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HLA Type in Minimal Lesion Nephrotic Syndrome (MLNS) in Childhood*

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Association of HLA antigens with certain diseases provide insights into genetically determined susceptibility to disease. Although nephrotic syndrome is one of the commonest diseases, it is poorly understood. A group of 57 patients suffering from a minimal lesion nephrotic syndrome (33 patients) and mesangioproliferative glomerulonephritis (24 patients) was studied for immunologic markers. The incidence of HLA-A w 24 is significantly greater in the minimal lesion nephrotic syndrome patients than in controls (18.7% in patients, 0% in controls, $p<0.01$). This report fails to show a high incidence of specific HLA antigen in mesangioproliferative glomerulonephritis patients. We believe that the high incidence of HLA-Aw 24 in minimal lesion nephrotic syndrome is indicative of a congenital predisposition to nephrotic syndrome.

Key Words: Minimal lesion nephrotic syndrome, Human Lymphocytes Antigen.

Although the minimal lesion nephrotic syndrome (MLNS) accounts for 80 to 90 percents of cases of the nephrotic syndrome in children, the etilogy is unknown. A review of the available data regarding immunity in nephrotic syndrome was published by Mallick (1977). Stühlinger *et al.* (1976) found nonspecific circulating immune complexes in nephrotic syndrome, but their significance was unclear. Several immunological diseases are known to be associated with HLA antigen (Ryder *et al,* 1979). Association of HLA Ag with certain diseases provide insights into genetically determined susceptibility to disease. Thomson *et al. (1976)* observed that atopic symptoms and HLA B_{12} Ag were more common in children with steroid responsive nephrotic syndrome than in adult controls. In order to examine the possible influence of the HLA system on the pathogenesis of MLNS, the association between HLA Ag and clinical and histopathological forms of the disease are looked for.

MATERIALS AND METHODS

A group of 57 patients suffering from MLNS and mesangioproliferative glomerulonephritis (MsPGN) were investigated. Diagnostic criteria of MLNS consist of massive proteinuria (0.1gm/kg/day) and hypoalbuminemia (<2.5gm/dl), generally with hyperlipidemia and generalized edema (Rance *et al,* 1976). Diagnostic criteria of MsPGN is a slight, diffuse increase in mesangial cells, together with a moderate increase in mesangial fibrils confirmed by renal biopsy. The diagnosis is: in 33 patients, MLNS; in 24 patients, MsPGN. Among 24 MsPGN patients, 14 patients, have the nephritis pattern and 10

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Table 1. HLA-A in Renal Diseases

Antigen	Controls		MLNS*		MsPGN** Nephritis		MsPGN** Nephrosis	
	No.	%	No.	%	No.	%	No.	%
Al	7	3.3	0	0	1	7.1	0	0
A2	131	61.3	13	40.6	11	78.6	5	50.0
A3	6	2.8	0	0	0	0	1	10.0
A9	102	47.6	8	25.0	8	57.1	2	20.0
A10	44	20.5	4	12.5	1	7.14	1	10.0
A11	25	11.7	6	18.8	3	21.4	2	20.1
A23	0	0	0	0	0	0	0	0
Aw24	0	0	6	18.7	2	14.3	1	10.0
A25	0	0	0	0	0	0	0	0
A26	0	0	0	0	1	7.1	1	10.0
A28	19	8.9	0	0	0	0	0	0
A29	0	0	4	12.5	1	7.1	1	10.0
A30	0	0	0	0	0	0	0	0
Aw32	0	0	1	3.1	0	0	0	0
Aw33	22	10.2	1	3.1	0	0	0	0
Blank	0	0	4	12.5	1	7.1	0	0
Total	214		33		14		10	

* Minimal lesion nephrotic syndrome.

** Mesangioproliferative glomerulonephritis.

patients have the nephrosis pattern. Thirty-four antigens of the HLA-A and B series are typed by the lymphocytotoxicity AMOS technique using antisera. Antisera which were confirmed at the International Histocompatibility Conference in 1977 are used (Huma type-filled typing tray from the Associated Biomedic System Inc.). Basis of statistical analysis is on differences between the respective frequencies of the involved antigen in the group of patients and a control group of healthy individuals. As control group healthy Korean individuals study of Chi *et al.* (1980) is used. Analysis was done with regard to the subgroups of patients with MLNS and MsPGN.

