Evaluation of Infectious Complications in the First Year After Kidney Transplantation

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ABSTRACT

Kidney transplantation (KT) is the best available therapy for patients with end-stage renal disease. Infectious complications are a common cause of morbidity and mortality. In this study, we evaluated the risk factors and outcomes of infectious complications in the first year after transplantation. This is a retrospective and observational study of kidney transplant recipients at Ankara University's Ibni Sina Hospital between January 2009 and August 2013. A total of 206 kidney transplant recipients were evaluated. In 129 patients, 298 infectious episodes occurred: 55 (26.7%) had 1; 33 (16%) 2; 19 (9.2%) 3; 7 (3.4%) 4; and 15 (7.3%) had 5 or more infectious episodes. The most common bacterial infection was urinary tract infection (128, 42.9%). Only 4 urinary tract infection episodes (3.1%) were associated with bacteriemia. Seventeen patients (5.7%) had bacteremia. Viral infections after transplantation were CMV infection (10.1%), BK virus infection (5.7%), and zona zoster (1.1%). Deceased donor kidney transplantation was the independent risk factor. Mean follow-up period was 66 months and was the same for the patients with and without infections. There was no significant difference in 5-year survival and creatinine levels at the last follow-up (logrank $P = .409$). Infections are the second most common cause of mortality in KT patients. The successful treatment of these complications and effective prophylaxis may decrease these complications.

KIDNEY TRANSPLANTATION (KT) is the best available therapy for patients with end-stage renal disease (ESRD). The 2 major factors for successful KT are better control of rejection and better prevention and treatment of infections [1]. Although infection-related mortality in the first year after transplantation has been reduced to less than 5%, these complications remain serious threats after renal transplantation [2]. Infection-associated mortality among dialysis patients on the waiting list for KT is greater than among transplant recipients [3].

Infections after transplantation are influenced by surgical procedure, immunosuppressive therapies, and other invasive interventions. Therefore, infectious agents and their distribution vary with respect to the period after transplantation [4]. Improvement in prophylaxis and more selective immunosuppressive drugs have made KT a secure procedure [5]. The greatest risk for life-threatening infections occurs during the first 6 months of after transplantation because of peak immunosuppressive therapy. After 6 months, the immunosuppressive therapy is at low level, and chronic infections, opportunistic infections, and general community-acquired infections are frequent. In this study, we evaluated the risk factors and outcomes of patients with infectious complications in the first year after transplantation.

PATIENTS AND METHODS

This is a retrospective, observational study of kidney transplant recipients at our hospital between January 2009 and August 2013. Transplantation procedures were performed using standard techniques by the same surgeon. After kidney transplantation, patient follow-up included 1 visit per week during the first month and 2

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0041-1345/15
http://dx.doi.org/10.1016/j.transproceed.2015.04.056

Table 1. Demographics, Underlying Diseases, and Risk Factors for Infection in RT Recipients

Characteristic	Total (N = 206)	Patients With Infection (n = 129)	Patients Without Infection (n = 77)	*P* Value
Age, mean ± SD	38.55 ± 13.314	39.3 ± 13.522	37.3 ± 12.948	NS
Gender, male (%)	112 (54.4%)	60 (46.5%)	47 (61%)	.045
Comorbidities				
Hypertension (n, %)	118 (60.8%)	64 (53.8%)	54 (72%)	<.011
Diabetes mellitis	46 (23.6)	28(23.3%)	18 (24%)	NS
COPD	5 (2.6%)	3 (2.5%)	2 (2.7%)	NS
CRF etiology				
Unknown etiology	46 (22.5%)	28 (21.9%)	19 (24.7%)	NS
Hypertension	25 (12.3%)	14 (11%)	11 (14.3%)	NS
Diabetes mellitus	31 (15.2%)	17 (13.4%)	14 (18.2%)	NS
VUR	14 (6.9%)	10 (7.8%)	4 (5.2%)	NS
Glomerulonephritis	16 (7.8%)	13 (10.2%)	7 (9.1%)	NS
Amiloidosis	13 (6.4%)	10 (7.8%)	3 (3.9%)	NS
Other	55 (26.8%)	36 (28.1%)	19 (24.7%)	NS
Deceased donor	37 (18.0%)	32 (24.8%)	5 (6.5%)	.001
Induction agent				
Basiliximab	93 (45.4%)	60 (46.5%)	33 (43.4%)	NS
ATG	23 (11.2%)	16 (12.4%)	7 (9.2%)	NS
Daclizumab	2 (1.0%)	2 (1.6%)	0 (0%)	NS
Antirejection therapy (%)	9 (4.4%)	6 (4.7%)	3 (3.9%)	NS

Abbreviations: COPD, chronic obstructive pulmonary disease; CRF, chronic renal failure; VUR, vesicoureteral reflux.

visits in the second month. Afterwards, patients visited the outpatient clinic once a month until the twelfth month. Patients who failed to follow up were excluded from the study.

