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An Allograft Kidney Showing Both Features of IgA Nephropathy and Membranous Glomerulonephritis

- A Case Report -

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We report a case of glomerular disease with both mesangial IgA and subepithelial IgG deposits in the allograft kidney. The patient was a 36 year-old man who had received a renal allograft 1 year previously. Fifteen days before admission, he discovered a microscopic hematuria without clinical evidences of allograft rejection. Light microscopy showed diffuse increase of mesangial matrix without mesangial cell proliferation. Capillary walls were diffusely and mildly thickened. Immunofluorescence microscopy demonstrated both granular deposits of IgA in the mesangium and IgG along the capillary walls. On electron microscopy, electron-dense deposits were identified not only in the mesangium but also on the epithelial side of the glomerular basement membrane.

Key Words : *IgA nephropathy, Membranous glomerulonephritis*

INTRODUCTION

IgA nephropathy(IgAN) has a feature of dense deposition of IgA in mesangium of glomerulus. Membranous glomerulopathy(MGN) is a disease with diffuse IgG deposition in the subepithelium of glomerular basement membrane(GBM). After renal transplantation, primary glomerulonephritis(GN) could recur or a new GN could be developed. IgAN or MGN is one of the most frequent diseases after renal transplantation, which is de novo or recurrent. Both GNs are rarely concurrent(Doi et al., 1983 ; Kobayashi et al., 1985 ; Magil et al., 1986 ; Jennette et al.,1987 ; Lai et al.,1987; Chen et al.,1988 ; Monga et al.,1990) and a few are thought to be related to hepatitis B(Magil et al.,1986 ; Lai et al.,1987 ; Chen et al.,1988 ; Monga et al.,1990). We experienced a case of the concurrent development of IgAN and MGN in a 36 year-old man with negative HBs antigen in the allograft kidney. Morphological features and possible mechanisms of this case are discussed.

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CASE REPORT

Case history : The patient was a 36 year-old male who received a renal allograft from a living unrelated donor in April 1991. There was one HLA-A and one DR antigen match. Original renal disease was unknown. He received hemodialysis for one month before transplantation. There was no episode of acute rejection. He was well until eleven months after transplantation, when he developed proteinuria. In Oct. 1993, he noticed microscopic hematuria. At this admission, serologic test revealed negative for HBs Ag, anti-HBc or HCV. Blood pressure was 170/100mmHg and urinalysis revealed 300mg/dl of proteinuria and microscopic hematuria. Blood urea nitrogen was 17.0mg/dl, and creatinine was 1.1mg/dl. A renal biopsy was performed.

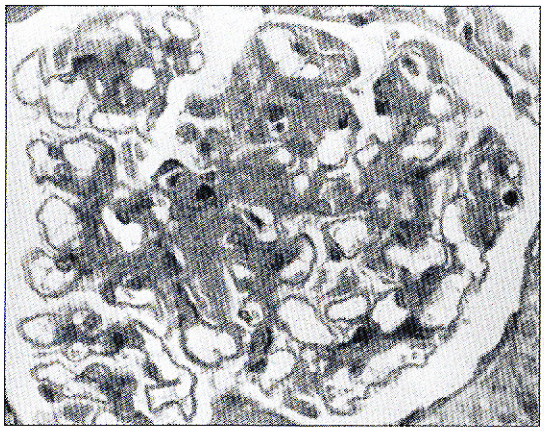

Fig. 1. The mesangial regions were expanded without increased mesangial cell proliferation.

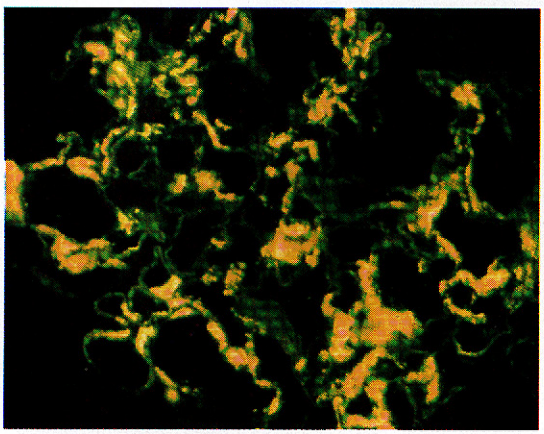

Fig. 2. Immunofluorescence microscopy showed nodular mesangial deposits of IgA.

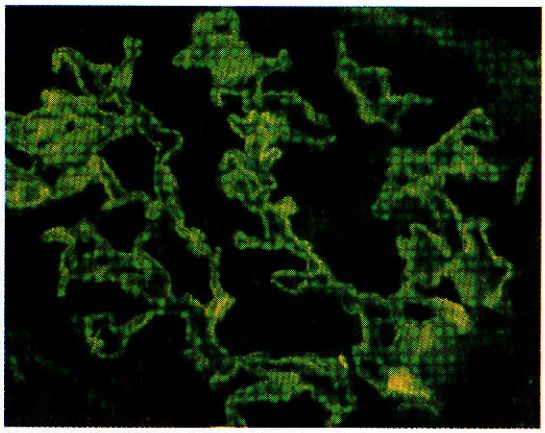

Fig. 3. Immunofluorescence microscopy showed weak granular pattern of IgG deposits along the capillary loops.

