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Carcinoembryonic Antigen in Pleural Effusions: A Diagnostic and Prognostic Indicator*

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Abstract—*The concentration of carcinoembryonic antigen (CEA) was determined in the serum and pleural fluid of* 114 *adult patients with a pleural effusion of various causes. With the cut-off level at* 5 ng/ml, *the serum level of CEA was raised in* 46% *of patients whose pleural effusion was caused by a malignant disease and in* 7% *of those with a pleural effusion caused by a non-malignant disease. The corresponding values in pleural fluid were* 59% *and* 8% *respectively. Among patients with malignant pleural effusion the difference in the survival rate at* 6 months *postassay between patients whose pleural fluid concentration of CEA was above and below* 5 ng/ml *was statistically significant* ($P < 0.001$). *A poorer prognosis was observed among patients with tumours producing CEA.*

INTRODUCTION

THE SERUM concentration of carcinoembryonic antigen (CEA) is frequently raised in patients with carcinoma of the gastrointestinal tract, but occasionally also with carcinoma of the lung, breast or urogenital tract and in patients with benign diseases [1]. Results to date indicate that the concentration of CEA is higher in effusion fluid secondary to malignant than in that secondary to non-malignant disease [2–5].

The present study investigates the diagnostic usefulness of the determination of CEA in the serum and pleural fluid of patients with pleural effusion due to a variety of diseases. It also examines the prognostic value of these determinations in patients with primary pulmonary and metastatic malignant diseases.

MATERIALS AND METHODS

Patients

The series consisted of 114 adult patients admitted to hospital for diagnostic or therapeutic evaluation of a uni- or bilateral pleural effusion. The final etiologic diagnosis was based on clinical, roentgenological and laboratory findings. Based on the final diagnosis the patients were divided into three groups (Table 1).

Patients with pleural effusion due to neither malignancy nor tuberculousis included patients with congestive heart failure, cirrhosis of the liver, pneumonia, connective tissue disease and empyema.

Blood and pleural fluid were collected on the same day. After being centrifuged the serum and pleural fluid were stored at −20° C until assayed. CEA was measured by a double antibody radioimmunoassay [6]. Concentrations below 5 ng/ml were considered normal. Statistical analysis on patient survival was performed with the Chi-square test.

RESULTS

Figure 1 shows the concentrations of CEA in serum and in pleural fluid in the entire series. Of the 41 patients with cancer, 19 (46%) had a CEA value greater than 5 ng/ml in serum (range 6–2400 ng/ml).

The serum CEA level was also greater than 5 ng/ml in two of the 28 patients with tuberculosis (7.0 and 7.4 ng/ml) and in three of the

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Table 1. Diagnoses of 114 patients studied for CEA concentration in serum and pleural fluid

Diagnoses	Number of patients
Group I	
Pulmonary carcinoma	32
Adenocarcinoma	15
Squamous cell carcinoma	9
Oat cell carcinoma	5
Anaplastic carcinoma	2
Alveolar cell carcinoma	1
Metastatic carcinoma	9
Breast	7
Stomach	1
Ovary	1
Group II	
Tuberculosis	28
Group III	
Non-malignant and non-tuberculous disease	45

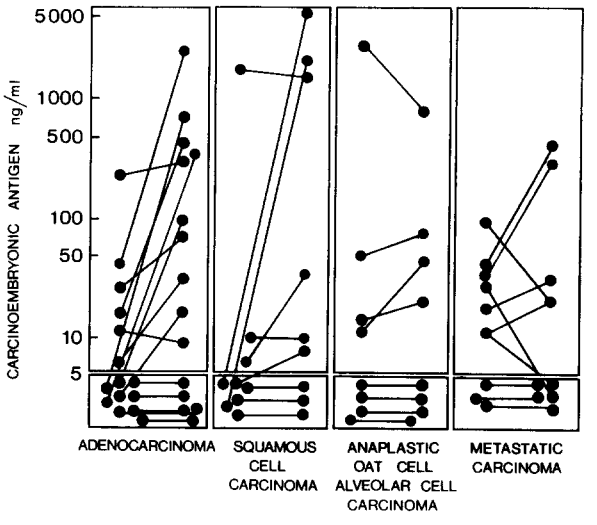

Fig. 2. The relationship between the CEA values in serum (on the left) and in pleural fluid (on the right) in a total of 41 patients with a malignant pleural effusion.

45 patients with non-malignant and non-tuberculous pleural effusion (range 5.2–5.5 ng/ml).

In pleural fluid the CEA level was raised in 24 (59%) of the 41 patients of group I (range 7.8–5600 ng/ml), in two of the 28 in group II (range 6.0–25.0 ng/ml) and in four of the 45 patients in group III (range 6–3600 ng/ml). In two patients with empyema the pleural fluid CEA values were 6.0 and 3600 ng/ml, respectively. The CEA value was 1150 ng/ml in one patient with effusion into therapeutic pneumothorax induced in 1952.

