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Effect of Hepatitis B Virus Infection of Membranous Nephropathy††

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=Abstract=To elucidate the effect of HBsAg on MN, 107 cases of MN admitted to SNUH from 1979 Jan. to 1985 Dec. were evaluated according to the markers of HBV.

Positive rate of HBsAg in MN was 48% which was higher than normal population and primary GN. Males were affected 4 times greater than females. MN with HBs antigenemia differed from MN without the antigen by having a lower incidence of nephrotic syndrome and azotemia. Serologically, positive rate of rheumatoid factor, ANA and rate of C4 decrement was higher in HBsAg positive patients, indicating the active participation of immune responses. Light microscopy demonstrated MPGN III-like lesions showing subendothelial deposit and double contour with mesangial hypercellularity, segmental change, tubular atrophy and interstitial fibrosis. Immunofluorescent microscopy showed frequent deposits of IgA and IgM in HBsAg positive group, and HBsAg, HBcAg were demonstrated in 76.9% and 31.4% of them.

Although the exact pathogenesis is not clear, the participation of multiple antigen and antibody system including HBsAg and HBcAg was clear, as well as the participation of hepatic dysfunction caused by liver cirrhosis on immune complex of rheumatoid factor, IgA deposit, subendothelial deposit have been proved to meet a concerted effect in the characterization of HBsAg related MN showing lupus-like features.

Key word: ***Hepatitis B virus, Membranous nephropathy***

INTRODUCTION

Most of the patients with membranous nephropathy (MN) do not present with any known causes, about 30% of them are associated with systemic illnesses such as sarcoidosis, malignancies, drugs or infections.

Hepatitis B virus (HBV) infection as a cause of MN was first demonstrated by Combes *et al.* (1971), who proved the existence of HBsAg in a glomerulus by indirect immunofluorescent method. Thereafter, HBsAg, HBcAg (Slusarczyk 1980) and HBeAg (Takekoshi 1979, Ito 1981, Fruse 1982, Collins 1983) depeosited in glome ruli had been proved, and this idea has been advanced that immune complexes formed by the BHBV antigens are deposited on the epithelial side of glomerular base ment membrane (Kohler 1973).

Although this causal relationship between HBV infection and MN is well established its clinical and pathological characteristics remained uncertain because most of the reports had been limited in number and to the pediatric patients. In Korea, where the positive rate of HBsAg is 5 to 12% (Kim 1975, Ahn 1983, Yu 1984) among the general population, it seems likely that many cases of MN which had been considered as idiopathic could well be the result of secondary lesions to HBV infection. If this could be proven it would lay an important ground on which the clinical and patho-

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logical differences between the idiopathic and HBV related MN could be better understood, especially in explaining the features of MN in Korea.

To elucidate the relationship of HBV infection to MN, we investigated clinical and pathological findings of MN patients based on studies of the patterns of HBV markers.

PATIENTS AND METHODS

1. Patients

107 patients of MN and 11 patients with lupus nephritis WHO class V membranous lupus were included for observation. The selection criteria were those diseases such as neoplasms, diabetes, amyloidosis or syphilis. Systemic lupus erythematosus was diagnosed by American Rheumatism Association (ARA) criteria. Pathological criteria for MN were to Ehrenreich and Churg (1968). these criteria are:1) thickening of glomerular capillary wall;2) absence of intra or extracapillary proliferation and exudation; and 3) demonstration of subepithelial and/or intramembranous deposit. Foca cell proliferation were included.

The patients were divided into four groups according to the paterns of HBV markers as follows:

Group I : HBsAg, HBsAb and HBcAb are all negative

Group II : HBsAg is negative, HBsAb and/or HBcAb are positive

Group III: HBsAg is positive regardless of the results of HBsAb or HBcAb tests

LN Class V: Lupus nephritis WHO Class V

Accordingly, 16 patients (15.0%) were Group I, 40 patients (37.4%) were Group II, and 51 patients (47.7%) were Group III (Fig. 1).

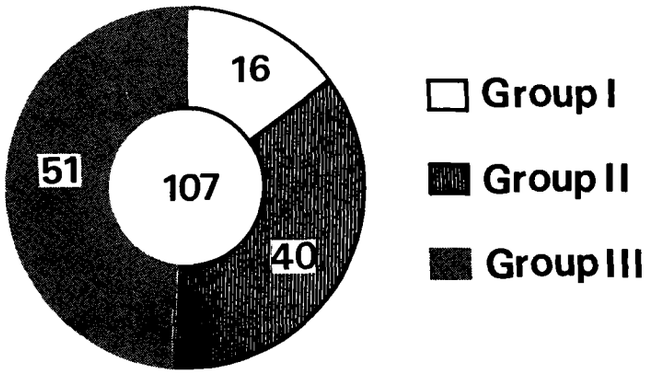

Fig. 1. Groups of MN according to the HBV markers (Group I: HBsAg, HBsAb, HBcAb are all negative; Group II: HBsAg is negative, HBsAb and/or HBcAb are positive; Group III:HBsAg is positive regardless of the results of HBsAb or HBcAb).

