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Pediatric Donor Glomerulopathy Is a Possible Cause of Abnormal Urinalysis in Adults Receiving Small Pediatric Donor Kidneys

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Background. Reports about prognosis of adults receiving small pediatric-donor kidneys (PDK) as compared to those receiving elder pediatric or adult donor kidneys (ADKs) are controversial. This study aimed to examine the outcomes of adults receiving small PDK and possible prognostic factors. **Methods.** The records of adults who received kidneys from donors < 10 years old at our center from July 1, 2011 to June 30, 2018 were reviewed. **Results.** A total of 121 adults were small PDK recipients. Twenty-three patients received 29 biopsies or nephrectomy between 6 and 896 days post-transplantation days. Seven patients (30.4%) had pediatric donor glomerulopathy (PDG), which developed from 113 to 615 days posttransplantation. The incidence of proteinuria and hematuria was significantly higher in the PDG group. The characteristic pathological finding in PDG was irregular lamination and splintering of the glomerular basement membrane (GBM). Donor age, donor weight, and donor kidney volume were significantly less in PDG cases compared with the non-PDG cases. For the risk factors of PDG, increasing urinary RBC count during follow-up was an independent predictor, while increasing donor age and body weight were protective factors. PDG was not a significant risk factor for Scr increasing of PDKs. **Conclusions.** PDG is a potential cause of abnormal urinalysis in adults receiving small PDKs. The pathological characteristic change of PDG is splitting and lamination of GBM. Persistent hematuria after transplantation in recipients of PDK is a predictor of PDG development.

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INTRODUCTION

Renal donation from pediatric donors is an effective means to expand the organ donor pool for adult patients with end-stage renal disease (ESRD).[1,2] Studies on prognosis of adults receiving small pediatric-donor kidneys (PDKs) compared with those receiving elder pediatric or adult donor kidneys (ADKs) are controversial. Studies have shown that the intermediated-term and long-term graft survival of adult patients receiving PDKs is comparable to, or better than that of patients receiving standard-criteria adult deceased donor kidneys (ADKs).[3-5] However, a disparity of recipient/donor body surface area > 1.3 m^2, recipients weighted more 30 kg than the donor and a kidney/recipient weight ratio < 2.3*g*/kg were reported to be associated with higher risk of graft loss.[6-8] These studies indicated that the outcomes of adults receiving PDKs are inferior to those of adults receiving ADKs.

The cause of renal allograft loss is multifactorial. Acute T-cell-mediated rejection (TCMR), antibody-mediated rejection, transplant glomerulopathy, de novo or recurrent glomerular pathologies, polyomavirus nephropathy, and chronic histological damage without specific causes are factors related to graft survival.[9,10] Glomerular diseases including recurrent/de novo glomerulonephritis and transplant glomerulopathy are common reasons for graft failure.[11]

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The incidence of posttransplant proteinuria is higher in adults who received small PDK compared to those who received ADK.[12-14] Choung et al[15] found that adults who received kidneys from pediatric donors < 10 years old had a higher incidence of a special glomerulopathy, pediatric donor glomerulopathy (PDG), which is characterized by spitting and lamination of the glomerular basement membrane (GBM), similar to the lesions seen in kidney of Alport syndrome (AS).

The aim of this study is to determine whether PDG is a cause of abnormal urinalysis (proteinuria and hematuria) in adults receiving small PDKs, to identify the specific pathological changes and to find predictors of occurrence of PDG.

PATIENTS AND METHODS

Patients

We retrospectively reviewed the renal transplant list from the First Affiliated Hospital of Sun Yat-sen University to identify adults who received single or en bloc kidney transplantation from pediatric donors < 10 years from July 1, 2011, to June 30, 2018, with follow-up through June 30, 2019. Because the thickness of GBM can grow to adult level of 300 ± 42 μm at around 10 years old, and will not increase thereafter,[16] we selected pediatric donors < 10 years in this study. The renal biopsy database was reviewed to identify patients who have renal allograft biopsies after transplantation for any cause during the follow-up period. Clinical and pathological data were collected from the databases.

