

A comparative study of protein expressions in primary colorectal cancer and synchronous hepatic metastases: The significance of MMP-1 expression

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Objective: This study was undertaken to determine the ability of protein expression in primary colorectal cancer and its metastatic liver tumour tissues to predict hepatic metastasis and intrahepatic recurrence.

Materials and Methods: A total of 60 patients with colorectal cancer were enrolled in this study. The expressions of 5 proteins, carcinoembryonic antigen (CEA), vascular endothelial growth factor (VEGF), matrix metalloproteinase (MMP)-1, MMP-7, and tissue inhibitor of metalloproteinases (TIMP)-1, were assessed by immunohistochemical (IHC) staining. Protein expressions were measured in primary colorectal cancer without liver metastasis (group A), in primary colorectal cancer with liver metastasis (primary tumour, group B), and in resected metastatic liver tumour tissues (liver metastasis, group C).

Results: IHC staining revealed more protease activity (MMP-1 and MMP-7) in group B than in group A. Angiogenic activity, positive VEGF expression, was significantly greater in group C than in group B. Multivariate analysis showed that positive MMP-1 expression, the presence of lymphovascular invasion, and an elevated preoperative serum CEA level (>5ng/ml) were significantly related to synchronous liver metastasis. However, intrahepatic recurrence was not found to be related to protein expressions, the presence of lymphovascular invasion, or preoperative CEA level.

Conclusions: Our findings suggest that protease activity is important for metastasis, and that angiogenic activity is essential for metastatic tumour growth. Furthermore, positive MMP-1 expression in primary colorectal tumour tissues was found to be a significant predictor of liver metastasis. However, the prognostic impact of protein marker expression in terms of intrahepatic recurrence appears to be minimal.

Figure 1. Tumour cell intensities of matrix metalloproteinase-1 (MMP-1) in primary colorectal cancer tissues: A (negative), B (weak), C (moderate), D (strong staining)

Histoscores were classified using a 4-point system: negative (histoscore=0), weak (histoscore 1-100), moderate (histoscore 101-200) and strong (201-300) staining.

