

O401

## Is Hypercalciuria a Promoting Factor to Urinary Tract Infection in Children?

Gheissari A, Adjoodani T, Eshraghi P

Isfahan University of Medical Sciences

**Introduction.** Urinary tract infection (UTI) is one of the most common diseases of urogenital tract in children. About 3% to 5% of girls and 1% of boys experience at least one period of UTI during childhood. It should be mentioned that UTI is an etiology for developing hypertension and various degrees of renal function impairment. Therefore, detecting predisposing factors to UTI takes an important place in managing patients with UTI. Some of these factors are as follows: vesicoureteral reflux, voiding dysfunction, urinary tract obstruction, poor hygiene, and anatomical abnormalities. However, a substantial number of these patients develop recurrent episodes of UTI without a clear evidence of known risk factors. Recently, few studies reported that idiopathic hypercalciuria is a predisposing factor for UTI. On the other hand, we have noticed that idiopathic hypercalciuria is a common finding among referral patients to pediatric nephrologists' offices. Therefore, we carried out a survey to find out whether idiopathic hypercalciuria is a contributing factor in children with UTI.

**Methods.** This is a cross sectional case-control study carried on 260 children between September 2003 and February 2005. The participants in this study were divided into two groups. Case group, contained 60 preadolescent children with the first episode of pyelonephritis admitted at St Al Zahra hospital and the control group contained 200 healthy preadolescents who referred to health care centers to assess their growth or attend their routine check ups. Inclusion criteria: 1-Children between 2-11 years old 2- No evidence or past history of kidney stone, urinary tract obstruction and high grade reflux. 3- Proven pyelonephritis for case group 4- negative urine culture at the time of determining urine calcium. Exclusion criteria: 1- secondary hypercalciuria such as RTA, hyperparathyroidism, and consuming loop diuretics 2- uncooperative children or parents. Mean age of case and control group were  $4.86 \pm 3.08$  years and  $4.22 \pm 2.9$  years, respectively. We used second fasting spot urine sample to measure calcium and creatinine. The measurements were repeated two times to increase the accuracy. Patients who had calcium/creatinine more than 0.25 in two measurements were considered as hypercalciuric. All samples were collected after completing the treatment course of UTI and achieving negative culture in case group. For those who had hypercalciuria; serum calcium, PTH, magnesium, phosphate, alkaline phosphatase and venous blood gas were determined to rule out most common causes of non-idiopathic hypercalciuria. Data was analyzed by SPSS10 software. Odds ratio with 95% confidence interval also measured.

**Results.** Approximately 63% of the participants were female and 37% were male. Fifteen percent of case group and 6% of control group had idiopathic hypercalciuria. The relative frequency of these two groups differed significantly (15% versus 6%;  $P < .05$ ). Odds ratio was 2.76 (95% CI, 1.03 to 7.3).

**Conclusions.** Hypercalciuria should be assessed in following up the patients with UTI.

O402

## Outcome After Renal Transplantation in Pediatric Patients: Results of 15-Year Experience in a Single Center

Mahdavi Zafarghandi R, Taghavi Razavizadeh SR, Darabi Mahboub MR, Naghibi M, Nazemian F, Shafipour F, Zeraati A, Hashemi S, Zolfaghari M, Baghestani G, Hosein-Zadeh M

Mashhad University of Medical Sciences

**Introduction.** The incidence of chronic renal failure (CRF) in children under 19 years has been put at approximately 11 per million population (US data system). In the recent years, the numbers of children who survive renal disease and become candidates for renal transplantation have been increased. In this study, we reviewed 15 years of our experience in pediatric renal transplantation to determine the rate of patient morbidity and graft survival.

**Methods.** Of 1250 renal transplantation performed in our center (1989-2005) 129 were done on children (6-18 years). Causes of renal failure were: neurogenic bladder 12 cases, reflux nephropathy 21 cases, posterior urethral valve 3 cases, prune belly syndrome 2 cases, chronic glomerulonephritis 28 cases. The remaining failures were of unknown etiology. Twenty percent of kidneys were retrieved from related living donor and, 66% from unrelated living donors and 14% from cadaveric donors. Immunosuppressive therapy was given with three drugs (prednisolon, azathioprine or mycophenolate mofetile and cyclosporine) in all of patients with the exception of 11 recipients of HLA identical sibling, who did not receive cyclosporine. The Kaplan-Meier curve was constructed to assess graft and patients survival and the long rank test was used to assess the effect of kidney source and date of renal transplantation.

**Results.** Immediate diuresis occurred in all grafts. Surgical complications included two urinary fistulas, two ureteral strictures and 3 clinical lymphocele which were all managed surgically. The most common causes of graft failure were chronic rejection and recurrence of primary renal disease. The graft survival rate after 1, 2, 5, 10 and 15 years were 97%, 88%, 79 %, 65 % and 53%, respectively.

**Conclusions.** Renal transplantation in children results in improvement in physical growth and mental

development. Rate of graft survival, chronic rejection, recurrence of primary renal disease and medical noncompliance, continue to be problematic.

#### O403

### Renal Function in Leukemic Children

Hooman N, Arjmandi K, Vosoug P

Ali-Asgar Children Hospital

**Introduction.** Renal dysfunction has been reported in survivors of neoplastic disease. Early diagnosis of renal damage may decrease the morbidity in those with partial or complete remission. This study assessed glomerular and tubular function in children with leukemia.

