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CLINICAL-DIAGNOSIS COORDINATES IN ETHYLENE GLYCOL INTOXICATION IN A CAT. CASE STUDY

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Abstract

The aim of this study is to underline the significance of ethylene glycol poisoning as a differential diagnosis in young outdoor cats presented with sudden onset of lethargy in the absence of other clinical signs whose state continues to degrade over a few hours. Ethylene glycol intoxication is more common in dogs than in cats, as they are more tempted by its sweet taste. Cats are more frequently intoxicated through cutaneous absorption and grooming and have a lower minimum toxic dose. Clinical signs include polyuria, hyporeflexia and ataxia, that progress to depression, stupor and hypothermia and signs of acute kidney failure. A 9 months-old male intact cat presented in a precomatose state in our clinic. The anamnesis indicated that it was an indoor-outdoor cat with no medical history which had been been away from home for a few hours. Clinically, it presented with inappetence and lethargy. The physical examination revealed a precomatose state with hypothermia (36.8°C), dehydration, cyanotic mucous membranes, uremic halitosis, mydriasis and an absent pupillary light reflex. Blood biochemistry revealed a blood urea nitrogen of 75 mg/dL and a creatinine of 11.8 mg/dL. Repeated blood glucose measurements revealed oscilations between hypo- and hyperglycemia despite therapeutical interventions. The ultrasonographic examination showed kidney lesions suggestive of ethylene glycol toxicity. The microscopic examination of the urinary sediment revealed calcium oxalate crystals. Based on the paraclinical evidence, we suspected an intoxication with antifreeze such as ethylene glycol. The cat was treated specifically and rehydrated, but after 48 hours the its clinical state had worsened and the decision was made to put the cat to sleep. Even though the incidence is lower in cats, ethylene glycol toxicity should be added to the list of differential diagnoses in cats, in particular during the cold season when antifreeze is more commonly used and mostly when the symptomatology is suggestive of an acute intoxication.

Key words: *ethylene glycol, intoxication, cat.*

INTRODUCTION

Ethylene glycol (EG) intoxication is one of the most common causes of acute kidney injury (AKI) and the second most common intoxication encountered in pet animals. Antifreeze is the main source of exposure, but ethylene glycol is also used in a variety of household products including cleaning products, varnishes, cosmetics and aromatic extracts[4]. Ethylene glycol as such is not directly nephrotoxic; its metabolites (glycolaldehydes, glycolic acid, glycolat and oxalic acid) are the cause of renal damage [7].

Ethylene glycol intoxication is more common in dogs[10] than in cats, as they are more tempted by the sweet taste [8].

Cats, on the other hand, are more frequently intoxicated through cutaneous absorption and grooming and have a lower minimum lethal dose of just 1.5 ml/kg with a recorded mortality after ingestion of EG of 96–100% [4,5].

Ethylene glycol is rapidly absorbed from the gastrointestinal tract. The peak plasma concentration occurs about 1 hour after ingestion and approximately 50% of the ingested ethylene glycol dose is eliminated unchanged by the kidneys; however a series of oxidative reactions in the liver and kidney metabolize the rest of ethylene glycol [6].

The first step of the metabolism is its conversion to glycoaldehyde by alcohol dehydrogenase. Further glycoaldehyde is then metabolised to glycolic acid.

The metabolites of glycolic acid turn to glyoxylic acid and then oxalate. The resulting toxic metabolites cause severe metabolic acidosis and impairment of the renal tubular epithelium. One of the most toxic metabolites is

oxalate, as it cannot be metabolized further and it is cytotoxic to the renal tubular epithelium and exacerbates metabolic acidosis. Glycolic acid and oxalate are considered to be the metabolites responsible for the acute tubular necrosis associated with ingestion of ethylene glycol. The oxalate combines with calcium to form a soluble complex that is eliminated by glomerular filtration. If the concentration of the glomerular filtrate increases and the pH decreases, calcium oxalate crystals can form in the lumen of the tubes [9,12] (Fig.1)

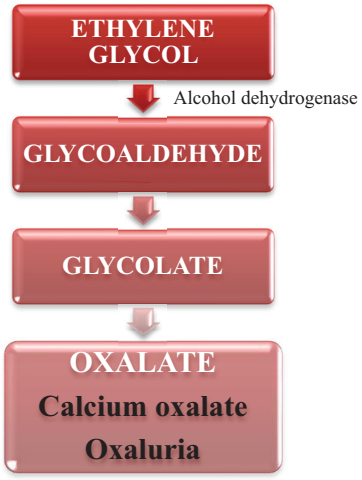

Fig. 1. Metabolic pathway of ethylene glycol

Clinical signs of EG toxicosis occur in III stages.

First stage (30 min–12 hours postingestion) is defined mainly by neurological signs such as depression, ataxia, seizures, coma, or death. As a consequence of the direct irritating effect of ethylene glycol on the mucosa, gastrointestinal signs may also appear. Research has shown that these clinical signs are due to aldehyde metabolites, hyperosmolarity, and metabolic acidosis, and resemble those of alcohol ingestion. Treatment is more likely to be successful if it is initiated in this stage [7].

The second stage occurs from 12 to 24 hours following ingestion and is determined by metabolic acidosis, CNS depression, miosis and the development of cardiopulmonary signs such as tachypnea or tachycardia [7].

