

THERAPEUTIC APPROACHES IN SEVERE, COMPLICATED CANINE BABESIOSIS: A CASE REPORT

Camelia ION, Ioan Liviu MITREA, Mariana IONITA

University of Agronomic Sciences and Veterinary Medicine of Bucharest, Faculty of Veterinary
Medicine, 105 Splaiul Independenței Street, District 5, Bucharest, Romania

Corresponding author email: ani.malz@yahoo.com

Abstract

Canine babesiosis is a potential life-threatening tick-borne disease affecting dogs worldwide. Early diagnostic and specific therapy in due time are emergency issues, as the infection may progress rapidly to severe, acute, and complicated potentially fatal disease. Here we describe a clinical case of babesiosis in a 6-year-old male Bichon Frise dog which was referred to the Clinic of Faculty of Veterinary Medicine of Bucharest, in April 2019, with clinical signs (fever, 39.9°C, jaundice, haemoglobinuria, weakness) compatible for babesiosis. Blood samples were collected and subjected for hematological and biochemical investigations, and for parasitological testing. The blood smear analysis showed intraerythrocytic piroplasms compatible for large Babesia form. Subsequently of the clinical and paraclinical investigations the dog was diagnosed with severe babesiosis, characterized by severe anemia (PCV=15.8%; Hgb=5.8 g/dL), neutropenia, trombocitopenia, and acute renal injury; a guarded to poor prognosis was considered. Accordingly, the therapeutic protocol aimed firstly to stabilize the animal by blood-transfusion, administering compatible tested blood, at a dose rate of 22 ml/kg body weight, over the course of 4 hours, followed by the babesiocidal therapy, using imidocarb dipropionate, at lower dose of 3 mg/kg b.w. (two intramuscular injections, 24 h apart). Additionally, supportive therapy was administered under permanent monitoring of the animal within the intensive care unit. Following the treatment, the dog's status improved rapidly and clinically recovered within 10 days. This case-report describes a successful complex therapeutic protocol based on multiple approaches (blood transfusion, specific treatment, intravenous fluids and oral supportive treatment) for critical, life-threatening cases of canine babesiosis.

Key words: dog, babesiosis, severe, clinical case, Romania.

INTRODUCTION

Canine babesiosis is a significant disease with specific tick vector transmission that affect dogs worldwide (Irwin, 2009). Currently it is emerging in many European countries (Schnitter et al., 2012). It is caused by large and small intra-erythrocytic protozoan piroplasms of the genus *Babesia* (Apicomplexa: Piroplasmia) (Carret et al., 1999; Mitrea, 2011). Clinical infection is usually characterized by fever, apathy, and anaemia, but single and/or multiple organ dysfunctions such as, kidney, liver, respiratory, nervous dysfunctions, associated with coagulation deficiencies and electrolyte imbalance, may occur (Lobetti et al., 1996; Leisewitz et al., 2001; Zygnier et al., 2014; Eichenberger et al., 2016). However, clinical presentation and disease progression are highly variable, characterized by mild, moderate up to severe anemia, depending of multiple factors, both parasite- (antigenic

properties, specific virulence, strain, and species) and/or host- (age, immunity and other concurrent diseases) related factors (Birkenheuer et al., 1999; Jacobson, 2006; Irwin, 2009).

Additionally, chronic evolution of the disease can be often associated with complex pathology (hepatic, renal, cardiac, and neurological dysfunctions).

The late diagnostic and lack or late babesiocidal treatment may lead to fulminating disease with high mortality (Ayoob, 2010; Leica et al., 2019). Therefore, early diagnostic and careful monitoring of disease's progression provides important data supporting adequate therapeutic protocols to be applied, according to the clinical presentation of infection (Lobetti et al., 1996; Leisewitz et al., 2001; Jacobson, 2006; Irwin, 2009).

In Romania, in the last decade, the epidemiology of canine babesiosis has been showing rapid changes, many reports

describing endemic foci, particularly in South-Eastern areas, with clinical presentation and pathological changes varying from mild, moderate up to severe, complicated diseases (Mitrea, 2011; Ionita et al., 2012; Leica et al., 2019). Additionally, increased abundance of tick populations associated with climate changes, socio-economic, and environmental related factors represent high potential risks for canine tick-borne diseases in Romania (Ionita et al., 2016; Ionita and Mitrea, 2017).

Therefore, there are strong evidences that clinicians should be aware that establishing early diagnostic is an emergency issue in canine babesiosis, as the clinical signs may progress rapidly to severe acute disease, evolving to complicated, life-threatening, fatal disease, especially on lack and/or delayed babesiid therapy (Irwin, 2009; Ayoob, 2010; Solano-Gallego et al., 2011).

Here we describe a clinical case of severe, complicated canine babesiosis. The therapeutically approaches and clinical follow-up are discussed.

