Carcinoma-containing CEA in colon cancers in primary and metastatic tumors

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ABSTRACT : Carcinoma-containing CEA was measured as compared with normal tissues and metastases in the lymph nodes and the liver.

The high CEA production was remarkable in the potent malignant tumors and metastases in the liver and the lymph nodes as compared with those in normal colon tissues as well as in non metastatic lymph nodes.

It is reasonable to consider that high plasma CEA may well indicate advancing or highly potent malignant diseases or recurrence of colon cancers due to destruction of vascular structure by cancer invasion.

INTRODUCTION

The measurement of carcinoembryonic antigen (CEA) in serum has been of use to clinically detect a presence of colon cancer and its recurrence. An extraordinarily clinical prevalance in use has been achieved, but the mechanism of CEA production and transmission to the serum is not clear yet.

This study is to clarify the mechanism as to where CEA is produced and how it is transmitted to the serum by means of measuring the tissue CEA in cancer mass and the surrounding tissues independently.

METERIAL AND METHOD

Fifty-seven cases surgically treated for colon cancers were eligible for this study. According to the location of colon cancers, 14 were in right half the colon, 19 in the left half and 24 in the rectum respectively.

According to the histologic type, 11 were well differentiated adenocarcinoma, 39 moderate, four undifferentiated and three mucinous respectively.

These included three with liver metastases, and the dissected lymph nodes were subjected to this study. There were 16 metastatic nodes and 24 normal one. Tissue-containing CEA were measured by using the surgical specimens and dissected nodes. These were cut into pieces of as large as 0.5 to 1g in 3-5ml cold normal saline per gram of tissue and homogenized at 4° C in phosphate buffer saline of pH 7.2-7.4 with ultrafurrox homogenizer (HITACHI 20 PR-52D). After centrifugation at 1600g for 20 min, the supernatant was tested by the micro immuno-assay method. Tissue CEA was calculated by ng/tissue weight (g).

In this study the surgical specimens were tak-

en from apparently proliferating part of the tumor mass near the margin of the tumor, avoiding to take the necrotic site in the middle of the tumor mass. Parts of the tissue, 3 cm proximal and distal to the visible tumor margin, were taken to compare with the tumor mass.

RESULT

Tissue CEA was compared in accordance with the location of the tumor as shown in Fig. 1.



Fig. 1. Relationship between tissue-containing CEA and the location of colon cancer.

There was no specific pattern concerning the tumor location, although tissue CEA of cancers originated from the right half of the colon showed somewhat low.

According to histologic differentiation, tissue CEA in undifferentiated adenocarcinoma were lower rather than those in well and moderate adenocarcinomas as shown in Fig. 2.



well : well differentiated adenocarcinoma mod. : moderately, undiff. : undifferentiated muci : mucinous

Fig. 2. Relationship between tissue-containing CEA and histologic patterns of differentiation.

Furthermore, that in mucinous carcinoma showed the lowest. It is a reflection that tissue-CEA is decreasing in accordance with the potent clinical malignancy. CEA in the tissues 3 cm distant from the tumor mass showed significantly lower than those in the tumor. However, there was no significant difference between the tissues 3 cm proximal and distal to the tumor in spite of presenting the lower CEA of the normal lymph nodes tissues.

Fig.3 indicates high CEA of the metastatic lymph nodes as compared with the non-metastatic one. It was almost the same as those of the tumor massess. Tissue CEA of the metastatic tumor into the liver had become higher than that of the metastatic lymph node.

It was evident that metastatic foci were containing and producing large amount of CEA.



Fig. 3. Tissue-containing CEA in each site

DISCUSSION

The measurement of CEA in colon cancer is of benefit to diagnose and \checkmark or treat in clinical use.^{1) 2) 3)}

It is well known that CEA is produced by cancer cells and transmitted to the portal vessel. However, the mechanism of an increase in CEA is not clearly understood, for example, 1)capacity of CEA production^{1) 2)} 2)transmission to the vessel and its speed³⁾⁻⁵⁾ 3)metabolism of CEA in the lung and the liver^{6) 7)} and 4)absorption of it from the intestinal epithelium.

The factors contributing to an increase in CEA are as follows, histologic types, depth of cancer invasion, vascular invasion, distant metastasis, staging classification by Dukes and so on.³⁾⁻⁵⁾ Of interest is the fact that a presence of vascular invasion is the most increasing factor. Bivns ³⁾ also reported that an increase in plasma CEA is mostly influenced by vascular invasion.

In this present study, it is worthwhile to emphasize that the more the potent malignancy of the tumor, the higher CEA in the tumor remains. It is suggested that higher malignant tumors including metastases in the lymph nodes and the liver have high activities of CEA production.

In fact, plasma CEA is not necessarily proportional to CEA production in the tumors. $P_{\rm ATT}$ ⁸ commented on this possibility that as soon as plasma CEA is derived from the tumor, it responds potentially to CEA antibody in plasma and changes into immunocomplex that makes CEA inactive.

REFERENCE

- MARTIN, F and MARTIN, M : Radioimmunoassay of carcinoembryonic antigen in extracts of human colon and stomach. Int. J. Cancer 9: 641, 1972.
- 2) WAGENER C, WALLRAF RN, NISSON S, et al. : Localization and concentration of carcinoembryonic antigen (CEA) in gastrointestinal tumors. Correlation with CEA levels in plasma. J. Natl. Cancer Inst. 67: 539, 1981.
- 3) BIVINS, BA, MECKER WR and GRIFFEN WO : Carcinoembryogenic antigen (CEA) levels and tumor histology in colon cancer. J. Surg. Res. 18 : 257, 1975.
- 4) DENK H, TAPPENINER G, ECKER STORFER R, et al. : Carcinoembryonic antigen (CEA) in gastrointestinal and extragastrointestinal tumors and its relationship to tumor cell differentiation.
- 5) HAMADA Y, YAMAMURA M, HIOKI K, et al. : Immunohistochemical study of carcinoembryonic antigen in patients with colorectal cancer. Correlation with plasma carcinoembryonic levels. Cancer 55 : 136, 1985.
- 6) SHUSTER J, SILVERMAN M and GOLD P : Metabolism of human carcinoembryonic antigen in xenogenic animals. *Cancer Res.* 33 : 65, 1973.
- THOMAS Pand Hems DM : The hepatic clearance of circulating carcinoembryonic antigen and asialocarcinoembryoni antigen by the rat. Biochem. Biophys. Res. Commun. 67 : 1205, 1975.
- 8) PATT YZ, MAVLIGIT G, CHUANG VP, et al. : Arteriovenous carcinoembryonic antigen gradient. Determination by selective angiography for localization of metastatic colorectal cancer. Arch. Surg. 115 : 1122, 1980.