Case Report

Cystic Urolithiasis in Dogs: A Case Report and Review of the Literature

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Abstract | A mildly dehydrated dog was presented at Veterinary Teaching Hospital, Paklihawa Campus, Tribhuvan University with symptoms of urinary inconsistency, haematuria, and inappetence. Radiography and ultrasonography revealed the presence of calculus in the urinary bladder. Cystolithotomy was performed and the dog responded to the intervention and recovered uneventfully.

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Introduction

Cystic-urolithiasis is defined as the formation of one or more urine crystalloids (uroliths) in the urinary bladder that may grow to fill the entire cavity. Uroliths are organized organic and inorganic solutes that precipitate around the nidus because of oversaturated urine (Breshears and Confer, 2017). The organic component known as mucoprotein acts as a cementing agent for the formation of calculi (Blood and Henderson, 1997). Cystolithotomy refers to the surgical opening made in the urinary bladder to remove the formed stones from the bladder. The formation of urolith has many etiological factors, and their chemical composition also differs according to the mode of formation (Sharun *et al.*, 2021). However, there are mainly four types of mineral deposits in uroliths: Urate, cystine, struvite (magnesium ammonium phosphate), and calcium (Tion *et al.*, 2015).

The most common mineral deposits are struvite and calcium-containing urolith (Low *et al.*, 2006). The etiology of struvite urolithin dogs is due to the concurrent urinary tract infection (Tiruneh and Abdisa, 2017). In addition, the urethra of a female is shorter than that of a male, which leads to more possibility of infection to reach the bladder from the urinary tract and vagina. This implies a higher incidence of cyst urolithiasis in females than males

(Tiruneh and Abdisa, 2017).

This case report explained the successful diagnosis and treatment of cystic-urolithiasis at the Veterinary Teaching Hospital (VTH) of the Institute of Agriculture and Animal Science (IAAS), Tribhuvan University, Nepal. A Japanese Spitz bitch with a reasonably big-sized urolith was successfully treated.

Case history

A seven years old intact female Japanese Spitz dog named Toffy was presented to VTH of IAAS on 20th November 2019 with complaints of inappetence for four days and dullness, depression and, hematuria for three days. The bitch was vaccinated against DHPPL (canine distemper, hepatitis, leptospirosis, parvovirus, and parainfluenza) and rabies, the recommended ones in this area. It was fed family meals supplemented with bones and sometimes commercial pet food. Toffy was kept under close observation, and further clinical as well as physical examination was performed. The physical examination revealed normal rectal temperature, heart rate, and respiratory rates of 101.2 F, 124 beats/min, and 22 cycles/min, respectively (Table 1). Observed clinical findings were hematuria, abnormal gait, urinary inconsistency, abnormal urinating position, and dysuria. Likewise, abdominal palpation revealed a hard mass in the bladder.

Table 1: *Physical parameters of the dog.*

Parameters	Test result	Reference value (Bukowski and Susan, 2011)
Heart rate	124 beats/min	70-120 beats/min
Respiration rate	22 cycles/min	18-34 cycles/min
Rectal temperature	101.2° Fahrenheit (F)	100.2°F-103.8°F
Dehydration	Mild: Skin tenting time	Normal 2 sec

Diagnosis

Based on the radiographic (Figure 1) and ultrasonography (Figure 2) findings, supported by the haemato-biochemical alterations (Table 2), the case was diagnosed to be a fairly large size cystic-urolithiasis and surgery performed by experienced veterinarians.

Treatment

Given the size and condition of Toffy, immediate surgery was recommended, and she was kept under supportive therapy, including intravenous (IV) normal saline and some essential nutrients of vitamins in the 250 ml of normal saline injection.

Figure 1: *Abdominal radiograph (lateral) showing large uroliths inside the urinary bladder of the dog.*

