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SIGNIFICANCE OF CEA AND CA242 IN THE DIAGNOSIS OF COLORECTAL CARCINOMA

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Carcinoembryonic antigen (CEA) is frequently used in the diagnosis of the colorectal carcinoma. CA242 is a novel unique tumor-associated antigen characterized by higher tumor specificity and sensitivity for colorectal cancer, as compared with other mucin antigens. In this study, preoperative levels of serum CEA and CA242 were measured in 63 cases of colorectal carcinoma. It was disclosed that the positive rate of CA242 was higher than that of CEA, particularly in patients with colon cancer. The combined determination of CEA and CA242 significantly increased the sensitivity and accuracy in the detection of colorectal cancer as compared with the use of CEA alone ($P<0.01$). In patients with advanced disease the positive rate was markedly elevated, especially in patients with liver metastasis. The results indicate that the combined use of CEA and CA242 assays is an useful adjunct diagnostic measure for colorectal carcinoma, and is helpful in the assessment of the stage of the disease as well as in making treatment plan.

Key words: Colorectal carcinoma, Rectal tumor, Carcinoembryonic antigen (CEA), Tumor-associated carbohydrate antigen

There are not any specific tumor markers for colorectal carcinoma (CRC). Carcinoembryonic antigen (CEA) is a proteidic marker, it is frequently used in the diagnosis of CRC. However, CEA have a poor tumor specificity and sensitivity. CA242 is a sialylated novel tumor-- associated mucin antigen, it can be determined with immunological methods using the CA242MAb. High CA242 levels are commonly found in the digestive tract malignant tumor. One of the effective methods of increasing diagnostic accuracy for CRC by measuring levels of serum tumor markers is that the combined use of several tumor markers. In this study, the significance of the combined determination of CEA and CA242 was analyzed in the diagnosis of CRC.

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MATERIALS AND METHODS

Specimens

Forty-seven serum samples were obtained from the fresh blood of healthy donors. Sixty-three serum samples of patients with CRC were obtained by venipuncture after fasting. All the specimens were taken during two weeks preoperatively. The cancer diagnosis was verified by histo-pathological examination in Department of Pathology, Cancer Hospital, Chinese Academy of Medical Sciences. The patients included 36 male and 27 female, their ages range from 27 to 82, with an average of 53.3.

Methods

CEA assay was performed, using the radioimmunoassay kit from China Institute of Atomic Energy. The positive value is over 15ng/ml. CA242

was detected using immunoradiometric assay kit, Beijing Jiake Biotechnical Company product, its positive cut-off value is 17U/ml. Statistical method: χ^2 test.

RESULTS

CEA and CA242 in Healthy Donors and CRC Patients

There were statistically significant differences in serum CEA and CA242 concentration between the patients with CRC and the healthy donors ($P<0.001$). In the healthy donors, the highest value of serum CEA was 7.3 ng/ml, and there was only a positive case for CA242 (22U/ml). In CRC the positive rate of serum CA242 was markedly higher than that of CEA, and the combination of CEA and CA242 significantly increases the diagnostic sensitivity for detection of CRC as compared with the use of CEA alone ($P<0.01$) (Table 1).

Table 1. Sensitivity of CEA, CA242 and the combination of CEA and CA242 in healthy donors and CRC patients

Group	Total	CEA		CA242		CEA+CA242	
		pos.(n)	%	pos.(n)	%	pos.(n)	%
Healthy donor	47	0	0	1	2.1	0	0
CRC	63	20	32	30	48	37	59

CEA and CA242 in Colon and Rectal Cancer

The positive rates of serum CEA and CA242 were higher in the patients with colon cancer than that in the cases with rectal carcinoma, particularly the difference of CA242 was statistically significant ($P<0.05$). (Table 2)

Table 2. Comparision of the CEA and CA242 assays in colon and rectal cancer patients

Group	cases	CA242		CEA	
	(n)	pos.(n)	%	pos.(n)	%
Rectal cancer	36	13	36*	8	22
Colon cancer	27	17	63*	12	44

*$P<0.05$

CEA, CA242 Liver Metastasis

In this group of patients with CRC, the combination of serum CEA and CA242 were positive in 7 of 9 cases (78%) with liver metastasis, and 5 of 9 cases were positive for the two markers. The positive rate was markedly higher than that in the cases with no liver metastasis. However, the differences was not statistically significant (Table 3).

Table 3. Sensitivity of the combination of CEA and CA242 in the CRC cases with and without liver metastasis

Group	Cases	CEA or/and CA242	
		pos.(n)	%
Liver metastasis	9	7	78
Non liver metastasis	54	30	56

CEA and CA242 in Clinical Staging of CRC

In CRC the positive rates of CEA and CA242 were higher in the patients with the Dukes C and D stages than that of Dukes A and B stages, but the differences were not statistically significant. (Table 4)

Table 4. Comparision of the CEA and CA242 assays in Dukes A-D stages of colorectal cancer

Marker	positive Total	Dukes A-B		Dukes C-D	
		pos.(n)	%	pos.(n)	%
CEA	20	9	45	11	55
CA242	30	13	43	17	57
CEA or/and CA242	37	16	43	21	57

