

Chapter 7 Prevalence of thrombocytopenia in canine with clinical signs of ehrlichiosis in Poza Rica, Veracruz

Capítulo 7 Prevalencia de trombocitopenia en caninos con signos clínicos de ehrlichiosis en Poza Rica, Veracruz

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DOI: 10.35429/H.2023.7.1.81.88

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Á. Marroquín, L. Castillo, J. Olivares and N. Olgún Cruz. (VV. AA.) CIERMMI Women in Science T-XXI Biological, Humanities and Social Sciences. Handbooks-©ECORFAN-México, Querétaro, 2023

Abstract

The objective of this study was to determine the prevalence of thrombocytopenia in dogs with clinical signs of canine Ehrlichiosis in the city of Poza Rica, Veracruz. It was used 32 blood samples from dogs with clinical signs compatible with canine ehrlichiosis. A platelet count by hematic biometry and the Uranotest Quattro test based on the immunochromatographic technique were used. To analyze the data, the Chi-square test of the statistical software SPSS 20 Windows was used. The results showed 43.8% positives samples for *E. canis* and the prevalence of thrombocytopenia was 81.3%. The statistical analysis carried out determined that the gender of the dogs was not a predisposing factor for the disease. Likewise, by age group, no statistically significant difference was shown. In addition, six animals positive for *Anaplasma* were detected, which represented 18.75% of prevalence in the sampled animals, of which five also presented thrombocytopenia and two of them were positive for both *Ehrlichia* and *Anaplasma*. Therefore, thrombocytopenia presented in canines may be due to other causes or other rickettsiae.

Prevalence, Thrombocytopenia, *Ehrlichia canis*, *Anaplasma*

Resumen

El objetivo de este trabajo de investigación fue determinar la prevalencia de trombocitopenia en perros con signos clínicos de Ehrlichiosis canina en la ciudad de Poza Rica, Veracruz. Se analizaron 32 muestras de sangre de caninos de diferente edad y sexo. Se utilizó un recuento de plaquetas mediante biometría hemática y la prueba URANOTEST QUATTRO basado en la técnica inmunocromatográfica. Para analizar los datos se utilizó la prueba Chi-cuadrada del paquete estadístico SPSS 20 Windows. Se detectó que el 43.8% de los caninos muestreados fueron positivos a *E. canis* y la prevalencia de trombocitopenia fue del 81.3%. El análisis estadístico realizado determinó que el género de los perros no fue un factor predisponente para la enfermedad. Así mismo, por grupo etario no se mostró una diferencia estadísticamente significativa. Además, se detectaron seis animales positivos a *Anaplasma* lo que representó el 18.75% de prevalencia en los animales muestreados, de los cuales cinco también presentaron trombocitopenia y dos de ellos resultaron positivos tanto a *Ehrlichia* como a *Anaplasma*. Por lo que, la trombocitopenia presentada en los caninos puede deberse a otras causas u otras rickettsias.

Prevalencia, Trombocitopenia, *Ehrlichia canis*, *Anaplasma*.

7.1 Introduction

Canine ehrlichiosis is a tick-borne infectious disease caused by *Ehrlichia* spp. whose main etiological agent is *Ehrlichia canis*, a gram-negative, obligate intracellular, rounded or pleomorphic bacterium. This bacterium is transmitted by the tick *Rhipicephalus sanguineus*, which is distributed worldwide and its main host is the domestic dog (Hoyos, 2007; Gutiérrez et al., 2016).

The infective action of *E. canis* is produced by invading the cells of the white package that serve as transport to reach other systems and organs, *E. canis* has an enormous ability to induce severe lymphoplasmacytosis in organs that present parenchymal structure, producing bleeding in vascular endothelial cells, thus giving rise to the classic hemorrhages present and a great variety of clinical signs (Waner and Harrus, 2013; Tamez, 2015).

Ehrlichiosis is a very important disease since, by attacking the aforementioned cells, it depresses the immune system, resulting in: bone marrow aplasia, increased susceptibility to infections with other secondary agents, anemia, hemorrhage, slow kidney injury that often causes irreversible renal failure; all this affects the health and quality of life of the canine (Vadillo et al., 2002).

Thrombocytopenia is considered the most common and consistent hematologic abnormality in dogs infected with *E. canis*. Mechanisms thought to be involved in the pathogenesis of thrombocytopenia include increased platelet sequestration in the spleen and immune destruction or injury resulting in decreased platelet lifespan. In addition, studies in which radioisotopes have been used have shown that platelet survival time decreases from an average of nine to four days from two to four days after infection with *E. canis* (Harrus et al., 1999).