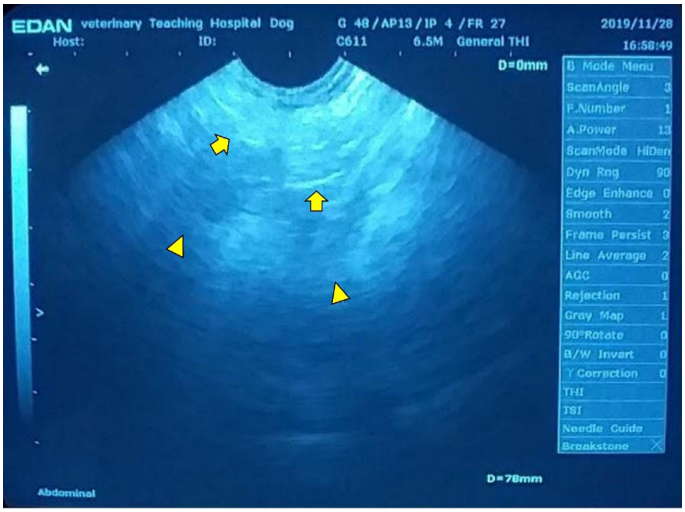

Figure 2: *Hyperechoic focal echogenicity (arrows) creating distal acoustic shadow (arrowheads) in the dependent portion of the bladder, confirming the presence of cystic calculus.*

Table 2: *Haemato-biochemical parameters of the dog.*

Parameters	Test result	Reference value (Fielder, 2015)
White blood cells (WBC)	36.2×10^9/l	$5\text{-}14.1\times10^9$/l
Lymphocytes (%)	25	8-21
Monocytes (%)	10	2-10
Granulocytes	29×10^9/l	$4.0\text{-}12.6\times10^9$/l
Hemoglobin (g/dl)	14.2	11.9-18.9
PCV (packed cell volume) %	42.7	35-57
ALT (alanine aminotransferase) (U/l)	36	10-109
Total Bilirubin (mg/dl)	0.1	0-0.3
Total Protein (g/dl)	7.0	5.4-7.5
Albumin (g/dl)	2.9	2.3-3.1
BUN (mg/dl)	75	8-28
Creatinine (mg/dl)	2.7	0.5-1.7

Anesthesia protocol

The animal was fasted for 12 hours, and the water was withheld three hours before surgery.

Sedation: Xylazine @ 1mg/kg slow IV.

Pre-operative medication: Pre-operative analgesia: Meloxicam @ 0.2 mg/kg IV; Pre-operative antibiotics: Ceftriaxone@ 20mg/kg IV.
Induction: Diazepam: Ketamine (1:1) @ 1ml/10kg IV.

Maintenance : Diazepam: Ketamine (1:2) ratio IV.

After Toffy was sedated, the surgical site was shaved and prepared for aseptic surgery from the umbilicus to the cranial brim of the pelvis using 2% Chlorhexidine and 70% methyl alcohol. The animal was placed in the dorsoventral position, and the limbs were tied to the surgical table. The sterile fenestrated drape was placed over the incision site to create a sterile field.

A ventral midline abdominal incision was made through the skin and Linea alba. The urinary bladder was located, which was distended and congested (Figure 3a). Next, a stab incision was made into the base of the bladder and extended cranially and caudally with scissors. The bladder was found to be distended with calculus (Figure 3b), and three large calculi were removed (Figure 3c). Each calculus had approximate dimensions of 2×3×2 cm and weighed 35 grams. After removing the calculi, a catheter was passed through the bladder to the urethral opening to check the patency (Figure 3d). However, obstructions were not evident. Then, the bladder was first flushed with normal saline, followed by a diluted iodine solution.

The bladder was sutured in double-layer using Vicryl 3-0 in Cushing followed by a Lembert suture pattern including serosa, muscularis, and submucosa avoiding the mucosa (Figure 3e). The bladder incision was apposed in an inverted fashion, and a leak test was performed. Then, muscle and subcutaneous layers were sutured with Vicryl 2-0 in a simple continuous pattern separately, whereas the skin was sutured with Nylon 2-0 in a simple interrupted pattern (Figure 3f). Vital signs like heart rate, respiration rate, and rectal temperature were monitored throughout the surgery. The dog recovered from anesthesia after 15 minutes of completion of surgery.

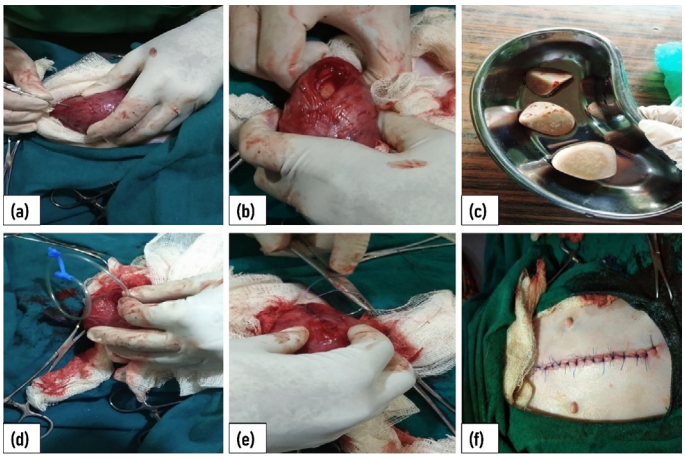

Figure 3: *Image showing the steps of cystotomy in a dog. Distended bladder incised at the base of the bladder (a), Bladder distended with calculi (b), Removed three bladder calculi (c), Inserting catheter from bladder to urethral opening (d), Double-layer suturing of the bladder (e), Skin closure by simple interrupted pattern (f).*

