TREATMENT OF *LEISHMANIA INFANTUM*-INFECTED HAMSTERS WITH A NEW IMMUNOCHEMOTHERAPY SCHEDULE: ANALYSIS OF INTRACELLULAR CYTOKINE PROFILE AND HISTOPATHOLOGY OF SPLEEN TISSUE

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Visceral leishmaniasis (VL) is a severe disease requiring new therapies due to current treatment limitations. Immunochemotherapy, which combines drugs and immunomodulators, emerges as a promising strategy to enhance therapeutic responses and reduce toxicity. Therefore, we aimed to evaluate the therapeutic efficacy of Chimera A adjuvanted with monophosphoryl lipid A (MPL) as immunotherapy or combined with Miltefosine as immunochemotherapy. Hamsters (*Mesocricetus auratus*) were infected with 5×10^7 stationary-phase *Leishmania infantum* promastigotes (MCAN/BR/2008/OP46) and received two treatment schedules. In the first approach, 60 days post-infection, the hamsters were treated with Miltefosine for 14 (M14) or 28 days (M28). In the second schedule, seven days after the chemotherapy treatment beginning, the animals submitted to immunotherapy (ChiA/MPL) and immunochemotherapy (ChiA/MPL +M14) received two series of five doses (ChiA/MPL) with 10-day intervals between series. Ninety days post-treatment, spleen samples were collected to assess intracellular cytokine profile (IFN-γ, TNF, and IL-10), parasite load, and histopathological analysis. Our study provides a robust evaluation of a specific compartmentalized immune response in the hamster model using multiparametric flow cytometry methodology. Chi A/MPL and ChiA/MPL+M14 treated hamsters showed increased IFN-γ and TNF-producing T cells and also reduced IL-10. Moreover, treated hamsters exhibited a remarkable reduction in the splenic parasite load. Considering the macroscopic structure of spleen tissue, we observed splenomegaly and thickening borders of the capsule of infected-nontreated hamsters. Treated hamsters presented a slight reduction in the follicle, suggesting efficient immune activation and contributing to parasite control. The results indicate that immunochemotherapy may be a promising alternative against VL while reinforcing the innovative potential of multiparametric flow cytometry in the hamster model.

Supported by: UFOP; PROPPI; CAPES; CNPq; FAPEMIG; INCT-DT; REDE IMUNOBIOLEISH; FINEP; CCA-UFOP; LMU-MAM; LMUCF.

Keywords: Visceral Leishmaniasis, Immunochemotherapy, Syrian golden hamster