

CLINICAL VALUE OF CARCINOEMBRYONIC ANTIGEN AND FERRITIN LEVELS IN THE BRONCHIAL LAVAGE FLUID OF LUNG CANCER PATIENTS

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SUMMARY : *The levels of carcinoembryonic antigen (CEA) and ferritin in the serum and bronchial lavage fluid of 17 patients with malignant and 14 patients with non-malignant lung diseases were determined. Bronchial lavage fluid CEA level was significantly higher in the malignant group than in non-malignant group whereas no significant difference was found in the ferritin levels between the groups. Measurement of venous blood and bronchial lavage fluid CEA levels may be helpful in the diagnosis of patients with lung cancer.*

Key Words : *Bronchial Lavage Fluid, CEA, Ferritin, Lung Cancer.*

INTRODUCTION

Various tumor markers including hormones (calcitonin), proteins (CEA), carbohydrates and nucleic acids have been identified in patients with cancer. Elevations of these tumor specific biochemical markers can be helpful in certain instances for the diagnosis of cancer. Most of the markers are not completely tumor specific. Some of them can be detected in the serum of the patients with benign diseases as well (Goldstein et al. 1985). In lung cancer, tumor markers as CEA, ferritin, calcitonin, neuron specific enolase, creatinine kinase BB, squamous cell carcinoma antigen etc. may also differ according to the histological type. In most studies tumor markers have been identified in the sera. In this study we have investigated the diagnostic value of two tumor markers: CEA and ferritin in the serum as well as in bronchial lavage fluid (BLF) of the patients having lung cancer.

MATERIALS AND METHODS

A total of thirty one patients, 17 with malignant and 14 with non-malignant lung disease were included in the study. 16 patients in the malignant group and 12 in the non-malignant group were male. Non-malignant lung diseases included: pleural effusion (2), benign pulmonary nodule (2), bronchiectasis (1), Behçets disease with pneumonia (1), radiation pneumonitis (1), chronic obstructive lung disease (COLD) (1), lung abscess (1), dermoid cyst (1), tuberculosis (1), lung fibrosis (1) and idiopathic hemoptysis (2) cases.

The diagnosis of malignancy was established either by fiberoptic bronchoscopy (biopsy and cytologic examination of the bronchial washing) or percutaneous fine needle aspiration biopsy. Among the 17 malignant patients, two were small cell and 15 were non-small cell carcinomas.

The mean age was 48.2 years in the benign gro-

up whereas 58.1 yrs and 62.5 yrs respectively in the non-small cell and the small cell carcinoma groups. Nine of 14 non-malignant and 13 of 17 malignant patients were smokers.

Flexible fiberoptic bronchoscopic examination was performed in all patients. Approximately 20 ml of BLF and venous blood samples were obtained on the same day. Ferritin and CEA levels were determined by IRMA (Immunoradiometric assay), which utilized the I^{120} antigenic labelling method. CEA was measured by Biomira Inc kit (Canada), and ferritin levels were determined by IDS kit (Immunodiagnostic Systems Limited, U.K.).

Mann Whitney U test was used in the statistical analysis of the data.

RESULTS

The mean concentrations of CEA and ferritin in serum and BLF are summarised in Table 1. The mean CEA level in BLF was 476.2 U/ml in the malignant group whereas it was 346.18 U/ml in the benign group. The mean serum CEA levels were 42.49 U/ml and 32.89 U/ml in the malignant and benign groups respectively. Lung cancer patients differed statistically from the benign group with regard to the average serum and BLF concentrations of CEA.

	Malignant (n : 17)	Benign (n : 14)	p
BLF CEA U/ml	476.21	346.18	<0.01
BLF ferritin ng/ml	151.34	192.33	NS
Serum CEA U/ml	42.49	32.89	<0.05
Serum ferritin ng/ml	366.62	264.17	<0.05

CEA : Carcinoembryonic antigen

BLF : Bronchial lavage fluid

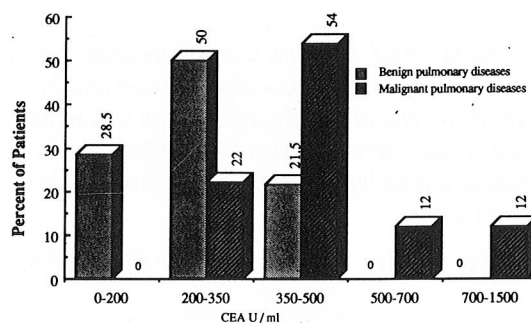
n : Number of patients

NS : Not significant

Table - 1 : The mean CEA and ferritin level in the serum and bronchial lavage fluid.

Bronchial lavage fluid ferritin levels showed no statistically significant difference between these groups. The mean ferritin level in the BLF was 151.34 ng/ml in the malignant group, and 192.33 ng/ml in the benign group. The difference between these two values was statistically significant within the 95 % confidence limits ($p < 0.05$).

In the benign group 28.5 % had BLF CEA level between 0-200 U/ml, 50 % between 200-350 U/ml and 21.5 % between 350-500 U/ml (Fig 1). None of the patients in the benign group had BLF CEA level over 500 U/ml. None of the malignant patients had a BLF CEA level between 0-200 U/ml, 22 % was between 200-350 U/ml, 54 % between 350-500 U/ml, 12 % between 500-700 U/ml and 12 % between 700-1500 U/ml. Based on these results and according to the literature (Blair and Goldenberg, 1974) when we tentatively set 350 U/ml as the cut off level for CEA in the bronchial lavage fluid, 11 out of 14 benign patients (78.5 %) had levels less than that. In the malignant group 13 of 17 patients (76.4 %) had BLF CEA level over 350 U/ml.



