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CEA, MCA AND CA 125 TUMOR MARKERS IN PREGNANT WOMEN

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Abstract – Changes in serum concentrations of tumor markers were studied in correlation with the duration of pregnancy. The study comprised 42 pregnant women distributed into 3 groups according to the trimester of pregnancy. The following tumor markes were determined: carcinoembryonic antigen (CEA) – specific for colorectal carcinoma, mucin-like carcinoma-associated antigen (MCA) – specific for breast cancer, and cancer antigen 125 (CA 125) – specific for nonmucinous epithelial ovarian carcinoma.
Elevated CEA concentrations exceeding the cut-off value (2.5 ng/ml) were found in 28.6% of pregnant women; the highest number of them were in the 1st trimester of pregnancy (40%). For the difference from CEA, MCA serum concentrations elevated above the cut-off value (17 U/ml) were established in all pregnant women during the 3rd trimester of pregnancy. Among the women in the 1st trimester of pregnancy, there were only 10% with elevated MCA serum concentrations. Ca 125 serum concentrations remained below the cut-off level (35 U/ml) in all cases. The obtained results indicate that pregnancy can be associated with elevated serum concentrations of tumor markers, which is particularly evident in MCA. Therefore, in the evaluation of relevant findings, pregnancy should be taken into consideration as a possible cause of elevated MCA and CEA serum concentrations.

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Introduction – The determination of various tumor markers in patients with malignant neoplasms has an important role in predicting the patients prognosis and monitoring the effects of treatment, such as possible occurrence after surgical excision, or in monitoring the response to therapy.

Carinoembryonic antigen (CEA), a glycoprotein with molecular weight of about 200 KD is produced by the fetal gastrointestinal tract. Increased CEA serum concentrations are found primarily in patients with colorectal carcinomas, but can be detected in gastrointestinal malignancies as well (1). Normal CEA values in the serum of helathy persons are up to 2.5 ng/ml.

Mucin–like carcinoma–associated antigen (MCA), a glycoprotein with molecular weight of approximately 350 KD, was recently described by Stahli et al. (2). Increased MCA serum concentrations are found in patients with breast cancer (2, 3, 4); normal serum concentrations of this marker in healthy persons are up to 17 U/ml.

Cancer antigen 125 (CA 125) is a glycoprotein with molecular weight in the range of 200 KD. A high number of patients with non-mucinous epithelial ovarian carcinoma had elevated CA 125 serum concentrations (5).

In the present report we present the results of our study on the serum concentrations of tumor markers (CEA, MCA, CA 125) during pregnancy, and try to explain the influence of pregnancy (in each trimester) on tumor marker serum concentrations.

Materials and methods – Subjects: The study comprised serum samples collected from 42 pregnant women who were distributed according to the duration of pregnancy as follows:

1) 10 women in the first trimester, age 23–25 years; of these, one woman was in the first, 3 in the second and 6 in the third month of pregnancy.

2) 11 women in the second trimester, age 20–28 years; 3 were in the fourth, 2 in the fifth and 6 in the sixth month of pregnancy.

3) 21 women in the third trimester, age 20–39 years; 7 were in the seventh, 7 in the eighth and 7 in the nienth month of pregnancy.

The serum samples were stored at the temperature of -20°C.

Methods: carcinoembryonic antigen levels were measured using CEA EIA Duomab 60 »Roche« kits. This is a solid phase enzyme immunoassay based on the sandwich principle

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using the highly specific murine monoclonal antibodies to CEA.

Mucin-like carcinoma-associated antigen levels were measured using MCA EIA »Roche« kits. The method is a two-step phase enzyme immunoassay based on the sandwich principle; the monoclonal antibody used was a highly specific murine monoclonal antibody b-12 (MAb b-12) to MCA.

Cancer antigen 125 levels were determined by the use of one-step solid phase enzyme immunoassay (sandwich principle). The CA 125 EIA »Roche« kits based on the murine Ca 125 monoclonal antibodies (MAb OC 125) were used.

Statistical evaluation: From the obtained data, arithmetic mean (AM), standard deviation (SD), standard error (SE), medium value (M) and geometric mean (GM) were calculated.

Results – CEA: The geometric mean (GM) of CEA serum concentrations in pregnant women was not higher than the cut-off limit (GM = 1.7 ng/ml). Also, the geometric mean values in the groups of pregnant women according to the trimester of their pregnancy were not above the cut-off limit (Table 1). The CEA serum concentrations were elevated above the cut-off limit in some cases of pregnant women (28.6%) only. The highest percentage (40%) of cases with elevated CEA serum concentrations was established in the first trimester; the percentages established in the second and third trimesters of pregnancy were 27.2% and 23.8% respectively. The highest CEA value (4.9 ng/ml) was found in an 8-month pregnant woman (Table 1, Figure 1).