DISCUSSION

The carcinoembryonic antigen (CEA) is a tumor-associated antigen. It was first isolated from the tissue of colonic adenocarcinoma and entodermal colon mucosa by Gold and Freedman in 1965. Because of having a poor specificity, the CEA was often used as a supplementary indication in the diagnosis of CRC. In the other hands,CEA is first degraded by the liver after it is released from the tissues of malignant digestive tract disease to the portal vein, and then to circulation.[1] Therefore, the

concentration of CEA is dropped in the peripheral blood. However, serum CA242 levels are usually elevated in the patients of malignant digestive tract disease. The exact chemical structure of the CA242 epitope has not been elucidated, but immuno-chemical studies have shown that CA242 is different from other known tumor-associated mucin antigens such as CA19-9, CA50, CA12-5, CA15-3, STN. CA242 is a novel unique tumor-associated epitope characterized by higher tumor specificity and sensitivity to pancreatic and colorectal cancer, as compared with other mucin antigens.[2-5] This study shown that CA242 was in a higher percentage of sera from patients with CRC than CEA. The combination of CEA and CA242 significantly increases the diagnostic sensitivity for detection of CRC as compared with the use of CEA alone, and can reduce the false positive rate.

Histochemistry studies have shown that in malignant tissues, expression of CA242 is seen in the majority of pancreatic and colon carcinomas, and it is also frequently expressed in adeno-carcinomas of other organs.[4] In this study, the positive rates of serum CEA and CA242 in the patients with colon carcinoma were markedly higher than that of rectal cancer, particularly the rate of CA242 was significantly increased.

It was disclosed that the level of serum CEA was obviously elevated in the pateints with advanced cancer and distant metastasis. The serum CEA concentration was evidently higher in the patients with metastasis of colorectal carcinoma than that of the patients with metastasis of lung, breast and gastric cancers. Therefore, CEA may be of additional value in the diagnosis of matestasis if combining other tumor markers.[6] A lot of clinical studies have proved that colorectal carcinoma patients with high preoperative level of serum CEA have bad prognoses. In dukes C and D stages diseases, patients with CEA serum concentration higher than normal level have a shorter disease free interval and lower survival rate than patients with normal CEA serum levels. These results have led to the speculation that the over-expression of CEA contributes directly to tumorigenesis or metastasis formation.[7] Cells of liver matastasis of colon carcinoma can express high level of CEA mRNA and CEA protein.[8] At present, it was disclosed that CEA is an adhesion molecules, has a function of immunodepression as well as play a promoting role in the development of metastasis. Some research in other countries reported that greatly elevated levels of CA242 are commonly found in pancreatic and advanced colorectal cancer. In colorectal cancer CA242 show higher sensitivity than CA50 and CA19-9. In a comparative study between CA_{50} and CA242 in colorectal cancer, CA242 have higher sensitivities in Dukes A,B,C and D stages than CA50.[5] In this study, the positive rates of CEA and CA242 were markedly higher in the patients with liver metastasis and Dukes C and D stages than that of non liver metastasis and early stages. The combination of CEA and CA242 levels were elevated in 7 of 9 patients with liver metastasis.

The results indicated that serum CA242 shows higher sensitivity than CEA in the patients with CRC, and the combination of CEA and CA242 signifi-cantly increases the diagnostic sensitivity and accuracy for detection of CRC as cmpared with the use of CEA alone, and reduce the false positive rate, particularly in patients with colon cancer. Serum CEA and CA242 have high positive rate in patients with advanced colorectal cancer, especially in patients with liver metastasis. The combined use of CEA and CA242 assays is an useful adjunct diagnostic measure for CRC, and is helpful in the assessment of the stage of the disease as well as in making treatment plan.

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Short Report

FINGERS METASTASES IN A WOMAN WITH LIVER CANCER

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CASE REPORT

A 51-year-old woman was admitted to our hospital on May 29, 1995 with the complaint of right upper abdominal pain, anorexia and weight less for more than 5 months. By CT scan, a round pathologic lesion with the size of 7.7 cm ×6.6 cm ×7.0 cm on the left lobe, and an irregular and lobulated focus with the size of 8.0 cm×8.0 cm×12 cm on the right lobe of liver were found. The result of chest radiograph showed that there were scattered nodular shadows on the lung. Serum HBV surface antigen (HBsAg) was positive, and the serum level of alpha-fetoprotein (AFP) was 1,650 ng/L. Primary liver cancer complicated with lung metastases was diagnosed. She received general chemotherapy and other supporting therapy. After 20 days, she left the hospital with the release of her abdominal pain and improve in appetite. Three weeks later, she came back for another course of chemotherapy. On physical examination, a red, cone and protruding vegetation with in length 0.6 cm, covered by a thin membrane, on the top of the ring finger of her left hand. The vegetation developed rapidly. After 2 weeks, it became a globular neoplasm with the size of 1.6 cm× 1.5 cm × 1.5 cm, full of bumps and holes
on outside appearance, and often bled because of the rupture of the membrane. Adenocarcinoma cells were observed through local secretion pathological examination. At that time, neoplasms as large as green beans appeared on the thumb and the little finger of the patient's left hand. After the treatment of injecting absolute alcohol to the bottom of the globular cancer swelling, local bleeding was controlled, and the focus was reduced gradually.

DISCUSSION

Advanced liver cancer may metastasize to other organs through the blood circulation, but it seldom metastasize to fingers. When the cancer cells circulate in the blood, any injury will give the chance to them to inoculate at the local site. The ring finger of the left hand is usually the site for routine exam of blood, so this may be the reason of finger metastasis. At first, the metastatic cancer cells formed a small subcutaneous nidus under the skin of the ring finger, then the cancer swelled and grew to the outside of the skin owing to frequent blood sampling. Therefore, we suggest that the examiner should pay more attention to the condition of the finger when he samples the blood in a cancer patient, and avoid hurting the finger which already has local metastasis.

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