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Research Article

Hematological Changes in Dogs Infected with *Ehrlichia canis* as a Diagnostic Contribution in the Clinical Routine

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Abstract

Canine Monocytic Ehrlichiosis (CME) is an infectious disease of dogs, responsible for hematological disorders, whose clinical picture is characterized by hemorrhages, immunosuppression and pancytopenia. Knowledge of the hematological profile of dogs infected with *Ehrlichia canis* is an essential tool for conducting diagnosis, prognosis and health monitoring, as well as the adoption of therapeutic practices. This article sought to analyze, based on a bibliographical research, the main hematological alterations observed in dogs infected by *Ehrlichia canis*, with the aim of indicating the contribution of these findings of clinical pathology to the direction of the prognosis, diagnosis and treatment of the animal. The results showed that anemia and thrombocytopenia are among the most prevalent and specific hematological changes in CME, being constantly observed in the acute and chronic phases of the disease. The high prevalence of anemic, thrombocytopenic and pancytopenic dogs contributes as an indicator of infection by *Ehrlichia canis*, however, it does not exclude the need to research the microorganism in the occurrence of these hematological alterations. Hematological parameters are pertinent to analyze, especially the clinical profile and general condition of the animal, also contributing to a reliable clinical diagnosis, prediction of prognosis and the adoption of appropriate clinical therapeutic approaches in sick animals. Thrombocytopenic and pancytopenic factors contribute as an indicator of infection by *Ehrlichia canis*, however, it does not exclude the need to research the microorganism in the occurrence of these hematological alterations. Hematological parameters are pertinent to analyze, especially the clinical profile and general condition of the animal, also contributing to a reliable clinical diagnosis, prediction of prognosis and the adoption of appropriate clinical therapeutic approaches in sick animals. Thrombocytopenic and pancytopenic factors contribute as an indicator of infection by *Ehrlichia canis*, however, it does not exclude the need to research the microorganism in the occurrence of these hematological alterations. Hematological parameters are pertinent to analyze, especially the clinical profile and general condition of the animal, also contributing to a reliable clinical diagnosis, prediction of prognosis and the adoption of appropriate clinical therapeutic approaches in sick animals.

Keywords: Ehrlichiosis; Anemia; Thrombocytopenia; Hematology

Introduction

Canine Monocytic Ehrlichiosis (CME) is an infectious and contagious hemoparasitosis caused by a rickettsia of the order Rickettsiales and the genus *Ehrlichia*. It is a serious disease, highly prevalent in the medical clinic of dogs and that affects several systems due to immunological and inflammatory alterations. Also

known as Tropical Canine Pancytopenia, Canine Hemorrhagic Fever or Canine Typhus, CME causes destruction of blood cells, such as red blood cells and platelets, in addition to the systemic impairment of several organs, which can lead the animal to death [17].

The main species of rickettsia that affects dogs is *Ehrlichia canis*, which is a bacterium of smaller dimensions, rudimentary, coccobacillary, pleomorphic, gram-negative and obligate intracellular of mature and immature hematopoietic cells, especially the mononuclear cells that make up the System Phagocytic Mononuclear, such as monocytes and macrophages [23].

EMC is transmitted to dogs through the bite of the brown canine tick, belonging to the species *Rhipicephalus sanguineus*, which acts both as a vector and as a reservoir of the disease. After inoculation, *Ehrlichia canis*, present in the tick's saliva, performs obligatory intracellular parasitism with reproduction by binary division and, therefore, causes destruction of red blood cells and platelets; which induces a hematic picture of anemia and thrombocytopenia [18].

Regarding predisposition, this hematological disorder is considered the parasitic disease most transmitted by ticks to dogs of all breeds, sex and age. In addition to dogs, *Ehrlichia canis* affects humans and is therefore considered a zoonosis. However, all evidence suggests that Human Ehrlichiosis is not transmitted directly by dogs, but by the vector tick in a blood meal situation [21].

EMC has a worldwide distribution, but its occurrence mainly covers the tropical and subtropical regions of the planet, due to the greater distribution and adaptation of its main vector, the tick *Rhipicephalus sanguineus*. In Brazil, this is quite widespread in the rural and urban environment, due to climatic conditions and the large population of stray or street dogs in its territory [8].

In recent years, the prevalence of CME has increased in several regions of Brazil, being reported in dogs from virtually all states, such as Espírito Santo, Santa Catarina and Rio Grande do Sul, with a higher occurrence in Minas Gerais and São Paulo. Epidemiological studies have revealed CME prevalences ranging from 4.8 to 65% in dogs from urban or rural areas [22].