Therefore, the objective was to calculate the prevalence of thrombocytopenia in dogs with clinical signs of canine Ehrlichiosis in the city of Poza Rica, Veracruz and to determine if the presence of thrombocytopenia in dogs with clinical signs of canine Ehrlichiosis is a common denominator of this disease.

7.2 Material and Methods

Samples were collected in three veterinary clinics in the city of Poza Rica, Veracruz during the autumn-winter season. The study area is located in the northern part of the state, at coordinates 20°32'00"N 97°27'00"W. It presents a warm climate, with a mean annual temperature of 24.4 °C, with abundant rainfall in summer and early autumn. The average annual precipitation is 1,010 mm (INEGI, 2019).

The sample size was 32 dogs, which were given a clinical record with general data such as age, sex, history of having had a tick, clinical signs of *E. canis*; neurological signs, seizures, ataxia, epistaxis, hemorrhages, petechiae, ecchymosis, anorexia, uveitis, hematuria, melena, generalized skin lesions, hyperemia, edema. Blood samples were collected in tubes containing the anticoagulant ethylenediaminetetraacetic acid (EDTA) by aseptic puncture of the cephalic vein. Subsequently, a platelet count was performed by manual method sent to the clinical analysis laboratory Animalandia Poza Rica.

Dogs with thrombocytopenia were tested for *Ehrlichia canis* antibodies by immunochromatographic technique using the URANOTEST QUATTRO® diagnostic kit, which requires whole blood, serum or plasma. Subsequently, the sample is taken with a capillary tube and deposited in each well together with two drops of buffer, obtaining the results in 15 minutes.

7.2.1 Platelet count

The platelet count consists of knowing the number of platelets found in one milliliter of blood. For this it is necessary to dilute the blood using a Thoma pipette for white blood cells and a special diluent liquid that makes the platelets visible while destroying the erythrocytes. Subsequently, a known volume of the sample is examined under the microscope in the Neubauer chamber, counting the number of platelets in the reticule and by means of a calculation the number of elements per mm³ is obtained (Rivadeneira, 2022).

7-2.2 Quattro Uranotest ® Diagnostic Kit

The URANOTEST QUATTRO diagnostic kit is based on the immunochromatographic technique and is designed for the qualitative determination of *Dirofilaria immitis* antigen and antibodies to *Ehrlichia canis*, *Anaplasma* and *Leishmania* in dog whole blood, serum or plasma. The test consists of four separate zones, one for the detection of *Ehrlichia* antibodies, one for the detection of *Anaplasma* antibodies, one for the detection of *Leishmania* antibodies and one for the detection of *Dirofilaria* antigen. Each test consists of a test strip with a zone where the sample is added and a result zone containing the T line (test line) and the C line (control line). Once the sample is applied to the rounded well and after the addition of the chromatography buffer, capillary migration along the membrane begins. If the result is negative, a single purple band will appear in the C-zone. The band in zone C always appears, as it is a control band indicating that the test has been performed correctly. If the result is positive, in addition to the C band, a purple band will appear in the test zone (T line) (URANOVet, 2022).

7.2.3 Reference value in platelets

In this work three different authors were taken into account, Tennant (1997) refers to a value to consider thrombocytopenia below $150 \times 10^9/L$ platelets, Lopez and Mesa (2015) speak of values of $175 \times 10^9 /L$ platelets. And Villiers and Blackwood (2013) of $200 \times 10^9/L$ in this work it was considered to take the mean of these three values and resulted in a value of $175 \times 10^9/L$ platelets.

7.2.4 Statistical analysis

The data were analyzed with the Chi-square statistical test using the SPSS 20 statistical package for Windows (IBM SPSS, 2011).

7.3 Results

The prevalence of thrombocytopenia in dogs with clinical signs of canine Ehrlichiosis was 81.3% (95%CI 67-96; Table 7.1) with a mean of $115.03 \pm 74.92 \times 10^9/L$ platelets. However, after analyzing the variable thrombocytopenia and presence of the disease, it was determined that there is no statistical evidence to affirm that there is a relationship between thrombocytopenia and Ehrlichiosis in the sampled dogs ($P=0.138$).

