Ethylene glycol toxicity: a retrospective pathological study in cats

Livia Amoroso¹, Cristiano Cocumelli²*, Giampaolo Bruni², Alberto Brozzi², Francesco Tancredi², Goffredo Grifoni², Antonio Mastromattei², Roberta Meoli², Giovanni Di Guardo¹ and Claudia Eleni²

¹ Veterinario Libero professionista.
² Istituto Zooprofilattico Sperimentale del Lazio e della Toscana "M. Aleandri", Rome, Italy.
³ University of Teramo, Faculty of Veterinary Medicine, Teramo, Italy.

*Corresponding author at: Istituto Zooprofilattico Sperimentale del Lazio e della Toscana "M. Aleandri", Ufficio di Staff Accettazione, Refertazione e Sportello dell’Utente, Laboratorio Anatomopatologia, Via Appia Nuova 1411, 00178 Roma (Capannele)
Tel.: +39 0679099468 - 442, Fax: +39 0679099331, e-mail: cristiano.cocumelli@izslt.it.

Keywords
Cat,
Ethylene glycol,
Ethylene glycol toxicity,
Pathological findings,
Poisoning.

Summary
Ethylene glycol (EG) is a well known toxic compound, the assumption of which can be fatal to pet animals as well as to humans. Limited information is available on the pathological features of EG poisoning in pet animals, with special emphasis on cats. Twenty-five cats with histologically confirmed EG intoxication were retrospectively investigated, in order to define more precisely the gross pathological findings and improve the diagnostic process. Furthermore, a brief comparison with the lesions reported in EG-poisoned human patients and dogs was also made.

Studio retrospettivo sull’avvelenamento da glicole etilenico nel gatto

Parole chiave
Avvelenamento,
Gatto,
Glicole etilenico,
Intossicazione,
Rilievi anatomopatologici.

Riassunto
Il glicole etilenico (GE) è una sostanza tossica ad ampia diffusione e di facile reperibilità. La sua ingestione, accidentale o volontaria, è responsabile di avvelenamento sia nell’uomo sia negli animali. Gli aspetti anatomopatologici dell’avvelenamento da GE negli animali, e in particolar modo nel gatto, sono poco conosciuti e la letteratura che li descrive è limitata e frammentaria. Per meglio definire il quadro anatomopatologico in corso di intossicazione e per migliorare l’accuratezza diagnostica in corso di sospetto avvelenamento da GE, è stato effettuato uno studio retrospettivo su 25 gatti nei quali l’avvelenamento da GE è stato confermato per mezzo dell’esame istologico. Le lesioni osservate sono state inoltre confrontate con quelle descritte in corso di intossicazione da GE nell’uomo e nel cane.

Ethylene glycol (EG) is a dihydric alcohol mainly used in anti-freezing solutions, with a high degree of toxicity in animals and humans. In pet animals, EG ingestion can lead to death within few hours. In Italy, there are no studies addressing the frequency (incidence and prevalence) of EG intoxication in cats and dogs, although in USA EG has been reported to be the second cause of poisoning for pets (Hornfeldt and Murphy 1997). Ethylene glycol is accidentally ingested by dogs and cats because of its sweet taste. After assumption, it is rapidly absorbed by the gastrointestinal mucosa and rapidly distributed to different body tissues through the bloodstream. Before being metabolized, much like the excessive consumption of alcohol in human patients, EG causes irritation of the gastric mucosa, along with central nervous system depression. Ethylene glycol is subsequently converted into more toxic metabolites, which are responsible for severe metabolic acidosis and acute renal failure. The terminal metabolite is calcium oxalate, which deposits in tissues, especially in the renal parenchyma, where it gives rise to crystal deposits and crystalluria (Grauer et al. 1984). Even though EG poisonings have been known for long time, the scientific literature concerning the pathological findings observed in EG-intoxicated...
Ethylene glycol toxicity in cats Amoroso et al.