**Methods.** A total of 115 pediatric leukemic patients (49 females, 66 males) enrolled in a prospective cross sectional study from 2003 to 2005 in oncology department of Ali asgar children hospital. Two groups were designed , pateints whose therapy were finished at least 12 months ( group 1) and those either on therapy or less than 12 months passed from the last protocol of cytostat ( group 2) . Demographic data, cumulative dosages of anticancer drugs, history of other nephrotoxic agents, nephrectomy, radiotherapy and acute renal failure were recorded. We used Common Toxicity Criteria version 2 (1999) to evaluate renal function. Chi2 and Mann Whitney U test and biniary logistic regression were used to compare percentage, scoring and correlation, respectively. P value less than 0.05 was considered significant.

**Results.** Fifty eight out of 115 patients were in group 1 and 57 ones were in group 2. The mean age was 11.86 years ( $\pm$  5.3 SD). The median (range) of therapy was 36 months (1- 156 months) in group 2 and 36 month ( 24 – 240 ) in group 1 . Chemotherapy was discontinued for median of 1 month (0-12 month) in former group and 51 months (15 to 120 months) in later group. The percentage of reversible renal failure, proteinuria, abnormal serum calcium and magnesium, metabolic acidosis and urinary concentration defect was higher in group 2 . These differences were statistically significant ( $P < .05$ ). We found no correlation CTC score neither of cumulative dosage of drugs , the age of initiation of treatment , duration of therapy , sex , history of radiotherapy nor prescription of other nephrotoxic agents ( $P > .05$ ).

**Conclusions.** Mild to moderate tubular dysfunction has been observed in survivors of leukemia. Routine follow up of renal functions is recommended.

#### O404

### Evaluation of Urine Macrophage Migration Inhibitory Factor in Children With Urinary Tract Infection: A Possible Predictor of Acute Pyelonephritis

Otukesh H, Hoseini R, Chalian M, Fereshteh-Nejad SM, Chalian H, Yazdi RS

Iran university of Medical Sciences

**Introduction.** Urinary tract infection is the second most common bacterial infection in children. During renal inflammation and all types of renal injury, macrophages infiltrate renal parenchyma, and their number correlates with the intensity of inflammation. By the way, macrophage migration inhibitory factor (MIF) is widely expressed and secreted in response to inflammatory stimuli, and plays an important role in renal tissue injury. However, the role of MIF is not evaluated in patients with pyelonephritis in any study. Therefore, the aim of our study was to compare urinary excretion of MIF in acute pyelonephritis, acute cystitis and also control group in order to find a non-invasive and sensitive method to differentiate them.

**Methods.** In this prospective analytical cross-sectional study, 31 pediatric patients with urinary tract infection (25 patients with acute pyelonephritis, 8 patients with acute cystitis) and 40 healthy children were recruited. Sterile midstream urine samples were taken to measure MIF concentration in all patients and healthy individuals. Urine MIF concentration was quantitated by ELISA and corrected for urine creatinine. The data were analyzed using SPSSv.13 software. Independent *t* test, 1-way ANOVA, correlation and receiver operating curve (ROC) analysis were performed.

**Results.** The mean ratios of urine MIF/Cr were calculated as 66.14 (SEM = 23.78) pg/ $\mu$ mol creatinine in acute pyelonephritis patients, 1.58 (SEM = 0.59) pg/ $\mu$ mol creatinine in acute cystitis patients and 1.85 (SEM = 0.35) pg/ $\mu$ mol creatinine in healthy individuals. It was significantly higher in pyelonephritis patients than the ones in acute cystitis patients ( $P < .001$ ) and control ( $P < .001$ ). ROC analysis demonstrated that urine MIF/Cr ratio could considered potentially useful index to detect acute pyelonephritis [ $P < .001$ , Area under curve (AUC) = 0.959], and also the optimal cut-point of 5.39 pg/ $\mu$ mol creatinine for urine MIF/Cr ratio could potentially separates acute pyelonephritis patients from healthy individuals with sensitivity and specificity of 92% and 92.5%, respectively.

**Conclusions.** To the best of our knowledge, urine MIF level of patients with cystitis, pyelonephritis and control group were compared with each other for the first time in our study. We showed that the urine MIF/Cr ratio does not rise in acute cystitis. Whereas, rising of this ratio in patients with acute pyelonephritis was remarkable in our study. It showed that urine MIF/Cr ratio is a sensitive test for differentiation of acute cystitis from pyelonephritis. The optimal cut-point of 5.39 pg/ $\mu$ mol creatinine for urine MIF/Cr ratio could potentially separates acute pyelonephritis patients from healthy individuals.

O405

## Renal Transplantation in Patients With Cystinosis

Sharifian-Dorcheh M, Dalirani R, Moshari F, Mohkam M

Shaheed Beheshti University of Medical Sciences, Tehran, Iran

**Introduction.** Cystinosis is an inherited metabolic disease in which transfer of cystine out of lysosome is impaired. This phenomenon leads to accumulation of cystine in different organs and causes organ dysfunction. Growth retardation seen in these patients and later they went on to develop renal failure and needed to dialysis or renal transplantation. This study aimed to evaluate the outcomes and complications of renal transplantation in patients with cystinosis.

