Studies on Streptococcal Type-Specific Antibody in Patients with Nephritis

TOSHIO NISHIMURA, NAOHIDE KUMAGAI, AND TACHIO KOBAYASHI

Using a hemagglutination technique, streptococcal type-specific antibody was studied in sera of patients with various types of nephritis. The close relationship between streptococcal infections and Ellis' Type I nephritis is presented.

THERE have been many studies implicating preceding streptococcal infection as a causative factor in acute glomerulo-nephritis.^{1-7,20} Since the advent of these studies there has been increased interest in streptococcal type-specific serum antibodies in patients with nephritis. The etiology of chronic diffuse glomerulo-nephritis still remains obscure. Any study that attempts to investigate the etiology of these various types of nephritis must consider infections, nephrotoxins, autoimmunity, renal circulation, etc.²¹. The purpose of this paper is to present evidence relating streptococcal infection and Ellis' Type I nephritis.

MATERIALS AND METHODS

Streptococcus: 42 of the 48 Lancefield's serological types of group A beta-hemolytic streptococci were used as previously reported.⁸

Hemagglutination: Modified BOYDEN's⁹ tannic acid hemagglutination technique¹⁰ was used as previously reported.⁸

Patient-sera: The blood was obtained from the patient's cubital veins, incubated for 30 minutes at 56°C in a water-bath, stored frozen at -20°C, and used by melting at room temperature as necessary. The cases were as follows: (i) 17 cases of acute diffuse glomerulonephritis, (ii) 4 cases of healthy persons having a past history of acute diffuse glomerulonephritis with complete recovery, (iii) 18 cases of chronic diffuse glomerulonephritis including 13 cases without nephrotic syndrome, and 5 cases with nephrotic syndrome, (iv) 2 children with lipid nephrosis,

(v) 8 cases of diabetic nephropathy, (vi) one case of nephropathy of pregnancy, (vii) 3 cases of lupus nephritis, (viii) 5 cases of a uremic stage of chronic nephritis, (ix) 273 cases of other diseases, (x) 73 healthy persons without past history of nephritis.

RESULTS

1. The number of serological type of group A beta hemolytic streptococcal type-specific antibodies with titers of 1 : 384 or above were increased in acute diffuse glomerulonephritis having high ASL-O (more than 500 Todd units) and in chronic diffuse glomerulonephritis without nephrotic syndrome, as shown in Table I and II.
2. High titers (1 : 384 or above) were observed in 4 of the 7 cases with acute diffuse glomerulonephritis having high ASL-O titers (more than 500 Todd units), in 2 of 4 healthy persons having a past history of acute diffuse glomerulonephritis with complete recovery, 10 of 13 cases with chronic diffuse glomerulonephritis without nephrotic syndrome, 1 of 5 cases with chronic diffuse glomerulonephritis with nephrotic syndrome, and 2 of 3 cases with lupus nephritis, as shown in Table III.
3. No correlation was observed between the number of serological type with high titers (1 : 384 or above) and Todd units of ASL-O, as shown in Fig. 1.
4. The frequency of serological types with high titers (1 : 384 or above) found in sera of patients with acute and chronic nephritis of Ellis' Type I

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The forth Department of Internal Medicine, Faculty of Medicine, University of Tokyo, Tokyo, Japan.

TABLE I NUMBER OF STREPTOCOCCAL SEROLOGICAL TYPES HAVING HIGH TITERS
(1 : 384 OR ABOVE) IN PATIENT-SERA OF VARIOUS DISEASE GROUPS

Diseases	Number of Serological Types							Total cases
	0	1	2-3	4-5	6-7	8-9	10	
<i>Nephritis of Various Etiology</i>	39	7	3	6	2	1		58
<i>Rheumatic Fever</i>	19	5	6	4	1	1		36
<i>Rheumatic H. D.</i>	8	8	23	10	2	2		53
<i>Other Heart D.</i>	31	7	5	2				45
<i>Scarlet Fever</i>	39	1	3	3				46
<i>Rheumatoid Arthritis</i>	35	6	10	2			1	54
<i>Simple Arthritis</i>	8	1						9
<i>Alveolar Pyorrhoe</i>	15	3						18
<i>Other Diseases</i>	7	5						12
<i>Apparently Healthy Persons</i>	61	11	1					73
Total								404

Fig. 1. Comparison of number of streptococcal serological types having high titers (1 : 384 or above) and ASL-O (Todd u.) in diffuse glomerulonephritis.

is shown in Table IV. Type 10 and Type 12 were observed in 11 cases of 16 cases of Ellis' Type I nephritis, as shown in Table IV.