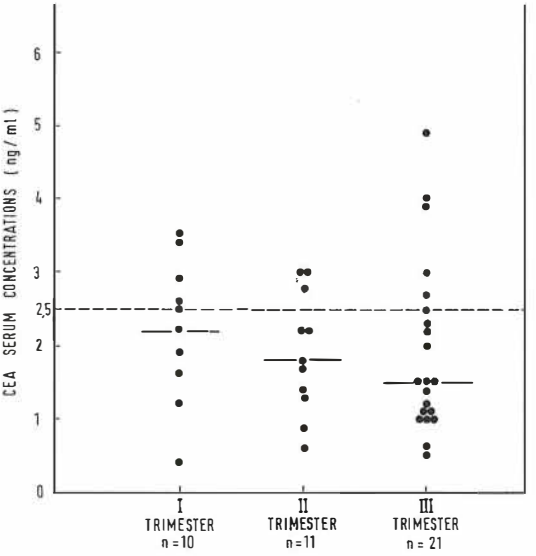

Fig. 1 – CEA sereum concentrations in pregnant women according to the trimester of pregnancy

MCA: For the difference from CEA, the GM of MCA serum concentrations was higher than cut-off limit (GM = 34.1 U/ml). In the first and the second group of pregnant women the GM values were not elevated (GM = 8.5 U/ml – 1st group; GM = 12.3 U/ml – 2nd group), whereas in the third group the same were markedly higher than the cut-off limit (GM = 109.6 U/ml vs. 17 U/ml) (Table 2).

MCA serum concentrations were elevated above the cut-off limit value in 57.2% of pregnant women.

Table 1 – CEA serum concentrations in pregnant women

Trimester	No. of cases	AM	SD	SE	M	GM	% < 2.5 ng/ml*
		ng/ml					
I	10	2.2	0.9	0.3	2.2	1.9	60.0
II	11	1.9	0.8	0.2	1.8	1.7	72.8
III	21	1.9	1.2	0.3	1.5	1.6	76.2
Total	42	2.0	1.0	0.2	1.9	1.7	71.4

* percent of cases with concentration < 2.5 ng/ml (cut-off value)

According to the present results, the obtained CEA serum levels in pregnant women were moderately elevated. However, regardless the GM and maximum value, it appeared that pregnancy did not greatly influence the CEA serum concentrations.

All cases (100%) in the third trimester had MCA serum concentrations higher than 17 U/ml. MCA serum concentrations were elevated in 10% and 18.2% of cases in the first and the second trimester of pregnancy (Table 2, Fig. 2).

Table 2 – MCA serum concentrations in pregnant women

Trimester	No. of cases	AM	SD	SE	M	GM	% < 17 U/ml*
		U/ml					
I	10	9.8	4.8	1.5	11.8	8.5	90.0
II	11	13.8	5.6	1.7	13.9	12.3	81.8
III	21	151.0	102.3	22.3	156.5	109.6	0.0
Total	42	81.4	100.4	15.5	22.2	34.1	42.8

* percent of cases with concentration < U/ml (cut-off value)

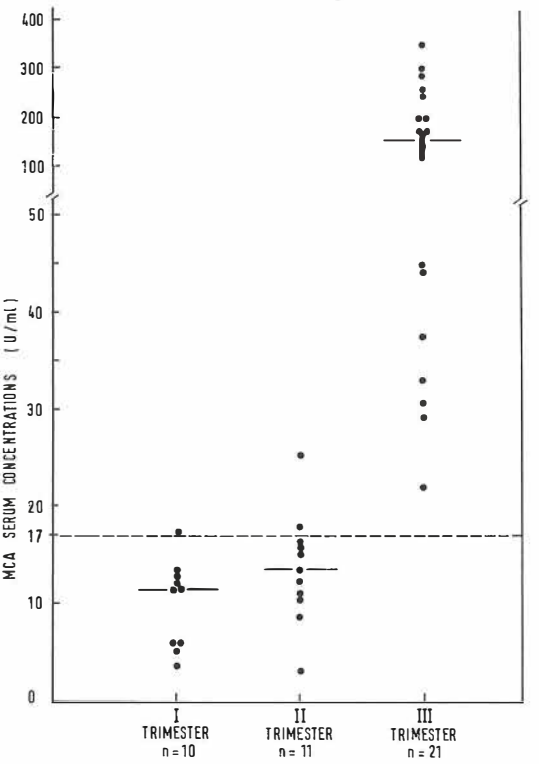

Fig. 2 – MCA serum concentrations in pregnant women according to the trimester of pregnancy

The highest MCA value (357.8 U/ml) was found in a 3-month pregnant woman.

These findings indicate that the period of pregnancy strongly influences the level of MCA serum concentrations: thus, in the last trimester of pregnancy these concentrations are markedly elevated.

CA 125: In our study however, Ca 125 levels never exceeded the cut-off value (35 U/ml). Accordingly, also the GM values in our groups were not above the cut-off values (Table 3, Fig.3).

The highest value (33.0 U/ml) was found in a 2-month pregnant woman.

The results indicate that Ca-125 serum concentrations were within normal range during different stages of pregnancy.

Discussion – In oncology, tumor markers are used for following the course of malignant disease, as well as for the assessment of treatment results, and early detection of recurrent disease.