This study was approved by the Institutional Review Board of our hospital, and because of the retrospective nature the requirement of informed patient consent was waived.

At our institution, renal allograft biopsies were typically performed in case of increased serum creatinine (Scr), proteinuria (urine protein positive or 24 h urinary protein >150 mg), or hematuria (>3 RBC/high power field or >5 RBC/μl). Biopsies were routinely examined by light, immunofluorescent, and electron microscopy. Light microscopy included hematoxylin and eosin, periodic acid-Schiff (PAS), Masson's trichrome, and silver methenamine stained specimens. Immunostaining for IgG, IgA, IgM, C3, C1q, Fib, and C4d was performed on frozen sections. Testing with monoclonal antibodies to the alpha 3 and alpha 5 chains of type IV collagen was performed when AS was suspected. Each kidney biopsy sample was subjected to electron microscope examination. At least one nonsclerotic glomerulus was examined if available for each patient, and the thickness of GBM was measured. GBM thickness defined as distance from endothelial to podocytic plasma membrane was measured on electronic microscope using the method reported by Hass.[17] Pathological diagnosis of renal allograft biopsy specimens were in accord with the published diagnostic categories of Banff criteria.[18]

In this study, considering no basic diseases in pediatric grafted kidney, time-zero biopsy was not performed. In addition, given that the recipients with stable disease (no proteinuria and hematuria) after transplantation did not agree to receive biopsy, we only performed indication biopsies but not protocol biopsy, which might affect the outcome.

Statistical Analysis

Descriptive statistics were expressed as mean ± SD, median values were presented for continuous variables, and percentages or ratios for categorical data. Comparisons between continuous variables were performed with Student's *t*-test or Mann-Whitney U-test for, as appropriate, while the chi-square test was used for categorical variables. For categorical variables, the predictive factor was performed with univariate logistic regression, multivariate logistic regression, and multinomial logistic regression. A 2-tailed value of $P < 0.05$ was considered statistically significant. Statistical analysis was performed using SPSS version 23.0 software for Windows.

RESULTS

Patients

During the study period, 121 adults received kidneys from pediatric donors < 10 years of age. Of the 121 adults, a total of 29 biopsies and nephrectomies were performed on 23 patients between 6 and 896 days posttransplantation. The number of biopsy was one in 17 cases and 2 in 5 cases. One case with en-bloc transplantation underwent nephrectomy. All biopsies were examined by light and immunofluorescent microscope, while only 20 biopsies were examined successfully by electron microscopy, 7 biopsies failed due to no glomeruli or only fibrous tissue was examined and 2 nephrectomy cases did not applied for EM. In 7 of the 23 cases, segmental or diffuse lamination of the GBM was noted, among which 3 allografts were from infants. Examination with monoclonal antibodies to the alpha 3 and alpha 5 chains of type IV collagen was performed in all of these 7 cases. Recipients and donors' characteristics of the 23 patients are presented in Table 1.

Each of the 29 allografts had at least 1 pathological diagnosis. Eight biopsies had rejections including 2 borderline rejections and 6 acute TCMR among which 3 combined with antibody-mediated rejection. Four cases were diagnosed with BK virus-associated nephropathy (BKVAN), 2 with acute tubular injury, 2 with IgA nephritis, 2 with focal segmental glomerulosclerosis (FSGS), 2 with graft vein rupture, 2 with nonspecific renal tubulointerstitial lesions, and 4 with nonspecific minor lesions.

In 7 of the 23 patients (30.4%), we identified PDG developed from 113 to 615 days posttransplantation. In

TABLE 1.

Recipients and donor demographic and clinical data

Recipients		Donors	
Age (y)	32 (13–49)	Age (y)	
Sex		<1	21.7 (n = 5)
Female	56.5 (n = 13)	1–4	30.4 (n = 7)
Male	43.5 (n=10)	5–9	47.8 (n = 11)
Body weight (kg)	51.6 (35.0–80.0)	Body weight (kg)	16 (3.3–31.0)
Primary disease		Kidney weight (g)	70.5 (15.0–102.0)
CGN, NST	60.9 (n = 14)	Kidney length (cm)	7.5 (2.5–10.1)
IgAN	13.0 (n = 3)		
LN	13.0 (n = 3)		
Other	13.0 (n = 3)		

Data presented a number and percentage, or median value.
CGN, NST, chronic glomerulonephritis, nonspecific type; IgAN, IgA nephropathy; LN, lupus nephritis.

these 7 patients, 2 had concurrent BKVAN, 1 had TCMR, 1 had FSGS, and 1 had IgA nephropathy which could not be determined recurrent or de novo because renal biopsy had not been performed in the recipients' native kidney before renal transplantation.

