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RESEARCH ARTICLE

ROLE OF ADA AND CYTOLOGY IN THE DIAGNOSIS OF EXUDATIVE PLEURAL EFFUSION

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ABSTRACT

Background: Exudative pleural effusions are a common diagnostic problem in clinical practice and it is difficult to determine the cause of pleural effusion.
Aims and objectives: to evaluate the role of ADA and cytology in diagnosis of exudative plural effusion
Materials and methods: 100 patients with exudative plural effusions were recruited
Results: Tuberculosis was the most common cause of plural effusion in 74% followed by malignancy 18% then synpneumonic 6%. majority of tubercular pleural effusions 86.47% were found in less than 50 years of age and majority of malignant pleural effusion found in more than 50 years of age (73.03%). 89.18 % and 84.62% are the sensitivity and specificity of the test if ADA 40 U/L cutoff is used for finding extra pulmonary TB, it is 67.5% and 100% when the ADA 63U/L cutoff is used and it is 83.78% and 96.15% when ADA and cytology both included.
Conclusion: In a clinically suspected case of plural effusion if the plural fluid ADA is >63U/L, it is virtually diagnostic of tubercular pleural effusion. If ADA is in between 40-63U/L it is highly suspicious of tubercular pleural effusion, and then the cytology report will aid in confirming the diagnosis.

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INTRODUCTION

Exudative pleural effusions are a common diagnostic problem in clinical practice, as the list of causes is quite exhaustive (Light, 2001), although sometimes they can be inferred from the clinical picture. The etiological distribution of pleural effusions in various series depends on the geographical area, patient's age, advances in the diagnostic methods and treatment of the underlying causes. The difficulty in determining the cause of pleural effusion is shown by the fact that in many series "unknown etiology" constitutes nearly 15% (Pleural effusion 2002). Exudative effusions require to be separated into infectious causes, noninfectious causes and malignancy. The most common causes in most series are infections and malignancy. In the West the most common cause is parapneumonic effusions followed by malignancy, while in India it is tubercular effusion followed by malignant effusion and a very few due to parapneumonic effusion. The clinical, biochemical and cytological parameters of tubercular effusion are shared by malignancy, both being exudates and predominantly lymphocytic effusions. This can pose a significant diagnostic dilemma. Adenosine deaminase enzyme activity, gamma interferon, polymerase chain reaction, lysozyme measurement, pleural fluid tuberculous protein antibodies and various tumor markers like CA15-3, squamous cell carcinoma antigen, etc have been used to differentiate TB from non TB. In India Five lakh patients of tuberculosis die every year (Tandon, 1999), in which most common is pulmonary tuberculosis and is often associated with effusion. In upto 25% of cases Delay in diagnosis and start of effective treatment results in poor prognosis and sequalae (Gecia-monco and Marra, 1999). All available methods of diagnosis of tubercular pleural effusion were evaluated and all of them were found to have low sensitivity and specificity. Thus we aimed to evaluate the role of ADA and cytology in diagnosis of exudative plural effusion.

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MATERIALS AND METHODS

This Hospital based prospective study was conducted in the Department of Respiratory Medicine, Govt. Medical College and hospital, Kota in the study period extending from 1st October to 31st September 2015. Our study included 100 consecutive patients with exudative pleural effusions. This study included patients with Age more than18 years having Exudative effusion as per Light's criteria and Chest X-ray evidence of pleural effusion. This study Excluded patients with

Transudative effusion, Patients who do not give their consent, Patient who have undergone repeated pleurocentesis. A detailed clinical history and general physical examination was done on all the patients. By a chest radiograph posterio anterior view the size of the effusion was estimated and after an informed consent Pleural Aspiration was done from all the patients with pleural effusion. The pleural fluid specimens were immediately carried to the biochemistry, pathology and microbiology laboratories. all parameters like Protein, Lactate dehydrogenase, Glucose, Adenosine deaminase, tubite blood cell count, Grams stain, Aerobic culture, Acid fast stain Cytology were estimated. Statistical analysis was done by using standard software.