RESULTS

Table 1 and 2 show the respective frequencies of the HLA Ag between the group of healthy control individuals and the study group. HLA Aw 24 is increased in the group of MLNS patients than the control group. The difference is statistically significant ($X^2=7.25$, $p<0.01$). Increases of frequency of the HLA Ag (HLA A_{11}, Aw 24, A26, Blank, Bw 44) between the group of MsPGN and the group of healthy control individuals are not significant statistically.

DISCUSSION

The HLA system is important because it exists

Table 2. HLA-B in Renal Diseases

Antigens	Controls		MLNS*		MsPGN** Nephritis		MsPGN** Nephrosis	
	No.	%	No.	%	No.	%	No.	%
B5	58	27.1	5	15.6	5	35.7	0	0
B7	14	6.5	4	12.5	0	0	0	0
B8	3	1.4	0	0	0	0	0	0
B12	38	17.8	8	25.0	0	0	0	0
B13	20	9.3	3	9.4	2	14.3	0	0
B14	2	0.9	0	0	0	0	1	20.0
B15	64	29.9	11	34.4	2	14.3	3	30.0
B17	20	9.3	1	3.1	2	14.3	2	20.0
B18	0	0	0	0	0	0	1	10.0
Bw35	29	13.6	1	3.1	0	0	1	10.0
B27	8	3.7	3	9.4	1	7.1	0	0
Bw35	19	8.9	1	3.1	2	14.3	2	20.0
B40	58	27.0	8	25.0	6	41.9	2	20.0
Bw44	0	0	0	0	2	14.3	1	10.0
Bw51	0	0	1	3.1	0	0	0	0
Bw6	0	0	0	0	0	0	0	0
Blank	0	0	2	6.2	4	28.6	0	0
Total	214		33		14		10	

* Minimal lesion nephrotic syndrome.

** Mesangioproliferative glomerulonephritis.

on the 6th chromosome in close proximity to several genes known to be important in the immune system, including loci determining synthesis or deficiency of various components of complement and perhaps loci determining immune responsiveness (Mc Devitt and Bondmer, 1972).

For the pathogenesis of glomerulonephritis two different mechanisms can be involved, anti-glomerular basement membrane immunity and circulating immune complexes trapped in glomeruli (Frank, 1968). Other mechanisms including serum complement abnormalities are perhaps also of great importance (Mallick *et al.*, 1972). But immune complex deposition is probably a very common mechanism (Cameron and Turner, 1979). Patel *et al.* (1969) concluded that an HLA-A_2 positive person was about 1.5 times as likely to develop chronic glomerulonephritis as an HLA-A_2 negative person. Nyulassy *et al.* (1977) observed significant association between the HLA-Bw 35 Ag and the subgroup of nonstreptococcal (probably viral) Schönlein-Henoch nephritis. Although nephrotic syndrome is one of the commonest diseases, it is poorly understood. On the whole, there is no evidence that a humoral immunological process is involved. The association of nephrotic syndrome with an atopic disease (Thomson *et al.*, 1976). exacerbations coexisting with allergic manifestation (Wittig and Goldman, 1970) and protracted remission following desensitization to the pre-

sumed allergen (Sandberg *et al.*, 1977) have suggested that reaginic immunity could be involved. Trompeter *et al.* (1980) found a higher incidence of HLA-B_{12} in steroid responsive nephrotic syndrome of children than control. Alfiler *et al. (1980) rep*orted that the incidence of HLA-DRw7 is significantly greater in steroid responsive nephrotic syndrome patients than in controls and relative risk factor for HLA-DRw7 in steroid responsive nephrotic syndrome was 5.9. In this study, HLA-Aw 24 is significantly increased statistically in MLNS patients over that of control. The high incidence in males and the high incidence of certain HLA antigens are indicative of a congenital predisposition of nephrotic syndrome. However the rarity of familial steroid-sensitive nephrotic syndrome suggests that hereditary factors play but a minor role.

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