13 cats (52%) (Figure 2 and 3). Finally, 2 animals (8%) had meningeal congestion, with 2 additional cats also exhibiting a subcutaneous oedema.

In the 25 cats herein investigated, the diagnostic confirmation of EG poisoning was made based on the presence of microscopically evident calcium oxalate deposits within their kidney tissue (Figure 4). In this respect, it is worth stressing that small amounts of calcium oxalate crystals can be found during chronic renal tubular obstruction, with occasional crystals being normally found in urine sediments from dogs (Maxie and Newmann 2007). In the present case series, the high amount of calcium oxalate crystals, which are considered a pathognomonic finding in pet animals, together with the mild to absent chronic renal changes, allowed us to confirm the diagnostic suspect of EG intoxication. Recently, several cases

Within the framework of the Italian Health Ministry Decree on animal poisoning\(^1\) from January 2011 to June 2015, 688 cats were submitted to the Istituto Zooprofilattico Sperimentale del Lazio e della Toscana “M. Aleandri” (IZSLT), in order to determine the cause of their death.

In all those cases in which microscopic evidence of high amounts of calcium oxalate crystals in kidneys was obtained, a diagnosis of EG intoxication was made, with the pathological findings observed in each of the aforementioned cats being retrospectively investigated.

The presumed cause of death could not be defined for 167 out of the 688 cats, and further histopathological investigations were requested. Microscopically, calcium oxalate crystals were detected in the kidney tissue of 25 animals. In these cats, macroscopic lesions (Table I) were characterized by enlarged (7/25) and pale (5/25) kidneys (Figure 1), which also showed more evident cortico-medullary junctions (3/25), and subcapsular capillaries’s congestion (1/25). As far as the respiratory system is concerned, 11 subjects (44%) had pulmonary hyperaemia associated with pneumonia (2/25), severe oedema (1/25), or both (1/25). Variable amounts of sero-haemorrhagic fluid also occurred within the pleural cavity from 13 cats (52%). As far for the digestive system, catarrhal gastritis was evident in 8 cats (32%), together with more or less extensive haemorrhagic foci (1/25).

Furthermore, hepatic degeneration was observed in 13 cats (52%) (Figure 2), while 11 subjects showed liver congestion (44%). Sero-haemorrhagic effusions were also detected in the peritoneal cavity from

animals is scanty, being it mainly focused on the lesions affecting the kidney tissue.

During acute EG intoxication, it is also possible to find uremic pneumonia, pulmonary oedema, and hyperaemia of the gastric mucosa (Marcato 2002). The observation of calcium oxalate crystals in histological sections of kidney is considered to be a pathognomonic lesion, while glomerular hyperaemia, vascular degeneration, and tubular renal necrosis are frequent in the acute poisoning, followed by fibrosis and tubular regeneration in the chronic phase of the intoxication. Crystals can also be found, though less commonly, in the blood vessels' endothelium within the intestinal sub mucosa as well as in the liver, heart, and brain. The present study aimed at characterizing more precisely the EG-related lesions' pattern in a number of cats succumbed to EG poisoning.

Within the framework of the Italian Health Ministry

<table>
<thead>
<tr>
<th>case</th>
</tr>
</thead>
<tbody>
<tr>
<td>enlarged</td>
</tr>
<tr>
<td>pale</td>
</tr>
<tr>
<td>pleural</td>
</tr>
<tr>
<td>peritoneal</td>
</tr>
<tr>
<td>congestion</td>
</tr>
<tr>
<td>oedema</td>
</tr>
<tr>
<td>degeneration</td>
</tr>
<tr>
<td>congestion</td>
</tr>
<tr>
<td>gastritis</td>
</tr>
</tbody>
</table>


Ordinanza Ministeriale 10/02/2012. Norme sul divieto di utilizzo e di detenzione di esche o di bocconcini avvelenati. Off J, 58, 09/03/2012.


