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Calcium oxalate nephrosis in a cat: Case report

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Abstract. The aim of this study was to report a case of sudden death due to acute renal failure by oxalate calcium nephrosis. Among the main differential diagnoses, there are ethylene glycol intoxication, lily intoxication and primary congenital hyperoxaluria. Epidemiology and clinical signs suggest intoxication by ethylene glycol, a nephrotoxic substance present in several products. There are few reports of this condition in Brazil, and it should be considered in cases of renal failure and sudden death.

Keywords: ethylene glycol, sudden death, nephrotoxicity

Nefrose por oxalato de cálcio em gato: Relato de caso

Resumo. O objetivo deste estudo foi relatar um caso de morte súbita por insuficiência renal aguda devido a um quadro de nefrose por cristais de oxalato de cálcio. Entre os principais diagnósticos diferenciais, cita-se a intoxicação por etilenoglicol, intoxicação por lírio e hiperoxalúria congênita primária. A epidemiologia e os sinais clínicos permitem sugerir intoxicação por etilenoglicol, uma substância nefrotóxica presente em diversos produtos. Há poucos relatos dessa condição no Brasil, e deve ser considerado em casos de insuficiência renal e de morte súbita.

Palavras-chave: Etilenoglicol, morte súbita, nefrotoxicidade

Nefrosis por oxalato de calcio en un gato: Reporte de caso

Resumen. El objetivo de este estudio fue reportar un caso de muerte súbita por insuficiencia renal aguda por nefrosis causada por cristales de oxalato de calcio. Entre los principales diagnósticos diferenciales se encuentran la intoxicación por etilenglicol, la intoxicación por azucenas y la hiperoxaluria congénita primaria. La epidemiología y los signos clínicos sugieren una intoxicación por etilenglicol, una sustancia nefrotóxica presente en varios productos. Hay pocos informes de esta afección en Brasil y debe considerarse en casos de insuficiencia renal y muerte súbita.

Palabras clave: Etilenglicol, muerte súbita, nefrotoxicidad

Introduction

In cats, one of the main causes of renal failure is acute tubular necrosis characterized by disruption of the cytoskeletal structure of renal tubular cells and loss of their apical microvilli and brush border. The death of these cells can occur due to ischemia or toxic injury (Monaghan et al., 2012a, 2012b).

Ethylene glycol is a bittersweet, odorless, colorless dihydric alcohol that can be found in antifreeze, brake fluid, industrial solvents, household cleaners, and cosmetics (Hristov et al., 2023). Ethylene glycol nephrotoxicity is associated with oxalate production during its metabolization process. Oxalate is then

combined with calcium ions resulting in calcium oxalate crystals, which are soluble complexes that reduce glomerular filtration and cause direct cellular toxicity to renal cells (Popa et al., 2018).

Renal oxalosis is a common histological finding in cases of ethylene glycol intoxication, however, there are other important differential diagnoses for calcium oxalate nephrosis in cats, such as intoxication by ingestion of lily (*Lilium* sp.) (Fitzgerald, 2010; Panziera et al., 2019) and congenital primary hyperoxaluria (Heiene et al., 2009). There are rare reports of primary or secondary hyperoxaluria in cats in Brazil (Bezerra et al., 2022; Santos et al., 2014).

Another important cause of renal failure in cats is polycystic kidney disease, which is characterized by the formation of multiple cysts that result in deterioration of the renal parenchyma. It is a genetic and progressive disease that initially presents itself in a subclinical form (Schirrer et al., 2021). The objective is to report a case of calcium oxalate nephrosis accompanied by polycystic kidney disease in a cat in Brazil, focusing on the anatomopathological findings.

Clinical case report

A 6-year-old male mixed-breed feline was referred for autopsy after sudden death. In the anamnesis, the owner revealed that the animal lived in an apartment and at the time of death, the animal was in a pet shop.

