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Clinical Article

CLINICAL MANAGEMENT OF INFECTION ASSOCIATED STRUVITE CYSTOLITHIASIS IN A BOXER DOG

ENSHA LOMIYA, M.A.[1], RAGUVARAN, R.[1], MONDAL, D.B.*[1], NAVJOT SINGH THAKUR[1] and SAXENA, A.C.[2]
[1]Division of Medicine, [2]Division of Surgery,
ICAR-Indian Veterinary Research Institute, Izatnagar-243122, U.P., India

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SUMMARY

A 12-years-old male Boxer dog was presented with history of pollakiuria, hematuria, anorexia and reduced water intake. Anamnesis revealed recurrent urinary tract infection in the past. Clinical examination revealed congested mucous membrane, pyrexia, tachycardia, tachypnea and pain on caudal abdominal palpation. Leukocytosis and hypophosphatemia was evident on haemato-biochemical examination. Abdominal radiography showed a large-sized radiopaque calculus in urinary bladder. Ultrasonography revealed distended bladder, increased wall thickness and large size calculus. Alkaline urine (pH-9), proteinuria and hematuria noticed on urinalysis. Urine sediment microscopy revealed significant number of erythrocytes, leucocytes, clumps of cocci and struvite crystals. Urine culture showed profuse growth of *Staphylococcus aureus*. Based on the findings such as alkalinity of the urine, urease positive bacteria on urine culture and radiopaque calculus in bladder, the case was presumed as infection associated struvite calculi and medical dissolution of cystolith was done using urinary acidifier L-methionine along with antibiotic and supportive therapy. The dog showed clinical (remission of clinical signs, hemogram, serum biochemistry and urinalysis findings) and microbiological cure on 14th day reexamination and the owner was advised to continue L-methionine for 30 more days for ensuring complete dissolution of calculus and it was confirmed by abdominal ultrasonography.

Keywords: CLED, Dog, L-methionine, *Staphylococcus aureus*, Struvite

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Urinary tract infection (UTI) is a common problem encountered in canine practice with a prevalence of 10% of total cases. International Society for Companion Animal Infectious Disease (ISCAID) grouped UTI into (i) simple uncomplicated cystitis (ii) recurrent bacterial cystitis (iii) subclinical bacteriuria and (iv) upper urinary tract infections. Most cases of canine UTI are originated from a single etiological agent; *Escherichia coli* followed by *Proteus* spp., *Staphylococcus* spp. and *Enterococcus* spp. (Hernando *et al.*, 2021). Urinary infection caused by urease producing bacteria such as *Staphylococcus*, *Proteus*, *Klebsiella*, *Escherichia coli*, *Corynebacterium urealyticum* makes the urine alkaline and increases the risk of struvite calculi formation in dogs. Struvite accounts for about 40% of urolithiasis in canines (Burggraaf *et al.*, 2021). It is primarily composed of magnesium ammonium phosphate hexahydrate. Although struvite calculi without infection have been reported, majority of canine struvite urolithiasis are infection related and it is commonly referred as infection stones or urease stones. A complete urinalysis and quantitative urine culture are minimally required for the diagnosis of UTI. Struvite crystals are large sized with coffin lid shape under microscopic examination. Being radiopaque nature, struvite stones can be visualized by radiography. In case of infection related struvite calculi medical management is preferred over surgery as most of the struvite stones confines to bladder, due to relative risk associated with surgery and chance of relapse after surgical removal (Jummai *et al.*, 2018). This report describes medical management of infection related struvite cystolithiasis.

*Corresponding author: dbmondal@gmail.com

A 12-year-old male Boxer dog was presented to the Referral Veterinary Policlinic, ICAR-Indian Veterinary Research Institute (IVRI) with history of pollakiuria, hematuria, anorexia and reduced water intake. According to the owner the dog had recurrent episodes of urinary tract infection and had been treated for the same. Clinical examination revealed congested mucous membrane, elevated rectal temperature (103.1F), tachycardia (120 bpm), tachypnea (60/min), mild dehydration, frequent dribbling of blood-tinged urine and pain on caudal abdominal palpation.

Blood and serum sample were collected for hematology and serum biochemistry. The results are illustrated in the table1. Haemato-biochemical examination revealed leukocytosis and hypophosphatemia. Abdominal radiography revealed a large-sized radiopaque calculus inside the urinary bladder (Fig. 1). Ultrasonography revealed a partially distended urinary bladder with the wall thickness of 7.6 mm (Fig. 2) containing markedly turbid contents, blood clots and a large-calculus measuring 3×4 cm in size (Fig. 3). Urine sample was collected by catheterization using an infant feeding tube size 6. On physical examination of the urine, it was dark red in color, watery in consistency with small quantities of blood clots and pus. Urinalysis was performed by reagent dipstick method and it revealed pH of 9 (alkaline), proteinuria and hematuria. Urine sediment examination under microscopy

