Medicinal Dissolution of Nephroliths in a Cat.

A clinical report submitted in partial satisfaction of the requirements for the degree of

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Table 1 : List of Abbreviations

Abbreviations	Meaning
ALP	Alkaline phosphatase
BUN	Blood urea nitrogen
CVASU	Chattogram Veterinary and Animal Sciences University.
g	Gram
g/dl	Hemoglobin
Hb	Hemoglobin
mg/dl	Milligrams per deciliter
mg/kg	Milligrams per kilogram
ml	Milliliters
pH	Potential of Hydrogen
SGOT	Serum Glutamic Oxaloacetic Transaminase
SGPT	Serum glutamic pyruvic transaminase
TTPHRC	Teaching and Training Pet Hospital and Research Center
u/l	Units per liter
USG	Ultrasound
UTI	Urinary tract infection

Abstract

Nephrolithiasis is a relatively rare clinical disorder in dogs and cats. Only 5-7% of feline uroliths are diagnosed as nephroliths when they are examined in the laboratories. In dogs and cats, the majority of nephroliths appear to be clinically asymptomatic and do not need treatment. However, some nephroliths do develop complications and cause problems. There are several treatment options for nephrolithiasis, including lithotripsy, surgical removal, and medical dissolving. Animal nephroliths may be removed surgically via nephrolithotomy, pyelolithotomy, and nephrectomy. Even though quick nephrolith removal through surgery has been successful, there are a number of disadvantages. For these disadvantages, medical dissolution of nephroliths can be first option. If medicinal dissolution is not effective, then surgery can be considered. The objective of this report is to describe the diagnosis and medicinal dissolution of nephroliths in a Persian cat. A 3-year-old Persian cat was brought to the TTPHRC with a history of weight loss, blood loss and saliva secretion. Physical examination revealed abnormal right kidney during palpation. Then in the ultrasonography, there was presence of acoustic shadow. Abdominal radiography revealed radiodense nephroliths at the same time. It could be infection-induced struvite as struvite results in relatively large radiodense nephroliths, same is this case. Conservative medical therapy was considered. The nephroliths were dissolved with a calculolytic, acidifying diet and antibiotic was given as adjunct.

Keywords: Cat, Nephroliths, Dissolution, Litholytic diet.

Chapter 1: Introduction

Nephrolithiasis is a rare condition in dogs and cats. When feline uroliths are referred to laboratory for examination, only 5-7% of them are nephroliths. The true incidence of nephroliths may be higher because many animals with nephroliths don't exhibit any symptoms (Osborne et al., 1995). Therefore, it appears that the majority of nephroliths in dogs and cats are clinically asymptomatic and do not need treatments (Lulich et al., 2016; Ross et al., 2007). The clinical signs and history of animals with nephroliths depend mostly on the level of renal pelvic obstruction and hydronephrosis, as well as the presence or absence of infection (Osborne et al., 1995).

Asymptomatic nephroliths are occasionally detected during the examination of various abdominal diseases by abdominal radiography or ultrasonography (Finco et al., 1970). However, some nephroliths cause complications and show problems like urinary flow obstruction from hydronephrosis or ureteropelvic junction obstruction, renal parenchyma compression from stone growth, discomfort, or they may act as a nidus for infection, so that they can cause recurrent urinary tract infections (Lulich et al., 2016; Berent and Adams, 2015).

Laboratory results have shown significant diversity in nephrolithiasis patients (Carter et al., 1993; Osborne et al., 1995). Medical dissolution, surgical removal, and lithotripsy are available management options for nephrolithiasis (Osborne et al., 1995). Nephrolithotomy, pyelolithotomy, and nephrectomy are surgical techniques that may be useful for removing nephroliths in animals (Osborne et al., 1995).

Surgery has considered a useful method for removing nephroliths right away, but it has a number of disadvantages, including the frequent recurrence of kidney stones persists despite surgery because of underlying reasons; certain health issues of a patient that make general anesthesia or surgery more harmful; and being unable to completely remove all nephroliths or nephrolith fragments by surgery. Thus, surgical treatments for the management of nephroliths, such as nephrotomy and pyelotomy, have been largely replaced by the adaptation of minimally invasive procedures from human to veterinary

patients (Cléroux, 2018). Besides, some pet owners are prepared to accept medical treatment but may not agree with surgical treatment for their pets. So, medical dissolution of nephrolith may be considered for these factors as well as others (such as asymptomatic renoliths) (Ross et al., 1999).

