COMPANION OR PET ANIMALS

Medical management of a unilateral obstructive ureterolith in a pet rabbit (Oryctolagus cuniculus)

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SUMMARY
A 5-year-old neutered male French lop rabbit presented with a 6-hour history of stranguria and reduced faecal output. Routine haematology, serum biochemistry, urinalysis and diagnostic imaging were performed. Ultrasonography revealed left renal pelvis and ureter distension due to the presence of a proximal and distal calculus and marked heterogenous bladder sediment. A diagnosis of left hydronephrosis due to ureteral obstruction with a suspected underlying pyelonephritis and hypercalciuria was made. The rabbit was treated medically with intravenous fluid therapy, prokinetic drugs, analgesia, systemic antibiotics and nutritional support, as well as closely monitored by ultrasonographic examination. Three days later, clinical signs and urinary tract findings had resolved. Repeat imaging at 7 days post-treatment was normal. This is the first report of successful medical management of obstructive ureterolithiasis in a pet rabbit. The small ureteral diameter in rabbits and consequent surgical limitations make medical therapy with close serial ultrasonographic monitoring an alternative option to surgical intervention in select cases that are evaluated as stable. Surgical intervention, however, should always be considered in cases that do not respond to medical therapy.

BACKGROUND
This case report is the first to describe successful diagnosis and medical management of obstructive ureterolithiasis in a pet rabbit. Despite urinary calculi being relatively commonly reported in pet rabbits, description of the successful treatment of obstructive ureteroliths is scarce in the literature, and only surgical management has been reported in this species, with variable and sometimes questionable success. Medical management of non-obstructive ureteroliths and renoliths has been suggested in pet rabbits in select cases. A variety of treatment options have been described in dogs, cats and humans for removal of ureteroliths also with varied success. The small ureteral diameter in rabbits and consequent surgical limitations make medical therapy with close serial ultrasonographic monitoring an alternative initial option to surgical intervention in select cases that are evaluated as stable. Surgical intervention, however, should always be considered in cases that do not respond to medical therapy. We believe that publication of this case report will significantly aid veterinarians in practice to better manage and treat similar cases, improving patient welfare and prognosis.

CASE PRESENTATION
A 5-year-old neutered male French lop rabbit presented with a 6-hour history of stranguria and reduced appetite and faecal output. Diet consisted of ad lib quality hay, fresh herbs and greens and 20-g/kg rabbit pellets daily (Burgess Excel Adult Rabbit Nuggets; Burgess Pet Care, Pollution, UK). The rabbit was in good body condition (Body Condition Score 3/5, weight 3.76 kg). Vital parameters and physical exam were within normal limits.

INVESTIGATIONS
The rabbit was admitted for further diagnostic workup. A free-catch urine sample was obtained and analysed by reagent strip and microscopy. All urinary parameters were within normal limits except for a trace of blood. Cytology of the urinary sediment revealed large numbers of calcium carbonate crystals, white blood cells, predominantly neutrophils, with clusters of rod-shaped bacteria, of doubtful significance, as the sample was free catch. A blood sample was taken from the left saphenous vein. Biochemistry revealed elevated creatine kinase (757 IU/l, normal reference interval 59–175 IU/l), lactate dehydrogenase (166 IU/l, normal reference interval 28–101 IU/l) and a lowered inorganic phosphate (0.61 mmol/l, reference interval 1.0–2.2 mmol/l), thought not to be clinically significant. Haematology showed a slightly low packed cell volume (0.309/l, reference interval 0.33–0.45/l) and an elevated neutrophil:lymphocyte ratio, consistent with a stress response, or a superimposed acute inflammatory response. Blood smear evaluation revealed mild non-regenerative anaemia possibly associated with inflammatory disease.

Abdominal B-mode ultrasound examination was performed (MyLab Twice Esacote, Genova, Italy) with microconvex (SC 3123) and electronic linear (LA 435) array probes, with frequencies ranging between 8 and 14 MHz. The exam revealed a right kidney within normal limits. The urinary bladder and urethra contained a moderate amount of echogenic, mineralised sediment. The left renal pelvis was mildly dilated, together with the proximal left ureter (3 mm, reference interval of 1–2 mm), which contained hyperechoic material (3 mm in length), with no acoustic shadowing. The distal left ureter was within normal limits (1 mm).

DIFFERENTIAL DIAGNOSIS
A provisional diagnosis of left proximal ureterolithiasis with partial ureteral obstruction and calcuria was made.

