IS ADA ACTIVITY IN PLEURAL FLUID AN EFFICIENT DIAGNOSTIC TOOL IN TUBERCULAR PLEURAL EFFUSION?

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ABSTRACT

BACKGROUND

The analysis of ADA activity is a very useful diagnostic approach to achieve a more rapid and precise diagnosis in the cases of pulmonary tuberculosis. Adenosine deaminase has been proposed to be a useful surrogate marker for tuberculosis in Pleural, pericardial and peritoneal fluids. Tuberculosis is a major cause of Pleural effusion, where in TB usually has lymphocytic and exudative characteristics.

MATERIALS & METHODS

The study was carried in 60 patients with history & clinical examination suggestive of Tubercular pleural effusion admitted in medical and chest units of Prathima Hospital, Karimnagar and these were labeled as group-I. In addition as a control study, the pleural fluid was aspirated in 30 selected patients having transudative pleural effusion secondary to CCF & cirrhosis of liver denoted as group II. ADA activity in pleural aspirate of all the subjects of group I & group II was estimated by Giusti & Galanti method.

RESULTS

The Results were analyzed by student 't' test and chi square test. The ADA activity was compared in both the groups by setting a cut off value 35U/L. The ADA activity of group I was 43.57±13.23 while that of group II was 21.37±8.41. The 'p' value was <0.001. There is significant increase in level of ADA in group I when compared to group II.

CONCLUSIONS

The results of this study favor the application of ADA activity in plural fluid as a diagnostic tool for tubercular pleural effusion without performing any invasive procedure like pleural biopsy.

KEYWORDS

Adenosine deaminase (ADA), Tubercular Pleural Effusion.

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INTRODUCTION: TB is one of the oldest and commonest infectious diseases also known as master of death or captain of death. TB usually affects lungs, but extra pulmonary TB is also common. TB has emerged as one of the most lethal diseases man has ever faced. It has become a major health problem in the 3rd world or developing countries in a short span of time. It affects all age groups irrespective of the sex. It has been estimated that nearly 500,000 people die of this disease every year. No other disease has so much socioeconomic health significance as TB in a country like India.[1]

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Pleural effusion develops because of excessive filtration or defective absorption of accumulated fluid. Effusion may be a primary manifestation or a secondary complication of many disorders. TB is the major cause of pleural effusion where in TB usually has lymphocytic and exudative characteristics.[2] Exudates are due to pleural inflammation (pleurisy) with an increased permeability of the pleural surface to proteinaceous fluid. Inflammation or Injury increases pleural membrane permeability to proteins and various types of cells and leads to the formation of educative effusion. In general, exudates have protein concentration higher than 3gmldl. Lymphatic obstruction may also contribute to accumulation of plural fluid.[3]

Conventionally, the diagnosis of tubercular pleural effusion is made on the basis of clinical data, biochemical and microscopic examination of pleural fluid as exudates and containing high count of lymphocytes which is nonspecific. Other methods are ZN staining & culture of pleural fluid lack sensitivity ie., 10-40% and 8-49% respectively. At the same

time culture identification takes long time i.e., 4-6 weeks. Pleural biopsy is an invasive procedure with sensitivity 50-80% and not a routine test.[4] The levels of ADA are increased in tubercular pleural effusion and its determination has acquired popularity as a diagnostic test which is non-invasive, not expensive and is readily accessible. Our study is aimed to assess the diagnostic importance of ADA in tubercular pleural effusion.

MATERIALS AND METHODS: This study was carried out in 60 patients with history and clinical examination suggestive of tubercular pleural effusion admitted in medical and chest units of Prathima Institute of Medical Sciences, Nagunur, Karimnagar were included in this study and denoted as Group-I. In addition as a control group of the study, the pleural fluid was aspirated in 30 selected patients having transudative pleural effusion secondary to congestive heart failure and cirrhosis of liver were included and denoted as Group-II. The detailed clinical history, physical examination and investigations like complete blood examination, urine analysis, chest x-ray PA and lateral view, tuberculin test, sputum for AFB for 3 consecutive days and wherever possible biopsy and histopathological examination of pleura and pleural fluid ADA estimations were carried out in all patients.

