Neotropical Helminthology, 2025, vol. 19 (1), XX-XX.

DOI: https://doi.org/10.62429/rnh20251911937

ORIGINAL ARTICLE / ARTÍCULO ORIGINAL

Rangelia Vitalii (Carini, 1908) (Apicomplexa, Piroplasmorida) in domestic dog in southern Brazil: a case report

Rangelia Vitalii (Carini, 1908) (Apicomplexa, Piroplasmorida) em canino doméstico no sul do Brasil: relato de caso

Rangelia Vitalii (Carini, 1908) (Apicomplexa, Piroplasmorida) en perro doméstico en el sur de Brasil: reporte de caso

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Running Head: *Rangelia Vitalii* in domestic dog in southern Brazil

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ABSTRACT

Rangeliosis is an extravascular hemolytic disease caused by the piroplasm *Rangelia vitalii* (Carini, 1908). This protozoan is transmitted by ticks of the species *Amblyomma aureolatum* (Pallas, 1772) and infects erythrocytes, endothelial cells, and leukocytes, leading to a variety of clinical signs such as anemia, thrombocytopenia, splenomegaly, hepatomegaly, jaundice, and bleeding from the nose, oral cavity, and ear tips. This study aims to report a case of rangeliosis in a domestic dog in southern Brazil. A female, adult, mixed-breed dog from a rural area was admitted to a Veterinary Hospital. Clinical examination revealed necrosis of the ear tips with active bleeding and abdominal hematomas. After a few days, the patient also developed jaundice, hematuria, bilirubinuria, subconjunctival hemorrhage, and epistaxis. Hematological analysis indicated anemia and thrombocytopenia, while biochemical tests revealed elevated serum urea levels. The definitive diagnosis was confirmed through a stained blood smear, which revealed the presence of *R. vitalii* inside leukocytes and free in plasma. In addition to supportive treatment, doxycycline and imidocarb dipropionate were administered. However, due to disease progression, the patient ultimately succumbed. Canine rangeliosis is likely an underdiagnosed disease; therefore, it is crucial to consider it as a differential diagnosis in patients presenting compatible clinical manifestations and laboratory findings, particularly in those from rural or forested areas or with access to such environments.

Keywords: bleeding – diagnosis – protozoan – rangeliosis – tick

RESUMO

Rangeliose é uma doença hemolítica extravascular, causada pelo piroplasma *Rangelia vitalli* (Carini, 1908). Este protozoário é transmitido através dos carrapatos da espécie *Amblyomma aureolatum* (Pallas, 1772) e infectam eritrócitos, células endoteliais e leucócitos, ocasionando uma variedade de sinais clínicos, como anemia, trombocitopenia, esplenomegalia, hepatomegalia, icterícia e sangramento pelo nariz, cavidade oral e ponta de orelha. Este trabalho teve como objetivo, relatar um caso de rangeliose em canino doméstico no sul do Brasil. Foi atendido num Hospital Veterinário, um canino, fêmea, adulto, sem raça definida, proveniente de área rural. No exame clínico, apresentava necrose de ponta de orelhas com sangramento ativo e hematomas no abdômen, e após alguns dias começou a apresentar também, icterícia, hematúria, bilirrubinúria, hemorragia subconjuntival e epistaxe. Anemia e trombocitopenia foram observadas no hemograma, e no exame bioquímico, aumento dos níveis séricos de uréia. O diagnóstico definitivo foi obtido através do esfregaço sanguíneo corado, onde observou-se a presença de *R. vitalii* no interior dos leucócitos e livre no plasma. Além do tratamento de suporte, foram utilizadas aplicações de doxiciclina e dipropionato de imidocarb, porém, devido ao agravamento do quadro, o paciente acabou evoluindo para óbito. A rangeliose canina é possivelmente uma doença subdiagnosticada, portanto, é importante que seja considerada como diagnóstico diferencial em pacientes com manifestações clínicas e achados laboratoriais compatíveis, principalmente naqueles procedentes de áreas rurais ou próximas a florestas ou que tenham tido acesso a estes locais.

