Proceedings of the Southern European Veterinary Conference
- SEVC -
Sep. 29-Oct. 2, 2011, Barcelona, Spain

Next SEVC Conference:
Oct. 18-21, 2012 - Barcelona, Spain

Reprinted in the IVIS website with the permission of the SEVC - AVEPA
Feline Urate Urolithiasis

After CaOx and struvite containing uroliths, urate uroliths appear to be the third most common mineral type submitted to our laboratory from cats. Although fluctuations in the percentage of struvite and CaOx containing uroliths have occurred over the past 25 years, the same does not appear to be true of urate uroliths. Therefore, it appears that whatever changes occurred in the feline diet market, these changes did not appear to influence cats that were predisposed to urate stones. No differences in gender were found in cats with urate urolithiasis (49% female and 51% males). Because it is reported that cats with urate stones may have a portosystemic shunt or other liver dysfunction, we have recently evaluated 143 records of cats that presented to primary care veterinarians for urate urolithiasis. Only two cases from our group we studied were diagnosed with a PSS. Although only two cases from the referral population were diagnosed with a PSS, it was impossible to identify which cats within this retrospective series had an underlying liver disorder because very few cases had full liver function evaluations, such as serum bile acids and imaging studies. Primary and secondary care veterinarians do not appear to evaluate cats for this issue, perhaps because most of these cats were reported to have normal physical examinations, biochemical panels, and no clinical signs (e.g. ptyalism, neurological signs, or lethargy) which made veterinarians suspect the presence of a hepatopathy. If one suspects a PSS in a cat, serum bile acids are much more sensitive for the diagnosis. Post prandial serum bile acids have been reported to have the highest sensitivity for evaluating hepatobiliary disease, including a PSS, in the cat. When reviewing the records from earlier cases, no cats were reported to develop clinical signs related to liver disease in subsequent years, suggesting that if an underlying hepatopathy such as a PSS was present in these cats, it was not severe enough to warrant evaluation for it by the owner or primary care veterinarian. When we reviewed cases presenting to the UC Davis Veterinary Medical Teaching Hospital, 5/16 cases had a PSS diagnosed. All of the cases diagnosed with a PSS from both populations of cats had biochemical parameters and/or clinical signs compatible with a PSS. Cats diagnosed with a PSS were generally younger than those without one. Specific breeds such as the Egyptian Mau and Siamese have been reported to be at increased risk for urate stones. Prospective studies are needed to see if full liver evaluations are warranted in breeds that are predisposed, as well as cats without a history, clinical signs and screening blood work suggestive of a PSS. When evaluating recurrence rates of 221 cats with urate stones, 10.9% had a recurrence of a urolith and 2.9% had a subsequent presentation for urolithiasis.

Management of Feline Urate Stones

In any cat that presents with a urate urolith, a full screening CBC and biochemical profile is warranted. If clinical signs and/or changes in the blood work are suggestive for a hepatopathy, further diagnostics such as abdominal ultrasound and serum bile acids are recommended. If urate stones are diagnosed in a cat with no history, clinical signs and clinicopathologic abnormalities suggestive for a hepatopathy, the costs of further tests can be discussed with the owner. In older cats, further testing may not be necessary, but no definitive studies have been done to support or refute this statement.
To prevent recurrence of urate stones in otherwise healthy cats, a high moisture diet that is restricted in protein is often recommended. Anecdotally, a commercially available hydrolyzed soy protein diet has been fed to these cats as well in hopes of providing an adequate protein intake in a low purine form (Royal Canin® Feline Hypoallergenic Hydrolyzed Adult HP). To the author’s knowledge no evidence of the effectiveness of any of these approaches has been evaluated in controlled trials in cats with urate stones. As with all stone disease, feeding a high moisture diet is the cornerstone of stone prevention management. Periodic imaging using ultrasound (as urate can be difficult to see on plain radiography) is also important to monitor for recurrence.

