ADENOSINE DEAMINASE ACTIVITY IN THE DIAGNOSIS OF PLEURAL EFFUSIONS*

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SUMMARY : The activity of adenosine deaminase (ADA) was determined in serum and pleural fluid of 63 patients with pleural effusions of various aetiology. Tuberculous pleural effusions and empyemas demonstrated significantly higher activities of ADA than pleural effusions due to malignancy and congestive heart failure. The determination of ADA activity in pleural fluids is valuable for differentiating exudates from transudates.

Determination of ADA is a low cost and easy test that we now consider in the early assessment of patients with effusions.

***Key Words** : Adenosine Deaminase, Pleural Effusions.*

INTRODUCTION

Pleural effusions are common in Turkey and because of the large number of underlying diseases, they often present a diagnostic challenge. In contrast to developed countries, tuberculosis is still the most common cause of exudative effusions, especially in the young adults of this country. The differential diagnosis is sometimes difficult between tuberculous pleural effusions and parapneumonic and malignant pleural effusions.

The diagnostic value of adenosine deaminase (ADA) in the sera and pleural effusion fluids of patients with various aetiology was investigated.

ADA is an enzyme in purine catabolism which catalyses the conversion of adenosine to inosine. ADA is essential for the differantiation of lymphoid cells, particularly T cells (Hovi et al. 1976; Shore et al. 1981) and plays a role in the maturation of monocytes to macrophages (Fisher, 1976). Activities of this enzyme have been reported to be high in the cerebrospinal fluid of patients with the tuberculous meningitis (Piras and Gakis, 1973) and also in tuberculous pleural effusions (Ocana et al. 1983; Pettersson et al. 1984; Piras et al. 1978).

The aim of our study was to evaluate the usefulness of determining ADA for the diagnosis of pleural effusions.

MATERIALS AND METHODS

Sixty three patients admitted to hospital with a diagnosis of pleural effusion were studied. In all cases, routine biochemical, microbiological and cytologic examinations of the fluid were carried out. In 44 patients a pleural biopsy was made with the Ramel or Cope needle.

ADA activity was determined in pleural fluid samples in all cases and in the sera of the 48 of them

simultaneously. It was also measured in the serum of 13 healthy controls. The assay for ADA was performed with the method of Solomon (Goldberg, 1965). According to the final clinical diagnosis achieved by standard methods, patients were subdivided into four groups : Empyema, Tuberculosis, Malignant neoplastic disease and Congestive heart failure.

One -way analysis of variance, Duncan test and Student's - t test were used for statistical calculations.

RESULTS

The mean serum ADA activity in the control subjects was found significantly higher than the patients with neoplasm and tuberculosis ($p < 0.05$).

Patients with empyema had a significantly higher mean ADA activity in pleural fluid than patients in the other three groups ($p < 0.01$). The mean pleural fluid level of ADA in the tuberculosis group was determined to be rather higher than the levels in the neoplastic and congestive heart failure group ($p < 0.01$). The activities of ADA in pleural fluid from the patients with neoplastic disease and congestive heart failure were not statistically different.

Patients with empyema had the highest mean pleural fluid / serum ADA ratio ($p < 0.01$). But there was no significant difference among the other three groups in respect to pleural fluid / serum ADA ratio (Table 1).

The mean ADA activity was determined in exudates and transudates. In exudates it was found markedly higher than that of transudates ($p < 0.01$). Another comparison was made between the mean values of ADA in biopsy positive and biopsy negative tuberculous pleural effusions. There was no significant difference between these two groups ($p > 0.05$) (Table 2).

DISCUSSION

Pleural effusions are frequent and often constitute diffucult diagnostic problems. In spite of careful diagnostic evaluation the aetiology of the effusion can not be established in about 20 % of patients (Storey et al. 1976).

This study showed that determination of ADA in pleural fluid helps to distinguish especially tuberculous pleural effusions from neoplastic and other pleural effusions.

