THE INFLUENCE OF TUBULAR PHENOTYPIC CHANGES ON THE DEVELOPMENT OF DIFFUSE INTERSTITIAL FIBROSIS IN RENAL ALLOGRAFTS

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It has been reported that myofibroblasts are the major cells in the development of interstitial fibrosis (IF) and therefore chronic graft dysfunction in renal allografts. In normal human kidney, tubular cells do not have myofibroblast differentiation and they don't have alpha-smooth muscle actin (alpha-SMA) expression.

In this study we aimed to show that tubular cells can undergo phenotypic changes toward myofibroblasts and induce early IF and poor graft outcome in renal allografts. The expression of alpha-SMA and the formation of vinculin and paxillin containing adhesion complexes are the primary criteria for determining the differentiation of non-muscle cells such as renal tubule cells into contractile myofibroblasts. For this reason we immunostained first year renal allograft biopsies of 74 patients with alpha-SMA, Vinculin and Paxillin primary antibodies and the expression of tubules and glomerular cells were evaluated.

Myofibroblast differentiation of renal tubules (alpha-SMA, vinculin and paxillin positive tubules) was found only 30 of 74 patients. In addition glomerular cells of 36 patients showed positive alpha-SMA, vinculin and paxillin staining. The development of diffuse IF was found significantly early in cases with tubules showing myofibroblast differentiation compared to cases with tubules that did not have myofibroblast differentiation ($p<0.01$). The presence of proteinuria in first year showed significant positive correlation with the glomerular alpha-SMA, vinculin and paxillin staining ($p<0.001$). Cases whom showed tubular and glomerular alpha-SMA, vinculin and paxillin staining showed worse graft outcome compared to cases that did not show tubular and glomerular staining ($p<0.001$).

In conclusion our results showed that renal tubular and glomerular cells can show myofibroblastic differentiation and these cells have a role in the development of diffuse interstitial fibrosis and early proteinuria in renal allografts.