**Methods.** In this case series done in years 1375 to 1385, all patients with renal failure due to cystinosis who received renal transplantation, were followed for 43 months. Definite diagnosis of this disease, classical, is made by measuring cystine in fibroblasts or leukocytes, but because this test cannot be done, diagnosis was made by clinical manifestations and observing corneal cystine crystals. Before operation, all patients were examined to determine if they are appropriate candidate for renal transplantation and after operation DPTA scan was done to evaluate graft function. In later follow up, necessary lab tests were done. In the presence of rejection symptoms such as fever and creatinine rise, graft rejection was confirmed by scan or sonography of transplanted kidney. All patients received triple immunosuppressive therapy includes cyclosporine, prednisolone, mycophenolate mofetil (cell cept). If symptoms of rejection or infection were seen, patients were hospitalized to receive treatment.

**Results.** In this study, 15 patients with cystinosis received renal transplantation from years 1375 to 1385, in Labbafinejad hospital. Patient survival was 100% at 50 months and graft survival was 86.7%. Mean creatinine level before operation was  $5.44 \pm 1.45$ , and its postoperative value was  $0.86 \pm 1.2$ . Mean hemoglobin level before operation was 8.22. The last GFR was 54.1. Six (40%) of patients were on dialysis  $\pm 1.01$  and post operation was 12.84 before operation, 5 (33%) of patients had acute rejection, 5 (33%) of patients suffered from UTI. Growth retardation was seen in all of patients. Fourteen (86%) of patients was affected by CMV infection and 6 (40%) by CMV disease; that were treated by Ganciclovir for 2 weeks. Nonrenal complications included: pneumonia (n = 3), hypothyroidism (n = 5), photophobia (n = 1), hypertension (n = 3), bladder stones (n = 1). One patient was affected by vessel thrombosis in post operation and in another one kink of vessel happened during operation, and had graft loss.

**Conclusions.** Renal transplantation in patients with cystinosis has favorable outcomes. Patients have effective

graft function, in spite of growth retardation. Renal transplantation is renal replacement therapy of choice for patients with cystinosis and End Stage Renal Failure.

O406

## Rituximab Treatment of Children With Steroid-Dependent and Frequently Relapsing Nephrotic Syndrome

Bitzan M,<sup>1</sup> Mamber S,<sup>2</sup> Abdel-Ouahed J<sup>2</sup>

<sup>1</sup>McGill University and Montreal Children's Hospital, Canada

<sup>2</sup>Montreal Children's Hospital, Canada

**Introduction.** Patients with frequently relapsing or steroid-dependent nephrotic syndrome risk serious complications due to long-term glucocorticoid or cytotoxic/immunosuppressive therapy, and disease-related morbidities. Recent studies suggest that minimal change disease (MCD) and some forms of focal segmental glomerulosclerosis (FSGS) are associated with altered T and B cell immunity. We sought to determine whether B cell depletion induces or maintains remission in steroid/calcineurin inhibitor (CI)-dependent or -resistant nephrotic syndrome and, if effective, to start defining dose requirements and predictors of outcome.

**Methods.** Six patients, median age 9.5 (range 3 to 17) yrs were treated with rituximab, five with a complicated history requiring frequent steroid and chronic CI and/or mycophenolate therapy (2 MCD, 2 mild FSGS, 1 collapsing glomerulopathy), and one with new onset, biopsy-proven MCD with primary steroid-dependence. Rituximab was given as 1 to 4 infusions of 375 mg/m<sup>2</sup> whilst patients were nephrotic or in relapse (n = 5), or after prednisone-induced remission (n = 1).

**Results.** B cells were effectively depleted to <1% of total lymphocyte counts within less than a week, and recovered relatively abruptly 5 to 6 months following treatment. All immunosuppressants were successfully discontinued in four patients two months after the first rituximab dose (range, 1.5 to 3 months). One child with MCD achieved remission with rituximab alone, whilst B cell depletion was associated with reduced proteinuria and delayed disease progression in the patient with collapsing glomerulopathy. Emergent adverse events included mild allergic reactions (n = 3), hypoglycemia (n = 1), worsening transient acute renal failure associated with profound hypoalbuminemia (n = 1), and possible rituximab-induced interstitial lung disease (R-ILD) following a second treatment course (n = 1).

**Conclusions.** Rituximab represents a potential therapeutic alternative for frequently relapsing and steroid/CI-dependent nephrotic syndromes. Less than "conventional" dosing may be effective, but the duration of remission is limited. Unexpected adverse effects of rituximab with this novel indication need be well documented and communicated.

O501

## Effects of Active Vitamin D on Costimulatory Molecules and HLA-DR Expression in Renal Transplantation

Ahmadpoor P, Ilkhanizadeh B, Ghasemmahdi L, Makhdoomi K, Ghafari A, Rahimi E, Salari-Lak S

Urmia University of Medical Sciences

**Introduction.** Full activation of T cells requires at least two distinct but synergistic signals, T cell receptor and co-stimulatory signal. It has been shown that 1, 25 (OH) 2 D3 inhibits T cell activation and maturation of dendritic cells and induces tolerogenic dendritic cells. This study was conducted to assess the effect of active vitamin D on co-stimulatory molecules and HLA-DR expression in renal transplant recipients.