Table 1 Number of canines with thrombocytopenia and clinical signs of canine Ehrlichiosis

		Diagnostic to <i>E. canis</i>		Total
		Negative	Positive	
Thrombocytopenia	Negative	5	1	6
	Positive	13	13	26
Total		18	14	32

Source: Own elaboration/2023

Regarding the prevalence of canine Ehrlichiosis, it was determined that of the 32 samples processed by the rapid test for the detection of antibodies to *E. canis*, 14 were positive for this bacterium, which represents 43.8% (IC95% 26-62). In addition, it was determined through data collection that the gender of the dogs sampled was not a predisposing factor for presenting the disease ($P=0.198$; Table 7.2). Likewise, when analyzing the results by age group, no statistically significant differences ($P=0.791$) were observed for the age of the sampled canines (Table 7.3).

Table 7.2 Detection of antibodies to *Ehrlichia canis* according to the sex of the animals sampled

Diagnostic	Sex		Total
	Female	Male	
Negative	5	13	18
Positive	7	7	14
Total	12	20	32

Source: Own elaboration/2023

Table 7.3 Detection of antibodies to *Ehrlichia canis* according to age group

Age group	Diagnostic		Total
	Negative	Positive	
Adult	7	7	14
Puppy	4	3	7
Geronte	7	4	11
Total	18	14	32

Source: Own elaboration/2023

In the laboratory analysis using the rapid test, it was also detected that six animals were positive to Anaplasmosis, which represents 18.75% (IC95% 4-33) of prevalence of the animals sampled, of which five also presented thrombocytopenia and two of them were positive to both Ehrlichiosis and Anaplasmosis (Table 7.4).

Table 7.4 Detection of antibodies to *Ehrlichia* and *Anaplasma platys*

Diagnostic	<i>Ehrlichia</i>	<i>Anaplasma</i>
Positive	14	6
Negative	18	26
Total	32	32

Source: Own elaboration/2023

7.4 Discussion

The results obtained in the laboratory analysis allowed determining that thrombocytopenia in dogs with clinical signs of canine Ehrlichiosis is not a determining factor for the diagnosis of this disease, since 81.3% (IC95% 67-96) of the animals sampled presented thrombocytopenia, but only 43.8% (IC95% 26-62) of the animals presented antibodies to *E. canis*, that is, of the 32 dogs sampled, 26 (81.3%) presented thrombocytopenia and of these, 13 animals (50%) were positive to *E. canis* and 13 (50%) animals were negative. Therefore, the thrombocytopenia presented in canines may be due to other causes, one of them being Anaplasmosis. In this study, the rapid test also detected the presence of Anaplasmosis in six animals, five of which had thrombocytopenia and four were negative for *E. canis*.

In Culiacán, Sinaloa Sosa-Gutierrez et al. (2013), evaluated 152 blood samples from dogs, with tick infestation and clinical signs of ECM, from six veterinary clinics and two shelters, 74.3% had anti-*E. canis* antibodies by Snap4Dx® ELISA from IDEXX Laboratory. In addition, 40.1% had morulae characteristic of *E. canis* in their blood smears. Regarding clinical manifestations, there was fever (91.2%), anorexia (86.7%), depression (85.0%), lethargy (72.6%) and petechiae (72.6%). Similarly, those positive for *E. canis*, 87.6% had thrombocytopenia.

Diaz et al. (2016), evaluated a population of 200 domestic dogs from Molas, Yucatan, Mexico, 70% were infested with 1,116 *R. sanguineus* ticks. In addition, a prevalence of *E. canis* of 71% was calculated. However, no association of gender, age, body condition, bleeding, thrombocytopenia and tick infestation with *E. canis* infection was found.

In the province of Maynas-Iquitos, Peru, Villaverde (2017), evaluated a group of dogs with clinical suspicion of Ehrlichiosis and thrombocytopenia and determined the presence of antibodies to *Ehrlichia* spp in 60% of the canines. It was also reported that the canines with thrombocytopenia had a median age of 18 months (inter-quartile range (IQR): 12 to 24 months), 16 (53%) were males, 22 (73%) were mongrels and 12 (40%) came from the Iquitos district. In the clinical examination, 13 (43%) canines had ticks, 23 (77%) had a history of having had ticks and 13 (43%) had fever. The mean platelet count was 33,000 platelets/ μ L (IQR: 23,000 to 69,000). Application of the IDEXX SNAP4DX diagnostic kit detected antibodies to *Ehrlichia* in 18 (60%) of the canines evaluated. Of the 18 canines with positive antibodies, 13 were mongrels, nine were males. On clinical examination, 14 had a history of having had ticks, seven had evidence of ticks and five had fever. Canines with positive antibodies to *Ehrlichia* spp had a median age of 24 months compared to 12 months for canines without infection, however, there was no statistically significant difference ($p = 0.06$). No statistically significant association was found between the presence of *Ehrlichia* antibodies and breed ($p = 0.6$), sex ($p = 0.4$), history of ticks ($p = 0.5$), presence of ticks at the time of evaluation ($p = 0.4$) and fever ($p = 0.06$). These results coincide with those reported in this study where no association was found between the variables sex, age and race. The platelet count was 28,500/ μ L in canines with positive antibodies to *Ehrlichia* compared to 37,000/ μ L in canines without infection, in our study it was found with a mean of $115.03 \pm 74.92 \times 10^9/L$ platelets.

