Dual infection of rabies virus and *Babesia canis* in a dog: a case report

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Abstract: A young adult labrador was presented for evaluation of hind leg weakness, depression, vomiting and severe icterus of skin and mucosa. Physical examination and laboratory findings suggested cerebral babesiosis. Unresponsiveness to treatment and unknown vaccinal status aroused suspicion of rabies which was confirmed post mortem.

Keywords: rabies virus; *Babesia canis*; dog

Rabies is an acute and fatal viral encephalitis caused by a single stranded RNA virus belonging to the genus *Lyssavirus* of the family *Rhabdoviridae*. It is one of the oldest diseases known to mankind and causes the deaths of thousands of people every year (Madhusudana, 2005), with 95% of human deaths occurring in the developing countries of Asia and Africa (WHO, 2005). However, despite all control and preventive measures taken, rabies is also still present in parts of south-eastern Europe. Epidemiological analyses, laboratory studies and modeling suggest that rabies in enzootic areas of Europe is propagated and maintained mainly by a single species, the red fox (*Vulpes vulpes*). The increased number of foxes and close contact with domestic animals result in occasional spillover (Briggs, 2002). Rabies among domestic animals, especially dogs, remains the major threat for transmitting rabies virus to humans (WHO, 2005).

Canine babesiosis is a tick-borne disease caused by hemoprotozoan parasites *Babesia canis* or *Babesia gibsoni*. Based on geographical distribution, epidemiological features, the tick species acting as vector and molecular characteristics, *B. canis* is subdivided into three subspecies: *B. canis canis*, *B. canis vogeli* and *Babesia canis rossi*. Although clinical signs related to acute haemolysis are the hallmark of the disease, numerous variations exist and complications involving multiple organs may develop (Uilenberg et al., 1989, Taboada and Lobetty, 2006).

Its rare appearance, atypical clinical manifestations and laboratory findings make diagnosis of canine rabies ante mortem extremely difficult. In contrast to rabies, *B. canis canis* is a very common cause of morbidity and mortality in our area and cases of cerebral babesiosis associated with nervous symptoms such as seizures and altered consciousness are well described in the literature (Lobetti, 1998; Matijatko et al., 2007; WHO, 2009).

The current report describes the clinical picture and details the overlapping symptoms in a dog with simultaneous infection with rabies virus and *Babesia canis*.

Case description

A 1.3 year old, male Labrador was referred to the Clinic for Infectious Diseases, Faculty of Veterinary Medicine, University of Zagreb for hind leg weakness, depression and vomiting. According to the owner's information onset of the symptoms had begun the day before, when the animal became anorexic and lethargic. The condition progressively worsened over the 24 hours prior to the emergency presentation. The animal was vaccinated once at the age of eight weeks against canine distemper virus,

parainfluenza virus, canine adenovirus-2, canine parvovirus (Vanguard Plus 5; Pfizer Animal Health, Exton, Pennsylvania, USA) and canine coronavirus (Vanguard CV, Pfizer Animal Health, Exton, Pennsylvania, USA). Allegedly, after that primary vaccination babesiosis was diagnosed twice in this dog and vaccination against rabies could not be performed. The animal was held in a fenced yard. The only close contact of the presented dog was with the neighbour's dog that came from the same litter and is allegedly regularly vaccinated. Walks through the woods at the edge of the city were reported, but owner claimed that the dog never left his sight and that he did not notice any scratches or bite wounds on the dog and that he declined all possible contacts with wild animals. On initial physical examination the dog was alert but unable to stand. The body temperature was elevated (40.1°C) and both tachypnoea (70 breaths/min) and tachycardia (150 beats/min) were present. Capillary refill time was shortened (CRT < 1 s). Severe icterus of skin and mucoses was noted. Urine was reddish, and vomiting with white foamy content was observed. During clinical examination and hospitalization the animal's condition worsened and depression advanced to the comatose condition. The dog was lying in lateral recumbent position with notable intermittent extensor rigidity. The animal was responsive to repeated auditory and noxious stimuli and scored eight according to the Modified Glasgow coma scale. Bilateral, unresponsive mydriasis with reduced oculocephalic reflexes was present. Horizontal nystagmus was also observed with a fast phase towards the right. Laboratory analysis revealed severe anaemia with a RBC count of 1.3×10^{12}/l, hematocrit 11% and severe thrombocytopenia (19×10^9/l). The white blood cell count (WBC) was within reference range (6.7×10^9/l). The biochemical profile showed an increase of bilirubin (383.1 μmol/l), urea (28.1 mmol/l) and creatinine (166 μmol/l), while total protein values were slightly lowered (51 g/l). Cytological evaluation of a peripheral blood smear revealed macrocytosis, anisocytosis and reactive lymphocytes. Multiple intra-erythrocytic, piriforme-shaped organisms compatible with *B. canis* were also detected. Treatment consisted of imidocarb diproprionate, metoclopramid, ranitidine and appropriate fluid therapy including the whole blood transfusion.

