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COAGULOPATHY AS A COMPLICATION OF BABESIOSIS IN A DOG WITH HEMOTHORAX: CLINICAL CASE REPORT

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Abstract

Canine babesiosis is a protozoan tick-borne disease affecting dogs worldwide, caused by intra-erythrocytic large and small piroplasms of the genus Babesia (Apicomplexa: Piroplasmida). Clinical manifestations are polymorph and evolution of the disease depends to a large extent on the virulence of the causative piroplasm species but also to host-related factors and as well as to the time of animal presentation for consultation, the early diagnostic and specific therapy administered in due time. The most frequent pathological changes of canine babesiosis are anemia and different degrees of thrombocytopenia. Additionally, the systemic inflammatory response syndrome and disseminated intravascular coagulation are described as possible complications. Here we present a clinical case of babesiosis complicated by coagulopathy in a 11 months-old male Beagle dog, which was presented at a veterinary clinic with dyspnoea and apathy. The clinical, radiological, and ultrasound examinations showed an active bleeding in the thoracic cavity, prolonged coagulation time and post-haemorrhagic anemia (packed cell volume of 22.2%). Based on these primary registered aspects, intoxication with anticoagulant rodenticides was suspected. As it was considered an emergency, the dog was transferred to a specialized clinic for hemo-transfusion and stabilized. However, a week later, the dog returned to the clinic with a febrile syndrome. Based on the hemo-parasitological investigations, the dog was diagnosed with babesiosis. Initially, a therapeutical protocol, based on clindamycin was administered, but without a satisfactory evolution; therefore, a babesiicid treatment, using imidocarb dipropionate, was administered, after which the clinical status of the dog rapidly improved. By this case report, the challenges for diagnostic and therapeutical management of canine babesiosis and its impact on the disease evolution, including potential complications, are emphasized.

Key words*: babesiosis, thrombocytopenia, clinical case, dog.*

INTRODUCTION

Canine babesiosis is a tick-borne protozoan disease that affects dogs all around the world. It is caused by intra-erytrocytic small and large piroplasms (Apicomplexa: Piroplasmida). Knowledge about the prevalence and the clinico-pathological aspects of this disease in dogs are of significant epidemiological and veterinary medical interest (Casapulla et al., 1998).

Infected dogs displays polymorphic clinical signs depending to a large extent on the virulence of the causative *Babesia* species, but also to the general status of animal, as well as the time of presentation at the consultation and the early administration of the specific therapy. Babesiosis in dogs is usually characterized by lethargy, anorexia, fever, pale mucous membrane, hemolytic anemia, icterus, and hemoglobinuria (Bourdoiseau, 2006).

Additionally, the most frequent pathological changes are anemia, ranging from mild, moderate to severe, and various degrees of thrombocytopenia (Irwin et al., 2010).

Systemic inflammatory response syndrome (SIRS) and disseminated intravascular coagulation (DIC) are two possible complications that lead to the syndrome of single and/or multiple organ dysfunction in canine babesiosis (Moore, 1979; Mathe et al., 1998; Welzl et al., 2001).

SIRS is commonly found in canine babesiosis. In veterinary medicine, several authors have proposed different SIRS criteria (Purvis and Kirby, 1994). Limit values for SIRS criteria are a major problem in veterinary medicine because normal values for temperature, heart

rate and respiratory rate vary in dogs due to major size differences (Huston and Radostitis, 2000). Use of SIRS criteria it is proposed by Okano et al. (2000), because this tested model showed the best prognostic value in canine babesiosis.

The therapeutic regimen used for treatment of of dogs with babesiosis differs depending on the clinical form they present, uncomplicated or severe, complicated disease, respectively.

In addition to the treatment administered to dogs with mild disease, rehydration, heparin, and blood transfusion along with other supportive therapy are recommended to dog with severe clinical babesiosis. Mortalities are reported primarly in dogs with severe disease and were attributed also to disseminated intravascular coagulation (Gopegui et al., 2007; Leica et al., 2019).

In addition to the directly pathogenic piroplasms (intraerythrocytic parasites' development, division and finally the cell lysis) resulting in hemolytic anaemia, parasitic antigens also act on lipoprotein metabolism, and on the complement system with the formation of anti-erythrocytic antibodies and immune complexes, all of which resulting in intra- and extravascular hemolysis (Ginger et al., 2005; Mitrea, 2011).

