underlying cause is known that will make it more difficult to resolve or where previous treatment failure has occurred. Causes of urinary tract infections include any anatomic abnormality allowing ascending infections (eg incontinence, diarrhoea, hooded vulva) to occur and most causes of polyuria as they are associated with decreased urinary defences in one capacity or another. Causes of persistence of infection include antibiotic resistance, ineffective access of antibiotics to the affected area or stagnation of urine preventing complete voiding of inhibited bacteria. Within this general list, there are many possible differential diagnoses, ranging from gastrointestinal disease preventing antibiotic absorption, urinary tract calculi, persistent urachus or chronic infection with deep infection of the bladder wall.

Antibiotic resistance should be particularly suspected whenever there is a hospital acquired infection or the patient has recently (in the past 4 weeks) been receiving antibiotics, for any reason.

Assessing Treatment Efficacy

As noted above, any suspicion of UTI is ideally confirmed with a urine culture, with therapeutic choices made on the basis of the antibiogram. In simple UTIs then clinical response may be adequate to assess efficacy. In most complex UTIs then antibiotic treatment for a minimum of 4 weeks is recommended but the basis for this recommendation is unclear. Urine should be cultured 2-3 weeks into this antibiotic course to check that the antibiotic is efficacious. Another culture should be performed 10-14 days after discontinuation of therapy to check whether treatment was successful. Timing of this sample is important as any sooner may be associated with bacterial inhibition and a false negative, without true cure. Any later may be associated with re-infection rather than persistence of the previous infection. If a sample is taken in this window and the same species of bacteria is identified, with a similar antibiogram, then failure to eradicate the infection can be suspected.

If recurrent infection is confirmed then a search for underlying causes and eradication of these should resolve the problem. If persistent infection is documented then this implies failure of antibiotics (if it was also represent at the mid-treatment sample) or a nidus of infection that must be identified and eliminated.

Dealing with Resistant Infections

Antibiotic Strategies

When increasingly resistant antibiograms are seen identified on repeat urine cultures, the temptation exists to reach for “bigger”, newer antibiotics. This temptation should be avoided, instead asking why the problem is occurring and trying to address this. Without doing so, changing antibiotics is unlikely to clear the problem but just lead to further resistance a potential problem for the patient and the population in general.

When antibiotic resistance is identified then I like to ask for MIC information, particularly for amoxicillin-clavulanate and fluroquinolones. These antibiotics are both readily excreted into the urine and generally tolerated at doses much higher than label doses (for enrofloxacin do not exceed 20mg/kg in dogs or 5mg/kg in cats). If an MIC is measurable but in excess of the breakpoint then increasing dosing may overcome this problem. One small study suggests that for E.Coli reported as resistant to co-amoxiclav then its use at 20-25mg/kg TID PO may be sufficient to clear the bacteria in many cases.

If resistance has developed in response to multiple failed treatments then new classes of antibiotics should only be introduced if the underlying cause of treatment failure has been identified and addressed and if the choice of antibiotic is appropriate for small animal patients (eg not drugs such as ticarcillin, impenenum or vancomycin which should be reserved for human use).

Non-antibiotic strategies

In addition to an escalating war of antibiotics and resistance, many non-antibiotic strategies exist for managing UTIs. These can be used in conjunction with antibiotics to aid clearance or as an alternative to reduce bacteria to tolerable levels.

- If the resistance pattern is marked and the clinical signs are negligible (more lie colonization) then consider stopping any antibiotics as this may be associated with the development of a more sensitive colonizing bacteria.
- D-mannose (either purified or in cranberry extract) has been shown to inhibit attachment of E.Coli in vitro and so may help with their clearance in vivo
- Oestrogens have been shown to be beneficial in clearance of UTIs in some post-menopausal women and may also be useful in spayed bitches. It is unclear in the latter case if this is due to effects on the urinary tract mucosa or because subclinical incontinence is being treated.
- Methenamine Hippurate (10mg/kg TID) is a urinary antiseptic that is converted to formaldehyde in acidic urine, preventing bacterial growth. In my experience it is very effective in maintaining urine sterility once antibiotics have suppressed bacterial numbers but it is not very effective at reducing bacterial numbers as a single agent.

It is only effective in acidic urine so cannot be used when significant numbers or urease producing bacteria are present to make the urine alkali and may need to be used with an acidifying diet or other urinary acidifiers.

