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# FIRST KIDNEY TRANSPLANTATION IN CHITTAGONG MEDICAL COLLEGE HOSPITAL

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**CASE 1**

Mr. Ali Abbas, a 19 year old patient hailing from Patiya, Chittagong was diagnosed as a case of End Stage Renal Disease (ESRD) due to chronic glomerulonephritis in the nephrology unit of Chittagong Medical College Hospital (CMCH) in April, 2008. Then he was put on maintenance hemodialysis (2 sessions per week and 4 hours per session) along with other supportive treatment including beta-erythropoetin (5000 units/week). His mother, Mrs. Julekha Begum, a house wife of 38 years old had consented to donate her kidney. Both the donor & recipient were investigated thoroughly according to the check-list. Both had blood group of A +ve and their HBsAg, Anti-HCV, Anti-CMV IgM were negative with Anti-CMV IgG positive.

Donor, Juleka Begum was normotensive and non-diabetic. Physical examination showed no abnormalities. Her urinalysis, blood count, liver function and kidney function tests were normal. X-ray chest, ECG & IVU reports were also normal. Renal angiogram showed single renal artery in each kidney.

Recipient, Ali Abbas was also normotensive (BP 120/80mm.of Hg) on admission. Respiratory and cardio vascular systems were normal. Urinalysis showed albumin "+", RBC- 2-4/HPF. Blood chemistry showed urea- 28 mmol/L, serum creatinine (Scr)-880 µmole/L, creatinine clearance (Ccr)- 5ml/min. Liver function test, X-ray chest and ECG were normal. Ultrasound examination showed bilateral smaller echogenic kidneys. Endoscopic examination of upper GIT was normal.

Although patient's micturating cysto-urethrogram showed normal urinary bladder and urethra but the patient developed UTI after the procedure. He was treated with two courses of Inj. Amikacin (dose-500 mg/d for 7 days each). Patient had cured but he developed bilateral ototoxicity. HLA typing showed 50% match of HLA-DR antigen between the donor and recipient, and cytotoxic cross match was negative.

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Transplantation was done on 25th October'2008 and that was the 1st kidney transplantation in Chittagong Medical College Hospital. The transplantation team of Bangobondhu Sheik Mujib Medical University (BSMMU), Dhaka carried out the transplantation surgery in collaboration with the surgical and anesthetic teams of this hospital. The nephrology team of this hospital took total care of the patient before and after the transplantation. The immunosuppressive protocol comprising of cyclosporine (8mg/kg/d) and mycofenolate moefetil (cellcept) (1G/day) was used in addition to intravenous methyl-prednisolone. Injection methyl-prednisolone was given at a dose of 500 mg IV intraoperatively and 500 mg daily on the 1st and 2nd post-operative day. From the 3rd post operative day he received oral prednisolone at a dose of 0.5mg/kg daily.

In the 1st 6 hours of postoperative day, urine output was 500 ml which increased to 3.6 liters in the next 24 hours. One unit of packed cell volume was transfused on the 2nd post-operative day. His serum creatinine level gradually reduced to 132 µmole/L after 10 days of transplantation. There was no episode of acute rejection. However he developed fever due to UTI and the pathogen, klebseilla was isolated, sensitive to imipenum and amikacin. He was treated first with IV imipenum for 10 days but he was not cured. Then, he was treated with IV amikacin (500 mg/d). Patient became afebrile with amikacin but there was persistent pyuria which subsided only after a prolonged use of cotrimoxazole (625 mg at night for 2 weeks). The patient was discharged after 3 months of transplantation with normal renal function (Scr-80 µmole/L).

On follow-up, the patient was physically and mentally alright except hypertension which was under control with anti-hypertensive drugs.

But he continued to have perceptive deafness in both ears (left>right) and since 1 year after transplantation he has been on hearing aid. After 18 months of transplantation, his serum creatinine level started to increase which was 109 µmole/L on 3rd May'10 and 150 µmole/L on 12th August'10.