RESULTS

There were total 100 study subjects. Mean age was 42 years. Majority were males (77%). Most common cause of pleural effusion among the study subjects was Tuberculosis (74%) followed by malignancy (18%) and sympneumonic (6%). Male preponderance was observed in the study both among tuberculous and non tuberculous group (Tuberculous 3.1: non tuberculous 2.5:1). Mean age of the study subjects with tubercular pleural effusion was 37.4 years. Majority (44.59%) were in the age group of 21-30 yrs. Result of pleural fluid ADA at 40 U/L cutoff values showed a Sensitivity of 89.18%, Specificity 84.62% Positive Predictive Value 94.29% and a Negetive Predictive Value 73.33%. A specificity of 100% obtained at a cutoff value of 63 U/L, but the sensivity of the test dropped to a low 67.57%. A definitive diagnosis of tuberculous pleural effusion can thus be made at ADA level above 63 U/L. Combination of both ADA and cytology results for diagnosis of tuberculous pleural effusion showed a Sensitivity 96.15%, Specificity 98.41%, Positive Predictive Value 67.57%,and a Negetive Predictive Value 67.57%.

Table 1. Comparison of various tests and their combination in the diagnosis of Tubercular pleural effusion

ADA cut off	Sensitivity	Specificity	PPV	NPV
40 U/L	89.18%	84.62%	94.29%	73.33%
63 U/L	67.57%	100%	100%	52%
Combination of both ADA and cytology	96.15%	98,41%	67.57%	67.57%.

DISCUSSION

Tuberculous pleurisy (TP) is caused by the delayed hypersensitivity reaction to the tubercle bacilli. Various diseases are manifested as Exudative pleural effusions. After a pleural tap only 10 to 25% of the cases will came positive by AFB staining, while culture for AFB is positive in less than 25% of the cases (Scharer and McClement, 1968). Perez *et al.* in their study have shown that tubercle bacilli will be present with smear alone in pleural fluid is only 11.1% (Perez-Rodriguez *et al*., 1999), with culture it shows 33.3% and with pleural biopsy it increases up to 96.2%. Among different workers these values may be differ (Antoniskis *et al*., 1990; Chan *et al*., 1987). One third of patients with exudative pleural effusion can have a negative tuberculin skin test (Antoniskis *et al*., 1990; Chan *et al*., 1987). PCR like Sensitive techniques shows positive results in about 50% of cases (Shah *et al*., 1998). In the patients of tuberculous exudative pleural effusion, predominatlyneutrophils presents in the early stages of the disease, while abundant mononuclear cells is believed to be due to the proliferation and differentiation of lymphocytes which release lymphokines, which in turn enhances the bactericidal activity by activating macrophages (Kataria and Khurshid, 2001). Even pleural fluid cytology takes a back seat while investigating the cause of an exudative pleural effusion, and is usually just evidence supporting our final diagnosis. Several bio-markers like interferon (IFN)-γ, ADA, a variety of tumor markers and cytokines, and C-reactive protein (CRP) have been proposed as alternative to invasive means of establishing tuberculous etiology in cases of exudative pleural effusion (Daniil *et al*., 2007). Adenosine deaminase estimation in pleural fluid has been taken as a marker for long time for tuberculous pleurisy. In our study At 40 U/L cut off value 66 cases of TPE gave a positive test leading to a sensitivity of 89.18% and specificity of 84.62%.We obtained a 100% specificity at a cut off value of 63U/L. At this value, the sensitivity decrease to a low 67.57%. In some works ADA cut off 40 U/L indicatestubercular pleural effusion with sensitivity 81 to 100% and specificity 83 to 100% (Muranishi *et al*., 1992; Valdes *et al*., 1993), while some other workers have shown that this cut-off denotes a still higher sensitivity of 90 - 100% and specificity of 89 - 100% (Roth, 1999). In conditions like empyema, lymphoma, malignancy, parapneumonic or collagen vascular disease False positive cases may be reported (Valdes *et al*., 1993; Ocana *et al*., 1988). In our study when we used a combination criteria of ADA 40U/L and a lymphocyte percentage >50% the sensitivity decreased to 83.78% but the specificity increased to 96.15%. PPV also increase to 98.41% like the observation of Oliveria *et al*. (1994) they used a combined criteria of ADA 40U/L & 50% Lymphocytes, they observed a sensitivity of 90.7% and specifity of 97.7%.

Conclusion

We conclude that India has a high prevalence of tuberculosis and for this population sensitivity and specificity also will be high for ADA test. As ADA estimation is a simple, rapid, low cost, and non-invasive it should become an integral part of the diagnostic work up of exudative pleural effusions in suspected cases of tuberculosis.

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