Involvement of erbB-2 and β-catenin oncogenes in stomach cancer

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1. Altered expression of β-catenin and c-erbB-2 in early gastric cancer

To investigate the possible relationship between altered expression (loss of membranous staining or nuclear accumulation) of β-catenin and invasion/metastasis in early gastric cancer (EGC), β-catenin was detected immunohistochemically in 116 cases of EGC, including 86 differentiated and 30 poorly differentiated carcinomas. In parallel, immunohistochemical expression of c-erbB-2 was analyzed in all EGC cases. Regardless of histological types, altered expression of β-catenin was found in 47% of mucosal carcinomas and 89% of carcinomas with submucosal invasion ($p<0.001$). Of particular interest is that β-catenin alteration was found in most EGCs wit lymph node metastasis, even though no significant statistical comparison could be made. These results suggest that molecular changes resulting in abnormal b-catenin expression participate in the process of submucosal invasion and metastasis to the lymph node. While loss of expressionwas preferentially observed in poorly differentiated EGCs, nuclear accumulation was found exclusively in 24% of differentiated EGCs. c-erbB-2 was overexpressed in only 16% of differentiated EGCs but there was no correlation between this overexpression and presence of invasion or metastasis. However, it is intriguing that 12 out of 14 cases with c-erbB-2 overexpression also showed altered β-catenin expression in the tumors, suggesting that both molecules are involved in the development of a certain set of differentiated EGCs.

2. Abnormal expression of E-cadherin, β-catenin and c-erbB-2 in advanced gastric cancer: its association with liver metastasis

Background and Aims. We investigated expression of E-cadherin, β-catenin and c-erbB-2 in gastric cancer to identify molecular factor(s) relevant to development of liver metastasis, which is a frequent cause of mortality in gastric cancer patients.

Patients and Methods. We analysed by immunohistochemistry and compared expression patterns of E-cadherin, β-catenin and c-erbB-2 in the tumor between 40 cases of gastric cancer (GC) without [GC-H(-)] and 16 with concurrent liver metastasis [GC-H(+)].

Results. Loss of E-cadherin expression in the primary tumor was found in 18% of GC-H (-) and in 19% of GC-H(+). Oncogenic β-catenin activation, represented by its nuclear translocation, was detected in 13% of GC-H(-) and in 31% of GC-H(+). There was no statistical difference in incidence of alteration in these molecules between the two groups of patients. c-erbB-2 overexpression was more frequently observed in GC-H(+) (10/16, 63%) than in GC-H(-) (5/40, 13%) ($p=0.0001$) while the distribution of histological types of the tumors was similar in the two groups of patients. This overexpression was also detected in metastatic liver tumors and biopsy specimens in the 10 of the former group of patients.

Conclusion. Our results strongly suggest a role of activated c-erbB-2 in the process of liver metastasis, and an importance of detection of this overexpression in biopsy specimens to identify GC patients who are at high risk of developing liver metastasis.