Case Report

Coinfection with multiple tick-borne and intestinal parasites in a 6-week-old dog

Arnon Gal, Shimon Harrus, Itamar Arcoh, Eran Lavy, Itzhak Aizenberg, Yael Mekuzas-Yisaschar, Gad Baneth

Abstract — Coinfection with *Ehrlichia canis*, *Babesia canis*, *Hepatozoon canis*, *Isospora* spp., *Giardia* spp., and *Dipylidium caninum* were detected in a 6-week-old dog. The effect of multi-pathogen infection was a fatal combination of gastrointestinal and hematologic abnormalities, including diarrhea, vomiting, anorexia, distended painful abdomen, intussusception, severe thrombocytopenia, anemia, and hypoproteinemia.


An intact female, 6-week-old, mixed-breed dog was referred to the Hebrew University Veterinary Teaching Hospital (HUVTH) with chief complaints of acute vomiting, anorexia, and intermittent diarrhea of 1-week duration, as well as a distended painful abdomen. The dog had been adopted from an animal shelter where it had been vaccinated against *Canine parvovirus* and dewormed 1 wk prior to presentation.

Case description

Upon presentation, the puppy had increased body temperature (39.4°C), tachycardia [heart rate 200 beats/min (bpm)], tachypnea [respiratory rate 160 breaths/min (brpm)], and slightly pale mucus membranes. The abdomen was soft, distended, and apparently painful, and bloody diarrhea was observed. Ectoparasites were not noted. A complete blood (cell) count (CBC) revealed normal white blood cell count (WBC) 13.4 × 10⁹/L (reference range, 6 to 17 × 10⁹/L), anemia [packed cell volume (PCV) 0.15 L/L (reference range, 0.258 to 0.552 L/L)], total solids (TS) 58 g/L (reference range, 60 to 80 g/L); red blood cell (RBC) 2.61 × 10¹²/L (reference range, 2.76 to 8.42 × 10¹²/L), hemoglobin 52 g/L (reference range, 64 to 189 g/L), and thrombocytopenia [platelets 2 × 10⁹/L (reference range, 200 to 500 × 10⁹/L)]; however, petechia or ecchymoses, were not detected either on the skin or on mucus membranes. Microscopic high power field examination of a giemsa-stained blood smear confirmed the thrombocytopenia and showed mild erythrocyte anisocytosis and polychromasia. The platelet number was estimated to be higher than counted by the automatic cell counter, but lower than normal, due to the presence of platelet clumps in the smear. A *Hepatozoon canis* gamont, as well as *Babesia canis* merozoite and trophozoite parasitemia was detected under high power field magnification, with 3% (15/500) of the neutrophils containing *H. canis* gamonts and 2.6% (13/500) of the erythrocytes parasitized by *B. canis* (Figure 1). In addition, *Ehrlichia canis* morulae were detected in several monocytes. *Ehrlichia canis* DNA was amplified from an EDTA-anticoagulated blood sample, using

Figure 1. Giemsa-stained blood smear showing concurrent *Hepatozoon canis* (wide arrow) and *Babesia canis* (thin arrows) parasitemia in a 6-week-old dog on the initial day of admission. Bar = 10 microns.

School of Veterinary Medicine, Hebrew University of Jerusalem, PO Box 12, Rehovot 76100, Israel.

Address all correspondence and reprint requests to Dr. Arnon Gal; e-mail: agal2@uiuc.edu

Dr. Gal’s current address is College of Veterinary Medicine, University of Illinois at Urbana-Champaign, 1008 West Hazelwood Drive, Urbana, Illinois 61802, USA.

