NEUTROPHIL STATE OF ACTIVATION MODULATES DENDRITIC CELLS SUSCEPTIBILITY TO LEISHMANIA AMAZONESIS INFECTION

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Introduction: Leishmaniasis remains as one of the most seriously neglected tropical diseases. The pathology is caused by an intracellular parasite transmitted to mammals through the bite of Leishmania-infected sandflies. Leishmania infects a wide range of cells. Neutrophils play a role in eliciting innate immune responses by releasing inflammatory mediators, (chemokines and cytokines) or through cell interaction, which collectively recruit and activate other leukocytes.**Hypothesis:**We propose that the DCs might resist to Leishmania amazonensis infection due the activation of appropriated molecular pathways elicited by neutrophil through inflammatory mediators and cell interaction. **Materials and methods:** To test this hypothesis, primarily, human monocyte-derived DCs and neutrophils were purified from peripheral blood of healthy donors. Neutrophils were activated with fibronectin at 10 µg/mL for 1 hour and DCs were infected with L. amazonensis stationary promastigotes (MHOM/BR/87/BA125 strain) and co-cultured with (activated or resting) neutrophils in the presence or absence of pharmacological inhibitors of myeloperoxidase (MPO), elastase (NE), metalloproteinase-9 (MMP-9) and TNFα for 18h. Subsequently, supernatants and cells were harvested to evaluate the release of granules enzymes (MPO and NE), and cytokine production (TNFα). To evaluate the role of DC activation through cell interaction, DCs were infected in transwell plates at the lower chamber and activated neutrophils were co-cultured in the upper chamber and, in other experiments, the co-culture of infected DCs and neutrophils was incubated with anti-DC-SIGN to assess the rate of infection of DCs and parasite burden. **Results and Discussion:** Our results demonstrated that neutrophil state of activation does not influence the rate of infected DCs and parasite load. Under inhibition of NE, MMP9, and MPO, there was no reduction in parasite load, despite the increase of MPO and NE in the supernatant of the cells co-culture. Activated neutrophils reduces DC infection, parasite load, and increase TNF production dependent of cell interaction, through DC-sign. **Conclusion:** Futher experiments will be made to evaluate how neutrophils influence the antigen presentation ability of DCs under infection by L. amazonensis.

Keywords : Leishmania amazonensis; Dendritic cells; Neutrophil

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