Plain Columns : Benign pulmonary diseases.

Crossed Columns : Malignant pulmonary diseases.

Fig. 1 : Bronchial lavage fluid CEA level

Although we have studied a small group of patients, we tried to get an idea about the specificity and sensitivity of the test. When we accepted 350 U/ml as the upper limit for BLF CEA level in the benign group we found the sensitivity of the test 76.5 % with the specificity of 78.5 % (Table 2).

	Malignant	Benign
CEA (+) (>350 U/ml)	13	3
CEA (-) (<350 U/ml)	4	11
Total	17	14

Sensitivity of the test : 13/17 (76.5 %)

Specificity of the test : 11/14 (78.5 %)

Table - 2 : The diagnostic value of bronchial lavage fluid CEA level.

Among the 17 patients with lung cancer, cytologic examination was found to be positive in 11 patients (65%). Combining sputum or lavage cytology with BLF CEA level (>350 U/ml) resulted in a positivity of 100% while CEA positivity alone was 76.5% (Table 3).

	Cytology (+)	Cytology (-)
CEA (+) (>350 U/ml)	7	6
CEA (-) (<350 U/ml)	4	0
Total	11	6

Cytology Positivity : 11/17 (65%)

CEA Positivity : 13/17 (76.5%)

CEA + Cytology : 17/17 (100%)

Table - 3 : Bronchial lavage fluid CEA and cytology results in lung cancer patients

DISCUSSION

One of the main goals of successful treatment of lung cancer is to diagnose the disease at an early stage. The recognition that lung cancer is often associated with changes in the levels of various plasma substances, has prompted many studies on the role of these measurements in the diagnosis of the disease. More than forty markers associated with lung tumors have been described in the literature (Lombardi et al. 1990). At the present time carcinoembryonic antigen is a marker of interest in lung cancer. It represents a group of cell surface glycoproteins initially identified in fetal gut tissue and colon carcinomas but subsequently noted in a variety of malignant and normal tissues. Bronchial carcinoma cells have been shown to release CEA in vitro and measurements of CEA levels may be useful in following the tumor burden or in diagnosis of patients with lung cancer (Wesselius et al. 1990).

Some investigators have found that CEA and ferritin are effective indicators for the presence of lung cancer only for normal population and the sensitivity of these markers thought to be low in discriminating between lung cancer and benign pulmonary disease (Blair and Goldenber, 1974).

In most studies, tumor markers have been identified in the sera. CEA levels in pleural fluid and serum have been evaluated for differentiating malignant and non-malignant pleural effusions. The sensitivity of pleural fluid CEA was determined to be 70%, which was 13% higher than sensitivity found in serum (Asseo and Tracopoulos, 1982). Elevated

levels of CEA were found in bronchoalveolar lavage fluid and in the serum of healthy smokers as well as in patients with benign pulmonary diseases such as chronic obstructive bronchitis (Merril et al. 1981; Stockley et al. 1986).

As the ultimate amount of tumor markers in body fluids depends on the balance between rate of release and degradation, no correlation could be found between lavage and plasma concentrations of CEA. When a tumor product is released in a large volume of interstitial fluid and/or blood stream it is diluted and may become undetectable with the contemporary assays. On the other hand a small volume of lavage fluid coming in close proximity to the affected lung segment or directly in touch with the tumor may yield much high marker concentrations.

In our study, both the serum and BLF concentrations of CEA were found to be markedly increased in patients with lung cancer compared with a group of patients with various benign lung diseases. This finding is in accord with the results of some previous investigations showing elevated serum or BLF CEA levels in patients with malignant lung diseases (Sculier et al. 1987).

In contrast to the results of Lombardi C et al, we could not find any significant difference between the ferritin levels of patients with malignant and benign pulmonary diseases.

When we considered the upper limit of BLF CEA level as 350 U/ml, we observed that 78.5% of the benign group had this level below the limit and 76.4% of the malignant group had levels above the cut off. So with the limit of 350 U/ml, bronchial lavage fluid CEA levels for lung cancer were found to have a sensitivity of 76.5% and a specificity of 78.5%. Previous studies indicate that sensitivity of a tumor marker alone varies from 50% to 70%. In combination with other parameters the test seems to be more sensitive but the specificity decreases as the number of markers increase (Goldstein et al, 1985). On the basis of these considerations we combined the BLF CEA positivity (>350 U/ml) with the cytologic examination results and we reached the sensitivity of 100% with these two parameters.

Conventional bronchoscopy is highly specific but has relatively low sensitivity particularly when dealing with solitary pulmonary nodules. Therefore, in the patients with negative bronchoscopic findings, further testing is necessary. The sensitivity of the procedure increases substantially when the

results of conventional bronchoscopy and tumor marker levels of the BLF are combined. In combination with careful clinical evaluation, serial CEA measurements can aid in assessing treatment associated tumor changes as well as early detection of recurrences in patients with lung cancer (Waalkes et al. 1980).

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