**Canine Urate Urolithiasis**

Urate containing calculi have comprised approximately 23% of the total number of stones analyzed at our laboratory from dogs. During the past 20 years, the proportion of urate containing uroliths (as well as cystine and silica containing uroliths) submitted to our laboratory decreased, however, the trend was not linear (Figure 1). Although an initial increase was noted, by the latter half of the 1990’s, submissions declined.

Unlike most other breeds of dogs, Dalmatian dogs have well described alterations in purine metabolism that lead to the excretion of uric acid in the urine rather than excretion of the more soluble metabolite, allantoin. All Dalmatians excrete relatively high amounts of uric acid (400-600 mg of uric acid per day as compared with 10-60 mg per day in non- Dalmatian dogs), however not all Dalmatians form urate stones. Genetic studies have reported that the mode of inheritance is not X-linked and the prevalence of the clinical disease in male Dalmatians ranges from 26-34%. Bannasch et al., identified the SLC2A9 transporter as the cause of the change in uric acid handling by Dalmatians by positional cloning using an interbreed backcross. We have also found an increased odds ratio for the English Bulldog breed with regards to urate containing calculi. Studies have shown that some individuals in this breed, as well as the Black Russian Terrier, were also homozygous for the same mutation in SLC2A9.

**Management of Urate Stones**

Management of urate calculi in Dalmatian dogs (and breeds with the similar genetic mutation) usually includes feeding a diet low in purines. This can be accomplished by feeding a diet low in protein (e.g. Hills Canine u/d); however newer diets higher in protein, but low in purines have recently become available (Royal Canin Canine U/C). Vegetarian diets have also been described for use in these breeds for management of urate stone recurrence. As with any animal that forms stones, the diet should be high in moisture. In larger breed dogs such as Dalmatians, feeding only canned food can be expensive; therefore, water can be added to the dry kibble if the dog will eat it. The author recommends adding approximately 1cup of water per cup of dry food, and then gradually increasing the water content over 3-4 weeks. Ideally, 3-4 cups of water per cup of dry food is recommended. Periodic urinalyses to evaluate the urine specific gravity and sediment should be performed and adjustments in water content made as needed. Ultrasounds or double contrast cystourethrograms should be evaluated to look for stone recurrence.

If dietary strategies are not successful, one can try the addition of the xanthine oxidase inhibitor, allopurinol. This drug will decrease the amount of uric acid formed in the urine. The exact dose is variable and studies have shown the metabolism of this drug varies from dog to dog. Ideally, the dose should be titrated based on 24 hour urine uric acid excretions. If the urine uric acid is
<300mg/day, the dose of allopurinol should be decreased so as not to predispose the dog to xanthine urolithiasis. Allopurinol should not be administered to animals unless a purine restricted diet is also provided.

If urate containing calculi are found in non-Dalmatian dogs, a search for an underlying portovascular anomaly or other cause for hepatic failure should be pursued. Urate stones have also been reported from dogs with microvascular dysplasia. Dogs with underlying liver disorders are likely predisposed to urate stone formation due to hyperammonuria and hyperuricosuria which result from the reduced ability to convert ammonia to urea and uric acid to allantoin. Allantoin is much more soluble in the urine compared to uric acid. Correction of the liver disorder should be addressed if possible to help prevent urate stone recurrence.

**Calcium Phosphate Containing Calculi in Cats and Dogs**

The number of calcium phosphate (in the form of apatite) containing uroliths in cats analyzed during the last 25 years comprised 5.6% of total stones we analyzed. A significant decrease in calcium phosphate containing uroliths in cats was found during this time period as compared with all other stone submittals. Similar to CaOx containing calculi, they occurred less commonly in young (<4 years of age) cats. No breed predilections were found. The most common site for urolith removal, was the bladder (71%) and 21% were removed from the upper urinary tract; ureteral calculi usually contained CaOx as well. Apatite tends to be less soluble in a urine pH>7.5.

