

The Ovarian Cancer Associated Antigen CA 125 in Patients with Pleural Effusions

JAN LINDGREN,* PENTTI KUUSELA,* PÄHR-EINAR HELLSTRÖM,† TOM PETTERSSON‡ and
MATTI KLOCKARS§

**Department of Bacteriology and Immunology, University of Helsinki, Helsinki, Finland, †Mjölbolsta Hospital, Finland, ‡Fourth Department of Medicine, Helsinki University Central Hospital, Finland and §Institute of Occupational Health, Helsinki, Finland*

Abstract—The concentration of the ovarian cancer associated antigen CA 125 was determined in the pleural fluid of 25 patients with lung cancer and of 40 patients with benign diseases. Paired serum and pleural fluid samples were measured in 21 tumor patients and 34 patients with nonmalignant diseases. Serum CA 125 was elevated (> 35 U/ml) in 16 of 25 (64%) patients with carcinoma and 13 of 34 (38%) patients with benign diseases. The CA 125 level in serum was markedly elevated (> 200 U/ml) in five of six adenocarcinomas whereas a slightly elevated level was associated with only one of four mesotheliomas and with one of three secondary carcinomas. The pleural fluid concentration of CA 125 was higher than the serum value in 90% of the patients, showing a median ratio of 4.9, respectively. Pleural fluid values higher than 250 U/ml were seen in 18 of 25 (72%) subjects with pleural effusion due to malignancy and in 10 of 40 (25%) patients in the benign group. There were no apparent differences in the pleural fluid CA 125 levels in patients having different types of cancer and different benign diseases.

INTRODUCTION

THE OVARIAN CANCER and coelomic epithelium associated antigen CA 125 is defined by the monoclonal antibody OC 125 raised against an established ovarian cancer cell line [1]. The nature of the antigen remains poorly understood.

The CA 125 antigen can be detected in the circulation of the majority of patients with ovarian cancer and the CA 125 determination is a promising new diagnostic tool for ovarian cancer [2-4]. However, the occurrence of this antigen in the circulation is not restricted to ovarian cancer but high concentrations can also be found in patients having other cancers and occasionally in patients with benign diseases [2, 4, 5].

More recently, high amounts of the antigen have been found in seminal plasma [6], endocervical mucus [7] and amniotic fluid [8].

Immunohistochemically, CA 125 has been demonstrated on frozen sections of most tissues derived from the fetal coelomic epithelium, i.e. endocervix, endometrium, Fallopian tube, peritoneum, pleura and pericardium [9]. Thus, it could

be expected that the CA 125 antigen could be found in pleural fluid.

PATIENTS AND METHODS

Patients included in the study consisted of 65 adult subjects admitted to hospital for diagnostic or therapeutic evaluation of uni- or bilateral pleural effusion. The final diagnosis was based on clinical, radiological and laboratory findings.

The patients were divided into two groups, i.e. (1) patients with pleural effusion due to malignant tumors and (2) patients with pleural effusion due to non-malignant disease. Twenty-five patients had pleural effusion resulting from a malignant disease. Six had adenocarcinoma of the lung, six had pleural mesothelioma, four had metastatic mammary carcinoma, four had squamous cell carcinoma, two had microcellular carcinoma, one had alveolar cell carcinoma and two had anaplastic carcinoma.

Forty patients with pleural effusions due to non-malignant disease included patients with congestive heart failure (4 patients), pulmonary tuberculosis (14), pneumonia (6), rheumatoid arthritis, systemic lupus erythematosus and non-defined connective tissue disease (9) and pleural effusion of unknown etiology (7).

Both serum and pleural fluid samples were obtained from 55 patients. Blood and pleural fluid

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Correspondence to: Jan Lindgren, M.D., Department of Bacteriology and Immunology, University of Helsinki, Haartmaninkatu 3, 00290 Helsinki, Finland.

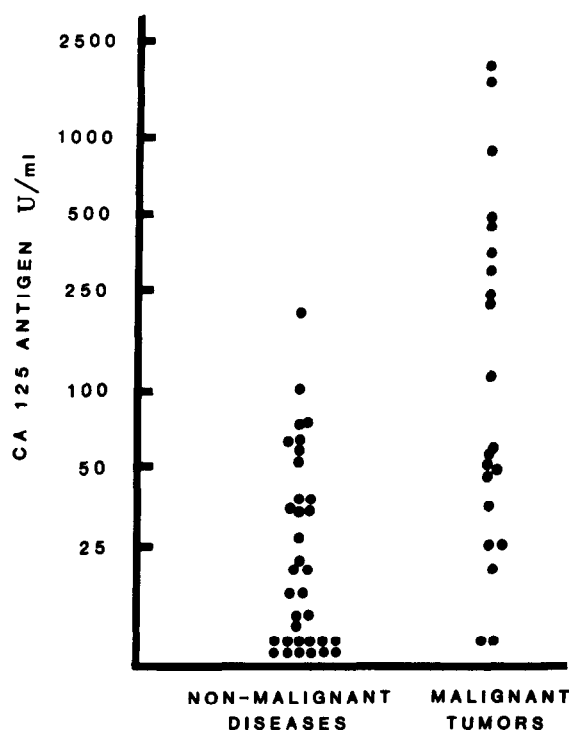


Fig. 1. Serum CA 125 concentrations of patients with malignant lung tumors and benign diseases.

