Macrophage cell responses in cutaneous leishmaniasis caused by Leishmania donovani

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Background: Leishmaniasis is a neglected tropical disease caused by parasitic protozoa of the genus Leishmania. It has a spectrum of manifestations including cutaneous, mucosal and visceral disease. The clinical outcome of infection in humans is determined primarily by the infecting species and the immune response by the host. Sri Lanka is endemic for localised cutaneous leishmaniasis (LCL) caused by Leishmania donovani; a species which usually causes visceral disease. The aim of this study was to characterize the immune response in LCL by macrophages; the cells responsible for survival as well as eventual elimination of the parasite.

Methods & Materials: Peripheral blood mononuclear cell (PBMC) derived macrophages from newly diagnosed LCL patients (n = 8) and healthy non endemic controls (n = 8) were stimulated with L. donovani antigen (50 µg/ml) in vitro. The production of IL-10, TNFα and Nitric Oxide (NO) were measured by ELISA and Griess reaction at predetermined time intervals. The differences between experimental groups were analysed using the Student’s t-test for parametric data and Mann-Whitney test for non-parametric data.

Results: Macrophages from patients produced more cytokines and NO at all time points. IL-10 production by patient macrophages was significantly higher (105.68 ± 26.05 vs 19.81 ± 28.24 pg/mL; p<0.01) at 72 hours but did not vary markedly at 24 and 48 hours. TNFα production by patient macrophages was significantly higher at both 24 hours (23.05 ± 13.97 vs 4.01 ± 2.26 pg/mL; p<0.01) and 48 hours (311.33 ± 206.29 vs 17.61 ± 21.09 pg/mL; p<0.01). Levels of production of NO remained similar at 24 and 48 hours but showed increased levels by patient macrophages at 72 hours (5.40 ± 1.15 vs 2.36 ± 1.21 pg/mL; p<0.01).

Conclusion: These data suggest that IL-10, TNFα and NO play a role in determining disease outcome in LCL due to L. donovani. In contrast to TNFα, the contribution of IL-10 and NO appear to be later in the infection. The findings should be interpreted in the context of changes in other inflammatory mediators, to better understand the underlying pathogenic mechanisms where a visceralizing Leishmania species is localized to the skin.

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