

Most Transmitted Glomerular Lesions in a Zero-Hour Biopsy of Allograft Kidney Have No Clinical Significance

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Background: The clinical significance of glomerular lesions detected in zero-hour renal allograft biopsies have yet to be fully examined.

Methods: We retrospectively reviewed 229 zero-hour renal allograft biopsies, and investigated the prevalence of transmitted glomerular lesions and their association with urinary abnormalities.

Results: Of 117 cases to which immunofluorescence microscopy was applied, immune complex-associated glomerular lesions were found in eight cases (6.8%). Seven cases were diagnosed with immunoglobulin A nephropathy and none accompanied significant urinary abnormalities during the mean follow-up period of 21.9 months. The other case was diagnosed as C1q nephropathy, revealing significant proteinuria and hematuria 1 month after transplantation. The remaining glomerular abnormalities included focal segmental glomerular sclerosis in five cases, focal endocapillary leukocyte infiltration in three cases, and glomerular fibrin thrombi in three cases. Urinary abnormalities were absent during the follow-up period in all of the cases.

Conclusions: Our observations suggest that most of the transmitted glomerular lesions were clinically irrelevant and that a renal biopsy is unnecessary to include in a pre-transplant donor evaluation procedure.

Key Words: Glomerulonephritis, Kidney transplantation, Time-zero renal biopsy

중심 단어: 사구체신염, 신장이식, 이식당시 신생검

Introduction

Various diseases can be transmitted from donors to recipients in kidney transplantation including infectious(1) and neoplastic conditions(2). The transmission of glomerulonephritis is also possible, and studies on transmitted glomerulonephritis were sporadically performed using pre-transplant donor biopsy or zero-hour renal biopsy in allograft kidneys(2-4). Authors in the pre-cyclosporine era reported that transmitted glomerulonephritis such as immunoglobulin A (IgA) nephropathy was a risk factor of acute rejection(4), however, not much concern has been paid to the natural history

and clinical significance of this condition in the era of advanced immunosuppressive agents and patient management technique.

In this study, we retrospectively reviewed zero-hour renal allograft biopsy to investigate the prevalence and clinical significance of transmitted glomerular lesions.

Materials and Methods

1) Materials

A total of 229 zero-hour renal allograft biopsies performed between 2006 and 2010 in Yonsei University Health System, Seoul, Korea were reviewed. Of which 131 were from male patients and 98 were from female patients and 124 patients received kidneys from living donors (79 related and 45 unrelated), and 105 from cadaveric donors. The mean age of the patients was 45.0 years. Patients' history and donor status were obtained from clinical records.

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2) Tissue processing

All the biopsy samples were examined by light microscopy. Immunofluorescence and electron microscopy were performed in 117 and 92 cases, respectively. For light microscopy, 2~3- μ m-thick sections were stained with hematoxylin-eosin, periodic acid-Schiff, aldehyde fuchsin orange G, and methenamine silver. Immunofluorescence was performed on 3- μ m-thick sections and antibodies applied were against IgG, IgA, IgM, C3, C4, C1q, and fibrinogen (DAKO Cytomation, Glostrup, Denmark). For electron microscopy, 1 mm³ renal tissue were double fixed with glutaraldehyde and osmium tetroxide and stained with uranyl acetate and lead citrate.

3) Histologic assessment

Glomerular lesion assessment included global and segmental sclerosis by light microscopy and the type and location of immune complex deposit by immunofluorescence and electron microscopy. Tubulointerstitial and vascular changes including tubular atrophy, interstitial fibrosis and inflammation, and arteriosclerosis were scored according to 2007 Banff classification of allograft rejection.

