

Urethral Plugs in Dogs

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Background: Crystalline-matrix urethral plugs have not been previously reported in dogs.

Hypothesis/Objectives: To report the composition of urethral plugs in dogs, describe clinical features of the disease, and identify overrepresented breeds.

Methods: Retrospective case series. A Minnesota Urolith Center (MUC) record search was performed for urethral plugs in dogs submitted during a 6-year period. The composition of the plugs and signalment of affected dogs were recorded. Breed risk analysis was performed using a control group without plugs from the Veterinary Medical Center, University of Minnesota (VMC UMN). Breed risk was also calculated for a group of dogs with struvite (plugs and uroliths). Medical records for the subset of plug cases from the VMC UMN were reviewed and described.

Results: Between 2006 and 2011, 42 urethral plugs from dogs were submitted to the MUC. All came from male dogs, and the mineral component of the majority (83%) was struvite. Thirty (71%) samples were from Pugs. Pugs were overrepresented in plug submissions (OR 179; CI 88–389; $P < .001$), and for struvite in general (OR 14.3; CI 7.9–24.4; $P < .001$). Nine of the dogs were treated at VMC UMN; all were castrated male Pugs. None of these cases had bacteriuria or positive urine cultures, and no underlying cause of plug formation was identified.

Conclusions and Clinical Importance: When evaluating dogs with urethral obstruction, plugs need to be considered, especially in male Pugs. Further investigation into the underlying cause of plug formation in dogs is warranted.

Key words: Lower urinary tract; Magnesium ammonium phosphate; Struvite; Urethral obstruction.

Crystalline-matrix plugs are a common cause of urethral obstruction in male cats.^{1–3} Urethral plugs in cats are soft and paste-like with a classic cylindrical shape. They are composed of matrix (mucoprotein, composed of mucus and inflammatory debris) and varying amounts of mineral.^{1,2} In greater than 80% of urethral plugs from cats, the mineral content is struvite (aka magnesium ammonium phosphate).¹ The etiology of this disease is not well understood. Over the past several years, we have observed a similar phenomenon of urethral plugs in male dogs. To our knowledge, this disease has not been previously described in dogs. The objective of this study was to report features of urethral plugs in dogs. This was achieved through 3 methods. First, we reported the composition of urethral plugs from dogs submitted to the Minnesota Urolith Center (MUC) during a 6-year period and provided signalment information on dogs diagnosed with this condition. Second, we performed statistical analyses to identify breeds that are overrepresented for urethral plugs; struvite breed data are provided as well to serve for comparison. Third, we described clinical data for a subset of cases that were evaluated at the Veterinary Medical Center, University of Minnesota (VMC UMN).

Abbreviations:

BUN	blood urea nitrogen
CBC	complete blood count
CT	computed tomography
H&E	hematoxylin and eosin
H ₂ PO ₄ ⁻	monobasic phosphate
HCO ₃	bicarbonate
HPO ₄ ²⁻	dibasic phosphate
MUC	Minnesota Urolith Center
OR	odds ratio
PCO ₂	partial pressure of carbon dioxide
PO ₄ ³⁻	trivalent phosphate ion
SD	standard deviation
TCO ₂	total carbon dioxide
VMC UMN	Veterinary Medical Center at the University of Minnesota

Materials and Methods

Study Population

Medical records of submissions to the MUC between January 1, 2006, and December 31, 2011 were searched using the terms urethral plug and dogs. A urethral plug was defined as deformable paste-like, crystalline-matrix material occluding the urethra. The mineral component of the plug and signalment of the affected dogs were recorded and used to calculate breed odds ratios (OR). The control population for this analysis consisted of all dogs admitted to the VMC UMN from January 1, 2006 to December 31, 2011 that did not have urethral plug submissions. Separate OR could not be calculated for the VMC UMN subset of plug cases, as all dogs were from a single breed.

To compare the breed data of dogs with urethral plugs, a separate MUC record search was performed for all struvite submissions (plug or urolith) from VMC UMN dogs during the study period. Breeds of the affected dogs were recorded, and ORs were calculated using the plug and struvite-free VMC UMN control population described above. To minimize the potential for overrepresentation, recurrences of plugs or struvite uroliths were not counted.