DISCUSSION

Although the classifications of nephritis differed according to investigators, a distinction has been drawn by many investigators between two main types within the group of diffuse nephritis. The first is the acute, usually recoverable, hemorrhagic type. While the second is the insidious, usually chronic nephritis associated with general-

ized edema. ELLIS¹¹ stated that, based on clinical and pathological studies over a twenty year period, the two types of nephritis differed in their relation to preceding infection, in their pattern of clinical symptoms, in course and prognosis, and in the character and reversibility of renal histological changes. A further clinicopathological study of DAVSON and PLATT¹³ provided support for ELLIS' classification. WILSON¹² was of the same opinion. JENINGS¹ proposed a term of post-streptococcal glomerulonephritis. We found a number of serological types of group

TABLE II NUMBER OF STREPTOCOCCAL SEROLOGICAL TYPES HAVING (1 : 384 OR ABOVE) IN PATIENT-SERA OF VARIOUS TYPES

Types of Nephritis			0	1	2
Ellis' Type I	Acute Diffuse Glomerulonephritis	ASL-O $\leq$ 333 Todd U.	10		
		ASL-O $\geq$ 500 Todd U.	3		
	Past History of Acute Diffuse Glomerulonephritis and Complete Recovery		2	1	1
Ellis' Type II	Chronic Diffuse Glomerulonephritis	Without Nephrotic Syndrome	3	5	
		With Nephrotic Syndrome	4		1
	Lipoidnephritis (Child)		2		
	Diabetic Nephropathy		8		
	Toxemia of Pregnancy		1		
Other Nephritis	Lupusnephritis		1	1	1
Uremia			5		
TOTAL					

TABLE III THE HIGHEST TITERS OF STREPTOCOCCAL TYPE-SPECIFIC ANTIBODY IN

Types of Nephritis			1 : 192	1 : 384	1 : 768
Ellis' Type I Nephritis	Acute Diffuse Glomerulonephritis	ASL-O $\leq$ 333 Todd U.	10		
		ASL-O $\geq$ 500 Todd U.	3		3
	Past History of Acute Diffuse Glomerulonephritis and Complete Recovery		2	2	
Ellis' Type II	Chronic Diffuse Glomerulonephritis	Without Nephrotic Syndrome	3	4	3
		With Nephrotic Syndrome	4		1
	Lipoidnephritis (Child)		2		
	Diabetic Nephropathy		8		
Other Nephritis	Toxemia of Pregnancy		1		
	Lupusnephritis		1	1	1
Uraemia			5		
TOTAL					

A beta hemolytic streptococcal type-specific antibodies with high titers in sera of patients with nephritis of Ellis' Type I, i.e., acute diffuse glomerulonephritis having high titers of ASL-O and

chronic diffuse glomerulonephritis without nephrotic syndrome. The reason for the increased number of serological types with high titers in Ellis' Type I nephritis may be accounted for by

HIGH TITERS
OF NEPHRITIS

Number of Serological Types						
3	4	5	6	7	8	Total
						10
	1	1	1		1	7
						4
	1	3	1			13
						5
						2
						8
						1
						3
						5
						58

VARIOUS TYPES OF NEPHRITIS

Titer of Antibody				
1:1500	1:3000	1:6000	1:12000	Total
				10
			1	7
				4
3				13
				5
				2
				8
				1
				3
				5
				58

the superimposed streptococcal infections, hypersensitive state of these patients against streptococcal antigens or anamnestic reaction of the past streptococcal infections. In acute diffuse

TABLE IV FREQUENCY OF STREPTOCOCCAL SEROLOGICAL TYPES HAVING HIGH TITERS (1 : 384 OR ABOVE) FOUND IN PATIENT-SERA OF ELLIS' TYPE I NEPHRITIS

Type 10 or Type 12	is found in	11 cases out of 16
Type 18	is found in	8 cases out of 16
Type 3	is found in	7 cases out of 16
Type 30	is found in	6 cases out of 16
Type 1	is found in	5 cases out of 16
Type 44	is found in	5 cases out of 16
Type 6	is found in	4 cases out of 16
Type 37	is found in	1 cases out of 16
Type 40	is found in	1 cases out of 16
Type 46	is found in	1 cases out of 16

glomerulonephritis having low ASL-O titers the type-specific antibodies were not high enough to be accepted as type-specific, i.e., 1 : 384 or above. It may have been too early to develop type-specific antibody or dependent on the strains of the preceding streptococcal infections, or causative agents other than streptococcus.

The frequency of the serological types of group A beta hemolytic streptococcal type-specific antibodies with high titers found in sera of patients in Ellis' Type I nephritis differs from that of patients with rheumatic fever and rheumatic heart diseases⁸ and from that of patients with scarlet fever¹⁹ as previously reported^{8,19} and does not accord with the frequency of serological types reported in throat cultures from patients with scarlet fever^{17,18} in Tokyo. This discrepancy may have resulted from many factors, i.e., the different nephritogenic capacity of each strain, different capacity of serological types to produce M-proteins, responses of patients against streptococcal infections, or serological types prevalent in epidemics when the investigations were performed, etc. . . . It is reasonable that type-specific antibody of Type 10 and 12 were most frequently encountered in sera of patients with Ellis' Type I nephritis since Type 10 and Type 12 were reported¹⁴ as having common antigenic M-proteins, and Type 12 is assumed as the most nephritogenic by RAMMELKAMP^{4,22} and other investigators.^{15,16}

Our present investigations based on streptococcal type-specific antibody did not demonstrate clearcut results, but it suggested a close relationship between Ellis' Type I nephritis and streptococcal infections.

CONCLUSION

Using a hemagglutination technique, streptococcal type-specific antibody was studied in the sera of patients with various types of nephritis. Antibodies against Type 12 and 10 were most frequently encountered in sera of patients with Ellis' Type I nephritis. The close relationship between streptococcal infections and Ellis' Type I nephritis is presented.

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