Original Research Article

Role of thoracoscopic pleural biopsy in low Adenosin DeAminase pleural effusions: A hospital based cross sectional study

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Abstract

Background: To obtain the good amount of specimen by biopsy for proper diagnosis, thoracoscopy is a very good tool. Using thoracoscopy the diagnostic accuracy can reach 100% whereas the diagnostic accuracy of the closed pleural biopsy is around 51-79%.
Aim: To study role of thoracoscopic pleural biopsy in low Adenosin DeAminase pleural effusions.
Material and Methods: A hospital based cross sectional study was carried out among 50 study subjects aged > 45 years. All were cases of pleural effusion. Thoracoscopic pleural biopsy was performed in all cases. The samples were sent for histopathology after biopsy.
Results: Majority of the study subjects were found to be in the age group of 45-55 years i.e. 60%. Males outnumbered females as the pleural effusion may be more common in males above the age of 45 years than among the females. Tuberculosis was more in females (60%) than males (40%). But malignancy – adenocarcinoma spreading to pleura was more common in males (90.5%) than females (9.5%). Only one female was found to have Meigs syndrom (ovarian tumor with secondaries pleura). Mesothelioma was seen in three cases and all of them were males. Normal histopathology finding was seen in five cases and all of them were males. It has been documented that pleural effusion due to tuberculosis was more common in females in the present study.

Conclusion: Thoracoscopic pleural biopsy diagnostic yield is high. Low ADA level in pleural fluid does not rule out kochs, incidence more in females.

Key words

Biopsy, Pleural effusion, Histopathology, Diagnostic yield.

Introduction

Pleural effusion is not so uncommon. It has varying causes. Acute diseases like pneumonia can lead to "Neutrophilic predominant exudative effusions". Lymphocytic effusions can be due to a variety of etiologies. But in tuberculosis high burden countries like India, the most common diagnosis of the lymphocytic pleural effusion which can be made is either tuberculosis or malignancy [1].

To find out the causes of exudative type of the pleural effusions, analysis of the pleural fluid as well as closed pleural biopsy are commonly used. Pleural fluid culture method is not found to be sufficient to diagnose that pleural effusion is due to tuberculosis as it gives only 36% of the accuracy. Biopsy gives best results. The problems associated with biopsy are that it is an invasive type of the procedure, and it takes a long time to give the results. Therefore use of "Pleural fluid adenosine deaminase (ADA)" to find out the causes of the pleural effusion is becoming more and more common now a days. It has more advantages like it is cheap, gives quick results, it is associated with more accuracy and at the same time it has a sensitivity of nearing 100% and useful especially to diagnose the pleural effusion due to tuberculosis [2].

ADA is an enzyme. It acts as a catalytic in the process of formation of inosine from adenosine. It has been found that ADA "plays an important role in the differentiation of lymphoid cells." Its activity is high in diseases in which cellular immunity is stimulated. Different cut off values of ADA ranging from 30–100 IU/L have been used in various studies, with differing sensitivities and specificities [3].

Tuberculosis prevalence has been reported to be different from different studies and this has been attributed to the adoption of different methods for analysis of the ADA samples. But these studies have noted that there is a positive association between CD4 lymphocyte counts and pleural ADA levels. These studies also observed that there is a positive association between pleural effusion due to tuberculosis and low ADA levels [4].

Patients with kidney disease of chronic nature usually have pleural effusion. It is due to variety of causes like overload of the fluids, low protein levels in the blood, heart failure, infections due to bacteria, tuberculosis and improper dialysis. Most patients in country like India are usually given anti-Koch treatment as tuberculosis is the leading cause of pleural effusions [5].

Pleural fluid analysis for tuberculosis is less sensitive. But ADA levels for the diagnosis of the pleural tuberculosis is more sensitive and very specific. But the sensitivity and specificity of the ADA is decreased in cases that have uremia. Uremia does not decrease even after hemodialysis [6]. To obtain the good amount of specimen by biopsy for proper diagnosis, thoracoscopy is a very good tool. Using thoracoscopy the diagnostic accuracy can reach 100% whereas the diagnostic accuracy of the closed pleural biopsy is around 51-79% [7].

Present study was carried out to study role of thoracoscopic pleural biopsy in low Adenosin DeAminase pleural effusions.

Materials and methods

Study design: Present study was hospital based cross sectional study.

Study place: Present study was carried out at Department of Pulmonary Medicine, Malla Reddy Medical College for Women, Quthbullapur, Medchal, Telangana, India.

Study duration: Present study was carried out over a period of six months from March 2018 to September 2018.

Sample size: During the study period of one year, it was possible to include 50 adults above the 45 years as per the inclusion and exclusion criteria laid down for the present study.

Inclusion criteria

- Age > 45 years
- ADA level < 30 IU/lit

Exclusion criteria

- Age < 45 years
- ADA level > 30 IU/lit
- Patients not willing to participate in the present study

Ethical considerations

The study proposal was submitted to the scientific research committee for primary approval. After approval from the scientific research committee of the Institute, the study proposal was submitted to the Institutional Ethics Committee for approval. After due presentation of the study proposal, the study protocol was approved. During the actual study, after the children eligible for the study were identified, their parents were contacted for due informed consent and it was obtained.

