의학석사 학위논문

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이식편 신장에서 **C1q** 침착의 임상 및 조직병리학적 특징

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서울대학교 대학원

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Clinical and Histopathologic Features of C1q Deposition in Transplanted Kidney Allograft

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A thesis submitted to the Department of Surgery in partial fulfillment of the requirements for the Degree of Master of Science in Medicine (Surgery) at Seoul National University College of Medicine

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Abstract

Background: C1q nephropathy is an uncommon type of glomerulonephritis and is characterized by an extensive and dominant C1q mesangial deposition in the absence of systemic lupus erythematosus. However, there are limited studies about C1q deposition in renal allografts. This study aims to report the incidence of C1q deposition in transplanted kidney allograft biopsies and describe clinical and histopathologic features.

Methods: Between January 2005 and December 2018, a total of 1742 kidney transplantations were performed at Seoul National University Hospital. All renal allograft biopsies (N=10,217) of these patients were retrospectively screened for C1q deposition. C1q deposition was detected in the renal allograft Bx of 104 (6.0%) patients. Only 28 (1.6%) cases had intense (≥2+) C1q-dominance and were reviewed in this study.

Results: Among the 28 cases, only 4 (14.3%) had accompanying proliferative glomerulonephritis. Most did not have any other glomerular changes in light microscopy. No patients had nephrotic-range proteinuria at the time of Bx. A follow-up Bx was undertaken in 15 (53.6%) of the cases. In these follow-up biopsies, C1q deposition either completely disappeared (n=13, 86.7%) or showed diminished staining (n=2, 13.3%).

Conclusion: The prevalence of dominant or codominant C1q deposition in transplanted renal allograft biopsies was 1.6%. Most did not have any other accompanying glomerular changes. The follow-up biopsies of these allografts showed spontaneous disappearance or diminished staining of C1q deposition. These findings suggest that incidental findings of C1q depositions found in routine biopsies are most likely clinically benign, which should be confirmed in further large-scale studies.

Keywords: Kidney transplantation; Biopsy; Allograft; C1q complement

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Introduction

C1q nephropathy is an uncommon type of glomerulonephritis that was first described by Jennette and Hipp in 1985 [1-4]. It is characterized by an extensive and dominant C1q mesangial deposition in the absence of systemic lupus erythematosus [1, 3, 5]. Its clinical and microscopic presentations are varied and diagnosis is based on histopathology [1, 6]. Typically, patients show proteinuria and is relatively resistant to steroid treatment [1, 6]. Despite decades of studies, a limited number of cases have been reported and C1q nephropathy is still poorly understood. The prognosis is generally favorable except in cases with nephrotic syndrome and focal segmental glomerulosclerosis [1].

There are even fewer studies about C1q depositions in transplanted renal allografts [5, 6]. Said et al. reported a series of cases with C1q deposition in renal allografts. Only half of the patients had proteinuria, of which 17% had proteinuria >1 g/day. The 1-year follow-up showed most had stable creatinine levels with no or stable proteinuria [6]. However, the clinicopathologic presentations and outcomes in transplanted kidney allografts have yet to be elucidated [5]. The purpose of this study is to retrospectively review and describe clinical presentations, histopathology and outcomes of kidney transplanted patients with C1q deposition in renal allografts.

Methods

Patient Selection and Data Collection

A retrospective review of kidney transplantations performed at Seoul National University Hospital (SNUH) between January 2005 and December 2018 was undertaken. Patients with both protocol and indication renal allograft biopsies were included and patients who displayed C1q depositions in the specimen were further selected.

For analysis, the patients were further divided into two groups based on the timing of initial C1q detection. The protocol Bx (PBx) group consisted of patients who had initial C1q detection in a protocol renal Bx including reperfusion Bx (Bx), a postoperative 2-week Bx or a postoperative 1-year Bx. The indication Bx (IBx) group consisted of patients who had initial C1q detection in a renal Bx performed at any other time periods due to a worsening of graft, defined as greater than 20% increase in baseline serum creatinine, or an appearance of *de novo* anti-human leukocyte antigen donor specific antigens (DSA).

The patients' electronic medical records were comprehensively reviewed to extract data for clinical variables, the type of transplantation, time interval since transplantation, the cause of end-stage renal disease, laboratory findings, immunosuppressive therapies, and infection history. Long-term patient outcomes, including serum creatinine, urine protein and creatinine, allograft survival and patient survival at last follow-up were also recorded. Nephrotic-range proteinuria was defined as spot urine protein to creatinine ratio >3.5 mg/mg, and a ratio of less than 0.2 was defined as normal.

