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Combination therapy with imidocarb dipropionate and doxycycline to clear infection of *Hepatozoon canis* in dog

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Abstract

A male Golden Retriever dog of five years of age was presented to VCC, CVAS Bikaner with the history of anorexia, fever, weight loss, depression, vomiting and diarrhea since last 2 days. On the basis of history and clinical examination dog was suspected for haemoprotozoan infection. Microscopic examination of blood film revealed ellipsoid, elongated, pale-staining cytoplasmic bodies inside neutrophils which identified as *H. canis* gametocytes. The case was treated with oxytetracycline, analgin, multivitamin, imidocarb dipropionate, prednisolone, doxycycline, fluid therapy and supplements.

Keywords: Anorexia, smear, dog, imidocarb

Introduction

Hepatozoon canis (James, 1905) [9] is a protozoan pathogen transmitted by *Rhipicephalus sanguineus* and has been reported worldwide (Baneth *et al.*, 1995) [2] in dogs and other carnivores from many regions around the world. Brown dog ticks *i.e.*, *Rhipicephalus sanguineus* are the main vector of *H. canis*, although several other species of ticks such as *Amblyomma ovale*, *Haemaphysalis longicornis*, *Haemaphysalis flava*, and *Rhipicephalus (Boophilus) microplus*, may play a role as vectors of this protozoan parasite (Aktas, 2014; Orkun and Nalbantoglu, 2018) [1, 11]. In addition, an experimental study has confirmed that *Rhipicephalus turanicus* plays a vital role in vectorial transmission (Giannelli *et al.*, 2017) [6]. The disease is transmitted to vertebrates by ingestion of the infected tick vectors, which carry mature oocysts of *H. canis* (Baneth, 2011) [5]. Generally, this protozoan causes a chronic infection in its host without causing any clinical manifestations (Baneth *et al.*, 2003) [3] but an excessive parasitaemia, characterized by high peripheral blood neutrophil levels, as well as severe illness, including fever, anorexia, weight loss, anaemia, ocular discharge, hindlimb weakness were present in some dogs (Gondim *et al.*, 1998) [7]. Hepatozoonosis is diagnosed by the detection of intracytoplasmic ellipsoidal-shaped gamonts in blood smear by microscopic examination (Klopper *et al.*, 1973) [10]. Anemia, neutrophilic leukocytosis, thrombocytopenia, hypoalbuminemia and an increase in serum alkaline phosphatase were among the abnormalities reported in blood and serum of affected dogs (Voyvoda *et al.*, 2004) [15]. Hypoalbuminemia detected in dog is probably a result of decreased protein production or chronic protein loss. An increase in serum alkaline phosphatase activity may indicate increased osteoblastic activity or liver damage (Rich and Coles, 1995) [13]. The cases can be treated with imidocarb dipropionate or a combination of imidocarb dipropionate and doxycycline. Imidocarb dipropionate with or without doxycycline, usually leads to rapid clinical remission and parasitaemia elimination (Pasa *et al.*, 2011) [12].

Case History

A five-year-old, male Golden Retriever dog weighing 32 kg was presented to medicine outdoor of Veterinary Clinical Complex, College of Veterinary and Animal Science, Bikaner with the history of anorexia, weight loss, depression, vomiting and diarrhea since last 2 days. The dog was fully vaccinated and had been kept at place where cattle were reared. On clinical examination temperature was high up to 104.8°F, severely dehydrated, lethargic, pale mucus membrane and ticks infestation. Blood was collected for the hematological, biochemical and blood protozoan examination. Blood picture revealed neutrophilia, moderate anemia and thrombocytopenia. Microscopic examination of giemsa stained blood smear revealed ellipsoid, elongated, pale-staining cytoplasmic bodies inside neutrophils which identified as *H. canis*

gametocytes based on their morphological characteristics. Blood examination revealed Hb 6.1 g/dl, TLC $36.25 \times 10^3 / \mu\text{l}$, TEC $3.5 \times 10^3 / \mu\text{l}$, platelets 98000, DLC neutrophils 67, leukocytes 16 and monocytes 17. Serum biochemical examination showed that the kidney function tests (creatinine, blood urea nitrogen levels) were normal, while in hepatic function tests low albumin, high alanine aminotransferase, aspartate aminotransferase and alkaline phosphatase were observed.

Diagnosis

The case was diagnosed on the basis of history, clinical signs and blood film examination as a *Hepatozoon canis* infection (Fig. 1)

Therapy

After the diagnosis the dog was treated with inj. oxytetracycline @15 mg/kg b.wt. iv in normal saline, inj. analgin 3 ml iv sos, inj. multivitamin 3 ml iv for 5 days. Inj. Imidocarb dipropionate @5mg/kg sc and inj. prednisolone @1mg/kg b.wt. were given once only. Supportive therapy for vomiting and diarrhea include inj. 5% dextrose normal saline 20 ml/kg b.wt. iv, inj. ringer lactate 20ml/kg iv, Inj. ondansetron 0.5mg/kg iv and Inj. Ranitidine 0.2mg/kg iv were given. On 5 days continue treatment vomiting and diarrhea stopped. After 5 days, the treatment was followed with tab doxycycline @10 mg/kg b.wt. od for 21 days, syrup platelet stimulator 10ml and syrup iron supplement 10ml bd for 1 month were given orally.

Results and Discussion

The most commonly used drug of choice for the treatment of *H. canis* infection is imidocarb dipropionate which administered intramuscularly or subcutaneously at 5–6 mg/kg twice a month and discontinued after 2–3 consecutive negative results in the microscopic examination of blood smear (Baneth and Weigler, 1997) [4]. At least eight weeks of treatment may be required in order to eliminate *Hepatozoon canis* gamonts from peripheral blood (Baneth *et al.*, 2003) [3]. Moreover, imidocarb dipropionate is frequently combined with doxycycline at 10 mg/kg for 21 days in order to treat concomitant tick-borne infections caused by *Ehrlichia canis* and *Anaplasma* spp.

Ondansetron (antiemetic) is a serotonin (5HT₃) receptor antagonist that inhibits vomiting by acting peripherally as well as centrally (Yatoo *et al.*, 2013) [16]. The serotonin receptor antagonists have been used as the most efficacious antiemetic (Greene and Decaro, 2012) [8]. H₂ blocker (ranitidine) also decreased the volume of gastric juice (Tams, 2009) [14] successfully used in clinical cases of gastritis. As long as vomiting or diarrhea or both persist, fluid therapy is probably the most important aspect of clinical management. The goal of fluid therapy is to correct dehydration, reestablish effective circulating blood volume, and correct electrolyte and acid-base disturbances.

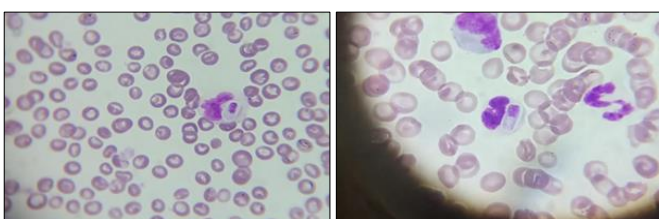


Fig 1: *Hepatozoon canis* (Capsule)

Conclusion

In conclusion, a combination of imidocarb dipropionate and doxycycline at the dosage given here cleared *Hepatozoon canis*. The combination therapy gives better clinical response than imidocarb mono therapy. It could prove useful to determine future directions for a treatment strategy from the results of this study.

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