Methodology

We selected 50 cases of pleural effusions, of age > 45 years, 30 were male and 15 were females. Pleural fluid is exudate (as per lights criteria), with ADA (adenosin de aminase) level less than 30IU/LIT. As high ADA level > 45 is one of the diagnostic feature of TB pleural effusions. So we selected exudative pleural effusion with low ADA, and subjected for thoracoscopy under sedation. Instrument was 10 mm storz rigid thoracoscopy. We performed thoracoscopy under sedation, 8 bits of parietal pleura taken from suspecious sites, and also from posterior diaphragmic resess of pleura and sent for histopathology and TB GENE X PERT analysis. All the procedures were uneventful.

Results

Table - 1 shows distribution of study subjects as per age. Majority of the study subjects were found to be in the age group of 45-55 years i.e. 60%. In the age group of 56-65 years, there were 20% of the study subjects and in the age group of more than 65 years, there were 20% of the study subjects.

Table - 1: Distribution of study subjects as per age.

Age (years)	Number	%
45-55	30	60
56-65	10	20
> 65	10	20
Total	50	100

Table - 2: Distribution of the study subjects as per sex.

Sex	Number	%
Male	35	70
Female	15	30
Total	50	100

Table - 2 shows distribution of the study subjects as per sex. There were 35 (70%) male study subjects and 15 (30%) female study subjects. Thus males outnumbered females as the pleural effusion may be more common in males above the age of 45 years than among the females.

Table - 3 shows distribution of the study subjects as per histopathology findings. Tuberculosis was more in females (60%) than males (40%). But malignancy – adenocarcinoma spreading to pleura was more common in males (90.5%) than females (9.5%). Only one female was found to have Meigs syndrom (ovarian tumor with secondaries pleura). Mesothelioma was seen in three cases and all of them were males. Normal histopathology finding was seen in five cases and all of them were males.

Table - 3: Distribution of the study subjects as per histopathology findings.

Histopathology findings	Male		Female		Total	
	Number	%	Number	%	Number	%
Caseating granulomas, with Tb gene test strongly positive	08	40	12	60	20	40
Malignancy – adenocarcinoma spreading to pleura	19	90.5	02	9.5	21	42
Meigs syndrom (ovarian tumor with secondaries pleura)	0	0	01	100	01	02
Mesothelioma	03	100	0	0	03	06
Normal	05	100	0	0	05	10
Total	35	70	15	30	50	100

Table - 4: Incidence of tuberculosis with low ADA.

Histopathology and gene test positive for tuberculosis	Male		Female		Total	
	Number	%	Number	%	Number	%
Positive for tuberculosis	08	22.9	12	80	20	40
Negative for tuberculosis	27	37.1	03	20	30	60
Total	35	70	15	30	50	100

Table - 4 shows incidence of tuberculosis with low ADA. Tuberculosis tested positive in 20 subjects (40%) of the total study subjects. Out of them, it was more common in females 12 (80%) compared to only eight cases i.e. 22.9% of the males. Thus it has been documented that pleural effusion due to tuberculosis was more common in females in the present study.

Discussion

We found that majority of the study subjects were found to be in the age group of 45-55 years i.e. 60%. Males outnumbered females as the pleural effusion may be more common in males above the age of 45 years than among the females. Tuberculosis was more in females (60%) than males (40%). But malignancy – adenocarcinoma spreading to pleura was more common in males (90.5%) than females (9.5%). Only one female was found to have Meigs syndrom (ovarian tumor with secondaries pleura). Mesothelioma was seen in three cases and all of them were males. Normal histopathology finding was seen in five cases and all of them were males. It has been documented that pleural effusion due to tuberculosis was more common in females in the present study.

Tay TR, et al. [8] found that the mean value of ADA taken from pleural fluid was more in pleural effusion due to tuberculosis cases compared to cases without pleural effusion without tuberculosis and this was statistically significant. ADA of pleural fluid was found to be associated with protein from pleural fluid, age, LDH. Age was strongly correlated. The sensitivity of ADA from pleural fluid was 95.1% at a level of 72 IU/L. The authors concluded that as the age increased, the ADA from the pleural fluid decreased significantly. Hence the authors recommended that for elderly cases, lower cut off should be used.

Kumar S, et al. [9] studied 107 patients with thoracocentesis. Out of them, 45 patients were diagnosed with pleural effusion of transudative type and 62 patients were diagnosed with pleural effusion of exudative type. Out of those 62 patients, thoracoscopy was done in 26 cases. Out of these 26 cases, pleurisy due to tuberculosis was found in six patients. The authors concluded that in patients with chronic kidney disease, uremia is the leading cause of pleural effusion in countries with high burden of tuberculosis. Thoracoscopy is useful in such cases.

Sakuraba M, et al. [10] carried out biopsy of the pleural region using thoracoscopy in 138 patients. They concluded that in pleural effusion patients and having ADA levels < 50 IU/L there is high probability of occult tuberculosis. There is chance that these patients may be diagnosed with non-specific pleurisy.

