ROCKS THAT ROLL NEVER FORGET: UROLITHIASIS – CALCIUM OXALATE AND NEW TREATMENTS

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- Calcium oxalate accounts for 40-50% of all uroliths and > 85% of nephroureteroliths
- **Risk factors** for calcium oxalate formation
  - Increased urinary calcium excretion (hypercalciuria)
    - May result from hypercalcemia, GI hyperabsorption (excessive absorption of calcium from the GI tract), resorptive (excessive calcium resorption from bone), or renal leak (decreased calcium reabsorption from the distal tubule)
  - Increased urinary oxalate excretion (hyperoxaluria)
    - May result from excessive absorption from the GI tract, excessive absorption from the GI tract due to deficiency of *Oxalobacter formigenes* (an enteric bacterial organism that metabolizes oxalate in the GI tract), and possibly from vitamin B6 deficiency (vitamin B6 is involved with oxalate metabolism)
  - In a small study of Miniature schnauzers, GI hyperabsorption appears to be the most likely cause as urinary calcium excretion decreased with fasting
  - Net result of risk factors is urinary oversaturation with calcium oxalate

- **Signalment**
  - **Cats**
    - Middle-aged or older
    - Males = females
    - Long-haired cats; Siamese and Ragdolls tend to form at young age
    - Overweight to obese body condition
  - **Dogs**
    - Middle-aged or older
    - Males > females
    - Small breed dogs (e.g. Miniature schnauzers, Lhasa apsos, Yorkshire terriers, Bichons). Bichons tend to form at young age
    - Overweight to obese body condition

- **Laboratory evaluation**
  - **Aciduria**
  - **Hypercalcemia**
    - 20-35% of cats – usually idiopathic hypercalcemia
    - 4% of dogs – usually primary hyperparathyroidism
  - **Crystalluria – not present in > 50% of cases with active stone disease**
  - **Renal azotemia – associated with nephroureteroliths**

**Management**

- Medical protocols that will promote dissolution of calcium oxalate uroliths are currently unavailable; therefore, uroliths must be removed physically
- **If urethral obstruction** is present, uroliths should be retropulsed into bladder and removed
  - If necessary urethrotomy or urethrostomy may be performed
- **If no clinical signs, then minimize growth** in size and number and monitor for urethral obstruction and clinical signs
- **Removal of calcium oxalate uroliths**
  - **Surgery** – cystotomy and / or urethrotomy / urethrostomy
  - **Catheter-assisted retrieval**
    - Technique can be used to retrieve “sand” or small uroliths
• Uroliths must be small enough to pass through the internal diameter of the lumen of the urethral catheter
• It is important to “jiggle” the urinary bladder to get the sand/uroliths “in motion” in order to facilitate retrieval through the catheter

Description of technique
1. Urinary bladder must be distended
2. As cleanly as possible, pass a urethral catheter. The rounded end of the catheter may be cut off to facilitate retrieval of larger uroliths.
3. Infuse sterile fluid if urinary bladder is not distended.
4. In lateral recumbency or in vertical position, agitate the urinary bladder to “put the uroliths in motion”.
5. Aspirate fluid from urinary bladder through urethral catheter.
6. Repeat if necessary.
7. Radiograph if an attempt was made to retrieve all urocystoliths.

• Complications
  • Occur very rarely
  • Iatrogenic bacterial urinary tract infection is most likely complication that might occur
  • Irritation from catheterization resulting in urethral spasm and lower urinary tract signs may also occur, but they occur rarely

• Voiding urohydropropulsion
  • Voiding urohydropropulsion is a non-surgical technique for removing bladder stones from dogs and cats
  • The technique is based on the idea of using gravity to assist an animal in voiding out stones

• Indications
  • The largest diameter stone must be able to pass through the urethra at its narrowest luminal diameter
  • We have retrieved stones with the following sizes:
    • 10 mm - 7.4 kg F / S K9
    • 5 mm - 9 kg M / C K9
    • 5 mm - 4.6 kg F / S Fel
    • 1 mm - 6.6 kg M / C Fel
  • It will not work in animals that present with urethral obstruction

