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TITLE

EVALUATION OF THE TH1/TH2/TH17 CYTOKINE PROFILE ASSOCIATION WITH LIVER FIBROSIS IN INDIVIDUALS INFECTED WITH SCHISTOSOMA MANSONI

AUTHORS

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ABSTRACT

Introduction: In Brazil, schistosomiasis is a parasitic disease caused by the blood parasite *Schistosoma mansoni*. Its clinical manifestations are due to hepatosplenic involvement resulting from the development of periportal fibrosis in response to the presence of the parasite egg in the tissue, which is responsible for the morbidity and mortality associated with the disease. However, the associated immunological mechanisms have been insufficiently explored regarding the search for biomarkers of clinical progression. The aim of this study was to associate the cytokine profile produced in vitro by peripheral blood mononuclear cells (PBMC) from infected individuals with different degrees of fibrosis. **Methodology:** soluble egg antigen (SEA) was produced from frozen eggs kindly provided by the Biomedical Research Institute's Schistosomiasis Resource Center (NIH-NIAID HHSN272201700014I). Briefly, the eggs were broken down using the cell and tissue disruptor L-BEADER 6 (Loccus, São Paulo, Brazil), followed by ultracentrifugation. Protein concentration was determined using the BCA kit (Thermo Scientific, Rockford, USA). Peripheral blood was collected and 3x10⁶ PBMCs were isolated from 10 infected individuals with ultrasonography (USG) patterns A or B (considered as group without fibrosis), 7 individuals with fibrosis pattern C, 6 individuals with fibrosis pattern D and 4 individuals with fibrosis pattern E. PBMC's were then stimulated with 10 ug/mL of SEA for 48 hours. Culture supernatant was collected and subjected to cytokine quantification using the BD™ Cytometric Bead Array (CBA) Human Th1/Th2/Th17 kit. Statistical analyses were carried out using GraphPad Prism 8.0.2 software. This project was approved by the Research Ethics Committee (protocol number 5.905.584). **Results:** A statistically significant reduction in IL-10 was observed in the group with fibrosis pattern E when compared to the group without fibrosis ($p = 0.04$). In the group of infected individuals without fibrosis, a significant positive correlation was observed between IL-6 and IFN- γ cytokines ($r = 0.74$, $p = 0.017$) and also between IL-6 and IL-10 ($r = 0.87$, $p = 0.02$). In the group with fibrosis pattern C, a significant positive correlation between IL-6 and IL-10 ($r = 0.96$, $p = 0.003$) also occurred. As the severity of fibrosis in the groups increased, an elevation of the IFN- γ levels ($R^2 = 0.899$, $p = 0.206$) and a reduction in IL-10 and IL-6 levels ($R^2 = 0.992$ and 0.947 , respectively) were noted. **Conclusion:** The results suggest that IL-10, IL-6 and IFN- γ cytokine levels may be associated with fibrosis patterns in the liver as revealed by USG. Ongoing experiments with a larger sample size of individuals may ascertain whether these cytokines can be utilized as blood markers for fibrosis in human schistosomiasis.

KEYWORDS

Schistosomiasis mansoni; Immunopathogenesis; Cytokines; Hepatic Fibrosis

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