Apatite-containing calculi in dogs have comprised an average of 38% of the stones we have analyzed in dogs from 1985-2006. Similar to cats, apatite containing uroliths in dogs occur most commonly with struvite uroliths, either mixed throughout or as single layers. Brushite (calcium hydroxide phosphate dihydrate) comprised on average only 1% of the stones we have analyzed from dogs during that same time period. These stones tend to occur as multiple small uroliths. Prevention of these uroliths in cats and dogs is unknown. Similar to CaOx management, a search for predisposing disorders that could result in hypercalcemia is recommended. Oftentimes, it is recommended the dog or cat be evaluated and managed similar to those patients with CaOx stones. A high moisture diet that produces a neutral urinary pH is advised.

**Cystine and Silica Urolithiasis in Cats and Dogs**

Cystine and silica-containing uroliths are very rare in the cat, and accounted for 0.15% and 0.3% respectively of the uroliths submitted to our laboratory. Cystine and silica containing calculi are uncommon in dogs and were noted in 1.3% and 6.6% respectively from all the canine urolith samples we have analyzed. Dogs with silica containing calculi are usually older and most affected dogs are male. Most silica calculi have a “jack stone” appearance, giving them a characteristic look on plain radiography. The recurrence rate of silica calculi is not well known, but these stones are generally slow growing. Dietary prevention strategies focus on providing a high moisture diet that is higher in animal proteins and lower in plant origins, particularly rice, soybean hulls, and corn gluten feed.

Cystine stones were reported more often in younger male dogs, and like urate containing calculi, research investigating a genetic mutation in dogs with cystinuria has been published. Testing for this mutation in Newfoundlands has been available for several years, and perhaps this information has lead to as steady decline in this metabolic stone. When cystine uroliths do occur, they recur frequently after removal. Dietary management can include feeding a diet high in moisture and moderately low in protein (e.g. Hill’s Canine u/d, Royal Canin Canine Urinary U/C). The drug, 2-MPG (Thiola®), can be used to help prevent or even dissolve some cystine stones, however this sulfhydryl compound can be cost prohibitive for many dog owners. Gastrointestinal side effects can occur.

**Dried Solidified Blood Calculi in Cats**

We have reported another stone type called dried solidified blood calculi (DSB) that we have only identified in cats. Although we have rarely noted small amounts of DSB on the surface of various canine stones, none of them were ever composed of 100% DSB that we analyzed in cats. DSB...
calculi were submitted to our laboratory and were reported to occur in various places in the urinary tract, including the upper urinary tract. These DSB calculi are very firm and “stone-like” but usually do not contain crystalline material. The incidence of DSB calculi in cats also seems to be increasing. Although these stones are not common, they can be a diagnostic challenge. We reported that many of these calculi were not radio-opaque (unless they contained a significant portion of CaOx, calcium phosphate or other radiodense mineral). Furthermore, they were oftentimes not identified on ultrasonographic examination. Infrared spectroscopy on a subset of 9 calculi did not identify the presence of any mineral crystals in six DSB calculi we analyzed but did identify the presence of minerals in the three control samples which contained DSB and CaOx or CaP. Quantitative elemental microprobe analysis on this same subset of 9 calculi revealed that the six DSB calculi contained significantly more carbon, nitrogen and sulfur as compared with the three control calculi suggesting that these DSB calculi are primarily formed from organic material. If a clinician suspects they may have DSB calculi, we recommend that they be submitted both in formalin and without formalin. The calculi submitted in formalin would be used for histopathology.

Conclusions
Whenever a stone is obtained from an animal (either surgically, catheter assisted, voided, or by lithotripsy), it is important that it be submitted for crystallographic analysis in order to properly identify the minerals present. Evaluating trends in feline and canine urolithiasis is important because it may assist clinicians in determining what if any effect current stone prevention strategies, including dietary modifications and drug therapy, are having in cats and dogs with urolithiasis.

References: