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Wuchereria bancrofti: Diminished platelet activation in filarial patients

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ABSTRACT

Blood platelets are the innate immune elements that have not been investigated in human filarial infections. Platelet activation status in the endemic normals (EN), microfilaria positive individuals (MF) and patients with chronic pathology (CP) was evaluated in whole blood, under unstimulated as well as antigen exposed (BmA, *E. coli*) conditions for PAC-1 expression by Flow cytometry. A diminished PAC-1 expression was observed in MF compared to CP and EN spontaneously as well as upon antigen exposure. Besides this, PAC-1 expression within the groups did not exhibit any significant difference under all the experimental conditions. However in CP patients, *E. coli* antigen exposure resulted in a significantly reduced PAC-1 expression compared to the spontaneous expression levels. NO release in platelet culture supernatants from EN was inversely proportional to platelet aggregation. Collagen stimulated platelets from EN, exposed to sera and immune complexes from CP and MF patients resulted in elevated Nitric Oxide (NO) release, compared to those exposed to autologous sera and fetal calf serum. In addition, under similar conditions, collagen stimulated platelets from EN, exposed to filarial antigen (BmA) exhibited increased NO compared to the *E. coli* antigen exposed ones and light microscopic observations of cultured platelets supported the above findings. Thus it appears from the results of the present study that filarial antigen may play a role in the loss of platelet aggregation, leading to platelet inactivation.

1. Introduction

Human lymphatic filariasis caused by nematode parasites *Wuchereria bancrofti*, *Brugia malayi* and *Brugia timori* is an endemic disease of tropical and sub tropical countries of the world. The parasite spells doom among the endemic inhabitants by causing severe suffering in the form of crippling disability leading to 'alienation' (Ramachandran, 1997). Parasite survival in the host is mediated by several factors that operate at various levels. These mechanisms collectively termed as immune evasion strategies facilitate parasite survival by modulating the function of host immune elements (Maizels et al., 2004). Studies on endemic population (Babu et al., 2006) as well as experimental models (Taylor et al., 2005, 2007) have demonstrated the activation of T-Regulatory cells (T-Regs) that contribute to parasite persistence. With respect to antigen presenting cells (APC), alternatively activated macrophages (AAMΦs), comprise of the special macrophage population that were implicated in parasite survival by studies with experimental models (Allen and Loke, 2001). Besides this, several other studies suggest impairment in dendritic cell function upon exposure to live MF, contributing to a reduction in $CD4^+$ T-cell activation (Semnani et al., 2003). In addition to this, studies from our lab (Sasisekhar et al., 2005), suggested monocyte dysfunction in microfilaremic patients as a probable reason for impaired antigen presentation and dampened immune responses of this cohort. However the cells that contribute to parasite persistence and disease transmittance have not been investigated. Blood platelets assume a prominent role in this context, as blood borne microfilariae circulate indefinitely in the host vasculature and are transmitted into a mosquito host, where they mature into L-3 larvae and infect a new human host to cause pathogenesis. Previous studies have shown that, survival of MF stage and its transmittance may be attributed to the inhibition of agonist induced platelet aggregation by *B. malayi* microfilariae (Liu and Weller, 1992). Besides this, there were no further attempts to investigate the role of blood platelets in the disease spectrum of human lymphatic filariasis.

An important role for platelets in parasitic infections comes from the studies showing the occurrence of thrombocytopenia in up to 80% of patients with malaria (Gerardin et al., 2002). In this

Abbreviations: BmA, adult *Brugia malayi* crude extracts; EN, endemic normal; MF, microfilaremic; CP, chronic pathology; NO, nitric oxide; FCS, foetal calf serum.

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