Production of Interleukin-1 by Mononuclear Leukocytes and Mesangial Cells in Experimental Nephrotoxic Nephritis

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Dear Sir,

The proliferation of mesangial cells (MC) – one of the important features of glomerulonephritis (GN) – is often associated with the infiltration of glomeruli by circulating mononuclear leukocytes (ML) which secrete different cytokines and other growth factors [1–4]. One of the important factors amongst these is interleukin-1 (IL-1), taking part in immunological and other inflammatory reactions resulting in the proliferation of many types of cells.

Attempting to understand the mechanisms of the MC proliferation in GN, the roles of infiltrating ML and IL-1 in this process, we investigated the intensity of MC proliferation, the number of ML, and IL-1 production in glomerular-cell cultures from control rats (C) and rats in the heterologous phase of nephrotoxic-serum nephritis (NTS).

Wistar rats were injected intravenously with rabbit nephrotoxic serum, and 4 days later, their kidneys were removed for morphological examination (fig. 1). Glomerular-cell cultures were made according to Lovett et al. [5]. On the 20th day, glomerular-cell cultures of rats with NTS showed an accumulation of round cells (fig. 2) and elongated MC which were growing in multilayers (fig. 3). On immunofluorescent study of cell cultures with anti-serum to bone marrow cells of rats, specific fluorescent reaction was seen only in round cells, suggesting that these cells are mononuclear leukocytes (fig. 4).

After 20 days in cultures, the intensity of the MC proliferation in glomerular-cell cultures (measured by ³H-Td incorporation) in NTS rats was significantly higher than in the C group ($X \pm m$, $1,383 \pm 288$ and 218 ± 58 cpm, respectively, $p < 0.05$). These data corresponded to the actual MC numbers measured by light microscopy direct counting of the MC nuclei in random-chosen fields of the stained glomerular-cell cultures

Fig. 1. Linear deposition of rabbit immunoglobulins along the glomerular basement membrane. Direct immunofluorescence method. $\times 400$.

Fig. 2. Assembly of the mononuclear cells and proliferative mesangial cells. Azur II-methylene blue-fuchsin. $\times 320$.

Fig. 3. Multilayers of MC in culture. Azur [1]-methylene blue-
of mononuclear cells with antiserum to cells

fuchsin. $\times 320$. of bone marrow. Indirect immunofluorescence method. $\times 320$.

(NTS = 155 ± 17 cell/HPF and C = 50 ± 3 cell/HPF, $p < 0.05$) as well as the IL-1 production measured by the mice thymocyte proliferation method. IL-1 activity in culture medium (CM) represented as stimulation index:

SI =

$\frac{\text{cpm of thymocytes with CM}}{\text{cpm of thymocytes without CM}}$

was more than 3 times higher in NTS compared to C cultures (2.8 vs. 0.8).

Comparing the active and prolonged proliferation of MC in NTS cultures and the presence of large numbers of ML capable of secreting IL-1, one must keep in mind that MC themselves act as source of these growth factors. There are two sources of IL-1 in our model: MC and ML. The fact that the prolonged active proliferation of MC and the production of IL-1 in glomerular-cell cultures of rats with NTS correlated with the presence of large numbers of ML makes it possible that particularly these cells, by the production of IL-1, induce and maintain the proliferation of MC and possibly account for similar processes in GN in man.

References

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Fig. 4. Specific stain