The purpose of medical treatment for nephroliths is to facilitate their dissolution. For treatment to be effective, urine must be undersaturated with calculogenic crystalloids. It can be achived by enhancing crystalloid solubility in urine, enhancing urine volume in which the crystalloids are dissolved or suspended, and decreasing the amount of lithogenic crystalloids in urine (Ross et al., 1999). For struvite, cystine, or urate nephroliths, conservative medical therapy may be taken into consideration. Struvite stones may dissolve when a calculolytic, acidifying diet (such as Hill's Prescription Diet s/d, Hill's Pet Nutrition, Inc., Topeka, KS) is given together with antibiotic treatment (Osborne et al., 1995).

In this case, there was no evidence of urinary outflow obstruction in this feline patient. Moreover, the radiography showed big rediodense kidney (right) stones. Which indicated that the patient's nephroliths were made of struvite due to an infection., mainly because struvite caused by infections makes quite big radiodense nephroliths. That is why the initial choice was medical dissolution of nephroliths with a calculolytic, acidifying diet together with antibiotic treatment. On that note, the objective of this report is to describe the diagnosis and medicinal dissolution of nephroliths of this Persian cat.

Chapter 2: Case Presentation

A 3-year-old non-spayed female Persian cat named “Shadow” was referred to the Teaching and Training Pet Hospital and Research Center (TTPHRC), Purbachal, Narayanganj under Chattogram Veterinary and Animal Sciences University (CVASU). The cat had been undergoing weight loss, blood loss and saliva secretion for two months. The cat was cachectic and very weak. Previous history included loss of appetite. But, there was no history of vomition. The defecation and urination were normal. Deworming and vaccination also were being done previously. The housing system was intensive in nature. The mucus membrane was pale. The rectal temperature was 101.5°F (normal range between 100.5°F and 102.5°F) , pulse rate was 130 per minute (normal range between 120 and 160 per minute), and respiration was 24 breaths every minute (normal range between 15-30 breaths every minute).

In urinalysis report, leucocytes were found in trace amount. The urobilinogen was found to be normal. The total protein was above 30 mg/dl. The pH was mild acidic. RBC was found in trace amount. The specific gravity was 1.020. Ketone, bilirubin, glucose and nitrate were absent in the urine.

The biochemical report revealed that the glucose was 165.3 mg/dl which was within reference value. The total protein was 8.9 g/dl which was higher than the reference value whereas the albumin was 2.4 g/dl which was less than reference value. The serum creatinine was 1.6 mg/dl which was higher than reference value and BUN was 26.2 mg/dl which was within reference value. The value of SGPT, SGOT and ALP were 46.3 u/l, 21.2 u/l and 22.8 u/l respectively, all were within normal ranges.

A palpable abnormality in the right kidney was found. Then in the ultrasonography there was presence of acoustic shadow in ultrasonography. Abdominal radiography revealed radiodense nephroliths at that time. Urinalysis of a cystocentesis urine sample revealed unconcentrated, mildly acidic urine with symptoms of inflammation (hematuria, pyuria, and proteinuria). General abdominal radiographs showed that the dimensions, shape, and echogenic texture of liver were within normal limits. Renal pelvis was dilated during abdominal ultrasonography, which is consistent with the size of the nephroliths. The lower urinary tract was found to be normal.

These all evidence of the nephroliths' mineral makeup of this patient indicates towards infection-induced struvite. Mainly, as struvite caused by infections makes quite big radiodense nephroliths. Medical dissolution was the first considered approach as there was no sign of a urine outflow blockage. A litholytic diet as well as amoxicillin and clavulinic acid (20 mg/kg body weight, Tab. Moxaclav® - Square Pharmaceuticals Ltd.) were the main components of medical treatment designed to cause struvite nephrolith dissolution.

Following radiological evidence of nephrolith dissolution, the owners were advised to continue the medication and feed just the recommended diet for one month. Serial evaluation of radiographs, urinalyses and urine cultures, serum analytes, and hemograms at intervals of four weeks were used to assess the therapeutic safety and effectiveness. The owners were advised to continue using the litholytic diet and amoxicillin - clavulanic acid for ongoing therapy.

