# Tumor-containing CEA in Colon Cancers

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Received for publication, June 20, 1988

**ABSTRACT :** Carcinoembryonic antigen (CEA) in serum and fresh cancer tissue taken at surgery was measured and analyzed in terms of the disease stage. The CEA level in serum (s-CEA) has become higher with advance in the disease stage. However, in stage V it was lowered as well as CEA level in cancer mass (ca-CEA).

It is suggested that S-CEA is influenced by cancer invasion into the vessel wall, tumor necrosis and/or degeneration which ca-CEA may well be migrated from the tumor cells.

#### INTRODUCTION

The measurement of carcinoembryonic antigen (CEA) was of use to detect colon cancer and its recurrence in follow-up study.

Recently it was defined that serum CEA levels were not specific to the patients with colon cancer and these were increased colon cancer as well as breast and gastric one.

In the present study, the clinical significance of CEA in patients with colon cancer was evaluated as compared between CEA in serum and tissues including cancer mass.

## MATERIAL AND METHOD

Fifty-nine cases of colon cancer treated in our clinics were eligible in this study, 13 of whom were advanced cases with peritoneal dissemination and hepatic metastasis.

CEA in serum (S-CEA) was measured by radioimmunoassay according to Sandwitch method using Dinabot-RIA kit, a normal values being less than 2.5 ng/ml. The fresh cancer mass CEA (ca-CEA) was measured from the primary tumor mass. These tissues as large as 0.5 to 1g were cut into pieces in 3-5 ml cold normal saline per gram of tissue and homogenized at  $4^{\circ}$ C in phosphate buffer saline of pH 7.2-7.4 with ultrafurrox homogenizer (HITACHI 20PR-52D). After centrifugation at 1600g for 20 min, the supernatant was tested by the microimmunoassay method. The CEA content of tissue was calculated by ng/tissue weight (g) using the same way as that in serum.



Fig. 1. Relationship between S-CEA level and tumor location, showing that S-CEA levels are not specific to the tumor locations.

#### RESULT

S-CEA levels were compared in association with tumor locations as shown in Fig. 1.

According to the tumor location, S-CEA levels were compared as shown in Fig. 1. There was no characteristics of the tumor location among the right colon, left colon and rectum.

In view of the histologic stages, S-CEA was increased with advances in the disease stage, in particular it was pronounced in Stage V. On the contrary, it was somewhat lowered in Stage I and II as indicated in Fig. 2. However, in this study ca-CEA values in cancer mass was measured and compared with those in serum. The results were shown in Fig. 3. According to an increase in S-CEA values, ca-CEA kevels were raised. The ca-CEA values were significantly higher than S-CEA one.

However, the S-CEA values of more than 10 ng/ml were not necessarily proportional to ca-CEA. The values of more than 10 ng/ml in ca-CEA were lowered rather than those in S-CEA. In advanced cases with peritoneal dissemination and hepatic metastasis, both of CEA levels did



Fig. 2. Relationship between S-CEA levels and histologic stages, indicating that S-CEA is increased with advancing histologic stages.



Fig. 3. Relationship between CEA levels in serum and cancer mass indicating that in advancing stage both are reduced.



Fig. 4. Relationship between S-CEA and ca-CEA, showing no correlation with advances in stages.

not necessarily remain high.

In view of the histologic stage, ca-CEA level did not proportionally varied as shown in Fig. 4 and in Stage V, it tended to be reduced, in particular, those of more than 2.5 ng/ml in serum changed with a wide range.

# DISCUSSION

CEA was first described by GOLD<sup>1)</sup> as an antigen associated with carcinoma of the digestive tract.

It is well known that S-CEA level is higher in colon cancer patients than in normal subject. The S-CEA levels in patients with colon cancer are ranging from 35.4 ng/g to 69.9 ng/g.<sup>2)</sup> It is recognized that when recurrence takes place, the CEA values reach 68.1-97.3 ng/g.<sup>2)</sup>

On the contrary, a resection of carcinoma contributes to lowering S-CEA.<sup>1)</sup> Therefore, the measurement of S-CEA is of help to detect colon cancer as well as appearance of its recurrence in follow-up study. It is not clear how CEA is moving from the tumor mass in which it is produced to the blood stream. It is assumed that complex factors such as degradation of  $CEA^{3)}$  and necrosis of the tumor mass<sup>4</sup> may be contributing. It is accepted that CEA is drained into the gut lumen of the colon and it is possible to understand that S-CEA level becomes elevated if cancer invades the adjacent vessel walls.

In this present study, there was a tendency toward increasing S-CEA with advancing disease stages of colon cancer. Of interest, however, is the fact that a rise of S-CEA becomes depressed according to advances in colon cancer. It may be in part attributed to tumor necrosis<sup>3)</sup> and  $\checkmark$  or CEA degeneration<sup>4)</sup> by rapid growth of the tumor mass. It is concluded that S-CEA level is elevated by colon cancer and with advancing disease stages. However, it was out of proportion to the disease stage in advanced disease, reflecting a presence of affecting factors.

### REFERENCE

- 1) GOLD P and FREEDMAN SO : Demonstration of tumor-specific antigens in human colonic carcinoma by immunological tolerance and absorption techniques. J. Exp. Med. 121 : 439-462, 1962.
- HIRAI H : Carcinoembryonic antigen (CEA). Clinic all-round 27:2437-2446, 1978 (Japanese).
- SIJUSSTEN J, SILVERMAN M and GOLD P : Metabolism of human carcinoembryonic antigen in exogeneic animals. *Cancer Res.*, 33 : 65-68, 1973.
- 4) ZAMCHECK N : Colorectal cancer markers
  " Clinical values of CEA in Oncodevelopmental Markers" ed. WH Fishman 339-349. Academic Press, New York.