Palavras chave: carrapato – diagnóstico – protozoário – rangeliose – sangramento

RESUMEN

La rangeliosis es una enfermedad hemolítica extravascular, causada por el piroplasma *Rangelia vitalli* (Carini, 1908). Este protozoario se transmite a través de garrapatas de la especie *Amblyomma aureolatum* (Pallas, 1772) e infecta eritrocitos, células endoteliales y leucocitos, provocando una variedad de signos clínicos como anemia, trombocitopenia, esplenomegalia, hepatomegalia, ictericia y hemorragias por la nariz, cavidad oral y punta de las orejas. Este trabajo tuvo como objetivo informar un caso de rangeliosis en un perro doméstico en el sur de Brasil. Fue atendido en un Hospital Veterinario, un perro, hembra, adulta, sin raza definida, proveniente de una zona rural.

En el examen clínico, presentaba necrosis en las puntas de las orejas con sangrado activo y hematomas en el abdomen, y después de algunos días comenzó a presentar también ictericia, hematuria, bilirrubinuria, hemorragia subconjuntival y epistaxis. Se observó anemia y trombocitopenia en el hemograma, y en el examen bioquímico, un aumento de los niveles séricos de urea. El diagnóstico definitivo se obtuvo a través del frotis sanguíneo teñido, donde se observó la presencia de *R. vitalli* dentro de los leucocitos y libre en el plasma. Además del tratamiento de soporte, se utilizaron aplicaciones de doxiciclina y dipropionato de imidocarb; sin embargo, debido al empeoramiento de la condición, el paciente terminó falleciendo. La rangeliosis canina es posiblemente una enfermedad subdiagnosticada, por lo tanto, es importante considerarla como diagnóstico diferencial en pacientes con manifestaciones clínicas y hallazgos de laboratorio compatibles, especialmente en aquellos provenientes de zonas rurales o cercanas a bosques, o que hayan tenido acceso a estos lugares.

Palabras clave: diagnóstico – garrapata – protozoario – rangeliosis – sangrado

INTRODUCTION

Rangelia vitalli (Carini, 1908) is a protozoan belonging to the Phylum Apicomplexa and Order Piroplasmorida, which infects canids. It is transmitted by ticks of the species *Amblyomma aureolatum* (Pallas, 1772), leading to extravascular hemolysis (Soares *et al.*, 2018).

Rangelia vitalii infects erythrocytes, endothelial cells, and leukocytes, causing a range of clinical signs such as anemia, thrombocytopenia, hemorrhage, fever, splenomegaly, hepatomegaly, lymphadenopathy, jaundice, and bleeding from the nose, oral cavity, and ear tips (Rodrigues *et al*., 2022; Silva *et al*., 2011; Soares *et al*., 2011).

While observing clinical signs is important, they are nonspecific and common to other hemoparasitic diseases. Therefore, the definitive diagnosis of canine rangeliosis involves a combination of clinical, laboratory, and imaging methods. Although clinical symptoms are crucial, confirmation requires specific laboratory tests. Serological tests, such as indirect immunofluorescence and polymerase chain reaction (PCR) (Soares *et al.*, 2011) and observation of parasites in peripheral blood smear (França *et al*., 2010) are commonly used to detect the presence of the protozoan in the animal's blood. Additionally, hematological analysis may reveal characteristic changes, such as hemolytic anemia (Soares *et al*., 2015).

Treatment of rangeliosis typically involves the administration of antiprotozoal drugs, such as imidocarb dipropionate (Borrás *et al*., 2020). Furthermore, supportive therapy is essential to address anemia and other complications, and blood transfusions may be necessary in severe cases (Loretti, 2012). Complete recovery depends on the severity of the infection and the individual response of each animal to treatment.

Therefore, the aim of this study was to report a case of rangeliosis in a domestic canine in southern Brazil.