Postoperative care

The patient was kept on postoperative antibiotics (ceftriaxone @20mg/kg), pain medication (meloxicam @ 0.2 mg/kg) for a week, and herbal medication Cystone tablets and Neeri tablets (urinary antiseptic and calculi dissolver). In addition, the surgical site was checked regularly for any swelling and discharge with a fresh dab of iodine solution.

The owner was advised to restrict the dog's movement, keep it clean, and provide a simple, balanced diet of boiled plain chicken with steamed rice or mashed carrot with a sprinkle of salt to induce thirst and production dilute urine. Toffy showed remarkable progress and the wound healed without any complications, and the skin sutures were removed on the 14th postoperative day.

Results and Discussion

VTH, IAAS, located close to the international with India in the Nepalese city of Sidharthanagar (gateway of Lumbini), is a relocated facility. It is now the center of referral for Western Nepal and part of India. The population of pet dogs in campus surroundings is fairly healthy. Besides the college animal farm, community dogs, cows, and rural farming communities are the primary beneficiaries of VTH's services. Complicated cases, including urolithiasis, can be handled comfortably. Urolith can develop in the kidney, ureter, bladder, or urethra and are referred to as nephrolith, ureterolith, urocystoliths, and urethroliths, respectively. Early detection of urolithiasis can be treated with dissolution therapy where clinical signs

are mild. Haematuria, polydipsia, polyuria, dysuria are the common clinical signs of cystic-urolithiasis in dogs. However, a definitive diagnosis cannot be made based on history and clinical signs. This emphasizes that diagnostic imaging is crucial for confirmative diagnosis of urolithiasis.

A hematological profile showed leukocytosis (36.2×10^9/l), which reveals the presence of infection. A marked increase in the blood urea nitrogen (BUN) and creatinine level correlates with partial or complete obstruction of urine due to calculi in the bladder. A plain abdominal radiograph was done, which revealed radio-opaque calculi in the urinary bladder (Figure 1). The ultrasonographic image revealed the subtly increased opacity over the dependent part of the bladder. Hyperechoic focal echogenicity creating distal acoustic shadow in the dependent portion of the urinary bladder can be noticed in the image (Figure 2). Surgery (cystolithotomy) was performed with minimal damage to the surrounding structure. The mechanism of each calculi formation is different, and it varies with etiological factors; however, the physicochemical mechanism for every urolith is the same as shown in Figure 4.

Figure 4: *Steps involved in lithogenesis (supersaturation, nucleation, crystal growth, and aggregation irrespective of crystal nature) (Espinosa-Ortiz et al., 2018).*

Factors associated with lithogenesis are:

1. Crystal formation depends on various factors such as supersaturation of urine, urine pH, absence or presence of crystallization inhibitors (nephrocalcin, osteopontin, crystal adhesion inhibitors, chondroitin sulfate, heparin sulfate, fibronectin) or promoters (collagen, hyaluronic acid, myeloperoxidase, nucleolin) (Aggarwal *et al.*, 2013).
2. Hypercalciuria is the most common pathophysiologic condition associated with calcium uroliths patients (O'Kell *et al.*, 2017) and oxalate concentration in urine enhances it (Bartges and Callens, 2015). High sodium intake reduces calcium reabsorption and increases calcium concentration in urine. Excessive protein use decreases the urine pH, ultimately increasing calcium through bone turnover and reducing tubular calcium reabsorption. Vitamin C helps in calculi formation via the conversion of ascorbic acid into oxalate (Butterweck and Khan, 2009).
3. Medicine that is insoluble in urine induces the precipitation of urine. For example, Sulfadiazine, ciprofloxacin, acyclovir, and oral sodium phosphate-containing preparations are known to cause crystal nephropathy (Yarlagadda and Perazella, 2008).
4. The urate crystal is formed due to liver disease or congenital defects in the metabolism of purines (Dalmatians and English Bulldogs) (Bartges and Callens, 2015).
5. The high concentration of cysteine amino acids in urine leads to cystine crystals (Espinosa-Ortiz *et al.*, 2018).
6. Urine pH influences crystal precipitation and calculi formation. At low pH, ammonium ion gets accumulated, but phosphate concentration is reduced. Moreover, at high pH, phosphate concentration is high, but ammonium ion is low. Therefore, struvite uroliths are formed only in the alkaline urine, while urate and cystine calculi are associated with acidic urine (Breshears and Confer, 2017).
7. Urinary tract infection (UTI) with urease producing bacteria, as the kidney cannot form struvite crystal (consist of ammonium, magnesium, and phosphate ion), produces urease that leads to urine alkalinization as well as increased concentration of ammonium and phosphate, ultimately forming uroliths (Coe and Parks, 2016).