- In cases of chronic, persistent UTI then biofilm may develop making it difficult to eradicate. Bladder lavage using TrisEDTA has been used in such instances although reports are rare and protocols are not standardised so this therapy must be considered experimental.
- Oral probiotics have been investigated to reduce recurrent infections in female dogs by increasing vaginal lactic acid producing bacteria. Some people anecdotally report success but supportive data is lacking.

Urinary Incontinence

Introduction

Urinary incontinence is a common problem, seen more commonly in dogs than cats and more commonly in females than males, but potentially in any of the above. While not life threatening and often no more than a minor annoyance for the patient themselves, it may be a more significant to concern to the patient if it is associated with urine scalding or recurrent ascending urinary tract infections. More commonly, incontinence represents a significant burden for the pet owner and this should not be underestimated as it commonly may lead to rehoming or euthanasia.

The common causes of incontinence are few but it can still present a significant diagnostic and therapeutic challenge. Incontinence is a common presenting complaint from owners but it is important that a careful history is obtained so that this may be differentiated from polyuria (which may manifest primarily as nocturia), periuria (which is typically behavioural), stranguria or dysuria (which are typically seen with infections, calculi, other causes of inflammation or neoplasia). Polyuria and dysuria warrant particular attention as various diseases may be associated with PU/PD AND incontinence, with one exacerbating the other. Similarly, incontinence of any cause predisposes to ascending urinary tract infections which may significantly worsen the incontinence. In addition to careful history taking, urinalysis, urine culture and serum biochemistry should be considered in every case of incontinence.

Urinary continence and normal micturition relies on the ureters emptying into the bladder, which relaxes as it fills while the urethral sphincters (internal and external) remain occluded. Once bladder stretch receptors are stimulated, the detrusor reflex is stimulated via the parasympathetic nervous system, causing bladder contraction. The internal urethral sphincter (smooth muscle) relaxes under sympathetic control and the external sphincter (skeletal muscle) is under somatic control via the pudendal nerve. Incontinence may be neurogenic or non-neurogenic but neurogenic incontinence is almost associated with more widespread, overt neurologic abnormalities such as paraparesis, decreased tail tone or faecal incontinence. Readers are referred to neurology texts for further discussion of neurogenic causes of incontinence. Common causes of non-neurogenic incontinence, their investigation and management is as follows.

Urine Pooling

Animals may have abnormal development of their urogenital tract such as vestibulovaginal septal remenants or intersex genitals that result in urine pooling distal to the urethra. In these cases urine is typically noted on bedding or after micturition from a young age. Diagnosis is based on identifying the physical abnormality. This may be through digital examination, vaginoscopy or retrograde, positive contrast radiography. Surgical correction is often curative in such cases and may range from balloon dilation or laser ablation of septal remnants to complex reconstructive procedures (rarely performed). Developmental abnormalities are often not isolated and so due consideration should be given to other developmental problems such as portosystemic shunts, ectopic ureters or renal dysplasia.

Ectopic Ureters

Whereas it was once thought that ureteral ectopia was seen exclusively in juvenile animals, it is now recognised as a problem that may present at any age. Ectopia is commonly seen concurrent with hydroureters and hydronephrosis or renal dysplasia. It may also exist concurrent with Urethral Sphincter Mechanism Incompetence (USMI) (see below) further confusing the picture as this may lead to its clinical manifestation being late onset and also result in a partial response to treatment with USMI medication.

Ureteral ectopia may be intramural (common in dogs), meaning that the ureters attach to the bladder in a relatively normal location before tunnelling through the bladder wall to enter the urethra distal to the trigone. Alternatively, ectopia may be extramural, meaning the ureteral insertion is distal to the trigone. Occasionally, multiple ureteral opening have been documented where there is a normal uretero-vesicular junction and then an intramural component with a more distal second opening.

Diagnosis

Diagnosis of ectopia is based on visualisation of the distal opening. Intravenous urograms (IVUs) are commonly used to visualise the ureters. Because the normal ureter is peristaltic, complete filling of the ureter is usually not seen and so multiple exposures are required to identify their termination confidently. Interpretation of IVUs can be challenging and greatly helped by CT, which allows 3D reconstruction of the trigonal region to better understand the anatomy. Because ectopia is often associated with hydroureter, retrograde urethrograms may often lead to distal ureteral filling and a diagnosis of ectopia.

Ultrasound can be used to look for renal and ureteral changes. A confident ultrasonographer will also be able to identify normal ureteral openings in the bladder, making a diagnosis of ecoptia very unlikely. Visualisation of “ureteric jets” (the turbulence caused by urine entering the bladder) can be enhanced by administration of intravenous fluids or furosemide but it remains a very tricky skill to reliably identify 2 separate jets.