Table 1

Haemato-biochemical changes in affected dog

Parameter	Observed value		Reference value	Impression
	Day 1	Day 14		
Hemoglobin (Hb) (g%)	16.3	15	11.9-18.9	Normal
Packed cell volume (PCV) (%)	49.1	48.6	35-57	Normal
Red blood cell count (10v /µl)	7.03	6.6	4.95-7.87	Normal
White blood cell count (10^3/µl)	25	13.8	5.0-14.1	Leukocytosis
Neutrophils (%)	82	76	58-85	Normal
Lymphocytes (%)	11	18	8-21	Normal
Monocytes (%)	7	5	2-10	Normal
Eosinophils (%)	0	1	0-9	Normal
Basophils (%)	0	0	0-1	Normal
Creatinine (mg/dL)	0.71	0.99	0.5-1.5	Normal
Blood urea nitrogen (BUN) (mg/dL)	32.03	30.8	8-28	Mild elevation
Alanine transaminase (ALT) (U/L)	87	56	10-109	Normal
Total protein (g/dL)	6.95	6.6	5.4-7.5	Normal
Albumin (g/dL)	2.95	3.2	2.3-3.1	Normal
Globulin (g/dL)	4	3.4	2.7-4.4	Normal
Calcium (mg/dL)	9.24	8.85	9.1-11.7	Normal
Phosphorus (mg/dL)	2.02	3.1	2.9-5.3	Hypophosphatemia

(Reference ranges: The Merck Veterinary Manual (10^{th} Edn.)

Table 2

Findings of urinalysis and urine culture

Parameters	Day 1	Day 14	Inference on 14^{th} day
Colour	Dark red	Yellow	Normal
Consistency	Turbid	Watery	Normal
Specific gravity	1.015	1.010	Normal
pH	9	6	Acidic
Protein (mg/dL)	100	Trace	Normal
Leucocytes (HPF)	10	4	Normal
Erythrocytes (HPF)	50	0	Normal
Crystals (HPF)	20 (Struvite)	Nil	Devoid of crytals
Urine culture	Positive: S. aureus (>10u CFU/ml)	Negative	Negative for UTI

revealed significant number of erythrocytes, leucocytes, clumps of cocci (Fig. 4) and struvite crystals (Fig. 5). The findings of urine examination are depicted in the table 2. Urine sample was cultured on CLED (Cystine Lactose Electrolyte Deficient) agar and profuse growth of Staphylococcus aureus (>10^5 CFU/ml) was observed. Urease production of isolated bacteria was confirmed by biochemical test (urease test). Antimicrobial susceptibility testing (ABST) was performed. The organism was found to be susceptible to amoxicillin-clavulanic acid, ampicillin, piperacillin-tazobactam, ceftazidime, cefepime, ciprofloxacin and nitrofurantoin and resistant to co-trimoxazole and gentamicin.

Based on the history, clinical signs, laboratory findings and diagnostic imaging findings, it was confirmed as cystitis and infection related struvite calculi.

In dogs, approximately 95% of struvite stones were confined to lower urinary tract, especially bladder and only 5% was observed in upper urinary tract. The value of RBC, Hb count and PCV were observed to be normal in cystitis affected dogs (Yassein *et al.*, 2021) and leukocytosis is a common finding in inflammatory conditions of urinary tract (Chethan *et al.*, 2020). The mean values of BUN, creatinine, ALT in cystitis affected dogs were found to be within the normal range (Yogeshpriya *et al.*, 2018). These findings are similar to the observations in present case. Medical management of infection related struvite urolith were accomplished by 1) elimination of the urease producing organisms 2) dietary modification and 3) urine acidification (Palma *et al.*, 2013). Appropriate antimicrobial