Diagnosed cases of infectious mononucleosis, enteric fever, leprosy, viral hepatitis, HIV, hematopoietic malignancies were excluded from the study. ADA level was estimated by Galanti and Giusti method[5] and Tulip kit was used. The ADA activity of pleural fluid of both the groups was statistically compared by setting the cut off at 35U/L for differentiation. The statistical analysis was done by applying chi square test.

RESULTS: The age of the patients of tubercular pleural effusion (Group-1) range from 15-60years with the mean age of 28.7±9.7yearsand in group-2 55.4±10.6years. The male patients were of older age as compared to female patients. In our study, the number of males with the disease was more compared to females.

The mean ADA level in pleural fluid of Group-I was 43.57±13.23 U/L, while that of Group-II was 21.77±8.41 U/L. The cutoff of ADA level was set at 35 U/L and chi square test was applied and 'p' value was calculated.

49 patients of Group-I and 2 subjects of Group-II were having ADA levels of >35 U/L while 11 patients of Group-I and 28 subjects of Group-II were having ADA levels <35 U/L and the 'p' value was <0.0001.

Sex	Patients Group-I (n=60)	%	Controls Group-II (n=30)	%
Age	28.7±9.7		55.4±10.6	
Male	34	57	15	50
Female	26	43	15	50

Table I: Demographic data of both groups showing age and gender distribution

ADA level	Patients Group-I (n=60)	Controls Group-II (n=30)	'p' value
Mean±SD	43.57±13.23	21.77±8.41	<0.0001
>35U/L	49	2	
<35U/L	21	28	

Table II: ADA level in pleural fluid of patients and controls

Sl. No.	Author	Year of publication	Cut off value
1	De-Olveira	1994	40U/L
2	Valdes L	1995	47U/L
3	Burgess LJ	1996	50U/L
4	Arif Rahim	2002	40U/L
5	S. K. Verma	2008	36U/L
6	Smitha C Patel	2012	45U/L
7	Asmita A Mehta	2014	40U/L

Table III: ADA activity levels in different studies

DISCUSSION: Tuberculosis has always been a serious health problem worldwide. Tubercular pleurisy usually occurs during primary infection, generally before the development of hypersensitivity due to sub pleural focus. Once the hypersensitivity develops, these sub pleural foci undergo necrosis and release antigenic material causing exudation of fluid and cells from the pleura.[6] Tuberculosis may also affect the pleural space by direct spread of the primary infection or as a result of haematogenous dissemination. The fluid accumulates in the pleural space as result of delayed hypersensitivity reaction to tuberculous proteins. The tubercular pleural fluid contains sensitive biomarkers like ADA, interferon-Gamma, tumor necrosis factor, IL-1. ADA is enzyme of purine catabolism which catalyzes the conversion of adenosine to inosine and is released by T-lymphocytes and macrophages during cellular immune response. Different studies have revealed high sensitivity and specificity of ADA for early diagnosis of tubercular pleural effusion. The pleural fluid ADA levels have higher positive predictive values in the region where pulmonary tuberculosis was prevalent.[7,8,9] Our results were statistically significant between tubercular and non-tubercular control group ('p' <0.0001). The results of our study are comparable with many national and international studies as depicted in table-3. Thus when compared with previous studies,[10,11,12] our study showed that in the region of high tuberculosis prevalence, determination of pleural fluid ADA level can provide a reliable basis to start anti-tubercular therapy before the results of biopsy and culture become available or without performing pleural biopsy.

CONCLUSION: We conclude that the ADA level in tuberculous pleural effusion is higher than the level in effusion of other etiology. Using 35U/L as the cut off, it is possible to avoid invasive pleural investigation in as much as 57% of patients to diagnose tuberculosis. Thus estimation of ADA activity may provide the basis for the rapid, non-

invasive and efficient diagnostic tool for tubercular pleural effusion in different clinical setting.

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