Minimal Change Nephrosis and Allergy

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Minimal change nephrotic syndrome (MCN) has proved so far to be an enigma. The prescribed treatment amounts to a trial of corticosteroid therapy [1,2] with the addition of cyclophosphamide for those who continue to relapse. Not surprisingly there are dissenting voices in respect of the steroid dosage schedule [3], and its duration [4, 5], and with regard to the ready use of cyclophosphamide [3]. Many, if not all, of these cases are associated with atopy [6]. Once the patient is receiving steroid therapy, this is an aspect that is difficult to investigate. There are good reports of the association of MCN in children with cow's milk allergy. There is improvement on withdrawal of the offending food [7, 8]. MCN can be associated with allergy to eggs [8] or pork [9], or inhaled pollen [10] or house dust [11]. The serum IgE can be raised [12], in spite of proteinuria, and the basophil degranulation test for allergens has yielded useful data [13].

Discussions of the immunological background have progressed from details of lymphocyte subsets [14] to acceptance of the fact that a vascular permeability-inducing cytokine [15] must be implicated. So there has been focus on tumour necrosis factor [16] and vascular endo-thelial growth factor. We are still not sure of the mediator.

Meantime one has begun to realize that division of helper T lymphocytes into Th-1 and Th-2 varieties, as was described in mice in the 1980s, is applicable to man. Thus in proliferative and progressive nephritides, in which a delayed hypersensitivity reaction accompanied by macro-phages is taking place in the glomeruli [17], the associated lymphocytes are of the Th-1 type and they are producing interleukin (IL)-2 and interferon- γ (IFN- γ) [18]. There is accompanying complement activation and production of

IgG2a and IgG3 antibodies. The reaction is the same as that used in the defence against bacteria, viruses and fungi, or intracellular parasites. On the other hand, if there are Th-2 helper lymphocytes producing the cytokines IL-4, IL-5 and IL-6, there is a long-lasting antibody response with production of IgE and IgG4 antibodies. This is the situation in allergic reactions and when there has to be defence against helminth parasites.

When cytokine analyses are performed on the supernatants of culture lymphocytes from grass pollen-allergic subjects to which grass pollen has been added, one can distinguish lymphocytes of allergic persons by their high production of IL-4 in relation to IFN- γ [19]. So one knows that these are Th-2 cells. As a result of many studies like this, one now realizes that allergy occurs in those persons who in early infancy have lymphocytes that produce little IFN- γ [20].

Clearly this approach should be useful in the study of patients with MCN. Initial studies from Seoul, Korea [21] revealed that B cells of children with MCN express increased membrane

type II IgE receptor (FcεR2/CD23) that are accompanied by elevated plasma-soluble CD23 and increased serum IgE. Furthermore, nonspecific stimulation of the T cells of those patients provoked production of cytokine IL-4, but IFN-γ formation by the cells was comparable to controls. In vitro treatment with methyl-prednisolone or IFN-γ resulted in inhibition of the IL-4-induced FcεR2 expression at both mRNA and protein levels. Also it was noted that MCN patients who went into remission with steroid therapy, then showed a reduction in expression of FcεR2 on their B cells. All this fits with the supposition of allergy in such patients. Indeed we know that successful hyposensitization of grass pollen-

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allergic subjects is accompanied by a reduction of CD23 expression on peripheral B cells [22].

To these findings one must add that Stachowski et al. [23] in Warsaw support the idea that there is a shift to Th-2 lymphocytes in children with MCN because when they cultured CD4 T cells with autologous monocytes that presented tetanus toxoid, production of cytokines, IL-4, and IL-6 and IL-10 was increased. Also, Neuhaus et al. [24] in London found that calcium ionophore stimulation

of lymphocytes from children with relapses of MCN often caused the release of large amounts of IL-4.

One has learned from the many studies of subjects with standard atopy that it is best to use freshly isolated lymphocytes that are stimulated with antigen in relatively short-term cultures with daily sampling of the elicited cytokines [19]. In this way one might soon know much more about the association between MCN and allergies.

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