Ethics

This study was approved by the Institutional Review Board at Seoul National University Hospital (IRB no. 2112-105-1284). The need for informed consent was waived due to the retrospective nature of the study.

Immunosuppression

All patients were prescribed a triple-immunosuppressant regimen comprised of tacrolimus, mycophenolate mofetil, and steroid (prednisone). During the first 3 months after operation, tacrolimus trough level was targeted to 8-12 ng/mL, followed by a concentration of 6-10 ng/mL until 1 year after transplantation, and 4-6 ng/mL thereafter. Mycophenolate mofetil was administered on a fixed dose of 500 mg twice a day. An intravenous dose of 10 mg/kg of steroid was administered during the operation, followed by rapid tapering to achieve a daily dose of 5 mg within the first month after transplantation. As induction immunosuppression, basiliximab was administered (20 mg) at days 0 and 4 after transplantation. In high-risk patients with high panel-reactive antibodies (>80%), DSAs, or ABO-incompatibility, induction with anti-thymoglobulin (1.5 mg/kg/day for 0-3 days) was administered instead of basiliximab.

Pathologic Findings

All Bx specimens were processed using standard protocols for light microscopy (LM), immunofluorescent microscopy (IF) and electron microscopy (EM). The degree of IF staining was graded as − (negative), ± (trace), 1+ (mild), 2+ (moderate), 3+ (marked), and 4+ (heavy) according to Jennette criteria [4]. IF stains with less than 2+ staining were excluded in this study. Other IF stain depositions greater than 2+ staining without a well-phenotype autoimmune disorder were classified as immune-complex glomerulopathy not otherwise specified (ICG-NOS) as suggested by Chin et al: Full-house (+IgG/+IgM/+IgA/+C3/+C1q), Quasi-full house (+IgG/+C3/+C1q), IgA-rich (IgA dominant/codominant), and C1q-rich (-IgG/+C1q) [5]. The specimens were classified in accordance with the Banff 2007 and 2013 classifications by experienced renal pathologists. C1q disappearance was defined as negative IF staining on a follow-up Bx. Diminished C1q was defined as diminished IF staining for C1q to either trace or 1+ (mild) in a follow-up Bx.

Statistical Analysis

The statistical analysis was conducted using SPSS version 21.0 (IBM Corp., Armonk, NY, USA). All tests were two-tailed and differences at P values <0.05 were considered statistically significant. Differences in mean values between groups were compared using Student t-test and categorical variables were compared by chi-square test or Fisher exact test.

Results

Eligible Cases

A total of 1,742 kidney transplantations were performed at SNUH from the period of January 2005 and December 2018. All protocol Bx including reperfusion Bx were performed in 1,357 of these cases (Fig.1). All renal allograft Bx samples (n=10,217) were retrospectively screened for C1q deposition. C1q deposition was detected in 367 of the Bx samples of 104 patients, and among them, patients with ≤+1 stain for C1q were excluded. Intense (≥+2) staining was found in 1.6% of the patients (n=28) (Fig. 2). Of these patients, C1q was initially detected in the PBx sample in 12 cases and in the IBx sample in 16 cases.

Histopathologic Findings

The mean number of sampled glomeruli was 8.0 (standard deviation, 3.6). Proliferative glomerular changes were found in four (14.3%) cases and the remaining 24 (85.7%) of the cases did not have any other lesions indicative of glomerular injury. Other findings in light microscopy accompanying C1q deposition were interstitial fibrosis and tubular atrophy in 11 (39.3%) cases, followed by 9 (32.1%) cases of borderline or acute cellular rejection and 1 (3.6%) case of mixed acute cellular and antibody-mediated rejection. There were no cases of antibody-mediated rejection. Three patients (10.7%) had histological evidence of BK polyoma nephropathy and five (17.8%) showed immunoglobulin A (IgA) nephropathy; these cases were *de novo* IgA nephropathy, except in one patient (Table1).

On electron microscopy, electron dense deposits were present in 92.3% (n=26) and four of the cases showed marked podocyte foot process effacement. In the analysis of immune complex subtypes, the most frequent type was C1q rich type (n=20, 71.4%) without IgG deposition, followed by full-house (n=4, 14.3%), Quasi-full (n=2, 7.1%) and IgA rich subtype (n=2, 7.1%).

On immunofluorescence microscopy, staining for C1q was 2+ in 85.7% (n=24/28) of the cases and 3+ in the remaining four cases. There were no cases of 4+ staining for C1q deposition. The most frequently accompanying

intense (≥2+) stains were IgA (n=11), followed by C3 (n=10), lambda (n=6), kappa and IgM (n=4 each) and lastly, IgG (n=3) (Table 2).

