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Case Report: Multiple Tick-Borne Diseases and Gastrointestinal Protozoal Infection in a Young Poodle Dog

I Putu Cahyadi Putra[1,2], Yeocelin Meida Utami[3], Ni Wayan Helpina Widyasanti[1, 4*]

Corresponding email: wayanhelpina@unud.ac.id

[1]Veterinary Teaching Hospital,
[2]Laboratory of Parasitology,
[3]Laboratory of Bacteriology and Mycology,
[4]Laboratory of Anatomy and Embryology
Faculty of Veterinary Medicine, University of Udayana
PB Sudirman Street, Denpasar 80226, Bali, Indonesia

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Abstract

Co-infections involving tick-borne diseases (TBD) alongside gastrointestinal protozoans are poorly understood in domestic dogs. This case report examines the occurrence of *Babesia* sp., *Ehrlichia* sp., and *Anaplasma* sp. co-infections with *Giardia* sp. and *Amoeba* sp. in a three-month-old female poodle. The owner complained that her dog had yellow vomiting and bloody diarrhea, and refused to eat. A physical examination was performed, revealing lethargy, 4% dehydration, bloody diarrhea, mandibular lymphoglandular swelling, and a Rhipicephalus sanguineus tick infestation in the case dog. The parvovirus antigen rapid test kit yielded negative results, whereas the TBD antibody test kit yielded positive results for *Anaplasma* sp., *Babesia* sp., and *Ehrlichia* sp. Infection with *Giardia* sp. and *Amoeba* sp. was detected by native stool examination. The dog had lymphocytosis, monocytosis, granulopenia, hyperchromic normocytic anemia, and thrombocytopenia. The therapy provided was metronidazole and doxycycline combination antibiotics, lactated ringer fluid (RL) therapy, vitamin B complex, Sangobion®, Fufang E'jiao Jiang® (FEJ), ondansetron, vitamin K1, kaolin-pectin, and Hill's Prescription Diet® A/D feed. The therapy showed significant improvement during the 3-day hospitalization, and the dog was declared clinically cured after two weeks of treatment.

Keywords

Amoeba sp., Anaplasmosis, Babesiosis, Ehrlichiosis, *Giardia* sp.

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Introduction

Tick-borne diseases (TBDs) are diseases transmitted by ticks. Many canine tick-borne pathogens have significant implications for both animal and human health due to their zoonotic potential (Springer *et al.,* 2021). TBDs are the leading cause of death in dogs worldwide (Huggins *et al.,* 2021). In dogs, the case fatality rate of TBDs is high at 33%, with all deaths occurring within four months of diagnosis (Kleeb *et al.,* 2021). *Rhipicephalus sanguineus* ticks are a TBD vector that includes *Anaplasma* sp., *Ehrlichia* sp., and *Babesia* sp. (Chirek *et al.,* 2018; Aziz *et al.,* 2023).

Anaplasmosis, Ehrlichiosis, and babesiosis are TBDs frequently reported in dogs in Indonesia (Hadi *et al.,* 2016; Perayadhista *et al.,* 2022; Suartha *et al.,* 2023). TBDs in Bali caused by *Anaplasma* sp. and *Ehrlichia* sp. have been reported to infect dogs infested with *R. sanguineus* ticks, with a seroprevalence of 73.3% (22/30) (Perayadhista *et al.,* 2022). *E. canis* is the causative agent of *Ehrlichiosis* in Bali (Suartha *et al.,* 2023), while *A. platys* is the causative agent of *Anaplasmosis* in Bali (Pradnyantari *et al.,* 2019) and Yogyakarta (Faizal *et al.,* 2019). Although cases of babesiosis in dogs have been reported in Indonesia, the species responsible for causing babesiosis remains unknown (Hadi *et al.,* 2016; Dwi *et al.,* 2018; Widyanjaya *et al.,* 2022). The prevalence of *Anaplasma* sp. and *Ehrlichia* sp. dual infection in Bali has also been reported as high as 54% (12/30) (Perayadhista *et al*., 2022). In addition, double infection with *Anaplasma* sp. and *Ehrlichia* sp. in Canidae, other than dogs, has been reported in timber wolves (Widyasanti *et al.,* 2025). Furthermore, double infections with anaplasmosis and babesiosis have also been reported (Widyanjaya *et al.,* 2022). The high prevalence of TBD in Bali causes cases frequently encountered by practicing veterinarians; thus, a potential combination of TBD and other diseases caused by protozoa and helminths may occur (Gal *et al.,* 2007).