Chapter 3: Result

A Persian can was referred to the TTPHRC, CVASU. In physical examination a palpable abnormality in the right kidney was found. Then in the ultrasonography there was presence of acoustic shadow. Abdominal radiography revealed radiodense nephroliths at that time. The tentative diagnosis was struvite nephroliths. The initial choice was medicinal dissolution of nephroliths with a calculolytic, acidifying diet together with antibiotic treatment. To continue monitoring the nephroliths' breakdown, monthly abdominal radiographies were taken. Twenty weeks after the start of the treatment, there was no longer any radiographic indication of nephroliths. The litholytic diet and antibiotics were continued for an additional month, at which time, abdominal radiographs confirmed the dissolution of the nephroliths. Polyuria and the excretion of dilute urine were related to the nephrolytic diet.

In urinalysis report leucocyte was absent. The nitrate was not found. The urobilinogen was found to be normal. Protein was above 30 mg/dl. The pH was 5.0. RBC was not found. The specific gravity was 1.025. Ketone was not present. No bilirubin was present and glucose was also absent.

The biochemical report revealed that calcium was 7.0 mg/dl and phosphorus was found 4.1 mg/dl, both were within reference values. The glucose was 89.5 mg/dl which was within reference value. Total protein was 8.3 g/dl which was also within reference value this time. The albumin was increased and it was 3.8 g/dl which was within the reference value. The serum creatinine was decrease and it was found 1.4 mg/dl which was within the reference value and BUN was 18.0 mg/dl which was also within reference value. The value of SGPT, SGOT and ALP were 45.5 u/l, 56.7 u/l and 27.3 u/l respectively, all were within reference values.

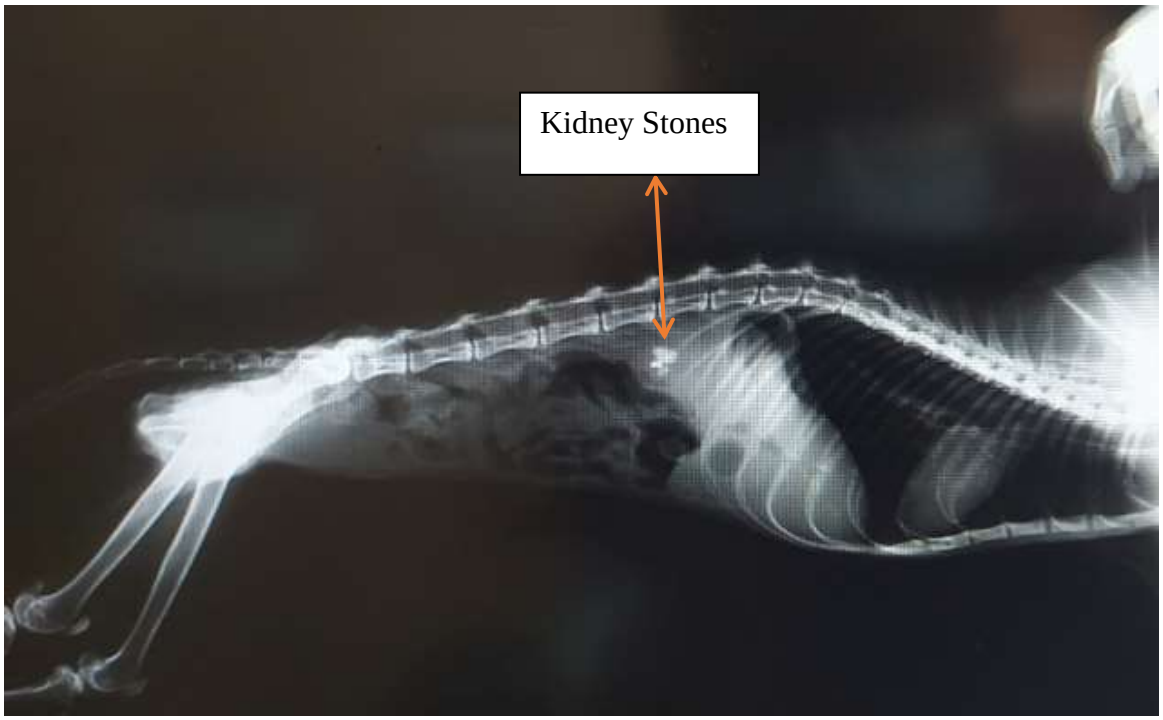
After cessation of antibiotic treatment, the cat was put on a maintenance diet that increases the production of acid urine. Alkaline phosphatase, alanine aminotransferase, and blood urea nitrogen levels all dropped four weeks after the maintenance diet was initiated. The cat was observed for a further 16 weeks at monthly intervals with abdominal radiography, serum chemical profiles, hematological, urinalysis, and quantitative urine cultures. No clinical abnormalities were observed at that time.