Clinical Data and Characteristics

The mean age was 37.6±17.1 years and 71.4% were male. None of the patients had underlying C1q nephropathy, or other types of auto-immune glomerulonephritis, such as systemic lupus erythematous. Among the 28 cases, 18 cases were from living donors, half of which were male with a mean age of 46.4±11.5 years.

C1q deposition was initially detected in PBx sample in 12 cases (42.9%) and in IBx sample in 16 cases (57.1%). All except two patients in the PBx group, had initial detection of C1q deposition during the reperfusion period. In these two patients, C1q was detected in postoperative 2 week and 1-year PBx. None of the patients in the IBx group had C1q detection in any previous biopsies, including the PBx. The mean time to initial C1q deposition in the IBx group was 1529±1254.8 days. The baseline characteristics were similar in both groups, with a mean follow-up of 7 years. The transplant characteristics were similar, except that preoperative desensitization was more frequent in the PBx group (p=0.034). This was due to pre-formed DSAs (n=2) and ABO incompatibility (n=1). The PBx group had worse initial serum creatinine levels (p=0.008) and eGFR at initial detection of C1q (p=0.002). However, after 3 years of follow-up, serum creatinine and eGFR showed no significant difference (Table 3).

Follow-up Bx Findings

Follow-up Bx were performed in only 15 cases (53.6%) (Table 4), including all of the PBx group (n=12), and three of the IBx group. The C1q depositions either disappeared (n=13, 86.7%) or diminished (n=2, 13.3%). The median interval to C1q diminishing or disappearance was 402 days (range, 8-2128). Two patients (13.3%) had borderline or acute cellular rejection in the follow-up Bx and three patients (20%) showed interstitial fibrosis and tubular atrophy. There were two cases (13.3%) of BK polyoma nephropathy.

Table 5 shows the detailed clinical characteristics of each patient. Patient 1-12 are from PBx group and of these cases, patient 1-10 are reperfusion Bx

cases. Patient 13-15 are from IBx group. The renal function at the time of C1q disappearance showed improvements in eGFR and proteinuria in all patients of the PBx group except patient 7 and 12. The fastest C1q disappearance occurred in the 2-week PBx in patient 6. Excluding patient 3, 4, 7 and 12 of the PBx group, the time to C1q disappearance occurred in the 1-year PBx.

Excluding three deceased donors with missing pretransplant information, the donors did not show preoperative proteinuria or renal dysfunction. Most of the patients had a C1q rich immune complex subtype. Patient 5, 8 and 12 showed full house and quasi-full house immune complexes that also diminished or disappeared in follow-up Bx.

Outcomes in Patients without Follow-up Bx

Table 6 shows the clinical details of each patients who did not have further follow-up Bx performed after the C1q detected Bx. All showed pathologic rejection or recurrence of original disease. Except for four patients, the original cause for end-stage renal disease was glomerulonephritis. With the exception of patient 21, all patients had recurrence of glomerulonephritis. In the latest follow-up, graft failure was found in 5 (38.5%) of these patients.

Discussion

The prevalence of dominant or codominant C1q deposition in kidney transplant recipients was 1.6% (n=28/1742). None of the 28 patients reviewed had underlying C1q nephropathy in the native kidney. However, the 10 cases of C1q deposition initially detected on reperfusion biopsies should be interpreted with caution. Since reperfusion Bx is undertaken immediately after reperfusion of the renal allograft, the C1q deposition in this group could signify the incidence of already existing C1q deposition in the donor allograft. Yet, the review of these patients' donors did not reveal any renal dysfunction or proteinuria. The retrospective design of this study makes it impossible to know exact appearance time of C1q deposition in the renal allografts. The remaining 18 cases (1.0%) could more accurately reflect the prevalence of C1q deposition in transplanted renal allografts. While the reported prevalence of C1q nephropathy in general population ranges from 0.2-16%, the reported prevalence in transplanted kidney is lower ranging from 0.01% to 3% [1, 3-7]. Despite this, along with focal segmental glomerulosclerosis and membranous glomerulonephritis, C1q deposition still accounts for one the three most common *de novo* morphological glomerular patterns in renal allografts [5, 6].

Except in one case that showed immune complex-mediated proliferative glomerulonephritis, there were no other accompanying glomerular changes. Upon review of other immune complexes on IF staining, the most common type of immune complex was C1q-rich subtype. In other studies, C1q was most frequently found with IgM and IgG, as they provide ligands for C1q immune complex formation [1, 5, 8]. The absence of other immune complexes in IF staining may support Kanai's hypothesis that C1q might only be an innocent bystander like IgA deposition, which is found in 4.8% of the general population, while the prevalence of IgA nephropathy is only 0.02% [3]. The spontaneous disappearance or diminishing of C1q deposition may further help support this hypothesis. Stable serum creatinine levels with stable or improved proteinuria were also seen. This is similar to other reports and as Said et al. [6] have suggested, the mild clinical and pathological features may be due to early disease detection and therapeutic effects of maintenance immunosuppression regimens or rejection treatment

The most common hypothesis of C1q nephropathy is the post-infection activation of the inflammatory cascade with subsequent complement activation, consumption and accumulation resulting in binding of C1q to other immunoglobulins and becoming entrapped in paramesangial region and increasing mesangial trafficking [1, 4, 7, 9]. In this study, three cases of BK nephropathy with C1q deposition showed disappearance of both BK nephropathy and C1q deposition in the follow-up Bx. Similarly, half of the patients in the report by Said et al. had preceding infections, but this prevalence of infection was not higher than that in the general renal transplant recipient population. The authors further argued that the absence of endocapillary hypercellularity or weaker staining for C3 than C1q or absence of subepithelial humps constitutes evidence against the possibility of such a hypothesis [6].

Other authors have suggested that C1q nephropathy may overlap with or be superimposed upon other glomerulopathies [3, 8, 10, 11]. All but one patient in the IBx group without follow-up Bx, showed recurrence of original GN disease. Only 3 of these patients showed C1q rich subtype and others were accompanied by various other intense IF stains. Based on this finding, C1q deposition may not simply be an innocent bystander. Nevertheless, in cases that showed C1q disappearance or diminution, C1q rich subtype with no other accompanying glomerulopathies were found in most patients.

Furthermore, C1q deposition in the IBx group was frequently accompanied by T-cell mediated rejection or interstitial fibrosis and tubular atrophy. This may have been the result of selection bias, as the IBx were performed due to either a worsening of graft function or an appearance of de novo DSAs. Some studies have suggested C1q-mediated antibody rejection leads to poorer allograft outcome; however, there was only one antibody mediated rejection and all other presensitized patients were in the PBx group and none had antibody mediated rejection [6, 10].

Although limited in number, as shown by the stabilization in serum creatinine levels and proteinuria and the diminution of C1q staining, the presence of C1q deposition in protocol Bx does not influence the graft failure rate and is most likely clinically silent. Similarly, other reports on C1q deposition or other immune complex depositions concluded that glomerular changes due to immune complex deposition are clinically silent and do not influence graft function [3, 5, 6, 8].

However, proteinuria after kidney transplantation is associated with reduced graft survival, independent of glomerular pathology, graft function, and

rejection [6]. The patients in the IBx group showed significant proteinuria and most showed recurrence of original GN. Therefore, if a patient presents proteinuria and C1q deposition appears in the Bx, active measures are recommended.

To our knowledge, this study reports the largest number of C1q deposition cases in transplanted renal allografts to date. Although a rare and poorly understood disease, the results from this cohort and other (few but existing) cohorts suggest that incidental finding of C1q deposition in a routine Bx is most likely clinically silent and will disappear or diminish spontaneously. However, due to the limited number of cases, firm conclusions about renal allograft outcomes could not be made.

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Table 1.

Table 1. Pathologic findings

Variable	Value
Light microscopy	
Glomeruli sampled (standard deviation)	8.0±3.6
Glomerular pattern	
No lesion	24 (85.7)
Proliferative GN	4 (14.3)
FSGS	0
Other findings	
Borderline or acute cellular rejection	9 (32.1)
Antibody-mediated rejection	0
Mixed acute cellular and antibody-mediated rejection	1 (3.6)
Interstitial fibrosis and tubular atrophy	11 (39.3)
BK nephropathy	3 (10.7)
IgA nephropathy	5 (17.8)
Electron microscopy	
Electron-dense deposition in mesangium	26 (92.8)
Podocyte foot effacement	4 (14.3)
Immune-complex subtypes	
C1q-rich type	20 (71.4)
Full house	4 (14.3)
Quasi-full	2 (7.1)
IgA-rich	2 (7.1)

Values are presented as mean±standard deviation or number (%).
GN, glomerulonephritis; FSGS, focal segmental glomerulosclerosis; Ig, immunoglobulin.

Table 2.

Table 2. Immunofluorescence findings

Stain	Positive case	Intensity when positive
C1q	28 (100)	2.4±0.3
C3	10 (35.7)	2.1±0.8
IgG	3 (10.7)	3.0±0.5
IgA	11 (39.3)	2.4±0.5
IgM	4 (14.3)	2.0±0.0
Kappa	4 (14.3)	2.5±0.5
Lambda	6 (21.4)	2.5±0.5

Values are presented as number (%) or mean±standard deviation.
Ig, immunoglobulin.

Table 3.

Table 3. Clinical data and characteristics

Variable	Protocol biopsy (n=12)	Indication biopsy (n=16)	Total (n=28)	P-value
Patient characteristics				
Age (yr)	43.9±14.4	32.9±17.9	37.6±17.1	0.092
Male	8 (66.7)	12 (75.0)	20 (71.4)	0.629
Cause of ESRD				0.671
GN	5 (41.7)	9 (56.2)	14 (50)	
Cystic kidney disease	3 (25)	2 (12.5)	5 (17.9)	
HTN	0	1 (6.2)	1 (3.6)	
Unknown	3 (25)	2 (16.7)	5 (17.9)	
Others	1 (8.3)	2 (16.7)	3 (10.7)	
Transplantation characteristics				
Living donor	8 (66.7)	10 (62.5)	18 (64.3)	0.820
Preoperative desensitization	3 (25.0)	0	3 (10.7)	0.034
ABOi	1 (8.3)	0	1 (3.6)	0.240
Donor age (yr)	44.5±14.4	47.7±9.8	46.4±11.5	0.469
Donor male	6 (50)	8 (50)	14 (50)	1.000
Time to C1q deposition finding from transplantation	0 (0–450)	1,479.5 (6–3,961)	3,961 (0–3,961)	<0.001
Follow-up (day)	2,088.0±1,383.4	3,195.6±1,113.4	2,721.0±1,334.2	0.027
Serum creatinine (mg/dL)				
At C1q detection	5.3±3.4	1.7±0.5	3.3±2.9	0.008
After 1 year	1.3±0.5	1.7±0.6	1.8±1.6	0.739
After 3 year	1.4±0.9	1.6±0.6	2.2±2.6	0.239
eGFR (mg/min/1.73 m^2)				
At C1q detection	20.7±18.7	49.1±13.2	37.3±24.7	0.002
After 1 year	57.2±13.7	45.7±10.8	51.9±17.9	0.502
After 3 year	55.4±20.8	45.7±10.8	39.4±15.1	0.062
Urine protein/creatinine ratio				
At C1q detection	0.4±0.9	0.7±0.6	0.5±0.6	0.493
After 1 year	0.3±0.7	0.7±0.6	0.5±0.1	0.146
After 3 year	1.0±2.1	0.6±0.6	0.5±0.7	0.938

Values are presented as mean±standard deviation, number (%), or median (range).

ESRD, end-stage renal disease; GN, glomerulonephritis; HTN, hypertension; ABOi, ABO incompatibility; eGFR, estimated glomerular filtration rate.

Table 4.

Table 4. Follow-up biopsy findings

Variable	Protocol biopsy(n=12)	Indication biopsy(n=3)	Total(n=15)	P-value
C1q intensity				0.448
Disappeared (0)	10 (83.3)	3 (100)	13 (86.7)	
Diminished (1+)	2 (16.7)	0	2 (13.3)	
Day from last biopsy	393.5 (8–2,128)	1,353 (1,191–1,872)	402 (8–2,128)	0.033
Other findings				
Borderline or acute cellular rejection	1 (8.3)	1 (33.3)	2 (13.3)	0.255
Antibody-mediated rejection	0	0	0	
Mixed acute cellular and antibody-mediated rejection	0	0	0	
Interstitial fibrosis and tubular atrophy	1 (8.3)	2 (66.7)	3 (20.0)	0.024
BK nephropathy	0	2 (66.7)	2 (13.3)	0.002
IgA nephropathy	0	0	0	
eGFR (mg/min/1.73 m^2)	49.1±13.2	20.7±18.7	53.5±19.1	0.029
Urine protein/creatinine ratio	0.4±0.9	0.7±0.6	0.1±0.8	0.719

Values are presented as number (%), median (range), or mean±standard deviation.

Ig, immunoglobulin; eGFR, estimated glomerular filtration rate.