Giardiasis and amoebiasis are zoonotic diseases that can be transmitted through the oral-fecal route, primarily by drinking untreated raw water and consuming contaminated food (Ngui *et al.,* 2020; Hardiyanti *et al.,* 2023). Giardiasis and amoebiasis are more common in young dogs (6 months to 1 year of age) than in older dogs (Uiterwijk *et al.,* 2019). Both organisms have been detected in feces, with the highest frequency of infection observed in dogs and cats (López-Arias et al., 019). Giardiasis and amoebiasis are diseases caused by intestinal protozoa *Giardia* sp. and *Entamoeba* sp., respectively. They are characterized by moderate to severe gastroenteritis, which, if persistent, can lead to anemia and liver abscesses that can spread to other organs, especially the lungs and brain (Ryan and Zahedi, 2019; Uiterwijk *et al.,* 2019). The occurrence of multiple TBDs, namely, a combination of *Anaplasma* sp., *Ehrlichia* sp., *Babesia* sp., *Hepatozoon* sp., and other blood parasites, has been widely reported (Widyanjaya *et al.,* 2022; Sukara *et al.,* 2023; Wongtawan *et al.,* 2024). However, reports of TBD cases with gastrointestinal protozoan infections are limited. The documented reports include multiple infections of *Ehrlichia canis*, *Babesia canis*, and *Hepatozoon canis*, accompanied by gastrointestinal protozoa (*Isospora* sp. and *Giardia* sp.), as well as *Dipylidium caninum* worms, in a 6-week-old puppy. This infection was fatal (Gal *et al.,* 2007). Multiple infections may be common in veterinary practice. To our knowledge, various

TBD infections accompanied by gastrointestinal protozoan infections have not been reported in Indonesia. This case report aimed to assess concurrent infections with *Anaplasma* sp., *Ehrlichia* sp., *Babesia* sp., *Amoeba* sp., *and Giardia* sp. in a young poodle dog.

Materials and Methods

Signalment and Anamnesis

A three-month-old female white-haired poodle dog presented to the Veterinary Teaching Hospital, Faculty of Veterinary Medicine, Udayana University (RSHP FKH UNUD) on 21 September 2021. The owner complained that the dog did not want to eat, had bloody stools three to four times a day, had been vomiting since 20 September 2021, and had a history of tick infestation. The dog was dewormed and vaccinated twice with a combination vaccine (DHPPL) that included canine parvovirus, canine distemper virus, canine hepatitis virus, canine parainfluenza virus, and leptospirosis.

Physical Examination

The patient's rectal temperature was 38.3°C, femoral artery pulses were 108 beats/min, respiration was 30 breaths/min, heart rate was 124 beats/min, body weight was 1.96 kg, capillary refill time (CRT) was < 2 seconds, slow turgor was present, and dehydration was estimated at 4%. The dog appeared lethargic. The left mandibular lymph node was swollen, and the diarrhea was bloody. After combing the hair, several *Rhipicephalus sanguineus* ticks were found.

Supporting Examination

A rapid test kit (Asan Easy Test® Parvo; Asan Pharm Co. Ltd., Korea) was used to detect canine parvovirus antigens, and the results were negative. A rapid test kit 4Dx-based enzyme-linked immunosorbent assay (ELISA) (A Pet Care One-Step Rapid Test Kit®, Shanghai Zhanxun Biotech Co. Ltd., China) against *Anaplasma* sp., *Babesia* sp., and *Ehrlichia* sp. antibodies showed positive results, and the canine heartworm (CHW) antigen showed negative results (Figure 1). A routine hematological examination (iCell-800Vet, Shenzhen Icubio Biomedical Technology Co., Ltd., China) revealed lymphocytosis, granulopenia, hyperchromic normocytic anemia, and thrombocytopenia (Table 1). The native stool examination was performed using a light microscope (Olympus CX23, OLYMPUS SE & CO, Japan) with a magnification of 40–400 times. The fecal-native examination revealed trophozoites of *Giardia* sp. that were motile, bilaterally symmetrical, kite-like, and flagellated. Another protozoan was the trophozoite stage of *Amoeba* sp., characterized by an oval shape, nucleus, and glycogen vacuoles (Figure 2). No helminth eggs were found during the fecal examination.