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The hospital records for the subset of urethral plug cases that were admitted to the VMC UMN during the study period were selected for full medical review. When available, results from medical imaging; CBC; serum biochemistry profile; blood gas; urinalysis; quantitative urine culture for aerobic bacteria; quantitative mineral analysis by optical crystallography, infrared spectroscopy, or both;⁴ and histopathology of plugs were evaluated in relation to this disease syndrome. Owners of the affected VMC UMN dogs were contacted and asked to return to the hospital for evaluation of serum concentrations of bile acids and fasting ammonia to determine if hepatic dysfunction might have contributed to plug formation.

Statistical Analysis

Descriptive statistics were calculated. Continuous data were expressed as mean and SD, unless not normally distributed, in which case the median and range were provided. Categorical data were expressed as counts. Odds ratios and 95% confidence intervals were used to assess breeds overrepresented for urethral plug formation and those overrepresented for struvite formation in general (plugs and uroliths). Chi-square tests were used to assess the significance of breed odds ratios and were corrected for multiple comparisons using the Bonferroni correction. For breeds with at least 3 struvite cases, ORs for sex were determined using Fisher's exact tests and were corrected for multiple comparisons using the Bonferroni correction. All analyses were performed with commercially available statistical software,^a and values of $P < .05$ were considered significant.

Results

MUC Urethral Plugs in Dogs

Between 2006 and 2011, 42 submissions for mineral analysis from dogs were plugs. The mineral component of 35 (83%) were struvite, 1 was calcium oxalate monohydrate, and 1 was 50% struvite and 50% ammonium urate. Five were composed of miscellaneous material without minerals. All plug submissions were from males and the mean age was 5.8 ± 2.5 years. Thirty (71%) urethral plugs were from Pugs; other affected breeds included mixed breed ($n = 4$) and 1 of each: Boxer, Shih Tzu, Miniature Schnauzer, Yorkshire Terrier, English Setter, Chihuahua, English Springer Spaniel, and Great Dane.

Urethral Plug and Struvite Breed Analyses

During 2006–2011, 64,129 dogs were evaluated at the VMC UMN. Of these dogs, 9 had urethral plugs and 579 had uroliths. The 64,120 dogs without urethral plugs served as the control population for the plug breed risk analysis. All 9 plugs and 16% (94/579) uroliths were struvite, resulting in a total struvite count (plugs and uroliths) of 103. The 64,026 dogs without struvite (plugs or uroliths) served as the control population for the struvite breed risk analysis.

Of the 10 MUC breeds with urethral plugs, only the Pug was found to be overrepresented relative to the control population (Table 1; OR = 179; CI: 88–389; $P < .001$). As mentioned in the Materials and Methods section, breed ORs could not be separately calculated

Table 1. Urethral plug breeds – Odds ratio (OR) for breed of 42 dogs with MUC urethral plug submission and 64,120 control dogs (dogs without plugs). P values corrected for multiple comparisons, $P < .05$ is considered significant.

Breed	Dogs with Plugs	Dogs without Plugs	OR	Confidence Interval	P value
Pug	30	881	179	88–389	<.001
English Setter	1	95	16	0.4–99	.5
Mixed	4	1,903	3.4	0.9–10	.3
Great Dane	1	576	2.7	0.1–16	1
Chihuahua	1	658	2.4	0.1–14	1
Miniature Schnauzer	1	1,043	1.5	0.0–8.7	1
English Springer Spaniel	1	1,098	1.4	0.0–8.3	1
Boxer	1	1,179	1.3	0.0–7.7	1
Yorkshire Terrier	1	1,206	1.3	0.0–7.5	1
Shih Tzu	1	1,284	1.2	0.0–7	1

for the VMC UMN plug cases, as all affected dogs were a single breed (the Pug).

