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DIAGNOSTIC VALUE OF ADENOSINE DEAMINASE TO DIFFERENTIATE EXUDATES AND TRANSUDATES

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Abstract : The differentiation of pleural effusions as exudates or transudates is the first step in the diagnosis of pleural effusions. The aim of this study was to evaluate the value of adenosine deaminase (ADA) concentration in the pleural effusions for differentiating exudates from transudates. Sixty indoor patients, admitted to our hospital, having pleural effusions and suffering from varying etiologies were included in this study. According to the final diagnosis, these 60 patients were divided into two groups: exudates (50) and transudates (10). The mean pleural ADA, serum ADA and pleural fluid/serum ADA ratio were significantly ($P<0.0001$) higher in exudates as compared to transudates. Using a cut-off point of 22 IU/L, the sensitivity and specificity of pleural ADA in the diagnosis of exudates was computed to be 90% and 90% respectively. At a cut-off point 1.28, pleural fluid/serum ADA ratio was found to have sensitivity 84% and specificity 90%, respectively. From this study it is concluded that, ADA is a useful biochemical marker to suggest exudative effusions.

Key words : pleural effusion, exudates, transudates, adenosine deaminase, diagnosis

INTRODUCTION

Pleural effusion is one of the most common clinical finding encountered in clinical practice. A primary diagnostic approach is the identification of the nature of effusion as exudate or transudate. A transudate, which is due to the systemic factor (e.g. congestive cardiac failure, liver cirrhosis, nephrotic syndrome and severe hypoprotienemia.) does not warrant further diagnostic procedures and one may not worry about therapeutic measures directed at pleura. On the other hand, an exudate requires more extensive diagnostic procedures in order to find out the cause of pleural disease.

The most commonly used method for differentiation between exudates from

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transudates was established by Light et al (1). A pleural fluid is classified as an exudate if it meets one or more of the following criteria: (1). A pleural fluid to serum protein ratio greater than 0.5; (2). A pleural fluid Lactate Dehydrogenase concentration greater than 200 IU/L; (3). A pleural fluid to serum Lactate Dehydrogenase ratio greater than 0.6. It has been suggested that the sensitivity and specificity of these criteria are both near 100 per cent. However, several recent articles (2–4) have indicated that it is of a low specificity. As a result, several recent classifications have been proposed. These include use of the pleural fluid cholesterol concentration (2), pleural fluid/ serum cholesterol ratio (3), serum-effusion albumin gradient (4) and pleural fluid/serum bilirubin ratio (5).

We could found only one study (6) about usefulness of adenosine deaminase (ADA) in pleural effusion for the purpose of differentiating exudates from transudates. Thus the purpose of this study was to assess the value of ADA in classifying the effusion in exudates and transudate. The purpose of this study was also to compare the usefulness of ADA with the Light's traditional criteria of pleural fluid to serum protein ratio (1).

METHODS

Sixty indoor patients, admitted to Government Medical College Aurangabad, having pleural effusion and suffering from varying etiologies were included in this study. In all these cases, a standard clinical protocol was followed and routine laboratory tests of pleural fluid were carried out that included total protein, glucose and pleural fluid cytology. Only the results of first thoracocentesis were used. Pleural fluid samples were cultured and pleural biopsy was also done to obtain a definitive diagnosis. Only patients in whom definitive diagnosis was established were included in the study. According to the final clinical diagnosis, these 60 patients were divided into two groups: exudates (n = 50) and transudates (n = 10) (Table I).

The following studies were performed on pleural fluid and serum of all patients: pleural fluid/serum protein ratio, pleural adenosine deaminase concentration, serum adenosine deaminase concentration, pleural fluid/serum adenosine deaminase ratio.

Biochemical analysis of protein was done on Erba Chem 5 plus semiautomatic analyzer using Erba Transasia kit. The assay of ADA activity was performed in these cases by a standard colorimetric method (7). One international unit of ADA represents the enzymatic activity that catalyzes a molecule of substrate in standardized conditions of pH and temperature.

Statistical analysis

Results are shown as means±SD. Student's t-test was employed to determine statistical significance. P value less than 0.05 was considered statistically significant.

RESULTS

Out of 60 cases studied, 40 were men and 20 women. According to the final clinical diagnosis, there were 50 cases of exudate of which 31 were men and 19 women with a

mean age of 41.46 (range 5–80) years. There were 10 cases of transudate of which 9 were men and one woman with a mean age of 25.5 (range 3–72) years.

In the group of patients with exudate, pleural fluid/serum protein ratio was significantly (P<0.0001) higher as compared to transudate (Table II). In the group of patients with exudate, mean ADA value, both in pleural fluid and serum, were significantly (P<0.0001) higher as compared to transudate (Table II). Patients with exudate had a significantly (P<0.0001) higher mean pleural fluid/serum ADA ratio than transudate (Table II).