Table 1. Results of routine hematology examination in young poodles

No	Item	Result	Unit	Reference	Information
1	WBC	10	$\times 10^3/\mu L$	6-15	Normal
2	Lymphocyte #	7.5	$\times 10^3/\mu L$	1.0-4.8	High
3	Monocytes #	1.9	$\times 10^3/\mu L$	0.3-1.5	High
4	Granulocytes #	1.2	$\times 10^3/\mu L$	6.2-14.8	Low
5	Lymphocyte %	71.1	%	10-30	High

No	Item	Result	Unit	Reference	Information
6	Monocytes %	17.5	%	3-10	High
7	Granulocytes %	11.4	%	63-87	Low
8	RBC	3.61	$\times 10^6/\mu L$	5-8.5	Low
9	Hemoglobin	11.2	g/dl	12-18	Low
10	MCV	66.8	fl	60-77	Normal
11	MCH	31.1	pg	14-25	High
12	MCHC	46.6	g/dL	31-36	High
13	RDW-CV	12	%	14-19	Low
14	RDW-SD	32	fl	20-70	Normal
15	HCT	24.1	%	37-55	Low
16	Platelets	15	$\times 10^3/\mu L$	160-625	Low
17	MPV	6.7	fL	6.1-13.1	Normal
18	PDW	7.4	L	10-24	Low
19	PCT	0.01	%	0.1-0.32	Low

Description: MCV = mean corpuscular volume; MCH = mean corpuscular hemoglobin; MCHC = mean corpuscular hemoglobin concentration; RDW-CV = red blood cell distribution width-coefficient variation; RDW-SD = red blood cell distribution width-standard deviation; PDW = platelet distribution width; PCT = procalcitonin. The reference was from the iCell-800Vet device (Shenzhen Icubio Biomedical Technology CO LTD, China).

Table 2. Therapy and clinical progress of poodle during hospitalization at RSHP FKH UNUD

Observation time		Clinical Measures and Signs	Treatment
Day 1	Morning	• The patient arrives. • Lactated ringer's infusion therapy • Stool examination and parvovirus antigen kit test • Manual removal of ticks	Ondansetron IV Vitamin K1 IV Vitamin B Complex IV Metronidazole PO Kaolin Pectin PO
Day 1	Night	• Temperature 37,9°C. The dog was observed to start eating wet food, having normal urination, no defecation, moderately active condition, and no vomiting.	Ondansetron IV Vitamin B Complex IV Metronidazole PO Kaolin Pectin PO *Hill's Prescription Diet*® A/D
Day 2	Morning	• Temperature 38°C. The dog has eaten wet food, has normal urination, no defecation, is moderately active, and has no vomiting. • Routine hematology and blood parasite kit tests are performed with the owner's consent.	Ondansetron IV Vitamin B Complex IV Metronidazole PO Kaolin Pectin PO *Hill's Prescription Diet*® A/D
Day 2	Night	• Temperature 38,3°C. The dog is willing to eat wet food, has normal urination, no vomiting, and has blackish paste-shaped feces.	Metronidazole PO Kaolin Pectin PO Fufang E'jiao Jiang® PO Sangobion® PO *Hill's Prescription Diet*® A/D
Day 3	Morning	• Temperature 38,9. The dog is willing to eat wet food, normal urination, and blackish paste-shaped feces.	Metronidazole PO Doxycycline PO Kaolin Pectin PO Fufang E'jiao Jiang® PO Sangobion® PO *Hill's Prescription Diet*® A/D

Observation time		Clinical Measures and Signs	Treatment
Day 3	Afternoon	• The owner decided to seek outpatient treatment due to financial constraints.	Continued oral therapy at the owner's home

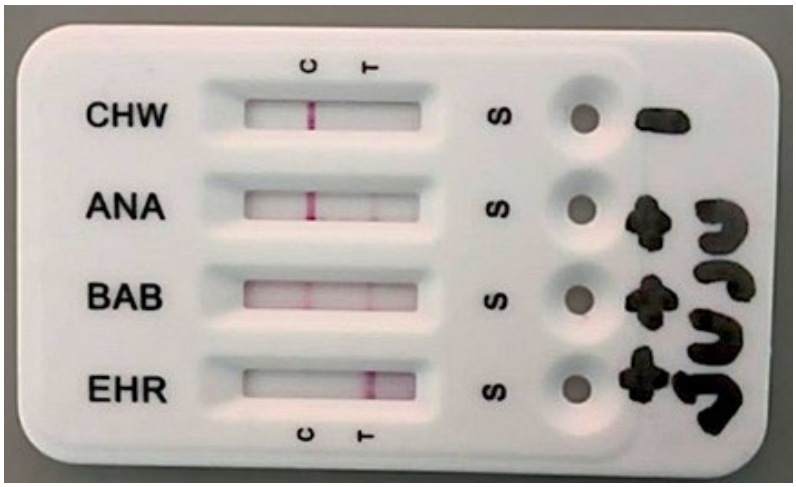

Figure 1. Rapid blood parasite test kit showing positive results for antibodies to *Anaplasma* sp., *Babesia* sp., and *Ehrlichia* sp. indicated by two strips on the test result.

