ADENOSINE DEAMINASE ACTIVITY IN PERICARDIAL EFFUSION

Adnan Gul, Muhammad Hafizullah, Zahoor Ullah, Tasleem Akhtar, Tasleem Ul Haq

Department of Cardiology, Postgraduate Medical Institute, Lady Reading Hospital, Peshawar

ABSTRACT

Objective: To test the efficacy of enzyme Adenosine Deaminase (ADA) in the early and rapid diagnosis of tuberculous pericarditis presenting as moderate and large pericardial effusions.

Material and Methods: The study was conducted at Lady Reading Hospital, Peshawar, from 1998 to 2000. Cases of moderate and large pericardial effusions were studied for ADA estimation. ADA activity was tested in four groups, Group A cases met the standard criteria of diagnosing tuberculosis, Group B included cases having high degree of suspicion of tuberculosis, Group C included cases having other etiologies except tuberculosis and Group D included the controls.

Results: Out of 102 cases of pericardial effusion, ADA estimation was done in 84 cases: Group A, 31 cases; Group B, 21 cases; Group C, 17 cases & Group D, 15 cases.

ADA levels in Group A were mean 93+ 21, Group B 84+16, Group C 51+12 and Group D 26+14.The Group A and B were having levels much above the cutoff range. The presence of high enzyme activity in Group C above the cutoff range limited its utility as a specific marker for TB. When combined Group A and B were compared against Group C and D, only then the difference reached to the level of statically significance making ADA a sensitive marker for TB.

Conclusion: ADA can be used as sensitive marker for the diagnosis of tuberculous activity however other large studies are further needed to test its efficacy in our setup.

Key Words: Adenosine Deaminase Enzyme, Tuberculosis, Pericardial Effusion

INTRODUCTION

Adenosine deaminase (ADA) is an enzyme, which catalyse the purine catabolism in body and is present in body fluid. The main reaction it catalysis and is the conversion of Adenosine to Insoine with the production of ammonia.[1] T-lymphocytes in the lymphoid system is the major activity site. It has been found and reported to be highly sensitive and specific in the diagnosis of tuberculous body effusions and can be developed as a quick and cheap marker for the diagnosis of tuberculosis[2-7].

In Pakistan where tuberculosis has emerged as a leading health problem and especially in NWFP over the last decades. There is a great need of such a diagnostic tool which is not only specific and sensitive but also simple and cost effective. ADA therefore can be one such potential marker if developed and can help in early diagnosis.

In this modest study, an attempt has been made to study its diagnostic value in pericardial fluid, as a part of major multidimensional study.

MATERIAL AND METHODS

This study has been conducted in cardiology unit, Post Graduate Medical Institute, Lady Reading Hospital Peshawar. Cases of moderate and large pericardial effusions reporting to echo room were enrolled in the study from 1998 to 2000. A total of 102 cases with moderate and large pericardial effusion were selected and enrolled in the study after obtaining their consent. The etiological work up was done using all the available diagnostic modalities including effusion culture for TB, cytology for AFB and pericardial biopsy. Cases were labeled as proven TB whenever they had a positive culture of TB or demonstration of AFB in smear of the effusion or a biopsy compatible with tuberculous granulommas. Cases were labeled as highly suggestive of TB according

EFFUSION CHARACTERISTICS

Group	Total	Hemorrhagic. Excluded	Cases Studied	% age
A	35	04	31	88.5
B	30	09	21	70.0
C	20	03	17	85.0
D	17	02	15	88.0
Total	102	18	84	

Table 1

to a Korean study[8], when they met either of the following criteria:

Criteria 1

- Positive Mantoux test
- Negative work up of other causes of pericardial effusion
- Absence of prodromal symptoms of upper respiratory tract infection
- Optimal response to anti tuberculous drugs

Criteria 2:

Presence pulmonary TB on chest X-ray but "sputum negative". ADA activity in effusion was determined within 2 hours of the aspiration using continuous spectrophotometer rate determination method9,10. Pakistan Medical Research Center laboratory facility in Khyber Medical Collage, Peshawar was used for the purpose.

The hypothesis was to test that can the cut off levels of >50U/lit were taken as to be diagnostic of tuberculous effusion in our setup.

Statistical Analysis: Student T test was used in the study for statistical analysis.

RESULTS

A total of 102 effusions samples were obtained. The males in the study were 66 and females were 36. The females presented at an early mean age of 29.47± SD 20.33 years than males who presented at the mean age of 40±46 years.

Out of 102 cases of pericardial effusion, 18 cases were found to be haemorrhagic and thus excluded because of the fact that RBC's have high degree of activity of ADA. ADA estimation was done in 84 cases. Exclusion were from all four groups as per following detail table 1:

Cases were assigned to four groups:

Group A comprised of 31 cases having proven TB.

