



Diagnostic Exercise

From The Davis-Thompson Foundation*

Case **172** Month: **September** Year: **2021**

Answer Sheet

Title: Cat, renal toxic disease

Contributors: Alex dos Santos*, DVM, MS, Doctorate candidate, Mariana Martins Flores*, DVM, MS, Doctor in Veterinary Pathology. *Laboratory of Veterinary Pathology, Universidade Federal de Santa Maria (UFSM), Santa Maria, Rio Grande do Sul, Brazil. mariana.flores@ufsm.br

Clinical History: This 8-month-old, male, mixed breed domestic shorthaired cat had a recent history of acute apathy and anorexia. It remained under hospital care for two days, during which it did not produce any urine. On the second day of hospitalization, another cat from the same household was brought in with similar clinical signs. These cats did not have any history of recent ingestion of antibiotics or other medication. Furthermore, they did not have any street or yard access since they were kept in an apartment. Both cats died spontaneously after a brief hospitalization period.

Laboratory Findings: Marked increase of urea and creatinine in both cats was reported (values not informed). On abdominal ultrasound, both cats had perirenal edema, and small amount of free abdominal effusion was observed in this cat.

Necropsy Findings: There was moderate amount of translucent, slightly yellowish fluid within the abdominal cavity, thoracic cavity and pericardial sac. There was moderate diffuse pulmonary edema. Moderate perirenal edema was observed bilaterally. The kidneys were diffusely swollen and pale (Fig. 1). On histopathologic exam, the cortical tubular epithelial cells were swollen, with hypereosinophilic cytoplasm and nuclear changes (karyolysis, pyknosis and karyorrhexis). These cells were frequently detached from the basement membrane. Some other tubular epithelial cells were swollen and markedly vacuolated. Accompanying these changes, multiple granular casts filled the tubular lumens in the cortical and medullar regions (Fig. 2).

Gross and Microscopic Images:

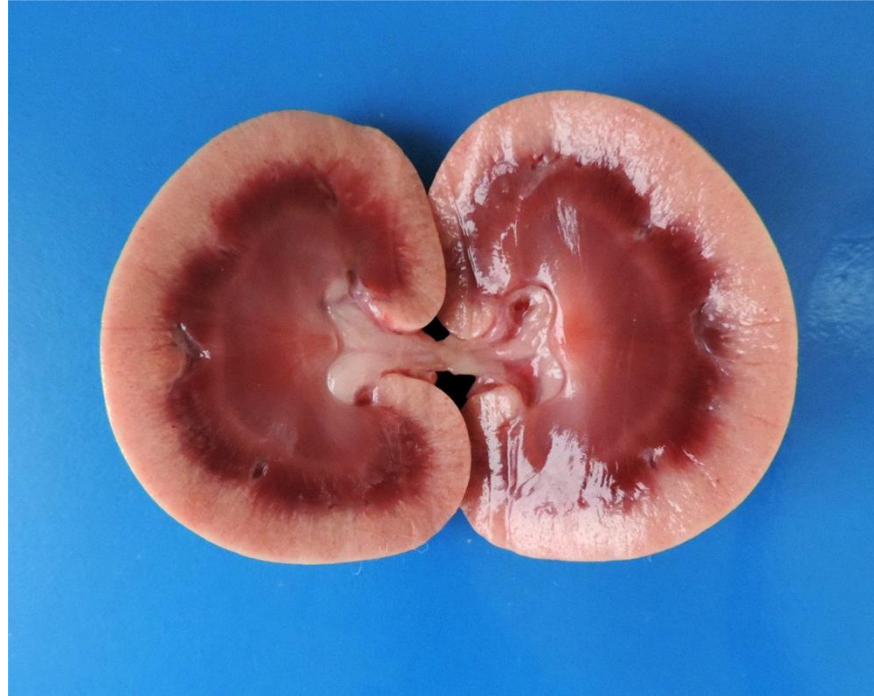


Figure 1

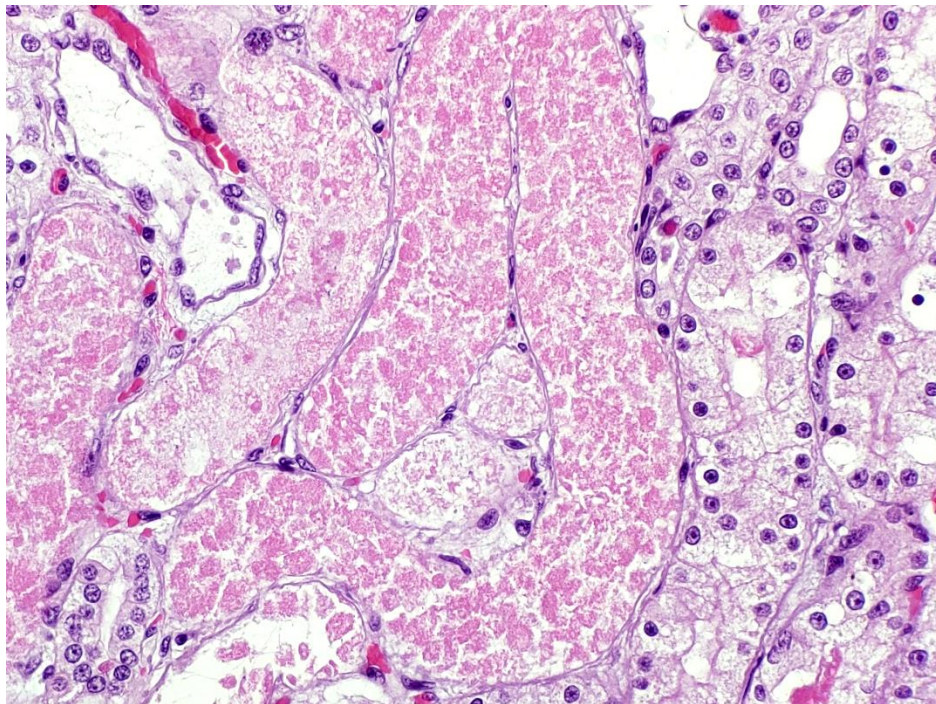


Figure 2

Follow-up Questions:

- *What is your morphologic diagnosis?*
- *What is your etiologic diagnosis?*
- *What is the pathogenesis for the acute anuria presented by this cat?*

- Can you name possible causes for this condition in cats?