Table 5. Detailed clinical characteristics of patients with follow-up biopsies

Patient	ESRD Cause	eGFR at initial C1q Detection (ml/min/1.72m²)	UPCR at initial C1q Detection	eGFR at C1q Disappearance (ml/min/1.72m²)	UPCR at C1q Disappearance	Days till C1q Disappearance	C1q Intensity change	Immune Complex Subtype	Donor age	Donor Sex	Donor relationship	Donor Creatinine (mg/dL)	Donor urine microalbumin (mg/dL)
1	ADPKD	10.22	0.66	43.60	0.05	343	2→0	C1q rich	40	F	Sibling	0.8	0.55
2	CGN	7.85	3.02	74.20	0.10	390	2→1	C1q rich	38	F	Sibling	0.65	0.43
3	Unknown	6.15	2.63	74.80	0.20	106	2→0	C1q rich	38	M	Deceased	-	-
4	IgAN	38.36	1.25	74.20	0.33	2128	3→0	C1q rich	44	M	Spouse	0.89	1.2
5	IgAN	5.20	0.08	53.90	0.06	402	2→0	Full house	31	M	Deceased	-	-
6	ADPKD	8.70	0.25	21.50	-	8	2→0	C1q rich	80	M	Deceased	0.93	0.6
7	Unknown	53.60	0.24	23.90	0.26	706	2→0	C1q rich	59	M	Spouse	0.76	1.4
8	ADPKD	32.90	0.10	77.30	0.05	371	3→0	Full house	45	F	Parent	0.56	0.4
9	Unknown	5.30	0.11	84.10	0.10	371	2→0	C1q rich	35	F	Spouse	0.66	0.4
10	CGN	14.40	0.11	53.30	0.09	441	2→0	C1q rich	46	F	Spouse	0.72	1.8
11	Other	12.10	0.26	51.40	0.17	397	2→0	C1q rich	41	M	Deceased	-	-
12	CGN	53.40	0.15	31.20	1.46	1459	2→1	Quasi-full house	47	F	Spouse	0.64	0.4
13	ADPKD	64.20	1.28	9.40	-	1872	2→0	C1q rich	51	F	Spouse	0.57	1.80
14	Unknown	39.50	0.63	40.70	0.39	1353	2→0	C1q rich	41	F	Sibling	0.68	0.80
15	Other	43.70	0.35	41.70	0.27	1191	2→0	C1q rich	46	M	Parent	1.20	0.40

ESRD, end stage renal disease. eGFR, estimated glomerular filtration rate. UPCR, urine protein creatinine ratio. ADPKD, autosomal dominant polycystic kidney disease. CGN, chronic glomerulonephritis. IgAN, IgA nephropathy. Other, malignancy or congenital abnormality

Table 5.

Table 6. Clinical outcomes of indication biopsy patients without further biopsy

Patient	ESRD Cause	C1q Intensity	Immune Complex Subtype	Pathologic rejection	Other accompanying pathology	eGFR at initial C1q Detection (ml/min/1.72m²)	UPCR at initial C1q Detection	eGFR at last FU (ml/min/1.72m²)	UPCR at last FU	Graft failure 0=No 1=Yes
16	CGN	2	IgA rich	ATMR	Recurred MPGN	23.50	1.30	6.8	12.8	1
17	IgAN	2	IgA rich	BDR	Recurred IgAN	50.10	1.71	26.8	2.33	0
18	Other	2	C1q rich	BDR	None	20.90	20.00	3.7	2.39	1
19	FSGS	2	Full house	BDR	IgAN	69.00	0.63	46.5	0.12	0
20	Unknown	3	Quasi-full house	BDR	MPGN	39.30	1.20	37.7	0.11	0
21	MPGN	2	C1q rich	ATMR	BKVN	26.80	0.10	45		0
22	ADPKD	2	C1q rich	BDR	ATN	94.22	0.09	54	0.58	0
23	IgAN	2	C1q rich	BDR	Recurred IgAN	34.10	1.47	22.4	3.84	0
24	MPGN	3	Full house	BDR	MN	74.15	2.37	78.8	0.21	0
25	FSGS	2	C1q rich	None	Recurred FSGS	59.90	0.57	63.8	0.15	0
26	HTN	2	C1q rich	ATMR & AAMR	ATN	32.40	1.19	4.1		1
27	CGN	2	IgA rich	None	IgAN	76.18	0.24	68.1	0.56	1
28	CGN	2	C1q rich	None	Recurred IgAN	49.00	0.33	8		1

ESRD, end stage renal disease. eGFR, estimated glomerular filtration rate. UPCR, urine protein creatinine ratio. FU, follow-up. ADPKD, autosomal dominant polycystic kidney disease. CGN, chronic glomerulonephritis. FSGS, Focal segmental glomerulosclerosis. IgAN, IgA nephropathy. BDR, borderline rejection. ATMR, acute t-cell mediated rejection. AAMR, acute anti-body mediated rejection. ATN, acute tubular necrosis.
MPGN, membranoproliferative glomerulonephritis. BKVN, BK virus nephropathy.