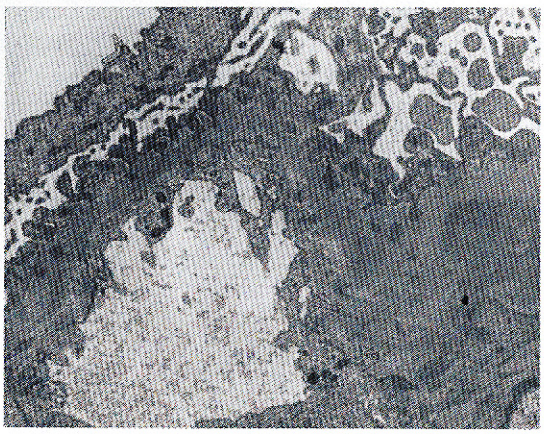

Fig. 4. Large amount of electron dense deposits were noted in the mesangium and small amount in the subepithelial side of glomerular basement membrane(×7500).

Light microscopic findings : A total of 17 glomeruli were present. The mesangial regions were slightly widened, but there was no proliferation of mesangial cells. The GBMs were diffusely thickened, but subepithelial spikes were not discernible on PAS-methenamine silver stain(Fig. 1). The features of acute rejection, such as tubulitis or vasculitis were not found. There was minimal focal tubular atrophy associated with interstitial fibrosis.

Immunofluorescence findings : IgG was diffusely deposited in the subepithelial side of peripheral capillary walls in a granular pattern. IgA was deposited in the mesangium as more coarse granules(Fig. 2 & 3). There were also a minimal deposits of IgM and C_3 in the mesangium.

Electron microscopic findings : A large amount of electron-dense deposits were observed in the mesangial regions. Evenly spaced small electron dense deposits were noted along the subepithelial and intramembranous portion of GBMs. Epithelial foot processes were diffusely effaced. But a new formation of basement membrane or spikes were not present(Fig. 4).

DISCUSSION

The chance of two GNs, having different and characteristic morphological and immunologic features, occuring simultaneously is rare. But there were a few reports of concurrences of MGN and crescentic GN, minimal

change disease and IgAN, IgAN and MGN. According to our native kidney biopsy data, the frequency of MGN was approxiamtely 8% and that of IgAN 18%(Choi et al., 1991). However, we could not find any such overlaping features in the native kidney or allograft kidney biopsy registry. This is the first case among over 300 cases of transplant biopsies in our experiences.

A total of thirteen cases of the concurrence of IgAN and MGN were reported in English literature (Doi et al., 1983 ; Kobayashi et al., 1985 ; Magil et al., 1986 ; Jennette et al., 1987 ; Lai et al., 1987 ; Chen et al., 1988 ; Monga et al., 1990). But they were all from native kidney. Eight cases were Oriental and five associated with hepatitis B surface antigenemia(Magil et al., 1986 ; Lai et al., 1987 ; Chen et al., 1988 ; Monga et al., 1990) and one with previous episode of viral hepatitis(Monga et al., 1990). The appearance of de novo MGN with recurrent IgAN after renal allograft has been reported once in France(Charpentier et al., 1982).

Whereas idiopathic MGN is characterized by the subepithelial immune deposition, MGN related to hepatitis B shows frequent immune complex deposition not only in the mesangium but also in the subendothelium (Margil et al., 1986 ; Chen et al., 1988). Therefore Chen et al.(1988) described this pattern as "HBV-associated membranous nephropathy with IgA deposits" instead of naming it as a "GN with a combination of MGN and IgAN".

This case and 7 other cases previously reported(Doi et al,. 1983 ; Yutaka et al., 1985 ; Jennette et al,. 1987), however, were negative for HBs Ag in neither the patient's serum or tissues nor any clues of the systemic disease associated. Because we had no knowledge of the primary renal disease in this case, it was difficult to decide whether the two forms of GN were recurrent or developed de novo. As for the possible pathogenesis, there are several hypotheses speculated. The first one is a chance occurrence of IgAN and MGN by two different mechanisms. One disease could have recurred while the other is newly developed. From a more general point of view, it includes a possibility that glomerular damage produced by one GN might favor the unmasking of previously protected glomerular antigen, the implantation of circulating antigens, or the deposition of nephritogenic immune complexes giving rise to the second(Monga et al.,1990). The incidence of de novo MGN is higher than that of recurrent form while IgAN recur in transplants in about 50%. There was the speculation that MGN might be initiated by the antigenic differences between the donor and the recipient. So, this patient was more likely to have recurrent IgAN and de novo MGN. The reverse senario, that is recurrent MGN and de novo IgAN, is possible also, although the possibility is much lower than that of the former. The second possibility is that both diseases could have recurred. The development of two patterns by one pathogenetic mechanism, or different but related mechanism is supported in hepatitis B associated disease. Magil et al.(1986) identified HBs antigen in the glomeruli of a case of IgAN and MGN and tried to document the role of this antigen in the development of the two GNs. But, up to date, concurrence of IgAN and MGN as a primary GN was rarely reported, so the recurrence seemed to be extremely rare. Furthermore, our case was negative for hepatitis markers. The third possibility is that both diseases could have newly begun. There could be an unknown immunologic response of IgG and IgA to an undetectable antigen which may lead to a GN with two features. But hardly any evidence supported this possibility.

IgAN can be developed de novo. However, we suspect this lesion to be a recurrence because the patient had an IgA deposit more than 2yrs post-transplantation, and no evidence of liver disease, and other systemic disease before or after transplantation, which was known to be related with mesangial IgA deposition. Considering an extremely rare coexistence of IgAN and MGN in our material, absence of infection and well known description of de novo MGN after transplantation, we think the chance occurrence of MGN and IgAN was the most likely apparent different operating mechanism.

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