Diagnostic yield of closed pleural biopsy in exudative pleural effusion

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ABSTRACT

Objectives: Closed pleural biopsy is known to be diagnostic in approximately 75% of pleural effusion undiagnosed by thoracocentesis or pleural fluid evaluation. The purpose of this study was to determine the efficacy of closed pleural biopsy in a Saudi tertiary care teaching hospital.

Methods: We retrospectively reviewed the diagnostic utility of all closed pleural biopsies performed from January 1988 to December 1997 at the King Fahad National Guard Hospital, Riyadh, Kingdom of Saudi Arabia.

Results: One hundred and twenty-two pleural biopsies were performed in 116 patients using cope needle in 39, Abram's needle in 82, and Trucut needle in one patient. Twelve cases were excluded due to transudative effusion (N=6) and obtaining no pleural tissue (N=6). Specific diagnoses were obtained in 54 cases giving a diagnostic yield of 49.1%. Of these 10 revealed neoplasia, 35 tuberculosis, and 9 empyema. A non-specific diagnosis was obtained in 56 (50.9%) cases.

Conclusion: By closed pleural biopsy 49.1% of undiagnosed exudative pleural effusions could be diagnosed. This shows that closed pleural biopsy is still of value as a diagnostic procedure, and should be carried out prior to invasive procedures such as thoracoscopy or open pleural biopsy.

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Pleural effusion, an abnormal accumulation of fluid in pleural space, develops as a common complication of many systemic and localized diseases[1] which include congestive heart failure, tuberculosis (TB), malignancy, empyema thoracis, parapneumonia and pulmonary embolism.[2,3] While the cause may often be evident from the underlying condition, it may be uncertain in many cases, particularly unilateral effusions, thus necessitating further diagnostic interventions.[4] Of pleural effusions, the exudative effusions which are usually of infectious origin in youth and malignant in aged,[2,5] are the most difficult to diagnose and require an extensive workup with many invasive and non invasive procedures, including pleural biopsy.[1,6] Diagnostic yield of pleural fluid analysis alone is low for TB and though sensitive for detecting malignancy, it is non-specific. Hence, pleural biopsy may be needed to obtain more tissue for definite histologic and bacteriologic analysis.[7-10] Major indications for closed pleural biopsy include a pleural effusion undiagnosed by routine analysis, evaluation of focal or diffuse pleural thickening or pleural masses, however, American Thoracic Society narrowed this indication to an undiagnosed pleural effusion suspicious for pleural TB or malignancy.[11] Closed needle biopsy of the pleura has been an important diagnostic tool since its first description by DeFrancis et al[12] in 1955 using Vim Silverman needle. Many modifications of the original needle have been used since then in an effort to obtain better biopsy specimens,[13-15] but the most popular ones are the Cope[16] and Abrams[17] needles. As early as 1960s, Kettel and Cugell[4] suggested that pleural biopsy should be a routine procedure. The refinements by Abrams[17] and Cope[16] simplified the technique, making the procedure a customary practice, with 98% of practicing pulmonologists in the United States of America (USA)

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performing pleural biopsy.[18] The objective of the present study was to determine the efficacy and diagnostic reliability of closed pleural biopsies performed from January1988 to December 1997 at the King Fahad National Guard Hospital, Riyadh, Kingdom of Saudi Arabia (KSA).

Methods. King Fahad National Guard Hospital where this study was carried out is a 560 bedded tertiary teaching hospital, and a major referral center for patients with pulmonary and pleural disorders. The study was a retrospective one, covering all patients on whom one or more closed pleural biopsy procedures were performed by Certified Pulmonologists for the diagnosis of pleural effusion during a period of 10 years from January 1988 to December 1997. The patients selected for closed pleural biopsy included (i) those having the generally accepted criteria of an exudative pleural effusion, and (ii) those for whom a thorough history, physical examination and the usual biochemical and laboratory (including acid-fast stains), cultural and cytological studies of pleural fluid and sputum were not diagnostic. The pleural biopsy specimens were sent for histopathologic and bacteriologic studies. Approximately 35 pleural biopsy specimens were not sent for *Mycobacterium tuberculosis* (*M. tuberculosis*) culture. Six of the cases with inconclusive initial biopsy had a repeat biopsy. The data were collected on patient's demographics and other variables such as underlying illness, character of the pleural fluid, number of pleural biopsies, histopathology and bacteriology reports. Complications following pleural biopsy were also recorded by taking inspiratory and expiratory chest roentgenograms to identify pneumothorax. The patients were followed up after the biopsy test to determine the causes of the undiagnosed cases. The criteria used for diagnosing the more common causes of exudative pleural effusion were: 1) Tuberculous effusion - exudative effusion with caseating granuloma on pleural biopsy specimen or positive smear for acid-fast bacillus or positive culture for *M. tuberculosis*. 2) Malignant effusion - an effusion associated with malignancy as demonstrated by the histopathological examination of the pleural biopsy specimen. 3) Empyema - the histopathological examination of the biopsy specimen showed a picture of acute inflammation consistent with empyema. Non-specific biopsy result was further followed up by other investigations to determine the specific cause. A biopsy specimen in which pleural tissue could not be identified, was deemed inadequate and not included in the study. Using a decision matrix, we calculated the true positive ratio (sensitivity), true negative ratio (specificity), and both positive and negative predictive values.[19]

