Cyclosporine에 의한 신간질 섬유화에서 Osteopontin의 역할

연세대학교 의과대학 병리학교실

정 현 주 · 임 범 진

The aim of this study was to evaluate the role of osteopontin (OPN) in cyclosporine (CsA) nephrotoxicity of the human kidney. Renal biopsy samples obtained before and after one to two years of CsA treatment were evaluated in 18 children (2.2-13.0 years, M : F=14 : 4) diagnosed of minimal change nephrotic syndrome. The changes in tubular OPN expression between pre- and post-treatment samples were correlated with interstitial macrophage infiltration, transforming growth factor-β (TGF-β) expression, interstitial fibrosis and microvascular density. OPN, TGF-beta, CD68 and CD34 positivity were quantitatively assessed by immunohistochemical staining. Light microscopy showed that interstitial fibrosis developed in two thirds of cases after CsA treatment. However, CD68-positive macrophages infiltrated minimally in fibrotic areas and were found in only one third of cases. OPN expression was significantly increased in the glomerular mesangium ($p=0.001$) and tubules ($p=0.025$) after CsA treatment, whereas the number of CD34-positive peritubular capillaries decreased ($p=0.022$). An inverse relationship was observed between tubular OPN expression and microvascular density ($r=-0.644$). However, tubular OPN expression was not related to proteinuria, interstitial fibrosis or interstitial or tubular TGF-β expression. This study indicates that increased OPN expression may be related to microvascular injury in human CsA nephrotoxicity. It also shows that OPN expression may be used as an early but nonspecific marker of CsA toxicity before the manifestation of interstitial fibrosis.