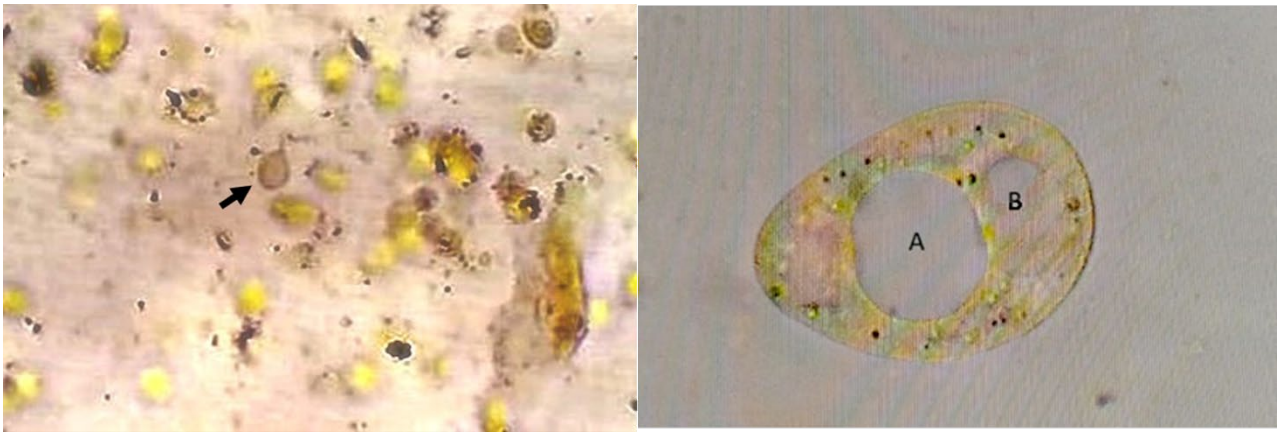

Figure 2. Examination results of the native stool sample in the case dog. *Giardia* sp. trophozoites (arrows) were bilaterally symmetrical, resembling kites and possessing flagella (100x) (left); *Amoeba* sp. trophozoite was oval and characterized by the observation

Diagnosis and Prognosis

Based on anamnesis, physical examination, and supportive examination, the dog was diagnosed with anaplasmosis, babesiosis, Ehrlichiosis, giardiasis, and amoebiasis, with a prognosis of Fausta to dubious. The differential diagnoses in this case were cryptosporidiosis, helminthiasis, canine Coronavirus, and intoxication.

Therapy

The therapy performed on the dog was divided into inpatient and outpatient stages. The patient received a three-day Ringer's lactate (RL) infusion fluid therapy during the inpatient stage. Furthermore, the treatment given is as follows: antiemetic ondansetron 0.1 mg/kg body weight (BW) q12h intravenously (IV), hemostatic vitamin K1 1 mg/kg BW IV once administration, supportive therapy of vitamin B complex 0.1 ml/kg BW q12h IV, Sangobion® supplement one cap/10 kg BW q24h orally (PO), Fufang E'jiao Jiang® (FEJ) supplement 0, 5 ml/kg BW q12h PO, metronidazole antibiotic 25 mg/kg BW q12h per-oral (PO), doxycycline antibiotic 10 mg/kg BW q24h PO, gastrointestinal protectant kaolin-pectin 1 ml/kg BW q12h PO, and Hill's Prescription Diet® A/D feed (Table 2). Outpatient therapy is a continuation of therapy performed at RSHP FKH UNUD. The drugs that were continued were metronidazole, kaolin-pectin, Sangobion®, and Fufang E'jiao Jiang® for seven days. The antibiotic doxycycline 10 mg/kg BW q24h was continued for up to 14 days (Plumb, 2011; Mylonakis *et al*, 2019). Telemedicine via the WhatsApp application during outpatient therapy was administered to monitor the continuation of therapy.

