

# NEUROLOGIC AND PSYCHOLOGIC COMPLICATIONS AFTER KIDNEY TRANSPLANTATION

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## ABSTRACT

Neurologic and psychologic complications are usually related to drug toxicity, infections or symptoms induced by deterioration of renal allograft function. Metabolic encephalopathy, hypertensive encephalopathy, cerebrovascular events, and new-onset seizures have all been reported in organ-transplant recipients. Infections can be caused by listeria, cryptococcus, nocardia, aspergillus and mucor. Toxoplasma, coccidia, cytomegalovirus (CMV) and herpes infections are also reported. Cerebral hemorrhage can occur secondary to septic emboli or intracerebral aneurysms. The aim of this study is to present the results of a review on 200 renal transplant recipients concerning neuropsychologic complications during a 12-year period in the Imam Khomeini Hospital affiliated to Tehran University of Medical Sciences.

According to this study, neuropsychologic disorders occurred in 30 (15%) of the recipients and of these, peripheral neuropathy, depression and tremor were the most common and were detected in 8 (4%), 5 (2.5%), and 4 (2%) of the recipients, respectively.

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## INTRODUCTION

Transplantation is now accepted as a lifesaving therapy. New discoveries in the field of immunology and development of better immunosuppressive therapy has led to greater success rates in transplantation and a decline in patient mortality.

Because of the importance of neuropsychologic complications related to metabolic and infectious causes and hypertension, drug toxicity and seizures, early detection and management of these complications are necessary.<sup>1</sup> The

neuropsychologic complications of 200 renal transplant recipients will be reviewed in this paper.

## MATERIALS AND METHODS

Between 1985 and 1996, 200 patients received renal transplantation in the Imam Khomeini Hospital. We retrospectively reviewed the medical records of these patients. 140 recipients (70%) were male and 60 (30%) were female. The mean age at the time of transplantation was  $33.74 \pm 0.7$  years. 164 patients (82%) received transplantation from living-unrelated donors, 35 patients (17.5%) from living-related donors and one (0.5%) from cadaver donor. The observation period ranged from one to 108 months. The immunosuppressive regimens consisted of azathioprine, cyclosporine and prednisolone and patients with acute re-

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jection received methylprednisolone pulse/ALG.

### RESULTS

Neuropsychologic disorders are shown in Table I. Peripheral neuropathy was diagnosed in 8 patients (4%). In 5 patients unilateral lower limb neuropathy was diagnosed in the first week after renal transplantation. They had decrease of muscle force, numbness, and paresthesia with documentation by electromyography and nerve conduction velocity (EMG, NCV) studies for involvement of the lumbosacral plexus and femoral nerve. In 3 patients bilateral neuropathy such as paresthesia in the hands was diagnosed about 2 years after transplantation. Depression was diagnosed in 5 patients (2.5%). In 3 patients, depression was accompanied by nightmares and irritability in the first month after transplantation. These three patients had acute rejection of their renal allograft concomitantly; two of them received methylprednisolone pulse and dialysis and one of them methylprednisolone pulse and plasmapheresis. In 2 patients depression was diagnosed 2 and 6 years after transplantation respectively.

Tremor was diagnosed in 4 patients (2%). In one of them the blood level of cyclosporine was above therapeutic level.

Hypertensive encephalopathy was diagnosed in 3 patients (1.5%). Acute rejection of renal allograft was propounded at the same time in these three patients. Hypertension in one patient in this group had progressed to malignant range, and allograft nephrectomy had been performed for the other one.

Convulsion was diagnosed in two patients: one with severe hyponatremia and the other with renal allograft dysfunction and uremia.

One patient of our series had post-herpetic neuralgia and persistent headache for 3 months after herpetic infection of the posterior neck and face. One patient presented with Ramsay-Hunt syndrome and involvement of the geniculate ganglion and facial nerve after herpetic infection of the face.

In another patient with pain in one half of the face, ptosis and diplopia, unilateral paralysis of the third cranial nerve due to atherosclerosis was diagnosed. One patient who presented with acute psychosis and disorientation responded to temporary discontinuation of cyclosporine.

Other neurologic disorders were: cerebrovascular accident (CVA) in a patient with hemorrhage in the parietal lobe; brain abscess in the frontal area and meningitis due to *Staph. aureus* in another patient; and acoustic neuroma in the cerebellopontine angle in a known case of Alport's syndrome.