Description of technique
1. Sedate or anesthetize the patient
2. If the urinary bladder is distended, proceed to #4. If the bladder is not distended, distend the bladder with a sterile physiological solution injected through a urethral catheter that is placed as cleanly as possible.
3. Remove the catheter; if the fluid is expelled prematurely, the vulva or penile urethra can be gently closed.
4. Position the patient so that the vertebral column is approximately vertical to the ground by supporting the animal under the axillae
  • In large dogs, place in dorsal recumbency on a table that can be tilted so that one end of the table is lower than the other
  • Support the dog under the axillae
5. Gently agitate the urinary bladder by palpation to promote gravitational movement of all urocystoliths into the trigone.
6. Apply steady digital pressure to the urinary bladder to induce micturition; once voiding begins, the bladder is more vigorously compressed; the object is to sustain maximum urine flow through the urethral lumen to keep it dilated as long as possible. The idea is to induce a micturition reflex, not to squeeze out the stones. Place a collection container under the urethral orifice or vulva to collect voided stones
7. Repeat steps 2 through 6 if the number of uroliths that are voided is less than that previously detected by radiography; if uroliths detected by radiography were too numerous to count, repeat voiding urohydropropulsion until uroliths are no longer detected in the expelled fluid.
8. If the number of uroliths retrieved equals the number observed by radiography, recover the patient. If there is a question concerning whether all of the uroliths were retrieved, repeat radiography.

9. Animals should be treated for 3 to 7 days with antibiotics due to catheterization. It is also a good idea to recheck a urinalysis and if necessary a urine culture 5 to 10 days after discontinuation of antibiotic therapy.

- **Contraindications**
  - Animals that present with urethral obstruction due to stones
  - Animals that have urethral outflow obstruction such as strictures, tumors
  - Do not perform in animals that have had a cystotomy in the previous 14 days – the bladder incision may not be strong
  - Use caution when applying pressure on the bladder in animals with a bacterial cystitis as this may cause reflux of infected urine up the ureters into the kidneys
  - Animals with other more serious disease should be stabilized or treated

- **Complications**
  - Hematuria occurs commonly
    - In dogs, this usually subsides in a couple of hours
    - In cats, this may persist for 12-24 hours
  - Urethral obstruction may occur if one or more stones are larger than the smallest diameter of the urethra
  - Bacterial urinary tract infection occurs uncommonly, but may occur secondary to poor technique and urethral catheterization
  - Bladder and/or urethral rupture could occur, but is very rare
  - Voiding urohydropropulsion can be used in combination with other treatment modalities for bladder stone disease
    - Stones amenable to medical dissolution can be dissolved to a size where they can be retrieved using voiding urohydropropulsion
    - Stones that are accidentally left behind at surgery may be retrieved with this technique if they are small enough
    - This technique can be done at time of induction for a cystotomy. If all stones are retrieved then the animal can be recovered. If not, then proceed with cystotomy.

- **Cystoscopy and retrieval and laser lithotripsy**
  - Cystoscopy can be performed using rigid cystoscope (in female dogs and cats) or flexible cystoscope (in male dogs)
    - A small “semi-rigid” cystoscope is available for use in male cats; however, due to its size (1 mm) there is no operating channel
    - This permits visualization of the lower urogenital tract
    - Procedures such as biopsy, urolith retrieval, injections, and use of laser can be performed through the operating channel
  - I perform cystoscopy usually with the patient in dorsal recumbency
    - Requires general anesthesia
    - Fluid for instillation through the scope for distention of the lower urogenital tract and for visualization
  - **Cystoscopic retrieval of uroliths**
    - Baskets and graspers can be inserted through the operating channel of the cystoscope for removal of uroliths
      - They must be small enough to be extracted through the most narrow portion of the urethra
  - **Laser lithotripsy**
    - Laser lithotripsy can be used to manage bladder stones
    - Cystoscopy is performed and a laser fiber – usually a Ho:YAG laser – is inserted through the operating channel
    - The laser energy is used to fragment the stone into small fragments that can be retrieved

- **Cystoscopic-assisted cystotomy**
A cystoscopic-assisted cystotomy is similar to laparoscopic removal
- A small incision is made on ventral midline
  - In male dogs, the incision is made just cranial to the preputial reflection
- The urinary bladder is grasped and brought to the incision edge of the linea
- It is sutured to the edges of the linea
- A stab incision is made and a rigid cystoscope is inserted into the urinary bladder
- Stones are retrieved using instruments passed through the cystoscope