TREATMENT
Supportive care consisted of maintenance intravenous fluid therapy (Hartman’s solution, Vetivex...
11; Dechra, Northwich, UK) at 4 ml/kg/hour via an indwelling marginal ear vein cannula. Analgesia was provided with oral meloxicam (Metacam; Boehringer Ingelheim, Ingelheim am Rhein, Germany) at 0.6 mg/kg every 12 hours, once renal parameters were found to be normal, and oral ranitidine (Ranitidine Oral Solution; Rosemont Pharmaceuticals, Leeds, UK) at 4 mg/kg was given every 12 hours for its prokinetic effect. The following day, the rabbit had eaten, drunk, urinated and defaecated normally.

Following discussion with the owner and since the rabbit was bright, showing no further clinical signs, it was discharged with medical treatment (consisting of oral meloxicam twice daily at 0.6 mg/kg for a further 5 days) and was booked the following week for a repeat ultrasound examination. Husbandry/dietary advice was given to reduce high-calcium foods (by gradually reducing the pelleted portion of the diet and avoiding high-calcium food items such as broccoli, alfalfa hay, clover, watercress, kale and Swiss chard) to increase water intake (by wetting hay, providing plant food with diuretic properties, such as dandelion and plantain, offering fresh grass in the diet, and providing water from both a bowl and a bottle) and to increase daily exercise to help encourage normal urination habits.

OUTCOME AND FOLLOW-UP

Four days later, the rabbit represented with reduced appetite, teeth grinding and stranguria. Clinical examination revealed pain on palpation of the caudal abdomen with an enlarged, firm bladder. Further diagnostics consisted of repeat blood analysis, ultrasonography with guided cystocentesis and radiography. Permission for anaesthesia with urethral catheterisation and bladder flushing was obtained.

Hartman’s fluids were administered via an intravenous cannula at a rate of 4 ml/kg/hour, and the rabbit was medicated with oral ranitidine at 4 mg/kg, oral meloxicam at 0.6 mg/kg and 0.03 mg/kg buprenorphine subcutaneously (Buprecare; Animalcare, York, UK). Biochemistry panel revealed elevation in creatinine level, within the normal limits (148 μmol/l, reference interval of 56–156 μmol/l). Haematology revealed a static anaemia (packed cell volume of 0.301/l, reference interval of 0.33–0.45 l/l). The rabbit was sedated with 5 mg/kg ketamine (Anaestamine, Animalcare) and 0.2 mg/kg midazolam (Hypnovel; Roche, Welwyn Garden City, UK) by slow intravenous injection and induced with 2 mg/kg alfaxalone intravenously to effect (Alfaxan multidose; Jurox Animal Health, Hunter Valley, Australia). It was intubated (3-mm uncuffed tube) using endoscopic visualisation of the glottis and maintained via an Ayre’s T-piece on 5% sevoflurane (Sevoflo; Zoetis, Parsippany, USA) and oxygen (1 l/minute). Heat was provided by a warm water circulating mat, and vital parameters were monitored (rectal thermometer, direct auscultation, Doppler ultrasound, capnography and pulse oximetry). Fluid therapy with Hartman’s solution was continued during the procedure at a rate of 10 ml/kg/hour.

Whole-body dorsoventral and right lateral radiographs (performed using a CR System Axiom HF-300 X-ray Unit with Fuji Computed Radiography System) revealed a 2-mm, triangular, mineralised structure superimposed over the caudodorsal peritoneum and marked radiopaque sediment within the urinary bladder (figure 1). There were no evident calculi within the urethra. Abdominal ultrasound revealed a worsening of the left renal pelvis distension (14 mm, reference interval of 7 mm) associated with pelvic steatitis. Perirenal steatitis was also detected, associated with a mild perirenal effusion. The left proximal ureter was still distended (2.7-mm diameter, reference interval of 1–2 mm, over 25 mm long) until the first proximal calculus (4.2 mm), and then tapered midureter, followed by a further mild distal distension of this ureter with a distal calculus (2.4 mm). Pelvic steatitis and thickening was evident, involving the right kidney. The right ureter was within normal limits. There was a marked heterogenous sediment, partially mineralised and partially mucoid (anechoic clumps) within the bladder (figure 2). A diagnosis of left renal progressive hydronephrosis due to ureteral obstruction with a suspected bilateral pelvonephritis and marked bladder sediment was made.

A sterile urine sample was collected via ultrasound-guided cystocentesis and was sent for urinalysis, culture and sensitivity, and urine protein:creatinine ratio.

A 4-Fr gauge sterile lubricated urinary catheter was passed into the urethra following topical local anaesthetic, and the bladder was flushed using a three-way tap with warm sterile saline (Vetivex 1; Dechra, Northwich, UK) until urine appeared clear. Topical analgesia was provided with 1 mg/kg lidocaine (Lidocaine 2 per cent; Hameln, Gloucester, UK) and 1 mg/kg bupivicaine (Marcain Polypam 0.5 per cent; Aspen, Durban, South Africa) applied directly into the bladder prior to catheter removal.