For differentiating exudate from transudate, we accepted the cut-off point as 0.5 for pleural fluid/serum protein ratio, 22 IU/L for pleural ADA level, 19 IU/L for serum ADA level and 1.28 for the pleural fluid/serum ADA ratio (Table III). Using cut-off point of 22 IU/L for pleural ADA, 6 were misclassified and of which 5 were exudates and one transudate. For serum ADA, using 19 IU/L as cut-off point, 10 were misclassified and all these were exudates. For pleural fluid/serum ADA ratio, using 1.28 as cut-off point, 9 were misclassified and of these 8 were exudates and one transudate. Hence the above data show that pleural ADA causes less misclassification in differentiating exudates from transudates as compared to serum ADA and pleural fluid/serum ADA ratio. However, using cut-off point of 0.5 for pleural fluid/serum ratio, only 3 were misclassified and all these were exudates.

The sensitivity, specificity, positive predictive value, negative predictive value and efficiency of the investigated parameters,

TABLE I: Causes of pleural effusions.

Cause	*No. of patients*
Exudate	**50**
Tuberculosis	30
Malignant effusion	08
Parapneumonic effusion	08
Empyema	01
Rheumatoid arthritis	01
Systemic lupus erythematosus	01
Liver abscess	01
Transudate	**10**
Nephrotic syndrome	03
Acute glomerulonephritis	02
Cirrhosis of liver	02
Congestive cardiac failure	01
Severe hypoprotienemia	01
Chronic renal failure	01

TABLE II: Mean values and SDs of pleural fluid/serum protein ratio, pleural ADA, serum ADA and pleural fluid/serum ADA ratio in exudate and transudate.

Criteria		*Exudate (n=50)*	*Transudate (n=10)*	*Statistical significance (P value)*
Pleural fluid/Serum protein	*x*	0.6424	0.387	0.0001
	SD	0.126	0.085	
Pleural ADA	*x*	80.66	16.40	0.0001
	SD	49.05	4.926	
Serum ADA	*x*	38.58	13.40	0.0001
	SD	22.81	3.62	
Pleural fluid/Serum ADA	*x*	2.0828	1.219	0.0001
	SD	0.682	0.100	

All values are expressed as means±standard deviation; n = number of patients.

TABLE III: Cut-off points for various biochemical parameters.

Criteria	*Exudate*	*Transudate*
Pleural fluid/serum protein ratio	≥ 0.5	< 0.5
Pleural ADA (IU/L)	≥ 22	< 22
Serum ADA (IU/L)	≥ 19	< 19
Pleural fluid/serum ADA ratio	≥ 1.28	< 1.28

TABLE IV: Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and efficiency of each parameter studied[1].

Criteria	*Sensitivity*	*Specificity*	*PPV*	*NPV*	*Efficiency*
Pleural fluid/serum protein ratio	94.00	100.00	100.00	76.92	95.00
Pleural ADA	90.00	90.00	97.82	64.28	90.00
Serum ADA	80.00	100.00	100.00	50.00	83.33
Pleural fluid/serum ADA ratio	84.00	90.00	97.67	52.94	85.00

[1]Shown in percent.

according to different cut-off points in the differentiation of exudates from transudates, are shown in Table IV.

DISCUSSION

Adenosine Deaminase (ADA, EC 3.5.4.4) is an enzyme of purine catabolism which catalyses the pathway from adenosine to inosine (8). Various authors have found higher ADA levels in tuberculous effusions (9–12). In the present study, we have found that the sensitivity and specificity of pleural ADA concentration for the diagnosis of exudates to be 90% and 90%, for serum ADA concentration 80% and 100% and for pleural fluid/serum ADA concentration 84% and 90% respectively. Also the value of pleural fluid and serum ADA, as well as pleural fluid/serum ADA ratio were higher in patients with exudates. Thus the results of present study confirm that ADA activity is a useful parameter for differentiating exudates from transudates. Using different cut-off point, out of pleural ADA, serum ADA and pleural fluid/serum ADA results, pleural ADA is most significant to differentiate effusion into exudates and transudate. Of all the biochemical parameter, pleural fluid/serum protein ratio (1) is more significant for differentiating exudates from transudate causing only 3 misclassifications as compared to other biochemical parameters.

Atalay et al. (6) carried out the only study available to our knowledge on pleural fluid ADA to differentiate between exudates and transudate. They claimed that pleural ADA separates pleural exudates from transudates. In addition, according to these authors, for detecting exudates, at a cut-off point of 15.3 IU/L for pleural ADA test yielded a sensitivity and specificity of 85.8% and 82.3% and at a cut-off point of 0.66 for pleural fluid/serum ADA ratio yielded 83.3% and 83.2% respectively. In the present study, we have found that at a cut-off point of 22 IU/L, the sensitivity and specificity of pleural ADA concentration for the diagnosis of exudates to be 90% and 90% and at a cut-off point of 1.28 for pleural fluid/serum ADA concentration 84% and 90% respectively. Hence the cut-off point established in our study yielded a better sensitivity and specificity as compared to the above study.

Thus, we conclude that adenosine deaminase is a useful biochemical marker to differentiate exudates from transudates. We further conclude that our results of adenosine deaminase had limited sensitivity and specificity for differentiating exudates from transudates as compared to Light's criteria. Thus, we propose that simultaneous use of adenosine deaminase may be helpful in separating exudates from transudates. However, further studies, involving larger

number of patients, to evaluate the parameters covered in our study are needed in order to draw any robust conclusion and to achieve higher sensitivity.

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