Figure 1

Figure 1. Flow chart of case selection

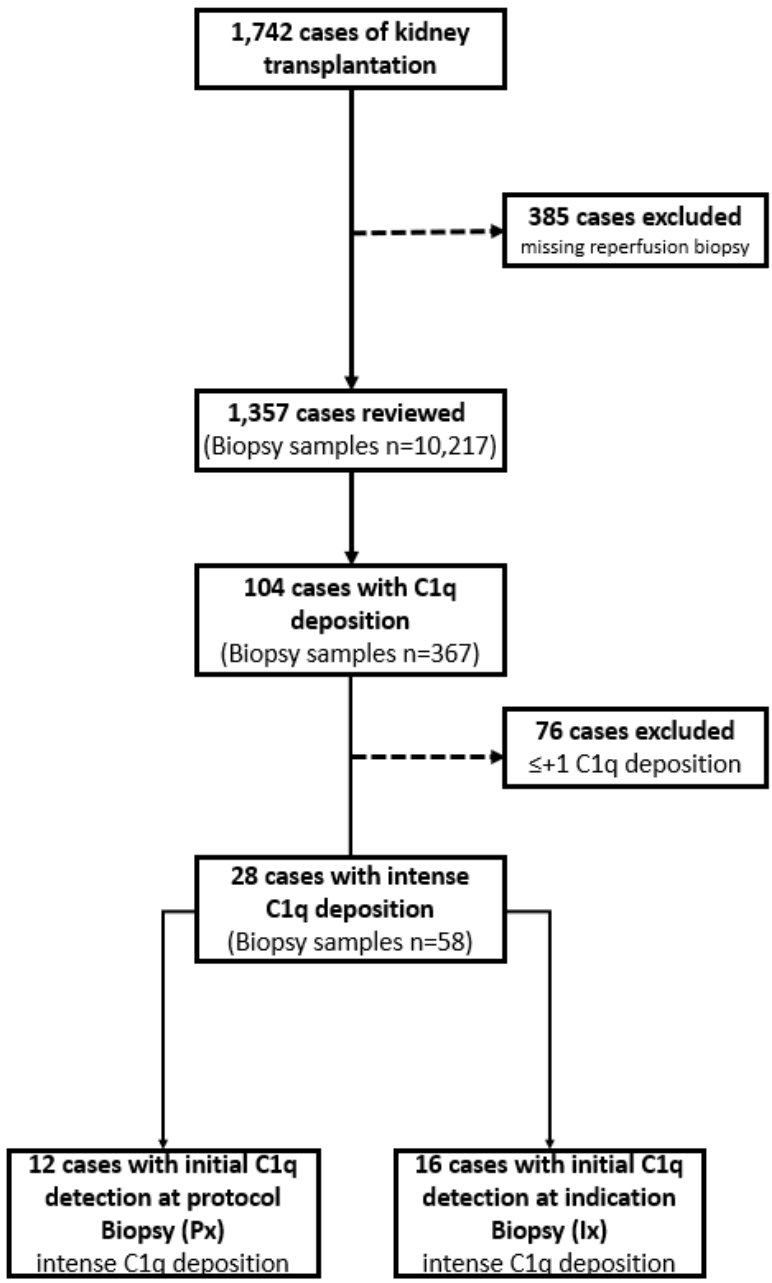
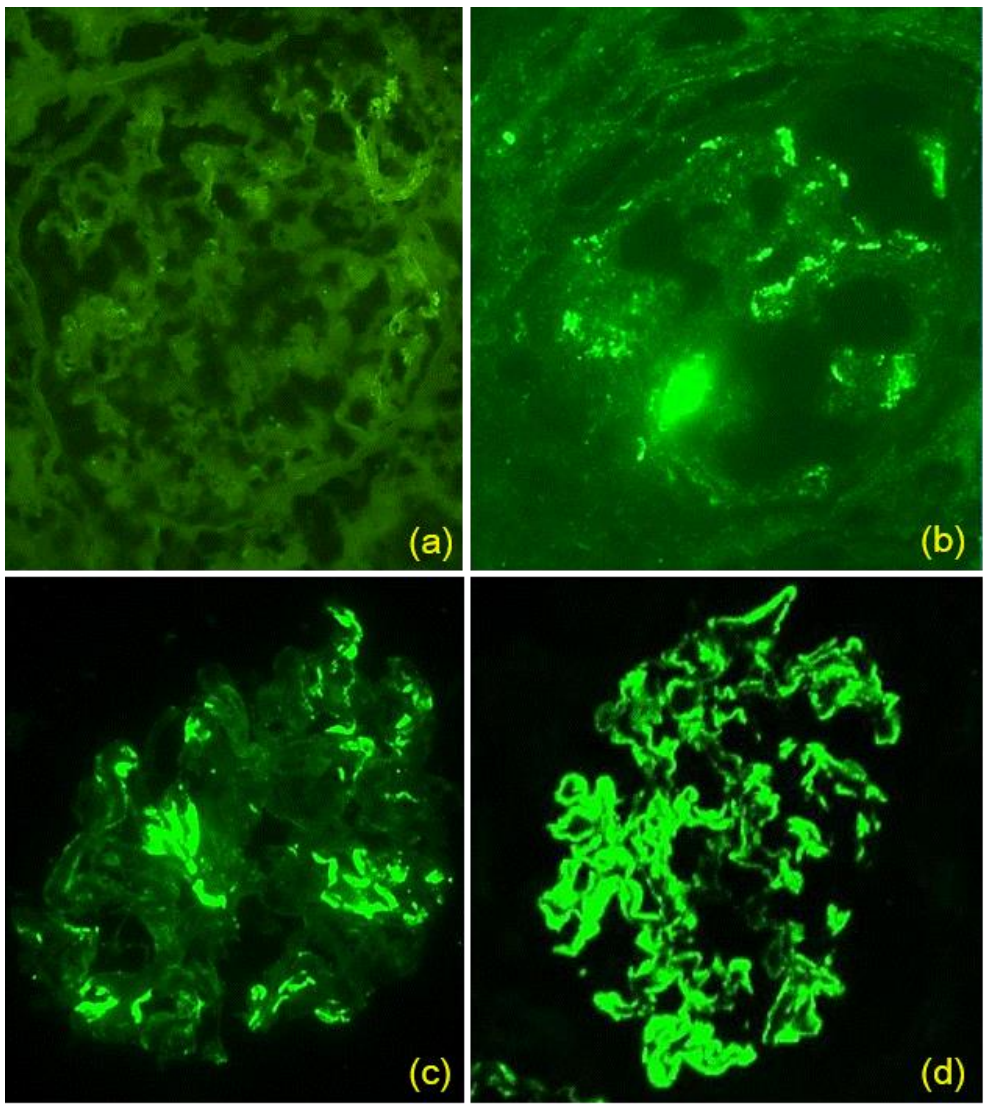