MATERIALS AND METHODS

A female adult, mixed-breed canine from a rural area was admitted at the Veterinary Hospital of the Federal University of Pelotas; Rio Grande do Sul state, Brazil. In the anamnesis, the owners reported that the animal was apathetic, hypothermic, with ear lesions that were not healing and were bleeding. Upon physical examination, it was noted that the patient was thin, with pale pink mucous membranes, and had fever (39.3ºC). The clinical exam revealed necrosis at the tips of the ears with active bleeding (Fig.1A) and bruising on the abdomen and around the body (with less intensity) (Figure 1B). A few days after hospitalization, the abdominal hematoma worsened, and the patient began to present with jaundice, hematuria (Figure 1C), bilirubinuria (Figure 1D), subconjunctival hemorrhage (Figure 1E), and epistaxis.

Complementary tests including a complete blood count, biochemical analysis, imaging via ultrasonography, and due to the clinical signs observed, a hemoparasite investigation was also requested.

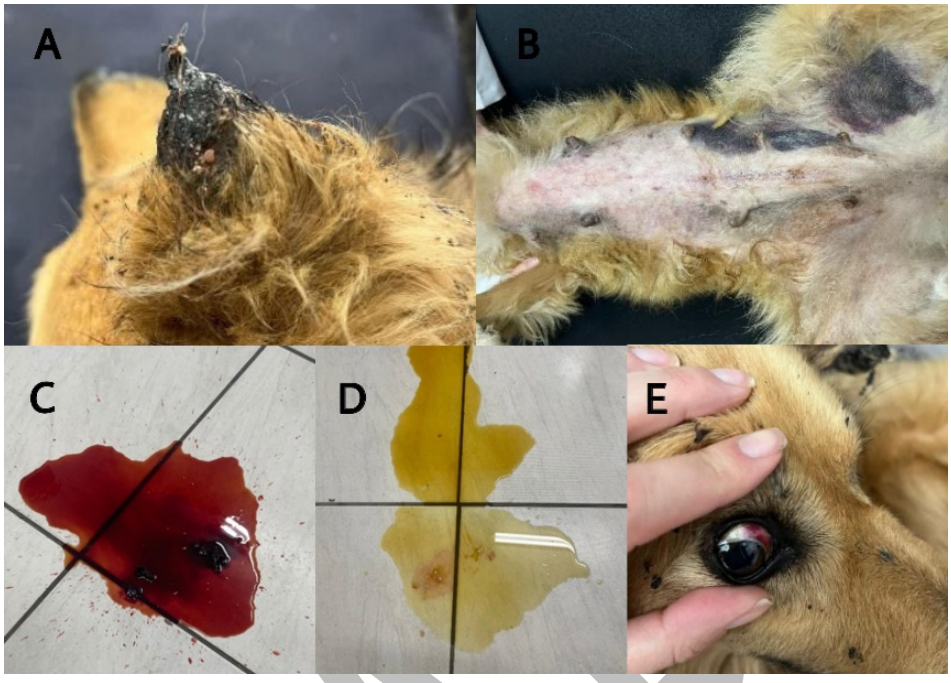

Figure 1. Dog with rangeliosis presenting ear tip necrosis (A), abdominal hematomas (B), hematuria (C), bilirubinuria (D) and subconjunctival hemorrhage (E).

Ethic aspects: The authors argue that all national and international ethical regulations were met.

RESULTS AND DISCUSSION

In the complete blood count performed on the day of admission, macrocytic/normochromic anemia and thrombocytopenia were observed. Morphological evaluation revealed anisocytosis, polychromasia, Howell-Jolly bodies, and platelet aggregation. In the biochemical analysis, increased urea levels (110.63 mg/dL) and icteric serum were noted. With the worsening of clinical signs, additional hematological tests were conducted, which confirmed the progression of the condition (Table 1). Abdominal ultrasonography revealed splenomegaly with enlargement of the splenic lymph nodes. Parasitized cells are recognized as foreign by the mononuclear phagocytic system and are then removed from the bloodstream in extra-vascular sites, such as the spleen and lymph nodes, justifying the occurrence of splenomegaly and lymphadenomegaly in cases of immune-mediated hemolytic anemia (Day, 2003). Through the examination of blood smears stained for hemoparasite investigation, structures compatible with *Rangeli vitalii* were observed within leukocytes and extracellularly (Fig. 2).