With regard to evolution, the CME develops in three different phases, the acute, the subclinical and the chronic phase, which are mainly characterized by thrombocytopenia. Anemia and thrombocytopenia are among the most prevalent and specific hematological alterations of the disease, being constantly observed both in the acute and chronic phases [9]. In the acute setting, the agent infects and multiplies in mononuclear cells and in organs, such as lymph nodes, liver and spleen; then the infected cells circulate through the bloodstream and reach other organs in the body, which makes the clinical signs nonspecific. In the subclinical phase, which develops after the acute phase, clinical signs are not evident and the agent remains in the infected animal, causing high titers of antibodies and discrete hematological alterations. In the chronic course.

Clinical signs are variable and nonspecific, which makes it difficult for tutors to perceive the onset of the disease. The most frequently observed clinical signs in dogs, unless asymptomatic, are fever, hyporexia, lethargy, pale mucous membranes and gastroenteritis, lymphadenopathy, splenomegaly, hepatomegaly, weight loss, epistaxis, petechiae, ecchymosis, and a significant result of anemia and thrombocytopenia [14].

EMC has been presenting a growing number of cases in the veterinary medical clinic and, therefore, knowledge of the hematological profile of dogs infected with *Ehrlichia canis* can be a valuable tool for establishing diagnosis, prognosis and health monitoring, in addition to the adoption of therapeutic approaches. in the outpatient routine. Thus, the general objective of this study was to analyze, based on the literature, the main hematological alterations in dogs infected with *Ehrlichia canis*. The specific objectives were to describe the occurrences of anemia, thrombocytopenia and pancytopenia resulting from the action of the hemoparasite, as well as to indicate the contribution of these findings of clinical pathology for the direction of the diagnosis, prognosis and treatment of the sick animal.

Methodology

The present study was carried out based on an exploratory bibliographical research with the scientific databases SciElo, PubMed, CAPES, LILACS, MEDLINE and Google Scholar. For the search, a time frame of publication between the years 2004 to 2021

was carried out, using the following keywords: Ehrlichiosis, dogs, alterations, hematology, hemorrhage, anemia, thrombocytopenia, pancytopenia, diagnosis, prognosis and medical clinic.

Articles that addressed the theme of hematological changes in dogs infected with *Ehrlichia canis* were included in the study, totaling 17 selected articles. From the collected material, a qualitative analysis of the selected articles was carried out, seeking to highlight hematological changes in dogs infected by *Ehrlichia canis*, as well as to apply knowledge of the hematological profile of infected animals to guide the diagnosis, prognosis and adoption of therapeutic practices in the clinical routine.

Results and Discussion

Canine Monocytic Ehrlichiosis (CME) is a severe infectious disease caused by rickettsia of the species *Ehrlichia canis*. Considered as one of the main parasitic diseases of dogs, it has a worldwide occurrence and high prevalence in the national territory. The results found in the present work point to the most frequent hematological alterations in the medical clinic of infected dogs described in the literature, whose attributes can be characterized by blood loss, followed by platelet lysis and persistent thrombocytopenia; that progress in cases of hemorrhages in membranes, mucous membranes or other organ systems.

Analysis of erythrograms from dogs infected with *Ehrlichia canis* demonstrated that the most frequent alteration is normochromic normocytic anemia, due to platelet destruction and persistent thrombocytopenia, followed by eosinopenia and neutropenia [15]. On the other hand, according to Gevehr., *et al*. [4], the most common findings were non-regenerative anemia in 37% of cases and regenerative in 13% of cases. According to these authors, the origin of anemia may be associated with the loss, destruction, deficiency in the production and sequestration of red blood cells. In cases where there is loss of red blood cells, either by hemorrhage or by destruction, the expected response is regenerative anemia.

According to González and Santos [5], an animal is considered anemic when the hematocrit, hemoglobin and/or erythrocyte count are below their reference values and, depending on the results, anemia is classified as regenerative or non-regenerative. Thus, when the erythrogram parameters are below the reference values, there are different possibilities for classifying the anemias and each one has its reference value. In addition, the origins of anemia within each category are very diverse and adjust according to the type, however, anemia resulting from chronic diseases is the most prevalent among species.

In studies of clinical pathology, dogs affected by CME were evaluated and the results showed normochromic normocytic anemia as the most common finding, however, a portion of the animals did not present alterations in red blood cells. The pathogenesis indicates that theanemia may be due to the removal of erythrocytes from the circulation by the phagocytic mononuclear system and the lysis caused by the complement system, in addition to bone marrow aplasia [15]. With the same diagnostic tool, Silveira., *et al*. [18] reported that the findings of thrombocytopenia occur due to the peripheral destruction of platelets or their sequestration, due to the vasculitis process.