Therefore, it is suggested that a great importance must be given to the second pathogenetic mechanism, that of parasitic antigens on the reticulo-histiocytic system in which cell hyperplasia occur (hyperplasia associated with the agglutination and adhesion to the vascular endothelium of the parasitized erythrocytes, platelets, and antigens from plasma) causing capillary blockage in different organs with varied consequences (Irwin, 2010).

Here, we present a case report on canine babesiosis complicated by coagulopathy.

MATERIALS AND METHODS

Case presentation

In October 2018, a 11-months old male Beagle dog was presented in a veterinary clinic with dyspnea and apathy, for a radiological examination, being suspected for pleural effusion.

The dog spent several days outdoors in a private yard (in Constanta county), and thereafter in Tulcea county (Isaccea), for a few days, where it was suspected for eating suspected food, as the owner stated. After that, the dog showed dyspnea, apathy, and the owner presented him at veterinary clinic.

The dog was subjected for a routine clinical examination followed by paraclinical investigations, including a count blood cells (hemoleucogram), radiological, and ultrasound investigations.

RESULTS AND DISCUSSIONS

Clinical history and investigations

At clinical examination, the dog displayed dyspnea and severe apathy.

The laboratory, radiological and ultrasound investigations revealed free fluids in the thoracic cavity (Figures 1, 2), prolonged coagulation time, and pronounced post haemorrhagic anemia (PCV of 22.2%).

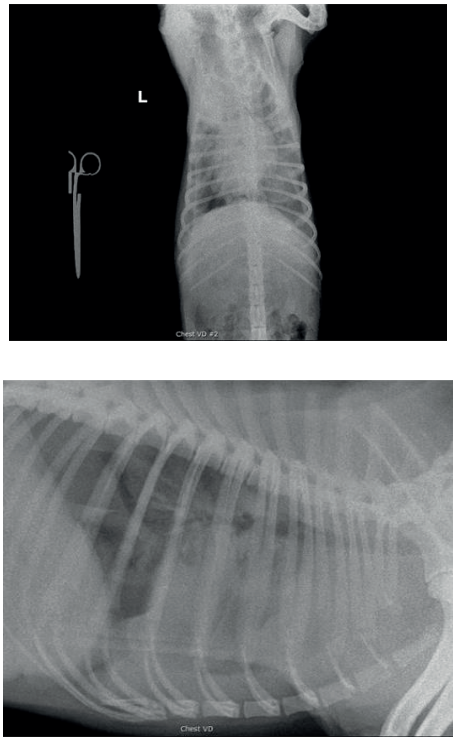

Figure 1. Pleural effusions in a 11-months Beagle dog (dorsal and lateral view) - radiography

Subsequently, in order to collect and examine the fluid, a puncture was performed. A total of

60 ml of bloody liquid (Figure 3) was collected, which was subjected for examination. An active bleeding in the thoracic cavity, was confirmed.

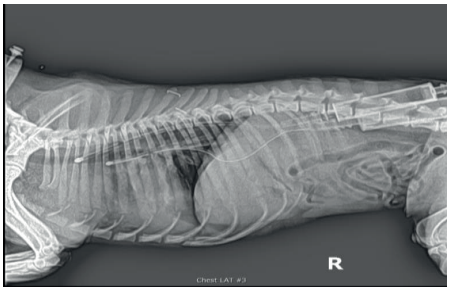

Figure 2. Dog with free fluid in the thoracic cavity

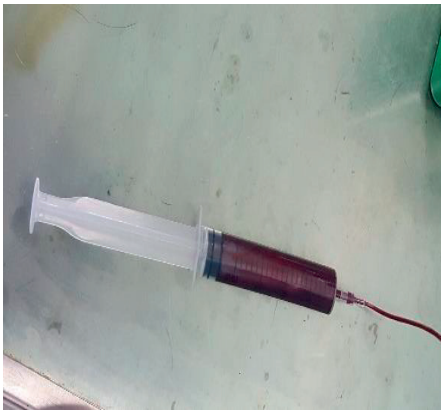

Figure 3. Bloody fluid drained from the thoracic cavity

Additionally, a drop of venous blood was collected to determine the coagulation time, which was longer than 10 minutes. Therefore, by corroborating the anamnesis and the clinical and pathological changes registered, an intoxication with anticoagulant rodenticides was suspected, and accordingly a therapy with vitamin K1 (phytomenadione) at a dose rate of 2.5 mg/kg body weight, s.c. was administered.
As it was considered an emergency, the dog was transferred to a specialized clinic for hemo-transfusion. Thereafter, the dog returned to the vet clinic where it was monitored post-transfusion, for a week. The haematological investigations performed during this period showed a stabilised condition (PCV improved from 22.2% to 32.0%); subsequently, the dog was released.

