[2003] [THU0293] LYMPHOCYTE APOPTOSIS, MACROPHAGE FUNCTION AND DISEASE ACTIVITY IN SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: The origin of numerous autoantibodies in SLE remains an enigma. Increased lymphocyte apoptosis and defects in macrophage removal of apoptotic cells have been suggested to contribute to the development of SLE. The reason why macrophages have defects in the clearance of apoptotic cells is unclear.
Objectives: To investigate the relationship between peripheral lymphocyte apoptosis, macrophage function as determined by the serum levels of neopterin and gama-interferon (gama-IFN), and SLE disease activity.
Methods: Peripheral apoptotic lymphtocytes (AL) were detected by annexin V-FITC staining and flow cytometry. Serum levels of neopterin and gama-IFN were measured by ELISA. SLE disease activity was determined using the systemic lupus activity measure (SLAM).
Results: (1) The % of AL in the peripheral blood of active SLE patients was significantly higher (13.07 ±7.39%, n=30) than that of the inactive SLE patients (4.08±3.55%, n=8, $p<0.001$) and normal controls (5.13 ±3.37%, n=11, $p<0.001$). (2) Serum levels of neopterin in SLE patients were significantly higher (1.39±1.10 mg/dl, n=22) than in controls (0.26±0.19 mg/dl, n=20, $p<0.01$). (3) Serum levels of gama-IFN in active SLE patients were elevated (58.97±34.52 ng/l, n=15) when compared with controls (28.06±2.35 ng/l, n=16, $p<0.05$). (4) The % of AL correlated significantly with serum levels of neopterin ($r=0.446$, $p<0.05$, n=22) and SLAM score ($r=0.533$, $p<0.001$, n=38), but not with the serum levels of gama-IFN. The SLAM score was also correlated with the serum levels of neopterin ($r=0.485$, $p<0.05$, n=22) but not with those of gama-IFN.
Conclusion: 1. Our study supported the hypothesis that increased lymphocyte apoptosis has a pathogenic role in SLE. 2. The increased levels of serum neopterin which are mainly released by actived macrophages may suggest an attempt of the patients' macrophage system to remove the apoptotic cell excess. 3. Since serum levels of neopterin are correlated with the % of apoptotic lymphocytes, so no imbalance was found between the macrophage cytokine production and increased lymphocyte apoptosis, suggesting that defects in removal of apoptotic cells by macrophages may be influenced by other factors, rather than a primary macrophage functional incapability. 4. Since serum levels of neopterin correlated with the lupus disease activity, they may be regarded as an index of SLE disease activity.1. Emlen W, Niebur J, Kadera R. Accelerated in vitro apoptosis of lymphocytes from patients with systemic lupus erythematosus. Journal of Immunology, 1994, 152(7):3685-3693.; 2. Baumann I, Kolowos W, Voll RE, et al. Impaired uptake of apoptotic cells into tingible body macrophages in germinal centers of patients with systemic lupus erythematosus. Arthritis and Rheumatism, 2002, 46(1):191-201.; 3. Hamerlinck FF. Neopterin: a review. Exp Dermatol,1999, 8(3):167-76.

Etiology and pathogenesis/Animal models