Results and Discussion

During hospitalization, the poodle dog showed significant improvement (Table 2). Immediately after the dog was admitted for hospitalization, 24 hours of fluid therapy were administered, and symptomatic and causative therapy were administered according to the results of the native stool examination. A routine hematological examination and a 4Dx rapid test kit for TBD were performed on the second day of hospitalization. The results showed a positive reaction to *Anaplasma* sp., *Babesia sp*., and *Ehrlichia* sp. antibodies and continued therapy on the 3rd day, namely doxycycline, Sangobion®, and Fufang E'jiao Jiang®. On the third day of hospitalization, the owner decided to transition to outpatient care due to the limited costs. In addition, the dog's condition improved, so it was decided to perform outpatient care with monitoring via telemedicine. The results of the WhatsApp chat interview revealed that the dog had never experienced vomiting after hospitalization during outpatient care. The patient's stool began to form a paste on the second day of outpatient care, and appetite increased. After two weeks of outpatient care, the dog was examined at the RSHP FKH UNUD and was found to be clinically healthy. However, the owner did not continue the routine hematology and rapid 4Dx test; therefore, her thrombocytopenia and antibodies to TBD were unknown. In the third week, the owner returned and underwent a physical examination to continue the rabies vaccination and was declared clinically healthy.

The dogs showed nonspecific clinical symptoms during physical examination, including bloody diarrhea, vomiting, dehydration, lethargy, enlarged lymph nodes, and tick infestation. The clinical symptoms found in dogs infected with anaplasmosis, Ehrlichiosis, babesiosis, amoebiasis, and giardiasis are generally lethargy, decreased activity, and anorexia. Lymphadenomegaly was observed in cases of acute Ehrlichiosis. Meanwhile, intermittent vomiting and diarrhea have been observed in cases of amoebiasis and giardiasis (Chirek *et al*., 2018; Fadhil *et al*., 2021; Remesar *et al*., 2022; Aziz *et al*., 2023). Typical clinical signs of TBDs, such

as epistaxis, jaundice, petechiae, or ecchymoses on the skin, were not observed in this case; however, swelling of the lymph nodes may indicate an ongoing blood parasite infection. In general, clinical signs of babesiosis in dogs include lethargy, pale mucous membranes, pigmenturia, jaundice, pyrexia, anorexia, vomiting, "water hammer" pulse, and epistaxis (Eichenberger *et al.,* 2016). The most common clinical signs in dogs with *A. phagocytophilum* infection are lethargy, decreased activity, acute fever, and decreased appetite (Chirek *et al.,* 2018). *A. platys* infection has been reported to exhibit a combination of the following clinical signs: epistaxis, fever, pale mucosal color, and tick infection (Perayadhista *et al.,* 2022). The clinical findings in Ehrlichiosis are not much different from those in anaplasmosis. The clinical symptoms of *E. canis* infection include nosebleeds, fever, pallor of the mucous membranes, infestation, or a history of tick infestation. The symptoms may appear separately or in combination with two or more otherymptoms simultaneously (Suartha *et al.,* 2023).

Blood tests revealed hyperchromic normocytic anemia, lymphocytosis, monocytosis, granulopenia, and thrombocytopenia. Combined infection with TBD and gastrointestinal protozoa results in complex hematological abnormalities. Anaplasmosis in dogs causes changes in hematological parameters, including thrombocytopenia, anemia, and leukocytosis (Chirek *et al.,* 2018). Acute and subclinical Ehrlichiosis cases often show no clinical symptoms or mild hematological changes (Mylonakis and Theodorou, 2017). In dogs infected with Ehrlichiosis, lower mean values of total erythrocytes, hematocrit, and platelets, along with higher counts of lymphocytes and monocytes, are observed (Bai *et al.,* 2017; Aziz *et al.,* 2023). Monocytosis is the main WBC abnormality in dogs with Ehrlichiosis, followed by eosinopenia and neutrophilia (Thongsahuan *et al.,* 2020). Eosinopenia was the most common WBC abnormality found in Ehrlichiosis in Yogyakarta, Indonesia; however, neutropenia, monocytopenia, leukopenia, and lymphopenia were also observed (Wuhan *et al.,* 2020). Babesiosis is characterized by significant changes in anemia, thrombocytopenia, eosinopenia, and lymphopenia associated with *Babesia canis* infection. Thrombocytopenia is a primary characteristic of Babesia canis infection, with 95.6% of infected dogs exhibiting this sign (Thongsahuan *et al.,* 2020). Thrombocytopenia results from increased platelet consumption during the acute phase of infection caused by inflammatory mechanisms (Solano-Gallego *et al.,* 2016). Meanwhile, all hematological and biochemical test parameters of dogs with giardiasis were within the normal range (Peruzzo *et al.,* 2023).

