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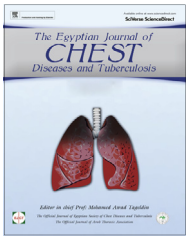

Comparison of the diagnostic utility of ADA and CA125 in tuberculous effusion

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Abstract *Background:* Pleural effusion can be due to various pleural infections like TB as well as neoplasia. CA125 is a tumor marker found on the surface of ovarian and other normal cells as pleural cells. CA125 has been found to increase in serum and hence pleural fluid of patients with pleural effusion due to malignancy as well as due to TB.

This study was conducted to evaluate the utility of CA125 in the diagnosis of pleural effusion resulting from TB, malignancy and pneumonia as well as to evaluate and compare the diagnostic utility of CA125 and ADA in the diagnosis of TB effusion.

Patients and methods: 20 patients with tuberculous effusion (group I), 20 patients with malignant effusion (group II) and 20 patients with parapneumonic effusions (group III) were evaluated for the levels of CA125 and ADA in their pleural fluid. In malignant cases, diagnosis was made through microscopic inspection of pleural biopsy samples and cytology of pleural fluid. For diagnosis of tuberculosis, Ziehl Neelsen sputum smear, pleural fluid smear and/ or culture. Parapneumonic effusions were confirmed by pleural fluid cell count and culture & sensitivity.

Results: The mean ± SD level of CA125 in pleural fluid was 41.732 ± 20.744 U/ml, 309.27 ± 79.564 U/ml and 7.040 ± 5.601 U/ml in tuberculous, malignant and parapneumonic effusions respectively; which showed a statistically significant difference between the three groups ($p < 0.01$). Pleural fluid CA125 was significantly higher in group II than group I ($P_1 = 0.000$), and group III ($P_3 = 0.000$). Pleural fluid CA125 was significantly higher in group I than group III ($P_2 = 0.000$). Pleural fluid ADA was significantly higher in group I than group II ($P_1 = 0.000$) and group III ($P_2 = 0.000$). For diagnosing TB, CA125 showed a sensitivity and specificity of 74.1%, 76.9%, respectively while ADA demonstrated a sensitivity and specificity of 75% and 75% respectively.

Conclusion: CA-125 levels in pleural fluid may be used for differentiation between TB, pneumonic, and malignancy-induced effusions.

Also CA125 may be added to the diagnostic workup of pleural fluid for accurate diagnosis of TB effusion.

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Introduction

In absence of inflammation, pleural space contains little transudate fluid with small amounts of protein, LDH and few cells, which are mainly lymphocytes, macrophages and endothelial cells. Pleural effusion may occur due to an inflammatory or non-inflammatory etiology. In non-inflammatory etiologies, there might be a decrease in oncotic pressure or an increase in hydrostatic pressure. Otherwise, changes in lymphatic drainage may play an important role. However, changes in the permeability of veins in the pleura result from cross reaction between infectious organisms and defensive inflammatory cells and the secreted cytokines and chemokines. Thus, diagnosis of the underlying cause is not simple in some cases. It is essential to keep this fact in mind for an appropriate treatment approach [1].

Mechanism of accumulation of pleural fluid in tuberculosis is somewhat chronic, just the same as in malignancy. This similarity makes differentiation of the cause of pleural effusion whether due to malignancy or TB difficult to detect. This makes the process of appropriate management also difficult despite the use of several parameters and techniques. Discriminating the etiology of pleural effusion in tuberculosis and malignant cases plays an important role in patients' treatment [1].

CA125 is glycoprotein with a high molecular weight, mucin-like, exists on the surface of ovarian, and some inflammatory and non-inflammatory cells like pleural cells. Proliferation of these cells causes this antigen to be released in serum. CA-125 was first known as a specific tumor marker that is the basis for a widely used serum assay for the monitoring of the ovary. Gradually it was found that inflammation even without polymorphism (as in the early stage of pregnancy, menstrual cycle, PID, and endometriosis) causes this tumor marker to increase. Increased CA-125 levels in response to tuberculosis were first observed in 1980's. Later, it was revealed that tuberculosis in various sites of the body causes increase in serum Antigen level [2–6].

This study was performed in order to investigate the ability of CA-125 levels to differentiate pleural effusion due to tuberculosis, pneumonias and malignancies. Also to compare the validity of the use of CA125 and ADA for the diagnosis of tuberculous effusion.

Aim of the work

The aim of the present study is to evaluate the diagnostic validity of CA125 and compare the diagnostic utilities of ADA and CA125 in tuberculous effusion.

Study population

This study included 60 patients who were admitted to Alexandria University Hospital during the period between December 2015 and July 2016. Patients were divided into 3 groups as follows: group I included 20 patients with tuberculous effusion, group II included 20 patients with malignant effusion and group III included 20 patients with pneumonic effusion.

Informed consent was obtained from all the participants before the study.

Patients and methods

All patients were subjected basically to thorough history-taking and clinical examination, routine laboratory investigations, plain chest radiography (posteroanterior and lateral views), CT chest and thoracocentesis. The pleural fluid obtained was examined for the following: gross appearance and nature of the fluid, total and differential cell count, total protein and albumin content (g/dl), lactate dehydrogenase enzyme, and bacteriological examination by culture and sensitivity. In malignant cases, diagnosis was made through microscopic inspection of biopsy samples and cytology of pleural fluid. For diagnosis of tuberculosis, Ziehl Neelsen smear and/ or culture of pleural fluid or in some cases pleural biopsy. Pneumonic effusions were confirmed by pleural fluid cell count and culture and sensitivity. CA125 was measured in pleural fluid in U/ml using the commercially available ELISA kit (CA125 Test System, Monobind Inc., CA, USA). Pleural fluid ADA measurements were done using Adenosine Deaminase BioAssay™ ELISA Kit, US Biological Life Sciences, Michigan, USA). By utilizing several different serum references of known antigen values, a dose response curve was generated from which the antigen concentration of the samples was ascertained.

ROC (receiver operating characteristic) curves were used to determine the optimal cut-off value of ADA and serum CA125 which could distinguish TB from other pulmonary infections with the highest sensitivity, specificity, and predictive values [7]. The curve obtained, allowed the calculation of the slope and the area under the curve (AUC).

The association between categorical variables was performed using Chisquared tests. Mann Whitney U test and SPSS ver. 11.5 software were used for statistical analysis to compare CA125 in the three groups and p-values < 0.05 were considered to be statistically significant.

Results

The study comprised 3 groups: group I which included 20 patients with confirmed diagnosis of tuberculous effusions.

In group II, 20 patients had confirmed malignant effusion through positive cytology of pleural fluid or biopsy samples.

In group III, 20 patients had a confirmed diagnosis of parapneumonic effusion.

Table 1 shows that the age of the studied patients ranged from 26 to 60 years with a mean of 44.87 ± 13.557 in group I, while it ranged from 24 to 68 years with a mean of 47.15 ± 12.963 in group II and it ranged from 23 to 66 years with a mean of 43.00 ± 14.008 in group III, with no statistically significant difference between the three groups as regards age.

Regarding gender, 12 patients (60%) were males whereas 8 patients (40%) were females in group I. 11 patients (55%) were males whereas 9 patients (45%) were females in group II, and 12 patients (60%) were males whereas 8 patients (40%) were females in group III with no statistically significant difference between the three groups as regards gender.

Regarding radiological findings, left pleural effusion was detected in 9 (45%) patients in group I, in 7 (35%) patients in group II and in 10 (50%) patients in group III. Right pleural effusion was detected in 11 (55%) patients in group I, in 13 (65%) patients in group II and in 10 (50%) patients in group

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