**Prevention**
- Calcium oxalate uroliths are recurrent; therefore, preventative measures are warranted
  - @ 8% recurrence at 6 months
  - @ 35% recurrence at 1 year
  - Recurrence increases with subsequent years
  - “Pseudorecurrence” refers to leaving uroliths behind after a procedure is performed
    - Occurs in 15-20% of cystotomies
- With hypercalcemia, potential causes should be investigated.
  - 4% of dogs with calcium oxalate uroliths have hypercalcemia – usually due to primary hyperparathyroidism
  - 20-35% of cats with calcium oxalate uroliths have hypercalcemia – usually idiopathic in nature

**Management**
- The goal of prevention is lower the urinary saturation for calcium oxalate by decreasing urinary levels of calcium and oxalate and by increasing urine volume in order to dilute the minerals
- **Cats with hypercalcemia**
  - Feed a high fiber, mineral restricted diet
  - Administer an alakinizing agent (Potassium citrate)
    - Citrate is an inhibitor of calcium oxalate crystallization and formation
  - In cats with idiopathic hypercalcemia, we have had success feeding a higher fiber diet (Hill’s Prescription Diet Feline w/d) and administering potassium citrate (see below)
- **Cats without hypercalcemia**
  - Feed a diet that induces a diuresis, is mineral restricted, and induces a neutral to alkaline urine pH
  - There are several “multiple use” feline diets formulated to prevent struvite and calcium oxalate
    - Prescription Diet c/d Multicare
    - Royal Canin S/O
    - Purina CNM UR st/ox
  - S/O and UR are higher in sodium than c/d
  - In a study comparing these 3 diets, they each induced a similar degree of urine undersaturation with calcium oxalate albeit by different mechanisms
  - Data from clinical studies is lacking, although in one clinical study of 10 cats with naturally-occurring calcium oxalate bladder stones, consumption of Prescription Diet Feline c/d<sub>old</sub> decreased urinary saturation level to the low end of the metastable range
  - Data from healthy, non-urolith-forming cats have demonstrated decreased urinary saturation with calcium oxalate when cats consumed c/d<sub>old</sub> or S/O
- **Dogs**
  - Feed a diet that is mineral restricted, diuresing, and alakinizing
    - Prescription Diet U/d
      - This is an “ultra-low” protein diet originally formulated for “uremic” dogs
      - It is also low in minerals, has increased vitamin D, has increased B vitamins, and is very alakinizing
    - Royal Canin S/O
      - Royal Canin s/o has been shown to decrease urine saturation with calcium oxalate but no clinical studies have been done
• These diets are higher in fat than maintenance foods.
  • Can feed a higher fiber diet and administer the alkanizing agent, potassium citrate

**Pharmacologic management**

- **Potassium citrate**
  - Citrate is an inhibitor of calcium oxalate crystal formation because it forms a soluble salt with calcium
  - Oral potassium citrate may be beneficial in managing calcium oxalate uroliths because it is a calcium oxalate inhibitor and because it is alkanizing in nature
  - Dosage is titrated to achieve a urine pH of approximately 7.5
  - Calcium oxalate preventative diets contain potassium citrate

- **Vitamin B6**
  - Vitamin B6 increases metabolism of glyoxylate, a precursor of oxalic acid, to glycine
  - Whether vitamin B6 deficiency occurs in adult animals, especially cats, with calcium oxalate uroliths is unknown, but unlikely
    - One study in adult calcium oxalate forming dogs showed lower plasma B6 levels when compared with non-urolith forming dogs
  - Vitamin B6 supplementation is inexpensive and safe and should be considered in pets that have difficult to control uroliths

- **Thiazide diuretics**
  - By inducing a diuresis and decreasing urinary calcium excretion, thiazide diuretic administration may be beneficial in pets with difficult to control calcium oxalate uroliths
    - Thiazide diuretics decrease urinary calcium excretion in human beings, dogs, and cats
    - In cats, thiazide diuretics have been shown to decrease urinary saturation for calcium oxalate in healthy cats only and they appear safe.
    - One 2-week study in calcium oxalate urolith forming dogs demonstrated decreased urinary calcium excretion
  - Diuretic administration may also be associated with dehydration and electrolyte imbalances and should be used cautiously in animals with renal failure

- **Other agents**
  - **Glucocorticoids** have been recommended to decrease blood calcium concentrations in cats with idiopathic hypercalcemia; however, they do so by increasing urinary excretion
  - **Bisphosphonates** have been recommended for cats with idiopathic hypercalcemia; however, no studies have been published