The finding of ticks, in this case, is instrumental in the transmission of anaplasmosis, babesiosis, and Ehrlichiosis (Pradnyantari *et al.,* 2019; Suartha *et al.,* 2023). *Rhipicephalus* sp. is an important vector for transstadial and intrastadial transmission of *Babesia* sp. and *Ehrlichia* sp. in dogs, but not for transovarial transmission. It plays a significant role in the transmission of pathogens from infected dogs during the acute phase of TBDs. *Babesia* sp. and *Ehrlichia* sp. infectious agents multiply in the gastrointestinal tract and move to the salivary glands to spread pathogens to other healthy dogs when ticks bite (Aziz *et al.,* 2023; Zygner *et al.,* 2023). *Ehrlichia* sp. bacteria are obligate intracellular to infect monocytes, macrophages, and lymphocytes to form

membrane-bound intracytoplasmic bacterial aggregates called morulae. The disease course begins with an incubation period of 8-20 days, followed by an acute period (2-4 weeks), a subclinical period (several months to years), and a chronic period (Mylonakis and Theodorou, 2017; Aziz *et al.,* 2023). *Babesia* sp. protozoa develop sexually in the vector gut and produce sporozoites that migrate to the salivary glands of the ticks. When ticks bite dogs, the sporozoites enter the bloodstream and infect erythrocytes, developing into trophozoites that then reproduce asexually into merozoites. This process causes damage to red blood cells, resulting in anemia and fever (Zygner *et al.,* 2023).

Meanwhile, *A. phagocytophilum,* when present in the bloodstream, infects and survives in neutrophils by disrupting key neutrophil functions. Neutrophils typically kill pathogens through phagocytosis and the release of reactive oxygen species (ROS) and antimicrobial peptides. However, *A. phagocytophilum* can survive these hostile conditions by interfering with the production of ROS and other antimicrobial mechanisms (Dumler *et al.,* 2020).

Giardia sp. infection in dogs involves both trophozoite and cyst stages, with transmission primarily occurring through the ingestion of water, food, or feces contaminated with trophozoites or cysts. Once ingested, binary fission occurs. This can disrupt normal intestinal absorption, causing clinical symptoms such as diarrhea, weight loss, and malnutrition. The trophozoites transform into cysts, which are then passed through the feces (Grüttner *et al.,* 2023; Barrera *et al.,* 2024). The *Giardia* sp. trophozoites identified in this study (Figure 2) were consistent with those reported by Harun *et al*. (2019), which are pear-shaped and convex on the dorsal part with spiral organelles. Otranto and Wall (2024) also described the morphology of *Giardia* sp. trophozoites as a bilaterally symmetrical body with a pyriform-to-ellipsoid shape. The dorsal part was convex, whereas the ventral side was equipped with a large sucking disc. This structure has two anterior nuclei, two slender axostyls, eight flagella divided into four pairs, and a pair of dark-colored median bodies. The median body was curved, resembling a hammer claw. Giardia cysts are ovoid and have four nuclei.

In the fecal examination of poodle dogs, an *Amoeba*, suspected to belong to the genus *Entamoeba*, was observed in the trophozoite phase of the minuta stage (Figure 2). *Entamoeba* spp. has several forms that may be found in stool samples depending on the phase of their life cycle, namely trophozoites and cysts (Fadhil *et al.,* 2021). The trophozoite phase consists of two stages: minuta (meta-cyst) and magna (adult stage). The minute stage is the initial stage of cyst formation (pre-cyst) or the transition from trophozoites to cysts, characterized by a size of 10-20 µm, a round or oval shape, and a colorless appearance, due to the slow formation of pseudopodia. In contrast, the magnum stage is a larger reproductive stage (20-60 µm), characterized by a large, clear entoplasm and thin, finger-like pseudopodia.

Meanwhile, the cyst stage is the infective form measuring 10-20 µm, with smooth and translucent walls and 1-4 cell nuclei. Large chromatoid bodies and glycogen vacuoles disappeared in the pre-cysts as they matured. The cyst wall, which consists of solid chitin, protects against damage caused by environmental change (Junaidi, 2021). *Entamoeba histolytica* infection in dogs can

cause diarrhea or dysentery. This pathogenic *Amoeba* strain penetrates the colon mucosa and multiplies to form small colonies that extend into the submucosa and muscularis (Otranto and Wall, 2024).