The 103 VMC UMN dogs with struvite (9 plugs and 94 uroliths) represented 29 breeds. Of these 29 breeds, 5 were found to be overrepresented relative to the struvite-free VMC UMN control population; the Pug, Bichon Frise, mixed breed, Shih Tzu, and Miniature Schnauzer (Table 2). Of the 5 overrepresented breeds, the male Bichon Frise had a significantly decreased risk of forming struvite relative to the female Bichon Frise (OR = 0; CI: 0–0.4; $P = .01$).

VMC UMN Subset of Urethral Plugs in Dogs

Signalment, Clinical History, and Physical Exam Findings. Nine of the 42 MUC urethral plugs originated from dogs treated at the VMC UMN. All of the dogs were neutered male Pugs. The mean \pm SD age was 5.8 ± 2.7 years. The mean \pm SD body weight was 10.5 ± 2 kg. All 9 dogs had urethral obstructions from the plugs. Eight of 9 dogs presented with acute onset of stranguria with little to no micturition. The remaining dogs presented for lethargy, decreased appetite, and vomiting for the past 48 hours. Physical exam revealed that all of the dogs had a palpably distended urinary bladder. Other pertinent physical exam and historical findings included neurologic deficits in 3 dogs: 1 had hindlimb ataxia and fecal incontinence, 1 had hindlimb paresis and conscious proprioceptive deficits in the hindlimbs, and the 3rd dog had conscious proprioceptive deficits in the hindlimbs. The owners of a 4th dog reported that he had always urinated only once daily.

Diet History. Diet was recorded for 6/9 dogs as follows: Solid Gold (2; kibble in 1 dog, not specified in 2nd dog), iVet Healthy Gourmet Canine Reduced Fat kibble (1), Pedigree canned and Nature's Choice kibble

Table 2. Struvite breeds – Odds ratio (OR) for breed of 103 VMC UMN dogs with struvite uroliths or plugs and 64,026 control dogs (dogs without struvite uroliths or plugs). *P* values corrected for multiple comparisons, *P* < .05 is considered significant.

Breed	Dogs with Struvite	Dogs without Struvite	OR	Confidence Interval	<i>P</i> value
	Uroliths or Plugs N (M/F)	Uroliths or Plugs N (M/F/Unknown)			
Pug	17 (13/4)	873 (450/422/1)	14.3	7.9–24.4	<.001
Japanese Chin	1 (0/1)	49 (27/22/0)	12.8	0.3–76.4	1
Bearded Collie	1 (0/1)	63 (36/27/0)	10.0	0.2–58.7	1
Bichon Frise	11 (0/11)	910 (440/468/2)	8.3	4.0–15.6	<.001
Mixed	16 (5/11)	1,887 (815/1,062/10)	6.0	3.3–10.4	<.001
Welsh Corgi	4 (0/4)	441 (210/228/3)	5.8	1.5–15.5	.15
Shih Tzu	10 (1/9)	1,274 (610/661/3)	5.3	2.5–10.2	.001
Lhasa Apso	2 (0/2)	257 (145/111/1)	4.9	0.6–18.4	1
Shar Pei	1 (1/0)	136 (69/67/0)	4.6	0.1–26.7	1
Miniature Schnauzer	7 (2/5)	1,036 (508/524/4)	4.4	1.7–9.5	.038
Papillon	1 (0/1)	164 (83/81/0)	3.8	0.1–22.0	1
Saint Bernard	1 (1/0)	189 (114/75/0)	3.3	0.1–19.1	1
Scottish Terrier	1 (0/1)	199 (92/107/0)	3.1	0.1–18.1	1
Wirehaired Fox Terrier	1 (0/1)	208 (108/99/1)	3.0	0.1–17.3	1
Mastiff	1 (0/1)	219 (118/97/4)	2.9	0.1–16.4	1
Cairn Terrier	1 (0/1)	242 (152/90/0)	2.6	0.1–14.9	1
Pomeranian	2 (0/2)	489 (232/256/1)	2.6	0.3–9.6	1
Havanese	1 (0/1)	274 (123/125/26)	2.3	0.1–13.1	1
Cavalier King Charles Spaniel	3 (0/3)	984 (454/493/37)	1.9	0.4–5.8	1
Viszla	1 (1/0)	331 (170/161/0)	1.9	0–10.8	1
Cocker Spaniel	3 (0/3)	1,148 (573/573/2)	1.6	0.3–5.0	1
Dachshund	4 (2/2)	1,792 (915/874/3)	1.4	0.4–3.7	1
Miniature Poodle	1 (0/1)	4,958 (240/255/3)	1.3	0.0–7.2	1
Australian Shepherd	1 (0/1)	540 (256/275/9)	1.2	0.0–6.6	1
English Springer Spaniel	2 (0/2)	1,096 (543/538/15)	1.1	0.1–4.3	1
Beagle	1 (0/1)	868 (429/423/16)	0.7	0.0–4.0	1
Yorkshire Terrier	1 (0/1)	1,205 (556/648/1)	0.5	0.0–2.9	1
Labrador Retriever	5 (5/0)	7,439 (3,693/3,715/31)	0.4	0.1–0.9	.99
Golden Retriever	2 (2/0)	4,263 (2,186/2,061/16)	0.3	0.0–1.0	1