Maintenance intravenous fluid therapy (4 ml/kg/hour, until the rabbit started eating), 0.03 mg/kg buprenorphine subcutaneously every 6 hours for the first 24 hours, oral meloxicam at 0.6 mg/kg and ranitidine at 4 mg/kg were continued every 12 hours for 5 days postoperatively. Trimethoprim sulfamethoxazole 15 mg/kg orally twice daily (Sulfatrim Oral Drops 96 mg/ml; Virbac, Carros, France) was started pending culture results. Nutritional support was provided with a convalescent diet (Critical Care Diet; Oxbow, Omaha, USA) at 20 ml/kg five times daily for the first 24 hours) until the rabbit fully recovered and started eating. Surgical intervention was planned for the next day, following repeat ultrasound examination.
Ultrasonic reference intervals for renal height, length and width of the urolith and assess any associated urinary tract changes, associated renal changes, locate accurately the anatomical position of the urolith and assess any associated urinary tract changes, such as ureteral distension, bladder wall thickening, renal pelvis distension and hydronephrosis. Its usefulness will also depend on other factors such as machine quality, operator experience and knowledge of rabbit anatomy, as well as patient compliance. Rabbits may be scanned conscious, tilted carefully onto their backs, supporting the spine, for visualisation of the kidneys irrespective of the radiographical view used, and therefore a dorsoventral view (as taken in this case) may be preferred in cases, for example, with respiratory disease, obesity or that are not intubated, where respiratory compromise could occur if placed in dorsal recumbency.

Radiography is useful to demonstrate the presence of a urolith but can prove difficult in determining its exact anatomical location. Ultrasonography is useful to assess and quantify any associated renal changes, locate accurately the anatomical position of the urolith and assess any associated urinary tract changes, such as ureteral distension, bladder wall thickening, renal pelvis distension and hydronephrosis. Its usefulness will also depend on other factors such as machine quality, operator experience and knowledge of rabbit anatomy, as well as patient compliance. Rabbits may be scanned conscious, tilted carefully onto their backs, supporting the spine, for visualisation of the kidneys using a transabdominal paravertebral approach. The ureters may be followed from the renal pelvis retroperitoneally along the dorsal body wall to where they enter the urinary bladder dorsally but may not always be visible unless distended. The internal surface is folded and normal diameter ranges from 1 to 2 mm. The bladder is easily visualised in the caudal abdomen. Ultrasonic reference intervals for renal height, length and width

Figure 2 Images collected at second presentation. (A) Short-axis view of the left kidney. Marked distension of the renal pelvis by anechoic content indicative of pyelectasia. (B) Long-axis view of the left ureter. Moderate distension of the left ureter by similar anechoic content indicative of hydrourereter, with a focal curvilinear intraluminal structure causing marked distal acoustic shadowing. (C) Long-axis view of the urinary bladder. Moderate amount of heterogeneously echogenic sediment within the urinary bladder lumen.

Figure 3 Follow-up images after treatment. (A) Short-axis view of the left kidney. Complete resolution of the pyelectasia. Normal kidney. Renal pelvis arrowed. (B) Long-axis view of the left ureter. Complete resolution of the hydrourereter. Normal ureter.
in rabbits have been reported. In one study, the renal pelvis was not visible in either scanning plane, in all animals scanned, whereas in another it was located centrally as a longitudinal structure. Ultrasonographic findings associated with ureteral obstruction have been well documented in cats and include ipsilateral nephromegaly, pelvic and/or ureteral dilatation and perinephric fluid. Antegrade pyelography is a useful adjunctive diagnostic tool in feline cases and could be considered in rabbits, although this procedure is more invasive.

A variety of treatment options have been described in dogs, cats and humans for removal of ureteroliths with varied success, but reports in pet rabbits are scarce. Traditionally, in feline and canine medicine, surgical intervention has been advocated for management of ureteroliths (primarily calcium oxalate), including ureterotomy, ureteronephrectomy or renal transplantation, but this has been associated with high morbidity and mortality. More recently, minimally invasive techniques such as ureteral stents, subcutaneous ureteral bypass and extracorporeal shockwave lithotripsy have been trialled with varied success. Mortality rates range from 5.6 per cent–8 per cent 1 week poststent or bypass procedure in cats, and success rates are low associated with lithotripsy (30 per cent). Surgical management of ureteroliths in pet rabbits has been rarely described in peer-reviewed literature and is associated with complications such as postoperative adhesions and a high perioperative mortality rate. Recurrence is common.