In the macroscopic evaluation, it was observed that both kidneys were diffuse and markedly pale and in the cortical region, there were multifocal cystic areas of 0.5 to 2.0 cm in diameter filled with translucent liquid content. In addition, bilateral and moderate diffuse pulmonary edema and congestion, discrete multifocal hepatic degeneration and moderate diffuse hemorrhagic gastritis were also visualized. Kidney samples were fixed in 10% buffered formalin solution, embedded in paraffin, sectioned at 4 µm and stained with hematoxylin and eosin, Von Kossa and Masson's trichrome.

On microscopy, a marked diffuse disorganization of the renal tubulointersticial architecture was noted, with the tubular epithelium with intense cytoplasmic vacuolation and marked diffuse loss of cellular detail, accompanied by increased cytoplasmic eosinophilia, pyknosis and nuclear karyorrhexis (acute tubular necrosis) (Figure 1A). Additionally, multiple translucent, pale-yellow crystals were observed; crystals were arranged in bundles, prisms and rosettes in the tubular lumens, often in contact with the basement membrane (Figure 1B). Von Kossa's stain stained the crystals black (Figure 1C and 1D); under polarized light they were birefringent (Figure 1E and 1F), making them compatible with calcium oxalate.

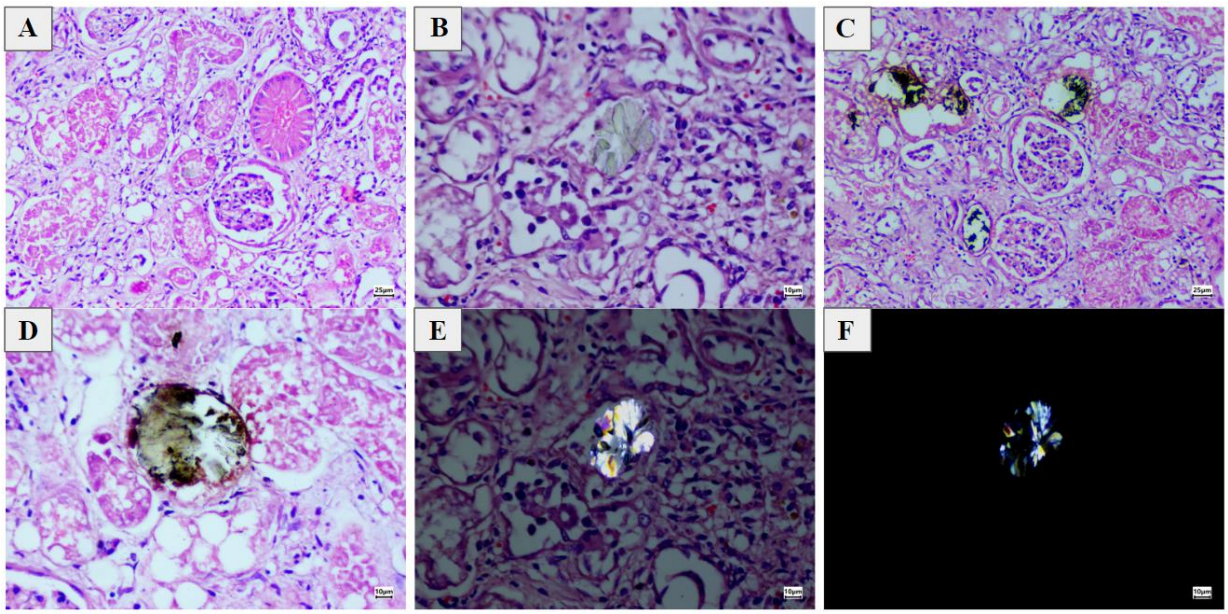

Figure 1. Kidney; cat. Calcium oxalate nephrosis. **A**) Severe epithelial cell necrosis of renal tubules (HE, 20x). **B**) Translucent, pale yellow crystal in prism in tubular lumen (HE, 40x). **C** and **D**) Crystals stained black in the Von Kossa stain (Von Kossa, 20x and 40x). **E** and **F**) Crystal's evidence under polarizes light (HE, under polarized light, 40x).