A total of 18 (78.3%) recipients developed posttransplantation proteinuria and/or hematuria, which were present before or after the biopsy. At the end of the follow-up, 23 recipients were followed regularly, 2 allograft lost function, 4 lost following up, and 2 died.

Outcomes of PDG Cases

Clinical data of the 7 PDG patients were summarized in Table 2. Six of the recipients were adults ranging from 23 to 38 years of age and one (case 5) was 13 years old. Native renal disease included IgA nephritis, FSGS not otherwise specified, focal glomerulonephritis, lupus nephritis, and chronic nephritis without a specific diagnosis. The donor's ages were from 22 days to 5 years, including 3 infants < 1 year old. Single kidney transplantation was performed in 6 cases and one case (case 4) was en bloc transplantation. Kidney length ranged from 2.5 to 8.0 cm. Kidney weight ranged from 15 to 88 g.

Six recipients showed urinary protein positive and 6 cases showed persistent hematuria until the end of follow-up or until the patient died. The death of case 2 was caused by pneumonia at 14 months posttransplantation. In addition to a pathological diagnosis of PDG, 3 patients were diagnosed with concurrent BKVAN or TCMR.

Each of the PDG cases had at least one glomerulus examined by electron microscopy. The most characteristic electron microscopy change in PDG cases was irregular lamination and splintering of GBM, leading to the increased thickness of GBM and irregular appearance of both outside and inside couture which resembled the morphologic changes in patients of AS (Figure 1). The GBM lesions were segmental or diffuse, involving mostly the lamina rara interna and externa, while the lamina densa was less affected. The lamination of lamina rara interna and externa resulted in increased distance from endothelial to podocytic plasma membrane, that is, GBM thickness, which varied from 900 to 2100 nm, while the relatively intact portion of GBM had a thickness of 120–390 nm. Segmental podocyte foot process effacement was found. No electronic dense deposits were noted within the GBM, while segments with lamination exhibited electron lucency. However, in 2 patients (case 3 and 7), electronic dense deposits were found in the mesangial area, suggesting an additional diagnosis of immune complex-mediated glomerulonephritis (Table 3).

Light microscopy of the PDG biopsy showed most of the glomeruli were small, some even immature. Segmental or global glomerulosclerosis was present in 2 biopsies, one of which was diagnosed with FSGS not otherwise specified. Mild mesangial expansion and mesangial hypercellularity was present in 2 biopsy specimens (Figure 2). Overall, mild chronic changes (<25%) including interstitial fibrosis and tubular atrophy were common in the biopsy. Focal Inflammation of the interstitium and peritubular capillaries was observed in 4 specimens. Changes suggestive of BKVAN were present in 2 cases (cases 3 and 4), and TCMR in 1 case (case 6). Other glomerular lesions including glomerulomegaly, glomerular hyalinosis, glomerular obsolescence, crescents, endothelial proliferation, basement membrane double couture, and arteriolar hyalinosis were rare in the PDG cases.

In most of the cases, immunofluorescent staining was negative for IgG, IgA, IgM, C3, C1q except for case 7 showing IgA dominant staining in mesangial area and IgM, C3 plus C1q positive in case 3 indicating immune complex-associated glomerulonephritis. C4d deposition in the peritubular capillaries was negative in all PDG cases. Immunofluorescence of alpha 3 and alpha 5 chains of type IV collagen was performed in all PDG cases, and strong staining along GBM and some TBM in PDG (Figure 3), which excluded the possibility of AS.

TABLE 2.