**Methods.** In a before and after study those renal transplant recipients who were transplanted 6-18 months before the study with stable allograft function, no episode of allograft dysfunction, or febrile episode in the last 2 months were administered oral calcitriol for 4 weeks. Expression of HLA-DR, CD28, CD86 (B7-2), and CD40 on peripheral blood leukocytes were checked by flowcytometry. Dose of immunosuppressive drugs were not changed during study. Exclusion criteria were induction with Anti IL-2 receptor blockers or ALG, history of vitamin D administration and change of immunosuppressive drugs or hypercalcemia during the study. Percent of blood leukocytes with given expressed marker were counted by flowcytometry in at least 15000 peripheral white blood cells before and after calcitriol administration.

**Results.** Expression of CD28 was decreased 30% (from  $2.30 \pm 0.74\%$  of peripheral WBC to  $1.61 \pm 0.91$ ,  $P = .004$ ), CD40 decreased 31.2% ( $3.07 \pm 1.51$  to  $2.11 \pm 1.71$ ,  $P = .0001$ ), CD86 (B7-2) decreased 36.7% ( $2.37 \pm 1.00$  to  $1.5 \pm 0.78$ ,  $P = 0.0001$ ) and HLA DR decreased 16.8% ( $9.99 \pm 3.02$  to  $8.31 \pm 2.93$ ,  $P = .0001$ ). Mean of serum calcium and creatinine were not changed statistically significant (9.4 and 1.12 before and 9.5 and 1.17 mg/dL after calcitriol).

**Conclusions.** By this study we have shown changes in co-stimulatory and HLA-DR molecules expression in these renal transplant recipients by active vitamin D that may influence allograft survival.

O502

## Study of Effect of G-CSF on Stem Cell Mobilization in Rat ATN

Sadeghi P, Nafar M

Shahid Beheshti University of Medical Sciences, Tehran, Iran

**Introduction.** Acute tubular necrosis (ATN) is a common problem, with a high rate of mortality and morbidity,

which occasionally progresses towards ESRD. So far, no effective therapeutic intervention for ATN has been proposed. New discoveries on the role of hematopoietic stem cells in healing process, and the possibility of increasing the number of these cells by the available drugs (eg, G-CSF) gave rise to a hope for finding a new treatment for ATN. The aim of this study is to assess the effects of G-CSF injection in the recovery of ischemic injury to the rat's kidney and the comparison between the number of stem cells in the peripheral circulation of G-CSF receivers and control group.

**Methods.** After midline incision nephrectomy of the right kidney was done by using a midline incision, the pedicle of the left kidney was clamped for 47 minutes. Rats have been divided into two groups. The first one received subcutaneous injection of G-CSF, 100  $\mu\text{g}/\text{kg}$ , for 6 days. The other group followed as control. Amount of BUN, Cr, and the number of CD34+ cells in peripheral circulation were used for the follow-up.

**Results.** The mean number of CD34+ cells in case group was 12433 (SD = 953.33) and in controls 14100 (SD=2624.24), which was statistically insignificant. Seventh day Cr in control group was 0.8 and 0.93 in case group ( $P < .05$ ).

**Conclusions.** Injection of G-CSF, 100  $\mu\text{g}/\text{kg}$ , for six days after induction of ATN in rat kidney did not improve healing process after 7 days follow-up.

O503

## Glutathione and Glutathione Related Enzymes in Hemodialysis Patients

Eftekhari E,<sup>1</sup> Ahmadpoor P,<sup>2</sup> Servat H,<sup>1</sup> Ghafari A<sup>2</sup>

<sup>1</sup>Department of Clinical Biochemistry, Urmia University of Medical Sciences

<sup>2</sup>Department of Nephrology, Urmia University of Medical Sciences

**Introduction.** Cardiovascular disease is the major cause of mortality in patients receiving hemodialysis for chronic renal failure. Increase production of reactive oxygen species and alteration in antioxidant defense mechanisms may contribute to increase risk of atherosclerosis. The aim of this study was to measure markers of antioxidant system including glutathione (GSH) as first line defense against oxidative stress, glutathione peroxidase (GPx) and glutathione reductase (GR) in hemodialysis patients.

**Methods.** In this study, 30 hemodialysis patients (16 males and 14 females, 35-60 years old) were recruited through the Department of Nephrology, Urmia University of Medical Sciences. Exclusion criteria were patients with diabetes, intercurrent infection and chronic inflammatory conditions. Twenty-Five age and sex matched controls used for comparison were healthy volunteers. All were on regular diet and did not have any history of hypertension, diabetes or renal disease. Erythrocyte



GSH level and plasma activities of GPx as well as GR were determined spectrophotometrically.

**Results.** Compared with controls, erythrocyte GSH level and plasma activity of GPx were significantly decreased ( $1.46 \pm 0.35$  versus  $1.26 \pm 0.34$   $\mu\text{mol/gHb}$  and  $141.95 \pm 33.5$  versus  $59.9 \pm 31.25$  U/L;  $P < .05$ , respectively), whereas plasma GR activity was significantly increased ( $33.49 \pm 9.5$  versus  $53.65 \pm 13.6$  U/L;  $P < .05$ ).