On the following day, despite the treatment, the dog's condition worsened. Body temperature varied during the day between 36.8°C to 41.1°C and heart rate was between 120 and 200 beats/min. Neurological status remained unchanged except for one episode of seizures that was noted during the day. This started with paddling and continued as tonic-clonic seizures that stopped immediately after application of diazepam. CBC count and biochemical findings showed only slight increases in RBC (2×10^{12}/l), hematocrit (16%), platelets (50×10^9/l), WBC (26×10^9/l), band neutrophils (5%) and monocytes (18%). Cytological evaluation of aperipheral blood smear revealed intravascular agglutination and extended haemolysis. Treatment was continued with fluid therapy (hydroxyethyl starch and crystalloids), metoclopramid, ranitidine, methylprednisolon and cefuroxime. On the third day, mental status remained unchanged without any seizures. Hematology showed a slight decrease in RBC count, hematocrit and hemoglobin concentrations. During the morning of the fourth day multiple seizures occurred. Trismus was also noted. Following advice, the owner elected to have the dog euthanized and the carcass was sent for rabies examination. Direct fluorescent antibody testing performed on fresh brain tissue was positive for rabies antigen. As human contact had occurred a PCR test was conducted as an additional confirmative method. A positive result in the PCR confirmed the presence of rabies virus in the brain tissue. The Public Health Department was notified and the owners received postexposure prophylaxis, as warranted.

DISCUSSION AND CONCLUSIONS

The classification and progression of rabies infection in dogs (so-called furious and paralytic forms) is artificial because rabies can be quite variable in its presentation and atypical signs are commonly seen (Green and Ruprecht, 2006; White et al., 2007). In addition, clinical and laboratory evaluation of dogs with rabies has rarely been reported due to the rapid fatal course of infection and risks associated with human exposure (Briggs et al., 1993; Barnes et al., 2003; White et al., 2007). All unvaccinated dogs with neurological dysfunction should be handled carefully, by a limited number of veterinary personnel, until diagnostic testing can be performed to identify or exclude other diseases and the clinical course is clarified (Green and Ruprecht, 2006).This case illustrates that despite the identification of some other infectious agent that can cause neuro-

logical symptoms the possibility of rabies shouldn't be ruled out.

There was no initial suspicion of rabies as a differential diagnosis in this case. There was no reported contact with other dogs, bats or terrestrial wildlife and no visible signs of a healing bite wound. Severe icterus, haematuria and laboratory findings were considered as characteristic symptoms of babesiosis. Subsequently, progressive deterioration in the dog's mentation, unresponsiveness to treatment and absence of obligate vaccination aroused suspicion of rabies. Definitive diagnosis was performed using a direct fluorescent antibody test (FAT) on the fresh brain tissue.

This report emphasizes the importance of early consideration of rabies as an important differential diagnosis in all, especially non-vaccinated dogs, with behavioural or neurological abnormalities. Animals may have a misleading combination of signs or as in this particular case other, more common, pathogens can complicate the clinical picture.

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