(1), Purina Mini Chunks kibble (1), Science Diet Light canned (1).

Abdominal Radiographs. Survey abdominal radiography was performed at initial presentation and before transurethral catheterization in 5 dogs. Radiography confirmed a distended urinary bladder in all 5 dogs. Four of the dogs had varying amounts of mineral opacity in the urinary bladder (1/5), urethra (2/5), or both (1/5; Fig 1). Mineral opacity within the lower urinary tract was not identified in the 5th dog. Abdominal radiographs were performed immediately after catheterization in 2 dogs. There was a faint mineral opacity, suggestive of bladder sand, in 1 dog; radiopaque material was not visualized in the urinary tract in the other dog. Two dogs were noted to have 6 lumbar vertebrae, and 1 dog had a transitional L₇ vertebra. The 2 remaining dogs did not have imaging at initial presentation.

Urinalysis and Urine Culture. Urine was obtained via cystocentesis in 4 dogs and via transurethral catheterization in 5 dogs. The median (range) urine pH and specific gravity measurements were 7.5 (6.5–9.0) and 1.021 (1.015–1.041). Six dogs had microscopic hematuria (>5

rbc/hpf), and 7 dogs had proteinuria (≥1+ via dipstick evaluation). Bacteria were not identified by microscopic evaluation of the urine sediment in any of the dogs; however, 5 dogs had crystalluria (4 with struvite crystalluria and 1 with calcium oxalate crystalluria).

Urine cultures were performed in 7/9 dogs. All cultures were negative for bacterial growth; however, 3 dogs received antimicrobials 2 weeks, 8 days, and 24 hours before sample collection.

Treatment

Transurethral Catheterization. Dogs were sedated with a combination of a benzodiazepine and an opioid administered IV. Transurethral catheterization was performed with sterile saline flushing. A portion of the plug was expelled from the distal urethra in 7/9 dogs (Fig 2). Transurethral catheterization was noted to be difficult in the remaining 2 dogs, and no material was flushed out. Once the catheter was in the urinary bladder, the bladder was drained and flushed several times, and in 7/9 cases, an indwelling urethral catheter was left in place overnight.

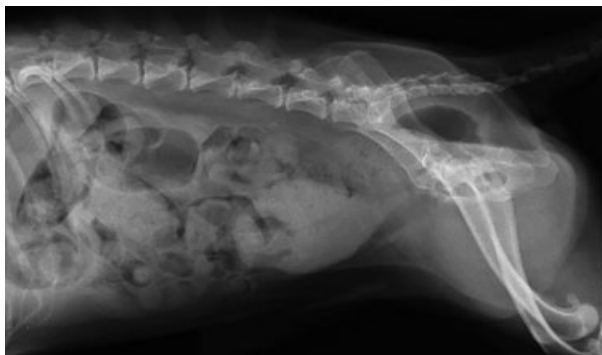


Fig 1. Survey abdominal radiograph of an 8-year-old castrated male Pug revealed mineral opacity throughout the bladder and proximal urethra. Large clumps of struvite crystalline material and several small struvite calculi were removed via cystotomy.