At present (after two and half years of transplantation); patient is hypertensive, his urinalysis is normal, serum creatinine is 187 µmole/L on 9th May'11. The graft is clinically and sonologically appears normal. There is no bruit over the graft and the resistive index is normal. Now he is under monthly follow-up. His present daily medications are cyclosporine-100 mg, prednisolone-05 mg, azathioprine-50 mg, atenolol-100 mg, amlodipine-10 mg and prazosine-2 mg.

**CASE 2**

Mr. Pranab Chakraborthy, a 32 yrs old man was admitted in the nephrology ward, Chittagong Medical College Hospital on 13th July 2008 with the complaints of anorexia, nausea, scanty urination and swelling of the body. He was thoroughly examined and investigated and diagnosed initially as a case of acute renal failure due to rapidly progressive glomerulonephritis (RPGN). He was treated with a course of iv Solumedrol (500 mg daily for 3 days) and urgent haemodialysis (HD). His renal function did not recover rather he gradually developed to end stage renal disease (ESRD). So, he continued maintenance hemodialysis (HD) since 13th August 2008. At that time, urinalysis showed albumin "++", pus cell 10-12/HPF, R.B.C. 6-7/HPF. His hemoglobulin level was 8.5 gm/dl, blood urea- 52 mmol/L, serum creatinine- 1232 µmole/L, serum potassium 6.7 mmol/L. Ultrasound study showed bilateral smaller echogenic kidneys. In the course of treatment, patient developed left ventricular failure and pericardial effusion which was improved by regular dialysis. He had asymptomatic cholecystitis which was treated by laparoscopic cholecystectomy as a part of preparation for kidney transplantation. He was also on weekly erythropoietin injection at a dose of 5000 i.u. subcutaneously.

His mother, Mrs. Tulu Rani Chakraborthy, a house wife of 62 yrs old was willing to donate her kidney. Both the donor & recipient were thoroughly investigated according to the check-list. Both the patient and donor had blood group of "0" positive and their HBsAg, Anti-HCV and Anti-CMV IgM were negative with Anti-CMV IgG positve. VDRL test was non-reactive.

Donor, Tulu Rani Chakraborthy was normotensive and non-diabetic. Urinalysis, blood count, and liver function tests were normal and kidney function test showed serum creatinine of 79 µmole/L. Her X-ray chest, ECG & IVU were normal. Renal angiogram showed single renal artery in each kidney.

The patient (recipient) was anemic. Blood Pressure was 140/85 mm of Hg. and body weight was 50 Kg. No other systemic abnormality was detected. Blood count showed Hb 8.5 gm/dl, total W.B.C. count-10,000/cumm, platelet count- 300,000/cumm. ECG, X-ray chest and KUB were normal. Endoscopy of upper G.I.T. showed pre-pyloric erosion.

Transplantation was done on 5th April 2009 and that was the 2nd kidney transplantation in CMCH. The transplantation team of BSMMU, Dhaka carried out the transplantation surgery in collaboration with the surgical and anesthetic teams of this hospital. The nephrology team took total care of the patient before and after the transplantation. The immunosuppressive protocol comprising of cyclosporine (8 mg/kg/day) and mycofenolate moefetil (cellcept) (1 g/day) was used in addition to intravenous methyl-prednisolone. Injection methyl-prednisolone was given at a dose of 500 mg IV intraoperatively and 500 mg daily on the 1st and 2nd post operative day. From 3rd post operative day he started to receive oral prednisolone at a dose of 0.5mg/kg daily.

