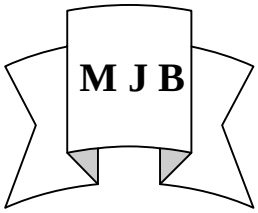
Efficacy of closed pleural biopsy in exudative pleural effusion

Moshtak A. Wtwt - Hadeel F. Farhood



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 exudative pleural effusion in marjan teaching hospital in Hilla.

Methods: We prospectively follow the diagnostic utility of closed pleural biopsies performed from May 2006 to November 2007 at the marjan teaching Hospital, Babylon, Iraq.

Results: fifty two pleural biopsies were performed in 52 patients using Abram's needle to obtain this biopsy. Twelve cases were excluded due to no pleural tissue obtaining .

Specific diagnosis was obtained in 22 cases giving a diagnostic yield of 55%. Of these 14 revealed tuberculosis, 4 neoplasia, & 4 post-pneumonic effusion. A non-specific diagnosis was obtained in 18 cases (45%).

Conclusion: By closed pleural biopsy 55% 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.

الخلاصة

الهدف من الدراسة هو لتقييم كفاءة خزعة الجنب في حالات الإصابة بانصباب الجنب الإفرازي في مستشفى مرجان التعليمي في الحلة . حيث تمت دراسة 52 عينة مأخوذة من غشاء الجنب في 52 مريض مصاب بانصباب الجنب الإفرازي للفترة (أيار 2006 – تشرين الثاني 2007) ،

باستعمال abram's needle للحصول على العينة من خلال الصدر تم استثناء 12 عينة بسبب عدم وجود نسيج جنبي .

حيث تم تشخيص 22 عينة (55%) من الحالات بواسطة هذه الخزعة ، و إن النسبة الكبرى من المصابين بانصباب جنبي يعانون من التدرن بنسبة 35%.

18 عينة (45%) من الحالات لم تصل الخزعة من خلالها إلى تشخيص معين ، لذلك من الأهمية القصوى عمل خزعة الجنب للمرضى المصابين بانصباب الجنب الإفرازي من خلال الصدر قبل عملها بطرق عميقة أكثر من خلال ناطور القصبة الهوائية أو فتح الصدر .

Introduction

Pleural effusion is defined as excess & abnormal fluid accumulation in pleural space[1]. The pleural effusion develops as a common complication of many systemic and localized diseases which include congestive heart failure, tuberculosis (TB), malignancy, empyema thoracis, parapneumonia and pulmonary embolism[2]. Of pleural effusions, the exudative effusions which are usually of infectious origin in youth and malignant in aged, are the most difficult to diagnose and require an extensive workup with many invasive and non invasive procedures, including pleural biopsy[3]. Major Percutaneous pleural biopsies are of greatest value in the diagnosis of granulomatous and malignant disease of the pleura. They are performed on patients with undiagnosed exudative effusions, with non-diagnostic cytology, and a clinical suspicion of tuberculosis or malignancy. Occasionally, a blind pleural biopsy may be performed at the same time

as the first pleural aspiration if clinical suspicion of tuberculosis is high[4]. however, American Thoracic Society narrowed this indication to an undiagnosed pleural effusion suspicious for pleural TB or malignancy[5]. Closed needle biopsy of the pleura has been an important diagnostic tool since its first description by DeFrancis et al in 1955 using Vim Silverman needle [6]. Many modifications of the original needle have been used since then in an effort to obtain better biopsy specimens[7], but the most popular ones are the Cope [8] and Abrams [9] needles. The refinements by Abrams [9] and Cope" simplified the technique, making the procedure a customary practice, with 98% of practicing pulmonologists in the United States of America (USA) performing pleural biopsy [10]. The objective of the present study was to determine the efficacy and diagnostic reliability of closed pleural biopsies performed from May 2006 to November 2007 at the marjan teaching Hospital, Babylon, Iraq.

Methods

At marjan teaching Hospital, this study was carried out. The study was a prospective one, covering 52 patients on whom closed pleural biopsy procedures were performed by Certified special doctor from May 2006 to November 2007. 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. We do a pleural biopsy on those patients (I usually use 6-8 ml of 2% xylocain to anesthetize the selected site, & making a generous incision through it & apply pressure over the site with gauze until the bleeding stops. With the stylet in place, I introduce the outer cannula into the selected site using rotary motion to advance the needle into the chest. A sudden give will indicate that entered the pleural space, then remove the stylet & introduce the biopsy needle which attached to a 50 cc syringe & apply downward & outward pressure until it hooks the parietal pleura. The pleural biopsy specimens were sent for histopathologic studies. The data were collected on patient's demographics and other variables such as underlying illness, character of the pleural fluid, & histopathology of pleural biopsy reports. Complications following pleural biopsy were also recorded by taking inspiratory & expiratory chest X-ray 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) post-pnemonic effusion - the histopathological examination of the biopsy specimen showed a picture of acute inflammation consistent. 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 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.