Fig 2. Urethral plug from a 2-year-old castrated male Pug protruding from the distal urethral opening. The crystalline portion of the plug was composed of 100% struvite interspersed in a matrix of cellular and proteinaceous material.

Transurethral catheterization was successful in relieving the obstruction in 5 dogs, whereas 4 dogs required additional procedures. In 1 dog, a contrast cystourethrogram revealed cystic and urethral calculi and a urethral diverticulum (Fig 3). Cystoscopy was performed so that laser lithotripsy and basket retrieval could be used to clear the urethral lumen. However, a urethral stricture prevented access, and a cystotomy was required. A large quantity of sludge-like material and small uroliths (<1 mm) was removed from the bladder and urethra. Retrograde transurethral catheterization was still not successful. Therefore, a scrotal urethrostomy was performed to allow urine voiding. The 2nd dog had a double contrast cystogram to further characterize the radio-opaque material identified on survey abdominal radiographs (Fig 1). Mineral opacity was present throughout the urinary bladder, raising concern for a large urocystolith. This dog had a cystotomy; the bladder was filled with large aggregations of struvite crystals; no urolith was found. It was noted in the last 2 dogs that urethral catheterization was difficult at initial presentation. In 1 dog, cystoscopy



Fig 3. Contrast cystourethrogram from an 8-year-old castrated male Pug revealed numerous cystic and urethral calculi and a urethral diverticulum in the proximal urethra. Sludge-like material and small uroliths (<1 mm) composed of 100% struvite were removed from the bladder and urethra via cystoscopy, followed by cystotomy.

revealed a urethral stricture and numerous small (<1 mm) uroliths dispersed within plug material. These were removed from the urinary tract, allowing the dog to urinate. In the other dog, a contrast cystourethrogram revealed cystic calculi and a thickened bladder wall. A cystotomy was performed; the bladder contained large clumps of crystalline material and several small calculi. Two of the 3 dogs with uroliths had a negative urine culture and no antimicrobial administration within the previous month. The 3rd dog did not have a urine culture.

Further Diagnostics

Clinicopathologic Data. A CBC was performed in 4/9 dogs; there were no clinically relevant abnormalities. Serum chemistries were performed in 8/9 dogs. In 2 dogs, postrenal azotemia (BUN 223 and 100 mg/dL; reference range 9–31 mg/dL and creatinine 11.1 and 9.7 mg/dL; reference range 0.6–1.6 mg/dL) and hyperkalemia (6.3 and 5.7 mmol/L; reference range 3.6–5.3 mmol/L) resolved with replacement fluid therapy. Venous blood gas was performed in 3 dogs before treatment. A mild metabolic acidosis was present in 1 dog with postrenal azotemia (pH 7.308; reference range 7.3–7.47, HCO₃ 17.3 mmol/L; reference range 17.8–27.2 mmol/L, pCO₂ 34.4 mmHg; reference range 28.9–44.4 mmHg.). The 2nd dog had a mild respiratory acidosis (pH 7.325; reference range 7.3–7.47, HCO₃ 23.5 mmol/L; reference range 17.8–27.2 mmol/L, pCO₂ 45 mmHg; reference range 28.9–44.4 mmHg). The remaining dogs had normal acid base status.

Owners of 3 dogs were available to bring the dog back to the VMC UMN for liver function analysis. One dog had serum bile acids within the reference range at the time of initial presentation. When this dog was evaluated 60 months later, serum concentrations of bile acids and fasting plasma ammonia were in the reference range. A 2nd dog had serum bile acids

and ammonia performed 27 months after urethral obstruction. After a 12-hour food restriction, the preprandial and postprandial serum bile acids concentrations were minimally increased (preprandial 10 $\mu\text{mol/L}$; reference range $<6 \mu\text{mol/L}$, postprandial 27.1 $\mu\text{mol/L}$; reference range $<15 \mu\text{mol/L}$), but the fasting plasma ammonia was unremarkable. A 3rd dog had serum bile acids and fasting plasma ammonia performed 7 months after urethral obstruction, and results were within the reference range.

