Cerebrospinal fluid and serum carcinoembryonic antigen in brain tumors

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Carcinoembryonic antigen (CEA) has been indicated to be a marker for brain tumors. In this study CEA was measured in serum and cerebrospinal fluid (CSF) of 14 patients with benign brain lesions, 16 with primary brain tumors and 8 with metastatic brain tumors by radioimmuno assay. Tumor cyst fluid CEA of 6 patients having intracranial tumors was also measured. The control group (n=20) had no neurological disease. The mean CEA levels in CSF for the control group, patients with benign tumors, primary tumors and metastatic tumors were 0.22 ng/ml, 0.31 ng/ml, 0.92 ng/ml, and 6.3 ng/ml respectively. Corresponding serum CEA levels were 2.5, 2.7, 3.0 and 5.2 ng/ml. Results showed that CEA level in CSF may play an important role in differential diagnosis of primary and metastatic brain tumors and consequently management of the treatment. To our knowledge this is the first such study on brain tumors from India.

Key words: CSF, CEA, brain, CNS.

CEA have been found to be elevated in blood and tissue extracts of patients with carcinomas of breast, uterus, ovary, testis, prostrate gland, kidney and lung [4, 7]. Determination of CEA levels has been found useful in the management of cancers including evaluation of treatment or detection of tumor recurrence [1–3, 12] and in screening of cancer [14]. Marked elevation of CEA in peripheral blood has been reported as an initial manifestation of meningeal carcinomatosis [13]. CSF CEA has been considered as a useful marker in cases of meningeal carcinomatosis in monitoring the course of the disease [7]. Statistically significant higher CEA levels in serum and CSF was found in patients with central nervous system (CNS) metastasis and primary brain tumors in a previous study [9].

This study was carried out to evaluate CEA levels in CSF and serum of patients with primary and metastatic brain tumors in relation to CEA levels in benign brain lesions and in patients without any neurological disease. The other objective was to examine whether high CEA levels in cyst fluid from the tumors were indicative of malignancy in brain.

Patients and methods

Samples were collected between March 2001 to Sept. 2002 from 58 patients admitted at the B.R. Singh Hospital, Kolkata, India. Their mean age was 51 years (range 49–56 yrs.). Among them 18 were female and 40 male. The patients were diagnosed clinically and evaluated by CT scan. Tumor type was histologically confirmed. The 16 primary brain tumors included 3 cases of medulloblastoma, 1 cerebellar hemangioma, 11 gliomas and 1 pineal germinoma. Out of the 8 metastatic brain tumors 4 metastasized from breast cancer, 3 from lung cancer and 1 from seminoma. The 14 benign tumors consisted of 4 cases of pituitary adenoma, 3 TB granuloma, 4 craniopharingioma, 1 acoustic neuroma and 2 meningioma. The 20 patients of the control group had backache and headache but no tumor or organic neurological diseases. Tumor cyst fluid was collected at the time of operation from 6 patients and 4 of them had glioma, 1 craniopharyngioma and 1 cerebellar epidermoid tumor. None of the patients had non-neoplastic diseases (liver cirrhosis, pancreatitis, ulcerative colitis, chronic lung disease) that could result in increased level of circulating CEA. CSF was collected by lumbar puncture during myelography or

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during surgical intervention. Serum was prepared from the venous blood. In operated cases blood was collected pre-operatively.

CEA in the serum, CSF and cyst fluid was determined using a double-antibody I^{125}-radioimmunoassay kit following protocol of the manufacturer (EURO/DPC, Oxfordshire, UK). Samples were centrifuged briefly (3000 rpm; 5 min.) and the supernatant was assayed for CEA. Samples were stored at –20 °C if not analyzed on the day of their collection.

Paired t-test was done to evaluate statistical significance in CEA levels between the control group and the benign, primary and metastatic brain tumor groups.

Results

Results of CEA measurements from the controls and different patient groups are summarised in Table 1. In all of the 20 control subjects CEA levels in CSF were less than 0.5 ng/ml and that in serum rarely exceeded 4.0 ng/ml. Hence, CEA levels in CSF and serum above 0.5 ng/ml and 4.0 ng/ml, respectively were considered abnormal. CEA in serum of patients, excepting those with metastatic lesions, were not significantly higher ($p>0.05$) compared to the control group. CEA in CSF of the patients with benign brain lesions was also similar to that in the control subjects. However, the CSF CEA levels in the patients having primary and metastatic tumors were significantly high ($p<0.001$) compared to that in the control/benign tumor groups.

CEA level was higher in serum as well as CSF of almost all the patients with metastatic tumor (Tab. 2). All of the 8 cases of metastatic brain tumors had CSF CEA values higher than 0.5 ng/ml. The serum CEA level was more than 4.0 ng/ml in 7 out of the 8 patients with metastatic tumors.

CSF CEA level was markedly high (compared to control/benign group) in 14/16 (87.5%) primary tumor cases (Tab. 3). One of the medulloblastomas (n=3) and the single case of pineal germinoma had lower values. However, most of the gliomas (8/11; 72.7%) showed pronounced higher (>0.80 ng/ml) CSF CEA level. Serum CEA levels of the patients with primary tumors were much less elevated (only 3 cases had >4.0 ng/ml) compared to control/benign group of patients.