2. Methods

clinical data were obtained by retrospective study of historical medical records. Hypertension was defined as diastolic pressure>90mmHg. Proteinuria was evaluated with 24-hour quantitative measurements performed on most patients, and nephrotic syndrome was defined as proteinuria > 0.05 g/kg/day. Hematuria was defined as centrifuged urine specimen containing>10 red cells per HPF.

On evaluation for clinical courses, patients who were followed-up for more than 25 weeks were included using the criteria mentioned by Noel (1979) with some modifications. Remission was defined as the total abscence of urinary abnormalities with normal renal function. Improvement was defined as disappearance of clinical symptoms, persisting mild proteinuria or hematuria with normal renal function. Progressive disease was defined as increment of serum creatinine level during the course of follow up.

Standard biochemical methods were used for the estimation of creatinine, protein, albumin, and cholesterol. HBsAg, HBsAb and HBcAb in the sera were tested with radioimmunoassay. Rheumatoid factor was measured with Latex test kit from Iatron company. To measure cryoglobulin, approximatly 5 ml of serum was incubated for 48 horus at 4°C. CH50 was measured by a hemolytic technique (Mayer 1961). C3 and C4 were determined by radial immunodiffusion using commercial anti C3 and anti-C4 serum (Behringwerke).

Liver biopsies were perfomed in 23 patients using Vim-Silverman needle.

The renal biopsy tissues obtained by percutaneous needle biopsy were evaluated with light microscopy and with immunofluorescence in each case; in selected cases, electron microscopy was also used. Specimens for light microscopy were fixed with Zenker's solution, embedded in paraffin, and cut into 2 μ sections. Sections were stained with hematoxylin and eosin, periodic acid-Schiff (PAS), silver-methanamine (PASM) and Masson's trichrome. A portion of renal tissue was embedded in OCT compound (Lab-Tek Oroducts) and snaped frozen in dry-ice and acetone. The forozen sections of 4 μ thickness were stained with fluorescien-isothiocyannate FITC conjugated antisera to human IgG, IgM, IgA, C3 and fibrinogen (Hyland, Costa Mesa, Co.) in frozen tissues prepared as above. Goat anti-HBsAg and rabbit anti-HBcAg were used

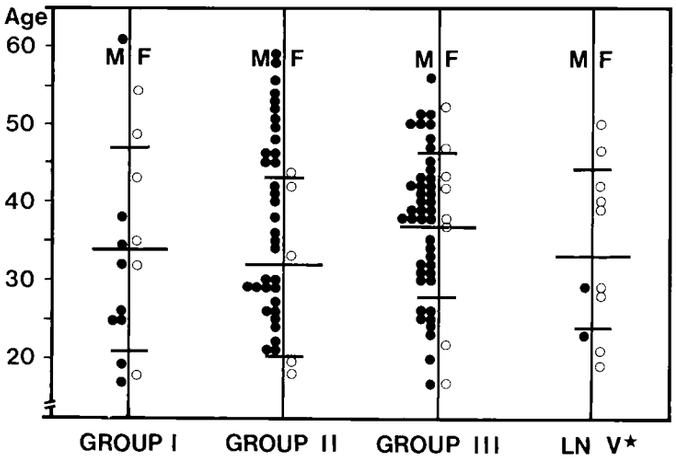

Fig. 2. Age and sex distribution of MN cases according to the HBV markers (mean ±SD, *LM class V: lupus nephritis class V).

for primary antibodies. Tissues for electron microscopy were fixed in glutaraldehyde, post-fixed in osmium and embeded in Epon. Ultrathin sections were cut on an LKB ultramicrotome, stained with lead citrate and uranyl acetated and examined on a TelsaBS 613 electron microscope. Abnormalities were graded semiquantitatively on a scale of 0 to 3 $^{+}$, as well as classified according to the criteria of Ehrenreich and Churg (1968).

RESULTS

1. Age and sex distributions

The mean age of Group I was 34.3 (range; 18-59) yr, Group II, 31.8 (range; 17-56) yr and Group III, 37.4 (range; 17-62) yr. Although there were no differences in age between the groups, the male to female sex ratio showed a higher incidence in male in Group II and Group III compared with that of Group I (Fig. 2).

2. Clinical findings

The incidences of clinical findings on admission had no differences among the groups (Table 1).

3. Laboratory findings

The massive proteinuria defined by 24 HU protein>50 mg/kg were found in 81.3% of Group I, 65. 0% of group II and 28.5% of group III. Hypercholesterolemia was observed at 81.3%, 55.0% and 46.9% of Group I, II and III, respectively (Table 2). In Group III, SGOT was elevated in 52.6%(20/38), SGPT in 56.4%(22/39), and HBeAg was found in 81.0%(34/42). Liver disease was confirmed in 27 patients by biopsy or endoscopy. The distribution of liver diagnosis were; AVH 1 case, CAH 8 cases, normal 1 case, CPH 8 cases and LC 9 cases.

