HISTOPATHOLOGICAL STUDY OF PLEURA IN 50 CASES OF PLEURAL EFFUSION

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ABSTRACT

BACKGROUND

Pleural effusion is very common worldwide, which is broadly differentiated into exudative and transudative types depending upon various characteristics of fluid. This broad division further classified depending upon aetiology. Main cause of pleural effusion in developing countries including India is tuberculosis. Effusion due to malignancy is also common in India especially among elderly age group individuals. Diagnostic methods include pleural fluid analysis, thoracoscopic studies and pleural biopsy. Histopathological examination of the pleura is very much important in deriving the definitive diagnosis of the pleural effusion.

MATERIALS AND METHODS

50 random cases were selected and made to undergo pleral biopsy with Abrams punch biopsy needle after ruling out bleeding diathesis. Citrated pleural fluid was collected for cytological and biochemical analysisas well. Simultaneously, sample of pleura was sent for histopathological analysis. Based on the presence or nature of mesothelial lining ,a reporting of normal pleura, inadequate for reorting,tuberculous or malignant was done.Sample was also sent for bacteriological studies. Four out of five transudates on biopsy showed normal pleura giving a specificity of 80%.

RESULTS

The age group ranged from 14 to 80 years. Male-to-female ratio was 3:1. Effusions were more frequent on right side as compared to left. Radiologically, all had pleural effusions and sputum for AFB was negative in all cases. Majority of the straw-coloured effusions were tubercular effusions, whereas most of malignant effusions were haemorrhagic. Two-third of these cases showed tubercular granuloma and a small number were found to have malignancy. A significant number (41%) showed nonspecific pleuritis.

CONCLUSION

A definitive diagnosis of tuberculosis or malignancy could be established in 16 (32%) cases by pleural biopsy alone, thus showing a sensitivity of 38%, which enhanced to 40% on combining histopathological and pleural fluid cytological examination.

KEYWORDS

Pleural Effusion, Histopathology.

HOW TO CITE THIS ARTICLE: Naik V, Shanbag N, Bharathraj MY. Histopathological study of pleura in 50 cases of pleural effusion. J. Evid. Based Med. Healthc. 2017; 4(31), 1840-1844. DOI: 10.18410/jebmh/2017/359

BACKGROUND

Pleural effusion is the most common manifestation of the pleural involvement. After routine haematological and radiological investigations, the diagnostic workup of patients with clinically significant pleural effusion usually begins with analysis of pleural fluid analysis after a thoracocentesis. Then, on the basis of whether the fluid is transudate or exudate (according to Light's Criteria), diagnostic insight is provided and further evaluation carried out.[1] Pleural biopsy is helpful to reach an aetiological diagnosis of exudative pleural effusion particularly when malignancy is suspected or when results of detailed pleural fluid study are inconclusive, especially in a setup where thoracoscope is not available. The role of needle biopsy for diagnosis of pleural effusion is well-defined. Multiple pleural biopsies (closed or open) increase the diagnostic potential and subsequent investigations will disclose if these patients are bearers of malignant or granulomatous pleuritis.[2]A significant percentage of pleural effusion remains undiagnosed. In such circumstances, the anatomical-pathological correlation of nonspecific chronic pleuritis should be taken into account mainly by the pneumologist who usually makes the clinical-pathological correlation and infer the final diagnosis. This study was undertaken to study histopathological changes of pleura in pleural effusion and to evaluate the efficacy of pleural biopsy as a diagnostic tool in pleural effusion.

Financial or Other, Competing Interest: None.
Submission 18-03-2017, Peer Review 25-03-2017,
Acceptance 07-04-2017, Published 15-04-2017.
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DOI: 10.18410/jebmh/2017/359

MATERIALS AND METHODS

The present study was undertaken at Karwar Institute of Medical Sciences, Karwar, comprising of 50 cases of pleural effusions admitted during the period from August 2015 to

January 2017. The cases taken up for study were randomly chosen. Patients whose general conditions was not satisfactory for performing pleural biopsy or those who refused to undergo the procedure were omitted from the study. A detailed clinical examination was done in all patients and the clinical data was recorded according to the proforma. Routine investigations were done in all cases including chest x-ray/screening and sputum investigations. After ruling out any bleeding diathesis, pleural fluid aspiration and biopsy were done in all cases. Pleural biopsy was done using Abrams punch biopsy needle in the posterior scapular line in the 8th or 7th intercostal space depending upon the area of maximum dullness. A citrated sample of fluid was sent for cytological evaluation. Simultaneously, a sample was sent for bacteriological studies. The biopsied specimen was sent for histopathological study with 10% formalin.