Medical management of this condition has been described in cats for partial ureteral obstructions using intravenous fluid therapy and diuretics to increase the hydraulic pressure on the ureterolith and promote antegrade movement, and in humans with mannitol intravenous infusions, amitriptyline, glucagon therapy and alpha-adrenergic blockade (prazocin or tamsulosin). One report suggests it should always be considered prior to any surgical intervention in cats. Medical therapy may not be successful in cases where calculus are adherent to the mucosa. It is interesting to note that despite the large size of the ureterolith in this case, it was possible to flush it down the ureter. In human medicine, medical management of ureteroliths (calcium oxalate primarily) with extracorporeal shockwave lithotripsy is highly successful compared with its use in dogs and cats. This technique causes pathology in rabbit models, associated with histopathological changes within the kidney and ureter, both in the shocked kidney and the contralateral kidney, as well as damage to extrarenal tissues such as liver and lung. Secondary bacterial infection is commonly reported in cases of ureteral obstruction in pet dogs (75 per cent) and cats (10 per cent–30 per cent), and therefore, urinary infection and culture are recommended in these cases, with administration of a broad spectrum antibiotic pending results of urine culture and sensitivity. The incidence of secondary bacterial infection in obstructive urinary cases in pet rabbits is currently unknown, and more work is needed to determine the significance of urinary tract infection as a predisposing cause for calculus formation in pet rabbits.

Analgesia is essential in cases of urolithiasis as this is often painful, causing signs of discomfort, such as the stranguria, teeth grinding and inappetence seen in this case. Opioid analgesics such as buprenorphine or morphine should be used in the first instance until renal parameters have been evaluated, and fluid therapy should be commenced to correct deficits. Buprenorphine could have been given on initial case presentation pending results but was not initially deemed necessary based on clinical findings. Following this, non-steroidal anti-inflammatory drugs may safely be instigated, such as meloxicam. In this case, meloxicam was given twice daily as pharmacokinetic studies have indicated a 6-hour half-life following oral administration of this drug and at a slightly higher overall 24-hour dose than 1 mg/kg oral daily dose described by Delk et al and Fredholm et al. A dose of 0.6 mg/kg has been shown to be clinically effective in one study. Clinical analgesic efficacy of this drug at varying dose rates and frequency is, however, greatly debated and more research based evidence is needed.

In future cases, the authors will hospitalise the patient on intravenous fluid therapy and appropriate analgesia and serially monitor the ureterolith via ultrasound examination prior to sending the rabbit home to avoid representation at a later date, as occurred in this case.

Renal dysfunction, despite partial ureteral obstruction and secondary renal pelvis distension, was not evident in this case based on the normal urine protein:creatinine ratio and serum biochemistry results, and therefore, maintenance fluid therapy rates were used to increase diuresis and to ensure adequate renal perfusion and normal urine output. In cases presenting with acute renal failure, immediate fluid therapy should be instigated aimed at correction of dehydration deficits, increasing perfusion and diuresis to correct azotaemia, acid–base imbalances and electrolytes.

This case demonstrates that severe renal changes visible on ultrasonography, which may occur secondary to ureteral obstruction, can quickly resolve on passage of the calculus and may not cause permanent damage to the kidneys. In dogs with full ureteral obstruction for a duration of 4 days, return to completely normal renal function was observed on removal of the obstruction. Surgical removal of the affected kidney may not therefore be necessary, and the authors recommend careful serial monitoring by ultrasound examination in these cases. There is evidence that this situation also occurs in feline cases of ureteral obstruction, with preoperative renal pelvis diameter not being significantly associated with postoperative survival. Long-term management should aim to identify and address any underlying causes. Increasing water intake, regular exercise, weight reduction and diets low in calcium should be considered. Patients should also be regularly monitored for recurrence of the condition.

The potential to treat non-obstructive ureteroliths medically in rabbits has been discussed; however this is the first report demonstrating successful medical management of obstructive ureterolithiasis in a pet rabbit. As this is only a single case report, more work is required to determine the reproducibility of the clinical management described and subsequent outcome in a larger select cohort of rabbits. The small ureteral diameter in rabbits and consequent surgical limitations make medical therapy with serial ultrasonographic monitoring a realistic initial

**Learning points**

- Urinary calculi are relatively commonly reported in pet rabbits and should be considered a differential diagnosis in cases presenting with reduced appetite and faecal output.
- A variety of treatment options have been described in dogs, cats and humans for removal of ureteroliths with varied success, but reports in pet rabbits are scarce and describe primarily surgical management.
- This case report describes a successful diagnosis and medical management of unilateral obstructive ureterolithiasis in a pet rabbit.
alternative in select cases that are evaluated as stable to surgical intervention in this species. Surgical intervention, however, should always be considered in cases that do not respond to medical therapy.

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