Table 1. Clinical findings of the patients with membranous nephropathy on admission(%)

Clinical findings	Group I	Group II	Group III	LN classV**
Hypertension(>140/90)	25.0	35.0	33.3	13.6
Edema	62.5	75.0	66.7	54.6
Oliguria(<500ml/d)	12.5	27.5	11.8	54.6
Gross hematuria	25.0	25.0	27.5	9.1

*LN classV: lupus nephritis WHO Class V

Table 2. Laboratory findings of patients with membranous nephrophathy on admission (% abnormal)

Laboratory Findings	Group I	Group II	Group III	LN classV**
Creatinine>1.4mg/dl	50.0*	22.5	23.5	26.4
24 HU Prot>0.05g/kg	81.3*	65.0*	28.6	36.4
Hematuria>10/HPF	56.3	35.0	56.9	72.7
Reversed A/G Ratio	56.3	37.5	43.1	72.7
Albumin<2.5g/dl	50.0	50.0	33.3	72.7
Cholesterol>270mg/dl	81.3*	55.0	46.9	36.4

*$p<0.05$, compared with Group III

**LN class V: lupus nephritis WHO classV

Table 3. Serologic findings of the patients on admission(% abnormal)

Serology	Group I	Group II	Group III	LN classV**
Rheumatoid Factor	0.0*	3.6*	36.4	18.2
Cryoglobulin	16.7	23.5	13.5	55.6
ANA	0.0	0.0*	7.4	54.6
Complement 3	0.0	0.0	4.1	72.7
Complement 4	0.0	0.0*	15.6	72.7
CH50	28.3	12.1*	39.0	77.8

*$p<0.05$, compared with Group III
**LN class V: lupus nephritis WHO classV

Table 4. Clinical course of the patients who were followed-up for more than 25 weeks (number of patients(%))

Clinical course	Group I	Group II	Group III	LN classV**
Remission	3(30.0)	5(16.2)	3(10.3)	1(14.3)
Improved	4(40.0)*	14(45.2)	1(3.4)	1(14.3)
Stable	2(20.0)	7(22.6)	19(65.5)	5(71.4)
Progress	1(10.0)	5(16.1)	6(20.7)	0(0.0)
Total	10	31	29	7

*LN class V: lupus nephritis class V

The serologic profile of group III showed the following characterisitics: a difference in RA positive rate compared with group II, and the reduction rate of C4 and CH50 were more common than in group II (Table 3).

In Group III, RA postitivity was related to liver cirrhosis and decrement in C4($P<0.05$*). Among 22 patients upon whom both RA test and liver diagnosis were performed the incidences of liver cirrhosis was 44% (4/9) for RA positive group, but 8%(1/13) for RA negative group. C4 was reduced in 33% (5/15) of RA poitive patients but 7% (2/21) in RA negative patients. Among 7 patients with decreased C4 levels, 5 had positive results for rheumatoid factor. Cryoglobulin or HBeAg test results showed no correlation with the results for rheumatoid factor or complement levels.

4. Clinical course

As the average periods from disease onset to the performance of renal biopsy were 9.2 months for group I, 16.2 months for group II, and 20.4 months for group III, there were no statistical differences among the groups.

The clinical courses for the patients who were followed-up for more than 25 weeks also showed no statistically significant difference among groups in the remission or the progression rate (Table 4). Six progressed patients of group III showed higher incidence of azotemia (66.7%) than the patients whose renal function were normal (8.9%) upon admission, and the incidences of hypertension,

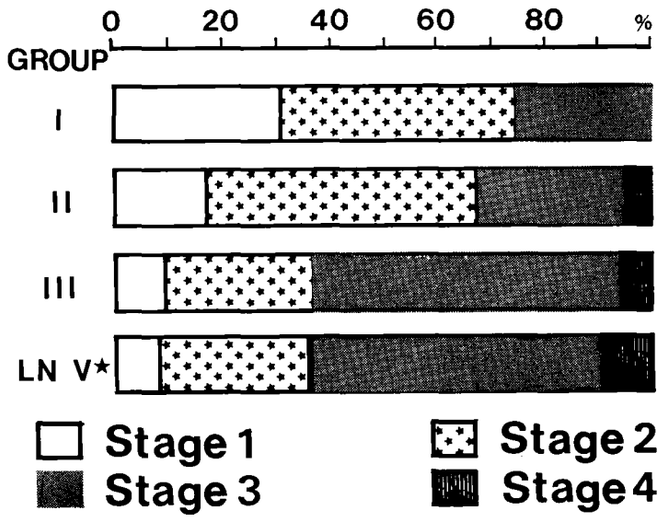

Fig. 3. Stage of MN of the 107 patients and 11 lupus nephritis class V cases.