Criteria for Histopathological Diagnosis

1. **Adequate Pleura**- The biopsy sample was considered to be adequate only when it showed mesothelial lining.
2. **Inadequate Pleura**- When mesothelial lining was not seen inadequate pleura was reported.
3. **Tuberculous Pleuritis**- It was reported when there was collection of epithelioid cells with or without a central caseation focus.
4. **Malignancy**- It was reported when the biopsy showed cells with hyperchromatic nuclei infiltrating between muscle bundles or the mesothelium. The cells could be anaplastic or differentiated.
5. **Nonspecific Inflammatory Changes**- It was reported when chronic inflammatory cells, viz. lymphocytes and plasma cells were seen with early evidence of fibrosis.
6. **Acute Inflammatory Reaction**- It was reported when acute inflammatory changes predominantly polymorphonuclear infiltration was seen.
7. **Normal Pleura**- It was reported when normal mesothelial lining was seen without any inflammatory changes.

RESULTS

Total number of patients studied were 50. The age group of patients ranged from 14 to 80 years. Maximum incidence of pleural effusion was in 31-40 age group, i.e. 15 (30%) cases. Total number of male patients were 38 (76%) and total number of female patients were 12 (24%). Location of effusion 26 patients had right-sided effusion, 22 patients had left-sided effusion and 2 patients had bilateral effusion (Figure 1). Physical appearance of pleural fluid was straw in color in 66% cases, haemorrhagic in 20% cases, clear in 8% cases and 6% cases had turbid pleural effusion (Figure 2). Out of 33 straw-coloured fluid, 2 were due to malignant effusions, 1 was due to CCF. Out of 10 haemorrhagic fluid, 2 were tubercular and 8 were malignant. Out of 3 turbid pleural fluid, 2 were in synpneumonic effusion and 1 in empyema. Clear fluid was found in CCF, nephrotic syndrome, cirrhosis with portal HTN, anaemia and hypoproteinaemia. The total protein content ranged from 1.5 gm% to 6.4 gm%. 41 (82%) cases had protein >3.0 gm%. 9 (18%) cases had protein <3.0 gm%. 22 cases of exudative effusions had cell count more than 1000/mm^3, i.e. 44%. None of the transudates had cell count more than 1000 cells/mm^3. Thus, it is obvious that the classification of exudates on the basis of cell count more than 1000/mm^3 is not reliable. Lymphocytes were predominant (more than 50%) in 40 cases (80%). Neutrophils were predominant in 5 (10%) cases of which two were in pneumonia, 1 was in empyema and 2 in malignancy. Lymphocytic predominance was seen in 50 cases of tubercular effusions and 6 cases of malignancy and 1 case of CCF. No case had significant mesothelial cells in pleural fluid, i.e. more than 1% of cell count, but occasional cells were found in 5 cases. Out of 10 suspected cases of malignant effusion, only two cases proved positive for malignancy. In the remaining cases, no evidence of malignancy could be established even after repeated examination of pleural fluid. Smear for AFB was negative in all cases. Culture of the pleural fluid was positive in three cases among, which Staphylococci in one case with empyema, 1 case had Klebsiella and 1 had pneumococci. Histopathology of pleura showed adequate tissue sample was obtained in 39 cases, i.e. yield was 78%. Inadequate tissue in 11 cases (22%).

Biopsy Diagnosis	Number of Cases	Percentage
Nonspecific Pleuritis (NSP)	16	32
TB pleuritis	11	22
Malignancy	5	10
Acute inflammatory	2	4
Normal pleura	4	8

Table 1. Analysis of Biopsy Diagnosis of Adequate Pleura

Out of the 16 cases of nonspecific pleuritis, tuberculosis formed 14 cases (87.5%) and malignancy formed 2 cases (12.5%).