Morphologic diagnosis: Kidneys, multifocal, severe, acute tubular degeneration and necrosis, with multifocal intratubular granular casts.

Etiologic diagnosis: Kidney, toxic nephropathy.

Typical gross findings: Acute tubular necrosis (ATN) is macroscopically characterized by swollen and pale kidneys. In some instances, perirenal edema is an important feature and is thought to be an ultrafiltrate associated with tubular back-leak into the renal interstitium, ultimately leaking into the perirenal and retroperitoneal connective tissues (Cianciolo & Mohr, 2015). Extrarenal lesions of uremia may additionally be observed; however, these lesions are less common in cats than in dogs. Feline uremia is commonly accompanied by pulmonary edema, with occasional cavitory effusions; other extrarenal lesions (such as soft tissue mineralization and oral ulcers) are uncommon (Ambrosio 2020).

Typical microscopic findings: Histologically, ATN affects the epithelial cells lining the renal tubules while the basement membrane remains intact. Proximal renal tubules are particularly susceptible to most nephrotoxins and are therefore predominantly affected in ATN cases. However, some toxins induce primarily distal tubule injury (Brown et al. 2007). Histologic changes have multifocal distribution and are characterized by epithelial cell swelling and vacuolation (degeneration), and cell detachment from the basement membrane, cytoplasmic hypereosinophilia and nuclear changes (pyknosis, karyolysis, and karyorrhexis) (necrosis). Some tubules are devoid of epithelial cells, constituted only by a denuded basement membrane, and occasionally filled with necrotic debris (granular casts) (Cianciolo & Mohr, 2015).

Discussion: Acute tubular injury refers to acute injury to the tubular portion of the nephron, which may include degeneration and necrosis. It may be referred to as acute tubular necrosis (ATN) or nephrosis (Cianciolo & Mohr, 2015). If severe enough, this condition may induce acute renal failure, as seen in this case. ATN is potentially reversible since epithelial cells from the kidney may regenerate and replace the necrotic cells. This regeneration is facilitated by the preservation of the basement membrane, a feature of ATN. The main causes of ATN in domestic animals are hypoxia and nephrotoxins (Cianciolo & Mohr, 2015). Nephrotoxins may include routinely used drugs (aminoglycosides, penicillin, polymyxins), plants (*Lilium* spp., *Amaranthus retroflexus*), insects (blister beetle), animal venoms, and other chemicals (organomercurials, chlorinated naphthalenes, ethylene glycol, paraquat) (Ross, 2011; Cianciolo & Mohr, 2015). Outbreaks of ATN have additionally been described in dogs and cats associated with pet-food contaminated with melamine and cyanuric acid (Brown et al. 2007). A thorough anamnesis may help to identify the animal's contact with potential nephrotoxins; however, it is not always easy to confirm the specific cause of ATN during clinical exam or necropsy. In some instances, the animal may have had contact with a nephrotoxin without the owners' knowledge. In other situations, information regarding the contact with potentially nephrotoxic drugs, substances, or plants is not shared by the owner. In this specific case, there was no history of use of any drugs prior to the clinical onset. The fact that both cats were from the same household led us to contact the owner and insist on trying to define the cause of ATN. When asked about the presence of specific plants in his apartment, the owner reported that his wife had bought *Lilium* sp. a week earlier and that both cats had played with the plant, even eating parts of it. Based on this information, we were able to confirm *Lilium* sp. intoxication. Several members of the

Liliaceae family of plants are nephrotoxic to domestic animals, including *Nartheceum ossifragum* in ruminants and *Lilium* spp. in cats (Cianciolo & Mohr, 2015). Most cat owners are not aware of the nephrotoxic potential of this plant, which facilitates the intoxication. *Lilium* spp. ingestion causes acute clinical disease associated with proximal tubular necrosis and may also induce pancreatic necrosis (Langston, 2002), the latter not being observed in this case. Clinically, ATN may cause acute oliguria and anuria; these are attributed, in part, to the high quantity of granular casts filling the renal tubules and obstructing the intratubular flow of glomerular filtrate, reducing urine formation (Ross, 2011; Cianciolo & Mohr, 2015). Histological changes are indistinguishable in different nephrotoxin-induced ATN, except for nephrotoxicoses associated with oxalates (ethylene glycol, fungal or plant-associated oxalates), which induce intraluminal crystal accumulation within the proximal renal tubules (Cianciolo & Mohr, 2015). Non-oxalate crystals were observed in several cases of pet-food melamine and cyanuric acid intoxication; however, they predominated in the distal tubules (Brown et al. 2007).

References and Recommended literature:

- Ambrosio M.B., Hennig M.M., Nascimento H.H.L., Santos A., Flores M.M., Figuera R.A, Irigoyen L.F., Kommers G.D. 2020. Non-Renal Lesions of Uraemia in Domestic Cats. 2020. J Comp Path 180:105-114.
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Associate Editor for this Diagnostic Exercise: Mariana M. Flores

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