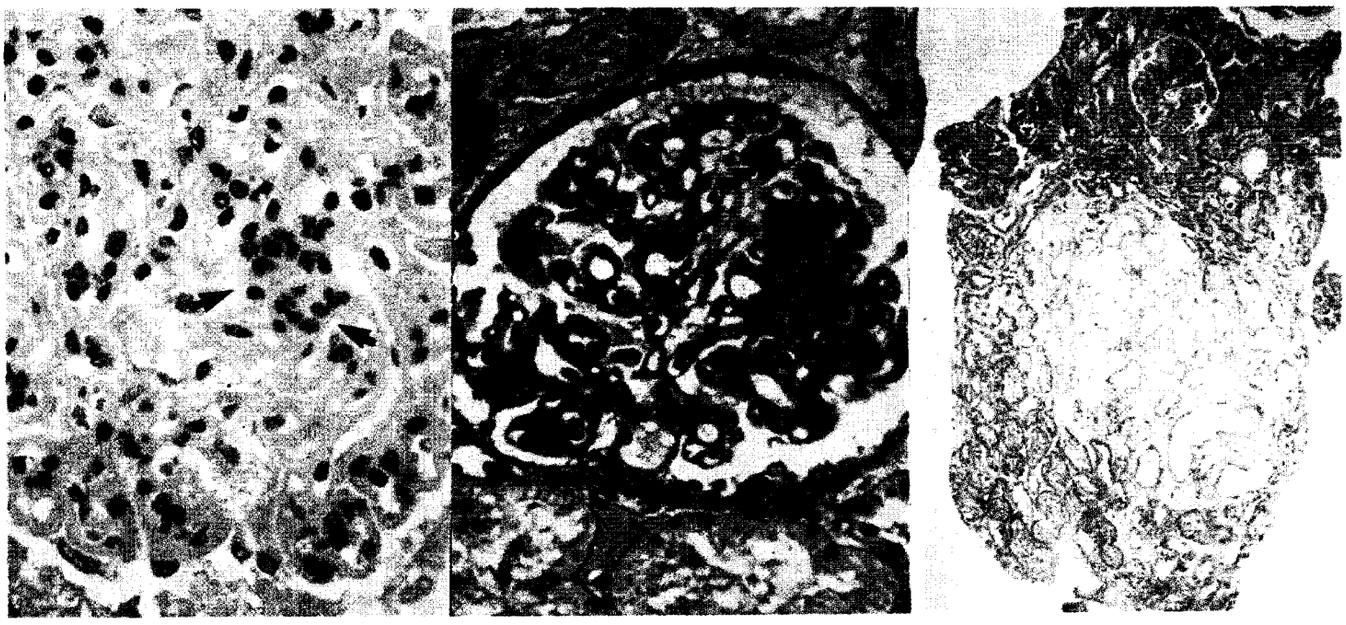

Fig. 4. Light microscopic findings of group III showing mesangial hypercellularity (right), segmental sclerosis(middle) and tubular atrophy(left).

Table 5. Light microscopic findings of patients in each group (% abnormal)

Findings	Group I	Group II	Group III	LN classV**
GLOMERULUS				
Size	43.8	65.0	52.9	45.5
Hypercellularity	0.0	2.5	13.7	45.5
Mes. expansion	31.3*	32.5*	68.6	100.0
Duplication	25.0*	15.0*	82.3	63.6
Segmental sclerosis	18.8	15.0	31.4	18.0
Cresent	6.3	5.0	5.9	36.4
TUBULE				
Atrophy	18.8*	17.5*	47.1	54.6
INTERSTITIUM				
Edema	37.5	27.5	43.1	81.8
Inflammation	31.3	32.5	29.4	90.9
Fibrosis	12.5	12.5	25.5	36.4

*$p<0.05$, compared with Group III

severity of proteinuria or the stage of MN gave no stastistically meaningful differences compared with other patients.

5. Morphologic findings

In accordance to the stage of MN classified by Ehrenreich and Churg (1968) advanced lesions of stage II and IV were 25% in Group I, 32.5% in Group II and 62.7% in group III (Fg. 3).

On light microscopic examination, group III was conspicuous from Group I and II in respect to showing frequent mesangial hypercellularity, mesangial expansion, duplication of capillary walls, segmental changes, tubular atrophy and interstitial fibrosis (Fig. 4, Table 5).

