PROSPECTIVE MONITORING OF ANTI-HLA ANTIBODIES AFTER KIDNEY TRANSPLANTATION AND THE RELATIONSHIP WITH ALLOGRAFT PATHOLOGY AND C4D

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Objective: The goal of this study was to follow systematically the appearance/increase of post-transplant anti-HLA antibodies (abs) and to evaluate their association with rejection episodes, C4d staining and transplant outcome in renal transplantation.

Methods: Between July/05 and July/06, sera of all transplanted patients who signed informed consent were collected before transplantation, at days 7, 14, 30, 60, 90, 180, and at the beginning and after rejection episodes. All patients who completed 6 months of follow-up (n=60) were analyzed. Donor-specific antibodies (DSA) were detected by flow cytometry analysis (FACS) and NIH-CDC-AGH technique. HLA specificity was studied using ELISA methods and rejection by graft biopsy and classified by Banff 97 classification (updated in 2003). C4d staining was performed on frozen biopsies.

Results: Pre-transplant PRA was ≥1% in 28% of the patients and 7 patients were highly sensitized (PRA > 50%). “De novo” anti-HLA abs were seen in 9,3% of all patients and increase in PRA was seen in 11 patients. Patients were classified in two groups: Group A (n=15) with evidence of antibody response by either developing “de novo” anti-HLA antibodies or increasing pre-transplant PRA and Group B (n=45) without evidence of antibody production. Groups were similar regarding gender, age, transplant number, previous transfusions and pregnancies. Acute rejection episodes (AR) occurred more frequently in the group A (6/15=40%) than in the group B (9/45=20%), p=0,01. In the group A: AR had higher Banff scores, were associated with positive C4d staining (>50% of PTCs) or with necrotic findings in biopsies (p=0,001) and donor-specific antibodies (DSA) in 50% of cases in the group. Patients who developed non-specific abs recovered graft function after IVIg treatment but patients who developed DSA lost the graft in spite of treatment with PP/IVIG or IVIG alone. In the group B, all rejections were milder and C4d negative. Graft loss occurred in 20% of GA patients vs 6,6% of GB patients, p=NS.

Conclusion: Development of new anti-HLA antibodies after kidney transplantation is associated with more frequent and severe acute rejection episodes and usually progress to graft loss, mainly when antibodies are donor specific. These data suggest that monitoring of anti-HLA abs may be a useful tool to follow antibody-mediated responses after kidney transplantation.