**Conclusions.** Our finding indicates that hemodialysis patients have an impaired antioxidant defense system. This condition may contribute to the increase in vascular disease in such patients.

#### O504

### The Expression Signature of End Stage Kidneys May Explain the High Risk of Tumor Development

Kovacs G, Nagy A

University of Heidelberg

**Introduction.** End stage renal disease (ESRD) is associated with hyperplastic-cystic remodelling of the kidneys (ARCD) and increased rate of renal cell cancer (RCC). We have investigated whether the remodelling resembles the embryonal development or regeneration of kidneys or corresponds to a novel type of disease.

**Methods.** Using the Affymetrix HG U133 oligoarray, we have established the gene expression signature of ESRD/ARCD kidneys and compared to those of fetal and adult kidneys and of distinct types of childhood and adult renal cell tumors. The gene expression was confirmed by quantitative RT-PCR and for selected genes by immunohistochemistry.

**Results.** We have observed a unique clustering of experiments stemming from ESRD/ARCD kidneys whereas embryonal/fetal kidneys and normal adult kidneys formed distinct clusters. Under stringent conditions overexpression of 79 genes were affiliated to ESRD/ARCD. Quantitative RT-PCR studies on ESRD/ARCD and control normal and tumor samples confirmed the specific expression of 47 genes. Immunohistological analysis of selected genes involved in distinct molecular mechanisms (GPR87, CSF2 and SCEL) revealed a high expression in hyperplastic tubular structures, cysts as well as in small atrophic epithelial clusters of ESRD/ARCD kidneys. The SCEL was also expressed in small papillary precursor lesions and papillary RCC as well suggesting its role in the tumorigenesis.

**Conclusions.** The unique expression signature indicates that ESKD/ARCD is a novel disease irrespective of the type of chronic renal failure leading to loss of kidney function. The specific gene expression profile may also explain the high frequency of RCCs in ESRD/ARCD kidneys.

#### O601

### Effect of Renin-Angiotensin System Polymorphisms on Renal Graft Function in Renal Transplant Recipients

Noroozianavval M, Argani H, Aghaeishahsavari M, Veisi P, Rashtchizadeh N, Ghorbanihaghjo N

Drug-Applied Research Center, Tabriz University of Medical Sciences

**Introduction.** As the renin-angiotensin system (RAS) plays a significant role in renal function and several polymorphisms of the RAS system have been associated with renal disease, the aim of this study was to analyze the role of three polymorphisms in renal transplant recipients (RTRs) and correlate them with graft function.

**Methods.** The present study was performed in Drug Applied Research Center (DARC) from September 2003 to December 2005 on 108 RTRs (66 males and 42 females, with mean age  $37.34 \pm 4.97$  years) with stable allograft function (creatinine  $\leq 2.2$  mg/dL). Following the DNA extraction from the blood leukocytes, the genotypes of the angiotensin converting enzyme (ACE I/D), angiotensinogen (ANG M235T) and angiotensin II type 1 receptor (ATR1 A1166C) were determined by polymerase chain reaction. The magnitude of clearance of creatinine (CICr) in the setting of each of the above RAS polymorphisms was determined. CICr was measured by Modification of Diet in Renal Disease (MDRD) formula. Values were expressed as the mean  $\pm$  SD;  $P < .05$  was considered to indicate statistical significance.

**Results.** There was no association of each genotype of RAS alone with CICr, serum urea, cyclosporine trough level and the degree of urinary protein excretion rate. But, patients with ACEDD + ATR1CC genotype had lower CICr and higher urinary protein excretion rate ( $P = .05$  and  $P = .03$ , respectively). Other combination genotypes of RAS had no effect on allograft function. Interestingly, the percent of hypertensive patients in C allele was more than A allele of ATR1 polymorphism (70% versus 30%,  $P = .04$ ; respectively).

**Conclusions.** Although, none of the single gene polymorphisms of the RAS had impact on renal allograft function, combinations of these genotypes are associated with the outcome of allograft function.

#### O602

### BK Polyoma Virus Nephropathy Among Iranian Renal Transplant Recipients

Ghafari A, Makhdoomi K, Ahmadpoor P, Akbari S, Safar-Shamspour S, Sepehrvand N, Ghasemi-Rad M

Urmia University of Medical Sciences

**Introduction.** BK virus nephropathy (BKN) is recognized

as a cause of graft loss in renal transplant patients (pts). This may be related to the introduction of new and potent immunosuppressive regimens. In Iran, our experience regarding its prevalence, clinical significance, and outcome is still limited. In this study, our primary purpose is to outline the prevalence, outcome, and clinical characteristics of BKN as observed at our hospital.

**Methods.** We retrospectively analyzed 160 specimens from episode biopsies. All transplantations were from living donors. Cyclosporine and corticosteroid were used in all pts; in addition azathioprine (AZA) was used in 41 (25.6%) patients and mycophenolate mofetil (MMF) in 119 (74.4%) patients. Antilymphocyte globulin was used in 84 (52.5%) patients. BKN was diagnosed by light microscopic examination and a positive immunohistochemical staining (formalin-fixed, paraffin-embedded tissue was processed using standard heat-induced antigen retrieval protocols and the monoclonal antibody to large T-Antigen of BKV). Data was analyzed using Fischer exact and T test.

