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Carcinoembryonic antigen (CEA), alphafetoprotein (AFP) alpha and beta subunits of human chorionic gonadotropin (hCG) in cerebrospinal fluid of children with acute lymphoblastic leukaemia

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The cerebrospinal fluid (CSF) and plasma levels of CEA, AFP, alpha and beta hCG were determined by radioimmunoassay in 19 children with acute lymphoblastic leukaemia (ALL). CSF in 15 patients at the onset of ALL was examined in the first week after diagnosis and subsequently every two months. In 4 other children in second complete remission of ALL, CSF was examined every two months as well. Elevated values of CEA_{CSF} were present in 1/15 patients at the onset of ALL, of AFP_{CSF} 0/15, alpha hCG_{CSF} in 2/15, beta hCG_{CSF} in 2/15 cases. The elevated levels of these markers in CSF became normal in successive lumbar punctures and none of these children developed central nervous system (CNS) relapse in further follow-up. Isolated CNS relapses were diagnosed 13 times in 7 children. Elevated CEA_{CSF} levels were found in 6/13 cases (maximum, 25.0 ng/ml) and in one patient CEA_{CSF} levels correlated well with pleocytosis. Elevated AFP_{CSF} values were present in 0/13 cases, alpha hCG_{CSF} in 0/13 and beta hCG_{CSF} in 3/13 patients and became normal by the next CSF examination. The determination of CEA, AFP, alpha and beta hCG in plasma did not play a role in monitoring CNS relapse in ALL patients.

In spite of prophylactic treatment against central nervous system (CNS) leukaemia, 10% of the children with acute lymphoblastic leukaemia (ALL) will suffer from extension of the disease to CNS [3, 4] This aggravates the prognosis considerably. In a previous paper we have pointed to the usefulness of plasma CEA determination in children with acute leukaemia [5].

The purpose of the present study was to determine the usefulness of serial measurements of CEA, AFP, alpha and beta hCG on cerebrospinal fluid (CSF) in children with acute leukaemia, especially in patients with CNS relapse.

Materials and Methods

A total of 19 patients with ALL aged from 2 to 14 years were studied, 15 of them at the onset of ALL, 4 patients were in second complete remission. CSF in 15 children at the onset of acute leukaemia was studied in the first week after diagnosis and subsequently every two months. In 4 patients in second complete remission of ALL, CSF was taken every months. Leu-

kaemia of CNS was not diagnosed in any examined patient at the onset of ALL. Isolated CNS relapses were diagnosed in 13 times in 7/19 patients with ALL: 3 times in 2 children, twice in 2 patients and once in 3 patients. Leukaemia of CNS was diagnosed on the basis of clinical symptoms and examination of CSF. All of these patients had received "prophylactic" CNS treatment including cranial irradiation and intrathecal injections of methotrexate. The CNS relapses were treated biweekly with intrathecal injections of methotrexate, arabinoside hydrochloride and hydrocortisone. CEA, AFT, alpha and beta subunits of hCG in CSF were determined by double-antibody radioimmunoassay technique as described earlier [1]. Plasma levels of these markers were determined simultaneously.

Results

Normal values of the investigated markers in plasma (P) and CSF

The upper limit for CEA, AFP alpha and beta hCG in plasma and CSF was found to be less than

CEA_P	— 4.1 ng/ml
AFP_P	—12.2 ng/ml
alpha hCG_P	— 1.0 ng/ml
beta hCG_P	— 0.4 ng/ml
CEA_{CSF}	— 0.0 ng/ml
AFP_{CSF}	—53.2 ng/ml
alpha hCG_{CSF}	— 0.0 ng/ml
beta hCG_{CSF}	— 0.4 ng/ml.

CSF CEA, AFP, alpha and beta hCG levels in 15 children with ALL at the first diagnostic lumbar puncture

Leukaemia of CNS was not diagnosed in any examined child at the onset of ALL. Results of marker levels in CSF are shown in Table I.

Table I

Cerebrospinal fluid CEA, AFP, alpha and beta hCG concentrations at the onset of childhood lymphoblastic leukaemia

No.	CEA	AFP	alpha hCG	beta hCG
1.	0.0	16.5	0.0	0.0
2.	0.0	20.0	0.0	0.1
3.	0.0	42.0	0.0	0.6*
4.	0.0	2.4	0.0	0.0
5.	0.0	5.0	0.3*	0.0
6.	0.0	40.0	0.0	0.0
7.	0.0	24.0	0.0	0.0
8.	0.0	12.0	0.0	0.0
9.	0.0	0.0	0.0	0.0
10.	0.0	0.0	0.0	0.7*
11.	0.0	6.6	0.0	0.0
12.	1.0*	11.0	0.0	0.4
13.	0.0	6.0	0.0	0.0
14.	0.0	6.4	0.4*	0.2
15.	0.0	6.0	0.0	0.2

* Values higher than normal

Elevated CEA_{CSF} levels were found in 1/15, AFP_{CSF} in 0/15, alpha hCG_{CSF} in 2/15, beta hCG_{CSF} in 2/15 cases. Plasma CEA, AFP, alpha and beta hCG levels in these children did not reach the upper limit of normal. The elevated CSF levels of these markers became normal in successive lumbar punctures. None of patients with elevated marker levels in CSF developed CNS relapse in further follow-up.

