A Case of Renal Oxalosis in a 3-Month-Old Cat Raised under Controlled Conditions

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ABSTRACT. The kidneys of a 3-month-old female cat were examined. The cat which had been raised under controlled conditions with no history of any poisoning showed progressive weight loss with increases in blood BUN and creatinine concentrations. At necropsy, both kidneys were firm in consistency with formation of focal scars. Histopathologically, widespread deposition of crystals was observed in the renal tubules (in both dilated lumina and degenerative epithelia) accompanying mild interstitial fibrosis with lymphocyte infiltration. The crystals were colorless or basophilic on the hematoxylin and eosin-stained section and could be visualized with polarized light as doubly refractile crystals. The crystals were identified as calcium oxalate crystals by histochemical examinations using von Kossa stain and alizarin red S stain under different conditions and by ultrastructural examination. Judging from the above-mentioned findings, the present renal lesion detected in an infant cat was diagnosed as renal oxalosis which was suspected to be hereditary in nature.

KEY WORDS: feline, nephrosis, oxalate.

Oxalosis is characterized by widespread deposition of calcium oxalate crystals in the kidneys, bones, arterial media and myocardium, following increased concentrations of oxalate in body fluids, including the urine (hyperoxaluria) [4–8, 14, 16]. Deposition of calcium oxalate crystals most frequently occurs in the kidneys, resulting in renal failure and/or urolithiasis in severe cases. This renal disorder is called renal oxalosis. This paper describes the results of histopathological, histochemical, and ultrastructural examinations on the kidneys of an infant cat with renal oxalosis.

A female mixed-breed cat which had been raised in a laboratory under controlled conditions with no history of any poisoning showed progressive weight loss with increases in BUN (from 140.1 to 388.5 mg/dl in 1 week – reference range 10–30 mg/dl) and creatinine (from 3.56 to 7.94 mg/dl in 1 week – reference range 0.8–1.4 mg/dl) concentrations, indicators of renal tubule disorder. At 3 months of age, the cat was euthanized and subjected to postmortem examination in the laboratory. At necropsy, both kidneys were firm in consistency with formation of focal scars. In the other organs, there were no gross abnormalities observed.

The kidneys were sent to the authors’ laboratory for histopathological, histochemical and ultrastructural examinations. Renal tissues were fixed in 4% phosphate-buffered paraformaldehyde (PFA) solution, embedded in paraffin, sectioned at 4 μm, and stained with hematoxylin and eosin (HE). Some sections were also subjected to von Kossa stain, alizarin red S stain with a modification of the previously published procedure [6, 17], periodic acid-Schiff (PAS) reaction, periodic acid-methenamine-silver (PAM) stain, masson trichrome stain or phosphotungstic acid hematoxylin (PTAH) stain.

For ultrastructural examination, small pieces of the PFA-fixed tissues were post-fixed in 1% osmium tetroxide and embedded in epoxy resin. Ultrathin sections were double-stained with uranyl acetate and lead citrate and were examined under transmission electron microscope (H600, Hitachi, Tokyo, Japan).

In the histopathological examination, there were several dents in the cortical surface accompanying ectatic or cystic renal tubules surrounded by focal interstitial fibrosis and lymphocyte infiltration (Fig. 1A). In addition, an extremely dilated blood vessel was observed at the renal capsular surface. Its lumen was occupied with organized thrombus accompanying calcium deposition and neutrophil infiltration. Some glomeruli appeared to be atrophic with an accumulation of eosinophilic materials in Bowman’s space, while clear glomerulonephritis or glomerulosclerosis was not detected on the results of PAS, PAM and Masson trichrome stains.

Deposition of crystals was detected in the renal tubules with dilated lumen and flattened or degenerative epithelium throughout the HE-stained section (Fig. 1A and 1B). They could be visualized with polarized light as doubly refractile crystals (Fig. 2A). The crystals were colorless or basophilic on the HE-stained section and arranged in sheaves or prisms (Fig. 2B). In addition, the crystals stained positive for von Kossa stain (Fig. 2C) and alizarin red S stain at pH7.0 even after treatment with 0.1N hydrochloric acid (Fig. 2D and 2E). The positive staining for alizarin red S was diminished at pH4.2, and also at pH7.0 after treatment with 0.1N hydrochloric acid (Fig. 2F and 2G).

