Rehabilitation of Two Cases Neurologic Complications Following Solid Organ Transplantation

Solid Organ Transplantasyonu Sonrası Nörolojik Komplikasyon Gelişen İki Olgunun Rehabilitasyonu

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ABSTRACT Patients developing neurologic complications following solid organ transplantation may require neurologic rehabilitation, as well. This is not commonly observed in rehabilitation clinics. The first case was a perioperative cerebrovascular accident that developed in a 13-year-old girl who had a cardiac transplantation upon the diagnosis of cardiomyopathy associated with myocarditis. The second case was a 63-year-old woman who had undergone a liver transplantation due to biliary cirrhosis that developed in the left hemiplegia during the postoperative period. Neurologic complications emerged in the early stages in both of the two transplant patients. They were admitted to the rehabilitation program in order to aid in the improvement of their motor and cognitive functions, and to provide mobility and independence in their daily life activities. The rehabilitation of transplant patients does require a different approach compared to other neurologic rehabilitations, since it involves the use of multiple medicines, high infection risk, a longer stay in intensive care units, and comorbidities (decubitus ulcer, and nutrition and respiration problems).

Key Words: Heart transplantation; liver transplantation; stroke; rehabilitation

ÖZET Solid organ nakli sonrası nörolojik komplikasyon gelişen hastalara yönelik nörolojik rehabilitasyon gerekebilir. Bu, rehabilitasyon kliniklerinde sık görülen bir durum değildir. Birinci olguda, miyokarditle ilişkili, kardiyomiyopati tanısı nedeniyle kalp nakli olan 13 yaşındaki bir kız çocuğunda perioperatif serebro-vasküler olay gelişmiştir. İkinci olgu, biliyer siroz nedeniyle karaciğer nakli olan 63 yaşındaki kadın hastada postoperatif dönemde sol hemipleji gelişmiştir. Her iki nakil hastasında, erken dönemde nörolojik komplikasyon ortaya çıkmıştır. Bu hastalar, motor ve bilişsel fonksiyonlarını iyileştirmek, mobilite ve günlük yaşam aktivitelerinde bağımsızlıklarını sağlamak amacıyla rehabilitasyon programına kabul edildi. Nakil hastalarının rehabilitasyonu, çok sayıda ilaç kullanımı, yüksek enfeksiyon riski, yoğun bakım ünitelerinde uzun süre kalma, komorbiditeleri (bası yarası, beslenme ve solunum problemleri) nedeniyle diğer nörolojik rehabilitasyon durumlarıyla karşılaştırıldığında farklı bir yaklaşım gerektirir.

Anahtar Kelimeler: Kalp nakli; karaciğer nakli; inme, felç; rehabilitasyon

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Cardiac transplantation (CT) is the most effective treatment for end-stage heart failure. While the most common cause of its etiology in adults is ischemic heart disease, congenital heart disease is the primary reason in children. Pediatric CT constitutes approximately 9% of all cardiac transplantations. Perioperative neurologic complications result in significant morbidity.[1] Neurologic complications (NC) are most frequently seen after CT. Prevalence has been reported as 7-70%.[2,3]

Orthotopic liver transplantation (LT) is the world's most effective treatment for all end-stage liver diseases.[4] NCs are common after LT, which are en-

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cephalopathy, peripheral motor disorder, attention-deficit disorder, seizures, tremor, peroneal neuropathy, central pontine myelinolysis (CPM), cerebral hemorrhage, transient ischemic attack, cerebral infarction, Guillain-Barre Syndrome, dizziness, dysarthria, and polyneuropathy.[5] The prevalence rate is between 13% to 47%. Acute cerebrovascular accident (CVA) is seen at a rate of 2-6.5%. Intracranial hemorrhage in LT is more frequent than ischemic infarction.[6-8] These complications have a major effect on patient survival, disability, and on quality of life.[5]

As these patients remain in the intensive care unit (ICU) for a long time, they suffer from problems associated with eating, swallowing, pressure sores, respiratory problems, and joint contractures. Neurologic rehabilitation requires an approach to solve all these problems. Transplant patients face a high risk of infection due to immunosuppressive drugs, and thus, precautions should be taken against infection. The levels of immunosuppressive drugs should be followed regularly.