Over other several days, the dog returned to the clinic with a febrile syndrome, showing apathy, and accelerated breathing. The dogs displayed clinical signs compatible for babesiosis, such as: hyperthermia (40.6ºC), pale mucous membranes, tachypnea. Therefore, blood sample was collected and subjected for hematological, biochemical, and parasitological investigations.
The results of hematological and biochemical investigations revealed moderate non-regenerative anemia (PCV: 28.8%) and trombocytopaenia (Table 1).
Additional, a rapid, in-clinic, immunochromatographic (Snap 4DX, Plus, Idexx Laboratories) for detection of arthropod-borne pathogens (*Dirofilaria immitis* antigen and antibodies for *Anaplasma* spp., *Ehrlichia* spp., and *Borrelia burgdorferi* sensu lato), which was negative.
At the miscroscopic examination of thin blood smears Diff-quick stained, intraerythrocytic large *Babesia* piroplasms were identified.

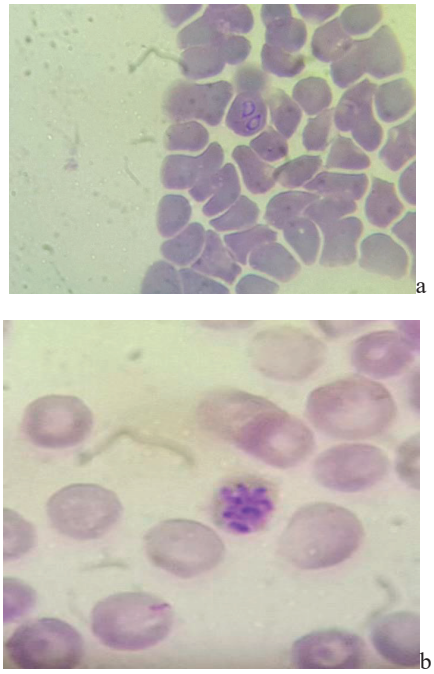

Figure 4. Dog peripheral blood smear showing intra-erythrocytic large *Babesia* piroplasms [paired (a) and multiple (b) intra-erythrocytic pyriform piroplasms] (Diff-quick staining; x1000)

Diagnostic, treatment, and follow-up
The owner was informed about the diagnostic, the potential severity of disease' evolution, and therapeutical protocol. Imidocarb dipropionate therapy was refused by the owner, who

requested for other therapeutic alternative. Therefore, a clindamycin-based therapy (Baneth, 2018) was initiated, at a dose rate of 15 mg/kg/day, *per-os*. Initially, an improvement in the dog's clinical status was observed, but the treatment has not been fully effective (Table 1, Figure 5). Due to the fact that a worsening of clinical condition and pathological changes were registered (PCV decreased at 33.7%; day 9 p.t.), finally the owner accepted the babesiicid treatment protocol, and imidocarb dipropionate was administered (6.0 mg/kg, body weight). At 48 hours p.t., the haematological parameters (PCV: 39.9%) and clinical status improved substantially.

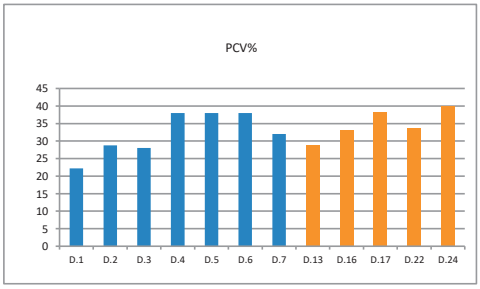

Figure 5. Dynamic of the packed cell volume (PCV%) in dog with coagulopathy and diagnosed with babesiosis (from the day of presentation-D.1 and the follow-up 24 days)

The second injection of imidocarb dipropionate was administered at 14 days, as manufacturer recommendations.

