Acute Humoral Rejection in Renal Transplantation: Experience in Children

Carmen García Meseguer, Jorge Martinez Sáenz de Jubera, Marta Melgosa Hijosa, Carlota Fernández Camblor, Antonia Peña Carrión, Ángel Alonso Melgar, J. Bravo Feito and Laura Espinosa Román

Department of Pediatric Nephrology, University Children's Hospital La Paz, Madrid, Spain

Abstract

Acute humoral rejection or antibody mediated rejection is a severe immunological complication after renal transplantation with a negative impact on graft outcome. Its treatment in children is not well defined. We have reviewed the medical history, clinical expression, and outcome of seven children with kidney transplants who have developed acute humoral rejection.

Acute humoral rejection was diagnosed in seven children (one girl, six boys) out of 128 transplanted children (5.5%) in our unit (19 non-primary transplants). Age at diagnosis was 12 years (range, 6-16 years). Acute humoral rejection developed in the first three months after transplantation (median five days). All except one were second or third transplants (acute humoral rejection occurred in 31.6% of all non-primary transplants). The main clinical manifestation of rejection (six patients) was serum creatinine increase, and in all graft biopsies peritubular capillary CD4 deposition was found.

The most frequently used treatments were immunoglobulins (five children) and plasmapheresis (four children), with complete resolution in five cases (complete recovery of renal function) and graft loss in two children. Other treatments proposed are rituximab, bortezomib, and eculizumab.

In conclusion, in our experience, acute humoral rejection incidence in children with renal transplantation has been 5.5%, but increases significantly in re-transplantation (up to 31.6%). There is great variability in the clinical outcome of these patients. Response to treatment was successful in 71.4% of children. **(Trends in Transplant. 2013;7:67-9)**

Corresponding author: Carmen García Meseguer, cgarciameseguer@salud.madrid.org

Key words

Children. Acute humoral rejection. Antibody mediated rejection. Renal transplantation.

Correspondence to:
Carmen García Meseguer
Servicio de Nefrología Pediátrica
Hospital Infantil Universitario La Paz
P.º Castellana, 261
28046 Madrid, España
E-mail: cgarciameseguer@salud.madrid.org

Introduction

Acute humoral rejection (AHR) or antibody mediated rejection is a clinicopathologic entity[1] defined by renal dysfunction with pathologic biopsy, peritubular capillary CD4 deposition, and presence of circulating donor-specific antibodies (DSA). The incidence, clinical expression, treatment, and outcome in pediatric renal transplantation are not well known[2].

Aim of the study

To describe the clinical presentation, treatment, and outcome of seven children who developed AHR at our Institute.

Patients and methods

We conducted a retrospective and descriptive study from January 2004 to October 2012. In this period we performed 128 renal transplants (19 were re-transplants) at our Hospital. We reviewed the medical records (clinical expression, treatment, and outcome) of the patients who developed AHR. All met the diagnostic criteria defined for AHR except for DSA (all had circulating antibodies class I or II, but only in the last cases did we demonstrate DSA).

Results

We diagnosed or suspected AHR in seven children (one girl, six boys) out of 128 transplanted children (5.5%) in our unit (19 non-primary transplants). Age at diagnosis was 12 years (range, 6-16 years). All except one were re-transplants with previous graft immune loss in 4/6 (31.6% of non-primary transplants in our experience suffered from AHR). Acute humoral rejection developed in the first three months after transplantation (median five days). Except for one patient, all were recipients of cadaveric donors. The range of panel reactivity antibody was 3-75%. Before transplantation, four patients had positive anti-HLA class I and one had class II antibodies and with AHR this increased up to six and two, respectively[3,4]. Pre-transplant complement-dependent cytotoxicity crossmatches were negative in all cases. Induction therapy was used in the seven patients (thymoglobulin in three) and the immunosuppression received was tacrolimus, mycophenolate, and steroids. Two patients underwent preemptive plasmapheresis prior to transplantation and in the immediate postoperative period.

The main clinical manifestation of rejection (six patients) was serum creatinine increase. The first case of AHR had non-primary graft function and was initially not suspected (the diagnosis was made retrospectively on transplantectomy). In all cases, mean tacrolimus serum levels were low (4.6 ± 1.7 ng/ml) before AHR developed. The most frequent pathological finding was peritubular capillaritis and in all graft biopsies peritubular capillary CD4 deposition was found.

The treatments most frequently used for AHR were immunoglobulins (five cases) and plasmapheresis (four children), with a complete resolution in five cases and graft loss in two children (one kidney never worked and the other was complicated by arteriovenous fistula post-biopsy). Two patients received rituximab without complications[5].

The mean follow-up was 14 months (0-48 months). One patient was discharged to the adult unit and the rest have a good renal function (mean glomerular filtration rate estimated by Swartz formula: 115 ml/mi/1.73 m^2). Currently, only one needs treatment for arterial hypertension.

Summary

Acute humoral rejection is more frequent in re-transplants (31.6% of non-primary transplants developed AHR). Early diagnosis and treatment is very important and a high index of suspicion is necessary. Outcome was favorable in 71% of children, but we need studies to better define the best treatment, the relationship with chronic humoral rejection, and the long-term evolution in children.

References

1. Colvin RB. Antibody-Mediated Renal Allograft Rejection.Diagnosis and Pathogenesis. J Am Soc Nephrol. 2007;18:1046-56.
2. Kranz B, Kelsch R, Kuwertz-Bröking E, Bröcker V, Wolters HH, Konrad M. Acute antibody-mediated rejection in paediatric renal transplant recipients. Pediatr Nephrol. 2011;26:1149-56.
3. Verghese PS, Smith JM, McDonald RA, Schwartz SM, Nelson KA, Warner PR. Impaired graft survival in pediatric renal transplant recipients with donor-specific antibodies detected by solid-phase assays. Pediatr Transplantation. 2010;14:730-4.
4. Miettinen J, Lauronen J, Qvist E, et al. Donor-specific HLA antibodies and graft function in children after transplantation. Pediatr Nephrol. 2012;27:1011-9.
5. Tullus K, Marks SD. Indications for use and safety of rituximab in childhood renal diseases. Pediatr Nephrol. DOI10.1007.Epub 2012.Sep 21.