Group B comprised of 20 cases, highly suggestive of TB.

Group C comprised of 18 cases not having any presenting feature for TB but other etiologies of pericardial effusion like pyogenic, parapneumonic, uremic or due to connective tissue disorders.

Group D comprised of 15 cases all having pleural effusion with CCF due to known cardiac causes.

Results reveal (table2) that mean total ADA activity in the first three groups remained above the cut of range for normal i.e. 50 units/l thus suggesting the marker as non-specific and non valid. The results also reveal that there is no statistically significant difference amongst the first three groups, and therefore the marker may not be termed as sensitive for any diagnostic conclusion. However when the data is analyzed separately for the ADA activity tested in cases of proven TB (Group A) and suggestive of TB group (Group B) fluid levels of ADA (93.5 and 84.0 u/l) and compared against the other two groups of non tuberculous etiologies (Group C) and CCF cases (Group D), ADA levels (51 and 26 u/l), difference found being statistically significant p value<0.05. However no intra group statistical significance has been found for group A and B for which purpose the marker may be considered as non-specific.

Marker gives high results above the cut off levels of 50 u/l for cases with non tuberculous etiology group C compared to controls group D having levels below cut off levels, is not reaching a level of statistical significance p=0.17. This combined group C and D result of ADA when compared to the result for proven and highly suggestive of TB, group A and B, again the difference reaches to a level of significance for the values for sensitivity, thus making ADA as a

ADA ACTIVITY IN PERICARDIAL EFFUSIONS

Group	Number n=84	Mean ADA Activity in clear pericardial fluid
A	31	93.5 ± 21
B	21	84.0 ± 16
C	17	51 ± 12
D	15	26 ± 14

Table 2

sensitive marker for the diagnosis of TB.

DISCUSSION

Tuberculosis is a worldwide killer whose occurrence is on the rise. The current gold standard test for the diagnosis of Mycobacterium tuberculosis infection is a positive culture. However this method takes 4-6 weeks to perform and is not readily available. The more rapid BACTEC culture method is not cost effective and requires about 10 days. To take tissue biopsy for granulommas compatible with tuberculosis is an invasive procedure and needs expertise and is also not readily available and cost effective. Tuberculin test and chest X-ray are more available, but are not conclusive for the diagnosis of tuberculosis. Presentation of disease varies widely and not all patients produce bacilli in their sputum or body fluids, which further complicates an accurate diagnosis of the disease. Because of the difficulty in isolating the causative organism, pericardial tuberculosis is hardly diagnosed[11]. Studies in patients with TB pericarditis have shown that ADA levels in pericardial fluids are diagnostically useful in early diagnosis of TB pericarditis, particularly when the results of other laboratory tests are negative[8,12].

Using a cutoff value of ADA activity of 40 U/L, the sensitivity and specificity of ADA in one series of nine patients with proven and five patients with suspected TB pericarditis were 93% and 97% respectivley[8]. In another series, there was a positive correlation between high pericardial adenosine deaminase levels and the subsequent development of constrictive pericarditis[11].

This modest study conducted on a small number of cases in a clinical set up where the chances of encounter with TB cases are very high. In search for looking a simple, cheaper and readily available marker as compared to routine culture for TB which is a much time consuming or pericardial biopsy which is a much invasive procedure with high morbidity. ADA activity has been selected for evaluation. Previous reports as already mentiond[2-7] have claimed that ADA activity in body fluid has got a high sensitivity and specificity for tuberculous pleural effusions as well as pericardial effusions [9-13].

Our finding also suggests that ADA activity in proven TB and highly suggestive cases is significantly high when compared with the control group. However no statistically difference has been seen in the proven TB and highly suggestive of TB groups.

Mean ADA activity in proven TB cases (93.5 u/l) is quite the same (92.43 u/l) as reported by Ocana et al[4]. However our values obtained for cases with other etiologics and CCF taken as control are significantly higher as compared to the report referred to. Wide spread TB in our community may account for these high ADA values.

In our study, ADA is found both specific and sensitive for the cases with proven and suggestive of TB groups as compared to controls. However it looses its specificity and sensitivity when intra group comparison is taken. Secondly the main high activity for controls than reported by others, lowers its sensitivity and its adoption as a diagnostic marker.

In conclusion on the basis of this preliminary analysis, we can say that ADA activity in non hemorrhagic pericardial fluid is significantly high in proven TB and highly suggestive of TB cases as compared to the activity of the enzyme in fluid from the cases with other etiologies and CCF due to known cardiac causes.

Further studies on large number of cases and improved methods for enzyme activity follow-up are suggested.

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Address for Correspondence:

Dr. Adnan Gul
Assistant Professor
Department of Cardiology,
Lady Reading Hospital,
Peshawar