The site of electron-dense deposits evaluated by light and electron microscopy showed massive deposits in subendothelial and mesangial area in Group III. This observation suggested that Group III be divided into two subgroups according to the main site of the deposits, that is, mainly subepithelial (ClassV) and subendothelial(Class IVa). Thirty patients were belonged to the former (Lee's class

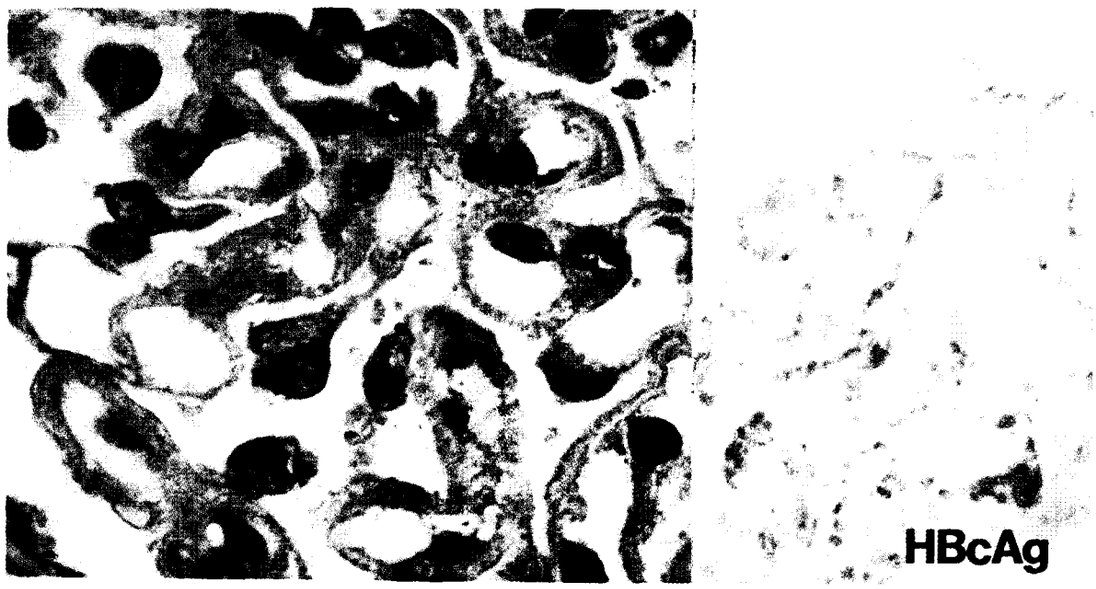

Fig. 5. Morphologic findings of a patient in group III showing classical findings of MN (Lee, SH)

