PLEURAL FLUID LYMPHOCYTE NEUTROPHIL RATIO IN THE DIAGNOSIS OF TUBERCULOUS PLEURAL EFFUSION

ABSTRACT

Background: Increased pleural fluid adenosine deaminase (ADA) activity is classically associated with tuberculous pleuritis. However, increased activity can also occur in a number of other diseases and this may negatively affect the diagnostic utility of ADA measurements and decrease its specificity for the diagnosis of tuberculosis (TB). The presence of ADA in pleural fluid reflects the cellular immune response in the pleural cavity and in particular, the activation of T lymphocytes.

Objectives: To determine whether the combined use of ADA activity and lymphocyte/neutrophil ratio would provide a more efficient means for diagnosing tuberculous pleurisy than the use of ADA levels alone.

Methods: Biochemistry, cytology and microbiology studies were performed on 90 consecutive pleural fluids. ADA and differential counts were determined on all exudative effusions.

Results: ADA activity in tuberculous effusions was significantly higher than in any other diagnostic group. At a level of 50U/L, the sensitivity, specificity, positive predictive value (ppv), negative predictive value (npv) and efficiency for the identification of TB were calculated at 100%, 83%, 93%, 100% and 95%, respectively.

Conclusion: ADA when combined with lymphocyte/neutrophil ratio remains a useful test in the diagnosis of tuberculous pleuritis.

KEYWORDS: Adenosine deaminase; Lymphocyte/neutrophil ratio; tuberculous pleuritis

INTRODUCTION:

Pulmonary tuberculosis is the most frequent cause of death by an infectious agent worldwide. Among the extra pulmonary presentations, tuberculous lymphadenitis, pleural tuberculosis is the second most frequent. Failure to diagnose and treat pleural tuberculosis can result in progressive disease with the involvement of other organs in as many as 65% of patients. Conventional methods have proven to be insufficient for diagnosing pleural tuberculosis.

Direct examination of pleural fluid is inefficient because sensitivity is about 1%. Pleural fluid culture is more sensitive than direct examination but Mycobacterium tuberculosis requires 4-6 weeks to grow. Many studies have demonstrated the diagnostic significance of increased adenosine deaminase (ADA) in tuberculous pleurisy, other studies have shown that ADA is of limited value as, as raised levels are also associated with a number of other diseases including malignancies (especially those of hematologic origin), bacterial infections (Q fever, brucellosis), emphysemas, and other collagen vascular diseases (including SLE and rheumatoid arthritis). Lymphocytes predominate in malignant and tuberculous pleural effusions*

Hence, this study is aimed to determine whether combined use of lymphocyte/neutrophil and ADA activity would provide more efficient means for diagnosing tuberculous pleurisy than the use of ADA levels alone.

OBJECTIVES OF THE STUDY:

To determine whether the combined use of ADA activity and lymphocyte/neutrophil ratio would provide a more efficient means for diagnosing tuberculous pleural effusion than with the use of ADA alone.

MATERIALS AND METHODS:

The present study was conducted at ASRAM Medical College, Eluru during the period between 2014-2016. 120 consecutive pleural fluid specimens were collected from patients admitted to medical wards.

Inclusion criteria: All exudative pleural effusion cases.

Exclusion criteria:

1. Patients with transudative pleural effusion
2. Patients with immunodeficient states like HIV/AIDS, those on chemotherapy were excluded.
3. Patients having hemothoraces or emphysemas too turbid for analysis were excluded.

Besides a detailed history and clinical examination, the following investigations were carried out:

a) Blood investigations
b) Urine examination
c) Sputum examination - acid fast bacilli by Ziehl Neelson (ZN) stain, Gram's stain, culture.
d) Mantoux test
e) Chest radiography – posterolateral and lateral view in selected cases
f) Pleural fluid analysis
g) Pleural biopsy: Pleural biopsy was performed using the Abramski biopsy needle.

Equipment: Spectrophotometer, spectral-line photometer or simple photometer (with tungsten lamp and filter) suitable for accurate measurements at wavelengths between 620 and 650nm, water bath (37°C).