Table 3.1 : Urinalysis report of a Persian cat with nephrolithiasis before and twenty weeks post-treatment.

Urinalysis Report		
Parameters	**Test Result**	
	Before Treatment	**After Treatment**
Leukocytes	Trace	Negative
Nitrite	Negative	Negative
Urobilinogen	Normal	Normal
Protein	30+	30+
pH	6.7	5.0
Blood	Trace (10)	Trace(10)
Specific Gravity	1.020	1.025
Ketone	Negative	Negative
Bilirubin	Negative	Negative
Glucose	Negative	Negative

Table 3.2 : Biochemical Report of a Persian cat with nephrolithiasis before and twenty weeks post-treatment.

Biochemical Report			
Parameters	**Reference Value***	**Test Result**	
		Before Treatment	**After Treatment**
Glucose	50 – 170 mg/dl	165.3 mg/dl	89.5 mg/dl
Total Protein	5.2 – 8.8 g/dl	8.9 g/dl	8.3 g/dl
Albumin	2.5 – 3.9 g/dl	2.4 g/dl	3.8 g/dl
SGPT	10 – 100 u/l	46.3 u/l	45.5 u/l
AST/SGOT	10 – 100 u/l	21.2 u/l	56.7 u/l
ALP	10 – 50 u/l	22.8 u/l	27.3 u/l
Serum Creatinine	0.6 – 1.5 mg/dl	1.6 mg/dl	1.4 mg/dl
BUN	14 – 36 mg/dl	26.2 mg/dl	18.0 mg/dl
*Cohn and Cote, 2019			



Before Treatment: Kidney Stones are Present

After Treatment: No Kidney Stone is Present

Figure 3.1 and 3.2 : Radiography of a Persian cat with nephrolithiasis before and twenty weeks post-treatment.

Before Treatment: Acoustic Shadow Observed.

After Treatment: No Acoustic Shadow Observed.

Figure 3.3 and 3.4 : Ultrasonography of a Persian cat with nephrolithiasis before and twenty weeks post-treatment.