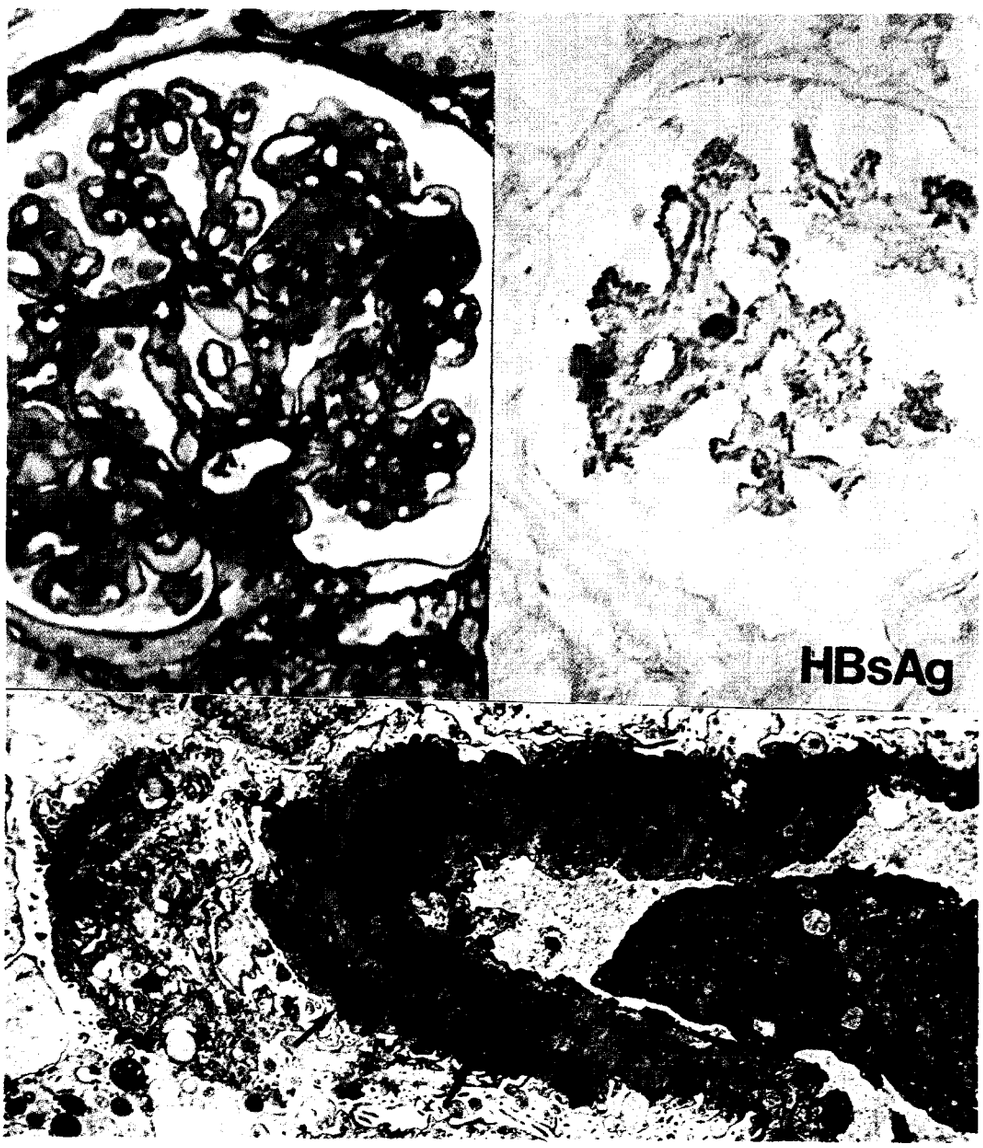

Fig. 6. Findings of a patient in group III showing massive subendothelial deposit, as well as subepithelial deposit (Kim IS)

Table 6. Site of deposit confirmed by light and electron microscopic examinations(%)

Site of deposit	Group I	Group II	Group III	LN classV**
Subepithelial	100.0	100.0	94.2	100.0
Mesangial	18.8*	22.5*	80.4	90.9
Subendothelial	18.8*	12.5*	71.6	72.7

*$p<0.05$, compared with Group III

Table 7. Immunofluorescent findings of the patient(% deposit more than 1+)

Antibody		Group I	Group II	Group III	LN classV**
IgG	capillary	82.8	96.2	86.4	80.0
	mesangium	0.0	3.9	11.4	20.0
IgM	capillary	18.2*	23.0*	56.8	30.0
	mesangium	0.0	3.9	22.7	30.0
IgA	capillary	0.0*	11.5*	36.4	70.0
	mesangium	0.0	0.0*	18.8	20.0

*$p<0.05$, compared with Group III
**LN class V: lupus nephritis WHO class V

Table 8. Positive rates of HBsAg and HBcAg demonstrated by PAP method in group III(number of patients(% positive))

		Tested	Positive	Positive Rate
HBsAg	capillary	26	20	76.9%
	mesangium		13	50.0%
	total		20	76.9%
HBcAg	capillary	28	9	31.4%
	mesangium		8	28.6%
	total		13	46.4%

Table 9. Effect of LC on MN group III (chi square test)

	C4		RA Factor		IgA(Cap)		IgA(Mes)		Class IVa*	
	+	−	+	−	+	−	+	−	+	−
LC*	1	6	4	1	6	2	4	4	7	1
nonLC	3	12	5	12	4	9	0	13	7	11
X^2	0.10		4.09		3.88		8.03		3.63	

*Class IV: MN with extensive subendothelial deposits without mesangial, endocapillary or mesangiocpillary proliferations.

V, Fig. 5), and 28 patients to the latter (Lee's class IVa, Fig. 4). there were no clinical differences between the two including the ages, serologic results and clinical courses except for a higher association with LC in class IVa(<0.10, $X^2=3.63$).

On immunofluorescent microscopic examination, Group III showed higher rate of IgM and IgA deposit than those of group I and group II ($p<0.05$). The rates of mesangial involvement were found in 9.1% of Group I, 8.7% of Group II, and 36.4% of Group III($P<0.05$*).

In Group III, HBsAg was demonstrated in 76.9%(20/26), 20 in capillary, 13 in mesangium. HBcAg was found in 46.4%(13/28) of cases, 9 in capillary, 8 in mesangium 4 in capillary and mesangium (Table 8).

6. Relation to liver cirrhosis

To evaluate the effect of hepatic dysfunction on HBsAg related MN, above findings were studied in relationship to liver cirrhosis. Liver cirrhosis was frequently combined with rheumatoid factor positivity, IgA deposit and class IVa lesions. Cryoglobulin, ANA, and complements were not influenced by terminal liver disease (Table 9).

DISCUSSION

Hepatitis B virus ifection as a cause of MN is well defined by seroepidemiologic studies. The positive rate of HBsAg in MN is reported to be about 45% (Kleinknecht 1979, Nagy 1982), with a wide range of variations according to the region and the age of the study groups. However, the positive rates in MN were higher than control populations. We observed HBsAg in 48% of MN, which was higher than 5-12%(Kim 1975, Ahn 1983) of general population and 24% of primary glomerulonephritis (Ahn 1984). Among the 257 cases with glomerulonephritis with HBV antigen in their glomeruli reported in English literature, 148 cases (58%) were MN. This suggested that the association between MN and HBs antigenemia is more than casual.

