DEFECTIVE IL-8 PRODUCTION AND ACCELERATED APOPTOSIS OF POLYMORPHONUCLEAR NEUTROPHILS IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Increased susceptibility to infection is a major cause of morbidity and mortality in patients with systemic lupus erythematosus (SLE). The polymorphonuclear neutrophils (PMN) derived from these patients have been found to exhibite many defects including decreased phagocytosis, defective membrane expression of complement receptors, decreased nitroblue tetrazolium reduction, and presence of serum inhibitors for PMN chemotaxis. Interleukin 8 (IL-8) is a specific potent activator for PMN and plays an essential role in amplifying the acute inflammatory reaction. In this study, we found the PMN from SLE produced decreased amount of IL-8 either spontaneously or in lipopolysaccharide (LPS) stimulation compared with normal PMN. This decreased production of IL-8 is disease-related, but not due to the effect of glucocorticoids. On the other hand, the responsiveness of SLE-PMN to exogenous IL-8 is also decreased. When we measure the percentage of pre-G0/G1 phase of PMN by flow cytometry or oligonucleosome release of PMN by ELISA after 48 hours incubation, accelerated apoptosis was noted in SLE. LPS, IL-1 β and IL-8 could protect PMN from apoptosis, but MCP-1, MIP-1 α, MIP-1 β, RANTES, GRO-α and fMLP failed to protect the cells from apoptosis. Both normal and SLE PMN may spontaneously express Fas antigens on the cell surface. The addition of anti-Fas antibodies exaggerated the death of PMN. These results suggest that accelerated apoptosis of PMN is one of the possible factors responsible for decreased IL-8 production of the cells in patients with SLE.