CANINE VISCERAL *LEISHMANIASIS* (CVL): SEROPREVALENCE, CLINICAL, HEMATOLOGICAL AND BIOCHEMICAL FINDINGS OF DOGS NATURALLY INFECTED IN AN ENDEMIC AREA OF SÃO JOSÉ DE RIBAMAR MUNICIPALITY, MARANHÃO STATE, BRAZIL

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ABSTRACT

This study aims at verifying the seroprevalence of dogs naturally infected with *Leishmania* in an endemic area together with clinical, hematological and biochemical parameters. A seroprevalence survey was conducted in 76 household mongrel dogs by an Indirect Antibody Test (IFAT). The results showed that 28 (36.84%) were positive; 15 (53.57%) were asymptomatic and 13 (46.43%) were symptomatic. The most frequent clinical signs were onychogryphosis, skin lesions (alopecia, ulcers, dry desquamation) and localized lymphadenopathy. In 6 out 22 dogs (27.27%) anemia was observed. The biochemical analyses indicated that infection caused by *Leishmania* can lead to hepatic changes. Kidney changes were not observed. In conclusion, the hematological and biochemical parameters would probably help to follow up the clinical stage of the disease.

KEY WORDS: Biochemical analyses, canine visceral *Leishmaniasis*, hematology.

RESUMO

LEISHMANIOSE VISCERAL CANINA (LVC): SOROPREVALÊNCIA, ASPECTOS CLÍNICOS, HEMATOLÓGICOS E BIOQUÍMICOS DE CÃES NATURALMENTE INFECTADOS EM UMA ÁREA ENDÊMICA NO MUNICÍPIO DE SÃO LUIS, ESTADO DO MARANHÃO, BRASIL

Objetivou-se verificar a soroprevalência e os parâmetros clínicos, hematológicos e bioquímicos de cães naturalmente infectados por *Leishmania* em uma área endêmica. Realizou-se a sorologia pela reação de imunofluorescência indireta (RIFI) em 76 cães sem raça definida. Os resultados demonstraram que 28 (36,84%) foram positivos, enquanto 15 (53,57%) eram assintomáticos e 13 (46,43%) sintomáticos. Os sinais clínicos mais freqüentes foram onicogrifose, lesões de pele (alopecia, úlceras, descamação furfurácea) e linfoadenopatia localizada. Em 6 de 22 animais (27,27%) observou-se anemia. As análises bioquímicas indicaram que a infecção causada por *Leishmania* pode levar a alterações hepáticas. Não se observaram alterações renais. Conclui-se que os parâmetros bioquímicos podem ser úteis para acompanhar os estágios clínicos da doença.

PALAVAS-CHAVES: Análises bioquímicas, hematologia, *Leishmaniose* visceral canina.

INTRODUCTION

Visceral Leishmaniasis (VL) or kala-azar is a chronic disease caused by protozoan parasites of *Leishmania donovani* complex (Kinetoplastidae). This disease is endemic in most of Brazil, but the major focus remains in the Northeastern region, mainly in states such as Ceará, Bahia, Piauí and Maranhão, the latter with 66% of all cases (MINISTÉRIO DA SAÚDE, 2003).

Infected dogs develop a wide spectrum of clinical signs such as lymphadenopathy, weight loss, emaciation, hepatospenomegaly, conjunctivitis, keratitis, onychogryphosis and cutaneous lesions (MARZOCHI et al., 1985; CARDOSO et al., 1986; SLAPPENDELL, 1988; ALMEIDA et al., 2005), which are frequent and include alopecia with extensive dry desquamation, ulcer in limbs and ear (FERRER, 1999). However, studies have shown that many dogs remain asymptomatic for long periods (BERRAHAL et al., 1996).

The most important and constant hematological change in cases of canine visceral leishmaniasis (CVL) is anemia. Another usual finding is an increase of total plasmatic protein levels. In some advanced stages of the disease, the total plasmatic protein levels may reach more than 10 g/dL (CIARAMELLA et al., 1997).

The kidney involvement, including interstitial and glomerular changes, has been observed in animals experimentally infected by *L. donovani* (CARAVACA et al., 1991).

Currently VL is a great public health concern in São Luís Island, Maranhão State, Brazil. There are four municipalities in this island and cases of human and canine visceral leishmaniasis have been reported in all of them. Therefore, the goal of this study was to investigate the seroprevalence, clinical, hematological and biochemical profiles of dogs naturally infected by *Leishmania chagasi* in a village of São José de Ribamar in São Luís Island, Brazil.

