Utility of renal allograft biopsy: An audit of 80 allograft biopsies

Sir,

Histologic analysis of allograft biopsies and their correlation with clinical features has helped in many revisions of the Banff classification for renal transplant pathology. We report an audit of allograft biopsy data of two years at our center and its correlation with clinical features.

A total of 80 biopsies were performed in 56 patients over a period of two years in 48 male and 8 female patients with the age range 5-67 years [Table 1]. These included five children (18 years). All were live-related transplants. The basic causes of end-stage renal disease were: hypertension (n = 24), diabetes mellitus (n = 17) or vesicoureteral reflux disease (6), IgA nephropathy (3), membranous nephropathy (2), postinfectious glomerulonephritis (2), Alport's disease (1), and traumatic damage of congenital single kidney (1).

Indication for biopsy included acute graft dysfunction (58), chronic graft dysfunction (14), proteinuria (n = 1), and change in immunosuppression protocol (n = 7). Serum creatinine level at the time of biopsy ranged from 1.4 to 7.1 mg/dl (Mean 2.4 mg/dl).

Acute cellular rejection (ACR) accounted for 7.5% of the cases which is comparable to other published studies from India[1] but less when compared to the western studies.[2] The discrepancy is attributable to the biopsy policies; ACR being higher in centers doing protocol biopsies. ACR is common in first two weeks post-transplant, but it ranged from 1 month to 16 years in our study.

Borderline rejection was seen in four of our biopsies (5%); three were done beyond the routine time for acute rejection. Some of the studies showed that borderline changes can progress to early Chronic allograft nephropathy (CAN) if left untreated.[3]

The morphologic features of acute humoral rejection (AHR) were identified in 9 biopsies (11.2%), two were C4d-positive. Donor-specific antibodies (DSA) were not available for these patients. All the patients showed dramatic response to anti-rejection treatment with mean follow-up creatinine level of 1.3 mg/dl. The incidence of AHR with analysis of morphologic features, C4d, and DSA ranges 0-8%.[4] Tubulitis or arterial fibrinoid necrosis was not seen in any of the biopsies. Some of the recent studies have also emphasized the existence of C4d-negative AHR.[5]

Table 1: Renal biopsy findings and clinical details (n=80)

Banff category	n=80 (%)	S Cr at Bx (mean) mg/dl	Time of Bx (median)	S Cr (mg/dl) on F/U
Acute rejection	15 (18.7)			
Borderline rejection	4 (5)	2.5	3 years	S Cr 1.8, Death (n=1)
ACR IA	2 (2.5)	2.7	2 month and 2 years	S Cr 1.7
AHR*	9 (11.2)	4.0	6 days	S Cr 1.3
CAN	7 (8.7)	3.7	4 years	S Cr 3.6, Death (n=1)
Acute pyelonephritis	4 (5)	3.0	1 month	S Cr 1.6, progressed to CAN (n=1), Death (n=1)
Glomerular diseases	2 (2.5)	2.3	3 and 10 year	Lost to F/U
CNI toxicity	7 (8.7)	1.7	1 month	S Cr 2.1, Death (n=1)
ATN	21 (26.2)	3.0	1 month	S Cr 1.3, Death (n=3)
Normal	24 (30)	2.8	45 days	S Cr 1.0, Death (n=3)

ACR: Acute cellular rejection, AHR: Acute humoral rejection, ATN: Acute tubular necrosis, Bx: Biopsy, CAN: Chronic allograft nephropathy, CNI: Calcinuric inhibitor, F/U: Follow up, S Cr: Serum Creatinine, *Donor-specific antibodies (DSA) not available

The causes of renal cortical necrosis (RCN) in transplant settings include technical problems related to the surgery, ABO incompatibility, hyperacute rejection, Hendytic Uremic Syndrome (HUS), and thrombotic microangiopathies.[6] All the three cases (3.8%) of RCN were seen in association of AHR. There was no evidence of renal artery thrombosis in any of these cases. Cortical necrosis in the setting of AHR is seen to be associated with positive DSA and negative C4d.[7] Cortical necrosis is an indicator of early graft loss and these patients need to be followed-up for changes of CAN.

The urine culture showed growth of *Pseudomonas* and *E. coli* in two of four patients reported as acute pyelonephritis (5%). Two of the patients responded to antibiotic treatment.

Six patients of calcinuric inhibitor (CNI) toxicity (8.7%) were on tacrolimus and one on cyclosporine. The reported incidence in literature is 12.1% in adult and as high as 35.5% of the pediatric transplants.[8]

Thrombotic microangiopathy (TMA) is caused by endothelial injury secondary to vasoconstriction-associated ischemia and is seen with CNI, infections, humoral rejection, ischemia, or recurrence of HUS.[9] Two cases of TMA were attributed to CNI toxicity, C4d was negative in both. Follow-up creatinine levels were high; one case showed significant chronicity changes.

Two cases with recurrence of disease presented with proteinuria. One was IgA nephropathy, presented after 3 years, one was focal segmental glomerulosclerosis (FSGS) presented after 10 years.

Seven biopsies showed CAN. Five of these patients had documentation of delayed graft function (n = 2), cyclosporine withdrawal (n = 1), recurrent infections (n = 2). The follow-up creatinine remained high (mean 3.6 mg/dl) in all the patients with three mortalities.

Banff (2003) has abolished the term CAN with the purpose of documenting the exact cause for chronicity.[10] Five cases in the present study showed non-specific features of interstitial fibrosis and tubular atrophy and two had transplant glomerulopathy (TG) with thickening and splitting of capillary loops. The reported incidence is 20% of biopsies at five years of transplantation. One of the biopsy with TG had positive C4d suggesting a possibility of chronic humoral rejection as per Banff (2007).

Acute tubular necrosis was noted in 26.2% of the biopsies. Twenty-four of the biopsies were normal on histology. Most of these biopsies were performed with clinical diagnosis of CNI toxicity.

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Quick Response Code:	Website: www.indianjnephrol.org
	DOI: 10.4103/0971-4065.109450