Up-regulation of VEGF in Alpha-fetoprotein-producing gastric cancer

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Alpha-fetoprotein (AFP)-producing gastric carcinoma (APGC) is well known to have a poor prognosis and high incidence of lymph node and liver metastases compared to non-producing carcinoma. Although the reason why APGC frequently metastasizes to the liver is not well known. We hypothesizes that angiogenesis is one of the important reasons for frequent liver metastases from APGC. In order to clarify this hypothesis, we examined the vessel density and vascular endothelial growth factor (VEGF) expression in APGC. Furthermore, we studied the effects of anti-AFP antibody for angiogenesis using APGC xenotransplanted mouse model.

Archival specimens of APGC (n=25) and non-APGC (n=68) were studied. Expressions of vessel density and VEGF were significantly higher in APGC than those in non-APGC ($p<0.001$). Immunohistochemical analysis of patients with gastric cancer shows that expression of VEGF and factor VIII are significantly higher in APGC than non-APGC. There is correlation among the AFP expression, the vessel density and the VEGF expression in APGC ($p<0.001$).

Next, we studied the effects of anti-AFP antibody on APGC xenotransplanted in nude mice. There is significant inhibition of tumor growth in the treatment groups compared to the control groups in two APGC lines ($p<0.01$). But, there is no difference in non-APGC cell line. Moreover, vessel densities of the treatment groups were significantly lower than those of the control groups in these two lines. These findings thus suggest that the biological behavior of APGC is angiogenesis-dependent. Down regulation of angiogenesis by anti-AFP antibody suggest that AFP itself may upregulate the angiogenesis, and the treatment by antibody could have anti-angiogenic effects, inhibiting metastasis, especially liver metastasis in APGC.