MATERIAL AND METHODS

Description of area

São José de Ribamar is a municipality lo-cated between 2º37'30"S and 44º07'30"L, in the north region of São Luís Island, Maranhão State, Brazil. It has a hot climate with annual average temperature around 26º C. The population is 107.333 inhabitants distributed in several villages. Studies have shown that original vegetation was modified, due to intense human occupation in the area and nowadays "capoeiras" replaced the original vegetation, although *Orbignya phalerata* (*babaçu*) palm trees are still present (MARANHÃO, 2002). This study was carried out in Jaguarema Village, where recent cases of human VL have been notified (FUNASA, 2004). This Village has 417 residences and 1097 inhabitants. Sanitary conditions are precarious (no water sanitation, open sewage and poor housing). The residences consist mainly of small shacks.

Survey design

A canine census was performed and all 76 household mongrel dogs were included in the study. The dogs were examined to search for clinical signs of *Leishmania* infection, and clinical epidemiological forms containing general information about the animals were filled out. The animals were classified as asymptomatic and symptomatic, while clinical signs were scored as follows: score 0 (no clinical signs), score 1 (skin lesions: ulcers, alopecia, dry desquamation, onychogryphosis), score 2 (visceral signs: lymphadenopathy, splenomegaly and hepatomegaly) and score 3 (skin lesions and visceral signs).

Peripheral blood samples were collected from cephalic vein. Five milliliter-samples were transferred to tubes with EDTA for hemogram and 5ml were transferred to tubes with no anticoagulant. The serum samples were stored in aliquots at -20ºC, for serological and biochemical tests.

An indirect fluorescent antibody test (IFAT), canine IFI-Leishmaniasis Kit (Bio-Manguinhos/FIOCRUZ), was used according to manufactures's recommendations. The threshold serum dilution for a positive test was 1:40 and the final dilution was 1:640.

Hemogram was performed by conventional technique of counting erythrocytes (DACE &

LEWIS, 1984) in an automatic cell counter. For biochemical analyses, available commercial kits for urea and creatinine and for Alanine Transferase (ALT) and Aspartate Transferase (AST) were used. The results obtained were compared to reference values according to SILVEIRA (1988).

For parasitological examination, bone marrow punctures were carried out and slides of Giemsa-stained bone marrow smears were examined for the presence of amastigote forms of *Leishmania*.

The project was submitted to and approved by the Ethics Committee of the State University of Maranhão (UEMA), under protocol 22/05. Written consent was obtained from each animal owner prior to its inclusion in the sampled group.

Statistical analysis

The Chi-square test was used to compare the clinical, serology, hematological and, biochemical data. Differences were considered statistically significant for p values < 0.05.

RESULTS

The IFAT was positive in 28 (36.84%) out of 76 dogs examined. Anti-*Leishmania* positive titers higher than 1: 40 were observed in 21 (75%) out of 28 dogs as follows: 1: 80 (05 animals); 1: 160 (05 animals); 1: 320 (05 animals) and 1: 640 (06 animals).

Among the 28 seropositive dogs 15 (53.57%) of them were asymptomatic and 13 (46.43%) were symptomatic. The most frequent clinical signs were onychogryphosis (60.71% - 17 out of 28), alopecia (39.28% - 11 out of 28), ulcers (39.28% - 11 out of 28), dry desquamation (28.57% - 08 out of 28) and localized lymphadenopathy (17.86% - 05 out of 28). Statistical analysis showed that there was no significant difference when the clinical score 0 (10 animals) and 1 (14 animals) were compared (p>0.05). Four animals presented score 3 and none of them presented score 2. The parasitological survey was positive in 2 (7.14%) out of 28 dogs examined.

The hematological and biochemical evaluations were performed in 22 seropositive

animals (six dogs were captured by Zoonosis Center Control). The assessment of hematological parameters demonstrated that 6 animals displayed anemia. The main finding in white blood cells count was eosinophilia (40.9%). Hyperproteinemia was detected in 63.63% cases. Biochemical analyses revealed that 22.72% dogs presented higher rates of urea in comparison to reference ranges (5-28mg/dL). There were no changes in creatinine values (reference ranges 0.5-1.5mg/dL). Concerning hepatic proofs, 63.63% of the animals displayed hepatic changes since ALT levels (4.8-24) and AST (6.2-13) were above the borderline values.

DISCUSSION

VL has assumed increasing public health importance due to the urbanization of the disease as well as the great number of cases among immune compromised patients. Changes in rural environment and the constant migratory movements of the population to the periphery of cities have facilitated this process (WHO, 1990). In the periurban and urban areas, dogs are the major reservoirs of the parasite (MARZOCHI et al., 1994). Villages located in São José de Ribamar (Sérgio Tamer and Quinta Villages), previously studied by GUIMARÃES et al. (2005), have suffered environmental changes in the last years, with poor conditions of infrastructure and sanitation, which contributed to the establishment of CVL.