Table 1. Dynamics of haematological parameters on the dog after diagnostic of babesiosis (day 0), during of the treatment (with different drugs) follow-up

Parameter	**Drug administered/Day post-treatment** (D.pt.)					Limits and units of measurement
	clindamycin				imidocarb dipropionate	
	D.0* (18.10)	D.3pt.* (21.10)	D.4pt.* (23.10)	D.9pt.* (27.10)	D.2pt.** (29.10)	
WBC (white blood cells)	7.9	17.85	**17.8**↑	**4.09**↓	13.69	6-17 *10^9/L
LYM (lymphocytes)	1.92	30.7	2.86	**0.87**↓	**4.9**↑	1.0-4.80 *10^9/L
MON (monocytes)	0.33	5.9	0.86	0.38	0.65	0.20-1.5 *10^9/L
NEU (neutrophils)	5.63	ND	**14.5**↑	**2.83**↓	8.09	3.0-12.0*10^9/L
EOS (eosinophiles)	**0.02**↓	ND	**0.02**↓	**0.02**↓	**0.06**↓	0.1-1.0*10^9/L
BAS (basophiles)	0	ND	0.01	0	0	0.00-0.50*10^9/L
LYM %	24.3	ND	16.1	21.2	**35.8**↑	12.0-30.0
MON %	**4.2**↑	ND	4.8↑	9.2	**4.7**↑	2.0-4.0
NEU %	71.2	ND	79	69.2	**59.1**↓	62.0-87.0
EOS %	**0.3**↓	ND	0.1	0.4↓	**0.4**↓	1.0-8.0
BAS %	0	ND	0	0	0	0.0-3.0
RBC (red blood cells\0	**3.66**↓	**4.69**↓	**4.85**↓	**4.24**↓	**5.15**↓	5.50-8.50*10^{12}/L
HGB (hemoglobine)	**8.4**↓	**11**↓	12.4	**10.3**↓	12.3	12.0-18.0 g/dL
HCT (haematocrite) = PCV (packed cell volume)	**28.88**↓	**33.2**↓	38.16	**33.77**↓	39.93	37.0-55.0
MCV	**79**↑	70.9	79	80	77	60-77 fL
MCH	**23.1**↓	23.4	25.6	24.3	23.9	19.5-24.5 pg
MCHC	29.2	33.1	32.5	**30.5**↓	**30.8**↓	31-34.0 g/dL
RDWc	14	12.1	15.9	14.8	15.4	
RDWs	45.3	ND	51.6	48.4	49.2	
PLT (platelets)	**95**↓	ND	240	58↓	**35**↓	200-500*10^9/L
MPV	**12.4**↑	ND	**12.8**↑	9.9	**11.9**↑	3.9-11.1
PCT	0.12	ND	0.31	0.06	0.04	
PDWc	41.5	ND	43.4	39.5	41.9	
PDWs	22.5	ND	26.9	18.6	23.4	

D.0: day of treatment; *: post-treatment with clindamycin; **: post-treatment with imidocarb dipropionate

During the whole period of antiparasitic therapy the patient received supportive therapy, including liver protectors.
One month later, at the check-up, the clinical condition of the dog was very good and at the microscopic examination of blood smears was negative for piroplasms.
The ultrasound examination did not revealed any thoracic or abdominal changes, and the coagulation time returned to normal.

