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Original Article

An Iranian experience on renal allograft diseases*

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Abstract

BACKGROUND: Renal transplantation is the treatment of choice for most patients with end stage renal disease. In addition, renal biopsy is the gold standard to assess the causes of renal allograft dysfunction. This study was designed to evaluate and designate renal lesions according to Banff schema.

METHODS: In this cross-sectional study, all renal allograft biopsies obtained from renal transplant patients at Alzahra and Noor referral hospitals in Isfahan during 2006-2008 were studied. Evaluations were made according to the Banff classification 2009. Clinical data was collected from the pathology database and analyzed using SPSS.

RESULTS: A total number of 161 specimens were studied from 68% male and 32% female subjects. The donor source was living unrelated in 85%, living related 9.9% and cadaveric in 5% of cases. Pathologic results showed 22.4% acute tubular necrosis (ATN), 13.7% interstitial fibrosis and tubular atrophy (IF/TA) grade II, 9.9% IF/TA (Grade III), 6.8% acute T-cell mediated rejection (TCMR-IA), 5.6% TCMR-IB, 5% borderline change, 5% infarction, 4.3% TCMR-IIA, 4.3% TA/IF (Grade I), 3.7% acute antibody-mediated rejection (ABMR), 1.9% TCMR-IIB and 17.4% other lesions.

CONCLUSIONS: The commonest causes of graft dysfunction after kidney transplant were IF/TA, no evidence of any specific etiology (NOS) and ATN. Living donors were found to be important sources for kidney transplantation in Iran.

KEYWORDS: Kidney Transplantation, Kidney Allograft, Transplantation Results, Renal Biopsy.

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Among renal replacement therapies, renal transplantation is the treatment of choice for most patients with end-stage renal disease (ESRD).[1] Factors such as donor quality, delayed graft function (DGF), acute rejection, immunosuppression and sometimes recurrence of primary disease threat the function of transplanted kidney.[2,3] Although there is great reduction in early acute rejection of allograft, chronic renal allograft failure is an underlying cause of poor outcome in some cases of kidney transplantation.[4-6] There are ways for measuring renal function and outcome of transplantation in kidney allograft. Serum creatinine level may help physicians assess transplanted kidney function. However, since changes in creatinine concentration occur late in disease progression, it is not a reliable marker for ongoing renal dysfunction.[4] Another way is conducting kidney protocol biopsy pre- and post-transplantation to evaluate short and long-term outcomes regarding histopathologic findings on biopsy.[7] The histologic findings on biopsy influence the prognosis and choice of therapy.[8-10] Factors such as geographic areas, socioeconomic conditions, race, age and indications for renal biopsy lead to variations in the pattern and prevalence of biopsy-

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proven renal disease.[11-18] Although sometimes biopsy findings may result in interstitial fibrosis and tubular atrophy with no specific cause, pathologists should try to define lesions and explain the pathologic process influencing allograft.[19] Using the Banff criteria makes a diagnostic uniformity worldwide.[20,21] There are diagnostic criteria on microscopic evaluation of donor biopsy for determination of post-transplant dysfunction in allograft. Gaber et al. found an association between biopsies with more than 20% glomerulosclerosis and more DGF, higher creatinine levels at 1 year and increased graft loss.[22] According to donor characteristics such as age (the most potent predictor of long-term outcome),[23-25] Bajwa et al. suggested that donor kidneys with less than 6% glomerulosclerosis were associated with better graft outcomes.[26] Vascular changes and tubulointerstitial findings may also be associated with early and late graft outcomes.[2,9,27-32]

The first kidney transplantation in Iran was performed in 1967.[33] In 2002, Iran stood at the 5th place in renal transplantation throughout the world.[33] However, there is no clinical data regarding transplanted kidney lesions on biopsy in Iran. Therefore, this study tried to categorize renal lesions by histopathologic findings in allograft biopsies after transplantation.