According to MARZOCHI & MARZOCHI (1997), environmental degradation and especially the lack of sanitation, that has been associated with the recent migration of rural populations to urban suburbs, are believed to have contributed to the urbanization of the disease as well as the adaptation of the inset vector. In fact, *Lutzomyia longipalpis*, known vector of VL, is commonly captured in the area, according to previous entomological studies (CARVALHO et al., 2000).

Clinical examination showed that 53.57% and 46.43% dog were asymptomatic and symptomatic, respectively. Similar results were

obtained by other authors such as MARZOCHI et al. (1985) and SILVA et al. (2001). Regarding the high percentage of asymptomatic dogs, BERRAHAL et al. (1996) found that many animals remain asymptomatic for long periods, in a similar way as it has been observed here. These animals constitute infection sources for the insect vector (ALVAR et al., 1994; MOLINA et al., 1994). FERREIRA et al. (2007) emphasizes that since CVL-infected dogs can remain asymptomatic for long periods of time, infection prevalence in an endemic area may be underestimated.

The more frequent clinical signs were onychogryphosis, skin lesions (alopecia, ulcers, dry desquamation) and lymphadenopathy. These findings have been extensively reported in the literature (SILVA et al., 2001; CAVALCANTI et al., 2005; GUIMARÃES et al., 2005; REIS et al., 2006). Despite of the great majority of dogs being asymptomatic, it is important to mention some clinical signs such as skin lesions, onychogryphosis and lymphadenopathy in endemic areas, since these signs are promptly recognized in CVL. The latent infections are important in maintaining the long-term presence of the parasite in endemic areas (PALATNIK-de-SOUSA et al., 2003).

The parasitological techniques employed to the direct detection of parasites in biological samples are invasive and of relatively low sensitivity (SCHALLIG et al., 2002). In this study a low parasite load in bone marrow was observed in the smears, whereas CORTADA et al. (2004) in Mato Grosso do Sul State and SILVA et al. (2001) in Minas Gerais State found greater parasite load, in which bone marrow presented both free amastigotes and macrophages filled with parasites. REIS et al. (2006) demonstrated that parasitological survey performed on tissue *in printing* smears (skin, spleen, liver and lymph node), as well as cultured bone marrow, proved to be more efficient to detect *Leishmania* organisms in asymptomatic dogs than direct bone marrow smear. An interesting feature is the great number of asymptomatic dogs and low parasite load, even in dogs that presented high titers of antibody against *Leishmania* (CORTADA et al., 2004).

Anemia was detected in 27.27% of the dogs. KEENAN et al. (1984) reported anemia as an usual finding in canine infection and REIS et al. (2006) found severe anemia in symptomatic dogs. It seems that anemia is related to the clinical stage of the disease. According to KIRAL et al. (2004), anemia was the most frequently observed hematological abnormality in *Leishmania* group. Hematological findings indicate that anemia developed after hyperactivity in the reticulo-endothelial system and also to the hemoglobin synthesis failure. Concerning the type of anemia, KEENAN et al. (1984), CIARAMELLA et al. (1997) and FEITOSA et al. (2003) reported that normocytic normochromic anemia is frequently found, but our results detected normocytic hypochromic anemia.

Eosinophilia was the unique leukocyte abnormality as opposed to the results presented by FEITOSA et al. (2003) and KIRAL et al. (2004). This finding has been reported in previous studies, which is typical for parasitic diseases as well as associated to skin disorders (DUNCAN & PRASSE, 1982; OLIVEIRA & POLINETO, 2004). Sampled dogs had ectoparasites (tick and fleas) and gastrointestinal parasites. Hyperproteinemia was observed as described by FEITOSA et al. (2003) and KIRAL et al. (2004). *Leishmania* infection can lead to hyperproteinemia probably due to increased globulin production.

Although KIRAL et al. (2004) did not find significant elevations in ALT and AST in infected dogs, we have detected significant elevation in ALT, what might indicate hepatic dysfunction. Not as expected, only concentration of urea was elevated, indicating no renal dysfunction. ALMEIDA et al. (2005) observed that kidney involvement is not frequent and AMUSATEGUI et al. (2003) stated that, in the advanced stage of CVL, mean values of urea, creatinine and ALT are high, but the percentage of these cases is relatively low.

All together, the clinical picture of the animals was typical of VL, while the hematological and biochemical parameters analyzed would probably help to follow up the clinical stage of the disease.

ACKNOWLEDGEMENTS

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