Figure 2 shows the relationship between the concentrations of CEA in peripheral blood and in pleural fluid in the 41 patients with different types of cancer. None of the different types of cancer was associated with any recognizable pattern of CEA levels. Three of the four patients with a significantly higher level of CEA in peripheral blood than in pleural fluid had a metastatic mammary carcinoma and all three had evidence of extensive metastases to the bones, lymph nodes or liver. Table 2 shows the survival rates among the 41 patients with cancer 2 and 6 months after the assay of CEA in blood and pleural fluid, respectively. The difference in the 6 month survival rate between patients with a pleural fluid CEA value below and above 5 ng/ml was statistically highly significant ($P<0.001$).

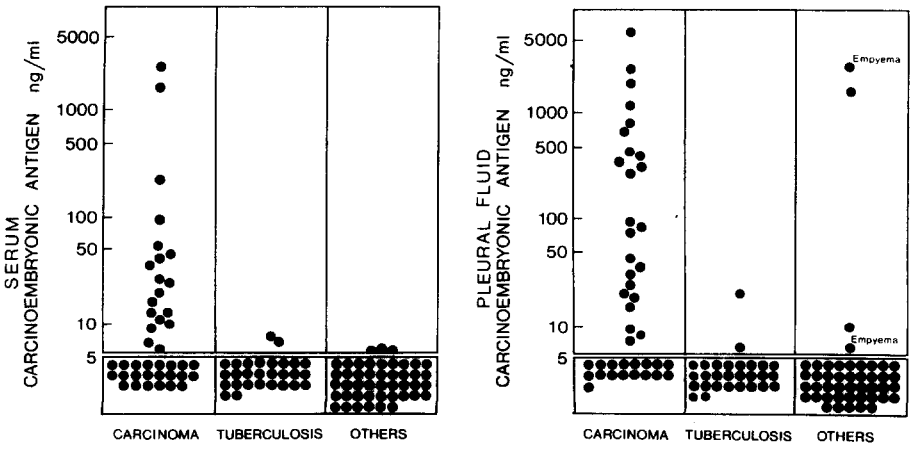

Fig. 1. The concentration of CEA in the serum and pleural fluid of 41 patients with a malignant pleural effusion, 28 patients with tuberculous pleurisy and 45 patients with pleural effusion due to non-malignant and non-tuberculous disease.

Table 2. Survival rate among 41 patients with malignant pleural effusion 2 and 6 months after the assay of CEA in serum and pleural fluid

		No. of patients alive	
		at 2 months	at 6 months
Serum	CEA < 5 ng/ml	20/22	16/22
	CEA > 5 ng/ml	13/19*	7/19†
Pleural fluid	CEA < 5 ng/ml	17/17	15/17
	CEA > 5 ng/ml	16/24‡	8/24§

Significance of difference:
*$\chi^2 = 3.28$, not sign.; †$\chi^2 = 5.33$, $P < 0.025$; ‡$\chi^2 = 4.71$, $P < 0.05$; §$\chi^2 = 12.18$, $P < 0.001$.

DISCUSSION

CEA levels in blood have been elevated in 47–77% of patients with lung cancer [7, 8]; determination of CEA in pleural fluid has been diagnostic in 34–57% of patients with pleural effusion due to cancer [4, 9]. Occasional 'falsely' raised concentrations of CEA in pleural fluid have been observed in tuberculous pleurisy and empyema [3, 10]. In the present study, when the cut-off value was 5 ng/ml, the assay for CEA in pleural effusion fluid was elevated in 59% of the cancer patients as compared with 46% in the serum determinations. The advantage in sensitivity gained by assaying CEA activity in secretions close to the tumour has been demonstrated by Bunn *et al.* [11] who reported that in patients with gastric cancer, the measurement of gastric CEA was a more sensitive diagnostic indicator than the plasma CEA. With the exclusion of pleural empyemas (easily and rapidly diagnosed by conventional methods ref. [12]), the specificity for malignancy of the pleural fluid CEA test reaches 97%.

It has been reported that at the time a malignant pleural effusion is diagnosed survival time is short [13] and most patients whose pleural fluid concentration of CEA is greater than 15 ng/ml at the time of initial examination have a locally extensive or disseminated disease with a poor prognosis [8]. A relationship has been described between survival rates and the presence of CEA in histological sections of breast carcinomas [14] but not in carcinomas of the uterine cervix [15]. In colorectal cancer, serum CEA concentrations are related to prognosis in patients with resectable tumors [16]. Our results indicate that the presence of CEA in pleural effusion fluid gives prognostic information about survival for 6 months and even for 2 months. It cannot be ruled out, however, that the poorer prognosis of those patients who had a greater concentration of CEA might reflect a greater tumour burden and not a more aggressive malignancy than in those patients in whom the tumour produced no CEA.

Whereas the determination of serum CEA cannot be used in the diagnosis of malignant disease, the assay of pleural fluid CEA seems to be an adjunct to other diagnostic procedures and prognostic indicators of malignant pleural effusions.

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