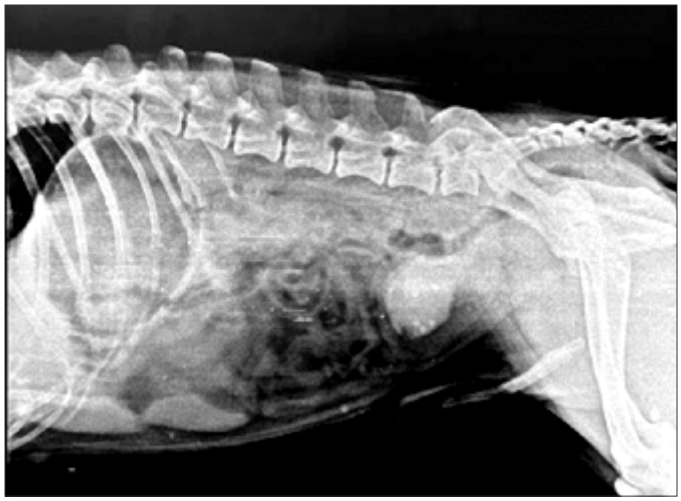

Fig. 1. Large sized radiopaque calculi inside the bladder

Fig. 2. Thickened the bladder wall with turbid content

Fig. 3. Hyper echoic structure (3×4 cm) with acoustic shadowing

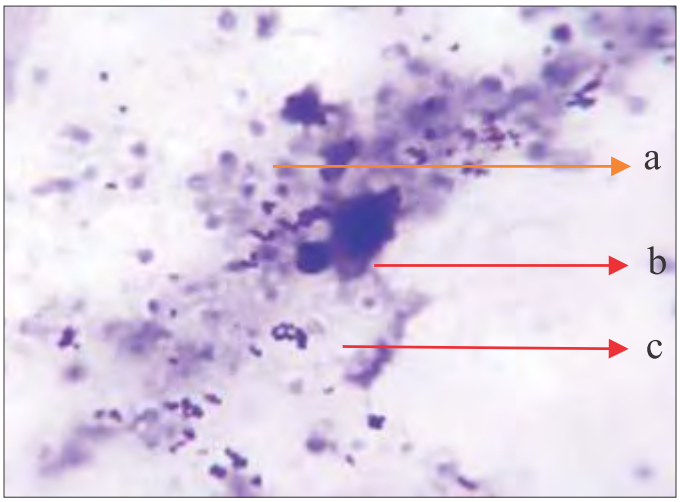

Fig. 4. Giemsa-stained smear (100x) showing RBC (a), WBC (b), Cocci (c)

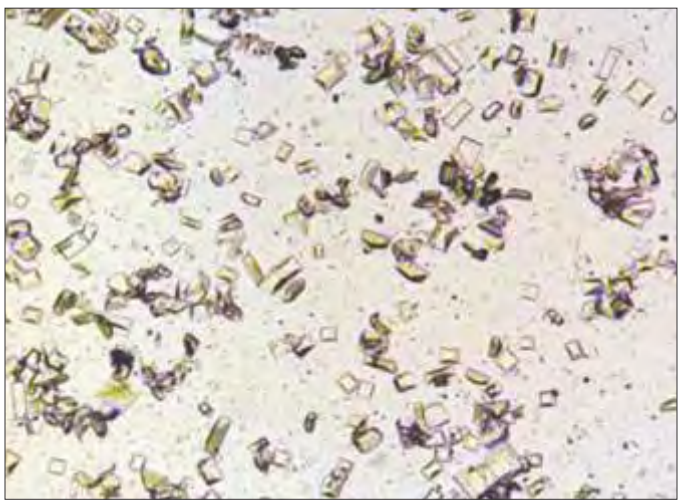

Fig. 5. Wet smear (10x) showing triple phosphate (struvite) crystals

Fig. 6. Ultrasonography of the patient after 45 days of dissolution therapy

therapy based on ABST result to eradicate UTI was the most important facet of treatment. The diet with restricted protein, magnesium and phosphorus is commonly recommended for dissolution of struvite. Low protein diet reduces the amount of urea available for bacterial conversions to ammonium (Osborne *et al.*, 1999). Normally dogs have acidic urine with pH of 6-7.5. Infection with urease producing bacteria makes the urine alkaline which favors the precipitation of magnesium and phosphate ions and formation of struvite calculi. Struvite crystals are soluble

in acidic urine therefore maintenance of acidic urine pH using urinary acidifiers is beneficial in inhibiting the stone growth.

As the stone size was larger in this, case was advised for surgical removal of calculi but surgery was denied due to age and anesthetic related risk factors. Then the dog was managed medically with amoxicillin-clavulanic acid (based on ABST) at dose rate of 12.5 mg/kg B. Wt PO, q 12 hr for 14 days. Beta lactams were recommended 1st tier antibiotics for the management of UTI (Weese *et al.*, 2019). Urinary acidifier L-methionine was given initially at rate of 50 mg/kg B. Wt PO, q 12 hr and the dose rate was gradually increased to 75 mg/kg B. Wt PO, q 12 hr or until the pH become acidic (Bartges and Moyers, 2010). Supportive treatment was given with fluid therapy (Inj. normal saline @ 30 ml/kg B. Wt IV q 24 hr for 3 days), NSAID (meloxicam @ 0.2 mg/kg B. Wt PO, q 12 hr for 3 days), antiulcer drug (pantoprazole @ 1 mg/kg B. Wt PO, q24 hr for 14 days), hemostat (Inj. Haemocoagulase @ 1 ml IM q 24 hr for 3 days) and herbal reno-protectant @ 5ml PO, q 12 hr for 14 days. Owner was advised to provide ad libitum drinking water and low protein diet. Haemato-serum biochemical parameters were reevaluated on day 14 which showed normal total leukocyte count ($13.8\times10^3/\mu l$) and serum inorganic phosphorus level (3.1 mg/dL). Finding of urinalysis on day 14 revealed acidic urine (pH-6) with trace leukocyte and protein and normal urine sediment cytology. The average urine pH value recommended for dissolution of struvite is 5.9-6.1 (Calabro *et al.*, 2011). Dog responded well to the medical management and had complete resolution of clinical signs on 14th day reexamination based on urine cytology examination. However, the dog was treated with L-methionine @ 75 mg/kg B. Wt PO, q 12 hr for 30 more days for the complete dissolution of calculus and it was confirmed by ultrasonography after 45 days of dissolution therapy (Fig. 6). The timely diagnosis and intervention are essential for the management of UTI and infection associated calculi.

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