The effects of *Ehrlichia canis* on the mononuclear phagocytic system and the reference values due to cell lysis occur as a result of the action of the complement system and the suppression of erythropoiesis by the bone marrow. As a result, the animal has anemia of significant proportions in the deficit of red blood cells, hemoglobin and/or hematocrit, which may be a secondary manifestation of a particular disease or one of the main laboratory findings associated with CME [3].

According to Gevehr., *et al*. [4], performing hematological measurements is important to assess and monitor the health status of animals. Accordingly, Mota., *et al*. [10] showed that the main hematological alterations in dogs with *Ehrlichia canis* are thrombocytopenia, anemia or leukopenia and, therefore, the diagnosis is based on the clinical signs presented by the animal and through changes observed in hematological exams.

Studies indicate that, despite being general and specific, clinical and laboratory changes in CME are important for the diagnosis. Silva [16] reports that there is no leukogram pattern among animals affected by the disease. In addition, he points out that anemia, leukopenia and thrombocytopenia can be observed alone or associated in sick dogs infected with *Ehrlichia canis*, and may even be absent in dogs with inapparent infections.

Cases of CME in clinically healthy dogs or dogs with inapparent infections are described with a clinical pathology characterized by moderate thrombocytopenia, caused by the consumption of platelets by the inflamed vascular endothelium [16]. For Bulla., *et al*. thrombocytopenia may be secondary to the increase in the concentration of platelet migration inhibition factor, which suggests increased sequestration and blood stagnation leading to platelet reduction [2].

According to Santos., *et al*. [15], laboratory findings associated with *Ehrlichia canis* vary according to the clinical phase of the disease, the parasitemia and the animal's own resistance. Still, in the absence of significant hematologic changes, thrombocytopenia is the most prevalent abnormality in infected dogs. In this sense, these studies corroborate Peixoto [13], who states that the intensity of thrombocytopenia attests to the reliability of diagnostic tests. In agreement, Silva [16] points out that anemia is associated with thrombocytopenia, and it is possible to infer that dogs with these alterations have a high possibility of infection by *Ehrlichia canis*.

Anemia and thrombocytopenia are among the most prevalent and specific hematological changes in Canine Ehrlichiosis [1], being constantly observed in both the acute and chronic phases [9]. Guedes., *et al*. [6] report that dogs can present different hematological responses in relation to the stage of development of CME, in addition to being able to present associated nonspecific signs and history of coinfections. Stella., *et al*. [20] also highlight that cases of co-infections are responsible for more significant changes in hematological aspects.

Dogs infected with *Ehrlichia canis* and submitted to clinical pathology analyzes showed normocytic and normochromic anemia, mild anisocytosis and polychromasia, in addition to thrombocytopenia [19]. Also, cases of reduction in the amount of red blood cells that are normocytic and normochromic are described, in addition to the decrease in hemoglobin and hematocrit; which are the characteristic attributes of discreet normocytic and normochromic anemia, with the presence of thrombocytopenia, due to multiplication in the organs of the phagocytic mononuclear system in an incubation period of 8 to 20 days [11]. Furthermore, analyzes obtained through hematocrit and platelet averages confirm that anemia and thrombocytopenia are common hematological alterations in CME-positive dogs [18].

Thrombocytopenia is a dominant and frequent sign in the results of clinical pathology found in dogs infected with *Ehrlichia canis.* Macrocytic and hypochromic anemia has been described as a frequent hematological alteration in dogs, being a regenerative anemia, which occurs during acute hemolysis or blood loss [7]. For Queiroz [12], thrombocytopenia and anemia are the most important hematological findings at all stages of the disease, and pancytopenia may also occur. However, thrombocytopenia is an important reference hematological parameter to be considered as a diagnostic tool.

Final Considerations

Performing hematological analyzes is extremely important to assess and monitor the health status of dogs infected with *Ehrlichia canis*. The main findings in the blood series of these animals are anemia, thrombocytopenia and pancytopenia, indicating a high prevalence of pathological conditions in canine populations affected by CME. Thrombocytopenia is the most evident and consistent hematological alteration, being more frequent in the chronic phase. However, in cases of normal platelet count, one should never rule out the disease.

It was concluded that the diagnosis of *Ehrlichia canis* infection in dogs should be based on hematological changes of anemia, thrombocytopenia and pancytopenia. In addition, studies on these hematological abnormalities found in infected dogs are necessary, mainly relating health status and living conditions, with a view to favoring a reliable clinical diagnosis, a predictive prognosis and the adoption of clinical therapeutic approaches in animals sick.

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