Escherichia coli-induced immune paralysis is not exacerbated during chronic filarial infection.

Abstract:
Sepsis initially starts with a systemic inflammatory response (SIRS phase) and is followed by a compensatory anti-inflammatory response syndrome (CARS) that causes impaired adaptive T-cell immunity, immune paralysis and an increased susceptibility to secondary infections. In contrast, parasitic filariae release thousands of microfilariae into the peripheral blood without triggering inflammation, as they induce regulatory, anti-inflammatory host responses. Hence, we investigated the impact of chronic filarial infection on adaptive T-cell responses during the SIRS and CARS phases of a systemic bacterial infection and analysed the development of T-cell paralysis following a subsequent adenovirus challenge in BALB/c mice. Chronic filarial infection impaired adenovirus-specific CD8(+) T-cell cytotoxicity and interferon-γ responses in the absence of a bacterial challenge and led to higher numbers of splenic CTLA-4(+) CD4(+) T cells, whereas splenic T-cell expression of CD69 and CD62 ligand, serum cytokine levels and regulatory T-cell frequencies were comparable to naive controls. Irrespective of filarial infection, the SIRS phase dominated 6-24 hr after intravenous Escherichia coli challenge with increased T-cell activation and pro-inflammatory cytokine production, whereas the CARS phase occurred 6 days post E. coli challenge and correlated with high levels of
transforming growth factor-? and increased CD62 ligand T-cell expression. Escherichia coli-induced impairment of adenovirus-specific CD8(+) T-cell cytotoxicity and interferon-? production was not additionally impaired by chronic filarial infection. This suggests that filarial immunoregulation does not exacerbate E. coli-induced T-cell paralysis.