Results. During the 10-year-period, 122 pleural biopsies were performed on 116 patients: Cope[16] needle (Randall Fachney, Avon, Massachests, USA) was used in 39 cases (32%), Abrams[17] needle (Harle's Inc, Cincinnati, Ohio, USA) in 82 cases (67.2%) and Trucut needle in one case (0.8%). Twelve biopsies were excluded for the following reasons 1) for being performed in a transudate effusion – 6 2) no pleural tissue obtained – 6. A review of the demographic profile of the 116 patients showed that the mean age group was 57.5 years ranging between 20-88 years. In the study group, 94 (81%) were male and 99 (85.3%) were Saudis. As shown in **Figure 1**, the specific diagnoses were obtained in 54 cases giving an overall diagnostic yield of 49.1%. Of these 54 biopsies, neoplastic diseases were found in 10 (9.1%); the benign diagnoses included 35 cases of TB (31.8%) and 9 cases of empyema (8.2%). No specific diagnosis was obtained on the remaining 56 biospy specimens constituting 50.9% of the biopsies. The follow-up showed a diagnosis of TB in 16 patients and malignancy in 14 patients. Eight patients lost follow-up and 16 remained undiagnosed after further work-up. Two were diagnosed as hydatid disease. Four cases developed pneumothorax giving an overall complication rate of 3.6%; 2 of them required chest tube drainage. No death was reported as a complication of the procedure. As shown in **Table 1**, the sensitivity of closed pleural biopsy for TB was 68.6% and for malignancy was 41.7% and specificity for both was 100%. The positive predictive value was 100% in both and negative predictive value was 76.1% for tuberculosis and 84.8% for malignancy.

Discussion. Closed pleural biopsy is an effective means of obtaining histologic samples of parietal pleura and define further the cause of a pleural effusion that remains undiagnosed after more routine analysis of the pleural fluid.[20,21] It is a minimally invasive, relatively simple and safe technique utilizing local anesthesia, and Cope,[16] Abrams[17] or Trucut needles. Sensitivity of closed pleural biopsy in detecting the 2 major causes of exudative pleural effusion range from 57%-80% for TB and 40%-73% for malignancy[7,9,10,22-26] as shown in various studies. Poe et al[7] reported a sensitivity of 68% and a specificity of 99% with a predictive value of 98% and 77% for positive and negative biopsy specimens. The positive predictive value in the above mentioned study was high as the procedure had a high specificity with few false positive results. Our study showed comparable results (**Table 2**) with sensitivity of 62.7% and specificity of 100% and predictive value of 100% and 33.3% for positive and negative biopsy specimen. In our study, the diagnostic yield of closed pleual biopsy was 49.1% which was less than the percentage reported in the literature. The anticipated low yield is probably due to: not all specimens were sent for microbiological culture for *M. tuberculosis* (approximately 35 biopsies) in our study. This could considerably affect the diagnostic yield for TB. The best sensitivity for pleural biopsy is 80%-95% when combined with pleural biopsy cuture.[9,27] Importantly, culture of the offending bacillus,