CASE REPORTS

CASE 1

F.I., a 13-year-old girl, received a CT in the Department of Cardiovascular Surgery at Gazi University in November 2008 upon the diagnosis of heart failure and dilated cardiomyopathy. She remained awake for a short duration during the postoperative period, but then became unconscious. She stayed in the ICU for 6 months.

During the cranial magnetic resonance imaging (MRI) that was conducted, regions of encephalomalacia were observed in the right frontal lobe and in the left frontoparietal region. Furthermore, in the diffusion MRI, cytotoxic edema and gliotic signal change were indicated in these areas. The MR spectroscopy revealed a significant decrease in N-acetyl aspartate (NAA) and creatinine, elevated choline, and the presence of lactate, lipids, and glutamate in the bilateral cerebral parenchyma. The findings were reported to be consistent with neuronal damage. A diagnosis of clinical and radiological CVA was then given.

After the patient was discharged from the ICU of the University Hospital, she was accepted to our clinic in June 2009 for rehabilitation.

PHYSICAL EXAMINATION

The patient's general condition was moderate, with no cooperation and disorientation. Eye tracking was only available for a short period. The patient was fed through a percutaneous endoscopic gastrostomy (PEG). She had urinary-fecal incontinence. The patient was not ambulated, had poor head control, and no turning in bed during the examination of the locomotors system. No active movement in the bilateral hips and contracture in bilateral ankles was observed. According to the Modified Ashworth Scale (MAS), bilateral shoulder flexion: stage 1, abduction: stage +1, external rotation: stage 1, internal rotation: stage 1, bilateral elbow flexion: stage 2, bilateral wrist flexion: stage 3, bilateral finger flexion: stage 3, and bilateral ankle plantar flexion and inventor: stage 2 spasticity were evaluated.[9] Deep tendon reflexes (DTR) were evaluated as hyperactive. The Babinski reflex was bilaterally positive. Tetraplegia was diagnosed and the functional independence measurement (FIM) score was 5.[10]

The patient was taking the following medications: mycophenolate mofetil 2 g/day, cyclosporine 250 mg/day, acyclovir 800 mg /day, trimethoprim sulfamethoxazole 160/800 mg/day, amlodipine 5 mg /day, baclofen 35 mg/day, calcium carbonate 1000 mg/day, prednisolone 10 mg/day, nistatin mouthwash 3x1/day, intestamin enteral feeding (500 ml) 3x1/day, enoxaparin 0.4 ml/day, ferrous glycine sulfate 576 mg/day, furosemide 40 mg/twice per week, pravastatin sodium 20 mg/day, and memantine 10 mg/day.

In the evaluation of the patient's echocardiography (ECHO), left ventricular function was adequate, no pleural effusion was seen, and ejection fraction was observed as 68%. ECHO and exercise capacity were evaluated as normal by the cardiologist.

The patient's hemogram, biochemistry, urinalysis, urine culture, cytomegalovirus (CMV), polymerase chain reaction (PCR), cyclosporine levels, electrocardiogram (ECG), PO2 saturation were monitored weekly.

A problem list for the follow-up of the patient, which included neurogenic bowel assessment, nutritional assessment, oral care, gastrostomy care was created.

The patient was provided with an elbow splint against the risk of contracture. A cervical collar was used in order to keep the patient's head upright. Serial castings were applied to both lower extremities against the contracture of the knees and ankles. Botulinum toxin A was applied to the muscles for the treatment of spasticity. The Botulinum toxin A dose was administered as follows: tibialis posterior: 40/40 Units, gastrocnemius: 40/40 U, flexor digitorum superficialis: 30/30 U, flexor carpi ulnaris: 30/30 U, brachialis: 10/10 U.