There was no immediate complication. Urine volume increased gradually to 5L/day. In the post-operative period, fluid and electrolyte balance was done according to the standard fluid replacement protocol. Patient's serum creatinine level came down to 141 µmole/L by a week. After 10 days of transplantation, abdominal stitches were cut off and penile catheter was removed. According to the protocol, cyclosporine dose was reduced by 25 mg/day on 21st day of operation, but the patient developed a rejection episode characterized by mild fever, malaise and rise of serum creatinine (132 µmole/L). He was treated with a course of anti-rejection therapy (inj. solumedrol 500 mg I.V. daily for three days) and his serum creatinine level reduced to normal. Seven days later (3rd May 2009), the patient again (2nd time) developed similar type of acute rejection for which he was retreated with the same course of i.v. Solumedrol. But his rejection trend continued for which on 10th May'09 another course of I.V. solumedrol was given at a dose of 250mg on 1st day, 125mg on 2nd day and 125mg on 3rd day. His cellcept dose was increased to 1 gm twice daily on 7th May'09.

However, on a stable condition the patient was discharged on 14th June'09. But he was readmitted after 1 week with chicken pox infection and was treated with inj. Supraviron (acyclovir) at a dose of 10 mg/kg for 7 days. Then, he had improved and was discharged from hospital. But after 7 days (13th July'09), he was again admitted with mild fever and pain into both knee joints. He also developed malena 2 days later after admission. The severity of malena and number of bowel movement had been increased day by day.

Endoscopy of upper G.I. tract revealed esophageal candidiasis, fundal gastric ulcer with pyloric erosion. He was managed with blood transfusion, inj. pantoprazole and inj. Traxyl (tranxic acid) in addition to the immunosuppressive drugs. But malena continued. Endoscopy of upper GIT was repeated and biopsy was taken from pyloric ulcer which revealed inflammatory granulation tissue. Colonoscopy showed normal mucosa of colon but ileo-caecal valve was edematious and blood was rushing through the valve. His serological test of anti-CMV IgG was positive but anti-CMV IgM was negative. Treatment was started with I.V. gangcyclovir (dose- 5 mg/kg 12 hrly) on 30th July'09. In the meantime, the patient had a total of 20 units of blood transfusion. Although his malena stopped after 2 days' treatment of gangciclovir but he developed pneumonia and septicemic shock. And at last, the patient died on 3rd August' 09.

**Discussion**

1st Kidney transplantation in the world was done on the 23rd December 1954 in Boston, USA[1]. In Bangladesh, 1st successful kidney transplant was done in October 1988 in the IPGMR (presently BSMMU), Dhaka from a live related donor[2]. Twenty years after that, on the 25th October, 2008 1st successful kidney transplantation was done in the Chittagong Medical College Hospital (CMCH) which was 1st time in any peripheral medical college hospital outside Dhaka. In the same year kidney transplantation was done 1st time in Nepal on 8th August 2008[3]

In 1988 the kidney transplantation program in Bangladesh was sponsored by the Government with a special transplantation fund. But in Chittagong Medical College Hospital the transplantation program was a collaborative approach program chiefly sponsored by the CMCH dialysis fund.

1st transplantation case was alright except that he developed deafness that was likely due to amikacin toxicity used for the treatment of UTI. This toxicity might be avoided if he could be treated by the sensitive but costly medicine like imipenum for two weeks or more.

As a transplantation preparation of the patient, micturating cysto-urethrogram (MCU) was done in the hospital which is no more required according to the recent protocol[4,5,6]. The UTI was likely to be acquired during the procedure of MCU and the subsequent oto-toxicity was likely due to prolonged use of amikacin. Previous study showed that the risk of aminoglycoside-induced ototoxicity is greater in patients with renal failure which is usually irreversible, and administration of amikacin followed by frusemide may further enhance the risk of ototoxicity[7].

Usually patients using amikacin needs to monitor for ototoxicity by doing serial audiograms, serum creatinine and amikacin blood levels which were not possible in this case due to financial constraints as well as unavailability of test facility.