CSF CEA, AFP, alpha and beta hCG levels in patients with CNS relapse

The results of marker levels in CSF and plasma are shown in Table II. Protein concentration in CSF was in the range of 16 mg to 284 mg/dl, and pleocytosis from 16 to 602 per mm^3. Elevated plasma CEA levels were

TABLE II

CEA, AFP, alpha and beta hCG levels in plasma and cerebrospinal fluid in children with CNS relapse

No.	Cerebrospinal fluid (CSF)		CEA ng/ml		AFP ng/ml		alpha hCG ng/ml		beta hCG ng/ml	
	Protein mg/dl	Pleocytosis 1 mm³	Plasma	CSF	Plasma	CSF	Plasma	CSF	Plasma	CSF
1.	26	113	0.0	0.0	6.0	25.0	0.0	0.0	0.0	0.0
2.	20	133	5.0*	3.0*	0.0	0.0	0.0	0.0	0.0	0.0
3.	16	16	9.5*	0.0	1.0	5.0	0.0	0.0	0.0	0.1
4.	34	290	(−)	2.0*	(−)	2.6	(−)	0.0	(−)	0.2
5.	284	602	0.0	4.0*	9.0	1.7	0.0	0.0	0.0	0.0
6.	50	49	0.0	25.0*	0.0	5.4	0.4	0.0	0.0	0.4
7.	18	28	6.0*	0.0	6.0	2.5	0.0	0.0	0.0	0.0
8.	32	80	0.0	0.0	1.5	27.0	0.5	0.0	0.0	0.5*
9.	30	80	4.0	0.0	0.0	10.0	0.0	0.0	0.0	0.2
10.	122	501	2.0	1.0*	0.0	7.0	0.4	0.0	0.0	1.0*
11.	96	39	2.0	2.0*	0.0	1.3	0.0	0.0	0.0	0.0
12.	20	381	24.0*	0.0	5.0	7.0	0.0	0.0	0.2	0.6*
13.	15	95	10.0*	0.0	7.0	3.0	0.0	0.1*	0.0	0.0

* values higher than normal
(−) markers were not determined since there was not enough plasma.

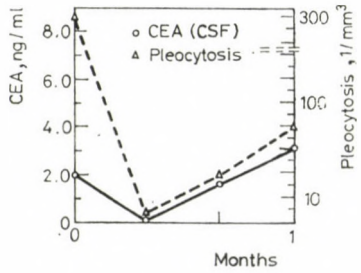

FIG. 1

observed in 5/12 patients and the highest CEA level was 24.0 ng/ml. Elevated CEA_{CSF} levels were noted in 6/13 cases, but in children with elevated CEA_{CSF} level we did not observe any simultaneous abnormal CEA level in plasma. The highest CEA_{CSF} concentration was 25.0 ng/ml. Elevated CEA_{CSF} levels became normal by the next CSF examination. In one patient the CEA_{CSF} level correlated well with pleocytosis (Fig. 1).

AFP levels in plasma and CSF were normal and so were the alpha and beta hCG levels in plasma. Elevated alpha hCG_{CSF} levels (0.1 ng/ml) were found in 1/13 cases and beta hCG_{CSF} in 3/13 patients at 0.5, 1.0, 0.6 ng/ml, respectively. Elevated alpha and beta hCG levels were normal in the next CSF examination. CNS leukaemia was not preceded by a rise of CEA_{CSF} or alpha and beta hCG_{CSF} in any case.

Discussion

Earlier we have reported on the usefulness of CEA determination in plasma in children with acute leukaemia [5]. Elevated plasma CEA levels were noted in 5/12 patients with CNS relapse. These findings suggested that CEA determination in CSF in children with ALL might prove useful in the early detection and monitoring of treatment of CNS leukaemia. Hill et al [2] observed an elevated CEA level (0.5 ng/ml) in the CSF of an adult patient with CNS leukaemia. In the present study elevated CEA_{CSF} levels (maximum, 25 ng/ml) occurred in 6/13 cases. In one patient with CNS relapse the CEA_{CSF} level correlated well with pleocytosis and reflected the activity of leucaemic involvement of the CNS. On the other hand, elevated CEA_{CSF} levels had normalized by the next CSF examination in spite of the activity of CNS leukaemia. CNS leukaemia was not preceded by a rise of CEA_{CSF} in any case. We did not observe CEA_{CSF} activity in 4/12 patients with elevated plasma CEA levels and, vice versa, we did note plasma CEA activity in 4 children with elevated CEA_{CSF} levels. Thus, we suggest that concentration of CEA in plasma and CSF are independent. Perhaps, an elevated plasma CEA level in these children might announce a bone marrow relapse as we showed in a previous study [5]. We also found elevated CEA_{CSF} levels in 9% of children with acute inflammatory CNS disease [1]. Similar observations concerning the activity of CEA in CSF in non-malignant patients were reported by Hill et al [2] and Suzuki and Tanaka [6].

We should consider whether the CEA_{CSF} activity in children with CNS relapse depends upon the production of CEA by leukaemia cells or whether anti-CEA antibodies used in our assay crossreacted with related CEA antigens i.e. NCA (nonspecific crossreacting antigen). The question requires further investigations of CEA in CSF in children with ALL and other malignant diseases. We have not found any data on the behaviour of AFP, alpha and beta hCG in CSF of patients with CNS leukaemia. In the present study, elevated AFP, alpha and beta hCG levels in CNS relapses had an incidental character and their behaviour in CSF did not reflect the activity of CNS leukaemia.

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