Three days after discharge, the dog was presented again with vomiting, diarrhea, anorexia, and painful, distended abdomen that had become apparent the night before. A direct fecal smear revealed numerous Isospora spp. oocysts and Dipylidium caninum eggs. Abdominal radiography and ultrasonography revealed gas-filled intestines with no evidence of obstruction, peritoneal effusion, or organomegaly. The dog was hospitalized and treatment was initiated. A combination of antibiotics [trimethoprim sulfamethoxazole (Resprim; Teva Pharmaceutical Industries, Jerusalem, Israel), 15 mg/kg body weight (BW), PO, q12h; metronidazole (Metronidazole; B. Brown, Melsungen AG, Germany), 10 mg/kg BW, IV, q12h; doxycycline (Doxyclin; Dexxon, Or-Akiva, Israel), 10 mg/kg BW, PO, q24h] was given to clear gastrointestinal infection of coccidian spp., for potential intestinal protozoa (giardiosis), as well as against anaerobic intestinal bacteria, and to treat tick-borne ricketsial infection. Other treatments given were the antiprotozoal drug imidiocarb dipropionate (Imizol; Schering-Plough, Kenilworth, New Jersey, USA), 0.2 mg/kg BW, IM, q14d, for a total of 2 treatments; the anthelmintics ivermectin (Ivomec; Merial, Lyon, France), 0.2 mg/kg BW, SC, single dose; and praziquantel-pyrantel-febantel (Drontal Plus; Bayer AG, Wuppertal, Germany), 1 tab/10 kg BW, PO, q10d; the IV fluid lactated Ringer’s solution (LRS) (Teva Pharmaceuticals Industries, Markham, Ontario), 5 mg/kg BW, PO, — single treatment— an anthelmintic [pyrantel pamoate (Combantrin; Pfizer, Markham, Ontario), 5 mg/kg BW, PO, — single treatment— and supportive care (LRS supplemented with 5% dextrose and 20 mmol/L K⁺ at 5 mL/kg BW/h). On day 11 from the initial presentation, signs of bloody diarrhea appeared, and abdominal palpation indicated an intussusception. The dog underwent an exploratory laparotomy and a 15-cm long reducible ileal intussusception was observed and reduced by gentle traction. Three days later, a cloudy fluid that contained bacteria within degenerated neutrophils was aspirated from the abdominal cavity. The dog was diagnosed with septic peritonitis and the owners opted for euthanasia, but denied a postmortem examination.

Discussion

This case demonstrates the complexity and clinically challenging multiple intestinal and hemopoietic coinfections, as well as the potential complications encountered during the management of such cases. The wide range of clinical signs found in such coinfections often leads to difficulties in the diagnosis and clinical management (2). The initial observation of some pathogens may hinder the diagnosis of other potentially more virulent infections or clinical diagnoses requiring specific therapy. Furthermore, coinfections often lead to a more serious disease course in pediatric patients, since at 3–6 wk of age, puppies may not have sufficient nutritional reserves to accommodate large parasitic burdens (3).

Puppies have an immature immune system and, thus, are predisposed to infection through environmental exposure and contact with adult animals that harbor infections. Environmental factors such as crowding in animal shelters, kennels, and pet shops may increase the exposure of young animals to pathogens (4). Fifty-four percent of the animals adopted from shelters in Perth, Australia, were reported to become ill and suffer from respiratory or gastrointestinal signs within 14 d of their acquisition, and 92% of the pet owners that returned their newly adopted animal to the shelter did so due to such illness (5). Hemoparasitic and gastrointestinal pathogens, such as ascarids, hook worms, cestodes, coccidia, and Giardia spp., have been reported to be prevalent in dogs housed in crowded conditions (3,4). Puppies 3 to 6 wk of age are especially susceptible to internal and external parasitic infection (6).
Puppies infected with tick-transmitted pathogens, such as *B. canis* and *H. canis*, can exhibit more severe clinical signs than older dogs (3,7). Moreover, *E. canis* infection has been reported to predispose dogs to opportunistic pathogens, such as *B. canis* and *H. canis* (8,9). Multiple tick-transmitted pathogen co-infections in dogs have been documented and associated with severe and fatal disease (9).