The decreased graft function after 22 months of transplantation is likely due to chronic allograft nephropathy (CAN). CAN is the most prevalent cause of graft dysfunction and failure in transplantation. CAN is characterized by a relatively slow but variable rate of decline in renal function after initial few post-transplant months, often in combination with proteinuria and aggravation of hypertension[8]. Although the pathogenesis of CAN is complex and poorly defined but a contributory role of acute rejection, donor age, anti-HLA antibodies, cyclosporine effects, hypertension have been suggested[9]. The calcineurin inhibitor, cyclosporine may play a role either related to the direct stimulation of profibrogenic cytokines (TGF) or indirect mechanisms through increase in blood pressure. Clinical study showed that cyclosporine dose reduction may help to reduce the rate of loss of renal function in patients with CAN[10]. In this case, we used cyclosporine dose according to the conventional protocol but we could not readjust its exact dose based on serum level due to unaffordability of blood cyclosporine estimation. Since there was no evidence of acute rejection or proteinuria in this case possibly hypertension and/or cyclosporine toxicity might be the underlying cause of CAN here. The exact cause may be established with graft (kidney) biopsy and estimation of cyclosporine level in blood which is now under process in this patient.

In the 2nd case, transplantation was uneventful and everything was running well. The cyclosporine dose was same as body weight of both was equal. But the 2nd case developed acute rejection on the 21st post-operative day. He was given repeated doses of methyl prednisolone for repeated episode of acute rejection. Subsequently the patient developed first chicken pox and then cytomegalo virus (CMV) infection. In fact, we diagnosed cytomegalo-virus infection lately and therefore the patient management was delayed. Lastly, he developed septicemia and died after 118 days of transplantation.

The chicken pox and CMV infection are two known complications of transplantation[4,5,6]. These infections may occur due to either de novo infection or reactivation of latent viral infection[5,6]. In this case the infection might be due to reactivation of latent viral infection as a result of repeated use of anti rejection therapy.

Although, it is known that the prophylaxis by gangcyclovir along with anti-rejection therapy is very much effective in prevention of CMV disease[4,5,6], which was not given in this case because of its high cost and poor economic condition of the patient.

One important observation was that both patients had same body weight and was prescribed the equal dose of cyclosporine. The second case devolved acute rejection on the 21st day but the 1st case did not. So it is speculated that there might be some individual variation in the pharmacokinetics and pharmacodynamics of cyclosporine. Therefore, cyclosporine dose should be adjusted according to the cyclospore level in blood, not on the body weight of the patients which was not possible because of patients' unaffordability.

**Conclusion**

As a beginner and also doing transplantations in such poor patients in a new st-up, we faced some problems in the overall management. We have understood that we should be more careful in patient selection in respect of social and financial status before transplantation. However, it is hoped that with the present experience it would be possible to overcome the problems and the outcome of the future transplant will be better.

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**References**

**1.** Merill JP, Murray JE, Harrison JH, Guild WR. Successful homotransplantations of the human kidney between identical twins. JAMA,1956; 160:277-282

**2.** Bangladesh Renal Journal

**3.** ISN News No. 28 page 9, December, 2008

**4.** Nauman Siddqui, Sundaram Hariharan, Gabriel Danovitech. Eva Luation and Preparation of Renal Transplant Candidates. In; Gabriel M Danovitch, Editor. Handbook of Kidney Transplantation. 4th ed. California : Lippincott williams and wilkins; 2001;169-192

**5.** Brenner and Recter's The Kidney, 8th edition page 2162-2163 Saunders, Philadelphia, 2008

**6.** Davison AM, Cameron JS, Granfeld JP, Pontecelli C, Ritz E, Winearl CG, Van Y Persele C et al Oxford Textbook of Clinical Nephrology,3rd edition, page 2040-2041,2097-2098 Oxford University Press,2005

**7.** Bates DE, Beaumont SJ, Baylis BW. Ototoxicity induced by gentamycin and frusemide. Ann Pharmacother, 2002;36:446-451

**8.** Paul LC. Chronic allograft nephropathy: An update. Kidney International, 1999;56:783-793

**9.** Can Li, Chul Woo Yang. The pathogenesis and treatment of chronic allograft nephropathy. Nature Review Nephrology, 2009;5:513-519

**10.** Paller MS. Cyclosporine nephrotoxicity and the role of cyclosporine in living related donor transplantation. Am J Kid Dis, 1990; 16:414-416