Blood Hepatocyte Growth Factor Levels in Chronic Renal Failure Patients

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1.2

1.0 -

0.8 -

Dear Sir,

Hepatocyte growth factor (HGF) was originally purified and cloned as a factor that promotes proliferation of parenchymal liver cells [1]. Subsequent studies have revealed that HGF has a wide range of cell types as its target, including renal tubular cells [2]. HGF stimulates DNA synthesis, increases motility and induces tubular formation of renal epithelial cells in vitro [2], suggesting that HGF may have a role in kidney organogenesis, hypertrophy or repair. This notion is further supported by the findings in vivo that, in experimental animals, maneuvers which reduce the number of functional nephrons, such as unilateral nephrectomy and application of nephrotoxic agents, increase the production of HGF in liver, lung and kidney [3]. In order to investigate whether a similar response of increased HGF production is operative in humans with renal damage, we have measured the blood HGF level in end-stage renal disease (ESRD) patients.

Blood serum was sampled from 14 ESRD patients requiring regular hemodialysis treatment and 195 healthy volunteers. ESRD patients consisted of 8 males and 6 females, were 49.4 ± 14.5 (mean $\pm$ s.d.) years old, had been treated with hemodialysis for 7.8 ± 6.1 years, and had predialysis serum creatinine level of 10.3 ± 1.4 mg/dl. Diseases which caused renal failure were chronic glomerulonephritis in 5 patients, diabetes mellitus in 2, IgA nephropathy in 1, systemic lupus erythematosus in 1, toxemia of pregnancy in 1, and unknown in

20.6

UL

σ

x

0.4 -

0.2

0.0

Fig. 1. Serum HGF levels of normal and ESRD patients. Each dot represents an individual measurement. Bars indicate means and standard deviations. HGF level was significantly different between normals and ESRD patients ($p < 0.01$, Student's t test).

the remaining 4. None of the subjects had active lung or liver disease as judged by physical examination, chest X-ray, serum GOT, GPT, and LDH levels. Serum HGF level was measured by sandwich-type immuno-radiometric assay. The serum specimen was incubated with anti-HGF monoclonal anti-

ESRD

Normal

body (mAb) coated beads. After washing, they were incubated with the ^{125}I -labeled anti-HGF mAb solution. They were washed again, and radioactivity on the beads was counted with a γ -counter. Figure 1 shows that the serum HGF level is significantly increased in ESRD patients as compared to normal con-

trols ($p < 0.01$, Student's t test). HGF level was 0.48 ± 0.20 ng/ml in ESRD patients and 0.26 ± 0.07 ng/ml in normals. Since HGF is cleared from the plasma mainly by the liver (96%) and the kidney contributes very little (less than 1%) to the total clearance [4], it is reasonable to conclude that increased blood HGF level in ESRD patients represents increased production instead of decreased destruction. This result is compatible with the notion that HGF production is increased in response to reduced renal mass in humans. The increased HGF might be involved in the increased incidence of renal tubular cysts and neoplasms in ESRD patients [5].

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