The current possibilities for the rapid transfer of animals between different countries and habitats create opportunities for invasion of new pathogens and disease vectors to nonendemic regions via automobiles, airplanes, and ships. In addition, exotic diseases are often detected in animals that return from travel outside their native environment. For these reasons, veterinary practitioners need to be alert and to consider nonendemic infections in their list of differential diagnoses for some disease conditions.

Anemia and thrombocytopenia are common findings in babesiosis and ehrlichiosis (9,10). Electrolyte abnormalities are frequent in animals with vomiting and diarrhea. Pain and anxiety combined with dehydration were probably responsible for the mixed acid base abnormalities that included respiratory alkalosis and metabolic acidosis. Protein losing enteropathy, malabsorption, and malnutrition, secondary to giardiasis, coccidiosis, and helmhinit infestation, were the likely sources of the paucity of one of the latter, probably led to the ascitic fluid transudate. Intussusception is a well-documented sequela to severe, continuous diarrhea or intestinal parasitic infestation altering the gut motility (11). The final complication of septic peritonitis might have been caused by a devitalized intestinal segment involved in the intussusception or perforation of the intestine after surgery.

The brown dog tick, *Rhipicephalus sanguineus*, is the main vector of *B. canis* and *H. canis*, and *E. canis*. The acquired *E. canis* and *B. canis* infections probably resulted from a *R. sanguineus* bite. *Hepatozoon canis* is transmitted by the same tick vector but infects dogs via a different route. *Hepatozoon canis* sporozoites present in the host tick’s haemocoele need to be ingested by the dog for infection to develop (12). The time interval from *H. canis* sporozoite ingestion to gamont parasitemia has been shown to be 28 d (12). Thus, the presence of gamont parasites upon presentation suggests that tick infection had occurred at least 4 wk before. Such an event, although possible, is unlikely. However, both *H. canis* and *B. canis* can be transmitted in-utero (13,14), and this was likely to have been the route of infection for *H. canis* and, possibly, *B. canis* in this case. In contrast, to date, there is no evidence that *E. canis* can be transmitted in-utero. Therefore, for the puppy to have ehrlichiosis during hospitalization, it had to have been exposed to the tick prior to admission to hospital. The incubation periods from bite to clinical signs with *E. canis* and *B. canis* has been shown to be 8 to 20 and 10 to 21 d, respectively (15,16). Thus the puppy could potentially have been infected after birth with *E. canis* and *B. canis*. Given that *R. sanguineus* is a 3-host tick and leaves the host for molting, the absence of ticks on physical examination does not rule out the possibility for tick-borne infections.

*Giardia* spp. and *Isospora* spp. are transmitted feco-orally. Giardiasis can be manifested in a wide spectrum of clinical signs, from none to those through mild to severe infection. It can induce acute to chronic vomiting, diarrhea, or both, as well as protein losing enteropathy (17). Giardial infection is often associated with young age and poor hygienic conditions, both in dogs and humans (18). Young dogs, as well as young children, are more prone to giardiasis and tend to develop a more severe disease (4,18). *Isospora* infection is usually self-limiting and without clinical signs, although puppies and immunosuppressed animals may develop mucoid to bloody diarrhea (17). The dog in the present report may have acquired giardiasis and coccidiosis at the animal shelter. Dogs in animal shelters are often housed in crowded and inadequate hygienic conditions, with no separation between young and adult animals. Under these conditions, the potential for the spread of infectious agents is increased. These factors were probably involved in the development of the presently described co-infection.

To the best of our knowledge, this is the first description of coinfection with all 6 of these pathogens. Puppies, especially when acquired from an animal shelter, should be carefully examined when transferred to a new environment, because they may harbor multiple infections that potentially can lead to a complex illness with mixed clinical signs. In addition, routine prophylactic measures should be taken, including ectoparasite prevention treatments, deworming, and vaccination. Lastly, when a vector-borne disease is diagnosed, other potential coexisting infections transmitted by the same arthropod vector should be ruled out.