Prophylactic antimicrobials included cefazolin for 3 days as surgical prophylaxis, trimethoprim/sulfamethoxasole against *Pneumocystis jirovecii*, fluconazole for fungal infections, and valgancyclovir against cytomegalovirus (CMV) starting from the fourth day of transplantation for 6 months. Additionally, patients with positive tuberculin skin test and no evidence of active tuberculosis received isoniazid 300 mg per day for 9 months. Standard immunosuppressive protocol included prednisone, tacrolimus, and mycophenolate mofetil. Antirejection treatment included methyl prednisolone and/or antithymocyte globulin and/or plasmapheresis.

We analyzed the infectious complications of the kidney transplant recipients in the first year after transplantation. Variables collected were as follows: gender, age at time of transplantation, cause of ESRD, comorbid diseases, type of dialysis before transplantation, length of dialysis, type of donor, transplant number, viral markers of the recipient before transplantation, and induction and maintenance immunosuppressive therapy. Variables that were evaluated related to the infections were as follows: Type of infection, type of microorganisms that were isolated, the time of infection, presence of "double J" catheter, and symptoms in urinary tract infections (UTIs).

An infectious episode was defined as a febrile episode and/or a laboratory diagnosis of infection. The site of infection was determined as urinary, pulmonary, surgical wound, intraabdominal, bacteremia, vascular catheter-related bloodstream, and diarrhea. UTIs were diagnosed clinically by fever, dysuria, frequency, suprapubic tenderness, and/or isolation of an infectious agent upon culture. Asymptomatic cases were diagnosed only by a positive urine culture ($\geq 10^5$ cfu/mL). We also followed the BK virus titers in patients' urine. Cases of pneumonia were diagnosed on a clinical and/or laboratory basis. Cases of bacteremia were defined as at least 1 or 2 positive blood cultures and evidence of systemic inflammatory response syndrome (SIRS). Patients with clinical gastrointestinal manifestations and significant clinical improvement after therapy with intravenous fluids and quinolones, and in whom certain gastrointestinal side effects of immunosuppressant therapy (including mycophenolate mofetil) were ruled out because reduction of drug dosage did not modify the acute diarrhea. CMV infection was defined as isolation of CMV-DNA in the blood. CMV disease was associated with the presence of organ-specific involvement. In order to assess the impact of infections on graft function, the last serum creatinine concentration measured was evaluated and 5-year survival was calculated.

Data were analyzed using SPSS statistics version 16 for Windows (SPSS, Inc., Chicago, Ill., United States). The χ^2 test, Student *t* test, or the Mann-Whitney *U* (Wilcoxon) sample were used for the statistical analysis. We also analyzed the 5-year survival of the patients using the Kaplan-Meier method. Patients were divided into 2 groups: cases with at least 1 infection in the first year after transplantation and cases without infection. Comparison between these 2 groups was performed by log rank test. All *P* values <.05 were considered to be statistically significant.

RESULTS

From January 1, 2009, to August 31, 2013, a total of 240 KT procedures were performed at Ankara University Ibni Sina Hospital's Transplantation Unit. A total of 34 patients were excluded from the study, 29 of whom were below 18 years of age, and 5 failed to follow up. The transplants were from a living donor in 169 cases and from a deceased donor in 37. During the study period, transplantation was performed twice on 1 patient. Eight patients had previously undergone a KT. Before KT, 116 patients (59.5%) had been on hemodialysis and 28 (14.4%) on peritoneal dialysis. In total, 41 patients (21%) underwent KT preemptively, and 161 recipients (95.8%) were CMV seropositive, whereas 7 (4.2%) were seronegative. Regarding donors, 129 (98.5%) were CMV