EXPRESSION OF CD20 IN RENAL ALLOGRAFT BIOPSIES IS NOT UNIQUE TO REJECTION AND IS NOT RELATED TO ALLOGRAFT FUNCTION

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The interstitial infiltrate in renal allograft rejection is usually dominated by cytotoxic T lymphocytes and macrophages. In addition, the presence of $CD20^+$ B lymphocytes or plasma cells can be observed in some biopsies with T cell mediated rejection (TCMR). Recent publications have identified lymphoid clusters containing CD20+ B cells in kidney allografts undergoing TCMR as a prognostic factor for glucocorticoid resistance and graft loss. However, the pathogenesis that underlies the recruitment of B cells into the graft and the significance of the presence of B lymphocytes remains unknown.

We measured expression of the CD20 transcript (a specific marker for B lymphocytes) as an indicator of the B cell burden in 143 renal allograft biopsies performed for clinical indication (deterioration in function, stable but impaired function, or proteinuria) and analyzed its relationship to histologic lesions, diagosis, and renal function. In addition, we analyzed expression of transcript sets that reflect the major components of graft rejection: cytotoxic T cell associated transcripts, interferon gamma effects, and renal transcripts, which reflect the integrity of the kidney epithelium.

Compared to control kidneys (histologically normal sections of tumor nephrectomies), biopsies for cause showed a wide range in expression of the CD20 transcript (between 0.3fold and 45fold). Biopsies classified as rejection (TCMR, ABMR, or mixed TCMR & ABMR) or borderline had higher CD20 expression (1.37 ± 1.73 or 1.46 ± 2.13, respectively (log2 values)) than biopsies with BK nephropathy (0.81 ± 1.74, log2) or other diagnoses (eg CNIT, recurrent GN) (0.50 ± 1.63, log2). However, CD20 expression was not different between biopsies with TCMR and ABMR (1.05 ± 1.72 and 1.26 ± 1.33, respectively (log2)). Not all cases with high CD20 expression had rejection. In relationship to histologic lesions, CD20 expression correlated best with interstitial inflammation (Banff i-score, r = 0.43), followed by interstitial fibrosis, tubular atrophy, and tubulitis (r = 0.40, r = 0.37, and r = 0.31, respectively). There was no relationship to intimal arteritis. Biopsies with positive C4d staining had higher CD20 expression (2.00 ± 1.17, log2) than C4d-negative biopsies (0.83 ± 1.78, log2). However, in those biopsies with rejection (TCMR, ABMR, or mixed TCMR & ABMR) or borderline rejection, there was no difference between C4d+ and C4d- biopsies (2.00 ± 1.17 and 1.30 ± 1.92, respectively (log2, p = n.s)). CD20 expression correlated with expression of cytotoxic T cell associated transcripts (r = 0.67) and interferon gamma effects in the graft (r = 0.53), but only moderately with transcripts indicative of a renal response to injury (r = 0.36) and correlated moderately with loss of renal parenchymal transcripts (r = -0.40, and r = -0.29). CD20 expression correlated with expression of the B-cell attracting chemokine CXCL13 and its receptor, CXCR5. CD20 expression did not correlate with renal function at the time of biopsy or change in function during the 3 months following the biopsy. There was no correlation between CD20 expression and kidney age or time post transplant.

Our study does not support a relationship between the presence of B cells in the graft and graft function or functional deterioration. The level of CD20 expression was not related to severity of rejection: biopsies classified as borderline had CD20 expression similar to those with TCMR and ABMR. The presence of B cells, indicated by CD20 expression, was not unique to biopsies with rejection, indicating that B cells may home to the graft non-specifically in response to injury. The correlation of CD20 expression with the histology score for tubular atrophy and interstitial fibrosis supports this hypothesis. The correlation with expression of CCXL13 and CXCR5 supports previous studies and suggests that this interaction may play a role in B cell homing to the graft. The mechanisms of B cell recruitment to the graft and the functional role of B cells present in allografts remain unknown, but a role for B cells in determining allograft function and outcome is not supported by this study.