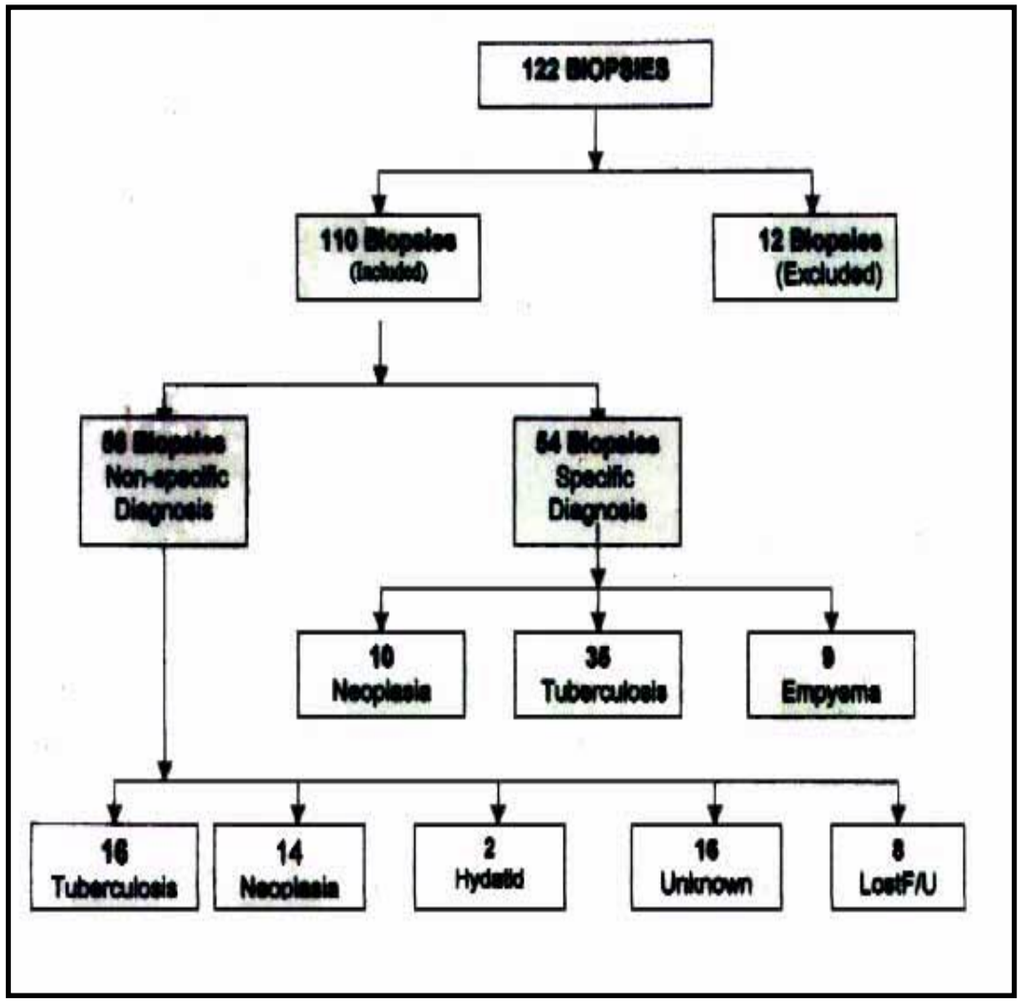

Figure 1 - Results of closed pleural biopsy. F/U - follow up.

Table 1 - Diagnostic value of closed pleural biopsy*

Parameter	Tuberculosis		Malignancy	
	Present	Absent	Present	Absent
Positive	35	0	10	0
Negative	16	51	14	78
Sensitivity (%)	(68.6)		(41.7)	
Specificity (%)	(100)		(100)	
Predictive value				
Positive (%)	(100)		(100)	
Negative (%)	(76.1)		(84.8)	

*patients who lost follow-up (8) are not included for the calculations

Table 2 - Results of initial closed pleural biopsy.

Studies	n patients	Sensitivity	Specificity	Predictive value	
				Positive	Negative
Poe et al[7]*	195	68	99	98	77
Scerbo et al[9]	149	40	100	100	33
VanHoff et al[10]*	265	40	96	98	28
Niden et al[22]	18	73	100	100	43
Hampson and Karlish[23]	114	72	100	100	71
Mestitz et al[24]	138	77	95	99	43
Bueno et al[25]†	414	72	100	100	56
Traczyk et al[26]	160	63	100	100	40.5
Al-Shimemeri et al‡	110	62.7	100	100	33.3

*pleural fluid cytology results are included, †calculations include first thoracocentesis and pleural biopsy results, ‡present study

which can be accomplished with pleural biopsy specimens, is essential for drug sensitivity testing with increasing multiple drug resistance. In our study, repeated pleural biopsy was carried out in 6 patients with inconclusive initial biopsy. Data indicates that repeated pleural biopsy increase the diagnostic yield.[9,10] Kirsch et al[28] found a direct correlation between the sensitivity of closed pleural biopsy and the number of samples submitted, the diagnostic sensitivity of closed pleural biopsy for pulmonary TB is the highest (100%) when more than 6 specimens were obtained which can be expected to contain, on an average, more than 2 samples of parietal pleura. While, Jimenez et al[29] concluded that 81% of pleural TB could be diagnosed with single good sample due to the disseminated nature of the disease which affects different areas more or less homogeneously. On the other hand, in malignant pleural pathology, a single biopsy sample provides a diagnosis of 54%, while the yield was 89% when 4 samples were examined as the pleural involvement is not homogeneous. Several studies have reported closed needle biopsy of the pleural space to be most successful in diagnosing pleural TB and less so for pleural malignancy.[7,20,23] Tomlinson and Sahn[20] from their review of over 2,500 pleural biopsies noted a yield of 75% for pleural TB and 57% for pleural carcinoma. In tuberculous pleural effusions, the reported diagnostic sensitivity of pleural biopsy ranges from 60%-95%.[6,7,9,20,24,27] In our study, the sensitivity for TB was 68.6%. In up to 80% of cases, pleural biopsy produces culture positivity or granulomas. However, granulomas are only presumptively diagnostic of TB given other possible etiologies, such as fungal infections and sarcoidosis.[6] The diagnostic sensitivity of closed pleural biopsy for TB can be improved by combining histology with pleural biopsy culture[7,27] (sensitivity improves to 80%-95%), but this approach requires more samples[28] (at least one biosy for culture). Combining pleural fluid studies with biopsy may push yields to 95%.[6] Missing the diagnosis and opportunity to treat tuberculous pleuritis may lead to pulmonary and extrapulmonary involvement in up to 65% of cases over the subsequent 5 years.[30]

