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Clinical Article

HYPERCALCIURIA IN THE HOUSE RABBIT: AN ECOLOGICAL ANOMALY

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SUMMARY

A four-year-old male, domestic rabbit was presented for treatment with the history of anorexia, oliguria and sluggish bowel movements. Radiography revealed ballooned urinary bladder, radiopacity virtually at par with bone. With signs of marked tissue dehydration, the pet, in acute agony, was stabilized with subcutaneous fluid therapy and pain medication. Later, the pet was referred to the veterinary emergency care centre, where a thorough clinical reappraisal confirmed poor prognosis because of intractable urolithiasis. Therefore, with the owner's formal consent the animal was euthanized humanely to relieve him from extreme suffering. The present communication on the highly challenging urolithiasis in rabbits aims to highlight this unique, virtually incurable, pathoclinical syndrome and call attention to the prophylactic measures including suitable diet modification and timely veterinary medical care.

Keywords: Cystocentesis, Diet, Fluid Therapy, Hypercalciuria, Rabbit

Humans as well as most animals absorb dietary calcium commensurate with the actual need of body tissues; the excess is excreted uneventfully via bile in the feces. However, calcium homeostasis in rabbits is not well-balanced; inhibited ammonia synthesis in the renal tubules is presumably the outcome of some queer twist in their ecological journey (Kampheus, 1991). Thus, rabbits absorb calcium directly in proportion to the dietary calcium intake, regardless of the metabolic demand, resulting in markedly increased circulatory titres (Kennedy, 1965). The average sized adult bunny weighing nearly 2.5 kg consumes around 0.51 g dietary calcium per day and excretes the excess mineral in the blood circulation-not through the normal hepatobiliary gastrointestinal tract channel-but mainly through the kidneys as calcium carbonate ($CaCO_3$) crystals. Some rabbits exhibit the clinical syndrome of hypercalciuria, named "bladder sludge" in the popular parlance (Hartcourt-Brown, 2002). The predisposing factors include genetic susceptibility of the individual subject, continuing reduced water intake resulting in accelerated tissue dehydration, urinary tract disorders, e.g. latent or patent microbial infection of the bladder with oliguria, postural defects, sore hocks and obesity, compounded with the lack of physical activity under prolonged house confinement (Richardson, 2008). With improved rabbit care protocols, the prognosis has improved significantly in recent years (Brown, 2020).

Rabbit urine, very dark when freshly voided and drying up leaving behind voluminous gray-white chalky material, clearly points to life-threatening tissue dehydration, necessitating the appropriate fluid replacement therapy on the topmost priority. In this clinical condition, bunnies often exhibit visible signs of stress, frequently voiding scanty, highly viscous, almost paste-like urine on each forced attempt, often outside the litter box. The hunched-up posture is typical. Grinding of the teeth in agony reflects trauma from the pricks of sharp-edged sludge crystals. Bald patches and markings "urine scalds" are often seen in the inner aspect of thighs. Anorexia and depression are the consequence of impaired renal function.

In the diagnostic protocol, anamnesis aims to solicit precise information from the owner on the exact duration of the disorder, major changes in the house rabbit's behavioral profile/food preferences/life style/micro-environment, or use of any home remedy. Clinical examination and abdominal survey radiography, the definitive tool to demonstrate sludge entrapped inside the "ballooned bladder"- with or without calculi in the urinary tract and kidneys - are the other basic components. Ultrasonography monitors the internal organs, especially the kidney. Blood work, urinalysis and serum biochemistry also provide valuable leads. The treatment options are flushing out the urinary bladder (cystocentesis), catheterization under anaesthesia, or surgery if absolutely unavoidable (Meredith and Flecknell, 2006).

A four-year-old male domestic breed rabbit was brought to the Angel Animal Hospital with the history of anorexia, oliguria, and turgid bowel movements. Clinical examination revealed subnormal rectal temperature (37.8 ºC). The exceptionally fast heart rate could not be recorded. However, the rate of respiration (40-45 beats/minute) was within the normal range. The capillary refill time was <2 seconds. The visible mucous membranes appeared pink. The slightly overweight (3.2 kg), nearly 8% dehydrated (skin tent test, 3 seconds) pet exhibited clear signs of depression. On anamnesis, the tentative diagnosis narrowed

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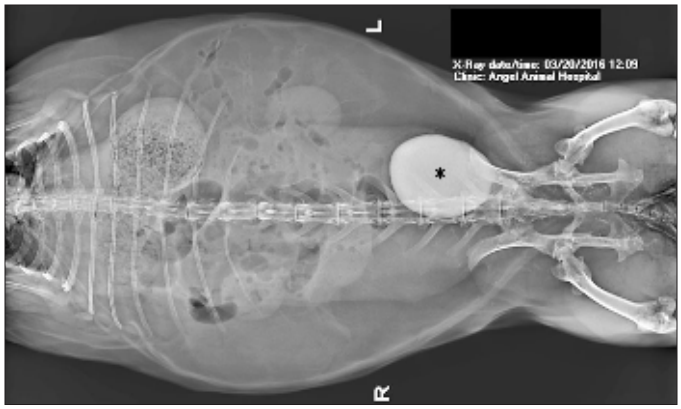

Fig. 1. Ventrodorsal survey radiograph: Note the radiopaque urinary bladder (*)

Fig. 2. Right Lateral survey radiograph: Note the urinary bladder sludge (*)

down to GI tract stasis, kidney disorder, cystitis, or mechanical obstruction of the urethra because of some growth/calculi, the most likely possibility. The in-house abdominal radiographs (Fig. 1 & 2) revealed ballooned urinary bladder with the increased radiopacity mimicking bone, the hallmark of severe hypercalciuria with no evidence of growth in the internal organs/ other body parts.

