SHORT COMMUNICATION

Oncologic markers in patients with colorectal cancer after a complex therapy

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Abstract

The authors present a prospective study on a value of oncologic markers CEA and CA 19-9 in patients after curative therapy for colorectal adenocarcinoma. During a five-year follow-up in 320 patients, a significant elevation of CEA or CA 19-9 was documented in 71 patients (22.8 %), and resulted in tumour detection in 39/71 patients (55 %). Although the levels were defined as false positive in 32 patients (45 %), the importance of CEA and CA 19-9 monitoring is documented by elevated levels of oncomakers in 39/55 patients (71 %) with metastases or local-regional recurrence of colorectal adenocarcinoma. ***(Tab. 3, Ref. 21.)***

Key words: oncologic markers, colorectal carcinoma, complex therapy.

To intervene in local-regional recurrence or metastases of colorectal cancer, the follow-up should detect the disease dissemination. Unfortunately, no reliable method indicating the progression of malignant disease is available, so the monitoring of patients requires a repeated examination using a combination of several methods. All laboratory and examination methods display either false positive or false negative results. The monitoring of patients after a complex therapy due to colorectal cancer is based on clinical examination, evaluation of oncologic markers, colonoscopy, liver sonogragraphy and X-ray examination of lungs. With respect to the obtained results, these basic examinations are supplemented with computer tomography, magnetic resonance, scintigraphy and positron emission tomography. The aim of the present study is to evaluate the monitoring of oncomarkers levels with respect to the false positive as well as false negative results.

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Tab. 1. Oncomarkers in 71 patients.

	Patients
Elevated CEA and CA 19-9	71/320 (22.2%)
Elevated oncomarkers - dissemination	39/71 (54.2%)
liver metastases	15
lung metastases	3
local-regional recurrence	8
generalization	13
Elevated oncomarkers - false positive	32/71 (44.8%)
Elevated CEA	15
Elevated CA 19-9	26

Tab. 2. Metastases or local-regional recurrence.

	Patients
Dissemination - normal oncomarkers	16/55 (54.2%)
Liver metastases	7
Lung metastases	4
Local-regional recurrence	2
Generalization	3

Tab. 3. Transient elevation of oncomarkers.

	Patients
Acute infections of upper respiratory tract	6
Inflammatory diseases (arthritis, erysipelas)	4
Exacerbation of chronic bronchial-pulmonary diseases (silicosis, asthma, bronchitis)	3
Cardiac disease (after bypass)	1
Urolithiasis	1
Diabetes mellitus - decompensation	1
Pregnancy	1
Liver cirrhosis	1
No reason found	14

Patients

The patients after a complex therapy for colorectal cancer have been monitored at our Coloproctologic Centre. During the first three years after operation have the patients been monitored in three-month intervals, then in six-month intervals. In the course of a five-year period (1998–2002), we have prospectively studied 320 patients after a complex therapy for colon and rectum adenocarcinoma, fulfilling the criteria of curative radical therapy of primary tumour and, at time of operation, without signs of distant dissemination of malignant tumour. In addition to clinical examination, we evaluated following tumour markers during each check-up: CEA, CA 19-9, CA 72-4. Every 6 months patients underwent an ultrasound examination (abdomen sonography focused on liver), every 12 months an endoscopy of colon as well as anterior-posterior X-ray examination of lungs. An elevated level of oncomarkers, particularly CEA and CA 19-9 was found in 71 patients (Tab. 1).

During a five-year follow-up, dissemination of colon and rectum adenocarcinoma was recorded in 55 patients (17.18 %), when the metastasizing malignant tumour manifested itself by elevated level of oncomarkers at the beginning, and oncomarkers were normal despite observed metastases or local-regional recurrence in 16/55 patients (29 %) (Tab. 2).

Discussion

Carcinoembryonic antigen (CEA) and carbohydrate antigen 19-9 (CA 19-9) are the most frequent tumour markers related to the diagnosis of colorectal cancer. Less important are CA 72-4, CA 242, TPS and TPA. More than thirty-year research of oncomarkers in colorectal cancer has led to the following conclusions:

1) A preoperative elevated markers are obtained in 30–60 % of patients with colorectal cancer (2, 20). The most frequent is an elevated level of CEA (50–60 %), then CA 242 (40–45 %), CA 19-9 (30–40 %) and CA 72-4 (20–25 %).

2) These tumour markers cannot be used as a screening test for diagnosis of colorectal cancer (6,13, 15, 18, 19).

3) Positivity and sensitivity of oncomarkers corresponds with tumour stage – A: 10.5 %, B: 38.8 %, C: 32.2 %, D: 72 % (1). Oncomarkers levels increase with the volume of tumorous infiltration; distant metastases are significantly more frequent in patients with CEA plasma level over 60 ng/ml (5, 11, 16). The level of CA 19-9 increases with advanced stages of colorectal carcinoma (5, 17).

4) Patients without preoperatively elevated CEA have a more favourable prognosis (16) and vice versa (preoperative high CEA levels indicate poor prognosis (3, 4, 10, 21).

5) Patients with metastasizing colorectal cancer have a significantly higher biliary CEA compared with colorectal cancer patients without liver metastases (7, 8, 12).

However, above-mentioned conclusions do not determine the reliability of oncologic markers in the monitoring of patients after a curative therapy of colorectal cancer. Only Spila et al reported an elevated levels of CEA and CA 19-9 in 63.9 % and 66.7 %, resp., patients with disseminated malignant tumour (14). In order to determine the value of CEA and CA 19-9 levels, we decided to monitor the levels of oncomarkers in patients who fulfilled the criteria of curative surgical treatment and were without distant metastases at the time of operation (at most metastatic involvement of pericolic lymph nodes). All patients were operated by the same surgical team and the applied oncologic-surgical strategy was the same. The postoperative oncologic therapy, chemotherapy in colon cancer and/or chemoradiotherapy in rectum cancer, was indicated by one oncologist on the basis of the operation record, histological finding and patient's co-morbidity. The group of patients in the study was not stratified according to primary tumour staging and grading, because only small subgroups would be evaluated. It can be concluded that in malignant tumour dissemination at the time of monitoring no difference in oncomarkers levels was found with regard to differentiation of metastatic cells. We believe that the grading and staging correspond only to the risk of metastasizing and that the volume of malignant tumour dissemination enhances the level of oncomarkers only secondary. Our group of

patients had been monitored by two surgeons who operated the patients and the analysis showed a significant repeated elevation of the studied oncomarkers in 71 patients (22.18 %), amongst 32/71 patients (45 %) had falsely negative findings. A probable reason of transient elevation of oncomarkers are presented in Table 3.

During the follow-up, metastasis, local-regional recurrence and generalization of the disease were found in 55 cases (17.18 %). In case of the disease dissemination, were the oncomarkers CEA and CA 19-9 elevated significantly in 39/55 patients (71 %) and quite normal in 28/55 patients (29 %). It can be concluded that elevated CEA and CA 19-9 require an immediate repeated evaluation of oncomarkers and in case of persisting higher values a complex examination of a patient is needed despite routine examinations done within the follow-up (sonography of abdomen, X-ray examination of lungs, colonoscopy). If oncomarkers are still elevated, we recommend following algorithm: CT of lungs, liver and abdomen, CT of brain, scintigraphy of skeleton and PET. If these methods bring negative results and the levels of oncomarkers are still elevated, we repeat above examinations after two months. Although our results show a high rate of false positive elevation of oncomarkers (32/71, 45 %), our study confirmed the importance of oncomarkers for the diagnosis of metastases and/or local-regional recurrence of colon and rectum carcinomas (39/55, 71 %).

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