The most outstanding difference among the groups was the sex difference. The male to female ratio in Group I was similar to those of other reports (Glasssok, 1986). Among the HBsAg related MN, more than 80% of male predominance has been reported (Takekoshi 1978, Kleinknecht 1979, Levi 1980, Hsu 1983, Vecchio-Blanco 1983, Myata 1984). Since the male to female ratio was high in both Group II and III in this series, and reported as 4:1 in HBsAg carriers in Korea (Ahn 1983), it suggested that the male preponderance could be attributed to higher chances of environmental exposure to the antigen or to possible association with cross reactivity between male sex antigen and HBsAg, rather than to association with the glomerulonephritis itself.

Eighty percent of MN is manifested by nephrotic syndrome (Mallik 1983) and this also applies to HBsAg related MN in pediatric patients (Takekoshi 1978, Kleinknecht 1979, Hsu 1983, Seggie 1984). In diagnosing NS in patients with liver disease, there are difficulties in determining the diagnostic standard, because serum albumin level may be reduced and the increase of serum cholesterol level may not be marked in the presence of liver disease. Therefore we made the diagnosis of nephrotic syndrome based on the definition of syndrome as 24 HU with protein more than 0.05g/kg, and on such bases Group III included 29% of nephrotic syndrome, which was lower than Group I or II. Azotemia was rare in Group III in spite of higher incidences of advanced lesions of MN stage III and IV in Group III compared with Group I and II. Other differences in clinical findings were negligible.

Proper evaluation of clinical course was impossible, because there were only few patients who were followed-up for more than 25 weeks. Slow or benign course in HBsAg related MN than in idiopathic group in pediatric patients (Wyznska 1979, Wiggelinkhuizen 1983) was reported as apparent. If it is true (Kleinknecht 1979) then age, in addition to azotemia would be a factor for prognosis. Remission with disappearance of circulating virus antigen (Knecht 1978, Luciani 1980, Nagata 1981, Yamashita 1985, Cadrobbi 1985) was not found in this series.

The complement levels in HBsAg related MN remain to be settled. While some reported hypocomplementemia, others did not (Combes 1971, Kohler 1974, Ainsworth 1974, Kamph 1978, CPC 1978, Kleinknecht 1979, Stratta 1979, Silver 1979, D'amico 1981, Nagy 1982, Cadrobbi 1985). The involved complements were C3(Takekoshi 1979, Cogan 1977, Yoshikawa 1985), C4 (Wieggelinkenhuisen 1983, Cadobbi 1985, Southwest Group 1985) or both (Scully 1982, Collins 1983). The mechanisms of hypocomplementemia in HBsAg related MN are likely due to i) consumption by immune complex formation(Thomas 1979) ii) decreased production in liver (Kourilsky 1973, Notch 1976) and there was no correlation between liver cirrhosis and hypocomplementemia, we ascribe

hypocomplementemia as secondary to increased consumption. However, the participation of dereased production could not be excluded unless radiolabelled complement test or measurement of acitation product were performed, as all of the 7 patients with C4 decrement had elevated SGOT and SGPT.

Chronic liver disease is known as one of the conditions showing more than 30% positivity for rheumatoid factor. Hepatocellullar disease in general shows 60-86% positivity and viral hepatitis 71 to 94% (Ziegenfuss 1971, Morris 1978). Some IgM rheumatoid factors comprised of HBsAg HBsAb or HBeAg containing immune complexes (Anderson-Visona 1980). A few case reports (Scully 1982, Collins 1983).

The morphological pictures in HBsAg positive MN can be characterized by mesangial expansion and cell proliferation, double contour, subendothelial and mesangial deposits, segmental changes, tubular atrophy, interstitial fibrosis, and IgM and IgA deposits. These features are not the same as in idiopathic MN previously reported (Porch 1973, Glassok 1986) except for the IgM deposit described in Row (1973) and in some series as being found in over 1/3 of biopsies. The lesions we observed showed much similarity with those of MPGN III except that there was no C3 decrease, mesangial interposition or marked diffuse hyper cellularity. Such findings were meaningful, however, cannot be a characteristic for HBs related MN, because the so-called "atypical", "mixed membranous and proliferative" or "intramembranous" membranous nephropathy had been mentioned in association with systemic disease (Cameron 1979). These features of MN with HBs antigenemia were prominent in some cases but in others the morphologic lesions were not different from the idiopathic type. Moreover, marked subendothelial and mesangial deposits were not frequently noted in MN with HBs antigenemia among the pediatric patients (Takekoshi 1978, Ito 1981, Fruse 1982). The 3 reports we found (Choi Y 1985, Yoshikawa 1985, Southwest 1985) with observation of subendothelial or mesangial deposits were by electron microscopy, and was different from our series, because they can be visualized clearly by light microscopy as well as electron microscopy. In adults, although the number of reported cases are few, mesangial cell proliferation (Combes 1971, Morzycka 1979, Scully 1982, Collins 1983, Myata 1984), subendothelial deposits, and mesangial deposits (Kohler 1974, Glassok 1982, Collins 1983) were frequently described.