Diagnosis	Number of Cases	Percentage
Tuberculosis	7	63.6
Malignancy	3	27.2
Pneumonia	1	9.0

Table 2. Analysis of Biopsy Diagnosis of Inadequate Pleura

Case distribution as per diagnosis showed that the study constituted of maximum number of tuberculosis cases with about 64% of cases 20% of cases were due to malignancy ,4% of cases were due to synpneumonic effusion, 4% of cases were due to congestive cardiac failure. Rest of the cases were due to empyema, anaemia, hypoproteinaemia, nephrotic syndrome, cirrhosis, portal hypertension, etc.

Diagnosis	Number of Cases	Positive by HPE	Percentage
Tuberculosis	32	11	34.3
Malignancy	10	5	50.0
Total	**42**	**16**	

Table 3. Analysis of Definitive Diagnosis Arrived by Histopathology alone in TB and Malignancy

Mild pneumothorax was produced in six cases. None required intercostal tube, but resolved spontaneously. In one case, minimal local surgical emphysema occurred.

Complication	Number of Cases	Percentage
Pneumothorax	6	12
Surgical emphysema	1	2
Total	**7**	**14**

Table 4. Complications of Pleural Biopsy

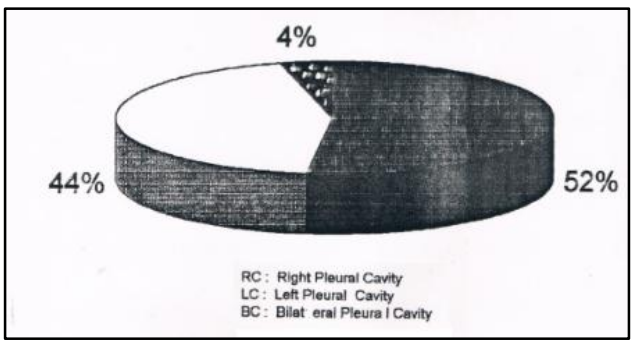

Figure 1. Site of Effusion

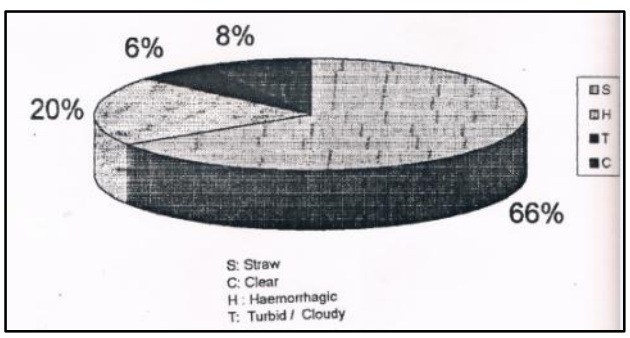

Figure 2. Physical Appearance of Pleural Effusion

DISCUSSION

Fifty cases of pleural effusions selected randomly from the inpatients of Karwar Institute of Medical Sciences were included in the present study. The total number of cases admitted with a diagnosis of pleural effusion from August 1996 to October 1998 were 431. There were 38 males (78%) and 12 females (24%) in the present study. Nakhate V. Rao[3] observed in his 124 patients, 85 males (69%) and 39 females (31%). Thiruvengadam et al[4] in 100 cases had 85 males and 15 females.

	Total Cases	Males	Females
Nakhate V. Rao	124	85 (69%)	39 (31%)
Thiruvengadam	100	85	15
Present study	50	38 (78%)	12 (224%)

Table 5. Sex Distribution of Cases

The preponderance of males in this study is consistent with earlier studies. The age incidence varied between 14 years and 80 years. The mean age being 41.18 years. The maximum cases were between 21-40 years, which is similar to that conducted by Thiruvengadam et al.[4]

	Number of Cases	Age Range	Maximum Incidence
Thiruvengadam et al	100	12-80 yrs.	21-40 yrs.
Present study	50	14-80 yrs.	21-40 yrs.

