

THE “g” SCORE AND CORRESPONDING CHANGES IN THE TRANSCRIPTOME

J. Riopel¹, B. Sis^{1,2}, G. Jhangri³ and P. Halloran²

Departments of ¹Pathology and Lab Medicine, ²Medicine, Division of Nephrology & Transplantation Immunology and ³Public Health Sciences, University of Alberta, Edmonton, Alberta, Canada.

Objectives: The significance and prognostic implications of glomerulitis in the context of transplantation are still unclear. The objectives of this study were to evaluate the frequency and distribution of glomerulitis in our study population and to see whether the “g” score shows a correlation with changes in the transcriptome, with C4d positivity and with the other Banff lesions.

Methods: Banff scores, C4d immunofluorescence results and expression of previously defined pathogenesis-based transcript sets (PBTs) as measured by Affymetrix microarrays were reviewed for 177 renal biopsies for cause done between September 2004 and March 2007.

Results: Glomerulitis (“g” = 1 to 3) was present in 24 % of biopsies and was more frequent in antibody-mediated rejection (ABMR) than in T-cell mediated rejection (TCMR) cases (80% vs 34%). Glomerulitis in the absence of rejection was infrequent, being found in 9.6% of biopsies mostly composed of borderline rejections or glomerulonephritis. When all biopsies were considered, the “g” score was significantly correlated with increased expression of certain PBTs: interferon- γ -induced transcripts (IMAT, GRIT; $p < 0.001$), cytotoxic T-lymphocyte associated transcripts (CAT; $p < 0.001$), constitutively expressed macrophage-associated transcripts (CMAT; $p < 0.002$) and transcripts associated to NK and endothelial cells (NKAT, ENDAT; $p < 0.001$). A trend towards increased expression of IMAT and GRIT with increasing “g” score was seen in TCMR cases but did not reach statistical significance ($p = 0.089, 0.064$ and 0.108). Statistically analysis could not be performed in the ABMR subset due to a low number of observations but expression of PBTs did not appear correlated to the “g” score. The “g” score significantly correlated with C4d positivity in peritubular capillaries ($p < 0.001$), with the degree of multilayering of the peritubular capillary basement membranes ($p = 0.016$) and with the “cg” ($p < 0.001$), “mm” ($p < 0.001$) and “i” ($p < 0.002$) scores.

Conclusions: Glomerulitis is present in a higher proportion of ABMR than TCMR cases and correlates with markers of antibody-mediated activity such as C4d positivity and with the “cg” score. The transcriptome changes show increased interferon- γ effects and inflammatory response in biopsies with glomerulitis suggesting a more intense alloresponse in these patients.