The distinguishing factors noted are 1) age, 2) antigen involved, 3) route of infection, and 4) state of liver disease. As for age, there was no difference in mean age between MN according to its groups and subgroups of MN with HBs antigenemia differenciated by main site of deposition, i.e. subendothelial or subepithelial.

The involvement of the antigens, HBsAg, HBcAg and HBeAg were poroved in the literatures, but it is not settled as of yet which antigen plays the main role in provoking MN. In pediatric patients, the relation between HBeAg and MN was demonstrated, its pathogenesis appropriately described as being due to the size of immune complexes of HBeAg small enough to deposit subepithelialy provoking typical membranous lesions (Takekoshi, 1979). In adults, 7 out of 11 cases reviewed had HBsAg in their glomeruli (Combes 1971, Kohler 1974, Ainsworth 1974, Cogan 1977, Kamph 1978, D'amico 1981, Scully 1982, Collins 1983); this is different from pediatric cases in which demonstration of HBsAg is rare (Takekoshi 1979, Ito 1981, Fruse 1982), but well correlated with the PAP staining results of ours, which suggesting participation of the multiple antigen-antibody system of HBV infection including HBsAg and HBcAg operating simultaneously inducing morphologic features look like those of lupus nephritis.

The vertical transmission of HBV (Takekoshi 1979) and the severity of associated liver disease may participate also in the production of the characteristic lesion of HBsAg related MN. Mild liver disease was mentioned among the pediatric patients (Takekoshi 1979, Kleinknecht 1979, Hsu 1983), but not in adult cases (Kohler 1974 *et al.*). This series showed the effect of liver cirrhosis on immunologic markers such as rheumatoid factors, IgA deposit and subendothelial deposit. In literatures, it was reported that LC without HBs antigenemia was associated with mesangial changes (Eknoyan 1978, Morzycka 1979), mesangial (Eknoyan 1978), subendothelial deposits (Eknoyan 1978, Wilkinson 1982), double contour (Fisher 1959, Jones 1961, Notch 1976, Wilkinson 1982) or IgA deposit (Callard 1975, Eknoyan 1978, Berger 1978, Woodroffe 1981). These findings support the view that advanced liver disease probably plays a role in contributing to the lesion formation of HBsAg related MN; whether it provokes the formation or decreases the clearance of immune com-

plexes remains yet unclear. Had dealt with rheumatoid factor, and many had commented on the relation of HBV immune complex and cryoglobulinemia (McINtosh 1976, Notch 1976, Levo 1978, Tiku 1979). However, the positive rate in MN did not show any differences for each groups. Therefore, cryoglobulin as a marker for active disease in HBV related MN serves no meanings, but is rather related to proliferative lesions (Notch 1976 or induces glomerulonephritis of mixed essential cryoglobulinemia (Levo 1979, Kumer 1982, Lee 1983). ANA of which the positivity was by 14-65% (Jain 1976, Morris 1978) showed higher positive rate in Group III than Group I or II; may be reflect a active immune response, even though HBV induced immune complexes may not been single contributing factor (Boucher 1964).

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＝국문초록＝

HBV抗原 및 抗體有無에 따른 膜性絲毬體腎炎의 臨床 및 病理學的 所見의 比較硏究

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B형간염감염이 막성사구체신염에 미치는 영향을 알아보기 위하여, 1979년 1월부터 1985년 12월 사이에 서울대학교 병원 내과에 입원하여 신생검을 시행하여 막성사구체신염으로 진단받았던 107명과 낭창성 신염 class V 11명의 임상, 병리적 소견을 비교 검토하였다.

107례를 HBV 표식자에 따라 분류하면 HBsAg가 양성인 경우는 51례(47.7%)였고 HBsAg가 양성인 환자의 임상소견은 음성인 군에 비하여 신증후군과 혈증 크레아티닌치의 상승이 적었다. 혈청학적으로는, 양성인 군에서 rheumatoid factor, ANA양성률과 C4 감소율이 증가되었다. 병리조직학적으로는 mesangial, subepithelial deposit외에 subendothelial deposit이 상당수 관찰되었고 double contour, mesangium의 확장, 신세뇨관 상피의 퇴행성 변화가 빈번하였으며, 면역형광 검사상 IgA의 침착을 볼 수 있었다. HBsAg은 76.9%에서, HBsAg은 31.4%에서 PAP법으로 증명되었다.

HBV에 의한 막성사구체 신염의 병태생리에 관하여는 아직 잘 밝혀져있지 않으나, HBsAg와 HBcAg을 포함한 여러 항원항체계에 의한 면역 복합체가 관여할 가능성이 증명되었으며 아울러 간경화같은 만성 간기능 장애가 HBsAg유발성 사구체신염의 임상적 형태적 변화 특히 RA factor나 IgA침착에 관여할 것으로 사료되었으며 이와 같은 system의 복합작용은 낭창성 신염에서와 유사한 임상 병리적 소견을 나타내게 하는 것으로 생각된다.