Mineral Analysis of Urethral Plugs. Mineral analysis of the urethral plugs from 8/9 dogs was composed of 100% magnesium ammonium phosphate (struvite) crystals admixed with cellular and proteinaceous material. The mineral component of 1 plug was 90% struvite and 10% calcium phosphate apatite. Mineral analysis of the uroliths was performed for 2 of the 3 dogs with concurrent urolithiasis. In 1 of these dogs, the accompanying stones were composed of a mixture of mostly struvite (70–95%) and smaller amounts of calcium phosphate carbonate (20%) and calcium oxalate monohydrate (5–10%) with a 100% struvite shell. In the 2nd dog, the stones were 100% struvite.

Histopathology of Urethral Plugs. Urethral plugs from 3/9 dogs were submitted for microscopic evaluation. Samples consist of variably shaped and sized (approximately $15 \times 25 \mu\text{m}$ to up to $150 \times 200 \mu\text{m}$) angular to slightly rounded clear spaces within eosinophilic amorphous material (Fig 4). Within the eosinophilic material there are low numbers of scattered degenerate cells with rounded margins and a single round condensed nucleus.

Prevention and Outcome. The dogs were discharged with various therapies for their urinary disease: struvite dissolution or prevention diets (Hill's s/d (5), Hill's c/d (1), or Royal Canin S/O (1)), antibiotics (6/9),

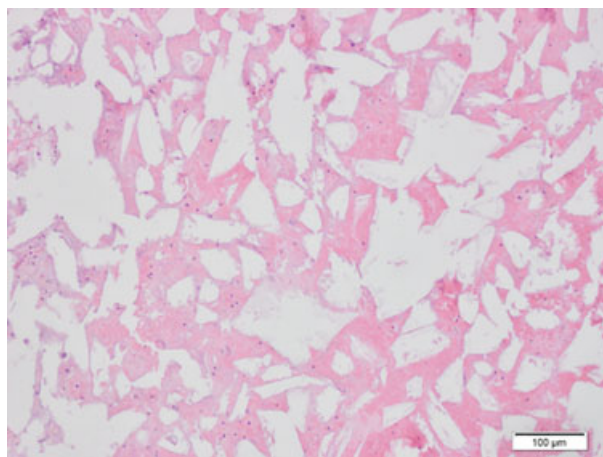


Fig 4. H&E stained section of urethral plug at 10 \times magnification. Amorphous angular to slightly rounded clear spaces, that once contained struvite crystals that were lost in processing, within eosinophilic amorphous material that might represent proteinaceous debris and degenerate cells. A portion of the plug was submitted for quantitative mineral analysis; the crystalline portion was composed of 100% struvite.

phenoxybenzamine (2/9), and oral diazepam (1/9). Follow up was available for 8 dogs, ranging from 21 to 1,800 days. One dog reobstructed 9 weeks after the initial obstruction and was euthanized by the referring veterinarian. No information regarding the cause of the urethral obstruction was available. One dog reobstructed 4 years later secondary to calcium oxalate urolithiasis. Neither of these 2 dogs had been diagnosed with uroliths or a urethral stricture at the time of their initial urethral obstruction.

Discussion

Review of the medical records from 9 affected dogs with struvite plugs that had been evaluated at the VMC UMN revealed several features that contrast starkly with the typical presentation of struvite urolithiasis in dogs. First, in urethral plugs, struvite was interspersed in a deformable matrix of cellular and proteinaceous material rather than as discrete uroliths. Of 42 plug samples from dogs analyzed by the MUC over a 6-year period, 83% had a struvite mineral component. One theoretical contributing factor in the development of urethral plugs in cats is that the bladder mucosal cells secrete excessive mucus in response to irritation or inflammation.³ The plug-forming dogs in this study could have had an underlying bladder disorder that was responsible for the production of the cellular and proteinaceous component of the plugs, but bladder mucosal biopsies were not available for evaluation. Three of the UMN VMC plug dogs had accompanying small uroliths. The presence of uroliths and secondary inflammation might have contributed to the formation of urethral plugs in these dogs.

