CHRONIC ALLOGRAFT NEPHROPATHY (CAN): AN OBSOLETE DIAGNOSTIC DESIGNATION?

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"A credible diagnostic designation always entails management decisions. This is particularly true in renal transplant biopsies."

The 2005 Banff report introduces two major changes; 1) the elimination of "chronic allograft nephropathy" as a diagnostic designation, replacing it with "interstitial fibrosis/tubular atrophy", a designation that omits the universally present chronic glomerular and vascular lesions, and 2) that chronic glomerular and vascular lesions constitute a diagnostic triad for chronic humoral rejection, in addition to C4d positive staining in peritubular capillaries (PTC) and the presence of donor specific antibodies. To investigate this assertion we reviewed 416 renal transplant biopsies immunostained with C4d from May 2002 to March 2007. 66 (16%) were C4d positive in PTC with the remaining 84% being negative. We examined the distribution of histological categories as defined by the Banff 1997 schema (Racusen et cal, Kidney International, 1999, 55: 713-723). In the 66 C4d positive biopsies only 23 (35%) were associated with chronic allograft nephropathy (CAN). 36 (54.5%) were associated with pure acute humoral rejection, while 28 biopsies (42.5%) were characterized by a combination of acute humoral rejection and acute cellular rejection. 179 (43%) of the biopsies showed evidence of CAN, of which 156 (87%) were pure CAN and 23 (13%) represent a combination of CAN with acute humoral rejection (17 specimens, 9.5%) or CAN with acute cellular rejection and acute humoral rejection (6 specimens, 3.5%). Of the 179 biopsies with CAN, 64 (36%) showed evidence of concomitant transplant glomerulopathy (TG). Of the CAN/TGP biopsies 13 (20%) showed C4d staining in the peritubular capillaries.

In conclusion, we recommend continuation of using "chronic allograft nephropathy" as a diagnostic designation which implies a) end stage irreversible and nonspecific sclerosing damage to the renal allograft; this non-committal diagnosis prevents selective and specific therapeutic interventions; b) inclusion of interstitial and tubular sclerosing damage as well as the universally present vascular and glomerular scarring of heterogeneous pathogenesis. The latter includes TG, a relatively common (36%) component of CAN. This glomerular process represents a heterogeneous, non-specific repair lesion resulting from a variety of etiopathogenic insults to the graft. Our results do not demonstrate a preferential association of TG and/or CAN with antibody-mediated humoral rejection.