MATERIALS AND METHODS

Case presentation

A 6-year-old male Bichon Frise dog was referred to the Clinic of Faculty of Veterinary Medicine of Bucharest, in April 2019 with clinical signs compatible with babesiosis (fever, 39.9°C, jaundice, haemoglobinuria, weakness).

The dog was subjected to a routine physical and clinical examination and thereafter blood samples were collected and subjected to hematological, biochemical, and parasitological investigations.

Hemathological parameters were determined by using IDEXX VetAutoread™ Hematology Analyzer. Serum biochemistry parameters' analysis was performed with VetTest 8008 / Catalyst Dx analyzer (IDEXX U.S.).

For parasitological testing, thin blood smears, Giemsa stained, were microscopically examined for intraerythrocytic piroplasms.

Imagistic investigations were performed using ultrasound examination according to abdominal assessment with sonography for triage (AFAST) (Codreanu et al., 2017).

RESULTS AND DISCUSSIONS

At clinical examination the dog displayed fever (39.9°C), generalised jaundice, dyspnoea, severe vomiting, and haemoglobinuria.

Microscopical examination of the blood smear showed large intra-erythrocytic piroplasms (Figure 1), compatible for *Babesia* large piroplasms. Additional, severe non-regenerative, normocytic, normochromic anemia, as well as neutropenia, vacuoles in monocyte's cytoplasm, and severe thrombocytopenia were registered.

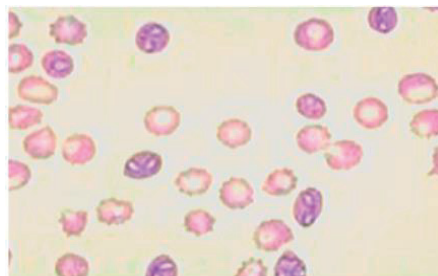


Figure 1. Dog blood smear, Giemsa stained, showing intraerythrocytic large piroplasms (x 1000)

Haematology parameters analysis revealed severe anaemia (packed red cell volume: PCV=15.8%; haemoglobin: HGB=5.8 g/dL), leukopenia and thrombocytopenia (Table 1).

Table 1. Dynamics of haematological parameters in a 6 year old Bichon Frise with babesiosis, during the follow-up period

Parameter tested*	Reference limits	Day 1	Day 2	Day 3	Day 18
PCV	37-55%	15.8↓	28.2↓	26.4↓	33.0↓
HGB	12-18 g/dL	5.8↓	8.4↓	9.7↓	10.7↓
MCHC	30-36.9 g/dL	36.7	29.8↓	36.7	32.4
WBC	6-16.9 K/ μ L	5.00↓	13.00	14.50	18.10
GRANS	3.3-12 K/ μ L	3.40	7.00	7.40	14.60
% GRANS	%	68%	53.8	51.0	80.7
NEUT	2.80-10.50 K/ μ L	2.80	5.98	NT	NT
EOS	0.5-1.50 K/ μ L	0.6	1.02	NT	NT
PLT	175-500 K/ μ L	>15↓	>932↑	67↓	499

*PCV=packed red cell volume; Hgb=hemoglobin; MCHC: mean corpuscular hemoglobin concentration; WBC= white blood cells; GRANS=total granulocyte count; NEUT= neutrophils; EOS: eosinophils; PLT: platelet count; D1=day of admission; D2-18=days after admission

Serum biochemistry panel's analysis showed acute renal injury (azotemia- BUN=126 mg/dL) and elevation of hepatic enzymes (TBIL >27.9 mg/dL; ALT 270 U/L) (Table 2). In Tables 1, 2 dynamics of the hematological and biochemical parameters, from day of dog admission and during of the follow-up period (approx. three weeks), are displayed.

Table 2. Dynamics of serum biochemistry parameters in a 6 year old Bichon Frise dog with severe babesiosis, during the follow-up period

Parameter tested*	Reference limits	Day 1	Day 2	Day 3	Day 18
GLU	74-143 mg/dL	87	NT	NT	97
CREA	0.5-1.8 mg/dL	0.8	1.1	NT	1.5
BUN	7-27 mg/dL	126†	124†	62†	56†
ALT	10-100 U/L	36	NT	NT	270†
ALKP	23-212 U/L	+++†	NT	NT	602†
TBIL 1:1	0.0-0.9 mg/dL	>27.9†	NT	>27.9 ↑	0.9
LIPA	200-1800 U/L	1884†	NT	NT	NT

*GLU=glucose; CREA=creatinine; BUN= blood urea nitrogen; ALT=alanine aminotransferase; ALKP= alkaline phosphatase; TBIL 1:1=total bilirubin; LIPA=lipase; D1=day of admission; D2, D3, D18=day after admission. +++†: over the detection limits.

The abdominal ultrasound examination showed enlarged spleen and liver, a fine layer of abdominal fluid.

Diagnostic

By corroborating the clinical and paraclinical investigations' results the dog was diagnosed with severe babesiosis, caused by piroplasms compatible for large *Babesia* form, and characterized by severe anaemia, complicated with acute renal and hepatic injuries.