Table 6. Age Incidence

Right-sided effusions were found in 26 (52%), left sided in 22 (44%) cases and bilateral effusion 2 (4%) of cases. Levallan et al[5] during their study found right-sided effusions in 51%, left-sided in 45.3% and bilateral in 4.75, so also Poe et al found right-sided effusion in 53.65 and left-sided effusion in 44% of cases.

	Number of Cases	Right	Left	Bilateral
Lev Allen	150	51%	45.3%	4.7%
R. Poe	80	53%	44.0%	1.0%
Present study	50	52%	44.0%	4.0%

Table 7. Side of Effusion

The results of predominance of right-sided effusions is similar to above studies.

Clinical Diagnosis on Admission

In the present study, out of 50 cases, 32 cases were due to tubercular effusion (64%) and in 10 cases (20%), malignant effusion was suspected. Among the studies conducted in India, the incidence of tuberculosis was 65% in studies by Thiruvengadam, 57.5% by Chouti and 74.6% by Rajkondawar. The high incidence of tuberculosis found in the present study is consistent with similar other Indian studies.

Investigative Findings

The haemoglobin ranged from 2.5 gm to 5 gm indicating a mild degree of anaemia. This was probably attributable to their low socioeconomic status. Also, many had round worm and Ancylostoma infestations. Four cases had radiological evidence of pulmonary tuberculosis. Berger et al[6] found associated parenchymal involvement in 18 cases out of 42 tuberculous pleurisy (37%). Sibley found this association in 15% of TB cases. One case showed mass lesion in the corresponding side of effusion and one case showed evidence of collapse consolidation of upper lobe among the 10 malignant cases. None of the cases tested positive for sputum AFB. But, Herbert Berger[6] demonstrated tubercle bacilli in sputum or gastric contents in 12 (30%) out of 40 cases. Ten of these patients had visible pulmonary lesions on their chest roentgenograms. Mantoux test was not done in the present study because it is positive in more than 30% of the Indian population above the age of 30 years since tuberculosis is endemic in our country. This finding is confirmed by Thiruvengadam et al (1965) and Levine et al (1967). Specific gravity estimations were also not done as they have been documented to be often quite inaccurate as it is dependent on many factors like temperature changes, hydrometric variation and other factors and is not reliable.

Protein Content

The protein content ranged between 1.5 gm/dL to 6.4 gm/dL. In 41 (82%) cases, the proteins was more than 3.0 gm/dL and in 9 (18%) cases less than 3.0 gm/dL. In 5 cases of exudates, the protein was less than 3.0 gm/dL, but all cases of transudates had protein content less than 3.0 gm/dL in the present study giving a high specificity for transudate classification. Carr and Pawar were misclassified by estimating protein alone. According to study conducted by M. Lakhotia et al (1996)[7] comparing biochemical parameters in pleural effusions. The sensitivity of pleural protein to classify exudates is 94% and to detect transudate is 100%.

Sugar Content

The sugar content in pleural fluid ranged from 40 mg/dL to 119 mg/dL. In 6 cases (18%) of tuberculous effusions, the blood sugar was more than 80 mg/dL and 6 cases had sugar less than 60 mg/dL. Thus, the pleural fluid glucose is not a reliable indicator of tuberculosis effusions. This is in agreement with Light et al (1973) and others. In 5 (50) cases of malignancy, the pleural fluid sugar was less than 60 mg% indicating that glucose level tends to be low in malignancy. In only one (10%) case, the sugar level was more than 80 mg/dL. Also, the sugar was low (<60 mg/dL) in parapneumonic effusions (2 cases). This has been documented by Alfred F. Connors[8] and our findings are similar to this.

Cell Counts

In the present study, 20 cases (40%) showed cell count more than 1000 cells/mm^3. Lymphocytes were predominant (more than 50% cells) in over 80% of cases and polymorphs predominant in less than 11% of cases. Lymphocytic predominant in less than 11% of cases. Lymphocytic predominance was found in equal proportions of tubercular and malignant effusions. But in addition, RBCs were found in plenty in malignant effusions.

