O29 ECULIZUMAB IN ANTIBODY MEDIATED REJECTION

M. Elias, S. Beaudreuil, E. Obada, C. Poitou, L. Weis, L. Iamandi, P. Mutinelli, B. Charpentier, A. Durrbach, H. Francois
CHU Kremlin Bicetre, Paris, France

Introduction: There is to date no gold standard treatment of antibody mediated rejection (AMR). Current therapeutic strategies rely on plasmapheresis combined with intravenous globulin (IVIg). Despite these treatments, 12%-37% of patients suffering from acute AMR eventually lose their grafts.

Eculizumab is a humanized monoclonal antibody that targets complement protein C5 and prevents the formation of the membrane attack complex. Therefore it could be efficient in treating complement mediated lesions during AMR. Few clinical cases describe the efficiency of Eculizumab in treating acute AMR.

Methodology: In this monocentric retrospective study we report 15 patients (7 men and 8 women) that have been treated between October 2011 and June 2013 for AMR using Eculizumab on top of plasmapheresis, IV Ig and a B-cell targeting agent. Patients were transplanted between January 2002 and November 2012. All AMR were documented by a graft biopsy according to the Banff 2009 criteria at diagnosis and we followed the patient and graft outcome after treatment. The biopsy was repeated whenever necessary. The mean follow up was 10.4 months.

Results: Seven patients out of 15 (47%) did not respond to the treatment and 5 lost their graft. 9 patients were diagnosed with AMR 27.2 months after their transplantation, out of which 6 (78%) did not respond to treatment. The remaining 6 were diagnosed with AMR in the first year following transplantation and only one lost its graft (17%), $p < 0.05$. Only one of the patients died and 7 experienced severe infections. In the responders group, the mean serum creatinine was 163 μmol/l 37.6 months after transplantation and 10.4 months after AMR diagnosis. No responding patients received eculizumab more than 3 months.

Conclusion: Eculizumab seems more efficient in early versus late AMR, which reflects a more prominent involvement of the complement cascade in early versus late AMR.

O30 THE PROGNOSTIC FACTORS IN CHRONIC ACTIVE ANTIBODY-MEDIATED REJECTION

A. Zniber[3], V. Pernin[3], A. Ramouneau-Pigot[2], T. Kanouni[1], J.E. Serre[3], V. Garrigue[3], J.F. Eliaou[2], G. Mourad[3]
[1]Hématologie; [2]Immunologie; [3]Néphrologie, Montpellier, France

Chronic active antibody-mediated rejection (CAMR) is an important cause of chronic allograft dysfunction and kidney graft loss. CAMR treatment is not well established and its effectiveness is discussed.

The aim of our work was to study the risk factors of graft loss in patients with CAMR.

Methods: we conducted a retrospective study of CAMR diagnosed in our center between January 2007 and June 2013. We performed a Cox regression analysis of risk factors of graft loss, having as variables the recipient clinical and biological characteristics, histological lesions (Banff 2007) and the treatment of CAMR.

Results: From 837 patients transplanted, 24 patients were diagnosed as CAMR (Graft biopsy and DSA). Mean age was 48 ± 18.8 years. The median duration of the diagnosis of CAMR was 38.5 months (3–261). Creatinine at diagnosis was 254 ± 92.8 μmol/l and proteinuria 1.32 g/d. 7 patients (29.2%) received only plasma exchanges (PE), 6 patients (25%) PE + low doses IvIg and 11 patients (45.8%) PE+IvIg+Rituximab.

10 patients lost their graft after a mean period of 16.9 months (5–52). 3 patients died (including on death complicating lymphoma).

The factors associated with graft loss were: recipient age >50 years (HR 1.15 [1.001–1.32], $p = 0.04$), CMV infection before CAMR (HR 4.46 [1.2–16.4], $p = 0.024$), GFR < 20 ml/min at time of rejection (HR 10.7 [1.6- 61.6], $p = 0.012$) and histological grade of cg2 (HR 8.7 [1.03–74], $p = 0.047$). The presence of C4d on biopsy, the MFI and the class (I or II) of DSA and the treatment modality did not significantly influence graft survival.

Conclusion: The CAMR is frequently complicated by graft loss. Recipient age >50 years, renal dysfunction and allograft glomerulopathy at diagnosis and CMV infection before rejection was associated with poor prognostic.

O31 MANAGEMENT OF SENSITIZED PATIENTS IN KIDNEY TRANSPLANTATION. PROSPECTIVE SINGLE CENTER STRATEGY

M. De Meyer, D. Latinne, C. Lambert, D. Chaib Eddour, L. De Pauw, N. Kanaan, E. Goffin, C. Hermans, M. Mourad
Cliniques universitaire St Luc UCL, Bruxelles, Belgique

Introduction: Many patients (pts) awaiting for a KT in our institution are highly sensitized (HS) because of HLA antibodies in their serum. In order to avoid early alloantibody mediated rejection (AMR) leading to a early graft loss, we prospectively proposed a therapeutic strategy by plasmapheresis (PP) and IVIg .