The patient's swallowing ability was evaluated by an otolaryngologist using a flexible laryngoscope. During the assessment, the patient could not voluntarily swallow, tongue movements and velum reflex were present, and gag reflex and effective laryngeal elevation were absent. Bilateral cord movements were normal. There was no coordination of swallowing. Fluids administered orally directly penetrated the larynx. Therefore, direct swallowing required dietary modifications and postural techniques were not implemented. Since the oral intake was absent, feeding was continued with PEG. When admitted to our clinics, the patient was taking fiber-containing enteral feeding (soy fiber) 50 g-8x1/day, fiber-free enteral feeding 100 g-3x1/day. A high protein supplement 225 g/day was added on the medicament as the patient's albumin and pre-albumin values were low.

REHABILITATION PROGRAM

For childhood stroke rehabilitation, both Bobath and Proprioceptive Neural Facilitation (PNF) therapeutic approaches were applied. Talking exercises, accompanied by a psychologist, were applied. There was short-term eye contact. A 10 mg/day dose of memantine was started to increase the state of alertness.

The patient was initially verticalized for 10 minutes at 20º on the tilt table in the exercise room. Range of motion (ROM) exercises, continuous passive motion (with a CPM device), pneumatic compression, and Russian electrical stimulation for the lower extremities (15 min, frequency 2.5 kHz, 5 seconds stimulation and 5 seconds rest) were performed. The patient was instructed to perform cat-camel exercise and assisted to develop sitting balance. The patient was ambulated inside the clinic to remain on a daily basis on the standing table at 45º for a period of 20 minutes. She began to sit in a wheelchair for 3 hours per day. The patient's rehabilitation program lasted for 55 days. She had only short-term control of the head and could sit with support when discharged. She was unable to turn around in bed, and had impaired swallowing function and only minimal cooperation. FIM was 18 at the time of discharge.

CASE 2

B.G, a 63-year-old female patient, had a liver transplant from a live donor in September 2009 in the Department of General Surgery at the Malatya Faculty of Medicine, following the diagnosis of primary biliary cirrhosis associated with hepatitis B. The patient had convulsions on the post-operative seventh day, resulting in a paralysis on the left side.

During the diffusion MRI of the brain, an acute ischemic focus at the right internal capsule posterior was observed. Periventricular changes were present in the pons, bilateral thalamus, and at the centrum semiovale level, and lacunar changes were present in the white matter. The carotid Doppler was evaluated as normal.

The patient was discharged after she had been monitored in the ICU for 4 months. The patient was admitted to our clinic on January 15, 2010 for rehabilitation.

Informed consent was obtained from both patients' families.

PHYSICAL EXAMINATION

The patient was partially cooperative, attempting to answer the questions. Tracheostomy was present and nutrition was conducted via a nasogastric probe. Due to urinary-fecal incontinence, a permanent catheter was applied.

The patient had poor head control, no sitting balance, and was unable to turn around in bed. There was no active movement on the left side, she had also neglect syndrome. A grade 3 (10x10 cm) decubitus ulcer was observed in the sacrum and a grade 2 (2x2 cm) was observed in the bilateral ankle. According to Brunnstrom staging, the upper extremities, arm stage 1, hand stage 2, lower-extremity stage

2 were determined to have active movements.[11] Stage 2 spasticity in the left upper and lower extremities were noticed with MAS. Left hemiplegia was diagnosed and the FIM score was 28.

The patient was taking the following medications: rapamune 3 mg/day, prednisolone 10 mg/day, valganciclovir 900 mg/day, sulfamethoxazole trimethoprim 160/800 mg/day, hydrochlorothiazide 160/12.5 mg/day, carvedilol 50 mg/day, acetylsalicylic acid 100 mg/day, enoxaparin 0.4 ml/day, levatiracetam 2000 mg/day, acetylcysteine, 15 ml/day, pantoprazole 40 mg/day, insulin 3x4 U/day, NPH insulin 1x6 U/day, fiber-free feed 100 cc/h, O_2 2 liters/min., and albumin 200 cc/day.

FOLLOW-UP IN THE REHABILITATION CLINIC

During the first week in the clinic, effusion was detected in patient's chest x-ray taken upon the patient's respiratory distress. A pulmonologist was consulted, who recommended postural drainage and follow-up.