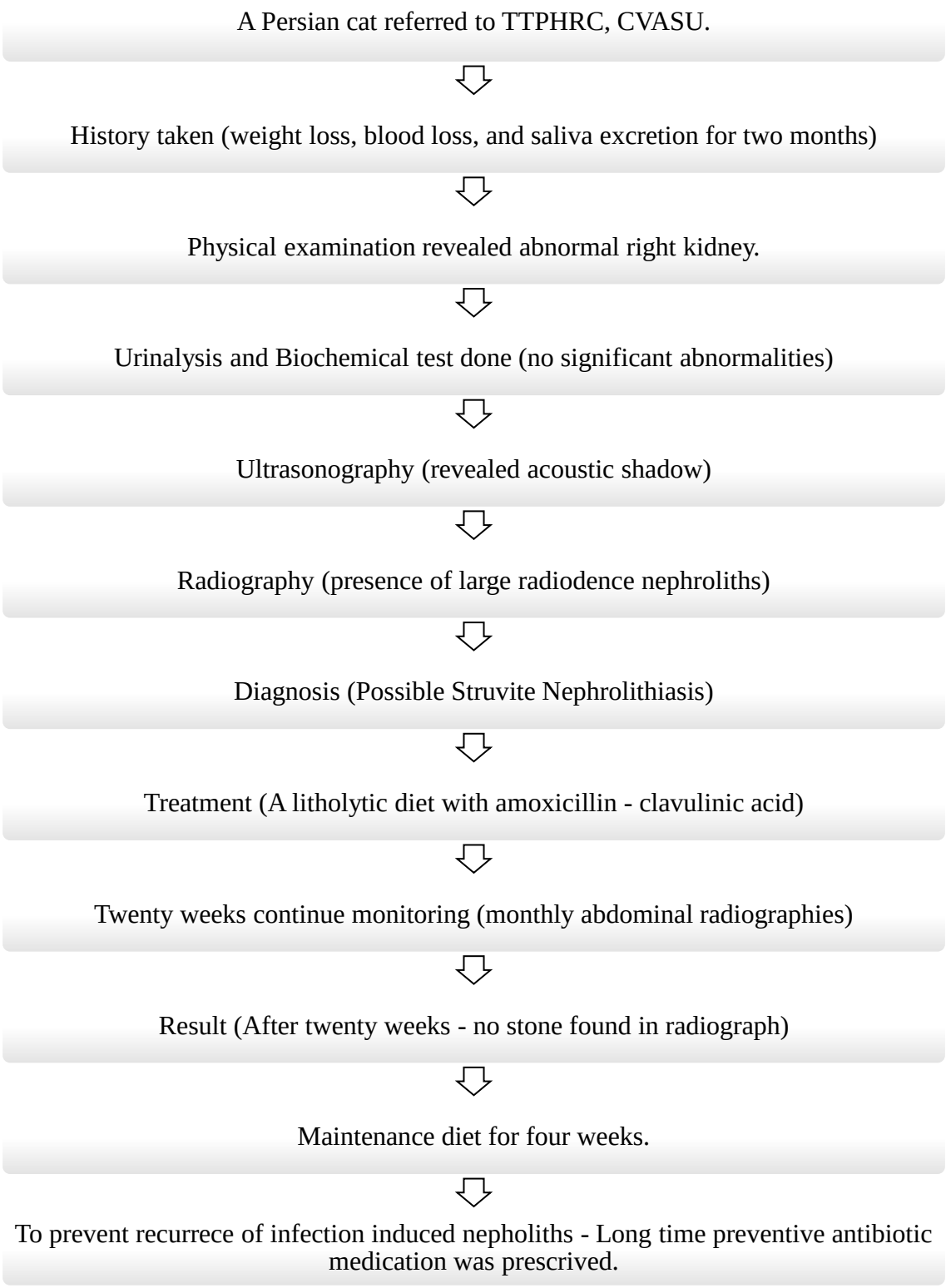


Figure 3.5 : Chronology of medicinal dissolution of nephroliths in a Persian cat.

Chapter 4: Discussion

Uroliths were found in more than 20% of the patients in a prospective diagnostic investigation of feline lower urinary tract diseases carried out at the University of Minnesota. When uroliths were sent to laboratory for examination, only 5-7% of them were nephroliths (Osborne et al., 1995).

A thorough diagnostic workup is necessary for the treatment of nephrolithiasis and includes urinalysis, urine culture, serum and urine chemistry, radiography or ultrasonography, and evaluation of the stone composition (Osborne et al., 1995). So, these tests were done first to understand the nature of stones and other possible complications. When there was found abnormal right kidney in palpation, then ultrasonography and radiography were done. Finding the site(s), number, density, and shape of the suspected stone(s) is the main goal of radiographic or ultrasonographic evaluation of patients (Osborne et al., 1996). In ultrasonography there was revealed acoustic shadow in renal pelvis. Although ultrasonography is a fairly sensitive method of detection, it is insufficient to make a treatment decision with regard to uroliths characteristics (size, shape, radio-opacity, quantity, etc.) (Lulich et al., 2011). In radiography there was found radiodense nephroliths.

Struvite occupies a significant portion of canine and feline cystic calculi, whereas calcium salts (oxalate and phosphate) form the majority of nephroliths (Ling, 1995). Ammonium urate, calcium oxalate, cystine, sodium urate, and uric acid stones are typically related with acid urine, while magnesium ammonium phosphate and calcium phosphate stones are typically associated with alkaline urine (Osborne et al., 1996). As the urine pH found acidic and the stones were quite big radiodense so the diagnosis was infection induced struvite nephrolithiasis.