The presence of calculi in the urinary tract (UT) results in obstruction, which leads to anuria. Uroliths act as foreign bodies that initiate irritation and damages the epithelium of UT. Chronic cases of urolithiasis may result in renal failure. The severity of pain varies from mild to severe, and it ends when there is no further obstruction in the flow of urine (Coe and Parks, 2016). The presence of calculi in the bladder causing hematuria and dysuria.

Differentiation of different crystals may be difficult as they vary in shape, size, and structure. However, crystals can be identified accurately by polarization microscopy, x-ray diffraction, and infrared spectroscopy (Coe and Parks, 2016). CT scan also is used for uroliths identification (Espinosa-Ortiz *et al.*, 2018). Urinalysis can be done for the detection of crystalluria. However, it does not present the definitive diagnosis for urolithiasis but can suggest

urine supersaturation (Bartges and Callens, 2015). Evaluation of the chemical nature of urine by estimating urine pH can also act as a practical measure. Urine with a pH of less than seven favors cystine, calcium oxalate, and purine crystal formation, while pH greater than seven favors struvite crystal growth (Bartges and Callens, 2015). In the case of infection-induced struvite crystal, urine culture and sensitivity test may additionally act as diagnostic as well as therapeutic tools, and measurement of urea, creatinine, minerals, and electrolytes may assist in diagnosis (Bartges and Callens, 2015). According to Houston *et al.* (2004), struvite uroliths were most common in female dogs, whereas oxalate uroliths were common in male dogs. Calcium oxalate urolithiasis was more common in shorthair, neutered dogs, male dogs, intact male dogs, and small breed dogs. Male dogs had the highest levels of cysteine and urate. Urate urolithiasis was most common in Dalmatians (Burggraaf *et al.*, 2021). In a study in Mexico, male dogs over the age of six and big breeds, particularly Labradors and Golden retrievers, were at high risk of canine silica urolithiasis (Mendoza-López et., 2020).

The line of treatment may vary with crystal nature, size, degree of obstruction, and location. However, some of them are as follows:

Surgical management

Surgical therapy for canine urolithiasis is successful, according to studies, with a cure rate of over 87.5 percent (Sodhi *et al.*, 2021). Every urolithiasis patient does not require surgery; however, the presence of large size, increased number of calculi, and unresponsiveness to therapy suggest surgery (Bartges and Callens, 2015; Kumar *et al.*, 2019). Open surgical procedures such as cystotomy, urethrotomy can be done for urolithiasis. Anatrophic nephrolithotomy is a surgical procedure with a longer recovery period than endoscopic methods, where the elimination rate is 80-100%. Robotic surgery is also successful for calculi removal with high efficacy (Espinosa-Ortiz *et al.*, 2018). Therefore, minimally invasive techniques have replaced the open surgical procedure.

Minimal invasive techniques

Extracorporeal shock wave lithotripsy (ESWL), percutaneous nephrolithotomy (PCNL), ureteroscopy with laser lithotripsy is used to break and remove the stone fragment (Espinosa-Ortiz *et al.*, 2018).

ESWL is a non-surgical approach where shock waves are used for fragmentation of calculi, and it is useful only for small calculi. The success rate depends on wave frequency, stone composition, size, and location. Damage to the surrounding structure is reported, and mostly renal hemorrhage is seen with hypertension and diabetes mellitus for the long term (Butterweck and Khan, 2019). Ureteroscopy is an endoscopic procedure used to treat lower ureteral stones and can be used safely for patients with coagulopathy disease (Espinosa-Ortiz *et al.*, 2018). PCNL is mainly used for large stones in renal with ultrasonography or fluoroscopy support. After the passage of the endoscope, the urolith can be broken with the help of laser, ultrasound, or pneumatic energy. The stone elimination rate is higher in PCNL as compared to internal surgery after an operation. However, complications such as infection, damage to the surrounding structure, hemorrhages are observed (Espinosa-Ortiz *et al.*, 2018).