Results

During the 19-month-period, 52 pleural biopsies were performed on 52 patients: Twelve biopsies were excluded because of inadequate pleural tissue obtained.

A review of the demographic profile of the 52 patients showed that the mean age group was 57.5 years ranging between 20-88 years. In the study group, 43 (85%) were male & 9 (15%) were female. As shown in Figure 1, the specific diagnoses were obtained in 22 cases giving an overall diagnostic yield of 55%. Of these

22 biopsies, neoplastic diseases were found in 4 (10%); the benign diagnoses included 14 cases of TB (35%) and 4 cases of post-pnemonic effusion (10%).

No specific diagnosis was obtained on the remaining 18 biopsy specimens constituting 45% of the biopsies. The follow-up showed a diagnosis of TB in 6 (15%) patients and malignancy in 5(12.5%) patients, 5 patients lost follow-up (12.5%) and 2 (5%) remained undiagnosed after further work-up. One case developed pneumothorax giving an overall complication rate of 2.5%; that 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 70% and for malignancy was 44.5% and specificity for both was 100%. The positive predictive value was 100% in both and negative predictive value was 77% for tuberculosis and 86.1% for malignancy.

Discussion

Closed pleural biopsy is an effective means of obtaining histologic samples of parietal pleura and defines further the cause of a pleural effusion that remains undiagnosed after more routine analysis of the pleural fluid [11]. It is a minimally invasive, relatively simple and safe technique utilizing local anesthesia, and Cope, Abrams[9]. 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 as shown in various studies[12]. Poe et al reported a sensitivity of 68% and a specificity of 99% with a predictive value of 98% and 77% for positive and negative biopsy specimens[13]. 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 70% and specificity of 100% and predictive value of 100% and 77.7% for positive and negative biopsy specimen. In our study, the diagnostic yield of closed pleural biopsy was 55%. The anticipated low yield is probably due to: not all specimens were sent for microbiological culture for *M. tuberculosis* in our study. This could considerably affect the diagnostic yield for TB. Importantly, culture of the offending bacillus, 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 not carried out in patients with inconclusive initial biopsy. Data indicates that repeated pleural biopsy increase the diagnostic yield [14], Kirsch et al 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 [15]. While, Jimenez et al 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 [16]. 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, Tomlinson and Sahn from their review of over 2,500 pleural biopsies noted a yield of 75% for pleural TB and 57% for pleural carcinoma [11].

In tuberculous pleural effusions, the reported diagnostic sensitivity of pleural biopsy ranges from 60%-95% [3,13,]. In our study, the sensitivity for TB was 70%. 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 [3]. The diagnostic sensitivity of closed pleural biopsy for TB can be improved by combining histology with pleural biopsy culture (sensitivity improves to 80%-95%)

[13], but this approach requires more samples (at least one biopsy for culture)[15]. Combining pleural fluid studies with biopsy may push yields to 95%[3]. missing the diagnosis and opportunity to treat tuberculous pleuritis may lead to pulmonary and extra pulmonary involvement in up to 65% of cases over the subsequent 5 years [17].

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% [18]. In our study the sensitivity for malignancy was 44.5%. Loddenkemper et al found a sensitivity of 44% for closed pleural biopsy, 62% for fluid cytology and 95% for thoracoscopy in diagnosing malignant pleural effusions [19]. 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 [12,20]. 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 [13]. Menzies and Charbonneau 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 [22]. Another option is the pleural brushings with reported yield of 91% [23]. Jimenez et al 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, but pleural fluid analysis cannot sub classify the malignant cell types, important for management of chemo sensitive malignancies [16]. Empyema, a pyogenic collection in pleural space commonly follows pneumonia, thoracic surgery or trauma.

In our study, post-pnemonic effusion was diagnosed in 4 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 reported 8% incidence of pneumothorax as complication - but not of much clinical significance and resolved spontaneously [13]. Another study by Bueno et al 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 [12]. In our study the complication rate was as low as 2.5% for pneumothorax, were required chest tube drainage. Operator experience is key to success [24], The lower complication rate in our study as compared to other studies could be because the biopsies were performed by Certified specialist doctor & low number of specimen . Only 6 (2.3%) procedures failed to obtain pleural tissue out of the biopsies performed on 46 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.

