Role of Poly (ADP-Ribose) Polymerase on Microvascular injury and Inflammation in Renal Allograft Rejection and Its Influence on Renal Graft Survival

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Introduction: The activation of poly (ADP-Ribose) polymerase (PARP) is well considered to play an augmenting role in inflammation and cell death. The aims of this study were to investigate the role of PARP in acute rejection (AR) and to assess the influence of PARP on renal survival.

Methods: Study compromised 81cases and 55 of them had AR. Twenty-six cases had no pathology and used as a control group. PARP and HLA-DR expression of tubules, interstitium, arteries and peritubular capillaries (PTC's) were studied immunohistochemically and CD68 positive macrophage infiltration of tubules, interstitium, PTC's and arterial walls were evaluated. The decreasing intensity of PTC HLA-DR (PTC-DR) expression was accepted as the increasing degree of the destruction of PTC's.

Results: AR cases showed higher degrees of tubular, interstitial and vascular PARP and HLA-DR expression compared to control group ($p<0.01$ for all). PTC-DR expression was lower and PTC-PARP expression was higher in AR cases compared to control group ($p<0.001$). Increasing of AR grade with the high level of PTC-PARP expression, caused decrease of PTC-DR expression and increase of PTC destruction ($p<0.01$). Tubular and interstitial HLA-DR expression, interstitial, tubular, vascular and PTC macrophage infiltration showed positive correlation with tubular, interstitial, PTC and vascular PARP expression ($p<0.01$ for all). In contrast PTC-DR expression showed negative correlation with all these parameters ($p<0.01$). Severity of PTC destruction with accompanying higher degrees of PARP expression on tubules, interstitium, arteries and PTC's caused unresponsiveness of steroid therapy ($p<0.01$) and poor graft outcome ($p<0.01$).

Conclusion: Increased PARP activation leads to higher degrees of cell death and inflammation that AR cases with high renal PARP expression showed significant PTC destruction and renal inflammation. Therefore we suggest that PARP inhibitor drugs can combine with immunosuppressive therapy in order to control PTC destruction and renal inflammation.