Immune Modulation and Cytomegalovirus Reactivation in Sepsis-Induced Immunosuppression

Authors: G. Lambe, D. Mansukhani, A. Shetty, S. Khodaiji, C. Rodrigues, F. Kapadia

Abstract: Introduction: Sepsis is known to cause impairment of both innate and adaptive immunity and involves an early uncontrolled inflammatory response, followed by a protracting immunosuppression phase, which includes decreased expression of cell receptors, T cell anergy and exhaustion, impaired cytokine production, which may cause high risk for secondary infections due to reduced response to antigens. Although human cytomegalovirus (CMV) is widely recognized as a serious viral pathogen in sepsis and immunocompromised patients, the incidence of CMV reactivation in patients with sepsis lacking strong evidence of immunosuppression is not well defined. Therefore, it is important to determine an association between CMV reactivation and sepsis-induced immunosuppression. Aim: To determine the association between incidence of CMV reactivation and immune modulation in sepsis-induced immunosuppression with time. Material and Methods: Ten CMVseropositive adult patients with severe sepsis were included in this study. Blood samples were collected on Day 0, and further weekly up to 21 days. CMV load was quantified by real-time PCR using plasma. The expression of immunosuppression markers, namely, HLA-DR, PD-1, and regulatory T cells, were determined by flow cytometry using whole blood. Results: At Day 0, no CMV reactivation was observed in 6/10 patients. In these patients, the median length for reactivation was 14 days (range, 7-14 days). The remaining four patients, at Day 0, had a mean viral load of 1802+2599 copies/ml, which increased with time. At Day 21, the mean viral load for all 10 patients was 60949+179700 copies/ml, indicating that viremia increased with the length of stay in the hospital. HLA-DR expression on monocytes significantly increased from Day 0 to Day 7 (p = 0.001), following which no significant change was observed until Day 21, for all patients except 3. In these three patients, HLA-DR expression on monocytes showed a decrease at elevated viral load (>5000 copies/ml), indicating immune suppression. However, the other markers, PD-1 and regulatory T cells, did not show any significant changes. Conclusion: These preliminary findings suggest that CMV reactivation can occur in patients with severe sepsis. In fact, the viral load continued to increase with the length of stay in the hospital. Immune suppression, indicated by decreased expression of HLA-DR alone, was observed in three patients with elevated viral load.

Keywords : CMV reactivation, immune suppression, sepsis immune modulation, CMV viral load **Conference Title :** ICHI 2019 : International Conference on Haematology and Immunology

Conference Location: Mumbai, India Conference Dates: February 07-08, 2019