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Therapeutic management of *Hepatozoon canis* induced acute hepatitis in a dog

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Abstract

A three year old Labrador retriever dog was presented to the Referral Veterinary Polyclinic, Indian Veterinary Research Institute, Izatnagar with a history of vomiting, anorexia, fever and tick infestation. Clinical examination revealed pyrexia, pale conjunctival and oral mucous membrane, hepatomegaly, peripheral lymphadenopathy. Haemato-biochemical evaluation revealed anemia (Hb- 8.1g/dl, RBC- 3.95 millions/mm³, PCV- 25.2%), leukocytosis (21.32×10³ cells/mm³), thrombocytopenia (1.12 lakhs/mm³), Hypoalbuminemia (1.44 g/dl), hyperglobulinemia (4.51 g/dl) and elevated levels of blood urea nitrogen (BUN) (37.4 mg/dl), creatinine (2.05 mg/dl), alanine aminotransferase (ALT) (162 U/L) and aspartate aminotransferase (AST) (48 U/L). Blood smear examination revealed *Hepatozoon canis* gamonts in the neutrophils. The animal was treated with a combination therapy including single dose of Inj. Imidocarb dipropionate (6.6 mg/kg, SC) and Tab. Doxycycline (5 mg/kg, PO, BID) for 28 days. Supportive treatment was done with antiemetics, hepatoprotectants, hematinics, plasma expanders and acaricides. An uneventful recovery was noticed after 28 days of treatment.

Keywords: *Hepatozoon canis*, hepatitis, imidocarb dipropionate, doxycycline

Introduction

Hepatozoon species is an epicomplexan parasite of family Hepatozoidae affecting primarily mammalian leukocytes [1]. *Hepatozoon* spp. undergoes asexual development with merogony followed by gamontogony in a vertebrate intermediate (dog) and sexual development leading to sporogony in a hematophagous invertebrate definitive host (tick) [2]. Two species of *Hepatozoon* has been identified namely: *Hepatozoon canis* and *Hepatozoon americanum*. Canine hepatozoonosis was reported first time from India by James [3]. Transmission of disease takes place by ingestion of *Rhipicephalus sanguineus* tick belonging to family Ixodidae. Mixed infections are possible with hepatozoonosis as single tick may harbor multiple pathogens [4]. Subclinical infection may remain unnoticed unless concurrent infection with other pathogens is present [5]. *H. canis* gamonts are usually detected in neutrophils and macrophages, but molecular detection techniques are highly sensitive [6]. The present case study represents the effect of combination therapy of imidocarb dipropionate and doxycycline against *Hepatozoon canis* infection.

2. Materials and Methods

A three year old Labrador retriever dog was presented to the Referral Veterinary Polyclinic, Indian Veterinary Research Institute, Izatnagar in March, 2017 with a history of vomiting, anorexia, fever and tick infestation. Deworming and vaccination history was proper. Since 2 days, the dog was exhibiting pain while lying down. Clinical examination revealed pyrexia (103.5°F), pale conjunctival and oral mucous membrane, hepatomegaly, peripheral lymphadenopathy. Blood and serum samples were collected for haematology and serum biochemistry, respectively. The peripheral blood smear was prepared and stained with Giemsa stain after methanol fixation [7]. The stained blood smear was screened for haemoprotozoa under light microscope. Haematological analysis was carried out as per standard method [8]. Biochemical analysis was done with semi-autoanalyzer. Ultrasonography of the abdominal region was performed as per standard method to see if there is any visceral organ abnormality is present or not [9]. The hemato-biochemical values were compared with normal reference values and interpreted.

3. Results and Discussion

Abdominal ultrasonographic examination revealed hepatomegaly with enlargement of hepatic lobes beyond costal arches and slight splenomegaly. The haematological analysis revealed anaemia (decreased level of haemoglobin, packed cell volume and red blood cell), thrombocytopenia, leukocytosis with neutrophilia. The serum biochemistry showed hypoalbuminemia, hyperglobulinemia and elevated levels of blood urea nitrogen (BUN), creatinine, alanine aminotransferase (ALT) and aspartate aminotransferase (AST). The detailed haematological and serum biochemical parameters before therapy and after therapy are mentioned in the Table 1. The stained peripheral blood smear was positive for *Hepatozoon canis* gamont in neutrophils (Fig. 1). On the basis of history, clinical and laboratory findings it was diagnosed as a case of *H. canis* induced acute hepatitis.

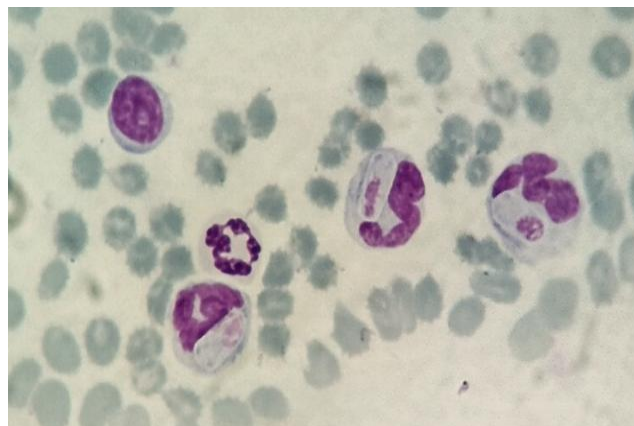


Fig 1: *Hepatozoon canis* gamont (arrow) in neutrophils (Giemsa stain X1000)