Groups	Number of Patients	Serum ADA (U / L)	Pleural Fluid ADA (U / L)	Pleural Fluid/Serum ADA ratio
Healthy Controls	(13)*	7.30 ± 4.66	--	--
Empyema	9 (9)*	4.22 ± 2.99	53.33 ± 18.35	19.81 ± 13.73
Tuberculosis	30 (25)*	4.12 ± 2.35	21.30 ± 7.87	6.76 ± 4.16
Malignant Neoplastic disease	12 (7)*	3.42 ± 1.61	7.53 ± 3.63	2.74 ± 1.70
Congestive heart failure	12 (7)*	3.42 ± 1.61	6.33 ± 3.82	1.88 ± 1.93

* Number of cases whose serum ADA level was determined

Table - 1 : ADA activity (mean ± SE) in serum and pleural fluid. Pleural fluid / Serum ADA ratio (mean ±SE).

Groups	Number of patients	Pleural Fluid ADA (U/ L)
Exudates	53	23.05 ± 17.89
Transudates	10	6.70 ± 3.94
Biopsy positive tuberculous pleural effusions	13	22.00 ± 8.67
Biopsy negative tuberculous pleural effusion	17	20.76 ± 7.61

Table - 2 : ADA activity (mean ± SE) in exudates and transudates and in biopsy positive and biopsy negative tuberculous pleural effusions.

In our study the mean ADA activity was highest in the empyema group. It was found apparently higher in the tuberculosis group than the patients in neoplastic and congestive heart failure groups. Ocana et al. (1983; 1986) found the same result before and emphasized that ADA activity was a good parameter particularly for diagnosis of tuberculous pleural effusion and its sensitivity and spesificity were very high. Pettersson et al. (1984) demonstrated that tuberculous pleural effusions, empyematous and rheumatoid pleural effusions had rather higher activities of ADA than parapneumonic, nonspesific and neoplastic pleural effusions and effusions in systemic lupus erythematosus on congestive heart failure. Sinha et al. (1985) obtained similar findings.

Some investigators emphasize that determining the ADA activity in pleural fluid, especially in tuberculosis will not be enough, but it is also necesarry to determine pleural fluid / serum ADA ratio, (Maritz et al. 1982; Pettersson et al. 1984). Maritz et al. (1982) concluded that ADA values over 40 U /L and pleural fluid / serum ADA ratio over 1.1 make tuberculosis very likely. However, according to Pettersson et al. (1984) a pleural fluid ADA activity over 50 U / L or a pleural fluid / serum ADA ratio over 2.5 always denote tuberculosis, empyema or rheumatoid arthritis. In our study, in the tuberculosis group, although the ADA activity in pleural fluid have been determined low; the ratio of pleural fluid ADA / serum ADA was found to be 6.76 which is a higher value when compared to literature.

When we made a comparison between 13 biopsy positive tuberculosis patients and negative ones, it was found that there was not any significant difference in their ADA levels of pleural fluid ($p > 0.05$). Also Pettersson et al. (1984) reported that there was not any difference of ADA values between the two groups (Pettersson et al. 1984). The above results emphasize the importance of determination of ADA activity in indefinitive diagnosis of tuberculosis.

Another comparison, in our study, was made between the mean ADA value of 53 exudates and 10 transudates. The mean ADA value of exudates have been determined to be markedly higher than that of transudates ($p < 0.01$). We have not yet come across with the determination of ADA activity for differentiation of exudates and transudates through the literature. We believe that, the ADA level determination in pleural fluids, could also be of great importance as well as other parameters in differantiation of exudates and transudates.

The reason of the increase in the activity of this enzyme in fluids of tuberculosis, empyema and rheumatoid arthritis is not yet obvious.

However it is thought that ADA is produced locally in pleural cavity by T lymphocytes and thus the activity in pleural fluid is greater than the activity in serum. Most probably it is due to the local inflammatory process in pleural fluid and membranes. This inflammatory process causes; an activation in T lymphocytes, change of monocytes to macrophages and increase in the activity of ADA, which is a predominantly lymphocytic enzyme.

The ADA determination in pleural fluid is inexpensive and easy to do. Ocana et al. (1983) suggest that ADA determination should be a routine test especially in countries where the prevalence of tuberculosis is still high.

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