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Glomerulonephritis Associated with Deposition of Heaptitis B Surface Antigen-Antibody Immune Complexes in Children*

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It has been reported that transient glomerulonephritis may accompany acute viral hepatitis[1] and chronic active hepatitis.[2] The accumulative evidence suggests that HB,Ag is closely related to a hepatitis virus.[3-6] The association of HB,Ag positive viral hepatitis with chronic glomeru lonephritis was recently described. In the patients deposits Hepatitis B antigen-containing immune complexes have been shown in arterioler and glomerular basementmembrane.[7,8]

During the past year we observed three patients with glomerulonephritis, in all of whom it had followed viral hepatitis. An attempt was made in all the patients to detect deposition of Hepatitis B antigen-antibody complexes in the kidney by the immunofluorescence technique.

Report of Cases

Case 1: (A. Y.) a two-year-old boy was admitted with the complaint of edema to Hacettepe Children's Medical Center on June 6,1974. He had a history of jaundice 3 months prior to admission.

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The pertinent phsyical findings on admission were edema and hepatomegaly. His blood pressure was 90/60 mm Hg. The following laboratory results were obtained: Proteinuria, 3-4 granular casts in the urine sediment. Blood chemical findings: BUN 10 mg/dl, total protein 3.9 g/dl, albumin 1.6 g/dl, total lipid 1550 mg/dl, cholesterol 320 mg/dl, SGOT 120 K. U., SGPT 30 K. U., complement C_3 10 mg/dl.

An intravenous pyelogram was normal. Percutaneous renal biopsy specimen showed epimembranous glomerulonephritis in light microscopy. Hepatitis B surface antigen was found positive in the serum.

Case 2: (O. B.) a 15-year-old boy who was admitted to our hospital with complaints of edema and vertigo, on Nov. 28, 1974.

Four months prior to admission he had had jaundice with dark colored urine and acholic feces. When he was admitted he had facial and pedal edema, which had started one month following the onset of jaundice; he also had a high blood pressure (140/100 mm Hg).

Laboratory findings: proteinuria and abundant RBC and WBC in the urine sediment. Serum chemical findings: BUN 134 mg/dl, creatinine 4.2 mg/dl, total protein 4.3 g /dl, albumin 2.1 g/dl, total lipid 750 mg/dl, cholesterol 185 mg/dl, SGOT 55 K.U., SGPT 44 K.U., C_3 level 68 mg/dl.

An intravenous pyelogram study showed bilateral paranchymal enlargement. Percutaneous renal biopsy specimen was diagnosed as subacute glomerulonephritis. Hepatitis B surface antigen was found negative in the serum.

Case 3: (O.F.) a two-and-a-half year-old boy was admitted with the complaint of edema, to the hospital on August 15, 1974. Physical examination upon admission showed edema, slight pallor and hepatomegaly. Blood pressure was 110/60 mm Hg. Laboratory findings included the following: BUN 20 mg/dl, total protein 4.7 g/dl, albumin 2.5 g/dl, total lipid 900 mg/dl, cholesterol 252 mg/dl, SGOT 110 K.U. SGPT 86. K.U. serum complement C_3 level 82 mg/dl, Proteinuria and 5-6 RBC were seen in the urine sediment.

An intraveneous pyelogram study was normal. A needle liver biopsy and percutaneous kidney biopsy showed hepatitis and membranous glomerulonephritis, respectively. Hepatitis B surface antigen was found positive in the serum.

Materials and Methods

Kidney-tissue specimens were obtained by percutaneous needle biopsy. A portion of each kidney biopsy specimen was examined routinely by light microscopy. The remaining portions were frozen immediately and 4-micron sections were cut in the cryostat; these were fixed with acetone for 10 minutes at room temperature and dried. The direct immunofluorescent method[9] was used for the detection of IgA, IgM, IgG and complement C_3 (β_1C). Indirect immunofluorescence technique[9] was used for the detection of HB_sAg in tissues. Tissue was obtained by liver biopsy from one patient (Case 3).

Serum samples were tested for the HB_sAg and antibody and the agar gel double immuno diffusion method was used (Ouchterlony).

Results

Serum HB_sAg was positive in two patients, but Hepatitis B antibody was found negative in all.

Liver biopsy was done in one patient in whom the clinical picture suggested the existence of aniteric hepatitis. In this patient histopathologic evidence of hepatitis was found by light microscopy. The results of immunofluorescent studies are shown in Table I. Immunofluorescence

TABLE I

HB_s ANTIGEN IN SERA AND THE RESULTS OF IMMUNOFLUORESCENT STUDIES.