CEA levels in the cyst fluid of 4 (66.6%) cases were similar to that in CSF of the control/benign group. Elevated CEA level in the cyst fluid was observed in one glioma case and in the cerebellar epidermoid tumor (Tab. 4).

Out of the 8 metastatic brain tumors (Tab. 2) serial numbers 2, 4 and 8 metastasized from lung cancer, serial numbers 3, 5, 6, 7 from breast cancer and serial number 1 from seminoma. Comparison of the CEA levels in serum or CSF of the metastatic tumors with each other showed no trend of increase or decrease in the levels on the basis of primary sites of the metastatic tumors.

Table 1. Levels of CEA in serum and CSF of the control group and patients with brain lesions

CEA (ng/ml)	Control (n=20)	Benign tumors (n=14)	Primary tumors (n=16)	Metastatic tumors (n=8)
Serum	2.5 ± 1.2 (1.1–4.1)	2.7 ± 1.6 (0.98–4.5)	3.0 ± 1.7 (1.2–4.8)	5.2 ± 2.0 (2.8–7.5)
CSF	0.22 ± 0.15 (0.06–0.45)	0.31 ± 0.23 (0.08–0.5)	0.92 ± 0.46 (0.3–2.0)	6.3 ± 3.8 (1.6–14.0)

Values are expressed as Mean $\pm$ SD; Number of subjects and range of values are shown in parenthesis.

Table 2. Serum and CSF CEA levels of the 8 metastatic brain tumors

Patient Sr. no.	Serum CEA (ng/ml)	CSF CEA (ng/ml)
1	2.8	1.6
2	4.4	6.6
3	5.6	4.4
4	4.8	8.0
5	5.0	3.5
6	7.5	5.1
7	4.5	14.0
8	6.8	6.6

Table 3. CEA levels (ng/ml) in serum and CSF of the patients (n=16) with primary brain tumors

Patient no.	Tumor	Serum CEA	CSF CEA
1	Medulloblastoma	1.5	0.46
2	Medulloblastoma	2.6	0.74
3	Medulloblastoma	3.4	0.68
4	Cerebellar hemangioma	1.9	0.92
5	Glioma	4.5	1.50
6	Glioma	2.0	0.74
7	Glioma	3.7	0.92
8	Glioma	4.8	2.00
9	Glioma	2.3	0.56
10	Glioma	4.0	1.40
11	Glioma	3.5	0.88
12	Glioma	3.2	0.85
13	Glioma	2.7	0.65
14	Glioma	3.8	0.94
15	Glioma	3.0	1.20
16	Pineal germinoma	1.2	0.30

Table 4. CEA levels in the tumor cyst fluids (n=6)

Tumor	CEA (ng/ml)
Craniopharingioma	0.56
Cerebellar epidermoid tumor	5.4
Glioma	0.42
Glioma	0.28
Glioma	6.0
Glioma	0.14

Discussion

Several studies have determined serum and CSF CEA to understand their clinical significance in brain tumors [9, 13]. In some cases of brain metastases determination of plasma CEA has been thought to be helpful in tumor control and its response to radiation and chemotherapy [5].

In the present study in many patients (12/16; 75%) with primary brain tumors the CSF CEA levels were very low (<1 ng/ml). But the level exceeded 1 ng/ml in all the patients with metastatic brain tumors and by several folds in many of them. Meaningful ($p<0.01$) differences in serum and CSF CEA levels were observed in the present study between metastatic and primary brain tumors. Other investigators [9, 11] also found similar results. An identical observation has been reported earlier [11] in cases of malignant lymphoma and metastatic tumors.

A previous study [6] with intracranial tumors showed that CEA plasma value above 5.0 ng/ml is indicative of metastasis with a probability of 91%. In conformation to this none of the patients with primary tumor of the present study had serum CEA above 5 ng/ml, whereas almost all (7 out of 8) the metastases tumors showed a level either very close to or above 5 ng/ml.

In a previous report [8] high levels of serum CEA did not always show similar elevated CEA in the CSF of patients with meningeal carcinomatosis. In the present study also proportionate concomitant elevation of CEA in serum and CSF was not observed in all cases of primary or metastatic tumors. This may be owing to unequal blood brain barrier crossing of the CEA in cases of the primary/metastatic brain tumors. Local production of CEA in the brain may also influence the level in CSF.

In this study elevated CEA level (>4.0 ng/ml) in cyst fluid was observed in 2 brain tumor cases. Thus such an investigation with small number of cyst fluid samples is inadequate to evaluate the role of cyst fluid CEA measurement in the pathological outcome. Analysis of the serum and CSF CEA levels of the metastatic tumors of this study yielded no clue towards understanding influence of the primary sites of the malignancies on the CEA levels.

Differential diagnosis between primary brain tumor especially malignant gliomas and metastatic brain tumors is often very difficult. Estimation of CSF CEA might be of great help in the differential diagnosis of brain tumors.

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