Flores(2020), determined that the prevalence of canine Anaplasmosis in dogs with thrombocytopenia in the province of Maynas, Iquitos, obtained antigenic evidence confirming the presence of *Anaplasma* spp. in the study sector of an overall prevalence of 20.10% \pm 0.02 with a confidence level of 95%, constituting a report of its presence in this study area. The studied area presents risk factors associated with Anaplasmosis. Due to the high rate of cases found in this research, this is considered of scientific connotation since it is a triggering factor of a large enzootic disease.

Harvey (1978), cited by Arraga-Alvarado et al. (2003) indicated that *Anaplasma platys* is the causal agent of clinical infectious thrombocytopenia. This gram-negative, obligate intracellular bacterium has an affinity for canine platelets and causes cyclic thrombocytopenia that can last between seven and 14 days (Ettinger, 1992). This thrombocytopenia is apparently of a regenerative type, due to the megakaryocytic hyperplasia found in the bone marrow of experimentally infected dogs (Gaunt et al., 1990).

Román (2021), comments that another disease causing thrombocytopenia is canine hepatozoonosis; it is caused by a protozoan called *Hepatozoon canis* which is found inside neutrophils and monocytes of vertebrates in the form of microgametes and macrogametes. It is transmitted by *Rhipicephalus sanguineus* which ingests the microorganism by feeding on the blood of an infected canine. Platelets originate from megakaryocytes present in bone marrow and to a lesser extent in the lung. The causes of decreased platelet production may be due to alterations in these precursor cells, but are usually disorders that also affect other hematopoietic cell lines (Weiss et al., 2010). Among the most frequent disorders we can mention bone marrow hypoplasia or aplasia, drug myelotoxicity, necrosis, myelofibrosis, sclerosis, myeloptosis, myelodysplasia, increased cell sequestration or destruction, immune-mediated alterations, sepsis, disseminated intravascular coagulation, hemangiosarcoma and splenomegaly (Nelson and Couto, 2010).

Recently, Christodoulou et al. (2023), by comparing the clinical and clinicopathological features of ehrlichiosis and primary immune thrombocytopenia in dogs diagnosed with these partially overlapping diseases, determined that dogs with ehrlichiosis had a lower albumin concentration, therefore, it may be a useful discriminator between the two diseases in the clinical setting.

Although the URANOTEST QUATTRO diagnostic kit has a high sensitivity and specificity, a small incidence of false positive or negative results cannot be ruled out. As with any other laboratory procedure, a definitive clinical diagnosis should not be based on the performance of a test alone, but should be the result of a series of clinical and laboratory findings. In case of doubt, repeat the test and/or contrast with other diagnostic methods (URANOvet, 2022).

Regarding susceptibility by gender, it was determined by statistical analysis to the antibody response against *E. canis* that there is no effect, this coincides with Franco-Zetina et al. (2022) in the city of Merida, Yucatan, who also indicates that the sex of the animals did not present differences, so it was not a factor associated with the antibody response against *E. canis*. Similarly, Requejo (2018), in the district la Victoria, Peru, in his research indicates that in females there is a prevalence of 65.85% (27/41) and in males of 70.18% (40/57). However, the number of male canines evaluated was higher than the number of females; therefore, it cannot be affirmed that canine ehrlichiosis is more prevalent in males than in females.

7.5 Conclusion

According to the results obtained it is concluded that 81.3% (CI95% 67-96) of the dogs sampled with clinical signs of canine Ehrlichiosis presented thrombocytopenia and only 43.8% (CI95% 26-62) were positive for *E. canis*, which determines that it is not a common denominator for the disease, since thrombocytopenia does not ensure a positive diagnosis of *E. canis* because it can be due to other causes. Likewise, 18.75% of the 32 dogs were positive for *Anaplasma*.

According to the statistical results of the chi-square test, the age and sex of the canines sampled were not predisposing factors for the presentation of canine ehrlichiosis.

7.6 Acknowledgements

MVZ Everardo Salas Pérez, MVZ Anna Maria Attwood Clarke and MVZ Emilia Elizabeth for all the facilities granted to obtain the samples used in the study.

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