Malignant Cells

In the present study, only 2 cases (20%) showed positive findings of malignant cells. Light et al found 77% positivity, and in some studies, it is documented that the percentage of positivity increases with multiple examinations. But, in present study, multiple examinations yielded no better results.

Pleural Fluid Culture

This was positive in three cases. Staphylococcus aureus was cultured from patient diagnosed as emphysema. Klebsiella and pneumococci were cultured from two cases with parapneumonic effusions.

AFB could not be cultured because of its long duration and laborious procedure. None of the pleural fluid samples were positive for AFB stain either.

Benjamin P.K. et al (1970) had 25% positivity and Sibley had 70% positivity of pleural fluid for AFB culture and AFB stain combined together.

Histopathology of Pleura (Pleural Biopsy)

Adequate tissue could be obtained in 38 (78%) cases. Of these, 11 cases (22%) showed tubercular pleuritis, 5 cases (10%) showed malignant cells, 16 (32%) showed nonspecific pleuritis, 2 (4%) showed acute inflammatory changes and in 4 cases the pleura was normal.

The diagnostic yield in our study using Abram's pleural punch biopsy was 78%. Biopsy was repeated on only 2 occasions where one showed evidence of malignancy and the other was reported as inadequate pleura.

According to J.C. Suri et al,[9] yield of first biopsy was 60.87%. However, this rose to 72.83% and 90.48%, following the second and third biopsies, respectively. On combining cytology and biopsy, the diagnostic yield rose to 94%.

In the present study, 5 cases (50%) were diagnosed to be malignant and this rose to 60% combining biopsy and cytology findings.

Only 11 cases showed positive findings of tuberculosis of 32 cases of tubercular effusions. The sensitivity being 34%.

Five cases showed biopsy findings suggestive of malignancy out of 10 malignant effusions giving a sensitivity of 50%.

Authors	Number of Cases	Biopsy Diagnosis of TB or Malignancy	Sensitivity
Donohoe et al	78	30	38.46%
Mestitz et al	200	104	52%
Legghat et al	20	12	60%
Hampson et al	118	49	41.5%
Thiruvegadam et al	100	50	50%
Present study	50	16	32%

Table 8. Comparing the Sensitivity of the Biopsy Procedure with Various Authors

Authors	Number of Cases	Instrument	M	TBP	NSP	NP	IAP	Yield	%
Donohoe et al	78	VS	8 10.2%	22 28.2%	29 37.1%	1	18	60	76
Mestitz et al	200	Abr	33	71	92	-	4	196	98
Leggat et al	20	Abr	12	-	7	-	1	19	85
Carpenter et al	47	Crp	13	1	26	3	4	43	91

Niden et al	44	Copr	16	4	20	3	1	43	97
Hampson et al	118	Abr	25	24	65	-	4	114	96
Thiruvengadam et al	100	Abr	17	33	4	-	5	94	94
Suri et al	155	Cope	18	86	15	-	25	129	83
Ratnakar and Maiya	25	Abr	1	15	6	-	3	22	84
Present study	50	Abr	5	11	16	4	12	38	76

Table 9. Summary of Previously Reported Needle Biopsies

Complications

In the present study, complications occurred in 7 patients (14%). In 6 cases, there was minimal pneumothorax, which did not require intercostal drainage. In one case, there was surgical emphysema. The complications encountered during pleural biopsy are comparable with those occurring with thoracentesis.[10,11,12] According to Anthony S. Floreni,[10] the most frequent complication of pleural biopsy is pneumothorax, which occurs in 3 to 20% of the time. There were no major complications seen during the present study.

CONCLUSION

Histopathological study of pleura is a useful tool in the aetiological diagnosis of pleural effusions particularly in exudative pleural effusions such as tuberculosis and malignancy. Closed pleural biopsy using the Abram's pleural punch biopsy needle is a simple, effective and safe procedure. Nonspecific inflammatory changes does not rule out tuberculosis or malignancy. Hence, histopathological findings should be correlated with other investigative procedures to arrive at the aetiological diagnosis of pleural effusions. Pleural biopsy is of limited value in transudative effusions and may help in excluding other coexisting disease.

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