Discussions
Overall, this case supports the statement that babesiosis can lead to systemic disorders (Jacobson, 2006). Some authors hypothesized that multiple organ dysfunction syndrome (MODS) in canine babesiosis appears as a consequence of the dysfunction of pro-inflammatory and anti-inflammatory mechanisms (Goris et al., 1985; Welzl et al., 2001). The circulatory complications of canine babesiosis arising from systemic inflammatory response syndrome and disseminated intravascular coagulation, may lead to multiple organ dysfunction syndrome in babesiosis.
In the last decades, a high prevalence of canine babesiosis is reported in Romania, with values ranging from 10.7% in western Romania, Banat area (Imre et al., 2013), to up 27.8% in Dobrogea (Leica et al., 2017; 2019), or from 26.10 to 30.5% in the metropolitan area of Bucharest (Anghel, 2016; 2017), even with severe, complicated, life-threatening clinical cases (Leica et al., 2019). Moreover, molecular testing of ticks infesting dogs revealed the presence of *Babesia canis* in 21% of the investigated *Dermacentor reticulatus* tick (Ionita et al., 2016). Additionally, an increasing frequency and abundance of the *D. reticulatus* tick populations in the last decades, particularly in southe-southeastern Romania suggests increasing risks as well for canine babesiosis (Ionita and Mitrea, 2017).
Moreover, apart of dogs, recently, in Romania, outbreaks of clinical babesiosis have been also reported for horses (Ionita et al., 2018).
By this case report, the challenges for diagnostic of babesiosis in the acute phase and its impact on the mechanisms of hematopoiesis, hemostasis and vascular integrity are emphasized.
Moreover, the importance of the monitoring ante- and post-hemotransfusion, as well as the administration of the babesiicide medication it is highlighted.

CONCLUSIONS

This case report emphasizes the importance of the early diagnostic and specific treatment in due time in canine babesiosis, in order to avoid occurrence of complications that may lead to multiple organ dysfunctions.
Despite of various ways for diagnosis and treatment, canine babesiosis still remain a disease with major potential risks and challenges.

REFERENCES

Anghel, R. G., Mitrea, I. L., Ionita, M. (2016). Retrospective study on prevalence of canine vector borne diseases in Bucharest area. *Revista Română de Medicină Veterinară*, 26(4): 27-32.

Anghel, R. G., Mitrea, I. L., Ionita, M. (2017). Clinico-pathological findings in vector-borne pathogen co-infections in dogs, from Bucharest area. *Scientific Works. Series C. Veterinary Medicine*, 63(1): 45-49.

Bohm, M., Leisewitz, A. L., Thompson, P. N., Schoeman, J. P. (2006). Capillary and venous *Babesia canis* rosi parasitaemia and their association with outcome of infection and circulatory compromise. *Veterinary Parasitology*, 141:18-29.

Bone, R. C., Balk, R. A., Cerra, F. B. , Dellinger, R. P., Fein, A. M. W., Knaus, A. (1992). Definitions for sepsis and organ failure and guidelines for the use of innovative therapies in sepsis. ACCP/SCCM consensus conference committee. *Chest,* 101: 1644-1655.

Brady, C. A., Otto, C. M. (2001). Systemic inflammatory response syndrome, sepsis, and multiple organ dysfunction. *Vet. Clin. North Am. Small Anim. Pract.* 31: 1147-1162.

Casapulla, R., Baldi, L., Avallone, V., Sannino, R., Pazzanese, L. and Mizzoni, V. (1998): Canine Piroplasmosis Due To Babesia Gibsoni: Clinical and Morphological Aspects. *Veterinary Record,* 142: 168-169.

Duh, D., Tozon, N., Petrovec, M., Strasek, K. and Avsic-Zupanc, T. (2004). Canine babesiosis in Slovenia: Molecular evidence of *Babesia canis canis* and *Babesia canis vogeli*. *Veterinary Research*, 35, 363-368.

Farwell, G. E., LeGrand, E. K., Cobb, C. C. (1982). Clinical observations on *Babesia gibsoni* and *Babesia canis* infections in Dogs. *J. Am. Vet. Med. Assoc.* 180, 507-511.

Ganeth, B. (2018). Antiprotozoal treatment of canine babesiosis. *Veterinary Parasitology*, 254: 58-63.

Giger, U. (2005). *Regenerative Anemias Caused by Blood Loss or Hemolysis*. In: Ettinger, S. J. and Feldman, E. C. (eds) *Textbook of Veterinary*

Internal Medicine. 6th Edition. Elsevier Saunders, St. Louis. pp. 1886-1907.

Gopegui R. R., Penalba B., Goicoa A., Espada Y., Fidalgo L., Espino L., 2007. Clinico-Pathological Findings and Coagulation Disorders in 45 Cases of Babesiosis in Spain. *Veterinary Journal*, 174: 129-132, 2007.

Goris, R. J., T. P. Bockhorst, J. K. Nuytinek, J. S. Gimbrere (1985): Multiple-Organ Failure. Generalized Autodestructive Inflammation? *Arch. Surg.* 120, 1109-1115.