Table 1. Hematological tests of the dog diagnosed with rangeliosis.

	Eritrogram 1	Eritrogram 2	Eritrogram 3	Reference value
Red blood cells	4.5	2.6	1.96	5-10 millions/ul
Hemoglobine	8.6	5.3	4.2	8 - 15 g/dL
Hematocrit	26.1	17.9	13.6	24 - 45 %
MCV	58.1	67.8	69.4	39 - 55 fL
MCHC	33	29.6	30.9	31 - 35 %
Blood platelets	25	38	13	300 - 800 (10^3/µL)
PPT	6.2	4.6	4.2 g/dL	6 - 8 g/dL

MCV = Mean corpuscular volume; MCHC = Mean Corpuscular Hemoglobin Concentration; TPP = Total plasma protein

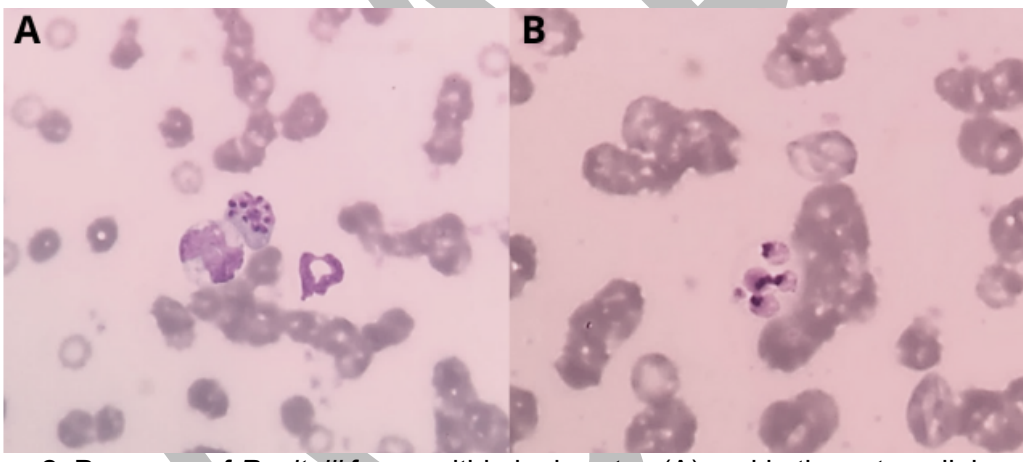

Figure 2. Presence of *R. vitalii* forms within leukocytes (A) and in the extracellular environment (B), observed under light microscopy at 1000x magnification.

The erythrogram of animals infected with *R. vitalii* typically exhibits findings characteristic of hemolytic anemia. This anemia is generally regenerative, ranging from normocytic/normochromic to macrocytic/hypochromic (Rodrigues *et al*., 2022). Morphological abnormalities include anisocytosis, polychromasia, spherocytosis, metarubricytosis, and the presence of Howell-Jolly bodies. Additionally, thrombocytopenia and alterations in biochemical parameters, such as elevated liver enzyme and bilirubin levels, are also commonly observed (França *et al*., 2013).

The main clinical signs presented by animals with rangeliosis include fever, apathy, anemia, jaundice, and splenomegaly (Fighera *et al*., 2010). Spontaneous bleeding is also commonly reported, which is correlated with intense platelet consumption, as this protozoan has the ability to parasitize and damage the vascular endothelium, potentially affecting the ears and skin (Soares *et al*., 2018). The clinical and hematological findings of the animal in this case report are consistent with those described in the literature.

