CORRELATION OF PERITUBULAR CAPILLARY BASEMENT MEMBRANE MULTILAYERING AND C4D IMMUNOSTAINING IN RENAL TRANSPLANT BIOSIES

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Background: Both peritubular capillary basement membrane multilayering (PTCBMML) and C4d positivity have been described in the Banff schema as diagnostic criteria for chronic or late antibody-mediated allograft rejection. The consensus at the 2005 Banff Meeting was that the criteria for diagnosing chronic antibody-mediated rejection includes: transplant glomerulopathy and/or PTCBMML, and/or peritubular capillary loss and fibrosis, and/or chronic arteriopathy. PTCBMML, in the absence of glomeruli in tissue sections under electron microscopy, has been considered indicative of transplant glomerulopathy. Positive C4d immunostaining in the peritubular capillaries is considered the hallmark of antibody mediated rejection. Moreover, PTCBMML has also been seen in native kidney diseases.

Methods: Transplant renal biopsies were examined histologically, by immunoflouresence, and by electron microscopy. We reviewed 81 transplant renal biopsies in which peritubular capillaries were evaluated by electron microscopy. The number of layers of the basement membranes in the capillary wall and the percentage of capillaries involved by the multilayering were recorded, along with the number of peritubular capillaries seen per case. The numbers of layers were compared to the disease process and the C4d staining. PTCBMML was defined as: no multilayering (one layer), mild (2-3 layers), moderate (4-6 layers), and severe (greater than 6 layers). The PTCBMML was correlated to the C4d positivity in the biopsies.

Results: Of the 81 kidney transplant biopsies evaluated, 59 also had C4d staining performed by immunoflouresence. A mean of 2.7 capillaries were evaluated on each case. 46 (78%) cases were C4d negative (78%) with a mean number of 3.7 ± 2.2 capillary layers per capillary. 13 (22%) cases were C4d positive (22%) with a mean number of 4.3 ± 2.1 capillary layers per capillary. The difference of the means was not statistically significant. Furthermore, 20 (43%) of the C4d negative biopsies had moderate to severe PTCBMML, while 5 (38%) of the C4d positive biopsies had negative or mild multilayering.

Conclusions: PTCBMML is seen in both transplant and native kidneys with a variety of pathologies such as diabetes mellitus, hypertension, and chronic systemic lupus. The overall difference in capillary basement membrane multilayering is not statistically different. More importantly, a lack of severe PTCBMML is seen in kidney transplant biopsies that are positive for C4d. C4d is regarded as the gold standard for humoral rejection. Therefore, PTCBMML as an indicator in the “diagnostic triad” for chronic humoral rejection is not warranted. PTCBMML may be a sign of general endothelial damage and subsequent repair, as opposed to specific damage diagnostic of humoral rejection.