Methods

In this cross-sectional study, all renal allograft biopsies were obtained from two referral hospitals in Isfahan (Alzahra and Noor Hospitals) between 2006 and 2008. Data about the type of transplantation (cadaveric or living related/unrelated donor), demographic information, as well as clinical data, was collected. All data was obtained and recorded in requisition forms by the nephrologist at the time of biopsy.

Inclusion criteria were sufficient number of glomeruli (7-10 glomeruli),[34] at least one artery in biopsies and completed requisition forms. Insufficient or suboptimal biopsies without enough glomeruli and artery for definite diagnosis were excluded.

All the specimens were studied by a nephropathologist based on the Banff classification.[21] Type of renal injuries in biopsies were determined by these terms: 1) Tubular atrophy and interstitial fibrosis (IF/TA) grade I, II and III; and 2) Acute T-cell mediated rejection (TCMR) including TCMR-IA, TCMR-IB, TCMR-IIA, TCMR-IIB and TCMR-III considering the intensity of TCMR injury.

Finally, clinical data collected from the pathology database and requisition forms was analyzed by $SPSS_{16}$ (Chicago, IL, USA).

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Results

There were 161 specimens from 110 male patients (68.3%) and 51 female patients (31.7%). The minimum age was 7.5 years and maximum age was 74 years. Mean age of patients who had undergone operation for biopsy was 37.1 years. Maximum and minimum mean ages were observed in the groups with IF/TA, no evidence of any specific etiology (NOS) I (45.5 years) and TCMRIIB (24 years), respectively.

Pathological results in specimens showed 22.4% ATN, 13.7% IF/TA (NOS) II, 9.9% IF/TA (NOS) III, 6.8% TCMR-IA, 5.6% TCMR-IB, 5% infarction, 5% borderline rejection, 4.3% TCMR-IIA, 4.3% IF/TA (NOS) I, 3.7% ABMR, 1.9% TCMR-IIB and 17.4% other lesions. Pathologic findings are categorized based on sex in Table 1.

Of all donors, 85.1% were living unrelated donors, 9.9% cadaveric and 5% were living related donors. The pathological diagnoses were 18.6% TCMR, 3.7% antibody-mediated rejection (ABMR), 5% borderline rejection, 27.9% IF/TA (NOS). Moreover, 44.8% of all biopsies had no pathologic evidences for rejection and the commonest pathologic finding in this group (22%) was acute tubular necrosis (ATN).

In addition, the commonest pathologic findings in patients with cadaveric, living related and living unrelated donors were ATN (81.2%), IF/TA (NOS) (37.5%), and ATN (16%), respectively. Type of donors and pathologic findings of renal allograft biopsies are seen in Table 2.

Table 1. Pathologic results based on sex

	Men		Women	
Pathologic finding	(n)	(%)	(n)	(%)
ATN	22	61.1	14	38.8
TCMR-IA	7	63.6	4	36.3
TCMR-IIA	7	100	0	0
TCMR-IB	7	77.7	2	22.2
TCMR-IIB	2	66.7	1	33.3
IF/TA I	4	57.1	3	42.8
IF/TA II	15	68.1	7	31.8
IF/TA III	13	81.3	3	18.7
ABMR	2	33.3	4	66.6
Calcineurine Inhibitor toxicity	12	85.7	2	14.2
Infarction	4	50	4	50
Borderline	6	75	2	25
BK Virus	3	75	1	25
Recurrence of DM Nephropathy	1	33.3	2	66.7
Recurrence of lupus nephritis	0	0	1	100
Tubulointerstitial nephritis	2	66.7	1	33.3
FSGS	2	100	0	0
CMV infection	1	100	0	0

ATN: Acute tubular necrosis; TCMR: Acute T-cell mediated rejection; IF/TA: Interstitial fibrosis and tubular atrophy; ABMR: Acute Antibody-mediated rejection; FSGS: Focal segmental glomerulosclerosis; CMV: Cytomegalovirus.