Clinical judgment dictated immediate relief to the patient in great agony: gently emptying the turgid urinary bladder. Since the attempted cystocentesis did not work, sterilized tom cat catheter was applied to collect the tenacious urine directly. When the catheter was withdrawn, a whitish beige coloured chalk-like, more precisely cement-like, highly viscous discharge was seen, slowly dribbling out from the penile urethral opening. Thus, this was a classic case of "bladder sludge" in rabbit. The patient was stabilized with pain medication Meloxicam® injectable 5 mg/ml (Putney, Inc., USA) @0.2 mg/kg S/Q (VIN portal, North America), and administered fluid therapy with Normosol® (Hospira, Inc., USA) balanced electrolytes solution @ 35ml S/Q : Na^+ 140, K^+ 5, Mg^{2+} 3, Cl^- 98, acetate 47 and gluconate 23 m Eq/l. However, in view of the fast deteriorating clinical condition, the patient was immediately referred to the emergency veterinary care centre, where clinical reappraisal established poor prognosis. Therefore, with the well-informed owner's formal consent, the animal was euthanized humanely (sodium pentobarbital 2 ml IV, following Telazole induced sedation) to relieve him from the excruciating pain and suffering. This episode, with an unhappy ending, would serve to highlight the mandatory long-term preventive measures including suitable dietary changes relating to the house rabbit, and timely veterinary care.

Biostatistics of the domestic rabbit will be of interest to pet practitioners. The life span ranges from 6 to 13 years. In healthy subjects, the 24-hour water intake is 50-100 ml/kg body weight, and total urinary output 20-25 ml/kg. The optimum ambient temperature is 15-20 ºC; normal rectal temperature 38.5-40 ºC, subnormal 38.0 ºC and below, and elevated 40.6 ºC and above. The heart rate is 130-325 beats/ minute, and respiratory rate 32-60 counts/ minute. The blood volume is 55-65 ml/kg weight; 10 ml jugular vein sample may be drawn for blood work (Hartcourt-Brown, 2002). The average life span of rabbit erythrocytes is 50 days, compared to 120 days in humans.

The unconventional *in vivo* calcium metabolic pathway in the rabbit results in the circulatory total calcium concentration varying over a wide range and 30-50% higher, compared to all other mammalian species (Buss and Bordeau, 1984). Dietary calcium is absorbed from the duodenum by passive diffusion and/or ATP-dependent active transport involving de novo synthesis of a specific carrier protein. Reduced blood ionized calcium [iCa^{2+}] triggers accelerated parathormone (PTH) release (Warren *et al.*, 1989) which, in turn, stimulates transformation of biologically inactive 25-hydroxy cholecalciferol, vitamin D_2 functional 1, 25-dihydroxy cholecalciferol, vitamin D_3 (calcitriol) in the renal parenchyma. This biomechanism is designed to ensure need-based intestinal absorption of calcium (Eckermann-Ross, 2008). In rabbits, for reasons not clearly defined yet, the passive pathway of intestinal calcium absorption predominates; the role of vitamin D_3-mediated pathway remains dormant (Bordeau *et al.*, 1986; Kampheus, 1991). As a consequence, the normal feed-back mechanism is non-existent; calcium is absorbed in direct proportion to the dietary calcium concentration (Cheeke and Amberg, 1973). This accounts for the increased blood calcium concentration in the rabbit in response to elevated dietary calcium level. The kidney reacts by excreting large quantities of blood calcium in the urine (Whiting and Quamme, 1984).

The normal rabbit urine varies markedly in

appearance, colour ranging from the characteristic pale yellow through different shades of orange and brown to deep red, closely resembling blood. Further, the voided urine colour mainly depends on the nature of the diet and the quantum of excreted plant pigments. Intake of vegetables such as cabbage, broccoli and dandelion (a common lawn grass with small yellow flowers) often results in red urine. A dipstick differentiates blood from the phytopigments. Urolithiasis or uterine/renal disorders may cause hematuria. "Bladder sludge" in rabbits, irrespective of the age gender and breed, is marked by hypercalciuria with massive accumulation of crystals. The excess mineral is voided via the renal excretory system, mostly in the form of $CaCO_3$ crystals, when the pH of excreted urine is increased to the exceptionally high alkaline range (8.5-9.5), compared to the average value of 8.2. In perspective, the treatment of choice is acidifying the urine concurrently with the use of staple diet of well-judged reduced calcium content (Johnson, 2009). Alfalfa hay component in commercial pellets is high in calcium (4.8%). Therefore, switching over to grass hay/ timothy hay (0.41% calcium) is recommended (Hartcourt-Brown, 2002). Surgical removal of uroliths is attempted only in emergency (Capello, 2005; Hoefer, 2006).

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