Hepatocyte Growth Factor Localization in Primary Glomerulonephritis and Drug-Induced Interstitial Nephritis

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Table 1. Correlation between the distribution of HGF on tubule epithelial cells and primary glomerulonephritis, drug-induced interstitial nephritis and control tissue.

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Dear Sir,

Hepatocyte growth factor (HGF) was initially identified as a mitogen for hepatocytes by Nakamura et al. [1] in 1984. Recently, HGF has been shown to be a mitogen for a variety of cell types, including renal tubular cells [2, 3]. Nagaike et al. [4] examined changes in HGF mRNA expression, HGF activity and HGF receptor in the rat kidney following unilateral nephrectomy or treatment with carbon tetrachloride, and suggested that HGF might function as a renotropic factor during renal regeneration after injury.

In this study, we present the immunohistochemical localization of HGF in patients with primary glomerulonephritis and drug-induced interstitial nephritis.

Hepatocyte growth factor (HGF) was initially identified as a mitogen for hepatocytes by Nakamura et al. [1] in 1984. Recently, HGF has been shown to be a mitogen for a variety of cell types, including renal tubular cells [2, 3]. Nagaike et al. [4] examined changes in HGF mRNA expression, HGF activity and HGF receptor in the rat kidney following unilateral nephrectomy or treatment with carbon tetrachloride, and suggested that HGF might function as a renotropic factor during renal regeneration after injury.

In this study, we present the immunohistochemical localization of HGF in patients with primary glomerulonephritis and drug-induced interstitial nephritis.

We examined 37 patients (18 males and 19 females; age: 15-74 years, mean ± SD; 40.9 ± 17.6) who underwent renal biopsy prior to treatment in the Second Department of Internal Medicine, Hiroshima University School of Medicine, Hiroshima, Japan. These patients were diagnosed as follows: primary glomerulonephritis, 25 patients (IgA nephropathy, 18 patients; membranous glomerulonephritis, 6 patients; focal glomerulosclerosis, 4 patients); drug-induced interstitial nephritis, 9 patients (NSAIDs, 4 patients; anticancer agents, 2 patients; antibiotics, 2 patients; interferon-γ, 1 patient), and minimal changes, for control tissue, 3 patients. Kidney tissue fixed in formalin and embedded in paraffin was used to localize HGF. The sections were deparaffinized using xylene and alcohol, and the antigen was unmasked in 0.06 M PBS, pH 7.2, for 30 min at 37°C. The primary antibody (monoclonal anti-HGF antibody, Otsuka Pharmaceuticals, Japan) was applied overnight at 4°C, followed by incubation with the secondary antibody for 30 min at room temperature. Immuno-products were visualized by applying DAB. The relationship between the presence of HGF and the histological stages of IgA nephropathy [5] was evaluated.
HGF was localized mainly on the epithelial cells in the tubules, but not in the glomeruli (fig. 1). The results of this study are summarized in table 1. The positive staining rate for HGF was 33.3% (5 of 15 patients) with IgA nephropathy, 66.7% (4 of 6 patients) with membranous glomerulonephritis and 50% (2 of 4 patients) with focal glomerulosclerosis.

Conversely, all patients with drug-induced interstitial nephritis were positive for HGF staining. No staining for HGF was observed in patients with minimal changes. There was a significant positive correlation between the distribution of HGF and the histological damage in patients with IgA nephropathy ($\chi^2 = 13.55, p < 0.01$). These findings suggest that HGF is correlated with tubular damage in primary glomerulonephritis, whose etiology remains unclear, as well as acute tubular damage from various drugs.

Fig. 1. Microscopic findings in the kidney. HGF was localized on the epithelial cells in the tubules of patients with IgA nephropathy, stage III (a) and in patients with drug-induced interstitial nephritis (b).

References

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