Circulating prophagocytic calreticulin and anti-phagocytic CD47 in renal transplant recipients: relation to allograft function

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Background: Chronic allograft dysfunction (CAD) is considered the leading cause of late allograft loss. Programmed cell removal is a process by which damaged or unwanted cells are recognized and phagocytosed and involves the expression of pro-phagocytic signals like calreticulin (CRT) on target cells, which is counterbalanced by anti-phagocytic signal CD47. The present study was conducted to assess circulating CRT and CD47 levels in renal transplant recipients (RTR) and their relation to allograft function.

Methods: Thirty RTR for more than 6 months (15 RTR with stable renal function and 15 RTR with CAD) and 15 healthy controls were enrolled in the study. Renal function was evaluated by serum creatinine, estimated glomerular filtration rate, and urinary alkaline phosphatase (u.ALP; a marker for tubular function). Serum levels of CRT, CD47 and high-sensitivity C-reactive protein (hsCRP; marker of systemic inflammation) were estimated using enzyme-linked immunosorbent assay. Renal interstitial fibrosis (IF) was graded in renal biopsies of CAD.

Results: Serum CRT, hsCRP and u.ALP levels showed significant increases and serum CD47 levels showed a significant decrease in RTR with CAD compared with RTR with stable renal function and healthy controls ($P<0.01$), while the differences were not statistically significant between the latter two groups ($P>0.05$). Serum CRT and CD47 levels were positively correlated with serum levels of creatinine and hsCRP and u.ALP in RTR and with the degree of renal IF in RTR with CAD ($P<0.05$). Serum CRT and CD47 showed high diagnostic accuracy in discriminating RTR with CAD from RTR with stable renal function (area under the curve, 0.842; $P=0.001$ and area under the curve, 0.824, $P=0.002$, respectively).

Conclusions: Alterations in circulating CRT and CD47 levels are associated with the development of CAD after renal transplantation and could be potential biomarkers for post-transplant outcome. Modulation of phagocytosis through CRT/CD47 pathway might be a therapeutic target for allograft dysfunction.

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