

## **PERITUBULAR CAPILLARY AND VASCULAR MACROPHAGE INFILTRATION CORRELATES WITH MICROVASCULAR DESTRUCTION AND WORSENS STEROID RESPONSE AND RENAL ALLOGRAFT OUTCOMES FOLLOWING C4d NEGATIVE ACUTE REJECTION EPISODES**

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We aimed to understand the influence of peritubular capillary (PTC) and vascular macrophage infiltration on steroid response and renal allograft outcomes after acute rejection (AR) episodes.

Seventy-nine patients with biopsy-proven AR in their first year after transplantation were included in the study. Thirty patients with normal first year renal allograft biopsies were also included in the study and used as a control group. All biopsies were C4d negative. Immunohistochemically we assessed the degree of macrophages (CD68) and HLA-DR-positive infiltrating cells in PTC's, glomeruli, and on vascular walls and tubules. In addition HLA-DR expression of PTC's was also evaluated. The decreasing intensity of peritubular capillary HLA-DR (PTC-DR) expression was accepted as the increasing degree of the destruction of PTC. Compared to control group AR cases showed significantly higher degree of macrophage and HLA-DR positive inflammatory cell infiltration in PTC's, glomeruli, and on vascular walls and tubules ( $P < 0.001$  for all). PTC destruction was significantly higher in AR cases than control group ( $p < 0.001$ ). PTC, glomerular and vascular macrophage infiltration showed significant correlation with PTC destruction and steroid response ( $p < 0.001$  for all).

Severity of PTC destruction with accompanying higher degrees of macrophage infiltration in PTC's, glomeruli and on vascular walls caused unresponsiveness to steroid therapy ( $p < 0.001$ ) and poor graft outcome ( $p < 0.001$ ). Five-year graft survival was 95%, 37% and 22 % for cases with grade 0, 1 and 2 PTC macrophage infiltration respectively ( $P < 0.001$ ). In addition five-year survival was 80%, 36% and 1% for cases with grade 0, 1 and 2 vascular macrophage infiltration respectively ( $p < 0.001$ ).

In conclusion peritubular capillary and vascular macrophage infiltration are important predictors of steroid response and renal outcome following acute rejection in cases whom especially had negative C4d.