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.

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.

References

1. Heffner J, Brown L, Barbieri C. "Diagnostic value of tests that discriminate between exudative & transudative pleural effusions". *Chest* 1997 (4):970-80.
2. Valdes L, Alvarez D, Valle JM, Pose A, San-Jose E. The aetiology of pleural effusions in an area with high incidence of tuberculosis. *Chest* 1996; 109: 158-162.
3. Sahn SA. State of the art: The pleura. Am Rev Respir Dis 1988; 138:184-234.
4. Ferrer A, Osset J, Alegre J, *etal* .Prospective clinical & microbiological study of pleural effusions. Eur J Clin Microbial infects Dis 1999; 18:237-41.
5. Sokolowski JW Jr, Burgher LW, Jones PL Jr, Patterson JR, Selecky PA. Guidelines for thoracocentesis and needle biopsy of the pleura. This position paper of the American Thoracic Society was adopted by the ATS Board of Directors, June 1988. *Am Rev* Respir Dis 1989; 140: 257-258.
6. DePrancis N, Kiosk E, Albano E. Needle biopsy of the parietal pleura. N Engl J Med 1955; 252: 948-949.
7. Ballestero RJ. A new reliable instrument for pleural biopsy. Chest 2000; 61:303-304.
8. Cope C. New pleural biopsy needle. JAMA 1958; 167: 1107-1108.
9. Abrams LD. A pleural-biopsy punch. Lancet 1958; 1:30-31.
10. Tape TO, Blank LL, Wigton RS. Procedural skills of practicing pulmonologists. A national survey of 1,000 members of the American College of Physicians. Am J Respir Crit Care Med. 1995; 151:282-287.
11. Tomlinson JR, Sahn SA. Invasive procedures in the diagnosis of pleural disease. Semin Respir Med 1987; 9: 30-36.
12. Bueno CE, Clemente MG, Castro CB, Martin ML, Ramos RS, Panizo GA et al. Cytologic and bacteriologic analysis of fluid and pleural biopsy specimens with cope's needle. Arch Intern Med 1999; 150: 1190-1194.
13. Poe RE, Israel RH, Utell MJ, Hall WJ, Greenblatt DW, Kallay MC. Sensitivity, specificity, and predictive values of closed pleural biopsy. Arch Intern Med 1984; 144: 325-328.
14. VanHoff DD, LiVoIsi V. Diagnostic reliability of needle biopsy of the parietal pleura: a review of 272 biopsies. Am J Clin Pathol 1975; 64:200-203.
15. Kirsch CM, Kroe M, Azzi RL, Jensen WA, Kagawa FT, Wehner JH. The optimal number of pleural biopsy specimens for a diagnosis of tuberculous pleurisy. Chest 1997; 112/3: 702-706.
16. Jimenez D, Perez-Rodriguez E, Diaz G, Fogue L, Light RW. Determining the optimal number of specimens to obtain with needle biopsy of the pleura. Respir Medicine 2002; 96: 14-17.
17. Roper W, Waring JJ. Primary serofibrinous pleural effusion in military personnel. Am Rev Tuber Pulm Dis 1995; 71: 616-635.
18. Light RW. Pleural diseases. 3rd ed. Baltimore (MD): Williams & Wilkins;1995.p.95- 116.
19. Loddenkempcr R, Grosser H, Gabler A, Mai J, Preussler H, Brandt HJ et al. Prospective evaluation of biopsy methods in the diagnosis of malignant pleural effusions: intrapatient comparison between pleural fluid cytology, blind needle biopsy and thoracoscopy. ACT Rev Respir Dis 1983; 127(suppl4): 114.
20. Nance KV, Shermer RW, Askin FB. Diagnostic efficacy of pleural biopsy as compared with that of pleural fluid examination. Mod Pathol 1991; 4: 320-324.
21. Hall WJ, Mayewski RJ. Developed for the Health and public policy committee, American college of Physicians, Philadelphia, Pennsylvania. Diagnostic thoracocentesis and

pleural biopsy in pleural effusions. Ann Intern Med 1985; 103: 799-802.

22. Menzies R, Charbonneau M. Thoracoscopy for the diagnosis of pleural disease. Ann Intern Med 1991; 114:271-276.

23. Emad A, Rezaian GR. Closed percutaneous pleural brushing: a new method for diagnosis of malignant pleural effusions. Respir Med 1998; 92: 659-663.