**Results.** Among the 160 patients, 109 (68.1%) were male; mean age was  $35.5 \pm 11.6$  year (range, 9 to 59). Twenty-one (13.1%) was diagnosed with BKN. Mean interval between biopsy and transplantation was  $13.6 \pm 10.67$  month. There were no significant differences between BKN patients and non-BKN patients with respect to age, sex, interval between diagnosis and transplantation, cyclosporine blood level and AZA versus MMF based immunosuppressant. Graft loss occurred in 57.1% of BKN pts versus 18.1% of non BKN pts ( $P = .005$ ). There was significant difference between ALG and non ALG group in respect to BKN (6.6% in nonALG versus 19% in ALG groups;  $P = .02$ ). BKN was diagnosed by immunohistochemistry in 40% of those specimens with acute rejection according to light microscopic evaluation.

**Conclusions.** This is the first report of BKN in Iranian renal allograft recipients. In our hospital, the prevalence of BKN was higher than those previously reported for non-Iranian recipients. BKN had a negative impact on graft survival.

### O603

## Angiotensin Converting Enzyme and Angiotensinogen Gene Polymorphism in Relation to Chronic Allograft Dysfunction

Azarpira N, Raisjalali GA, Nikeghbalian S, Darai M, Aghdaie MH, Behzadie S, Sagheb M, Bagheri M, Ashraf MJ, Roozbeh J, Geramizadeh B, Rahsaz M

Shiraz University of Medical Sciences

**Introduction.** Chronic allograft dysfunction (CAD) is the most common cause of allograft failure in the long-term, and current immunologic strategies have little effect on

this condition. The renin-angiotensin-aldosterone system (RAAS) plays important roles in progression of chronic renal disease. It is thought that plasminogen activator inhibitor-1 (PAI-1) functions in the RAS, in addition to involvement in fibrosis. This study investigates possible links between angiotensin converting enzyme (ACE I/D) genotypes (DD, ID, II), angiotensinogen (AGT) genotypes (M235T/MM, MT, TT) and PAI-1 genotypes (4G4G, 4G5G, 5G5G) with CAD.

**Methods.** These assessments were performed in 126 renal allograft recipients, 76 patients with chronic allograft nephropathy and 50 patients with normal kidney function for at least five years follow up after transplantation. Genotypes were determined using polymerase chain reaction (PCR) sequence-specific primers (for ACE and PAI-1), and PCR -RFLP (for AGT).

**Results.** Kidney recipients without CAD had significantly lower frequencies of the DD genotype (8%) than the recipients with CAD (29%) ( $p < 0.05$ ). The transplant recipients without CAD also had significantly lower frequencies of the TT genotype (4%) than those with CAD (24%) ( $P < .05$ ). There were no significant differences between PAI-1 genotypes between two groups. The differences between two groups regarding recipient demographic characteristics, type of donor, number and severity of acute rejections, and immunosuppressant treatment were not significant.

**Conclusions.** Pretransplantation testing of the ACE and AGT genotypes may assist clinicians in identifying patients at risk for chronic renal transplant dysfunction.

### O604

## Dysregulated Cytokine Responses During Cytomegalovirus Infection in Renal Transplant Recipients

Sadeghi M,<sup>1</sup> Daniel V,<sup>1</sup> Naujokat C,<sup>1</sup> Schmidt J,<sup>2</sup> Mehrabi A,<sup>2</sup> Zeier M,<sup>3</sup> Schnitzler P,<sup>4</sup> Opelz G<sup>1</sup>

<sup>1</sup>Immunology, Germany

<sup>2</sup>Surgery, Germany

<sup>3</sup>Nephrology, Germany

<sup>4</sup>Virology, Germany

**Introduction.** Cytomegalovirus (CMV) infection remains a major threat for renal transplant recipients. Pre- and posttransplant predisposing factors for CMV activation and disease are not well defined. The aim of this study was to examine whether there are differences in plasma cytokine levels pretransplant, prior to and during CMV replication in renal transplant recipients.

**Methods.** We studied 76 renal transplant recipients in whom CMV DNA was studied at regular intervals posttransplant. Thirty-eight patients were CMV DNA positive (CMV+) and 38 negative (CMV-). The two groups were matched for age, gender, pretransplant CMV antibody status, immunosuppressive protocol

and posttransplant day of investigation. sIL-1RA, IL-2, sIL-2R, IL-3, IL-4, IL-6, sIL-6R, IL-10, TNF-alpha, TGF-beta2, and IFN-gamma plasma levels were measured pretransplant, pre- and during CMV-viremia.

**Results.** After transplantation, sIL-2R, IL-6, and IFN-decreased in both patient groups (CMV+:  $P = .002$ ;  $P = .028$ ;  $P = .032$ ; CMV-:  $P = .001$ ;  $P = .040$ ;  $P = .030$ ) whereas IL-10 plasma levels remained constant ( $P = NS$ ) compared to pretransplant cytokine levels. When patients developed CMV viremia, sIL-2R ( $P = .015$ ) and IL-6 plasma levels ( $P = .006$ ) increased compared to previremia but remained constant in CMV- patients matched for the posttransplant day ( $P = NS$ ). Simultaneously, IFN-gamma plasma levels increased in CMV- patients ( $P = .008$ ) and remained constant in CMV+ patients ( $P = NS$ ). During CMV viremia, IL-10 ( $P = .002$ ) and sIL-2R ( $P = .007$ ) plasma levels were significantly higher in CMV+ than CMV- patients.

