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DONOR SPECIFIC ANTIBODY CHANGES AFTER NEPHRECTOMY

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Introduction: Many centers avoid nephrectomy of chronically rejected kidneys from fear of inducing production of anti-HLA antibodies (HLA). It is not clear if the rise in such antibodies is non-specific, resulting from a general inflammatory response or specific, resulting from removal of the donor organ (e.g. sponge effect). We analyzed donor specific (DSA) HLA antibodies and anti-tetanus (TET) and anti-CMV antibodies to determine a broad sensitization. Methods: Twenty-seven patients (21 male), who underwent transplant nephrectomy for cause, had serum samples obtained at the time of nephrectomy and 8.4 ± 11.3 weeks after nephrectomy. No patient was immunized with tetanus during this period. The study was approved as an exempt study by the IRB. The serum samples were tested on a Luminex platform with Single Antigen Class I and Class II specific beads for DSA HLA and by ELISA for the level of anti-TET antibody and anti-CMV antibodies. Nonparametric Spearman rank correlations tested associations of change in TET or CMV antibodies to anti-DSA and between anti-HLA-A locus and anti-HLA-B locus and Class II. ANOVA tested significant changes in anti-HLA. Results: Anti-HLA-A locus antibodies rose from 1480 to 9799 mean channel fluorescence (MFI), p = 0.099. Anti-HLA-B locus antibodies rose from 125 to 7798 MFI, p= 0.04. Total anti-Class I (i.e. anti-HLA-A locus plus anti-HLA-B locus) rose from 2033 to 11157 MFI, p = 0.007, anti-Class II rose from p = 222 to 6051 MFI, p = 0.036. Eight patients of 27 (30%) had an increase in total Class I DSA only, 2/27 (7%) had an increase in Class II only, 10/27 (37%) had an increase in both Class I and Class II, and 7 (26%) had no increase in either Class I or Class II. Anti-CMV (1.92 IU/mL pre and 2.12 IU/mL post nephrectomy, p = 0.3) and TET (13.54 IU/mL pre and 14.87 IU/mL post nephrectomy, p = 0.062) did not change. There were no correlations between changes in anti-CMV or TET with changes in anti-HLA. Change in anti-HLA-A locus correlated with change in anti-HLA-B locus p= 0.001. Change in anti-HLA-B locus, but not anti-HLA-A locus correlated positively with change in anti-Class II, p=0.042. Conclusion: After nephrectomy, there was an increase in donor specific anti-HLA antibodies that did not appear to be the result of a generalized inflammatory response.

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EPITOPE SPECIFICITY OF HLA DQA1 AND DQB1 ANTIBODIES DETECTED IN SERA FROM RENAL TRANSPLANT RECIPIENTS.

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Introduction. The precise characterization of HLA antibodies is important for the management of sensitized renal transplant candidates. Sensitization to HLA molecules is due to recognition of mismatched HLA epitopes of the sensitizing event which led to the production of antibodies specific for "private" or "public" epitopes of the immunizing HLA molecule. The recent development of assays using Single Antigen beads coated with DQ heterodimers (DQA1 and DQB1) permits to distinguish DQA1 from DQB1 alloantibodies. Besides, analyzing the beads' reaction patterns in relation to amino acid sequences of antibody-reactive alleles it is possible to identify DQA1 and DQB1 sensitizing epitopes. Methods. In 173 renal transplant candidates showing production of HLA class II antibodies we characterized anti-DQ antibodies using HLA class II Single Antigen beads containing 12 DQA1 and 14 DQB1 alleles variously combined each other. Results. One hundred and four (60%) of the HLA class II positive patients produced anti-DQ antibodies; 88 of the 104 recipients had had a previous transplant. Sixty-eight patients only anti-DQB1 antibodies, 2 had only anti-DQA1 and the remaining 34 had both anti-DQB1 and anti-DQA1. Anti-DQ positive patients were typed for DQA1 and DQB1 alleles by PCR-SSP technique. Correlating the reaction pattern of each antibody to the amino acid sequences of DQA1/DQB1 alleles, we could identify 9 epitopes characteristic of DQA1 molecules and 14 epitopes characteristic of DQB1. Seven (30%) of these 23 epitopes had not been reported yet; 6 were DQA1-epitopes (41K/130A=DQA1*0103; 160D=DQA1*0302, 0303; 75S/107I/161E/163S/175K=DQA1*05; 50L=DQA1*02, 03; 69T=DQA1*04, 06; 75I=DQA1*01, 02, 03, 04, 06) and one was a DQB1-epitope (87Y=DQB1*05, 0604, 0605, 0607, 0609, ...). Conclusions. This study, carried out on a large number of HLA-DQA1/DQB1 sensitized patients, confirms the great immunogenicity of mismatched DQ molecules especially of a previous kidney transplant. Since we have ascertained the different clinical impact of anti-DQB1 and anti-DQA1 donor specific antibodies on graft outcome, the accurate characterization of anti-DQ antibodies may be helpful in transplanting high sensitized transplant candidates.

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