Ureteral openings can also be visualised by cystoscopy. Cystoscopy has the advantages that it also allows through evaluation of the vagina and urethra for other lesions and in the case of intramural ectopia, lasers ablation can be used to open up the ureter back to a more normal location as a treatment.

Treatment

If a diagnosis of ectopia is made then treatment options include laser ablation, as noted above, or surgical re-implantation. If ectopia is bilateral then surgical correction is sometimes staged as surgical manipulation of one side leads to significant oedema, complicating surgery for the other side. Incontinence is completely cured only in approximately 50% of cases with some residual incontinence in the others. Possible causes of this include concurrent USMI (treatment of this improves cure rate to ~80%), re-canalisation of the ectopic ureter or bladder hypoplasia due to incomplete filling during development.

Urethral Sphincter Mechanism Incompetence (USMI)

USMI is incontinence due to an inability of the urethra to occlude tightly enough to prevent urine leakage. It is most commonly seen in older neutered bitches but may be seen with any signalment. There are many cited causes of USMI and in reality it is likely to be multifactorial. Although early neutering is often cited as a cause, a meta-analysis of available studies was only able to conclude that neutering prior to 3 months of age was weakly associated with an increase risk.

Diagnosis

Diagnosis of USMI in clinical cases is a diagnosis of exclusion. An intra-pelvic bladder may be seen on radiographs and it is thought that this contributes towards clinical signs by allowing greater pressure to develop in the bladder body compared to the bladder neck when the animal lies down but this finding is not consistent in dogs with USMI and its presence does not mean that the dog has USMI. Urethral pressure profiles are measured in a research setting to investigate USMI and its treatments but this is not practical for the vast majority of clinical cases.

Medical and surgical treatment options exist for USMI exist. Surgical treatment is recommended in young patients to avoid the need for life long therapy or in older patients where medical therapy has been unsuccessful. Surgical treatments may be curative in some instances but in others they augment medical therapy, improving its efficacy and reducing dose requirements.

Medical management

Medical management of USMI is mainly through the use of 2 licensed products. The sympathomimetic phenylpropanolamine (upto 1mk/g PO q8 hours) increases tone in urethral smooth muscles. It is generally well tolerated but may be associated with hyper-excitability and hypertension so blood pressure monitoring is periodically advised and its use is cautioned in patients with CKD, hyperadrenocorticism or other risk factors for hypertension. Because of the potential for tachyarrhythmias to develop, use with concurrent heart disease is also cautioned.

The oestrogen estriol (upto 2mg SID) is the other licensed treatment. This leads to development and thickening of the urethral mucosa and may increase sensitivity to sympathetic stimulation, making it synergistic with phenylpropanolamine. It is also very well tolerated by high doses of oestrogens may be associated with mammary neoplasia or myelosuppression.

Surgical Management

Numerous surgical treatments have been described for USMI and are continuing to be developed, indicating that the perfect treatment has not yet been identified. As noted above, these procedures are sometimes curative but they may also augment medical therapy.

Colposupsension has been performed for many years and is curative in approximately 50% of patients with some benefit seen in another 35%. It has been combined with urethropexy to be curative in upto 70% of cases.

The urethral bulk can be increased by cystoscopic injection of polytetrafluoroethylene or collagen. These procedures are reported to have a very high rate for cure but are typically only temporary, with some return of incontinence within a year in most cases due to redistribution of the agent. Treatments can be repeated if this is the case.

Transobturator vaginal tape inside out has been described in 7 dogs where an episiotomy is used to place tape around the mid-urethra, stabilising it during increased abdominal pressure. The results are encouraging but widespread use of the technique has not been reported.

A commonly applied surgical technique in recent years is placement of an artificial hydraulic urethral sphincter. This involves placement of a balloon around the urethra, linked to a subcutaneous port. In some cases, placement of the device itself leads to fibrosis around the urethra, increasing tone to the point of returning continence. In other cases, the balloon can be gradually inflated using saline (in a cautious stepwise fashion, by a veterinary surgeon) until such a time as urethral tone is adequate to maintain continence. A common misconception with these devices is that they must be inflated/deflated by the owner each time the animal urinates. This is not the case but rather they provide a continuous increase in urethral tone. Similar to SUB devices (see ureteral notes) the ports must only be injected using a Huber needle to avoid causing port damage and leakage. Long term follow-up on these devices is currently lacking but short term impressions are rare. Major complications are rare but minor complications such as dysuria are reported.