**Conclusions.** Our results indicate that CMV activation in renal transplant recipients is associated with increased sIL-2R, IL-6, and IL-10 plasma levels pointing to monocyte/Th2 activation. High IL-10 production might down-regulate the plasma IFN-gamma level. The Th1 deficiency in our CMV+ patients might promote development of CMV disease.

#### O605

### Effect of Prophylaxis with Low-Dose Anti-Thymocyte Globulin on Prevention of Acute Kidney Allgraft Rejection: A Comparative Study

Tayebi-Khosroshahi H, Mohajel Shoja MA, Shamsi-Khosroshahi R, Badr-Ogli N, Noshad H

Tabriz University of Medical Sciences

**Introduction.** During kidney transplantation, the first contact between the recipient's immune system and the donor organ takes place following the arterial anastomoses. The aim of this prospective study was to evaluate the efficacy of a single, low-dose anti-thymocyte globulin (ATG) prophylaxis in the reduction of early acute rejection in the renal allograft recipients

**Methods.** In a prospective randomized and controlled clinical trial, we studied the rate of acute rejection within the first month of kidney transplantation in patients who had received their transplant at a single center between the years 2004 and 2006. The patients were divided into two groups: Group 1 ( $n = 37$ ) received cyclosporine, mycophenolate mofetil or azathioprine, and prednisolone. Group 2 ( $n = 31$ ) received the above-mentioned agents plus a single ATG bolus (4-5 mg/kg) the night before the transplantation (~12 hours before operation). Blood urea and serum creatinine levels as well as complete blood count were measured regularly in the post transplant period. Acute allograft rejection was justified clinically

and/or pathologically. Statistical analysis was performed using student *t* test, Fisher exact test and multinomial logistic regression (MLR) analysis.

**Results.** There was no significant difference regarding age, gender and renal function tests between the two groups. Acute rejection was found in 31.3% of group 1 patients and was reduced to 13.8% in group 2 that was statistically significant ( $P = 0.05$ ). MLR analysis also revealed that age and gender were not related to the risk of acute renal allograft rejection.

**Conclusions.** Prophylactic administration of a single and low-dose ATG at the night before kidney transplantation dose reduce the risk of acute allograft rejection in renal transplant recipients. However, further studies with a greater number of patients should be conducted to confirm these Results.

#### O606

### Polyomavirus Infections in Pediatric Renal Transplant Recipients

Bitzan M, Ho-Wo-Cheong E, Burns A, Bernard C, Bell LE

McGill University and Montreal Children's Hospital, Canada

**Introduction.** Polyomavirus (PV) nephropathy (PVN) is being increasingly recognized as a cause of irreversible graft loss in adult kidney transplant (KT) recipients. The frequency and clinical evolution of PV infections and PVN in children with renal transplants is not known. The aims of the present retrospective cohort study are to (1) determine the prevalence of BK and JC viral infection in pediatric KT patients, and (2) examine the clinical implications of PV replication in this population.

**Methods.** All KT recipients with functioning graft followed in our program were routinely screened over a period of 8 months for BK and JC virus from urine and serum by quantitative PCR (National Microbiology Laboratory, Public Health Agency of Canada) and urine cytology (decoy cells). Allograft biopsies, performed during this period for suspected rejection and/or PVN, were also stained for (large) T antigen.

**Results.** Fifty patients (median age 13; range, 2 to 18 years) were evaluated  $4.6 \pm 3.5$  (median 3.6) yrs post transplantation. BK or JC virus-specific PCR amplification products were demonstrated in urine of 33 and 35% of the patients, and in serum of 12 and 8%, respectively, compared with a 10% detection rate of decoy cells. During the 8-month observation period, six additional, initially negative patients became positive for BK and one for JC virus. Overall, 32 children (64%) had evidence of PV replication (26% BK only, 20% JC only, 18% BK and JC). Of 20 patients with biopsies, three demonstrated T antigen expression and evidence of virus-associated tubulointerstitial nephritis, all with high-grade BK viremia ( $\geq 10^3$  copies/mL serum).

**Conclusions.** Approximately two-third of our pediatric

KT population has evidence of PV replication. The incidence of bona fide PVN is  $\geq 6\%$  per yr and associated with high BK viral load. Active surveillance, at least for BKV replication, and early intervention appear indicated while long-term outcome data are awaited.

## O607

### Tacrolimus Rescue Therapy in Corticosteroid and Polyclonal Antibody-Resistant Renal Allograft Rejection

Naderi G, Mehraban D, Ganji MR, Yahyazadeh R

Tehran University of Medical Sciences

**Introduction.** Conventional treatment for acute renal allograft rejection is high-dose pulses of corticosteroids. Treatment of corticosteroid resistant rejection is with antilymphocyte antibody preparations. We report our experience with tacrolimus for rescue therapy in 34 patients with acute allograft rejection resistant to corticosteroids and anti thymocyte/antilymphocyte globulin.