Clinical data of pediatric donor kidneys developing PDG in adult recipients

	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6	Case 7
Recipient age	30	23	30	27	13	38	34
Recipient sex	F	F	F	F	M	F	F
Primary renal disease	IgAN	CGN	FSGS	IgAN	Focal GN	CGN	LN
Donor age	1 y	8 m	2 y	2 m	22 d	5 y	2 y
Single/en bloc	Single	Single	Single	En bloc	Single	Single	Single
Kidney length (cm)	6.0	5.5	6.0	2.5/3.7	4.5	8.0	6.7
Kidney volume (cm^3)	6.0 × 4.0 × 2.5	5.5 × 2.5 × 1.5	6.0 × 4.0 × 1.5	L: 3.7 × 2.5 × 1.5 R: 2.5 × 2.5 × 1.5	4.5 × 2.5 × 1.0	/	6.7 × 4.6 × 2.1
Kidney weight (g)	/	27	/	/	15	88	/
Proteinuria (g/24 h) Bx	0.180	2.089	0.338	0.276	1.210	0.320	1.956
Proteinuria (g/24 h)[a]	–[b]	1.548	–[b]	1.802	–[b]	–[b]	1.246
Urinary RBC/HPF[a]	9	73[c]	7	69	1	27	63
Proteinuria test[a]	N	Y	N	Y	N	Y	Y
Scr[a]	66	111[c]	142	95	79	210	118

[a]Tested at the end of follow-up.
[b]Did not test due to urinary routine test negative.
[c]Tested before death. Grading: –, absent; 1+, mild; 2+, moderate; 3+, prominent.
Bx, biopsy time; CG, chronic nephritis; FSGS, focal segmental glomerulosclerosis; HPF, high power field; LN, lupus nephritis; PDG, pediatric donor glomerulopathy; Scr, serum creatinine.