A small portable, programmable device (Chattananooga) was used to deliver a high-voltage, twin-peaked monophasic pulsed current (15 min, 1800 Hz, 0.5-10 seconds) for hip wounds while a laser (emulsion 5 Hz, 15 min) was applied to small wounds. This application continued every day for three weeks; the heel wounds healed. Upon the recognition of the lack of healing in the sacral wounds, the patient was operated on in the plastic surgery clinic. As the protein level of the patient was low, reduced carbohydrate, modified-fat, fiber-containing nutrition of 200 g/day and resource glutamine 100 g/day were started by the dietitian. Electroencephalography requested by the neurologist revealed the presence of an active epileptic focus. Continuation of the levetiracetam treatment was recommended.

An otolaryngologist was consulted for the tracheostomy cannula and swallowing. The patient's swallow was evaluated to be disordered. Oral feeding could not be initiated.

The patient's hemogram, biochemistry, urinalysis, urine culture, CMV, PCR, cyclosporine levels, ECG, and PO2 saturation were monitored weekly.

REHABILITATION PROGRAM

During respiratory assessment, the tracheostomy was decannulated; O2 saturation did not decrease. The patient was aided in the performance of breathing exercises. A vest device was used 2-3 times a day for 5 minutes each in order to facilitate the secretions. Dressing containing thiocillin ointment was applied, and powder with zinc and boric acid was administered daily for the decubitus ulcer, and a vacuum assisted closure (VAC) was performed. The patient was placed on a tilt table at 30° for 15 minutes to verticalize the patient. The angle was then increased to 50° and 60°. Patient failed to tolerate 60° at the tilt table, with decreasing blood pressure. She could only be made to stand up at the bedside the next day for a short period. The patient was able to turn around on the bed, and managed to sit for a short duration with support. The Brunnstrom therapeutic technique was applied in the rehabilitation of the patient. Prior to discharge, the Brunnstrom stage of the left upper extremity was grade 2-3, hand was grade 2, and the lower extremities were evaluated as grade 2-3. A day later, the patient's general condition deteriorated, with increasing trend towards sleeping. The transplant team was consulted due to increases in the liver enzymes. A gastroenterology specialist considered the presence of chronic rejection and suggested biopsy. For this reason, the patient was transported by an ambulance helicopter to the clinic she was operated on before completing the rehabilitation program.

At the time of discharge, FIM value was 51, indicating partial improvement. The patient's rehabilitation time was 40 days.

DISCUSSION

Neurologic complications are most commonly observed following CT. They cause morbidity and lower the quality of life.[12,13] However, there were no studies or case reports regarding the neurological rehabilitation of these cases except for the study by Cortazzo et al.[14]

The study by Andrews et al. reported the onset of perioperative cerebral infarction in 75 male patients between the ages of 10-65 years, and in 6 (7%) of 15 CT patients.[15,16] Zierer determined early

neurologic complication in 46 (23%) of their 200 CT patients, reporting CVA in 11 patients (7 with embolism and 4 with hemorrhage).[17]

There is a difference between adult and pediatric patients with respect to NC spectrum. While peripheral neuropathy and reversible encephalopathy are more frequent in adults, seizures and vascular complications are more predominant in children.[6] Mayer, in his study examining 77 CT patients, reported cerebrovascular complication development in 5 patients (22%) during the postoperative period.[18]

The present patient had ischemia-induced infarct in the right lentiform nucleus, caudate nucleus, left frontoparietal junction, and in the deep white matter. There was a clinically severe cognitive, motor impairment due to diffuse cerebral involvement.

