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THE SIGNIFYING VALUE OF CA 19-9 COMPARED TO CEA IN GASTRIC AND COLORECTAL CARCINOMA

F. Safi, R. Bittner, R. Roscher, H.G. Beger

It is well-known fact that tumor markers are used to investigate whether malignant tumors have been operated sufficiently and radically and to rectify or falsify a renewed growth of the tumor. After CA 19-9 had proved to be a highly sensitive marker in the differential diagnosis between pancreatic carcinoma and chronic pancreatitis as well as in the perioperative follow-up, it was the aim of the present study to compare the monoganglioside antigen CA19-9 with CEA with regard to its sensitivity (SE) and specificity (SP) in diagnosing the different stages of colorectal and gastric carcinoma and in detecting recidivation during the aftercare treatment. Pre- and postoperatively CA 19-9 and CEA are estimated in 82 pts. with colorectal carcinoma (CRC) and in 57 pts. with gastric carcinoma (GC) radioimmunologically.

Results:	Tumor stages (GC)				Tumor stages (CRC)			
	I	II	III	IV	I	II	III	IV
CA 19-9								
6-37 U/ml	15	10	4	7	22	23	7	15
>37 U/ml	1	4	5	11	1	2	1	11
CEA								
< 3 ng/ml	11	8	3	5	16	14	3	8
> 3 ng/ml	5	6	6	13	7	10	6	18

The comparison depending on stages between the markers CEA and CA 19-9 shows an increased sensitivity of the CEA in all stages of GC and CRC. In our cases of 66 pts. with GC and 165 pts. with CRC who were all surgically treated, CA 19-9 and CEA were estimated at the same time in the outpatients' department. From the exact clinical evaluation of CA 19-9 and CEA estimation in these patients the following conclusion could be established: CEA is more sensitive than CA 19-9, but CA 19-9 is more specific. The specificity, sensitivity, and total accuracy increases, if both markers are used.

Dep. of General Surgery, Univ. of Ulm, Steinhövelstr., D-7900 Ulm

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FADING CLINICAL RELIABILITY OF SERIAL LONG-TERM CEA-DETERMINATIONS DUE TO MULTIPLE RIA-KITS

J. Spitz

In the last years the consequent monitoring of serum CEA values has become a solid pillar in the follow-up control of GI cancer patients. Consequently an increasing number of CEA-RIA kits appeared on the European market. Previous own observations as well as sporadic hints in the literature indicate, that there is a lack of comparability between the results of different kits.

Material and Methods: We therefore checked 12 different products (Abbott monoclonal and polyclonal, Amersham, Behring, Bio Sorin, Byk Mallinckrodt, Hybritech, ID CIS polyclonal and monoclonal, Medtro and Sero), simulating a follow-up study of cancer patients, using the same serum probes for CEA determination with the different kits (380 probes für 3594 estimations).

Results: While the overall correlation of the kits was quite good, ($r = 0,73 - 0,89$), the slopes of the correlation curves varied remarkably ($0,7 - 2,1$). The comparison of individual results however was alarming:

A pooled serum for quality control differed over 100% ($19,0 - 42,5$). A 1:1 dilution of the WHO-standard 2/22 J corresponding to 20 ng CEA/ml showed variations over 500% ($5,9 - 30,2$). Depending on the "accidental" sequence of the used kits, patients showed remission ($46-39-31-25-24-23-21-20-19-18-7$) or bad progress ($4-5-6-7-7-9-10-11-11-17-19-23$) or intermittent course of tumor disease ($17-14-10-11-15-18-12-11-3-11-16-20$).

Conclusion: Serum-CEA-values of one patient estimated by different products must not be compared with each other and are worthless for long-term follow-up control! CEA values therefore can only be accepted, if the name of the kit producing company is declared. Differs the company from the one in the own lab, the value has to be controlled to assure a correct long-term follow-up and to avoid annoying pitfalls.

Städt. Klin. Wiesbaden, L.-Erhardstr. 100, D 62 Wiesbaden

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C3-ACTIVATION CAPACITY IN THE SERUM OF COLORECTAL CANCER-PATIENTS-TUMOR DRAINING-BLOOD VERSUS PERIPHERAL BLOOD

M. Betzler, H.K. Schackert, M. Ernst, D. Flad, L. Edler

Opsonization of bacteria or fragments of the bacterial cell wall increases the binding to and phagocytosis by monocytes. Specific IgG binding or C3b activation and binding are two different pathways. Monocytes are stimulated as even via Fc receptors as via C3b receptors. The stimulation of monocytes is followed by a respiratory burst which is characterized by a non mitochondrial oxygen consumption. There is a consecutive production of activated oxygen species, which generate chemiluminescence after relaxation and photon emission. The aim of this study was to evaluate the C3 activation capacity (AC) in controls and colorectal cancer patients of different stages by monocyte mediated chemiluminescence.