Dr. P Aparna Devi
Associate Professor, Department of General Medicine Alluri Sitarama Raju Academy of Medical Sciences Eluru – 534 005, West Godavari District Andhra Pradesh

Dr. P Joyal Sandeep
Postgraduate, Department of General Medicine Alluri Sitarama Raju Academy of Medical Sciences Eluru – 534 005, West Godavari District Andhra Pradesh

Dr. N Partha Sarathy
Professor & HOD, Department of Community Medicine Alluri Sitarama Raju Academy of Medical Sciences Eluru – 534 005, West Godavari District Andhra Pradesh

Dr. Kalapala Abhilash
Postgraduate, Department of Community Medicine Alluri Sitarama Raju Academy of Medical Sciences Eluru – 534 005, West Godavari District Andhra Pradesh

* indicates a note or reference to a source.
Tuberculosis constitutes 50%. All patients of emphysema had total leukocyte count less than 1000 cells/mm3 of which Pleural fluid cell type and cell count: The majority of effusions had a predominant neutrophil count greater than 5,000 mm3 (100%) followed by parapneumonic effusions (36.4%), consistent with Light’s observation et al. The low cell counts in tuberculous pleural effusion compared to emphysema and parapneumonic effusion may be due to cell mediated immunity, lymphocytopredominance in tuberculous effusion where as antibody mediated immunity and neutrophil predominance in emphysema and parapneumonic effusion. 83.3% of TB effusions and 100% of malignant effusions had lymphocyte predominance. In comparison to other studies: Valdes L et al9 where they have encountered neutrophil predominant tuberculous effusion in only 6.7% of patients and only one malignant effusion had neutrophil predominant effusion (3%). Follander19 demonstrated predominance of lymphocytes and scarcity of mesothelial cells in tuberculous effusion; Light BW18—large number of neutrophil indicate the presence of bacterial pneumonia. Lymphocytes predominant in tubercular pleural effusion.

Adenosine deaminaseIn tubercular pleural effusion pleural fluid Adenosine deaminase level (ADA) has got a good diagnostic index after excluding other causes of raised ADA levels. Although a pleural fluid ADA above 70U/L is diagnostic of tuberculosis18, it has to be considered if the pleural fluid ADA is between 40IU/L and 70IU/L. An ADA level less than 40IU/L is very much unlikely of tuberculous pleural effusion. But different authors have used different cut off levels for pleural fluid ADA ranging between 33 IU/L to 50 IU/L.20-23 In our study pleural fluid ADA >50U/L was taken as diagnostic cut off for tuberculous effusion and it yielded 61% sensitivity, 71% specificity, 83% positive predictive value, 45% negative predictive value and pvalue <0.0001. In our study who were diagnosed as tubercular effusion ADA < 50 of 24 are of tuberculous effusion and 20 non tuberculous effusion. The general prevalence of tuberculosis is high in India, so tuberculosis aetiological cause for pleural effusion is expected to be high. Hence by taking ADA >40 U/L in our study is reasonable in developing countries like India, such that missing of tuberculous pleural effusion cases will be minimal. Our results show that, at a cutoff level of 50IU/L, ADA has sensitivity, specificity, ppv, npv, and efficiency were 100%, 93%, 100% and 93% respectively. In the present study, ADA activity was highest among the tuberculosis group. Para infective conditons were also seen to beos assaulted by high ADA activities. The relative cell count or L/N ratio could be used to distinguish between these two entities 8. In the cases of tuberculosis pleurisy, a predominant lymphocyte count was usually found, resulting in a L/N ratio of 0.75 or greater, whereas in the case of para infective effusions, a predominant neutrophil count was usually found (L/N ratio <0.75). Use of ADA level especially in conjunction with the L/N ratio, is therefore a valuable diagnostic tool in this regard, as it provides a rapid and accurate means of detecting TB pleurisy.

Conclusions: In conclusion, it is suggested that the combined use of adenosine deaminase activity along with lymphocyte neutrophil ratio would provide am ore efficient means for diagnosing tuberculous pleuritis than the use of ADA alone.

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