### DISCUSSION

Peripheral neuropathy was diagnosed in 4% of our series. One of its causes is trauma to the lumbosacral plexus and femoral nerve at the time of operation for transplantation. As a consequence, there will be weakness of the muscles

for knee extension, diminished patellar reflex, and disturbance of sensation of the anterior thigh and medial calf. Ischemic lesions of the lumbosacral plexus are more severe in diabetic patients and if this happens, they will complain of pain in the gluteal area and weakness of calf muscles. Sometimes subacute tetraparesis after kidney transplantation is due to reactivation or primary infection of CMV.

One entity which must be differentiated from cyclosporine toxicity, encephalitis, malignant hypertension, pseudotumor cerebri and brain lymphoma is rejection encephalopathy. This encephalopathy is an acute and reversible neurologic syndrome, especially in young males at the time of rejection episodes and is accompanied by headache, giddiness, irritability, convulsion and papilledema.<sup>2</sup>

Diffuse encephalopathy which can range from disturbance in consciousness to coma, has many causes: cyclosporine toxicity with tremor, convulsions and visual disturbances; meningoencephalitis; encephalopathy due to listeria infection with motor and speech disorders; cryptococcal infection; or encephalopathy due to hypertension or hyponatremia.

Nervous system infections can be caused by aspergillus,

**Table I.** Neurologic and psychologic complications in 200 renal transplant recipients during 1985-1996 at Imam Khomeini Hospital.

| Neuropsychologic disease    | No. | %     |
|-----------------------------|-----|-------|
| Hemorrhagic CVA             | 1   | 3.3%  |
| Convulsion                  | 2   | 6.6%  |
| Post-herpetic neuralgia     | 1   | 3.3%  |
| IIIrd cranial nerve palsy   | 1   | 3.3%  |
| Ramsay-Hunt Syndrome        | 1   | 3.3%  |
| Tremor                      | 4   | 13.3% |
| Peripheral neuropathy       | 8   | 26.6% |
| Headache                    | 1   | 3.3%  |
| Psychosis                   | 1   | 3.3%  |
| Depression                  | 5   | 16.6% |
| Brain abscess               | 1   | 3.3%  |
| Brain tumor                 | 1   | 3.3%  |
| Hypertensive encephalopathy | 3   | 10%   |
|                             | 30  | 100%  |

listeria, nocardia, toxoplasma, candida, herpes virus, cryptococcus, *Mycobacterium tuberculosis* and the agent of progressive multifocal leukoencephalopathy. One article has mentioned neurologic complications in 30% of renal transplant recipients and mentioned that infections were the most common disorder in their study group.<sup>3</sup>

Sometimes focal disturbances of the central nervous system can be caused by nocardia, toxoplasma, aspergillus, brain

lymphoma and central pontine myelinolysis.<sup>2</sup>

Cerebral stroke is reported in 3% of renal transplant recipients and is more common in patients with a history of chronic dialysis therapy, hypertension, age more than 40 years, diabetes, lupus erythematosus, hyperlipidemia and atherosclerosis.<sup>2</sup>

Convulsion in these patients can be due to brain lymphoma, infections, brain infarction, acute rejection, or cyclosporine toxicity. Cyclosporine will diminish the convulsion threshold. That's why in cases of convulsion one should measure the cyclosporine blood level, serum sodium, sugar, calcium and also magnesium, because of the possibility of hypomagnesemia due to cyclosporine.

Some neuropsychologic side effects of immunosuppressive drugs are as follows: cyclosporine induces tremor, paresthesia, leukoencephalopathy, visual hallucinations, depression, insomnia, cortical blindness, decline of convulsion threshold, mood disorder and psychosis.<sup>2</sup> Reflex sympathetic dystrophy syndrome (RSDS) with pain and tenderness in the extremities, vasomotor instability, trophic changes of skin and bone demineralization has also been reported due to this drug.<sup>4</sup>

Corticosteroids can induce pseudotumor cerebri syndrome, psychosis, epidural lipomatosis and insomnia.<sup>5</sup>

Tacrolimus (FK506), which has not been used in our patients yet, is reported to induce myalgia, tremor and fatigue in one study in pediatric renal transplant recipients.<sup>6</sup>

Other complications which should be differentiated from neurologic disorders are those which cause myopathy, such

as hypophosphatemia, hypokalemia, and drugs like cimetidine, lovastatine, clofibrate, gemfibrozil, cyclosporine and corticosteroids. Myopathy due to corticosteroids, which more commonly involves proximal muscles, is more often seen when using divided doses of the drug.<sup>3</sup>

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