A 2nd unique feature was that at least 4/9 VMC UMN dogs formed sterile struvite plugs. These 4 dogs had a negative urine culture and no history of antimicrobial therapy within the previous month. Two of these dogs also had concurrent struvite cystoliths. Bacterial culture results from 3 additional dogs were also negative. However, these dogs had received antimicrobials within the previous month. Although 2 dogs were only given a single dose, recent antibacterial therapy could have interfered with our ability to document concomitant bacterial infection. Bacteriuria was not observed for the 2 dogs in which urine cultures were not performed, but these data are insufficient to rule out the presence of a bacterial infection. Urine culture data were not available for the 33 other MUC plug submissions, and infection might have contributed to plug formation in these dogs.

Alkaluria favors dissociation of monobasic phosphate (H_2PO_4^-) and dibasic phosphate (HPO_4^{2-}) to trivalent phosphate ions (PO_4^{3-}). Increasing the concentrations of the trivalent form of phosphate is a risk factor for struvite precipitation. In the absence of a urinary tract infection with urease producing microbes, other risk factors promoting alkaline urine must be considered. Diseases resulting in chronic respiratory alkalosis or chronic metabolic alkalosis would contribute to persistent alkaluria. Three of the breeds (Pug,

Boxer, and Shih Tzu) with MUC plug submissions are brachycephalic and have been reported to develop brachycephalic obstructive airway syndrome.⁵ Dogs affected with this syndrome typically display excessive panting and hyperventilation. Hyperventilation can result in decreased partial pressure of carbon dioxide and subsequent respiratory alkalosis. To mitigate increasing blood pH, bicarbonate is excreted in the urine. However, in 1 study, arterial partial pressure of carbon dioxide was significantly higher in brachycephalic dogs ($n = 11$) when compared to nonbrachycephalic controls ($n = 11$); urine pH was not measured.⁶ Venous blood gases from 3 VMC UMN Pugs in our study did not support respiratory alkalosis as a contributing factor for struvite formation, but we cannot definitively rule out an underlying acid base disorder as a contributing factor to struvite plug formation.

Sterile struvite formation has been reported in 2 dogs suspected to have renal tubular acidosis.^{7,8} Distal renal tubular acidosis is characterized by a decrease in net H^+ secretion in the collecting tubules. This condition should be suspected in dogs with hyperchloremic metabolic acidosis with a urine pH of >6.0 . In the 3 VMC UMN dogs in this study with blood gas analysis and electrolytes, laboratory findings were not supportive of renal tubular acidosis. Three additional dogs had normal serum concentrations of bicarbonate or TCO_2 at presentation, ruling out primary metabolic acidosis. None of the dogs had hyperchloremia.

In vitro studies with sterile human urine revealed that the addition of magnesium, ammonium, or phosphate with a pH range of 5.0–9.6 resulted in formation of struvite crystals.⁹ They determined that if the concentrations of these solutes were high enough, struvite crystallization would occur in acidic urine. In our study, struvite precursors were not measured in the urine from dogs with plugs. Therefore, we were unable to determine if the concentrations of magnesium, ammonium, or phosphate were sufficiently elevated to promote struvite precipitation irrespective of urine pH. We did not observe conditions associated with phosphaturia (hyperparathyroidism, hypophosphatemic rickets, or Fanconi syndrome) or magnesuria (excessive dietary magnesium, renal tubular disorders, or medications containing magnesium) in the VMC UMN plug cases. Liver insufficiency is a potential cause of hyperammonemia and subsequent hyperammonuria. Ammonia will hydrolyze with available carbon dioxide and form ammonium and bicarbonate, resulting in alkaline urine and dissociation of phosphate ions. Ammonium binding with magnesium and phosphate ions would result in precipitation of magnesium ammonium phosphate. Although several of the breeds (Pug, Yorkshire Terrier, Miniature Schnauzer, Shih Tzu, Great Dane) in the MUC plug submission group are reported to be at risk for hepatic portovascular anomalies,^{10,11} struvite uroliths are not typically associated with hepatic insufficiency. Three of the VMC UMN dogs in this study were evaluated for hepatic dysfunction with bile acids and fasting ammonia levels. Though only a subset of dogs was screened,

liver disease was considered an unlikely cause of struvite plugs in dogs.