For struvite, cystine, or urate nephroliths, conservative medical therapy can be an ideal solution. A calculolytic, acidifying diet (such as Hill's Prescription Diet s/d, Hill's Pet Nutrition, Inc., Topeka, KS) with antibiotic treatment for a urinary tract infection may cause struvite stones to dissolve (Osborne et al., 1995). Prior to starting treatment, a urine analysis and urine culture are advised. Based on sensitivity data, patients with a positive culture should get the appropriate antibiotic medication (Cléroux, 2018). When a normal

lower urinary tract was confirmed, medicinal dissolution of stones advised as there was no indication of a blocked urine outflow. The primary treatments used to dissolve struvite nephroliths included a litholytic diet and amoxicillin-clavulanic acid preparation.

UTIs with urease-producing bacteria are present in the majority of individuals with struvite uroliths (especially staphylococci, Proteus spp., or ureaplasmas). As long as the stones are radiographically visible, appropriate antibiotic therapy should be maintained since bacteria present deep within the stones may be resistant to antimicrobials. The solubility of struvite crystals increases along with a usual decrease in urine pH as the infection is treated (Ross et al., 1999). Compared to bladder stones, kidney stones require more time to dissolve (Lulich et al., 2011). In one case it was reported that the mean time for dissolution of infection-induced struvite nephroliths in six dogs was 184 ± 99 days (Osborne et al., 1995). In this patient nephrolith was invisible twenty weeks after the beginning of treatment. Then treatment was continued for an additional month to confirm the complete absence of nephroliths.

The consumption of a struvite calculolytic diet carries several complications. As a result, not all patients are suitable for specific dietary medical therapy. These diets are often not recommended for those with medical issues like heart disease or hypertension that could be made worse by eating a lot of sodium. Additionally, if consumed for a longer period of time, the decreased protein composition of these diets may cause or worsen protein deficiency. Cats exhibiting signs of moderate to severe primary renal failure should receive special attention since they need more protein for anabolism than healthy cats. When there is evidence of an underlying metabolic acidosis, urine acidifiers should not be administered concurrently with an acidifying diet (Ross et al., 1999). So, the cat was under continuous monitoring with nephrolytic diet. Polyuria and the generation of diluted urine were related to the nephrolytic diet. No other abnormalities were noticed. The cat was put on a maintenance diet that boosts the production of acid urine after the antibiotic therapy was stopped. Four weeks after the maintenance diet was started, there was a decrease in the levels of alkaline phosphatase, alanine aminotransferase, and blood urea nitrogen.

A cat cannot be supposed to eat more water on its own, but cats will consume food that has had water mixed into it just as readily as food that is served dry. The average daily

urine volume rises from 70 to 105 ml when 40 ml of water are added to every 200 g of meals. This procedure lowers the urine's specific gravity, osmolarity, and struvite crystal content. Magnesium is a very abundant element in the diet of carnivores, and struvite, a magnesium salt, is one of the essential excretory cations in the cat nephron. For struvite nephrolithiasis, litholytic diets lower the concentration of urea, phosphorus, and magnesium in the urine. The production of urea is decreased when there is a restriction on high-quality protein in the diet. Increased sodium chloride levels may be present in litholytic diets to promote polydipsia and subsequent polyuria (Cowgill, 1995).

Controlling urease-producing bacterial-induced urinary tract infections is crucial for preventing the recurrence of infection-induced nephroliths. Diagnostic strategies should be developed to find an underlying anatomical or physiological explanation if the patient has recurring bacterial urinary tract infections. Long-term preventive antibiotic medication should be taken into consideration in the absence of predisposing conditions. Animals that continue to build nephroliths despite having acidified urine, more urine formed, and a bacterial urinary tract infection under control should not be given litholytic diets on a regular basis (Ross et al., 1999).

Conclusion

Nephrolithiasis treatment requires a detailed diagnostic workup that includes urinalysis, urine culture, serum and urine chemistry, radiography or ultrasonography, and assessment of the composition of uroliths. Among them ultrasonography and radiography are proved the most essential clinical tools to diagnosis of a nephrolith. Medical therapy in nephrolithiasis aims to promote their disintegration or, at the very least, prevent nephroliths from increasing in their size and number by correcting or lowering underlying risk factors. Litholytic diet along with an antibiotic therapy are found effective to resolve nephroliths. Consuming a struvite calculolytic diet has a number of problems. Because of this, not all patients are appropriate for a given dietary medical therapy.

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Biography

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