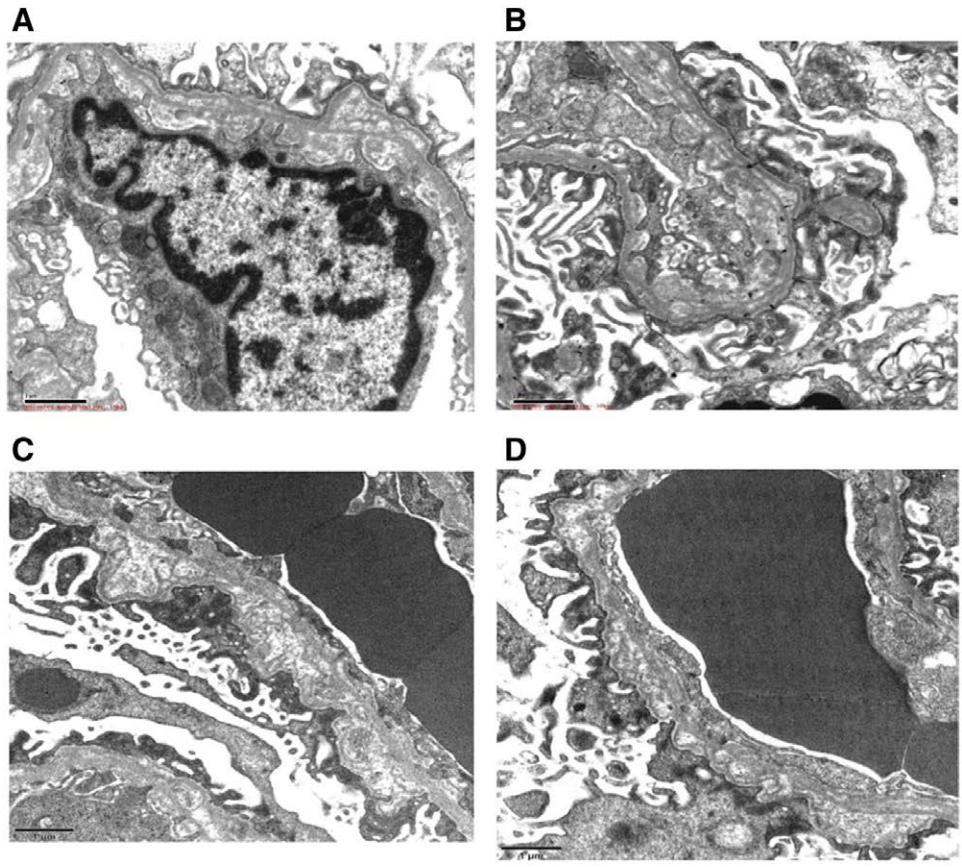

FIGURE 1. Electron microscopy image of pediatric donor glomerulopathy. A and B, Case 5. C and D, Case 7. Images show irregular lamination and splintering of the glomerular basement membrane (GBM), especially in the lamina rara interna and externa, with segmental foot process effacement. Areas of the GBM with lamination are thickened. Magnification ×12 000.

TABLE 3.

Electron microscopy findings of PDG kidneys

	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6	Case 7
Biopsy time (d posttransplant)	135	243	196	615	356	239	346
Number of examined glomeruli	1	2	1	1	1	1	1
Degree of GBM lamination	1+	3+	2+	1+	3+	1+	3+
Thickness of GBM with lamination (nm)	543 ± 357	622 ± 378	930 ± 670	683 ± 317	820 ± 680	689 ± 318	1367 ± 933
Thickness of relatively normal GBM (nm)	185 ± 15	245 ± 15	245 ± 95	285 ± 85	140 ± 20	320 ± 70	295 ± 45
Podocyte effacement	+	+	+	±	+, diffuse	+	+
Electron dense immune deposits	–	–	+, M	–	–	–	+, M
Pathological diagnosis	PDG	PDG FSGS, NOS	BKVAN PDG MPGN	BKVAN PDG	PDG	TCMR PDG	PDG ICGN

Grading: –, absent; 1+, mild; 2+, moderate; 3+, prominent.
BKVAN, BK virus-associated nephropathy; FSGS NOS, focal segmental glomerulosclerosis, not otherwise specified; GBM, glomerular basement membrane; ICGN, immune complex mediated glomerulonephritis; M, mesangial area; MPGN, membranoproliferative glomerulonephritis; PDG, pediatric donor glomerulopathy; TCMR, T-cell-mediated rejection.

Immunohistochemistry staining for SV40-T was performed in each biopsy and tubular epithelial cells were positive in cases 3 and 4, indicating an additional diagnosis of BKVAN.

For further analysis, recipients were divided into PDG group and non-PDG group (Table 4). Time from the day of transplantation to biopsy in PDG group was longer than that in non-PDG group ($P < 0.05$). The incidence of proteinuria and hematuria at biopsy time were significantly higher in PDG group ($P < 0.05$). Donor age, donor weight, donor kidney length, and serum creatinine at biopsy time were significantly less in PDG group compared with non-PDG group ($P < 0.05$), while the recipient weight in non-PDG group was significantly greater than that of PDG group ($P < 0.05$). Single kidney transplantation, recipient age, and recipient gender were not different between the 2 groups (all, $P > 0.05$). The presence of FSGS, IgA nephropathy, rejection, and BKVAN were not associated with PDG development.

The predictor of PDG incidence was analyzed by univariate and multivariable logistic regression. The donor age, donor weight, recipient age and weight, 24-hour urinary protein, and urinary RBC count until follow-up were analyzed in the logistic regression model. The