Ordinanza Ministeriale 10/02/2012. Norme sul divieto di utilizzo e di detenzione di esche o di bocconcini avvelenati. Off J, 58, 09/03/2012.
of acute renal failure secondary to melamine in association with cyanuric acid ingestion have been reported in pet animals, thus making necessary to include also this poisoning in the differential diagnosis investigation’s protocol. In the cases reported here and in agreement with the literature (Brown et al. 2007, Cocchi et al. 2009), however, the crystals observed in the renal parenchyma from the cats under study were morphologically different from melamine/cyanuric acid-induced crystals, as they were also also deposited in different kidney tissue compartments.

Oxalate crystals deposition is predominant in proximal tubules and they are lightly green with a glassy appearance. In contrast, melamine/cyanuric acid crystals are predominantly distributed within distal tubular segments, and are green to blue in appearance. In this respect, as also suggested by the relevant literature, selected renal tissue sections from the cats under investigation were histochemically stained using Pizzolato’s method (Figure 5), which is able to confirm the oxalate composition of the kidney stones (Yamaguchi et al. 2005).

In human patients, a number of gross pathological findings during EG poisoning have been reported (Davis et al. 1997). The most commonly observed findings are: enlarged kidneys with sharper cortico-medullary demarcation, associated with cerebral oedema; multiorganic congestion and haemorrhage; as well as liver degeneration (Leth et al. 2005).

In dogs, although limited information is available, post mortem findings are reminiscent of those seen in human patients, with enlarged and pale kidneys showing cortical petechiae, cardiac distension and left ventricular enlargement, pale myocardium, pulmonary oedema, splenomegaly and splenic congestion, as well as gastric and intestinal haemorrhagic lesions (Pasca et al. 2000).

In cats with confirmed EG intoxication, the renal macroscopic alterations were similar to those described in humans and dogs, although the aforementioned lesions were inconstantly detected. By contrast, hepatic degeneration and pulmonary congestion were frequently observed, in a similar manner to what reported in human patients, who commonly show hepatic lipidosis. This finding differs from those reported for dogs (Pasca et al. 2000), for
which available, microscopic examination of the liver revealed a variable degree of degeneration, from hydropic degeneration to lipoidosis, with no lesion prevailing on the other ones. Additionally, pleural and peritoneal effusions, which have been described neither in EG-poisoned human patients nor in dogs, were observed in more than half of the cats under investigation.

Based upon the herein reported data, lesions such as catarrhal gastritis, pulmonary congestion and/or liver degeneration, associated (or not) with pericardial and pleural effusions, should be considered as "non-specific" whenever the typical EG poisoning-associated macroscopic changes were missing. Alternatively, the aforementioned lesions should be regarded as compatible with other aetiologies, thereby leading to diagnostic misinterpretation. In some circumstances gross findings like pleural and/or abdominal effusion together with renal damage and sometimes pericardial effusion had been connected to Feline Coronavirus-1 infection (feline infectious peritonitis), but microscopic observation of oxalate crystals in renal parenchyma, in absence of typical pyogranulomatous nephritis clearly proved the diagnosis of EG poisoning.

This retrospective study provides some additional information on gross and microscopic lesions’ morphology in EG-poisoned cats, although it does not permit to highlight specific diagnostic elements. This is the main reason why we believe that EG intoxication is greatly underestimated in companion animals, with special reference to cats and, mainly, to those living in rural environments, where this toxic compound is widely distributed. An accurate case history collection, followed by detailed anatomo-histopathological investigations, are therefore of paramount relevance. Indeed, this information would be crucial to provide adequate support to the diagnostic process. Finally, further pathomorphological studies on EG-poisoned cats are warranted.

References


Tipişcă V., Solcan C., Nechita E.L., Ciompe C. & Vulpe V. 2012. Comparative histological aspects in some nephropathies in cat. Book from University of Agricultural Sciences and Veterinary Medicine, Romania, 438-443.