Role of Cytokines in Parasitic Disease

Cytokines also called Interleukins are hormone like polypeptides produced by lymphocytes, mbocytes or macrohage and consist of lymphokines and monokines. Interleukins are released in response to inflammatory stimuli and act on other cells of the immune system to regulate their function. Interleukins are of different types and the relationship of IL 2, IL 4, IL 5 and IL 10 and tumour necrosis factor (TNF) is present in parasitic disease. IL 2 protein is produced mainly by helper T cells and acts synergistically with IL 4 to stimulate the growth ofB cells. IL 4 and IL, 5 are protein produced by helper T cells. They promote the growth and differentiation of B cells. IL 4 is required for isotype switching from one class of antibody to another, within the antibody producing cells. It also enhances the synthesis of IgB and IgA and stimulate the production and activation of eosinophils which are an important host defence against many helminths. IL 10 regulates the production of cells that mediate delayed hypersensitivity and inhibit the development of these cells by limiting interferon production.

Studies link enhancement of IL 5 production and the associated eosinophilia with parasitic disease in mice and humans. Parasitic infection that persists for a long time involves high antigen load. Nippostrogylus brasiliensis infestation induces high level of parasite specific and polyclonal IgB and increased eosinophil levels which is due to IL 4 and IL 5 production. Infection with Schistosoma mansoni results in a strong immune response after the production of eggs by the parasite. The egg antigen induces high production of IL 4, IL 5 and IL 10. Antigen stimulation in culture does not induce high levels of Interferon (IFN) secretion but addition of IL 10 antibodies to these cultures results in high levels of IFN secretion. IL 4 has been implicated in the pathogenesis of leishmaniasis by its ability to inhibit macrophage function suggesting the possible role of an anti-IL 4 antibodies in treatment.

IL 2 and IL 5 production in response to G. lamblia trophozoites were strongly depressed in the retrovirus infected group while IFN was increased. Depressed cytokine was not due to depressed T cell number. Tumour necrosis factor alpha (TNF), a cytokine produced by macrophage is a portend mediator of inflammatory and immunological reaction. The alpha plays an important role in a variety of parasitic diseases. Its production by macrophage is altered during entamoeba histolytica infection and in response to B. histolytica IFN and prostaglandin E2 regulates TNF alpha production. An inflammatory response involving polymorphonuclear and mononuclear cells in the epitheliurn occurs in giardiasis. These cells secrete inflammatory mediators like kinins which alter epithelial structure and function. Cytokine gene expression was not altered after infection of colonic epithelial cells with non-invasive protozoa like 0. lamblia. None of the patients with cryptosporidium, rota-virus or monospecific diarrhoea or healthy controls had TNF alpha or IL 6. Local release of TNF alpha and IL 6 occurs mainly in Shigella dysenteriae infection. TNF alpha appears to act synergistically with other cytokines. Cytokine IL 6 and TNF alpha are released in response to endotoxin causing endothelial damage and multi-organ failure. Serum TNF alpha was released in acute phase but no correlation was observed with the disease severity and complication. Overproduction of TNF alpha has been implicated in septic shock following infection with gram negative bacteria. TNF alpha may also be of therapeutic benefit in the treatment of parasitic infection. Macrophage treated with recombinant IFN and bacterial lipopolysaccharide ingested significantly higher numbers of invitro grown trophozoites than untreated macrophage. Interleukin, colony stimulating factor or TNIF alone or
in combination with lipopolysaccharide failed to activate macrophage to phagocytose G. lamblia. Role of cytokines in G. lamblia infection is being investigated at our centre but there appears to be no significant relationship of interleukin IL 2 or IL 10 in giardiasis. IL 4 was found to be elevated (826 pg/ml) in 2/52 patients and low (165 pg/ml) in 2/36 controls. The study is still in progress and more cases will be studied to determine any relationship between cytokines and G. lamblia infection.

References