The fact that the same tumor markers can be found in some healthy tissues as well as in a few benign tumorous tissues and in several types of malignant tissues indicates that the presently known tumor markers are insufficiently specific for a particular malignant disease (6, 7, 8, 9).

Our study was aimed to explain possible influence of pregnancy on the serum concentrations of tumor markers in pregnant women by

Table 3 – CA-125 serum concentrations in pregnant women

Trimester	No. of cases	AM	SD	SE	M	GM	% < 35 U/ml*
		U/ml					
I	10	8.4	10.3	3.2	2.8	4.7	100.0
II	11	2.0	1.6	0.5	1.8	1.2	100.0
III	21	8.7	4.5	1.0	8.1	6.4	100.0
Total	42	6.8	6.5	1.0	4.7	3.8	100.0

* percent of cases with concentration < 35 U/ml (cut-off value)

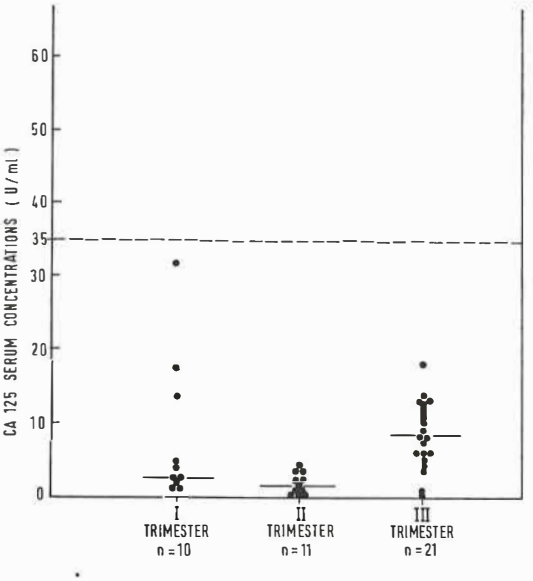

Fig. 3 – CA 125 serum concentrations in pregnant women according to the trimester of pregnancy

dtermining the following tumor markers: CEA, MCA and CA 125.

Gold and Freedman detected CEA or CEA-like molecules in the liver and pancreatic tissue of normal human fetuses between the second and sixth month of gestation (1). Our data are consistent with those from literature, indicating that the highest percent of cases with concentrations above the cut-off limit are in the first trimester of pregnancy; int the last trimester of pregnancy CEA serum concentrations are rarely elevated.

According to the data from literature, MCA is formed in the normal ductal epithelium of the breast and is present in the human milk too (9). Increased secretion activity of the ductal epithelium and mammary gland in the pre-lactation period may explain the elevated serum concentrations of this marker in late stages of pregnancy.

It was presumed that CA 125 serum concentrations would be elevated particularly during the early pregnancy, because high concentrations were detected in amniotic fluid during early stages of pregnancy (10). In our study, however, CA 125 serum levels never exceeded the cut-off value. However, any conclusions in this respect would be premature because of a rather small number of cases under investigation.

Tumor markers show a partial specificity for the type of malignant disease. Elevated CEA or MCA serum concentrations exceeding the cutoff limit need not be due to the presence of tumor only, but could be caused by pregnancy as well; this fact, however, does not render the role of tumor markers in following the course of malignant disease in female patients less important; it just point out that in the evaluation of results, pregnancy as a possible cause of elevated CEA and MCA serum concentrations should not be neglected.

Povzetek

PRISOTNOST TUMORSKIH MARKERJEV CEA, MCA IN CA 125 PRI NOSEČNICAH

V študiji smo pručevali spreminjanje serumskih koncentracij tumorskih markerjev v odvisnosti od trajanja nosečnosti. Tako smo v študijo uvrstili 42 nosečnic razdeljenih v 3 skupine po tromesečjih nosečnosti. Od tumorskih markerjev smo določali carcinoembryonic antigen (CEA) specifičen za kolorektalne karcinome, mucin-like carcinoma-associated antigen (MCA) specifičen za karcinom dojke, ter cancer antigen 125 (CA 125) specifičen za nemukozne epitelijske ovarijske karcinome. CEA je bil zvišan nad mejno vrednost (2.5 ng/ml) pri 28.6% nosečnic; največje število nosečnic s povišanimi vrednostmi CEA smo zasledili med tistimi v 1. tromesečju nosečnosti (40%). Za razliko od CEA so bile serumske koncentracije MCA zvišane nad mejno vrednostjo (17 U/ml) pri vseh nosečnicah v 3. tromesečju. V 1. tromesečju smo zasledili samo 10% nosečnic s povišanimi serumskimi koncentracijami MCA. Serumske koncentracije CA-125 niso niti v enem primeru bile povišane nad mejno vrednstjo (35 U/ml). Na osnovi rezultatov študije je očitno, da med nosečnostjo prihaja do zvišanja serumskih koncentracij tumorskih markerjev, kar še zlasti velja za MCA. Zaradi tega je potrebno pri vrednotenju izvidov bolnic upoštevati tudi nosečnost kot možen vrzok za zvišane koncentracije MCA in CEA v serumu.

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