In malignant pleural effusions, the diagnostic value of pleural biopsy is less as compared to the pleural fluid cytology, with cytologic yields ranging from 40%-87%.[1] In our study the sensitivity for malignancy was 41.7%. Loddenkemper et al[31] found a sensitivity of 44% for closed pleural biopsy, 62% for fluid cytology and 95% for thoracoscopy in diagnosing malignant pleural effusions. The limited diagnostic value of pleural biopsy for malignancy can be attributed to the fact that seeding of parietal pleura by the tumor cells is mandatory for biopsy to be positive and the biopsy might have been taken from the unaffected sites.[3,25] Furthermore, if the pleural space is completely drained obtaining a pleural biopsy on a subsequent occasion becomes much more difficult.[21] Another common reason for relative lack of sensitivity of pleural biopsy for the detection of malignancy is due to common occurrence of a histologically diagnosed "non-specific inflammation". This finding is reported in 50%-75% of patients examined by pleural biopsy in most series.[7,9] Menzies and Charbonneau[32] recommend thoracoscopy over closed needle biopsy in such cases as it has an excellent diagnostic yield for malignant pleural disease, with a sensitivity as high as 91%, a specificity of 100%, and a negative predictive value of 93% and it allows direct visualization of both parietal and visceral pleura and biopsy can be taken from grossly affected sites. Another option is the pleural brushings with reported yield of 91%.[33] Salyer et al[8] and Jimenez et al[29] found that simultaneous biopsy and pleural fluid cytology in patients with malignant pleural effusion improved diagnostic yield up to 91%. Serial thoracocentesis increases diagnostic yield of pleural fluid cytology generated by newly shed malignant cells.[8] But pleural fluid analysis cannot subclassify the malignant cell types, important for management of chemosensitive malignancies. Empyema, a pyogenic collection in pleural space commonly follows pneumonia, thoracic surgery or trauma. In our study, empyema was diagnosed in 9 cases on initial closed pleural biopsy. Though not a preferable method for diagnosing empyema, (better diagnosed by pleural fluid examination), the biopsy specimen showed an acute inflammatory picture consistent with empyema. Closed pleural biopsy is related with very low complication rates. Poe et al[7] reported 8% incidence of pneumothorax as complication – but not of much clinical significance and resolved spontaneously. Another study by Bueno et al[25] on the dual diagnostic procedure of thoracocentesis and closed pleural biopsy reported a complication rate of 11% with 10% having pneumothorax (with one third of them requiring chest tube drainage and rest resolving spontaneously) and 1% having subcutaneous emphysema which resolved completely without treatment. In our study the complication rate was as low as 3.6% for pneumothorax. Out of these only 2 required chest tube drainage and the rest resolved spontaneously. Operator experience is key to success.[34] The lower complication rate in our study as compared to other studies could be because the biopsies were performed by Certified Pulmonologists. Only 6 (5.8%) procedures failed to obtain pleural tissue out of the biopsies performed on 116 patients and had to be repeated in our study. There are no absolute contraindications for this procedure, bleeding diathesis is a relative contraindication and needs to be corrected before any invasive procedure.

In conclusion, the high diagnostic yield of closed pleural biopsy especially in TB makes it still a valuable diagnostic procedure, though not a perfect diagnostic test. Culture of the specimen especially for *M. tuberculosis* is a must to enhance the diagnostic yield especially in endemic regions. As was expected tuberculous pleural effusions were more compared to malignant pleural effusions, the reason for this being the endemicity of TB in our population. Repeated biopsies

may increase the sensitivity. Closed pleural biopsy is a low risk procedure with a very low complication rate. Invasive procedures, such as thoracoscopy or open pleural biopsy, should be considered in cases undiagnosed after closed pleural biopsy to further define the causes of undiagnosed exudative pleural effusion.

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