The list of problems of the current CT case included cognitive impairment, lack of mobility, joint contractures, spasticity, and food issues. The patient was evaluated regularly by a cardiologist, she was placed in the intensive rehabilitation program as her exercise capacity was appropriate, and passive exercises were applied.[19] Along with these exercises, a focus was made on sitting balance exercises aiming to help the CT patient sit in the wheelchair. Botulinum toxin A and splints were utilized in the treatment of spasticity, which was only partially successful. Electrical stimulation was applied to the muscles against atrophy due to disuse. Cognitive training was provided by a psychologist, and neurostimulant drugs, such as Memantine, were administered to increase alertness. As indicated by Zierer's long-term study, being dependent on the ventilation device (mechanical ventilator) for a long period, an extended stay in the ICU, a high incidence of pneumonia and suffering from sepsis increase the severity neurologic complication.[17] The patient remained in the ICU for 6 months, remained dependent on the mechanical ventilator and developed an infection. She also had multiple joint contractures. Therefore, the outcome of the rehabilitation was poor. A longer stay in outpatient in rehabilitation was associated with the presence of several comorbidities. However, a closer look into FIM values at the admission and at the discharge indicated an improvement, though slight, with respect to cognitive function and mobility.

In the second case, there was a stroke after LT. NC was reported in 49 (15.4%) of 319 LT patients in Kim's study. Of these NC-presenting patients, one had leukoencephalopathy, one had cerebral hemorrhage, and one had cerebral infarction. The authors drew attention to the fact that the hospitalization period of the latter patients was longer and their mortality rate was higher compared to the others.[5]

In their study, Ling et al. also reported the development of cerebrovascular complications in 10 (3%) of the 337 post-orthotropic LT patients. In this group of 10 patients, 8 had cerebral hemorrhage and 2 had cerebral infarct, and 6 were reported to have died.[4] Infarct treatment is possible while cerebral hemorrhage presents itself with high mortality.[20] Infarct or ischemic changes observed in LT patients often take place in the cortex and in the basal ganglia. Their sizes are small and medium.[21] As our patient had infarction, her prognosis was considered to be relatively good and was potentially placed into the rehabilitation program.

The patient was breathing by tracheostomy at the time of admission. In addition, emphasis was placed on pulmonary rehabilitation due to a lung infection and an increase in secretions. Weaning was achieved in a short time period. She was not included in the intensive exercise program due to the presence of comorbid diseases. The LT patient was placed into the rehabilitation program after a 45-day postoperative ICU period. In our opinion, a lack of early rehabilitation and pulmonary exercise during the ICU period facilitated the emergence of respiratory problems and decubitus. Low albumin levels and prolonged ICU stay were also other reasons for developing decubitus ulcers. Therefore, protein supplements were administered for nutrition in our clinic. Electrotherapy was applied to accelerate wound tissue healing.[22] The rehabilitation period, on the other hand, was 40 days for our patient. The FIM value was 28 at admission and 51 at discharge. We believe that our patient benefited partially from the rehabilitation program.

Cortazzo researched rehabilitation durations, FIM scores, albumin levels, complications, and dis-

charge statuses of 55 LT patients. Twenty-two percent of their patients had neuropathy while 20% had bed sores. The mean duration of hospitalization was reported to be 30 days. In conclusion, low albumin levels were found to be correlated with a longer duration of hospitalization. Longer rehabilitation periods increased FIM gains and those patients with an apparent increase in FIM values were discharged, but 15% of the patients had to return to intensive care clinics due to medical problems.[14]

Team work is required for the rehabilitation of NC developing in transplant patients. In addition, communication should be maintained with the surgeon, cardiologists, and gastroenterologists who perform transplantation. The success of rehabilitation depends mostly on the seriousness of the CVA. Furthermore, the patient's comorbidities (respiratory problems, pressure sores, PEG feeding, and infection) cause prolongation of the rehabilitation program. Patients must be protected against the development of infection due to the use of immunosuppressive drugs during rehabilitation. As patients use many drugs, the systemic, metabolic side effects of these drugs should be closely monitored.[23]

CONCLUSION

Patients with CVA, which appear as a transplantation complication, are rarely hospitalized. However, the need for hospitalizing patients with complications may increase with the increasing number of transplantation procedures. Therefore, the features of transplantation patients should be well- known. In conclusion, we believe that an improvement can be initiated in the patient's mobility and cognitive functions, as well as in the FIM score, through an intensive rehabilitation program.

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