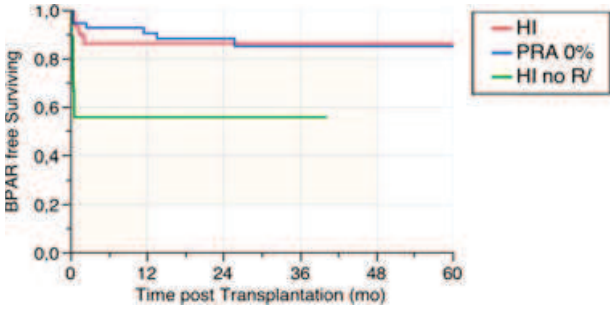
Materials and Methods: The first PP (1.4 X plasma volume of the patient) is performed before surgery. Then a total dose of 2gr/kg IVIG is infused during 48 hours postoperatively. At day5, PP are reinitiated (3/week for 1 month).

IS regimen include tacrolimus, MMF and low-dose steroids. Donors with extended criteria are excluded as well as positive virtual crossmatch.

This prospective study compares the evolution of three groups (G) of pts.

G1: 27 HS pts treated by PP and IVIg; G2: 54 pts without immunological risk (PRA 0%), paired with G1 for age, sex and year of KT and G3: 9 HS pts not treated by IVIG and PP. The mean follow-up is 24 months.

Results: Patient survival was similar in the three groups. In G1 and G2, we observe the same cellular acute rejection rate (10% at 1 year fig 1), none AMR, graft survival was 100% at the end of the follow-up, the GFR is equivalent (G1: 55, G2: 51 ml / min). In the other hand, G3 develops a high AMR rate (40%) and a significantly reduced graft survival.



The main morbidity in G1 is a high rate of hematoma arround the graft (in 9 cases) requiring further surgery in 6 pts.

Conclusion: AMR were avoided in pts HS treated by PP and IV Ig according to our therapeutic strategy started at the time of KT

The cellular acute rejection rate, the graft survival rate and renal function are similar in treated HS pts and in the reference population (without antibodies). HS pts in who we don't follow our strategy, a high AMR rate and a poor graft survival is observed.

O32 EVALUATION OF THE EFFICACY AND SAFETY OF BASILIXIMAB AS CURATIVE TREATMENT OF PERSISTENT OR COMPLICATED ACUTE REJECTION IN CARDIAC TRANSPLANTATION

S. Bouregaa[2], M. Larger[2,4], P. Boissonnat[1], A. Roussoulieres[1], J.F. Obadia[1,3], J. Neidecker[1], L. Sebbag[1,3]
[1]Pole de Transplantation Cardiaque; [2]Service Pharmaceutique, Hopital Louis Pradel; [3]CarMeN laboratoire, INSERM U 1060; [4]Université Claude Bernard Lyon1, Lyon, France

Basiliximab (Simulect) is a monoclonal antibody directed against the alpha chain (CD25) of the interleukin 2 receptor. It inhibits the activation of T lymphocytes and is indicated for prevention of acute rejection in *de novo* allogeneic renal transplantation in adults and children and is commonly used as induction therapy in solid organ transplantation.

Our retrospective study involved the treatment of 22 cellular rejection in 17 patients failing to control rejection by conventional strategies (corticosteroid resistant: $n = 12$; intolerance or contraindications to switched or increased immunosuppression $n = 8$). Basiliximab was administered in two doses of 20 mg IV over 20 min with 4 days intervals. A semi -quantitative score of rejection was used to compare the results of biopsies before and after treatment with basiliximab. We respectively assigned a score of 0, 1, 2, 3 or 4 to stages ISHLT 0R -1A- 1B -3A- 3B. The analysis is made from the patient records.

After basiliximab, the semi- quantitative score of rejection dropped from 50 to 18 (64% reduction), reflecting improved histology. Rejection is considered resolved in 47.6% of cases. There were four treatment failures (unmodified rejection) and the use of two courses of basiliximab for five patients and three times in one case. The cure of basiliximab was the only intervention for 6 patients (28%) and accompanied by an adjustment or change of immunosuppressants in other cases. The global efficiency is 81%, taking into account both resolved rejections ($n = 10$) and improved ($n = 7$) after treatment with basiliximab. No adverse effects related to basiliximab have been observed.

This study reports the first use of basiliximab in heart transplantation for treatment of acute cellular rejection in the absence of alternative or in addition to an adjustment of the immunosuppressive treatment. No incidents have been observed and these encouraging results suggest the need for prospective studies.