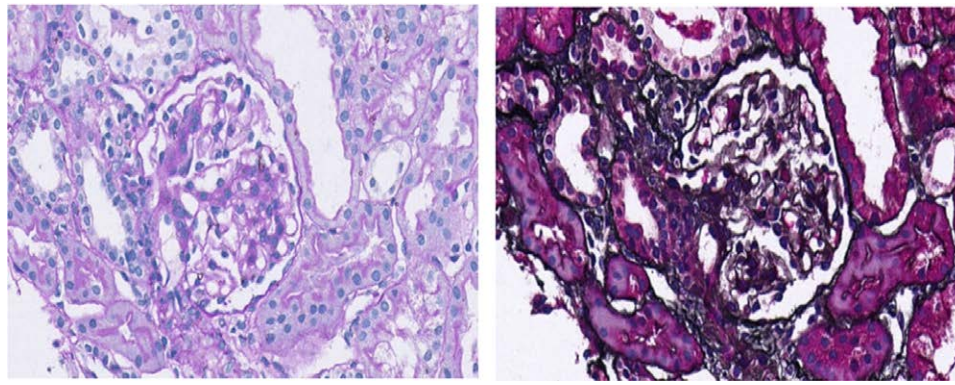

FIGURE 2. Light microscopy image of pediatric donor glomerulopathy. The glomerulus was noted to be small, with minimal changes, with some immature glomeruli present. Left: PAS staining; Right: PASM staining. Magnification ×400. PAS, periodic acid-Schiff; PASM, periodic Schiff-methenamine.

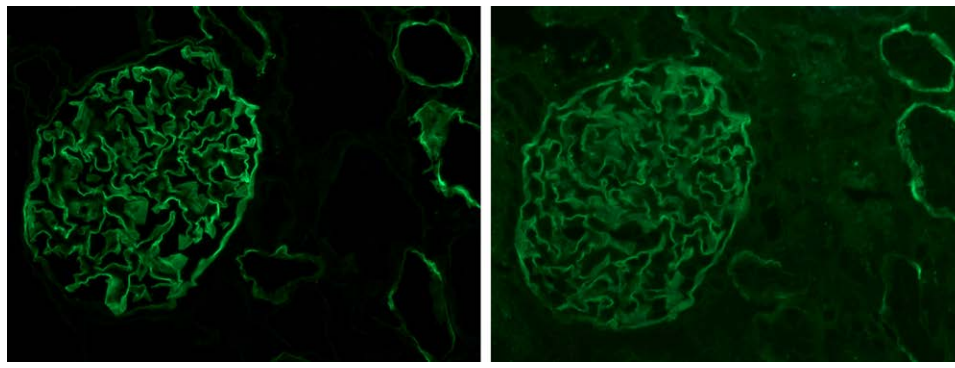

FIGURE 3. Immunofluorescence staining of alpha 3 and alpha 5 chains of type IV collagen showed strongly positive along GBM and some TBM in PDG. GBM, glomerular basement membrane; PDG, pediatric donor glomerulopathy; TBM, tubular basement membrane.

TABLE 4.

Comparisons of PDG group and non-PDG group

	PDG group (n = 7)	Non-PDG group (n = 16)	*P*
Number of biopsies	8	21	–
Biopsy time (posttransplantation)	241 (113–615)	115 (6-896)	0.048
Single donor kidney	6	15	0.526
Proteinuria (routine test positive)	6 (86%)	4 (25%)	0.034
24-h Proteinuria Bx[a]	1.38	2.29	0.315
Urine RBC/HPF until follow-up[a]	35.6 (1–73)	9.6 (1–43)	0.05
Scr at biopsy time[a]	111.9 (62–137)	267.1 (53–724)	0.009
Donor kidney volume(cm^3)[a]	33.1 (11.3–64.7)	157.6 (36.0–319.3)	0.03
Donor kidney length (cm)[b]	5.60 (2.5–8.0)	8.94 (6.0–10.1)	0.003
Donor weight (kg)[b]	8.5 (3.9–23.0)	21.5 (3.3–31.0)	0.016
Donor age (y)[b]	1 (22 d–5 y)	6.5 (2–9)	0.001
Recipient weight (kg)[b]	43.5 (35.0–62.0)	51.5 (39.0–80.0)	0.141
Recipient sex (female)	6 (85.7%)	7 (43.8%)	0.089
Recipient age (y)[b]	30 (13–38)	32.5 (18–49)	0.166
Combined with FSGS	1	1	0.526
Combined with IgAN	0	2	1.000
Combined with rejection	1	6	0.366
Combined with BKVAN	2	1	0.209

[a]Mean value.
[b]Median value.
BKVAN, BK virus-associated nephropathy; Bx, biopsy time; FSGS, focal segmental glomerulosclerosis; IgAN, IgA nephropathy; PDG, pediatric donor glomerulopathy.

data showed that increased urinary RBC count during follow-up was an independent predictor for the occurrence of PDG (Table 5), while proteinuria was not an independent predictor. Furthermore, the increasing donor age and donor weight were protective factors for PDG incidence (Table 5), which further suggested that PDG mainly occurred in pediatric donor kidney transplantation.

