

Neurologic Complications of Renal Transplant

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Abstract

Objectives: Neurologic problems have a major effect on the survival and quality of life in renal transplant recipients. This study sought to review the incidence and character of neurologic complications after renal transplant.

Materials and Methods: Medical records of 319 renal transplant recipients admitted to the Transplant Outpatient Clinic were reviewed retrospectively for neurologic complications.

Results: Of the 319 transplant recipient patients reviewed, 124 patients (39%) were women and 193 patients (61%) were men. The mean patient age was 41 ± 11 years, and the transplanted kidney was received from deceased donors in 161 patients (51%) and living donors in 158 patients (49%). There were 50 patients (16%) who had neurologic complications, most commonly herpes zoster infection associated with immunosuppressive medication. Only 1 patient, who had glioblastoma multiforme, died. Treatment included corticosteroids in 296 patients (93%) and calcineurin inhibitors (including tacrolimus) in 111 patients (35%).

Conclusions: Neurologic complications are common after renal transplant. Most complications are associated with immunosuppressive medications.

Key words: Neurology, Kidney, Renal failure, Herpes zoster, Immunosuppression

Introduction

Renal transplant is a life-saving procedure for patients with end-stage renal disease. Advances in surgical procedures and perioperative care have improved outcomes. However, neurologic complications constitute a serious concern both for the mortality and morbidity of the recipients.¹ The major neurologic complications after renal transplant include neurotoxicity associated with immunosuppressive therapies, infections, malignancies, peripheral nervous system involvement, and stroke.² The aim of the present study was to evaluate the frequency and type of the neurologic complications after renal transplant.

Materials and Methods

The medical records of the 319 renal transplant recipients who were followed at the Izmir Bozyaka Training and Research Hospital Organ Transplant Outpatient Clinic were reviewed after Local Ethical Committee approval was obtained. All protocols conformed to the ethical guidelines of the 1975 Helsinki Declaration. Data regarding the age and sex of subjects, date and cause of renal transplant, type of donor, and the neurologic symptoms were recorded. Statistical analyses were performed with SPSS software (SPSS: An IBM Company, version 16.0, IBM Corporation, Armonk, New York, USA).

Results

Of the 319 patients (renal transplant recipients) included in the study, 193 patients (61%) were men and 126 patients (39%) were women. The mean age of the patients was 41 ± 11 years (range, 14-71 y); 161 patients (51%) received transplants from deceased donors and 158 patients (49%) received transplants

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Acknowledgements: The authors declare no conflicts of interest.

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Experimental and Clinical Transplantation (2012) 3: 243-246

from living donors. There were 46 patients (14%) with hypertension and 17 patients (5%) with diabetes. There were 15 patients (5%) who were positive for hepatitis C, 1 patient had chronic hepatitis B infection, and 1 patient was a hepatitis B carrier.

Before the transplant procedure, 2 patients had a recent stroke, and 1 patient, each, had epilepsy, migraine headaches, and neurologic complications of Behçet disease. The mean follow-up was 6 ± 4 years (range, 1-33 y). The cause of end-stage renal disease was chronic glomerulonephritis in 113 patients (35%), tubular interstitial nephritis in 31 patients (10%), polycystic renal disease in 19 patients (6%), hypertensive nephrosclerosis in 18 patients (6%), diabetic nephrosclerosis in 17 patients (5%), amyloidosis in 18 patients (6%), congenital renal disease in 9 patients (3%), preeclampsia in 4 patients (1%), and toxic nephropathy in 3 patients (1%). The cause of end-stage renal disease could not be identified in 87 patients (27%).

Neurologic complications were observed in 50 patients (16%) (Table 1), of whom 32 (10%) had severe neurologic problems resulting in a disability (Table 2). The most-common neurologic complications were herpes zoster infections, tension headaches, vertigo, and femoral neuropathy (Table 1). The most-common drugs used after renal transplant included corticosteroids in 296 patients (93%) and calcineurin inhibitors (including tacrolimus) in 111 patients (35%). There was no significant difference in frequency of neurologic

complications between male and female patients (Table 3) or between patients who received kidney transplants from living or deceased donors (Table 4).