In the ultrastructural examination, crystals were observed not only in the renal tubule but also in the interstitium as radially or concentrically organized materials or crystal ghosts (Fig. 3A and 3B). Destruction of the renal tubule basement membrane by crystal ghosts was sometimes found (Fig. 3B). In proximal renal tubules, epithelial cells show-
ing destruction of brush borders with disorganized or ruptured cytoplasm containing swollen or broken mitochondria were detected (Fig. 3C).

Judging from the above-mentioned results of histopathological, histochemical and ultrastructural examinations, the crystals were identified as calcium oxalate, and the renal lesion in the present case was diagnosed as renal oxalosis with interstitial nephritis.

Two types of oxalosis, or hyperoxaluria, are known; the first is an acquired disorder, and the second is one aspect of a heritable disorder. Hereditary oxalosis, or primary hyperoxaluria, is known as an autosomal recessive disorder in human beings which contributes to the deficiencies in alanin:glyoxylate aminotransferase (AGT) and glyoxylate/
hydroxypruvate reductase (GR/HPR). These enzymatic deficiencies, which are categorized as type 1 and type 2, respectively, lead to an increase in oxalate production and subsequent development of oxalosis or hyperoxaluria [16]. On the other hand, acquired oxalosis, or secondary hyperoxaluria, is said to be caused by ethylene glycol poisoning, specific plant intoxication, infection by oxalate-producing microorganisms, such as Aspergillus niger and A. flavus, and low intake of pyridoxine (vitamin B6) [13]. Both types of oxalosis or hyperoxaluria have been reported in many species including humans, dogs, cows, and cats [1, 3, 5, 6, 8, 13, 14]. In cats, most cases of renal oxalosis are an acquired disorder, and dietary components are noted as risk factors for increase of oxalate urolithiasis [13]. On the other hand, there are only a few reports of primary hyperoxaluria or hereditary renal oxalosis including both type 1 and type 2 in cats [1, 3, 5, 8, 14]. In the previous reports, primary hyperoxaluria in cats showed clinical features including acute renal failure and neurological signs and histological findings such as interstitial nephritis and fibrosis with crystal deposits, swollen axon in spinal cord and variation in fibre size in skeletal muscle [5, 8, 14]. In the present case, clinical dysfunction and histological findings in the kidney were similar with previous reports, but clear neurological signs were not observed. However, the presence of any histopathological changes in spinal cord was not confirmed in this case.

Unfortunately, family history of renal oxalosis in this case is unknown. However, the present case was suspected to be hereditary renal oxalosis, because the cat was 3 months old and had been raised indoors under controlled conditions with no history of exposure to chemicals known to be able to cause oxalosis.

The cause of organized thrombus at the renal capsular surface in this case was not histopathologically clarified, because no crystallized CaOx was detected in renal vessel lumens or walls which cause vascular necrosis and hemorrhage. However, arterial wall oxalosis and atherosclerotic oxalosis have been reported in human beings [6] and so, the formation of this thrombus might be associated with the deposition of CaOx in the blood vessels.

In the previous study, it has been suggested that tubular epithelial cells endocytose CaOx crystals on the luminal surface and exocytose them on the basolateral side. Consequently, crystals move from the tubular lumen to the interstitium of the kidney [9–11, 18–20]. In this case, it was observed ultrastructurally that some crystal ghosts are extending from the tubular epithelium to the interstitium through the basement membrane, which suggests that similar transport of calcium oxalate crystals from the luminal surface to the peritubular interstitium might also occur in the present case.

The cat has been proposed as a model for human hyperoxaluria [5] and could provide a useful model to assess enzyme inhibitors which reduce the formation of oxalate [14]. Furthermore, oxalate urolithiasis in cats is often related with diet as a cause, and the case has been increasingly reported [2, 12, 15]. Therefore, the histopathological and ultrastructural analyses of kidney lesions in the present case will provide additional information of feline renal oxalosis, and may be useful for the future study of oxalosis in humans and animals.

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