TABLE 5.

Predicting factors of PDG incidence (n = 23)

Predicting factors	*exp(b)*	*P*
Urine RBC/HPF until follow-up	1.054	0.042
Donor weight	0.849	0.035
Donor age	0.355	0.023

PDG, pediatric donor glomerulopathy.

Finally, risk factors for increasing Scr in 23 cases of PDK and 7 cases of PDG were analyzed by multivariate logistic regression and multinomial logistic regression. Age difference between recipient and donor, posttransplant rejection, immune complex-mediated glomerulonephritis, BKVAN, and PDG was analyzed in the logistic regression model. Increasing Scr post kidney transplantation was defined as increased by >30% as compared with posttransplant baseline. As shown in Table 6, for all PDK cases, age difference itself was not a risk factor of increasing Scr, but it had an interaction effect with rejection, suggesting that the age difference becomes a significant risk factor when a rejection occurred ($P < 0.05$). Notably, PDG did not contribute to increasing Scr of PDKs ($P = 0.941$). As for the PDG cases, when there were no accompanied complications, such as posttransplant rejection, immune complex-mediated glomerulonephritis or BKVAN, recipients were less prone to increasing Scr ($P < 0.001$). PDG itself did not contribute to increasing Scr. One possible explanation was that the injury of GBM was reversible to some extent and proteinuria or hematuria disappeared with the growth of the allograft. However, once PDG was accompanied with rejection and immune complex-mediated glomerulonephritis, the immature allograft was relatively more susceptible to these factors, thus leading to increasing Scr.

DISCUSSION

PDG characterized by GBM lamination has only been reported in a few studies, and the first case was reported in 1991.[19] The earliest case showing a 24-year-old female received a kidney from an 8-year-old boy and developed proteinuria of 8.5 g/24 hours 33 months after transplantation. The graft biopsy revealed diffuse GBM lamination. Nadasdy et al[20] reported 6 cases of diffuse GBM lamination in 44 kidneys transplanted into adults from pediatric donors < 10 years old during a 10-year period from 1986 to 1995. The series showing GBM lamination was presented from 10 weeks to 36 months posttransplantation. The donor age ranged from 1 month to 6 years, and the recipient age ranged from 28 to 59 years. Four of the 6 grafts developed dysfunction after 3 months to 3 years posttransplantation, and in all cases AS was excluded. In 2014, Choung and Meleg-Smith[15] reported a unique lesion of the glomerular in pediatric grafts transplanted into adults identifiable on electron microscopy, and named the lesion PDG.

To some extent, the ultrastructural lesions of the GBM in patients with PDG are similar to those seen in AS.[21] However, in AS lamination of the GBM is severe, widespread, and the lamina densa is often affected, while in PDG the AS-like change mostly affected the lamina rara interna and externa. The lesion could be segmental or diffuse. Compared to diffuse AS-like GBM change reported by Nadasdy et al,[20] only 3 cases in our series showed diffuse lesion, while the other 4 only segmental. Choung and Meleg-Smith[15] described that PDG affected GBM mainly on the epithelial side, external lamina rara, while in our series both the internal and external lamina rara were thickened.

Most PDG cases developed proteinuria after transplantation. Up to now, there was still no threshold of proteinuria in the kidney allograft. Living kidney donors with only one functional kidney left, often have increased urinary protein after donation.[22] Similarly, the recipients usually have only one functional kidney, and as such protein excretion may differ from the normal condition. The incidence of proteinuria in renal transplant patients ranges from 7.5% to 45%, depending on the definition of proteinuria.[23-25] For renal transplant patients, proteinuria is the most common indicator of kidney injury, and is an independent risk factor for reduced graft and patient survival,[23,24] especially when creeping persistent proteinuria is present.[26] Possible reasons for posttransplant proteinuria include glomerulonephritis, chronic or acute rejection, chronic transplant glomerulopathy, and cyclosporine nephrotoxicity.[27]