Discussion

Renal transplant recipient patients are at high risk of developing neurologic problems,³ and the reported risk varies from 13% to 60%.^{4, 5} Neurologic complications can be related to surgical procedures, immunosuppression after transplant (including opportunistic infections or neurotoxicity of drugs), metabolic disturbances, malignancies, and stroke.⁶⁻⁸

A common neurologic complication of kidney transplant at our hospital was femoral neuropathy (Table 1), similar to previous reports.⁹⁻¹⁰ Approximately 2% patients may develop femoral neuropathy after renal transplant surgery because of focal nerve compression. In the present study, femoral neuropathy was mild in all 5 patients, and only 1 patient required a cane. The iliac arteries were used as the allograft blood supply in the present patients; although this procedure may increase the risk of spinal cord ischemia, no case of spinal infarction occurred.

Cerebrovascular events can occur in 4% to 8% of renal transplant recipients.¹¹ The cause may be atherosclerosis, vasculitis, or endocarditis. In the present study, cerebrovascular events occurred in only 2 (0.6%) of the 319 patients, less frequently than previous studies. Headache was a frequent complaint in the present patients; the differential diagnosis for headaches includes tension headache, migraine headache, and sinusitis.

Neurotoxic drugs, such as calcineurin inhibitors (tacrolimus) or cyclosporine, are frequently used in renal transplant recipients.^{4, 12} The most-frequent adverse events of these medications include tremor, encephalopathy, seizures, and headache. Tremor may be disabling but this was not observed in the present patients. Corticosteroids are commonly used for maintenance therapy and management of acute transplant rejection. Psychosis and myopathy are reported adverse events of corticosteroids. However, most present patients had been on corticosteroid therapy and only 1 case of myopathy was attributed directly to corticosteroids; therefore, corticosteroids could be regarded as a safe treatment. The frequency of complications in patients using tacrolimus or cyclosporine was low.

Table 1. Neurologic complications in 319 renal transplant recipient patients.

Neurologic complication	Patients	
	Number	Percentage
Herpes zoster	16	32
Tension headaches	9	18
Vertigo	6	12
Femoral neuropathy	5	10
Seizure*	3	6
Migraine headache	2	4
Cerebrovascular disease†	2	4
Peripheral facial paralysis	1	2
Diffuse myopathy	1	2
Glioblastoma multiforme‡	1	2
Ventricular cyst and hydrocephalus§	1	2
Transverse myelitis from herpes simplex	1	2
Pneumococcal meningitis	1	2
Amyotrophic lateral sclerosis	1	2
Total	50	100

*Seizures were caused by hypocalcemia, epilepsy after stroke, and cryptogenic epilepsy in 1 patient each. In the patient with cryptogenic epilepsy, seizures began 7 years after transplant, and no obvious cause was found.

†Cerebrovascular disease: 1 patient had a transient ischemic attack, and 1 patient had ischemic stroke with right hemiparesis.

‡Patient died from glioblastoma multiforme.

§Hydrocephalus was treated with ventriculoperitoneal shunt procedure.

Table 2. Demographic and clinical data of the 32 renal transplant recipient patients with severe neurologic complications resulting in disability.