Houston, D. M., O. M. Radostitis (2000). The Clinical Examination. In: *Veterinary Clinical Examination and Diagnosis* (Radostits, O. M., I. G. Mayhew, D. M. Houston, Eds.). W.B. Saunders. London. pp. 91-124.

Ionita, M., Mitrea, I. L. (2017). Actualities on vector-borne disease: risks for the human and animal health in Romania (a review). *Revista Română de Medicină Veterinară*, 27(2): 8-14.

Ionita M., Mitrea, I.L. (2013). *Diagnosticul parazitozelor la animale (vol. 1): Tehnici şi metode de diagnostic parazitologic. Diagnosticul protozoozelor,* Bucharest, RO: Ceres Publishing House.

Ionita, M. Nicorescu, I.M., Pfister, K., Mitrea, I. L. (2018). Parasitological and molecular diagnostic of a clinical *Babesia caballi* outbreak in Southern Romania. *Parasitology Research*, 117(7): 2333-2339.

Ionita, M., Silaghi, C., Mitrea, I. L., Edouard, S., Parola, P., Pfister, K. (2016). Molecular detection of *Rickettsia conorii* and other zoonotic spotted fever group rickettsiae in ticks, Romania. *Ticks and Tick Borne Diseases*, 7(1): 150-153.

Ionita M., Mitrea I.L., Pfister K., Hamel D., Buzatu C.M, Silaghi C. (2012). Canine babesiosis in Romania due to *Babesia canis* and *Babesia vogeli*: a molecular approach. *Parasitology Research* 110(5): 1659-1664.

Irwin J.P. (2010). Canine babesiosis. *Vet Clin Small Anim.,* 40: 1141-1156.

Jacobson, L. S. (2006). The South African Form of Severe and Complicated Canine Babesiosis: Clinical Advances 1994-2004. *Vet. Parasitol.* 138, 126-139

Leica, L., Mitrea, I. L, Ionita M. (2019). Clinical occurrence of canine babesiosis in the coastal area of the Black Sea (Dobrogea) in Southeastern Romania and associated epidemiological implications. *Journal of Parasitology,* 105(4): 491-496.

Leica, L., Mitrea, I. L., Ionita, M. (2017). Clinical study and pathological findings on babesiosis in dogs, on seaside of romania. The International *Scientific Works. Series C. Veterinary Medicine*, 63(2): 73-78.

Lobetti R.G. (2006). *Babesiosis in Infectious diseases of the dog and cat*, 3rd ed., edited by C.E. Greene. Philadelphia: W.B. Saunders.

Lobetti, R. G. (2000). Canine babesiosis. In: Day, M., Mackin, A. and Littlewood, J. (eds), *Manual of Canine and Feline Haematology and Transfusion Medicine.* British Small Animal Veterinary Association, Gloucester. pp. 85-91.

Máthé, Á., Vörös, K., Vajdovich, P., Kótai, I. and Soós, P. (1998). Immunohaemolytic anaemia of dogs. Review and Case Report. *Magyar Állatorvosok Lapja* 120, 261-267.

Mathe, A., Voros K., Papp, L., Reiczigel J. (2006) Clinical manifestation of canine babesiosis in Hungary (63 cases). *Acta Veterinarian Hungarica* 54(3):.367-385.

Moore, D. J. and Williams, M. C. (1979): Disseminated Intravascular Coagulation: A Complication of *Babesia canis* Infection in the Dog. *J. S. Afr. Vet. Assoc.* 50, 265-275.

Purvis, D., R. Kirby (1994). Systemic Inflammatory Respose Syndrome: eptic Shock. *Vet. Clin. North Am. Small Anim.* Pract. 24, 1225-1247.

Slappendel, R. J. (1986): Interpretation of Tests for Immune-mediated Blood Diseases. In: Kirk, R. W. (ed.), *Current Veterinary Therapy*. W. B. Saunders Co., Philadelphia. pp. 498-505.

Welzl, C., Leisewitz, A. L., Jacobson, L. S., Vaughan-Scott, T., Myburgh, E. (2001). Systemic Inflammatory Response Syndrome and Multiple-Organ Damage/Dysfunction in Complicated Canine Babesiosis. *J. South Afr. Vet. Assoc.* 72, 158-162.