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Original Article

Neurological complications in renal transplant patients: A single-center experience

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ABSTRACT

Aims: To evaluate the nature and incidence of neurologic complications in recipients of living donor renal transplantation. Neurologic complications are a significant cause of morbidity and mortality in patients who undergo transplants and there is paucity of data regarding the same. The epidemiology of infective agents varies according to geographical locations.

Methods: We included 856 patients of live related renal transplantation at our institution between January 2002 and December 2009. All recipients who were found to have some clinical, laboratory, or radiological evidence of neurological involvement were considered. Associated comorbid medical conditions, presenting neurologic symptoms, and type of immunosuppression were recorded. Occurrence of acute rejections, chronic allograft nephropathy (CAN), delayed graft function, and new onset diabetes after transplant (NODAT) were recorded.

Results: Of the total 856 renal transplant recipients, a total of 93 (10.8%) patients were found to have some clinical, laboratory, or radiological evidence of neurological involvement. A total of 69 (73.3%) developed CNS complications with a mortality rate of 37.7%. CNS infections occurred in 47 (5% of total) recipients and accounted for the largest group (68.1%). Fungi were the commonest etiological agents, 22 (46.8%), and were associated with 40% mortality. Cryptococcal meningitis was occurring in 19 (27.5%), with mortality in 31.6% of these. Other fungal infections were aspergillosis in two and mucormycosis in one. All patients with aspergillosis and mucormycosis had a fatal outcome. The second largest group on CNS complications comprised of patients with cerebrovascular accidents, which occurred in 13 patients (18.8%), and were associated with a mortality of 23%. Eight patients with ischemic stroke had survived. Two had hemorrhagic stroke and both had a fatal outcome. Three patients had subdural hematoma with 33.3% mortality. Four patients had toxic encephalopathy as a result of fulminant systemic sepsis with mortality in all. Other less common CNS complications included intracranial space occupying lesion in two, postoperative psychosis in two, and hypoglycemic coma in one. There was no relationship between the development of infection or stroke and the type of maintenance immunosuppression

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used. A total 61 (65.5%) patients, which comprises 7% of the total transplant recipients, presented with some complications involving the peripheral nervous system (PNS). The most common manifestations were tremor in 26.5%, followed by paresthesias in 18.3%, steroid-induced myopathy in 11.8%, ulnar neuropathy in 4.4, and femoral neuropathy in 2.2%. These complications were more common with tacrolimus.

Conclusion: We conclude that complications involving the neurological system occur in 10.5% of all transplant patients with 8% involving CNS and 7% involving the PNS. The high mortality rates associated with CNS complications warrant early diagnosis and aggressive treatment in renal transplant recipients.

1. Introduction

The kidney is the most frequently transplanted organ with more than 10,000 transplants occurring per year worldwide. Since the landmark operation by Murray in Boston in 1954 in which an identical twin received a donated sibling kidney, kidney transplants have developed into the best-accepted therapy for most causes of end-stage renal failure.[1] The 1-year survival rate is close to 100%, with an 85–95% graft survival rate.[2] However, despite these advances, neurologic complications after renal transplants occur in a significant percentage of patients. An early, large retrospective study found neurological complication to be 30% over an 18-year period.[7] Two more recent studies have found lower rates, 8% and 10% over a 26-year period and 19-year period, respectively.[5,6]

Several characteristics of renal transplant patients make overall complication rates in these persons different from those of other organ transplant recipients. Many renal transplant patients have some degree of vascular compromise either as a result of their underlying disease (e.g., hypertension, diabetes) or because of emboli associated with underlying atherosclerosis or heart disease.[8] After transplant, neurologic complications may develop secondary to the transplant itself, the immunosuppressive agent, or a previously known organ parenchymal failure. The most common neurological complications seen with renal transplantation are neurotoxicity attributable to immunosuppressive drugs, opportunistic central nervous system (CNS) infections, cerebrovascular events, encephalopathy, and de novo CNS neoplasms. Amongst immunosuppressants, calcineurin inhibitors are the main drugs involved in neurotoxicity, leading to complications, which range from mild symptoms, such as tremors and paresthesias, to severe symptoms, such as disabling pain syndrome and leukoencephalopathy. Indeed in some reports, opportunistic infections of the CNS are second in frequency to those of the lung as a cause of morbidity and mortality.[9] Neurological complications can be broadly divided into those involving the CNS and the peripheral nervous system (PNS). CNS dysfunction localizes to any abnormality of brain and spinal cord. PNS dysfunction localizes to nerve roots (radiculopathy), peripheral nerves (neuropathy), and muscle (myopathy). Since there are not many reports on this subject and because epidemiology of various infective agents varies according to geographical locations, we present our experience on various neurological complications encountered in renal transplant patients in our institute over a period of 8 years, from 2002 to 2009.

2. Patients and methods

The medical reports of 856 renal transplant recipients who underwent renal transplantation between January 2002 and December 2009 were analyzed retrospectively for presence of neurologic complications. The cut-off time for follow-up was December 2009. All patients presenting with symptoms or signs pertaining to neurological involvement were included excepting those with a uremic encephalopathy due to severe graft dysfunction. Investigations performed on patients with neurological complications were primarily guided by their clinical manifestation. Investigations included hemoglobin (Hb%), blood counts, RBC morphology, ESR, serum creatinine, blood urea nitrogen (BUN), serum electrolytes, serum calcium, phosphorus, alkaline phosphatase, parathyroid hormone (PTH) level, radiological investigations like chest X-ray, abdominal ultrasound, CT, and MRI scan as and when required. Cerebrospinal fluid examination, serology, NCV, EMG, and EEG were performed as and when required. All patients who were positive by ELISA were confirmed by DNA and RNA PCR studies.

Occurrence of acute rejections, biopsy proven chronic allograft nephropathy (CAN), delayed graft function (DGF), and new onset diabetes after transplant (NODAT) were recorded. All acute rejections were confirmed by graft biopsy, and delayed graft function (DGF) was defined as need of dialysis within 1 week after transplantation; new onset diabetes (NODAT) was defined as per the American Diabetes Association criteria. The use of immunosuppressive drugs with doses and induction with anti-thymocyte globulin (ATG) and IL-2Rα blockers were recorded.

Neurological complications were broadly categorized into complications involving the CNS and those involving the PNS. The type and incidence of neurologic complications, the type of immunosuppressive medication used, the type of antirejection treatment used, and the onset of symptoms were evaluated.

The causes of end-stage renal disease in all of the patients and significant medical histories other than chronic renal disease for these patients also were evaluated.