To the best of our knowledge, only one case report, Gal *et al*. (2007), has shown a co-infection pattern of TBDs (*E. canis, B. canis*, and *H. canis*), protozoa (*Isospora* spp. and *Giardia* spp.), and gastrointestinal helminths (*Dipylidium caninum*), which can worsen clinical manifestations and be fatal in a 4-month-old young dog. Gal *et al*. (2007) suggested that the co-infection relationship was due to overpopulation in the shelter where the case animals originated. In addition, co-infections with triple TBDs (*B. vogeli, E. canis*, and *A. platys*) have been reported. One such report came from Thailand, where the condition was observed in 9.05% (34/375) of dogs in shelters, despite the absence of gastrointestinal protozoan infection (Wongtawan *et al.,* 2024). Another case report described co-infection with *E. canis, H. canis*, and *A. phagocytophilum* in a 5-month-old mongrel dog (Mylonakis *et al.,* 2004). In the present case, it occurred in a young dog (3 months). We suspect a correlation between the age of the dog and the occurrence of multiple TBD infections, which warrants further investigation.

In this case, the treatment was both symptomatic and supportive, as well as causative. Symptomatic therapy involved the administration of RL infusion to correct the 4% dehydration that occurred. Ondansetron is an antiemetic that works as a 5-HT3 (serotonin type 3) receptor antagonist. 5-HT3 receptors are found peripherally and centrally in the vagus nerve endings in the chemoreceptor trigger zone (CTZ). Kaolin pectin is an adsorbent agent used to treat diarrhea and remove toxins from the gastrointestinal tract. Kaolin-pectin acts as a coating that protects the inflamed mucosa from bacteria and toxins. The pectin component that forms galacturonic acid has been shown to lower the pH of the intestinal lumen. Vitamin K1 (phytonadione) is used to treat bleeding disorders during episodes of bloody diarrhea (Plumb, 2011).

Supportive treatment, in the form of vitamin B complex, Sangobion®, and Fufang E'jiao Jiang® supplements, aims to increase the body's metabolism to generate energy and stimulate the production of red blood cells and platelets (Li *et al.,* 2018; Batool *et al.,* 2022; Yang *et al.,* 2023). Sangobion is a supplement for treating anemia that contains ferrous gluconate, copper sulfate, folic acid, Vitamin C, vitamin B12, and vitamin B6 (Batool *et al.,* 2022). Sangobion® supplements have been used to treat Ehrlichiosis in dogs with gallbladder mucoceles (Nurullah *et al.,* 2023). Sangobion® has also been used in dogs with anaplasmosis and babesiosis (Widyanjaya *et al.,* 2022). Although it has been widely used in dogs, no clinical studies have been conducted to evaluate its effectiveness, leaving only anecdotal evidence.

Fufang E'jiao Jiang® (FEJ) is a traditional Chinese medicine consisting of a combination of ingredients: donkey skin gelatin prepared by boiling and concentrating the skin of *Equus asinus Linnaeus*, *Codonopsis pilosula* root, steamed and dried root of *Panax ginseng*, fruit of *Crataegus pinnatifida Bunge*, and steamed and dried tuber of *Rehmannia glutinosa*. FEJ is claimed to increase vital energy, nourish the blood, and treat symptoms of dizziness, palpitations, insomnia, loss of appetite, and anemia in humans (Li *et al.,* 2023). Several case reports on dogs suffering from TBD have used

FEJ as therapy (Widyanjaya *et al.,* 2022; Nurullah *et al.,* 2023). However, no studies have specifically addressed the effectiveness of FEJ and its effects on dogs suffering from TBD. Its use is based solely on anecdotal evidence. However, studies have been conducted on the effects of FEJ in experimental animals and humans (Li *et al.,* 2018; Li *et al*., 2023; Zhang *et al.,* 2021). The Ejiao (donkey skin gelatin) content of FEJ in humans has been used to supplement blood and increase white blood cell counts; however, these effects are still within the normal range (Zhang *et al.,* 2021). FEJ has also been reported to improve hematopoietic function and rapidly and significantly increase hemoglobin levels in postpartum women with anemia (Li *et al.,* 2018).

The causative therapy was a combination of metronidazole and doxycycline antibiotics. Metronidazole is used as an antiprotozoal to treat giardiasis and amoebiasis. There is no significant difference in the cure rates of fenbendazole and metronidazole for treating giardiasis in dogs (Ciuca *et al.,* 2021). Metronidazole is widely recognized as an effective treatment for amoebiasis. It is the drug of choice due to its efficacy and low cost (Hemmati *et al.,* 2016). Metronidazole can also be used in various TBD treatments in combination with several other antibiotics and antiprotozoans (Gal *et al.,* 2007; An *et al*., 2019; Almendros *et al.,* 2020; Mohammed *et al.,* 2021). Combination therapy with metronidazole and doxycycline is superior to combination therapy with quinine and clindamycin in improving blood parameters in dogs with babesiosis and theileriosis, including decreased liver enzyme levels, increased platelet counts, and improved cure rates (Mohammed *et al.,* 2021). A three-antibiotic combination protocol (metronidazole, clindamycin, and doxycycline) increased the cure rate to 87% in dogs infected with *B. gibsoni* (Almendros *et al.,* 2020). This combination may also be an effective option for treating B. gibsoni infections resistant to atovaquone and azithromycin, and canelp improve clinical symptoms (An *et al.,* 2019).