Table 2. Type of donor and pathologic findings of renal allograft biopsies

	Cadaveric		Living related donor		Living unrelated donor	
Pathologic finding	(n)	(%)	(n)	(%)	(n)	(%)
ATN	13	36.1	1	2.7	22	61.1
TCMR-IA	1	9	0	0	10	91
TCMR-IIA	0	0	0	0	7	100
TCMR-IB	1	14.2	1	14.2	7	77.7
TCMR-IIB	0	0	0	0	3	100
IF/TA I	0	0	1	14.2	6	85.7
IF/TA II	0	0	3	13.6	19	86.3
IF/TA III	0	0	1	6.2	15	93.7
ABMR	0	0	0	0	6	100
Calcineurine inhibitor toxicity	0	0	0	0	14	100
Infarction	1	12.5	0	0	7	87.5
Borderline	0	0	1	12.5	7	87.5
BK Virus	0	0	0	0	4	100
Recurrence of DM nephropathy	0	0	0	0	3	100
Recurrence of lupus nephritis	0	0	0	0	1	100
Tubulointerstitial nephritis	0	0	0	0	3	100
FSGS	0	0	0	0	2	100
CMV infection	0	0	0	0	1	100

ATN: Acute tubular necrosis; TCMR: Acute T-cell mediated rejection; IF/TA: Interstitial fibrosis and tubular atrophy; ABMR: Acute Antibody-mediated rejection; FSGS: Focal segmental glomerulosclerosis; CMV: Cytomegalovirus.

Discussion

Kidney allograft loss in the first 10 years after transplantation is a major problem for both patients and physicians.[35] Although knowing the etiologies of allograft dysfunction helps physicians manage patients with renal dysfunction in a better way, based on our knowledge, no similar studies on kidney allograft diseases were performed in Iran.

In our study, based on Banff classification,

we found that the commonest pathology in Iranian renal allograft biopsies were IF/TA (NOS) and ATN. Both of them were seen more in men than women. Living donors are most important donors and the commonest pathologic process leading to renal allograft dysfunction was ATN in living related and IF/TA in living unrelated donors. Future studies may suggest a stronger association between type of donor and pathologic findings in renal allograft biopsies. In a 10-year study of graft survival of deceased-donor kidney transplantation, Hashiani et al. showed that graft survival rate in patients undergone kidney transplantation was related to recipients and donors' ages, donor source and creatinine level at discharge.[36] Another study of BK viruria in renal transplanted recipients by Taheri et al. revealed that polyomaviruses (BK and JC) were very prevalent among Iranian transplanted kidney biopsies in the first 2 years after transplantation.[37]

In a study in Bahrain, 10year renal allograft biopsies were evaluated for lesions. While the lesions were 34.6% acute rejection and 42.2% chronic rejection, 23.2% of all biopsies did not show any pathologic evidences of rejection. The most histopathologic findings were IF/TA II (26.9%), IF/TA III (7.5%), acute rejection III (ARIII) (15.3%), ARIB (11.5%), ARIIA (4%), IF/TA I (7.6%), ARIA (4%), antibody-mediated changes (4%) and others (19.2%).[38] It is noteworthy that the term "AR" referrs to acute rejection which was modified into TCMR in Banff 09.[21]

In another study in Oxford Transplantation Center, 20% of cases were not associated with rejection. However, 34.1% borderline findings, 17.7% ARIA, 14.3% ARIIB, 9.3% ARIB and 6.1% ARIIA were reported.[39]

Comparing these centers, Bahrain and Iran were more similar in biopsy results and IF/TA (NOS) was the commonest pathologic finding in both centers.

Various factors may affect function of the transplanted kidney.[35] Therefore, long-term follow-up of patients with transplanted kidney will show the outcome and survival duration of allograft kidney. In our study, we did not follow patients for a long period of time and future studies with stronger assessment of long-term pathologic results are required.

Conflict of Interests

Authors have no conflict of interests.

Authors' Contributions

DT and PM supervised data collection and pathology interpretation. SD, AT and VS contributed equally during data collection and analysis. They also helped MF, DT and PM prepare the manuscript. DT, MF and SD edited the manuscript before submission

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