Results

The average number of glomeruli in each slide for light microscopy was 14.2 (range; 0~59). Glomerular sclerosis was observed in 77 cases, and the mean percentage of globally sclerotic glomeruli in each case was $4.6 \pm 8.5\%$. Glomerular abnormalities other than global sclerosis were found in 19 biopsies (8.3%). Among them, immune complex-associated lesions were observed in eight cases, 6.8% of cases to which immunofluorescence microscopy had been applied (eight out of 117 cases). Seven of them were IgA nephropathy (five Haas subclass I and two subclass II) and the remaining one was C1q nephropathy. All the patients with IgA nephropathy received kidneys from living donors (five related and two unrelated) and C1q nephropathy patient from a cadaveric donor. In IgA nephropathy cases, the amount of IgA deposits was 2+

in one case, but only trace or 1+ in all the remaining cases. Co-deposition of C3 was observed in five cases, but all of them were of trace amount. All the patients did not accompany urinary abnormalities during a mean follow-up of 21.9 months. Immune deposits disappeared in the case with 2+ deposits 12 months later. In C1q nephropathy, the amount of mesangial C1q deposit was 1+. The patient presented significant (3+) proteinuria and hematuria at the time of biopsy. The deposits almost disappeared in a follow-up biopsy 1 month later, however, proteinuria and hematuria persisted. Graft failure occurred due to renal artery pseudoaneurysm 3 months later post-transplant, and no more information on urinalysis or histologic change was obtained.

The remaining glomerular abnormalities are as follows: Five biopsies showed focal segmental glomerulosclerosis. Three of them were from cadaveric donors and the other two from living related donors. None of the patients showed urinary abnormality at the time of biopsy and during follow-up (mean; 37.0 months). Focal endocapillary infiltration of leukocytes was observed in other three cases (two from cadaveric donors and one from living related donor) and none of them showed clinical significance. Glomerular fibrin thrombi were observed in three cases and all the patients received kidneys from cadaveric donors (Table 1). Interstitial inflammation and fibrosis and tubular atrophy were rarely observed and all of them were of mild degree.

Discussion

Although glomerular sclerosis in zero-our biopsies has been known to be a worse prognostic factor of allograft kidney(5), the significance of other transmitted glomerular lesions has not been fully examined yet. This study was designed to evaluate the prevalence of glomerular lesions transmitted from donors and their clinical significance. We found glomerular abnormalities other than global sclerosis in 8.3% of the cases, and especially immune complex-associated lesions in 6.8% of the cases. Curschellas et al.(6) reviewed 147 zero-hour renal biopsies and reported that non-specific

Table 1. Transmitted glomerular lesions in zero-hour biopsies and their characteristics

No.	Sex/Age	Donor	Diagnosis	Follow-up
1	F/44	LUR	IgA nephropathy, subclass I by Haas	No proteinuria and intermittent 1+hematuria for 8 mo
2	M/25	LR	IgA nephropathy, subclass I by Haas	No proteinuria and 1+intermittent hematuria for 8 mo
3	M/60	LR	IgA nephropathy, subclass II by Haas	No proteinuria/hematuria for 48 mo
4	F/55	LR	IgA nephropathy, subclass I by Haas	No proteinuria/hematuria for 47 mo
5	M/49	LUR	IgA nephropathy, subclass II by Haas	No proteinuria/hematuria for 16 mo
6	F/48	LR	IgA nephropathy, subclass I by Haas	No proteinuria/hematuria for 15 mo
7	F/56	LR	IgA nephropathy, subclass I by Haas	No proteinuria/hematuria for 11 mo
8	M/52	D	C1q nephropathy	3+proteinuria and 3+hematuria at 1 mo
9	F/50	D	FSGS	No proteinuria/hematuria for 61 mo
10	F/48	LR	FSGS	No proteinuria/hematuria for 53 mo
11	M/62	D	FSGS	No proteinuria/hematuria for 36 mo
12	M/41	D	FSGS	No proteinuria/hematuria for 25 mo
13	M/42	LR	FSGS	No proteinuria/hematuria for 10 mo
14	F/57	D	Endocapillary leukocyte infiltration	No proteinuria/hematuria for 1 mo
15	F/33	D	Endocapillary leukocyte infiltration	No proteinuria/hematuria for 33 mo
16	F/47	LR	Endocapillary leukocyte infiltration	No proteinuria/hematuria for 53 mo
17	M/45	D	Glomerular fibrin thrombi	No proteinuria/hematuria for 26 mo
18	M/51	D	Glomerular fibrin thrombi	Intermittent 1+proteinuria and hematuria for 25 mo
19	F/61	D	Glomerular fibrin thrombi	No proteinuria/hematuria for 24 mo