**Methods.** From 2001 to 2006, 34 patients (18 men and 16 women) with clinically diagnosed acute allograft rejection received (graft biopsies done in 21 patients) tacrolimus (Prograf) rescue therapy after unsuccessful treatment with corticosteroid and ATG/ALG.

**Results.** The patients mean age was 42.2 (22 to 62) years. Of 34 patients 27 (79.4%) were from living unrelated donors and others (20.6%) from deceased donors. Three patients underwent transplantation for second time from living unrelated donors. Pathologic reports for patients were: acute humoral rejection in 6 (31.6%), acute cellular rejection in 6 (31.6%) and acute vascular rejection in 7 (36.8%). Mean follow up time for patients was 31.7 months. Graft nephrectomy was done in 8 patients (23.5%). The other 26 patients (76.5%) discharged after response to therapy with good general condition. One of these patients died of herpes encephalitis one month after discharge.

**Conclusions.** We conclude that tacrolimus therapy is able to salvage kidneys with acute refractory rejection. We recommend that Tacrolimus be used as an alternative to the conventional drugs used for antirejection therapy in renal transplantation. However, severe infectious complications must be considered.

## O608

### Effect of Living Unrelated Donor Bone Marrow Cells Infusion on Kidney Allograft Function

Pourmand G, Nikbin B, Mehrsai AR, Taherimahmoudi M, Asadpour A, Solgi G

Tehran University of Medical Sciences

**Introduction.** Donor bone marrow infusion (DBMI) has been used in kidney transplantation with the idea of inducing specific immunological unresponsiveness and augmenting the survival of solid organ transplantation. It seems this procedure could have a positive effect on the long term graft survival due to the enhancement of microchimerism state.

**Methods.** Between November 2006 to July 2007, 20 patients receiving concurrent infusion of living unrelated donor bone marrow (6 to  $55 \times 10^6$  cells/kg) were compared prospectively with 20 patients that received kidney transplant alone. Both group received the same base immunosuppressant (cyclosporine A, cellcept, and prednisolone). Serum creatinine level, pre and post transplantation cytokine level, necessity of using ATG, delayed graft function (DGF) and acute rejection episodes within at least 6 month after transplantation were recorded.

**Results.** The mean serum creatinine level for the DBMI group was 2.62 mg/dL during 2 weeks after transplantation and 1.18 mg/dL during follow up period, and for the control group were 2.34 mg/dL and 1.16 mg/dL, respectively. Eight clinical manifestations of acute rejection in DBMI group and 5 in control group were seen. Seven of 20 cases in DBMI group and 5 of 20 cases in control group had DGF, 5/20 and 4/20 cases received ATG. Serum level of IL-2, IFN-gamma, IL-4 cytokines and TGF-beta1 before and 14 days after transplantation did not show significant difference between both group, but IL-10 had a significant difference.

**Conclusions.** Infusion of DBM cells was perfectly tolerated. Decreasing of creatinine level in DBMI groups was slower than control group. Long term follow up will show the effects of DBMI in graft survival.

## O609

### The Incidence of BK Virus Nephropathy in Iranian Kidney Transplant Recipients

Soleimani T, Najafi I, Rasolzadegan MH, Setoudeh M, Ganji MR, Naderi GR, Hakemi M, Saddadi F, Amini M

Tabriz University of Medical Sciences

**Introduction.** Polyoma virus associated nephropathy (PAN) in renal transplant recipients has been observed with increasing frequency in recent years. Highly potent immunosuppressive drugs like Tacrolimus and Mycophenolate Mofetil (MMF) have been accused as risk factors for this increase. The incidence of PAN in different reports is between 1 to 10% with allograft loss in over 50% of patients, particularly when timely diagnosis and treatment is delayed. In this study, we report our experience on BKV nephropathy in our institute.

**Methods.** All renal transplant biopsies performed at Shariati Hospital between 2001 and 2006 (n = 108) were immunohistochemically screened for the presence of



PV-specific protein (SV40 Ag). The histologic diagnosis of PAN was made upon observation of morphologic changes in tubular epithelium and confirmation with immunohistochemical staining. We also reviewed the charts of the subjects (n = 96) for demographic, clinical, and laboratory data.

**Results.** BKV nephropathy was found in 0.93% of all investigated allograft biopsies (1/108) and in 1.04% of all recipients (1/96). Mean age of recipients was 36.48 ± 14.10 (range, 13 to 74) years, and 54 (57%) of them were male. Type of kidney transplantation was living unrelated donor 76 (79%), living related donor 13 (14%), and deceased donor 7.17 (18%) patients were transplanted for second time. Immunosuppressive drugs in 87 (90%) of recipients were the combination of cyclosporine, MMF, and prednisolone. The recipient with BKV nephropathy

diagnosis was a 37-year old man with a female living unrelated donor. His maintenance immunosuppressive therapies were cyclosporine, azathioprine, and steroid. The time to diagnosis of PAN was nine months after kidney transplantation, with a serum creatinine of 3.5 mg/dL. He had clinical diagnosis of acute rejection six weeks earlier for which he had received steroid pulses, and Azathioprine had been replaced by MMF. After four months of BKV nephropathy diagnosis, he lost his graft.

**Conclusions.** Although BKV nephropathy after renal transplantation is uncommon, it is a serious complication causing loss of allograft. Therefore, it should be included in the clinical differential diagnosis of transplant dysfunction.