Leishmania (Leishmania) infantum Infection in Americas: What Factors Could be Involved in the Development of Visceral or Cutaneous Disease?

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Received: June 03, 2019; Published: June 21, 2019

Leishmaniasis is a tropical and subtropical disease caused by an intracellular parasite transmitted to humans by the bite of a sand fly that presents a broad spectrum of clinical manifestations depending on the causative parasite species and the host immune and genetic background. *Leishmania (Leishmania) infantum* causes subclinical or active visceral leishmaniasis (LV) that is characterized by irregular fever, hepatosplenomegaly, lymphadenomegaly, anemia with leucopenia, hypergammaglobulinemia with hypoalbuminenmia, lost weight, edema and progressive weakness leading to cachexia and is potentially fatal if untreated. American visceral leishmaniasis is considered an important zoonosis involving wild and domestic animals as reservoirs. Dogs are considered the main urban reservoir of *L. (L.) infantum*, acting as an important source of infection for the sand fly vector, *Lutzomyia longipalpis*. From the epidemiological point of view, canine disease is quite relevant since dog infection is much more prevalent than human infection, and canine leishmaniasis precedes the occurrence of human cases of visceral leishmaniasis. For this reason, most of the control programs of this important zoonosis are based on the elimination of seropositive dogs, since the available vaccines do not show 100% effectiveness, and drugs for the treatment of canine disease fail to completely eliminate the parasites, and the animals may remain in the environment as a source of infection.

However, in some countries of Central America such as Honduras, El Salvador and Nicaragua, human infection by L. (L.) infantum has presented atypical behavior, causing both visceral leishmaniasis (VL) in children younger than 10 years and non-ulcerated cutaneous leishmaniasis (NUCL) in adolescents and young adults. This atypical cutaneous form is clinically characterized by non-ulcerated skin lesions; of small size and few numbers, with chronic evolution, affecting the skin in the form of papules, nodules and erythematous plaques, painless and surrounded by a hypopigmented halo. Histopathological studies showed that they are characterized by a mononuclear inflammatory infiltrate, predominantly by lymphocytes, with the presence of granulomas and scarce parasitism. In endemic areas of NUCL transmission, the prevalence of canine infection is very low and the great majority of the animals are asymptomatic. While in high transmission endemic areas of South America the prevalence of canine infection is close to 50% and the human infection is near to 10%, in Central America occurs exactly the opposite, since the prevalence of human infection is higher than the canine infection and the role of dogs as an important reservoir is not proved yet. It is important to mention that most of the humans affected by NUCL present circulating parasites detected by molecular tests, which could represent a potential source of infection for the phlebotomine vector. In fact, the epidemiology and features of L. (L.) infantum infection in Central America is yet to be better understood and need more investigative studies to determine whether the genetic and immunological background of humans as well as genetic mutations of the parasites could be involved in determining the atypical cutaneous or the visceral form, and also the role of the different species of Leishmania (L.) infantum vectors, since in the endemic areas of transmission there is abundance not only of Lutzomyia longipalpis but also of Lutzomyia evansi with different seasonality during the year, diverging between rainy and dry periods. In addition, it is of pivotal importance to investigate the wild animals and especially the dog involvement in the biological cycle of the parasite in Central America.

Acknowledgment

FAPESP, CNPq, CAPES and LIM50 HC-FMUSP.

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Citation: Márcia Dalastra Laurenti. "*Leishmania (Leishmania) infantum* Infection in Americas: What Factors Could be Involved in the Development of Visceral or Cutaneous Disease?". *EC Veterinary Science* 4.5 (2019): 324.