Abbreviations: F, female; LUR, living unrelated donor; M, male; LR, living related donor; D, deceased donor; FSGS, focal segmental glomerulosclerosis.

lesions such as arteriolar intimal fibrosis and hyalinosis were found in 44% of the samples, and specific lesions such as glomerulosclerosis, glomerulonephritis, and intravascular coagulation were found in 18%. All these specific lesions did not affect the renal function and immune complex deposits were disappeared within 4 months. A few years later, Cosyns et al.(3) presented similar, but more detailed data obtained from 114 zero-hour renal biopsies, all of which were from cadaveric donors. They reported that zero-hour biopsies contained various acute and chronic non-specific lesions, and the latter were related with donor age. Most immune deposits were non-specific pattern, however, 9% of the cases showed the pattern of IgA nephropathy. Both patterns of deposit did not affect clinical course at 3 years post-transplant.

In our study, the proportion of living donors was much higher than previous reports, reflecting the donor procurement situation in Korea. The relatively low prevalence of glomerular lesions in our series can be explained partially by the difference of donor characteristic. Our cases also showed that glomerulosclerosis, intravascular coagulation, and other non-specific tubulointerstitial changes did not affect patients'

outcome. We focused on the evaluation of immune complex-associated glomerular lesions, because their clinical significance has not been settled yet.

Transmission of IgA nephropathy or mesangial IgA deposit in donor kidney is a well known phenomenon from decades ago. According to Japanese data, latent mesangial IgA deposit was observed in 16.1% of zero-hour biopsies out of 510 allografts (446 living donors and 64 cadaveric donors). Microscopic hematuria was more frequently observed in IgA deposit group, however, the authors did not present long term follow-up data(7). Both Japanese data and ours showed predominance of living donors over cadaveric donors, however, the IgA deposit is much more common in Japanese. Data from China also showed high prevalence of IgA deposit (24.3%)(8). Most recently, a Spanish data showed that 6.6% of zero-hour renal biopsies (10 out of 151 cases) had IgA nephropathy, and they were associated with decreased glomerular filtration rate after 3 years follow-up(9). This difference might be influenced by the different sensitivity of IgA detection among institutes, but more importantly, caused by ethnic difference in IgA deposition in healthy population. The Japanese data also empha-

sized that C3 co-deposition was an important cause of histologic change. However, C3 was of trace amount in five out of seven IgA nephropathy cases in our series and was not associated with mesangial proliferation. Another difference between our series and those of other countries was that all the IgA nephropathy cases in our series were not associated with urinary abnormality. Although Japanese(7), Chinese(8), and Spanish patients(9) accompanied more frequent urinary abnormalities or decreased renal function, there is no evidence that transmitted IgA nephropathy is associated with severe renal impairment or worse long-term outcome.

Predominant C1q deposition in zero-hour renal biopsy has never been reported in English literature. We experienced one case of C1q nephropathy in this series who had received kidney from a cadaveric donor. Significant proteinuria and hematuria were observed for 1 month, however, their clinical significance cannot be determined due to loss of allograft associated with surgical problem.

Conclusion

Our observation indicated that most of the transmitted glomerular lesions detected by zero-hour allograft renal biopsies did not accompany severe impairment of renal function. Therefore, there seems to be no necessity for including histologic evaluation into a donor selection procedure in fear of incidental glomerulonephritides in candidates without urinary abnormal-

ity, especially in living donors.

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