Doxycycline is one of the first-choice antibiotics for treating anaplasmosis, Ehrlichiosis, or babesiosis in dogs (Mylonakis *et al.,* 2019; Almendros *et al.,* 2020; Maheshwarappa *et al.,* 2020). The therapeutic dose of doxycycline for TBDs is 5 mg/kg BW q12h or 10 mg/kg BW q24h, with the duration of therapy varying from 2 to 4 weeks (Mylonakis *et al.,* 2019; Wongtawan *et al.,* 2024). Single doxycycline therapy for triple infections with *Babesia vogeli*, *Ehrlichia canis*, and *Anaplasma platys* has been reported. Most pathogens were undetectable by PCR by day 14, and all pathogens had been eliminated by day 28. Most blood profiles were significantly improved after 14 d. This improvement persisted for 28 days (Wongtawan *et al.,* 2024). In this case, we conducted therapy for 14 days, as clinical considerations indicated significant progress and the use of metronidazole in combination with other medications during treatment. Post-therapy tests were not performed due to cost constraints by the owner; therefore, therapy was not continued, and the dog was declared clinically cured after 14 days of treatment.

Combination treatment with doxycycline and various antibiotics, antiprotozoans, and anthelmintics has been reported for combined TBDs and gastrointestinal parasite infections. Mylonakis *et al*. (2004) reported a combination treatment of doxycycline (5 mg/kg BW PO q24h for 4 weeks) and imidocarb dipropionate

(5 mg/kg BW SC, twice, 14 days apart) in mixed infections with *E. canis, Hepatozoon canis*, and *A. phagocytophilum*. The therapy results showed clinical recovery within 48 hours, characterized by the return of appetite, followed by the resolution of clinical and pathological abnormalities and the disappearance of parasitemia by day 28. Gal *et al*. (2007) reported a combination of doxycycline (10 mg/kg BW PO q24h), metronidazole (10 mg/kg BW IV q24h), trimethoprim-sulfamethoxazole (15 mg/kg BW PO q24 h), imidocarb dipropionate (5 mg/kg BW IM q14d for two treatments), ivermectin (0.2 mg/kg BW SC one dose), and praziquantel-pyrantel-febantel (Drontal Plus. One tablet/10 kg BW PO q10d) was administered for the treatment of combined infections with *E. canis, B. canis, H. canis*, *Isospora* spp., *Giardia* spp., and *Dipylidium caninum* in 6-week-old dogs. Despite the complex therapy, the dog did not show significant progress; therefore, it was euthanized due to complications of septic peritonitis. In contrast, in our case, significant clinical improvement was observed starting on the third day, possibly because of the less severe symptoms reported by Gal *et al*. (2007) and the absence of further complications.

Conclusion

The dog was diagnosed with multiple TBDs and gastrointestinal protozoan infections based on clinical signs, hematology, rapid test kits, and fecal examination. The prognosis was good, and the dog was declared clinically cured two weeks after outpatient care. Combined therapy with metronidazole and doxycycline effectively treated this case of combined infection.

Approval of Ethical Commission

We declare that the clinical cases in this report occurred at RSHP FKH UNUD and did not require ethics commission approval, as the procedures performed were standard medical actions according to existing protocols, without involving experiments or data collection that contradicted ethical guidelines. All actions were carried out with the consent of the animal owner and with due regard to animal welfare.

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Author's Contribution

IPCP: supervision, conceptualization, methodology, and visualization. YMU: visualization and data curation. NWHW: investigation, supervision, and resources. All authors wrote the original draft, edited, and reviewed the manuscript. All authors made equal contributions to the writing of this case report.

Conflict of Interest

The authors declare that there is no conflict of interest.

Data Availability Statement

The data in this case report were obtained from the patient's medical records at RSHP FKH UNUD and could only be accessed by authorized parties. This data is not publicly accessible, but requests to obtain it can be submitted via email (wayanhelpina@unud.ac.id). The author will evaluate the request based on the research needs and applicable privacy policy.

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