Age (y)	Sex	History	Neurologic complication	Transplant donor type	Immunosuppressive medication
41	F	Familial Mediterranean fever, amyloidosis, preeclampsia	Femoral neuropathy	Deceased	Corticosteroid, mycophenolate, tacrolimus
50	M	Hypertension	Femoral neuropathy	Living	Corticosteroid, mycophenolate, cyclosporine
57	F	Hypertension	Femoral neuropathy	Deceased	Corticosteroid, azathioprine, sirolimus
50	M	None	Femoral neuropathy	Living	Corticosteroid, mycophenolate, tacrolimus
61	M	None	Femoral neuropathy	Deceased	Corticosteroid, mycophenolate, tacrolimus
69	M	Coronary artery bypass graft	Femoral neuropathy	Deceased	Mycophenolate, tacrolimus, azathioprine
35	F	Familial Mediterranean fever	Myopathy	Deceased	Corticosteroid, mycophenolate
55	M	None	Herpes zoster	Living	Corticosteroid, azathioprine, cyclosporine
30	M	Hypospadias	Herpes zoster	Living	Corticosteroid, azathioprine, tacrolimus
26	F	Hypertension	Herpes zoster	Deceased	Corticosteroid, azathioprine, cyclosporine
59	M	None	Herpes zoster	Deceased	Corticosteroid, azathioprine, tacrolimus
48	M	None	Herpes zoster	Living	Corticosteroid, tacrolimus
52	F	Cerebrovascular disease	Herpes zoster	Deceased	Corticosteroid, azathioprine, sirolimus
32	F	None	Herpes zoster	Living	Corticosteroid, azathioprine, tacrolimus
64	M	None	Herpes zoster	Deceased	Azathioprine, cyclosporine
35	M	None	Herpes zoster	Deceased	Corticosteroid, mycophenolate, cyclosporine, everolimus
54	F	None	Herpes zoster	Living	Corticosteroid, mycophenolate, sirolimus
54	M	None	Herpes zoster	Living	Corticosteroid, azathioprine, cyclosporine
26	F	Hypertension	Herpes zoster	Deceased	Corticosteroid, azathioprine, cyclosporine
61	M	None	Herpes zoster	Living	Corticosteroid, azathioprine, cyclosporine
40	M	None	Herpes zoster	Living	Corticosteroid, azathioprine, mycophenolate
43	M	None	Hydrocephalus	Living	Azathioprine, cyclosporine
45	M	None	Glioblastoma multiforme	Deceased	Corticosteroid, mycophenolate, everolimus
26	F	None	Facial paralysis	Living	Corticosteroid, mycophenolate, tacrolimus
37	F	Thalassemia minor	Seizure (hypocalcemia)	Deceased	Corticosteroid, mycophenolate, tacrolimus
55	M	Cerebrovascular disease, myocardial infarction	Epilepsy after stroke	Living	Azathioprine, cyclosporine
56	F	Hypertension	Seizure (metabolic)	Deceased	Corticosteroid, azathioprine, cyclosporine
60	M	None	Herpes myelitis	Deceased	Corticosteroid, azathioprine, cyclosporine
64	F	None	Meningitis	Living	Corticosteroid, azathioprine, cyclosporine
45	F	Hypertension, thalassemia minor	Transient ischemic attack	Living	Corticosteroid, mycophenolate, sirolimus
47	M	Hypertension	Intracerebral hemorrhage	Deceased	Corticosteroid, mycophenolate, tacrolimus
44	M	None	Central nervous system lymphoma, amyotrophic lateral sclerosis	Deceased	Corticosteroid, tacrolimus

Table 3. Distribution of renal transplant recipient patients with or without neurologic complications according to sex.

Neurologic complications	Number of patients (percentage)		
	Male	Female	Total
Absent	164	105	269 (84)
Present*	29	21	50 (16)
Total	193 (61)	126 (39)	319

*Difference between male and female patients: not significant ($P = .84$).

Table 4. Distribution of renal transplant recipient patients with or without neurologic complications according to sex.

Neurologic complications	Number of patients (percentage)		
	Living donor	Deceased donor	Total
Absent	137	132	269 (84)
Present *	24	26	50 (16)
Total	161 (51)	158 (49)	319

*Difference between patients with transplant from living versus deceased donor: not significant ($P = .82$).

Opportunistic infections also can occur in renal transplant recipients. The most-common opportunistic infection in the present study was herpes zoster infection, which was observed in 16 of

319 patients (5%). In a previous study of 681 renal transplant recipients, 18 patients (2.6%) had dermatomal herpes zoster.¹³ The incidence of central nervous system infection, which has high risk of mortality, is 10% to 16% in autopsy studies.^{2, 14} However, the present study included patients with pneumococcal meningitis and herpes myelitis without any fatality (Table 1).

Seizures have been reported frequently in renal transplant patients.^{15, 16} The cause of seizures in transplanted patients includes metabolic disturbances (such as electrolyte imbalance or glucose metabolism disorders), drug toxicity (such as cyclosporine, tacrolimus, theophylline, or imipenem), and local central nervous system lesions (such as tumor, infarction, or hemorrhage).⁴ In the present study, seizures occurred in 3 of 319 patients (0.9%).

Although de novo malignancies of the central nervous system are observed after renal transplant, only 1 patient in the present study developed glioblastoma multiforme and died. Another patient developed hydrocephalus that resulted from a benign cyst in the third ventricle, and this patient was operated on for this complication and had a good prognosis.

In conclusion, the present study showed that neurologic complications after renal transplant were common, having occurred in 50 of 319 patients (16%). It is important for health care providers to familiarize themselves about neurologic symptoms that may occur after renal transplant. Identifying and monitoring these symptoms may decrease the potential morbidity and mortality in renal transplant recipients.

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