Treatment and follow-up

Due to the severe, life-threatening anemia (PCV of 15.8%), blood-transfusion was the first therapy approach. Fresh whole tested blood (D.E.A.1.1 negative) was administered, at a rate of 22 ml/kg body weight, over the course of 4 hours. No side effects following the blood transfusion were registered, therefore, after completion of the blood transfusion, a babesiid therapy with imidocarb dipropionate (Imizol®, Merck, Animal Health, Intervet Inc.) was administered, as follows: firstly, one intramuscular injection of at a dose of 3 mg/kg, followed by a second injection in the next day

(at 24 h). No side effects were registered after the babesiid therapy.

Additionally, supportive therapy including intravenous fluids (continuous rate infusion with aminoacids, isotone cristaloids - ringer solution, at a rate of 5 ml/kg/h), antibiotics (ceftriaxone 20 mg/kg every 12 hours), renal and hepatic supplements (metoclopramide 0.5 mg/kg, at 12 hours, and cyanocobalamin, 50 mcg/kg/day) were administered. The dog was close monitorized for vital functions (breathing rate, heart rate, capillary refill time, temperature, blood pressure and urinary output) within the intensive care unit.

A rapid improvement of the clinical signs was registered after the babesiid therapy, and both hematological and biochemical parameters showed improved values in the next 3-10 days post-treatment (Tables 1, 2).

Over the course of 10 days in intensive care unit, the dog responded well to the treatment, its general status showing substantially improvement. Therefore, at 10 days post-admission, the dog was released, with recommendation to continue the supportive therapy (Doxycycline 10 mg/kg/day, supplements for supporting renal function, and liver supplements, for 30 days; B12 vitamin, 100 mcg/kg, once a week, for 4 weeks; probiotics), and tick prevention.

A clinical and parasitological follow-up was established a week post-releasing (D-18), when the blood smear examination was negative for intraerythrocytic piroplasms. Additionally, the relevant haematological and serum biochemistry parameters showed substantially improvement. The supportive therapeutic protocol continued, as recommended.

Discussions

The clinical case described in the present paper, clearly demonstrates that canine babesiosis represents an emergency in certain situations such as a late diagnostic, which may impact the prognosis, and may lead to severe disease progression with complex pathology, as previously described (Furlanello et al., 2005; Ayoob, 2010). In such cases, hemotransfusion may be used for controlling anemia (Uilenberg et al., 1981).

From clinical and pathological point of view, monitoring disease progression, assessment of

the clinical signs, as well as the outcome of treatment all represent the base for optimizing the therapeutic protocol, as described in the present case.

Blood transfusion should be correlated with the clinical status of the patient, in cases of acute anemia with a haematocrit lower than 20.0% (Costea, 2016). The hematocrit value increased rapidly after the fresh whole blood administration (from 15.8% to 28.2% at 24 h), and continued to improve during the monitoring period (up to 33.0%, two weeks post-treatment; Table 1), along with improving of the dog clinical presentation.

Babesioid therapy is based on imidocarb dipropionate injection, usually recommended at a dose rate of 6.6 mg/kg (Plumb, 2015). However, due to the critical clinical presentation of the dog, a therapy protocol with a lower dosage of imidocarb dipropionate (3.3 mg/kg, 24 h apart) was chosen, in order to avoid potential side effects, associated with permanent monitoring.

Additionally, supporting and fluid therapy, in order to recover and maintain the optimal vital signs (cardiac frequency, pulse, diuresis), including restoring electrolyte levels and reducing dehydration, was administered (Ayoob et al., 2010). Continuous rate infusion and symptomatic treatment continued until clinical monitoring revealed vital signs stabilisation and the dog was able to receive oral feeding and therapy.

The additional therapy with doxycycline (10 mg/kg/day for 30 days) was recommended as there are reports on other drugs that can positively contribute to the babesiosis management (Solano-Gallego et al., 2016). For instance, doxycycline has been described as reducing the severity of clinical signs, along with reduction of morbidity and mortality for *B. canis* and *B. gibsoni* infections (Vercammen et al., 1996; Lin and Huang, 2010). Additionally, experimental studies on plant extracts (i.e. artemisinin and its derivatives inhibited the *in vitro* growth of *B. gibsoni*) might be potential drugs for treatment of babesiosis (Goo et al., 2010; Iguchi et al., 2015).

In our case, the therapeutical approach, under a continuous monitoring, showed a rapid clinical improvement of the dog, despite of the severe

clinical presentation and pronounced pathological changes. Nonetheless, the severity of organ dysfunctions, early diagnostic, and specific and supportive treatment may have a serious impact on the efficacy of therapy and diseases' progression.

CONCLUSIONS

This case-report describes a complex successful therapeutic protocol based on multiple approaches (blood transfusion, specific treatment, intravenous fluids and oral treatment) on severe cases, with life-threatening disease. Additionally, it is emphasized that early diagnostic and specific therapy administered in due time are critical points of successful management of babesiosis.

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