Arnold DT, et al. [11] found that pleural effusion due to tuberculosis was present in 2% of the 338 cases studied. All these cases were having predominance of lymphocytes. The ADA levels were increased. They concluded that if the pfADA levels are more than 35 IU/L then mycobacterium tuberculosis should be suspected.

Pandit S, et al. [12] observed in their study that among the elderly population, the rate of malignancy was more than that of tuberculosis. In the absence of thoracoscope, cytology of the pleural fluid and biopsy from pleural area can be useful. They noted that if the ADA level is more than 70 IU/L then the diagnosis of tuberculosis is almost certain.

Boutin C, et al. [13] noted that where all other tests fail or likely to fail, diagnostic thoracoscopy should be used. The uncertainty can be reduced from 20% to less than 4% in the diagnosis of etiology specific pleural effusions. Thoracoscopic procedure in not time consuming and the rate of complications is comparatively lesser.

Thomas M, et al. [14] in their study carried out in Qatar found that in 84.5% of the cases of pleural effusion of exudative nature the most common cause was tuberculosis. Younger age group was commonly affected. Most of them were males. The diagnostic accuracy of thoracoscopy was 91.4%. Almost 5.2% of the cases, the cause was malignancy. There were no thoracoscopy related complications except minor bleeding in one or two cases. Thus the authors concluded that thoracoscopy was safe.

Conclusion

Thoracoscopic pleural biopsy diagnostic yield is high. Low ADA level in pleural fluid does not rule out kochs, incidence more in females. Males with age > 45 with low ADA – malignancy should stongly be suspected. Tissue gene x pert analysis is very good diagnostic test to confirm TB, is matching 100% with histopathology diagnosed TB cases.

References

1. Liam CK, Lim KH, Wong CM. Causes of pleural exudates in a region with a high incidence of tuberculosis. Respirology, 2000 Mar; 5(1): 33-8.
2. Valdés L, San José E, Alvarez D, Sarandeses A, Pose A, Chomón B, et al. Diagnosis of tuberculous pleurisy using the biologic parameters adenosine deaminase, lysozyme, and interferon gamma. Chest, 1993 Feb; 103(2): 458-65.
3. Gopi A, Madhavan SM, Sharma SK, Sahn SA. Diagnosis and treatment of tuberculous pleural effusion in 2006. Chest, 2007 Mar; 131(3): 880-889.
4. Niwa Y, Kishimoto H, Shimokata K. Carcinomatous and tuberculous pleural effusions. Comparison of tumor markers. Chest, 1985 Mar; 87(3): 351-5.
5. McGrath EE, Anderson PB. Diagnostic tests for tuberculous pleural effusion. Eur J Clin Microbiol Infect Dis., 2010 Oct; 29(10): 1187-93.
6. Pai M, Flores LL, Hubbard A, Riley LW, Colford JM Jr. Nucleic acid amplification tests in the diagnosis of tuberculous pleuritis: a systematic review and meta-analysis. BMC Infect Dis., 2004 Feb 23; 4: 6.
7. Loddenkemper R. Thoracoscopy--state of the art. Eur Respir J., 1998 Jan; 11(1): 213-21.
8. Tay TR, Tee A. Factors affecting pleural fluid adenosine deaminase level and the implication on the diagnosis of tuberculous pleural effusion: a

retrospective cohort study. BMC Infect Dis., 2013; 13: 546.

9. Kumar S, Agarwal R, Bal A, Sharma K, Singh N, Aggarwal AN, et al. Utility of adenosine deaminase (ADA), PCR & thoracoscopy in differentiating tuberculous & non-tuberculous pleural effusion complicating chronic kidney disease. Indian J Med Res., 2015 Mar; 141(3): 308–314.
10. Sakuraba M, Masuda K, Hebisawa A, Sagara Y, Komatsu H. Pleural effusion adenosine deaminase (ADA) level and occult tuberculous pleurisy. Ann Thorac Cardiovsc Surg., 2009 Oct; 15(5): 294-6.
11. Arnold DT, Bhatnagar R, Fairbanks LD, Zahan-Evans N, Clive AO, Morley AJ, et al. Pleural Fluid Adenosine Deaminase (Pfada) in the Diagnosis of Tuberculous Effusions in a Low Incidence Population. PLoS One, 2015; 10(2): e0113047.
12. Pandit S, Chaudhari AD, Bhuniya S, Datta S, Dey A, Bhanja P. Role of pleural biopsy in etiological diagnosis of pleural effusion. Lung India, 2010 Oct-Dec; 27(4): 202–204.
13. Boutin C, Astoul P, Seitz B. The role of thoracoscopy in the evaluation and management of pleural effusions. Lung, 1990; 168 Suppl: 1113-21.
14. Thomas M, Ibrahim WH, Raza T, Mushtaq K, Arshad A, Ahmed M, et al. Medical thoracoscopy for exudative pleural effusion: an eight-year experience from a country with a young population. BMC Pulm Med., 2017; 17: 151.