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DIAGNOSTIC VALIDITY OF SERIAL CEA DETERMINATIONS IN METASTATIC BREAST CANCER

G. Krieger, M. Prangen, R. Klar, M. Kneba, G. Bandlow and G.A. Nagel

Carcinoembryonic antigen (CEA) can be used as a monitor of metastatic breast cancer, however, its validity in terms of specifity and sensitivity when monitoring tumor mass has not been clearly defined. The aim of the present study was to investigate the diagnostic validity of CEA levels for assessing response to chemotherapy. These investigations were performed in 150 patients with advanced breast cancer who had clinical follow-ups and serial CEA determinations one to three monthly. The CEA values within eight weeks after start of therapy were correlated with the response to therapy. Diagnostic validity of CEA levels was only achieved, if the patients were selected and appropriate definitions of significant changes in CEA used. Thus, 83% of the responders (sensitivity) could be identified by a significant decrease of CEA titers in patients with CEA levels > 10 ng/ml. A decrease of more than 10% of pretreatment levels during the first 4 - 8 weeks after start of therapy proved to be the appropriate definition of a significant decrease of CEA titers. However, 32% of the nonresponders were misclassified as responders (unspecifity) using these criteria.
The positive predictive value of a significant decrease of CEA for response to therapy was 72% (prevalence 45%), the negative predictive value 82% (prevalence 55%). Serial CEA determinations were of predictive value in monitoring response to therapy, however, CEA values only reached diagnostic validity in selected patients, representing one third of all patients in this present study.

Abt, Hämatologie/Onkologie, Zentrum Innere Medizin, Universität Göttingen, Robert-Koch-Str. 40, D-3400 Göttingen

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PREOPERATIVE CEA SERUM CONCENTRATION AS PREDICTOR OF EARLY RECURRENCE IN BREAST CANCER PATIENTS

W. Jäger, P. Braun and G. Leyendecker

Increased CEA serum concentrations can be detected in 60-70 % of patients with metastatic breast cancer.
In order to evaluate if preoperative CEA serum levels could predict the course of the disease we measured the CEA serum concentrations of 209 breast cancer patients in three monthly intervals from 1978 until 1983.
The upper limit of normal range was formerly defined as 12 ng/ml, using polyclonal CEA assay (CEAK-PR, ID-CIS, DREIEICH, FRG) with a detection limit of 5 ng/ml.
20.6 % of all patients developed metastases within the time of our retrospective analysis (2 to 6 years). Most of these patients (79 %) had axillary metastases at primary operation whereas in 21 % the tumor was confined to the breast.
45 % of all patients had no detectable amounts of CEA preoperatively, 34 % concentrations between 5 and 12 ng/ml and 21 % serum concentrations above the normal range. The incidence of patients establishing metastases increased from 16.7 % (CEA < 5 ng/ml) over 21.1 % (CEA between 5 and 12 ng/ml) to 79 % of patients with elevated preoperative CEA serum levels.
Within the group of patients with lymph node involvement preoperative CEA serum concentrations seemed to be associated with early recurrence as 57 % of patients with increased and 31 % of patients with levels between 5 and 12 ng/ml developed metastases compared to 9 % of patients with no detectable amounts of CEA.
Preoperative CEA measurements may therefore be a useful indicator for early recurrence in breast cancer patients.

University of Erlangen-Nürnberg, Department of Gynecology and Obstetrics, Universitätsstraße 21/23, D-8520 Erlangen, FRG.

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CLINICAL RELEVANCE OF THE TUMOR MARKER CA 15-3 IN BREAST CANCER

F. Safi, M. Kreibich, H.O. Kleine, H.G. Beger

The value of tumor markers basically depends on their usefulness in diagnosing early tumor stages or metastases which can be treated successfully. The monoclonal antibodies CA 15-3 were developed against the two antibodies 115D8 of the human milk fat-globulin membrane and DF3 of breast cancer. In a prospective study the new radioimmunoassay was determined pre- and postoperatively in our own patients. Results: Group I (GI): breast cancer n=26; group II (GII): benign disease of the breast n=15; group III (III) benign surgical disease n=96; group IV (GIV): healthy blood donors n=57; group V (GV): malignomes outside the breast n=76.

CA 15-3 (U/ml)	G I	G II	G III	G IV	G V
Minimum	12.0	12.0	5.4	5.4	4.6
Maximum	357.0	39.0	48.9	28.1	75.0
Median	46.8	21.0	19.5	17.2	23.5

The sensitivity of the CA 15-3 RIA for breast carcinoma is remarkable, because in group I the median value is pathological with more than 25 U/ml (=above the normal level) and contrasts strongly with the median values of the four control groups, which ranges below 25 U/ml. In the course of the follow-up treatment CA 15-3 and CEA were determined simultaneously in 109 pts. who had been treated surgically because of breast cancer. The sensitivity rate in detecting metastases or recidivation was 79% in CA 15-3 and 25% in CEA. The CA 15-3 RIA turned out to be not mammaspecific for screening, but it is definitely superior to CEA for the detection of recidivation from breast cancer in the tumor follow-up treatment.

Abt.f.Allgem.Chirurgie, Universität Ulm, Steinhövelstr.9 D-7900 Ulm

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MONITORING BREAST CARCINOMA WITH CA 15-3 AND CEA

L. Hoffmann, D. Heinzerling, R. Klapdor, E. Schäfer

CA 15-3 is a circulating antigen excreted by cells of human breast carcinoma which reacts with a mixture of two monoclonal antibodies. We analysed 123 sera of 67 patients with metastasising breast carcinoma. Besides CA 15-3 (cut off value 40 U/ml) CEA (5 µg/l) was evaluated. Sensitivity of CA 15-3 was 55% (37/67) versus 51% (34/67) for CEA. Combining CA 15-3 and CEA false negative concentrations were found in 32,8% (22/67). Serum concentration above normal were found as follows:

	bone metastasis	liver	large tumor
CA15-3	9/18(50%)	10/11(91%)	21/26(81%)
CEA	10/18(55%)	7/11(64%)	19/26(73%)

Median (m) and medium ($\bar{x}$) concentrations:

	all cases		bone metastasis		liver		large tumor mass	
	m	$\bar{x}$	m	$\bar{x}$	m	$\bar{x}$	m	$\bar{x}$
CA15-3	43	182	43	139	74	123	78	329
CEA	4,6	73	9,4	43	8,7	238	264	287

17 out of 20 pts (85%) with poor prognosis (liver-/lung metastasis, negative hormone receptors, short free interval) had elevated CA 15-3 concentrations and 15 (75%) elevated CEA concentrations. These samples showed the highest (m- and x-levels) concentrations for CA 15-3 and CEA.
Tumor progress correlated well with CA 15-3 in 65%(11/17) and with CEA in 47%(8/17). Tumor regression correlated well with CA 15-3 and CEA in 67% (6/9).
CA 15-3 is a usefull marker in monitoring treatment of human metastasing breast carcinoma.

Onkologische Abteilung Allgemeines Krankenhaus Barmbek Rübenkamp 148, D-2000 Hamburg