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P215 -The role of HLA mismatch and HLA-Cw7 in the development and clearance of polyoma virus following kidney transplantation

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The role of HLA mismatch and specific HLA alleles in the risk for, and resolution of, polyoma viral nephropathy (PVIN) following kidney transplantation has been investigated, but with highly conflicting results. This study re-evaluated these potential immuno-genetic determinants in a large single-centre cohort.

We studied 1649 patients (and their donors) who received kidney transplants between 2007 and 2017 using a standardised tacrolimus and mycophenolate-based immunosuppression protocol. Clinical and demographic data were extracted from the prospectively maintained departmental database. HLA typing was undertaken in the accredited immuno-genetics laboratory linked to the transplant unit. We were especially interested in the role of HLA Cw7 status in the donor and recipient based on previous provocative but conflicting data in regard to the role of this specific allele in determining PVIN. PVIN diagnosis was based on indication-biopsy findings, with SV40 antigen expression, with or without inflammation and/or fibrosis, and supported by detectable blood viraemia. Departmental practice was to stop (or significantly reduce) mycophenolate, and to reduce (generally by half) tacrolimus dose at the time of PVIN diagnosis.

A total of 54 patients (3%) developed biopsy-proven PVIN. No difference in total HLA mismatch, or mismatch at the HLA-A, or HLA-DR loci was observed between patients with and without PVIN. A small, but statistically significant difference in HLA-B locus mismatch was seen (1.1 versus 0.9 antigens in those developing and not developing PVIN respectively; p=0.02).

Expression of HLA-Cw7 was seen in 51.6% and 55.8% of recipients and donors respectively. No difference in frequency of expression within the donor or recipient was seen when patients with and without PVIN were compared.

In contrast, a marked difference in recipient HLA-Cw7 expression was seen when recipients who cleared the virus, and those who failed to do so, were compared. Crude analysis revealed HLA-Cw7 was expressed in 23/39 (59%) of patients who experienced viral clearance at the end of follow-up, in comparison to only 3/15 (20%) patients who failed to clear the virus from blood (p=01). More accurately, Kaplan-Meier analysis revealed a significantly longer time to viral clearance in patients failing to express the HLA-Cw7 allele (p=0.02). Cox regression analysis, adjusted for relevant demographic and recipient variables, confirmed this association (p=0.01).

Secondary analysis, this time considering patients with ‘presumptive PVIN’ (defined as peripheral blood viral load>7000 copies/ml) but in the absence of SV40 expression on the biopsy yielded similar results for all analyses. In none of the analyses was an effect seen for donor HLA-Cw7 expression.

This study adds to the prevailing literature in regard to the role of the HLA system in defining PVIN prevalence ad outcome. Although a biologically plausible association between Class I mismatch (specifically HLA-B) and the development of PVIN was seen, we believe the magnitude of this effect is too small to be of clinical utility. However, the association between recipient HLA-Cw7 expression and the rate of viral

clearance, also biologically plausible, may indeed be of a magnitude sufficient to modify clinical practice. The efficacy and safety of such an approach requires prospective evaluation.