	Serum		Kidney (Glomeruli)				
Cases	HB_sAg	Anti-HB_s	HB_sAg	IgG	IgM	IgA	$C_3(\beta_1C)$
1	+	−	+	+	−	−	+
2	−	−	+	+	−	−	+
3	+	−	+	+	−	−	ND

ND = Not done.

for HB_sAg and IgG were positive in the three kidney biopsy specimens. Complement component C_3 was carried out for Cases 1 and 2; They were stained by anti-complement C_3 labelled fluorescent, but this was not done in Case 3 for technical reasons. No fluorescence for IgM and IgA could be observed. Kidney staining (Case 1) is shown in Figures 1-3. Irregular granular deposits were seen in the glomerular capillary loops.

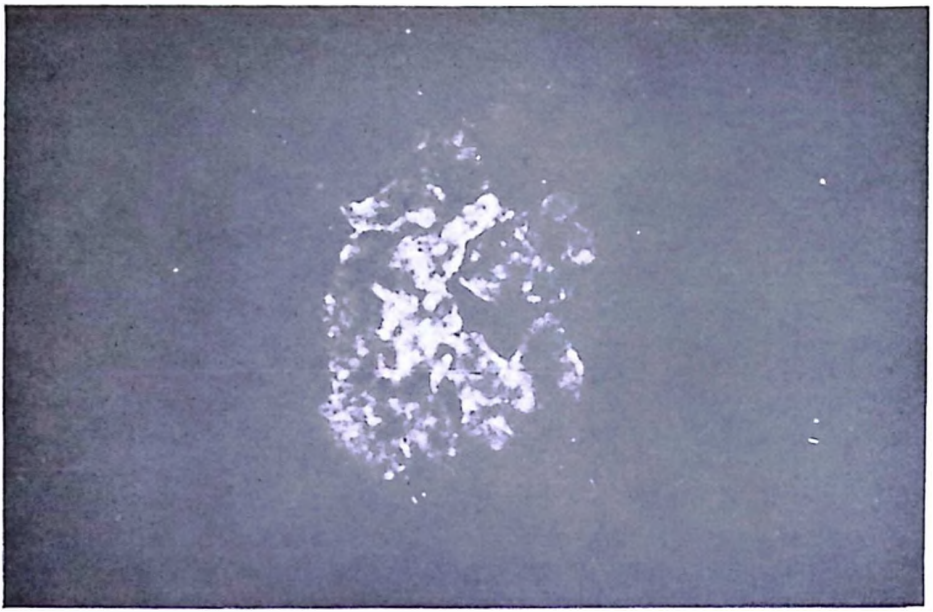

Figure 1
Frozen section of the kidney stained with fluorecein in conjugated anti-human IgG of the first patient, showing granular deposits along the glomerular capillary walls.

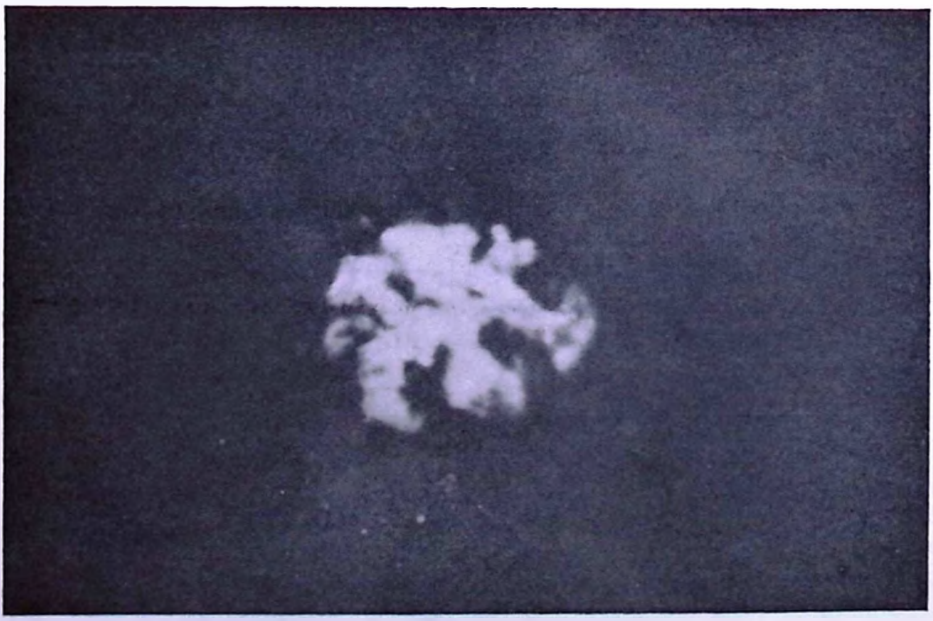

Figure 2
Section of the first patient's kidney stained for complement component C_3. Fluorescence along capillary loops.