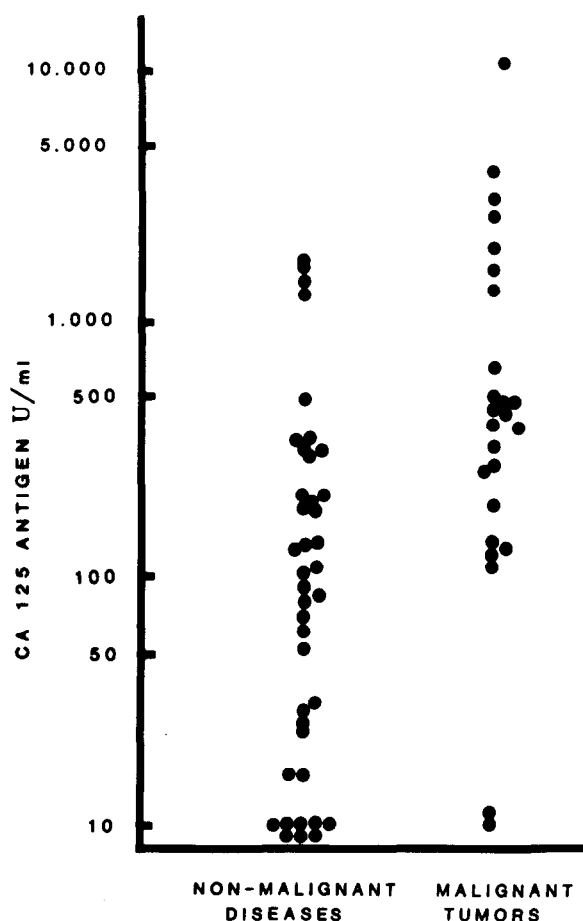


Fig. 2. Pleural fluid CA 125 concentrations of the patients.

were collected on the same day. After centrifugation, the samples were stored at -20°C .

CA 125 levels were measured by the double determinant radioimmunoassay kit by Abbott Diagnostic Products GmbH (Wiesbaden-Delkenheim, F.R.G.) according to the manufacturer's instructions. The recommended upper normal level for serum concentration is 35 U/ml.

RESULTS

Serum concentrations

Serum CA 125 values were elevated (> 35 U/ml) in 16 of 21 (64%) patients having malignant pulmonary disease (median 58 U/ml) and in 13 of 34 (38%) of the subjects with benign disease (median 20 U/ml) (Fig. 1).

Pleural fluid concentrations

CA 125 was detected in 56 of 65 (86%) samples of pleural effusion. The pleural fluid CA 125 level exceeded the cut-off value of 35 U/ml in 23 of 25 patients with malignant disease (median 450 U/ml) and in 26 of 40 subjects with benign disease (median 95 U/ml) (Fig. 2). Elevated CA 125 levels were not associated with any particular tumor type or benign disease.

Pleural fluid/serum ratio

The ratio of CA 125 concentrations in pleural fluid and serum exceeded 1 in 48 of 53 patients.

There were no significant differences between the groups of patients.

DISCUSSION

We found detectable amounts of the CA 125 antigen in the majority of pleural fluid samples. This is not surprising since Kabawat *et al.* [9] demonstrated the antigen immunohistochemically in normal pleural epithelium. Our results are suggestive of local production of the antigen in the pleural cavity because the pleural fluid concentration exceeded that of the serum in nearly all cases. We also found elevated serum CA 125 concentrations in benign diseases more frequently (38%) than in previous studies on patients with a wider variety of benign diseases (about 6%) [2, 3].

Several tumor markers have been suggested to be useful in the diagnosis and treatment of lung cancer. The best marker so far is carcinoembryonic antigen (CEA) [10]. The concentrations of CEA in pleural fluid have been shown to be of diagnostic help and to correlate with the survival of the patients [11]. The CEA assay seems also to be useful in differentiating between mesothelioma and other types of pulmonary neoplasias [12].

Our present results show that the majority of adenocarcinomas of the lung are associated with a

clearly elevated serum CA 125 level. However, the CA 125 determination in pleural fluid seems to have limited clinical application, since the marker is elevated in a large number of patients with pleural effusion of benign origin.

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