Figure 2

Figure 2. (a) Negative C1q staining. (b) C1q 1+ staining (c) C1q 2+ staining. (d) C1q 3+ staining. (x400)



초 록

배경

C1q 신병증은 흔하지 않은 유형의 사구체신염이며 전신성 홍반성 루푸스 없는 환자에서 메산지움에 광범위하고 우세한 C1q 침착을 특징으로 한다. 그러나 신장 동종이식편에서 C1q 침착에 대한 연구는 제한적이다. 이 연구는 이식된 신장 동종이식편 생검에서 C1q 침착의 발생률을 보고하고 임상 및 조직병리학적 특징을 설명하는 것을 목표로 한다.

방법

2005년 1월부터 2018년 12월까지 서울대학교병원에서 총 1,742건의 신장이식이 시행되었다. 이들 환자의 모든 신장 동종이식편 생검(N=10,217)을 후향적으로 C1q 침착에 대해 스크리닝 하였다. C1q 침착은 104명(6.0%)의 신장 동종이식편 생검에서 검출되었다. 28건(1.6%)의 사례만이 우세한(≥2+) C1q 침착을 보였고 이 연구에 포함되었다.

결과

28례 중 4례(14.3%)만이 증식성 사구체신염이 동반되었다. 대부분은 광학 현미경에서 다른 사구체 변화가 없었다. 생검 당시 신증범위의 단백뇨가 있었던 환자는 없었다. 15례(53.6%)에서 추적 생검을 시행하였다. 이러한 후속 생검에서 C1q 침착은 완전히 사라졌거나(n=13, 86.7%) 염색이 감소된 것으로 나타났다 (n=2, 13.3%).

결론

이식된 신장 동종이식 생검에서 우세한 C1q 침착의 유병률은 1.6%였다. 대부분은 동반되는 다른 사구체 변화가 없었다. 이들 동종이식편의 후속 생검은 C1q 침착의 자발적 소실 또는 감소된 염색을 나타냈다. 이러한 결과는 신장 동종이식편에서 우연히 발견되는 C1q 침착은 임상적으로 양성일 가능성이 높으며 이는 추가 대규모 연구에서 확인되어야 함을 시사한다.

주요어: 신장이식; 생검; 동종이식편; C1q 침착
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