Table 1: Haemato-biochemical changes in dog before and after therapy

Haematological Parameters				
Parameter	Day 0	Day 28	Reference range [*]	Key findings
RBC count (millions/mm ³)	3.95	6.4	5.0-7.9	• Anaemia
PCV (%)	25.2	35.6	35-57	
Hemoglobin (g/dl)	8.1	12.1	12-19	
Total WBC count (10 ³ cells/mm ³)	21.32	12.2	5.0-14.1	• Neutrophilic leukocytosis • Acute inflammatory reaction
Neutrophils (%)	89	68	58-85	
Lymphocyte (%)	07	24	8-21	
Monocytes (%)	02	05	2-10	
Eosinophils (%)	02	02	0-9	
Basophils (%)	00	01	0-1	• Thrombocytopenia
Platelets (lakhs/mm ³)	1.12	2.98	2.11-6.21	
Serum Biochemical Parameters				
Parameter	Day 0	Day 28	Reference range [#]	Inferences
Total protein (g/dl)	5.95	6.1	5.4-7.5	• Hypoalbuminemia • Hyperglobulinemia
Albumin (g/dl)	1.44	3.0	2.3-3.1	
Globulin (g/dl)	4.51	3.1	2.4-4.4	
A:G ratio	0.319	0.967	0.6-1.3	• Normal bilirubin level
Total bilirubin (mg/dl)	0.3	0.2	0-0.3	
Direct	0.2	0.2	0-0.2	
Indirect	0.1	0	0-0.1	• Increased liver specific enzymes
ALT (U/L)	162	52	10-109	
AST (U/L)	48	17	13-15	
BUN (mg/dl)	37.4	21.6	8-28	• Azotemia
Creatinine (mg/dl)	2.05	1.14	0.5-1.7	

* March 2012: Haematology reference ranges, 10th edn. The Merck Veterinary Manual

March 2012: Serum biochemical reference ranges, 10th edn. The Merck Veterinary Manual

The treatment was started with combination therapy including single dose of Inj. Imidocarb dipropionate @ 6.6 mg/kg, SC and Tab. Doxyxyclyne @ 5 mg/kg, PO, BID for 28 days. Fiprofort PlusTM (Fipronil + S-methoprene) spot on was applied topically for tick management. Supportive treatment was done with Inj. NS @ 250 ml very slow IV, Inj. HaemacelTM (5 ml/kg, IV, SID), Inj. Meloxicam @ 0.5 mg/kg, IM, BID, Inj. Pantoprazole 1 mg/kg, IV, SID, Inj. Ondansetron @ 0.2 mg/kg, IV, BID and Inj. NeohepatexTM (liver extract with vit B₁₂, Biological E limited, India) @ 2 ml IM, BID was given for management of gastritis and hepatic damage for 3 days. Along with this, hematonic (Syp. DexorangeTM @ 10 ml, PO, BID) and hepatoprotectant (Syp. SylibonTM 10 ml, PO, BID) were given for 4 weeks. After 4 weeks of therapy, the dog showed marked improvement in condition. Haemato-biochemical values were found within a normal range and peripheral blood smear was negative for *H. canis* on 28th day of post therapy.

Canine hepatozoonosis caused by *H. canis* is an important haemoprotozoan disease of dogs occurring throughout the world [10, 11]. Although hepatozoonosis occurs in subclinical

form, age related acute form has been reported in young aged dogs [12]. Generally canine hepatozoonosis is considered as mild infection but underdeveloped immune system in young animals flares up on the pathogenesis and resulting in acute fatal nature in puppies [13]. Clinical signs like lymphadenopathy, weight loss and pale mucous membranes were in accordance with the report of previous workers [14, 15]. Anaemia, thrombocytopenia, leukocytosis with neutrophilia and elevated levels of BUN, creatinine and liver specific enzymes are may be due to acute inflammatory response to *H. canis* infection [16]. Anemia in hepatozoonosis may be due to massive tick infestation or bone marrow suppression; similarly, thrombocytopenia may be due to bone marrow depression [14, 17]. Neutrophilic leukocytosis in a dog with acute hepatozoonosis has been reported [12]. Increase in total leukocyte count may be due to inflammatory conditions induced by *H. canis* infection, which reduced towards normal level in response to therapy and similar findings were reported by Kaur *et al.* [18]. Hypoproteinemia may be due to increased destruction of hepatocytes as *H. canis* is believed to affect liver and spleen on a great scale [19]. Serum biochemical

abnormalities like Hypoalbuminemia and hyperglobulinemia have been noticed in canine hepatozoonosis, as site of albumin synthesis is liver which is mostly affected in hepatozoonosis^[15, 20]. Increased levels of BUN and creatinine points towards damage to kidney as *H. canis* has also been incriminated as cause of glomerulonephritis, schizogony can also progress in kidney^[21].

Doxycycline is the first line of treatment of hepatozoonosis in canines^[22]. Successful treatment of *H. canis* infected dogs with combination therapy including doxycycline and oxytetracycline has been reported by Sarma *et al.*^[16]. It has been reported that imidocarb dipropionate fails to eliminate *H. canis* infection when given as a sole therapy by Baneth *et al.*^[23]. Imidocarb dipropionate was once considered as a drug of choice for canine hepatozoonosis, but recent reports suggest a failure of combination therapy of imidocarb dipropionate and toltazuril/emodepside plus clindamycin in treatment of *Hepatozoon canis* infection^[24]. In the present case, imidocarb dipropionate was used in combination therapy with doxycycline for treatment of canine hepatozoonosis resulted in elimination of *H. canis* infection.

4. Conclusion

Combination therapy including imidocarb dipropionate and doxycycline along with supportive treatment like fluids, anti-emetics, hematinic and liver protectives may be a possible choice for management of *H. canis* induced acute hepatitis in a dog.

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6. Conflicts of interest

The authors declare no conflicts of interest.

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