All of the plugs were from male dogs, whereas struvite urolithiasis is more common in females. The female predisposition for struvite is generally attributed to an increased risk for urinary tract infections. If urethral plugs in dogs are a microbiologically sterile disease, female dogs would no longer be expected to be at increased risk. In fact, because plugs are an obstructive disease, the male predisposition is logical. Male dogs have longer, narrower urethras, which place them at increased risk for urethral obstruction.

One of the most impressive features of the urethral plugs was their breed-specific nature. The majority of the MUC plugs were from Pugs. Odds ratios were calculated for the MUC population using a VMC UMN plug-free control group. The only breed found to be overrepresented for plug formation was the Pug with a significant OR of 179. A limitation of this calculation is that the MUC case population did not have the same geographical distribution as the VMC UMN control population, and there might be differences in breed popularity between these 2 sampled populations. A control population better matched to the MUC case submissions would provide more accurate estimates of breeds at risk for urethral plugs. All of the VMC UMN plug cases were Pugs, and this prohibited us from calculating breed-specific ORs for this subset of dogs.

Because most plugs from dogs had a struvite component, we also calculated breed ORs for a VMC UMN struvite (combined plug and urolith) case population. We found that Pugs were significantly overrepresented for precipitation of struvite in general (OR = 14.3). One other study evaluating urolith submissions from 1981 through 2001 also found that male Pugs had an increased risk (OR: 2.09; CI: 1.03–4.25) for struvite urolithiasis.¹²

Breed predispositions are often an indication of a genetic or familial disorder. Sterile struvite urolithiasis has been reported in 3 related Cocker Spaniels.¹³ These dogs had normal urine acidification after ammonium chloride administration, ruling out renal tubular acidosis. Because of the retrospective nature in this case series, pedigrees from Pugs were not available to assess for familial tendencies beyond recognition of the breed. It is of interest that Pugs are also commonly affected by congenital vertebral abnormalities.¹⁴ Abnormalities of the lumbosacral vertebra could potentially affect innervation to the bladder, resulting in urine retention, urinary incontinence, and increased risk for urinary tract infections, and subsequently influence struvite crystal formation and retention. On abdominal radiographs, 2 dogs were noted to have 6 lumbar vertebrae and 1 dog had a transitional L_7 vertebra. The only clinical sign or physical exam abnormality to suggest spinal cord disease in these 3 dogs was infrequent voiding (once daily) in a single dog, suggesting urine retention. Three other dogs had neurologic deficits on physical examination. The 7 dogs that had a urine culture were negative for aerobic bacterial growth; however, 3 had recently received

antibiotics. Advanced imaging, such as spinal CT or myelogram, was not performed in these 9 dogs. Therefore, compressive lesions of the spinal cord cannot be ruled out.

Conclusions

This report describes urethral plugs in dogs. The crystalline component of the majority of plugs was struvite. Close evaluation of 9 dogs diagnosed with plugs (all struvite) at the VMC UMN did not reveal an explanation of predisposition toward plug or struvite formation. Urinary tract infections were not diagnosed in any of the 9 dogs; however, some dogs had received antimicrobials before sample collection. Two signalment features did stand out in both the larger MUC group and the smaller VMC UMN subset: sex and breed. All plug submissions came from male dogs, and the majority was from Pugs. Anatomical differences between sexes might explain the male predisposition, and the overrepresentation of the Pug suggests a genetic component to disease risk. Further investigation as to the underlying cause of struvite plug formation in dogs is warranted.

Footnotes

^a R Core Team (2012). R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. ISBN 3-900051-07-0, URL <http://www.R-project.org/>

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