Multiple cystic areas of different sizes were also visualized, covered by flattened epithelium and delineated by a variable amount of connective tissue. The cysts were filled with amorphous eosinophilic material and sometimes with red blood cells. The interstitium was multifocally expanded by a moderate amount of inflammatory infiltrate composed of lymphocytes (interstitial nephritis) and by the deposition of a moderate amount of fibrous connective tissue (interstitial fibrosis). Interstitial fibrosis was evidenced in blue by Masson's trichrome stain.

The anatomopathological findings were compatible with acute tubular necrosis due to calcium oxalate and polycystic kidney disease. Due to the severity of the impairment of the renal tissue, it was concluded that the cause of death of this animal was acute renal failure.

Discussion and conclusion

Calcium oxalate crystals result in renal injury due to their precipitation in the tubular lumen and consequent obstruction accompanied by loss of glomerular filtration (McQuade et al., 2014). Crystalluria can occur not only from calcium oxalate, but also from calcium phosphate or melamine-containing crystals. To differentiate these crystals, a histomorphological analysis must be performed using hematoxylin and eosin stain associated with special stains. Other possible techniques are infrared microspectroscopy or scanning electron microscopy with dispersive energy X-ray analysis (Thompson et al., 2008). In this case, the crystals were Von Kossa positive indicating calcium ions in their composition. In addition, the crystals were colored and showed a prismatic effect -under hematoxylin and eosin staining confirming the origin as calcium oxalate crystals.

Ethylene glycol intoxication is the main diagnosis for this case, due to its severe calcium oxalate nephrosis, but it is a challenging diagnosis in cases where there is no clear history of deliberate or accidental ingestion since it is a substance that may be present inside houses or contaminating food products due to errors in industrial production (Bezerra, et al., 2022; Pereira et al., 2022; Smit et al., 2021). This condition is more frequent in dogs than in cats; however, cats show a lower lethal dose, a mortality rate of 96-100% and the main route of intoxication is cutaneous absorption (Popa et al., 2018)

Another differential diagnosis in cats is the intoxication caused by the ingestion of *Lilium* sp., an ornamental and toxic plant often present in houses (Fitzgerald, 2010; Fitzgerald et al., 2013). The main microscopic finding is acute tubular necrosis with the presence of occasional birefringent calcium oxalate crystals (Panziera et al., 2019). Epidemiologically, it is possible to exclude this cause in the present case, since the owner reported that there were no lilies in his apartment and the animal did not have access to the street.

Primary hyperoxaluria is a genetic disorder that results in the accumulation of glyoxalate, the precursor of oxalate, due to a deficiency of the enzyme alanine: glyoxylate aminotransferase (Heiene et al., 2009). In addition to renal lesions, there are neuromuscular impairment due to the accumulation of neuronal neurofilaments in peripheral nerves and consequent muscle atrophy (De Lorenzi et al., 2005). The animal in this case did not present neuromotor alterations.

The anatomopathological findings in this case associated with the epidemiology allow us to conclude that it is a case of ethylene glycol intoxication, even though the origin of the toxic substance has been not determined. This diagnosis is common in countries with severe winters, since is used as an antifreeze product (McQuade et al., 2014; Porter, 2012; Santos et al., 2014). However, in Brazilian veterinary literature there are rare reports in dogs, but none in cats (Santos et al., 2014). Recently, outbreaks in dogs consuming contaminated treat (Bezerra et al., 2022) and in human beings consuming contaminated beer by an industrial error were reported in Brazil (Pereira et al., 2022). Thus, ethylene glycol intoxication should be considered as an important differential diagnosis for acute renal failure or in cases of sudden death, since it is a substance present in several products.

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