The degree of proteinuria in PDG patients varies considerably, which may be related to the severity of GBM lesions. In our series, 6 of 7 PDG patients had mild-to-moderate proteinuria. Cases 2, 5, and 7 which developed diffused GBM change had a higher level of proteinuria, ranging from 1.210 to 2.089 g/24 hours compared to those with only segmental GBM lesion. Some reports have suggested that en bloc kidney transplantation may reduce the incidence of proteinuria, and had better long-term function if the allograft survives the early postoperative period.[28] In our series, case 4 received en bloc transplantation and developed proteinuria at 615 days posttransplantation which is the latest, suggesting an en bloc transplantation might delay the occurrence of PDG.

Donor/recipient age and body weight mismatch contribute to posttransplantation complications.[6,7,29] In our study, we found differences in some clinical factors between the PDG and non-PDG patients. A donor/recipient body weight mismatch was closely related with PDG incidence.

TABLE 6.

Predicting factors for increasing creatinine in PDK allograft

PDK (n = 23)	*exp(b)*	*P*	PDG (n=7)	*exp(b)*	*P*
Age difference between recipient and donor	0.708	0.044	No complications[a]	2.530E-10	<0.001
Age difference between recipient and donor by rejection	1.178	0.048			
PDG	0.889	0.941			

[a]Complications: rejection, ICGN, and BKVAN.

BKVAN, BK virus-associated nephropathy; ICGN, immune complex mediated glomerulonephritis; PDG, pediatric donor glomerulopathy; PDK, pediatric donor kidney.

PDG patients had younger PDKs compared with non-PDG. The decreasing age or weight of the pediatric donor caused increasing incidence of PDG. Persistent hematuria in recipients of PDK could be a predictor of PDG incidence. In our continuous follow-up, proteinuria in 4 PDG cases at biopsy time could gradually decrease and finally disappeared (mean: 458 d, range from 113 to 774 d) at the end of follow-up time, while hematuria persisted.

The persistent hematuria in PDG patients was not related to declined renal function made us think more about the events occurred after PDK transplantation. Kawaguchi et al[30] reported that in the body weight mismatch group, the mean GBM was significantly thinner at 1-hour post-transplantation, while at 1-year posttransplantation, the mean GBM thickness has no significant difference compared with the control group. Hirukawa et al[31] reported that the size of PDK grafts in adult recipient increased to adult size by 3 months posttransplant, but the glomerular area and volume were less than half of adult size at 3.5 years posttransplant, while at this time, podocytes was mature. Sureshkumar et al[32] found that the glomerular filtration rate was significantly higher in PDK recipients, and Mueller-Deile et al[33] demonstrated that hyperfiltration is the key trigger inducing the rapid growth response of glomerulus. All these research studies proved that hyperfusion did exist in PDK recipients and played an important role in the rapidly grow of the glomeruli and thickening of GBM, while these 2 processes might not parallel with each other. In our study, PDG was found between 3 months and 2 year (113–615 d, mean 241 d) after kidney transplantation during which the glomeruli were hyper-fused and gradually expanded together with the thickening of GBM, while podocyte was not yet mature. We also tracked the cases of PDG and found that in some cases proteinuria gradually decreased to negative in the later stage, which might represent the phenomenon of self-healing of GBM in some patients.

On the basis of previous studies and our findings, we proposed a possible pathogenesis of PDG. At the time of transplantation, GBM was initially thin. Small PDKs had a smaller glomerular volume and less total filtration area and the nephron units were relatively insufficient for adults. With the increasing glomerular filtration rate in PDK grafts, the sizes of kidney kept growing and reached adult size at about 3 months. The glomerular basement membrane began to splitting and forming GBM lamination due to high filtration pressure. At the same time, the glomerular inner cells including podocytes kept growing and differentiating. The filtration barrier became mature and reached adult level over several years after transplantation. Our findings suggest that PDG is a potential cause of abnormal urinalysis in adults receiving small PDKs, and clinically, it may be confused with recurrent or de novo glomerulonephritis without biopsy. The predominant change of PDG is GBM splitting and lamination ultrastructurally. Persistent hematuria after transplantation in recipients of PDK is a predictor of PDG development.

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