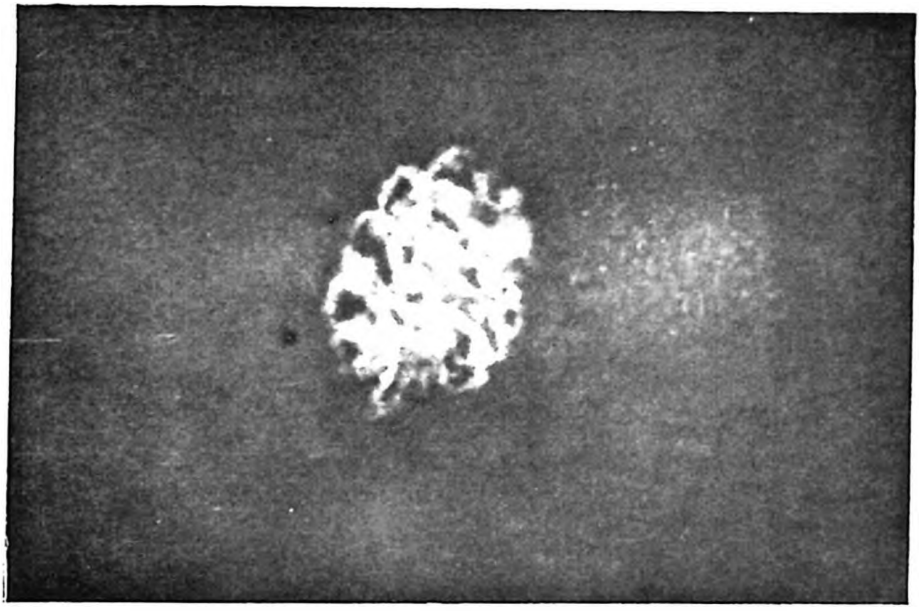

Figure 3
Section of the first patient's kidney stained for HB_sAg by the indirect immuno-fluorescent technique; there is heavy staining in the glomerulus

Discussion

The deposition of immune complexes in glomeruli is generally accepted as an important pathogenetic factor in the development of glomerulonephritis. As is well known, two different mechanisms have been proposed. The first depends upon the production of antigen-antibody complexes, which are subsequently trapped in the glomerular cappillary walls during filtration. The second mechanism involves the antigenic formation of infectious agents capable of reaction with the renal basement membrane tissue of the host.

Experimental evidence suggests that HB_sAg positive hepatitis may be associated with circulating immune complexes. Arthritis and urticaria associated with acute viral hepatitis deserves re-emphasis. The role of Hepatitis B antigen-antibody complexes in periarteritis nodosa has also been reported.[10]

The high frequency (20.3 %) of HB_s-antigenaemia in South African Bantus with chronic glomerulonephritis has been considered as an indication that HB_sAg immune complexes are involved in the pathogenesis of glomerul onephritis.[11] No characteristic glomerulonephritis type due to HB_sAg immune complexes has been described. It has been shown

experimentally that during the deposition of the immune complexes in the glomeruli the third component (C_3) of the complement is stored there, resulting in a lower C_3 level than normal in the patients' serum.

We studied three patients with glomerulonephritis, all of which were thought to have immune complex disease because of the deposition of IgG, HB_sAg, and C_3 in the glomeruli. Their serum complement levels were lower than normal; HB_sAg in the serum was found positive in two patients and the third one was negative. This negative result may however, reflect the insensitivity of our method. On the other hand, two of these three patients had a history of jaundice 3 and 4 months before the renal disease and the third patient had hepatitis which was confirmed by liver biopsy.

The possibility exists that our patients were exposed to Hepatitis B virus before the onset of renal disease. In accordance with these findings, we concluded that HB_sAg was the responsible antigenic agent in our three cases.

Summary

Deposition of immunoglobin G, HB_sAg and C_3 were shown by immunofluorescence in 3 kidney biopsy specimens from patients with clinical and laboratory diagnosis of glomerulonephritis. HB_sAg was found positive in the sera of two out of three patients. One of these patients had aniteric hepatitis and the others had a history of jaundice. The clinical features of the illness and laboratory data, support a role for Hepatitis B antigen in the development of the renal disease.

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