After the definitive diagnosis, treatment was initiated with imidocarb dipropionate (5 mg/kg IM) and doxycycline (10 mg/kg SID). Due to the worsening of anemia and clinical signs, supportive care was also provided, including blood transfusion and fluid therapy, as well as the administration of an antiemetic (maropitant citrate), anti-inflammatory (meloxicam), analgesic (tramadol), and vitamin supplements. The patient remained hospitalized for 7 days, however, due to the worsening of her condition, she ended up dying.

The treatment of rangeliosis involves the use of chemotherapeutic agents to eliminate the protozoan from the host. Among the drugs reported for treating canine rangeliosis are diminazene aceturate, imidocarb dipropionate, and doxycycline (França, 2014). Doxycycline is considered ineffective when administered alone (Quadros *et al*., 2015; Silva *et al*., 2019). However, the combination of doxycycline with imidocarb dipropionate has been found effective in the treatment of rangeliosis (França, 2010). Blood transfusion and supportive fluid therapy are necessary in cases of severe anemia (Loretti, 2012). Corticosteroid therapy may also be required to manage immune-mediated hemolytic anemia.

Rangeliosis mainly affects dogs from rural areas or those with access to such environments due to the presence of the tick *Amblyomma aureolatum* (Loretti & Barros, 2005; Fighera, 2007), the vector of the disease. Soares *et al.* (2018) conducted a study to evaluate the vector competence of *Rhipicephalus sanguineus* (tropical and temperate

lineages) (Latreille, 1906), *Amblyomma aureolatum* (Pallas, 1772), *Amblyomma ovale* (Koch,1844), *Amblyomma tigrinum* (Koch, 1844), and *Amblyomma sculptum* (Berlese, 1888) for *R. vitalii*. Among the six species, only *A. aureolatum* ticks were competent to transmit *R. vitalii* to dogs.

There is a higher incidence of cases in the southern and southeastern regions of Brazil, as reported by several authors in the states of Santa Catarina (Rodrigues *et al*., 2022), Rio Grande do Sul (Gottlieb *et al*., 2016; Malheiros *et al*., 2016; França *et al*., 2010), Paraná (Mongruel *et al*., 2017), Rio de Janeiro (Lemos *et al*., 2012), and Minas Gerais (Moreira *et a*l., 2013). Cases have also been reported in Argentina (Eiras *et al*., 2014) and Uruguay (Soares *et al*., 2015).

It is also possible that a wild reservoir exists in the biological cycle of *R. vitalii*, capable of maintaining this protozoan without causing disease (Loretti *et al*., 2003). In the state of Rio Grande do Sul, it is believed that this parasite is sustained in the environment by wild animals such as the crab-eating fox (*Cerdocyon thous*) (Linnaeus, 1758), the pampas fox or "zorro de campo" (*Pseudalopex gymnocercus*) (Fischer, 1814), and the raccoon (*Procyon cancrivorus*) (Cuvier, 1798) (Fredo *et al.,* 2015).

Additionally, it is important to consider tick control, as transmission occurs through *A. aureolatum*, highlighting the need for more rigorous environmental and preventive measures, such as the regular use of ectoparasiticides, particularly in dogs from endemic areas. Silva *et al.* (2020) emphasize that effective prevention of tick infestations can significantly reduce the incidence of rangeliosis, especially in rural regions where dogs have greater exposure to the vector.

This case report also raises questions about the possible underreporting of rangeliosis in urban areas. Although traditionally associated with rural regions, the expansion of urban areas into previously tick-endemic regions may be contributing to an increase in cases in urban environments.

Canine rangeliosis is possibly an underdiagnosed disease, as many professionals are unaware of its existence, which may contribute to the underdiagnosis of *R. vitalii* infections in dogs. Therefore, it is crucial to consider rangeliosis as a differential diagnosis in cases presenting with hemorrhage, anemia, thrombocytopenia, and splenomegaly, particularly in patients from rural areas, forested regions, or those with access to such environments.

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Received March 25, 2025.
Accepted May 5, 2025.