

ACETAMINOPHEN INDUCED HEPATOSIS IN A PUP - A CASE REPORT

K. Krithiga and M.J. Abraham

Department of Veterinary Pathology, College of Veterinary and Animal Sciences,
Mannuthy, Thrissur, Kerala - 680 651

Received: 07-11-2017 Accepted: 29-11-2017

ABSTRACT

Acetaminophen induced hepatitis in a pup is being reported. Acetaminophen toxicity in dogs results in hepatic damage. Suspecting pyrexia the animal was medicated with about 300 mg of acetaminophen (Paracetamol). It exhibited nausea, vomiting and respiratory distress and collapsed before treatment could be instituted. Grossly, the liver appeared very pale. The histopathological examination revealed well demarcated vacuolations in the hepatocytes and necrosis. Infiltration of inflammatory cells could be observed in the periportal area.

Keywords: Acetaminophen toxicity, hepatitis, pup

INTRODUCTION

Acetaminophen (Paracetamol) is an anti-pyretic and analgesic drug used commonly for human medication. However, the drug is contraindicated in dogs and cats. Acetaminophen in doses higher than 200 mg/ kg body weight can cause methaemoglobinemia, hemolysis and acute liver necrosis in dogs (Villar and Buck, 1998). Acetaminophen undergoes both toxic and non-toxic transformation in the

liver. In dogs, most of acetaminophen is conjugated with glucuronide and sulphate by transferase enzymes and only a small portion of the dose is converted to reactive metabolites by the cytochrome P-450-dependent mixed function oxidase (MFO) system (Nash and Oehme, 1984; Savides *et al.*, 1984 and Parkinson, 1996). The reactive metabolites formed may subsequently become conjugated with glutathione (GSH) and excreted in the urine as nontoxic metabolites (Nash and Oehme, 1984 and Savides *et al.*, 1984). The cytotoxic metabolite of acetaminophen, N-acetyl benzoquinoneimine tends to bind to liver proteins and cause centrilobular necrosis (Parkinson, 1996). Here we report a case of acetaminophen induced hepatitis in a pup due to improper medication.

MATERIALS AND METHODS

The carcass of a one month old Rottweiler pup weighing around 2 kg was brought for necropsy examination to the Department of Veterinary Pathology, College of Veterinary and animal Sciences, Mannuthy. The owner had tried to treat the animal with acetaminophen (Paracetamol) suspecting pyrexia as the animal was not taking food properly. The animal was given

with 300 mg of acetaminophen (half-a tablet of 600 mg paracetamol).

The animal exhibited weakness and shivering after the medication in the previous night. The animal was brought to the hospital, but collapsed before treatment could be initiated and the carcass was submitted for necropsy examination.

RESULTS AND DISCUSSION

Necropsy examination revealed a very pale liver (Fig.1) and few ulcers in the large intestine. Blood was oozing out from the tissues which lead to dark brown appearance of the tissues. Tissue samples were collected in 10 per cent neutral buffered formalin for histopathological examination. Histopathology revealed predominant changes in the liver with severe necrosis and fatty change. Whole parenchyma revealed cells with vacuolated cytoplasm, indicative of a fatty degeneration and necrosis (Fig.2). Infiltration of inflammatory cells could be observed in the periportal areas.

In dogs, the organ targeted by paracetamol toxicity is the liver. The animal was administered at a dose of about 300 mg of acetaminophen which has resulted in clinical signs like nausea, vomiting and has resulted in hepatic necrosis. Such clinical signs were generally observed at doses more than 200 mg/kg body weight (Villar and Buck, 1998) however the same were also reported when the dosage exceeded 100 mg/kg body weight (Sellon, 2006). As the given dosage exceeded 100 mg/kg body weight and due to variation in individual susceptibility, the animal succumbed to toxicity of acetaminophen.

The gross appearance of a very pale liver and histopathological observation of hepatic necrosis and fatty change indicate severe hepatic damage as biotransformation in the liver has been reported earlier (Parkinson, 1996). The wide spread necrosis noticed in the liver was also observed by Parkinson (1996), due to the cytotoxic metabolite, N-acetyl benzoquinoneimine, which could bind to liver proteins and produce necrosis. In the present study wide spread changes in the liver parenchyma could be observed against centrilobular necrosis reported by Parkinson (1996), which could be due to the variation in the amount of acetaminophen ingested or due to individual variation.

The dark brownish discolouration of blood oozing out from the tissue could be due to formation of methaemoglobin. Similar finding was made in acetaminophen toxicity by earlier researchers (MacNaughton, 2003 and Cortinovic *et al.*, 2015). Methaemoglobinemia would also have been a contributing factor resulting in death of the animal along with acute hepatitis.



Fig.1. Gross- Liver- Very pale appearance

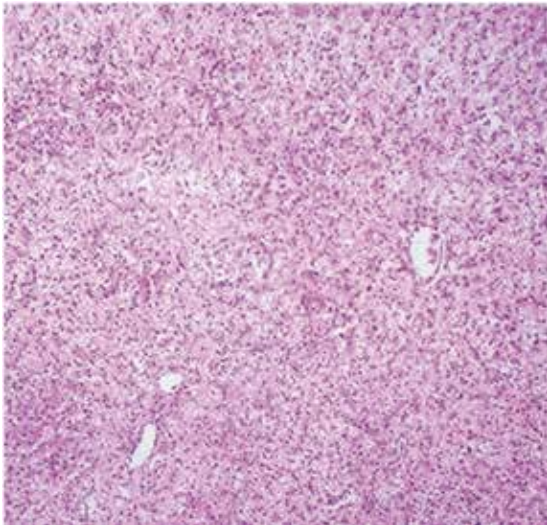


Fig.2. Histopathology- Liver- Necrosed and vacuolated hepatocytes. H & EX100

REFERENCES

- Cortinovis, C., Pizzo, F. and Caloni, F. 2015. Poisoning of dogs and cats by drugs intended for human use. *Vet. J.* **203**: 52-58.
- MacNaughton, S.M. 2003. Acetaminophen toxicosis in a Dalmatian. *Can. Vet. J.* **44**:142-144.
- Nash, S.L. and Oehme, F.W. 1984. A review of acetaminophen's effect on methemoglobin, glutathione, and some related enzymes. *Vet. Hum. Toxicol.* **26**: 123-132.
- Parkinson, A. 1996. Biotransformation of xenobiotics. In: Klaassen, C. D., Amdur, M.O., Doull, J., (Eds.), Casarett and Doull's *Toxicology: The Basic Science of Poisons*. 5th ed. New York: McGraw-Hill. pp. 113-186.
- Savides, M.C., Oehme, F.W., Nash, S.L., Leipold, H.W. 1984. The toxicity and biotransformation of single doses of acetaminophen in dogs and cats. *Toxicol. Appl. Pharmacol.* **74**: 26-34.
- Sellon, R. K. 2006. Acetaminophen. In: Petersen, M.E. and Talcott, P.A. (Eds.), *Small Animal Toxicology*, 2nd ed. Saunders, USA, pp: 550-558.
- Villar, D. and Buck, W.B. 1998. Ibuprofen, aspirin and acetaminophen toxicosis and treatment in dogs and cats. *Vet. Hum. Toxicol.* **40**: 156-162.