24. Walsh LJ, Macfarlane JT, Manhire AR, Sheppard M, Jones JS et al. Audit of pleural biopsies: an argument for a pleural biopsy service. Respir Med 1994; 88: 503-505.

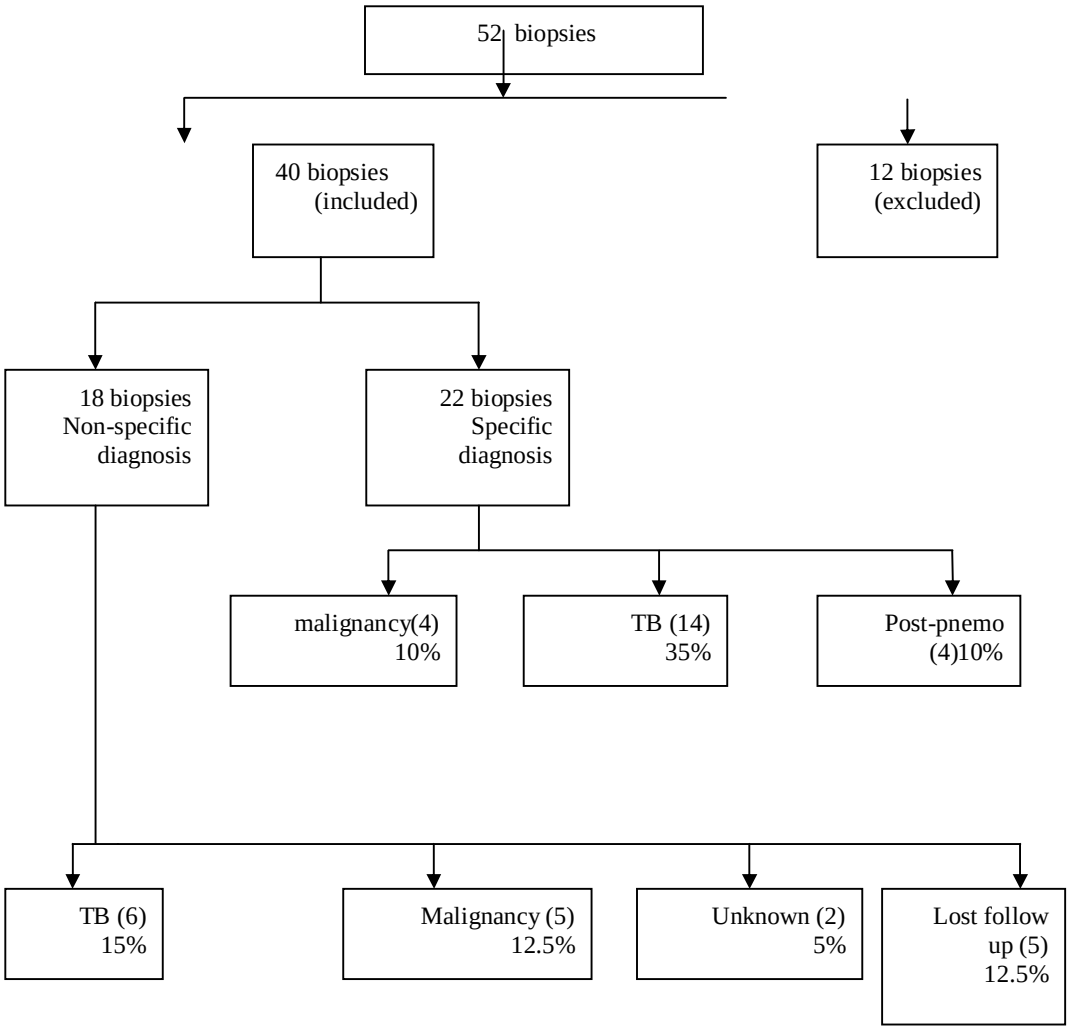


Figure 1- Results of closed pleural biopsy .

Table 1- diagnostic value of closed pleural

Parameter	TB		malignancy	
	Present	absent	present	absent
Positive	14	0	4	0
Negative	6	20	5	31
Sensitivity(%)	(70)			(44.5)
Specificity(%)	(100)			(100)
			Predictive value	
Positive(%)	(100)			(100)
Negative(%)	(77)			(86.1)

Table 2- results of initial closed pleural

Studies	n patients	sensitivity	specificity	predictive value + ve	-ve
Poe et al	195	68	99	98	77
VanHoff et al	265	40	96	98	33
Karlish	114	72	100	100	71
Mestitz et al	138	77	95	99	43
Bueno et al	414	72	100	100	56