The third and final stage (24–72 hours postingestion of a lethal dose) is characterized by acute renal failure and associated clinical signs (anorexia, vomiting, and other signs of uremia).

The ultrasonographic image of kidney with oxalate nephrosis points out ultrasonographic changes that varies from mild to marked increased renal cortical echogenicity with varying degrees of intensity of the corticomedullary junction ('halo' sign) and is supportive of the presumptive diagnosis of ethylene glycol intoxication [2].

MATERIALS AND METHODS

The clinical investigations, ultrasound examination and treatment methods described herein were performed in the Clinic of Medical Pathology, Faculty of Veterinary Medicine, Bucharest, on a 9 months-old intact male cat, presented in a precomatose state in our clinic. Haematological, biochemical and urine tests were conducted in the Laboratory Clinics, belonging to the Faculty of Veterinary Medicine.

The ultrasonographic examination was performed using the Esaote Pie Medical MyLab, in M and B-modes, with convex, micro-convex and linear probes with a frequency range of 5-18 MHz.

Storing and analyzing the image obtained was performed with the computer using specific morphometry software.

The anamnesis indicated that it was an indoor-outdoor cat with no medical history which had been away for a few hours.

Clinically, it presented with inappetence and lethargy. The physical examination revealed a precomatose state with hypothermia (36.8°C), capillary refill time was within 2-3 seconds, cyanotic mucous membranes, heart rate – 136 min, respiratory rate – 32 min, dehydration, uremic halitosis, mydriasis and an absent pupillary light reflex.

Blood biochemistry revealed a blood urea nitrogen of 75 mg/dL and a creatinine of 11.8 mg/dL. Repeated blood glucose measurements revealed oscilations between hypo- and hyperglycemia despite therapeutical intervention.

The ultrasonographic examination showed nephromegaly, increased renal cortical echogenicity, being markedly more echogenic than the adjacent liver with sonolucency in the

corticomedullary junction and central medullary region (the "halo sign") due to accumulation of multiple calcium oxalate crystals, particularly in the cortex and the corticomedullary junction.
The microscopic examination of the urinary sediment revealed calcium oxalate crystals, which can be detected in the urine of most animal species approximately 6–8 h after ingestion of ethylene glycol, and in cats as early as 3 h after ingestion (Fig.2)

Fig. 2. Urine sediment: the presence of calcium oxalate crystal (Courtesy of the Laboratory of the Faculty of Veterinary Medicine).

The diagnosis of oxalate nephropathy associated with ethylene glycol toxicosis as the cause was supported by the history and further corroborated by the analytical findings.
Based on the paraclinical evidence, we suspected an intoxication with antifreeze such as ethylene glycol. The cat was treated specifically and rehydrated, but after 48 hours its clinical state had worsened and the decision was made to euthanise the cat.

RESULTS AND DISCUSSIONS

The clinical diagnosis of ethylene glycol poisoning can be challenging, taking into account the fact that in this case, the actual ingestion couldn't have been noticed by the owner due to the absence of the cat from home.
Clinical signs were not specific especially when considering that the simptoms could have been representative of a large number of toxic or infectious agents and are variable depending on the stage of intoxication[7].
Ethylene glycol intoxication should be suspected in cats with acute onset of signs, high values of urea, creatinine, hypocalcaemia, hyperglycaemia (50% of patients develop hyperglicemia due to inhibition of glucose metabolism, increased blood epinephrine or cortisol, uraemia[7]), azotaemia or uraemia and depression, metabolic acidosis and calcium oxalate crystalluria[13].
Ultrasound examination offered valuable information regarding renal ultrasonographic appearances, which were strongly suggestive of ethylene glycol intoxication with increased renal cortical echogenicity and the presence of a 'halo' sign (an echogenic line in the outer zone of the renal medulla, paralleling the corticomedullary junction, described also as the renal medullary rim sign).
The detection of ethylene glycol in the body can also be aided by the fact that many antifreeze liquids contain fluorescein, which is easily detectable in urine by Wood lamp examination up to 6 h after ingestion[1].
Therapy. The deciding factor in the treatment of ethylene glycol intoxication is the administration of the antidote as soon as possible. The antidote of choice is ethanol, which competes with the ethylene glycol at the active site of the enzyme alcohol dehydrogenase. Its affinity is higher than that of ethylene glycol, which leads to the excretion of ethylene glycol in an unchanged form. The second antidote, 4-methylpyrazole (fomepizole), has a similar mechanism of action – with only minor adverse effects compared to ethanol, but it is very expensive and rarely quickly accessible in common veterinary practice [6,13].

CONCLUSIONS

Ethylene glycol ingestion is a common cause of lethal intoxication particularly in cats, but prompt diagnosis and treatment with ethanol therapy can be life-saving. However, in many cases the early signs may be missed, as they can be vague and non-specific, which results in a tardy presentation of the animal to the vet.

Diagnosis of EG toxicity in the clinical setting must be made based on clinical signs as well as history and clinicopathologic findings.

The speed with which the correct diagnosis is made directly influences the prognosis as the antidote is salutary when administered within the first five hours after ingestion. Otherwise, due to the enzymatic change into metabolites, the administration of an antidote is useless.

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