Medical management

Struvite crystal: Treatment of sterile struvite (without infection) can be done by consuming dissolution and prevention diets that have limited amounts of magnesium, phosphorus, acidifying diets, and increased water intake, and in case of infection-induced struvite, appropriate antibiotics should be used (Sodhi *et al.*, 2021; Bartges and Callens, 2015).

Calcium oxalate crystal: Hypercalciuria can be reduced by bicarbonate administration. Calcium oxalate should be removed physically because a dissolution diet doesn't work. So, prevention strategy includes reducing calcium and oxalate concentration in urine by using urine alkalizing agent, increasing urine volume, increasing inhibitors (citrate, magnesium, pyrophosphate, nephrocalcin) concentration and function (Bartges and Callens, 2015). Thiazide diuretics can be used due to their hypocalciuric action. Also, potassium citrate increases the pH of urine and citrate, which has an inhibitory effect on calcium oxalate crystallization (Butterweck and Khan, 2019).

Urate crystal: Uric acid is the metabolic product of purines. Dissolution therapy includes an alkalizing agent, purine limited diet, xanthine oxidase inhibitors, allopurinol with the proper functioning of the liver. However, without the proper function of the liver, such treatment may be inefficient (Bartges and Callens, 2015).

Herbal treatment

Either in the use of medicine or surgical approach, there is the presence of side effects. So, herbal use may have a beneficial effect on it. For example, extract from the herb *Herniariahirsuta, Phyllanthusniruri, Dolichosbiflorus*are used to treat calculi through their inhibitory effect on the lithogenesis process since they interfere with calcium oxalate crystallization (Butterweck and Khan, 2019).

Increasing urine volume is the major preventive approach for every crystal because it increases urination frequency, decreases crystal growth and aggregation time, and dilutes solutes in urine (Bartges and Callens, 2015). Treatment protocols for urolithiasis are well advanced. However, its formation cannot be eradicated because of broad etiology, and it also varies with individuals. A lot of research was done on urolithiasis but couldn't cover every etiology and its mechanism. Therefore, further study can be done on it.

Nutritional management of urolithiasis

The goal of urolithiasis dietary therapy is to dissolve calculi (struvite, urate, cystine) and/or limit the risk of recurrence. Dietary treatment for mixed or compound stones should be dependent on the salt content of the nidus. When it comes to any form of stone, the goal should always be to promote urine dilution, which is best accomplished by giving high-moisture meals whenever feasible. Controlling the quantity of crystal precursors in the food as well as the pH of the urine is critical for all stones, while the case for calcium oxalate is less clear (Queau, 2019).

Conclusions and Recommendations

The occurrence of urolithiasis relies upon various etiologic factors. Each crystal has a distinct etiological mechanism of formation and chemical composition. Furthermore, the therapeutic and preventive measures additionally fluctuate with crystal composition and mode of formation. Concisely, the predisposing elements can be stated as kidney disease, urinary infection, medication, and congenital disorder. With the assist of appropriate diagnostic testing and surgical intervention, the dog recovered well. However, there would be continually the threat of reoccurrence of stone. Recurrence can be prevented by measures like using a urinary alkalizer or acidifier according to the nature of the crystal. Moreover, increased water intake along with regular veterinary consultation is beneficial. Mishandling by quacks and most likely excess medication could have played a part in the genesis of the problem in the first place. Hence, IAAS needs to support VTH in its outreach activities to sensitize pet owners on ethical and proper care of pet animals from the welfare and prevention of zoonotic disease perspectives.

Ethical animal research

The dog owner signed a release form to consent to perform clinical study and surgery on his pet dog. The study was approved by Veterinary Teaching Hospital (VTH), Paklihawa Campus, Institute of Agriculture and Animal Science (IAAS), Tribhuvan University (TU).

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Novelty Statement

This case report describes the successful diagnosis and treatment of cystic-urolithiasis along with a detailed literature analysis.

Author's Contribution

Conceptualization C.R., manuscript preparation C.R., D.S., S.K. (Shanti Kunwar), and R.N., review and editing C.R, D.S., B.S, S.K. (Sharun Khan), K.K, and DK.S. All authors have agreed to the final version of the manuscript.

Conflict of interest

The authors have declared no conflict of interest.

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