Effect of Thymic Humoral Factor on a Local Graft-versus-Host Reaction of Lymphocytes in Patients with Lipoid Nephrosis

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Sir,

The etiology of lipoid nephrosis (LN) is poorly understood. We have recently shown that patients with LN have a systemic disorder of cell-mediated immunity, characterized by decreased T cell numbers, depressed delayed hypersensitivity reactions and impaired local graft-versus-host reaction (GVHR) [3, 4]. Our previous study [5] also illustrated an increase in concanavalin-A-induced suppressor cell activity in the majority of LN patients in relapse. Our present study is designed to compare the effect of thymic humoral factor (THF) on local GVHR in 16 patients with renal disease and 17 normal individuals. In all patients, the diagnosis was made by renal biopsy. All LN patients with nephrotic syndrome (NS) were receiving no medication at the time of the study. Donor peripheral blood lymphocytes (PBL) were isolated by separation on Ficoll-Hypaque gradients. The THF was prepared from young calf thymus according to the method described by Kook et al. [2]. The effect of THF on the patients' PBL was studied by preincubating 10×10^6 PBL with 100 μ g of THF for 1 h at 37 °C. Control experiments as above using normal PBL and THF treatment were also performed. A suspension of 10×10^6 PBL with or without THF treatment in a volume of 0.1 ml RPMI 1640 medium was injected intradermally into the closely shaven abdominal skin of Lewis rats immunosuppressed previously with 100 mg/kg cytoxan according to the method of Shohat and Joshua [6]. On day 5, the mean of the maximum and minimum diameters of the area of induration were measured with calipers.

The magnitude of local GVHR in the PBL of LN patients with NS was significantly ($p < 0.01$) lower than in normal subjects: 0.9 ± 0.4 vs. 2.5 ± 0.5 mm. Results in figure 1 indicate that THF significantly ($P < 0.01$) increased local GVHR in LN patients but had no significant effect on local GVHR in normal individuals and patients with chronic mesangial proliferative glomerulonephritis. That is, pre-incubation of the PBL from LN patients with THF resulted in a normalization of the local GVHR.

The local GVHR has been reported by Shohat and Joshua [6] to be a very sensitive test for measuring the functional activity of T cells. As far as we know, our article is the first to demonstrate a significant increase in the local GVHR by preincubation of the PBL from LN patients with THF. It has been shown that THF induces a rapid activation of membranal adenyl

cyclase in spleen cells, and an increase in cellular levels of cyclic AMP in thymocytes [1]. The precise mechanism by which THF increases local GVHR in our experiments is unclear. THF may increase local GVHR in LN patients via an effect on a specific subpopulation of LN lymphocytes. One might also speculate a direct effect of THF on PBL or on other cellular immune

Fig.1. Effect of THF on local GVHR in normal controls and patients with LN and chronic mesangial proliferative glomerulonephritis (CGN). Patients with LN were classified into two groups: patients with NS and patients without NS. * $p < 0.01$; ** $p < 0.05$ (significantly different from untreated values; p values by Student's t test). Open columns = untreated subjects; filled columns = subjects treated with THF.

response in LN. More data of a similar nature will be required to substantiate the hypothesis. Our investigation has shown that after preincubation with THF PBL from LN patients returned to normal levels. A study of this kind could provide further insight into the pathophysiology of LN and probably help in the design of a better therapeutic approach. However, owing to the limited number of cases studied, further investigations involving larger numbers of patients are needed in order to draw firm conclusions.

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References

- Kook, A. I.; Trainin, N.: Hormon-like activity of a thymus hormonal factor on the induction of immune competence in lymphoid cells. *J. exp. Med.* 139: 193–207 (1974).
- Kook, A. I.; Yakir, Y.; Trainin, N.: Isolation and partial chemical characterization of THF, a thymus hormone involved in immune maturation of lymphoid cells. *Cell. Immunol.* 19:151–157 (1975).
- Matsumoto, K.; Osakabe, K.; Harada, M.; Hatano, M.: Impaired cell-mediated immunity in lipoid nephrosis. *Nephron* 29: 190–194(1981).
- Matsumoto, K.: Impaired local graft-versus-host reaction in lipoid nephrosis. *Nephron* (in press).
- Osakabe, K.; Matsumoto, K.: Concanavalin A-induced suppressor cell activity in lipoid nephrosis. *Scand. J. Immunol.* 14: 161–166(1981).
- Shohat B.; Joshua H.: Assessment of the functional activity of human lymphocytes in malignant disease by the local graft-versus-host reaction in rats and the T rosette-forming cell test. *Clin. exp. Immunol.* 24: 534–537 (1976).