Methods: 48 patients (14 controls and 34 colorectal cancer) were examined for the C3 activating capacity. Blood was drawn from the cubital vein and separated serum was frozen at -70°C . To evaluate the C3 AC each serum sample was divided in two portions, one remaining untreated (active) and the other being inactivated (inactive) at 56°C for 30 min. 4×10^5 isolated mononuclear cells including monocytes and lymphocytes of healthy donors were incubated in 300 μl DMEM and 10 μl (2 mg/ml) luminol. 36 μl of either active or inactive serum was added and CL-reaction was started by adding 10 μl zymosan (5mg/ml). 20 minute integral relation of the dynamic CL-measurement of activated and inactivated serum was named C3b-index and expressed as percentage of a standard serum AC.

Results: Controls had the highest C3 AC ($14/92.5/85.2-99.8/95\%$ confidence interval). Colorectal cancer patients with the stage T₁N₀M₀ had significantly lower values ($18/72.2/57.0-87.4/p=0.009$) in contrast to T₁N₀M₀ patients ($12/81.6/69.7-93.8/n.s.$). The mean AC in T₁N₀M₀ cancer patients was found to be 54.7 ($n=4$); significance was set at $p<0.05$ using the Wilcoxon signed rank test.

Conclusion: These results indicate that the demonstrated phenomena of a decreased CA in colorectal cancer patients which was more pronounced in the tumor draining than in the peripheral blood could be related to a complement consumption in tumor patients, especially in the tumor region. This effects may be due to an increased complement activation by tumor antigens.

Chir. Univ. Klinik Heidelberg, Abtl. 2.1.1, 6900 Heidelberg (1)

Forschungsinstitut Borstel, 2061 Borstel (2)

DKFZ Heidelberg, Abtl. Biostatistik, 6900 Heidelberg (3)

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PLASMA MELATONIN IN PATIENTS WITH GASTROINTESTINAL CARCINOMA

D. Stenne, R. Khoo, Skaliky and V. Schlot

The pineal gland is a neuroendocrine transducer which is involved in the process of biological rhythms of the organism. The link between the pineal gland and its specific hormone melatonin and malignancy is discussed since morphological change in this gland in autopsied cases bearing neoplasias were made (N. Lapin; Pineal Gland and Malignancy, 2. Onkol. 3, 51-60, 1976). In animal models melatonin is known to decrease the growth of tumours and their metastasis (L.R. Stanberry et al.; Photoperiodic Control of Melanoma Growth in Hamsters; Influence of Pinealectomy and Melatonin, Endocrinology 113, 469-473, 1983). A reduced melatonin production during nighttime (L. Tarmarkin et al.; Decreased Nocturnal Plasma Melatonin Peak in Patients with Estrogen Receptor Positive Breast Cancer, Science 216, 1003-1005, 1982) or the absence of physiological day-night-rhythm in plasma melatonin levels in patients with cancer (Er+ breast cancer, prostata cancer) were found (C. Bartsch et al.; Circadian Rhythms of Serum Melatonin, Prolactin and Growth Hormone in Patients with benign and malignant Tumors of the Prostate and in non-tumor Controls, Neuroendocrinol. Lett. 5, 377-386, 1983). We thus examined melatonin levels in patients suffering from gastrointestinal carcinoma. Blood samples were collected between 11,30 and 12,30 hours (daytime) and between 23,30 and 0,30 hours (nighttime) from 34 patients hospitalized for non-malignant diseases and from 12 patients with diagnosis of gastrointestinal carcinoma. A iodinated melatonin RIA has been used for the determination of plasma melatonin concentrations.

In controls we observed great interindividual variability in melatonin levels during daytime. Mean value for this sample was $40 \text{ pg/ml} \pm 7 \text{ SEM}$. Mean daytime value for patients with gastrointestinal carcinoma was $26 \text{ pg/ml} \pm 6 \text{ SEM}$. Nighttime values were even more variable in both groups. Mean value for controls during nighttime was $94 \text{ pg/ml} \pm 24 \text{ SEM}$. Nighttime value of gastrointestinal carcinoma was $42 \text{ pg/ml} \pm 6 \text{ SEM}$. There was no statistical significance between daytime or nighttime melatonin levels in patients with gastrointestinal carcinoma and controls. The ratio night/day melatonin level in controls was 2,9; in patients with gastrointestinal carcinoma 1,6. This difference was statistically significant on $p < 0,05$ (student-t-test). Thus, the absence of nocturnal peak melatonin (indicated by decreased ratio of night/day-melatonin plasma level) may serve as a biochemical marker for increased risk of developing gastrointestinal cancer as discussed by others for breast cancer (see L. Tarmarkin). But because of the high interindividual variability in plasma melatonin levels in patients with gastrointestinal carcinoma and in controls further investigations about this phenomenon are necessary. Chirurg. Klinik, ZKH Links der Weser, 2800 Bremen