### References

1. v. e) Arsenic poisoning is characterized by gastrointestinal hyperemia.
   v. e) L’empoisonnement à l’arsenic est caractérisé par de l’hyperémie gastrointestinale.
   w. b) Animals poisoned with strychnine tend to develop rigor mortis relatively soon after death.
   w. b) Les animaux empoisonnés à la strychnine ont tendance à développer de la rigueur mortis peu de temps après la mort.
   x. a) Ergot alkaloids cause marked peripheral vasoconstriction, with subsequent dry gangrene.
   x. a) Les alcaloïdes de l’ergot causent une vasoconstriction périphérique importante, ce qui conduit par la suite à la gangrène sèche.
   y. c) The blood of animals poisoned with cyanogenetic plants tends to be bright red.
   y. c) Le sang des animaux empoisonnés par des plantes cyanogénétiques a tendance à être rouge vif.
   z. d) Warfarin poisoning is characterized by hemorrhage into body cavities.
   z. d) L’empoisonnement par la warfarine est caractérisé par des hémorragies dans les cavités corporelles.

2. e) Nonsteroidal antiinflammatory drugs (NSAIDs) are a major cause of gastrointestinal ulceration in dogs. Corticosteroids have comparatively low ulcerogenic potential compared with NSAIDs.
   e) Les anti-inflammatoires non stéroïdiens (AINS) sont une cause majeure d’ulcération gastrointestinale chez le chien. Les corticostéroïdes ont un potentiel ulcérogène relativement faible par rapport aux AINS.

3. e) FIP produces a high-protein exudate that is nonseptic and contains relatively few cells. The relative cellularity may vary with the stage of the disease, however.
   e) La péritonite infectieuse féline provoque un exsudat riche en protéines qui est non septic et renferme peu de cellules. Toutefois, la cellularité relative peut varier avec le stade de la maladie.

   d) Un lobe pulmonaire tordu et les broncho-alvéoles terminales se gorgent de sang, produisant un lobe radio-opaque.

5. b) 0.08 × 12.5 = approximately 1 kg, which, in fluid weight, is equivalent to 1 L (1000 mL). Not mentioned in the question, but also necessary to consider when treating with fluids, are maintenance needs and continuing losses (vomiting, diarrhea).
   b) 0.08 × 12,5 = environ 1 kg, ce qui, en poids de liquide, équivaut à 1 L (1000 mL). Ce qui n’est pas mentionné dans la question, mais qui est aussi nécessaire à considérer lors d’une fluidothérapie, ce sont les besoins d’entretien et les pertes continues (vomissements, diarrhée).

6. e) Histamine, serotonin, and bradykinin act during the immediate response. Leukotriene B4 and prostaglandin D2 are part of the late-phase type-I hypersensitivity response. Only prostaglandin D2 causes smooth muscle contraction.
   e) L’histamine, la sérotonine et la bradykinine agissent durant la réponse immédiate. La leucotriène B4 et la prostaglandine D2 font partie de la phase tardive type 1 de la réponse d’hypersensibilité. Seulement la prostaglandine D2 cause la contraction des muscles lisses.

7. d) All the other diseases listed primarily affect the placenta.
   d) Toutes les autres maladies énumérées affectent principalement le placenta.

8. c) Dietary selenium deficiency may cause placental retention, downer cow syndrome, premature and weak calves, and sudden death in young calves.
   c) Une carence alimentaire en sélénium peut causer une rétention placentaire, le syndrome de la vache par terre, des veaux prématurés et faibles ainsi que des morts subites chez les jeunes vaches.

9. b) This is a typical pattern at the onset of the breeding season.
   b) Ce sont les manifestations caractéristiques du début de la saison d’accouplement.

10. c) None of the other skin diseases listed causes pruritus.
    c) Aucune autre maladie de la peau énumérée ne cause du prurit.