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Received: 22 June 2012

Revised: 15 Oct 2012

Accepted: 13 Nov 2012

Approach to undiagnosed exudative pleural effusion: the diagnostic yield of blind pleural biopsy

Abstract

Background: Blind percutaneous pleural biopsy has traditionally been performed to investigate the etiology of exudative pleural effusion in which the initial thoracentesis has been non-diagnostic. In view of the increasing use of image-guided and thoracoscopic pleural biopsies, this study examined the role of blind Abrams pleural biopsy in the investigation of the exudative pleural effusion in the largest tertiary pulmonary center in Tehran, Iran.

Methods: All patients with pleural effusion admitted from September 2007 to April 2009 entered in this study. The patients with exudative pleural effusion underwent blind Abrams pleural biopsy when the initial thoracentesis was non-diagnostic. The patients with non-diagnostic blind biopsy underwent surgical biopsy or other investigations based on the physician's decision. The data were collected and analyzed.

Results: Blind percutaneous pleural biopsy was performed in 171 patients. Malignancy was diagnosed in 56 and tuberculosis in 52 cases with blind biopsy. For all the diagnoses, blind biopsy had a sensitivity of 70.1% and negative predictive value of 14.8%. For malignant diagnosis, the sensitivity value was 58.9%, specificity 100% and negative predictive value 63.2%. For TB diagnosis, sensitivity value was 88.1%, specificity 100% and negative predictive value 93.6%. The overall malignancy was diagnosed in 95 (58.6%) and TB in 59 (36.4%) patients.

Conclusion: Blind Abrams needle biopsy was diagnostic in approximately three out four patients presented with undiagnosed exudative pleural effusion. The data support the use of the Abrams needle in the investigation of pleural effusion especially in the less developed countries.

Keywords: Abrams needle, Pleural biopsy, Pleural effusion, Malignancy, Tuberculosis

Caspian J Intern Med 2013; 4(2): 642-647

Exudative pleural effusions are common in the clinical practice of both respiratory and non-respiratory specialists. The most common causes of undiagnosed exudative pleural effusion are tuberculosis and malignancy. To find out the cause of pleural effusion, biochemical, cytological and microbiological analysis of pleural fluid is a common practice. It may provide good diagnostic evidence for para-pneumonic effusion, however this initial analysis can not detect many cases of tuberculosis and malignancy. Pleural biopsy provides diagnostic evidence for both tuberculosis and malignancy. Biopsy has traditionally been performed blindly using an Abrams needle (1). The Abrams needle biopsy was found to be easy to perform, safe, and inexpensive, and rapidly became the standard method to obtain pleural tissue samples. The blind pleural biopsy is also well established in the diagnosis of tuberculous pleuritis in which the yield from microbial analysis of pleural fluid may be poor (2). The value of blind biopsy in diagnosing malignant effusion is controversial due to its diagnostic sensitivity being less than that of the image-guided and thoracoscopic pleural biopsies (3, 4).

The present study was undertaken to find relative frequency of TB and malignancy in undiagnosed exudative pleural effusion in a large referral pulmonary hospital. The main aim of our study was to identify the diagnostic yield of blind pleural biopsy especially in comparison with surgical biopsy.

Methods

This study was conducted at Massih-Daneshvari Tertiary Care Specialty Teaching Hospital (the largest pulmonary center in Iran). All consecutive patients with clinical and radiographic evidence of pleural effusion, over a period of 20 months (from September 2007 to April 2009) were included in the study. All patients routinely underwent diagnostic thoracentesis to obtain pleural fluid specimens. Differential cell counts, protein, lactate dehydrogenase (LDH), adenosine deaminase (ADA), cytological examination, gram-stain, culture, Ziehl-Neelsen stain and culture for mycobacterial of the specimens were performed. Serum was taken at the same time for the measurement of protein and LDH levels.

The patients were categorized as exudative pleural effusion based on Light's criteria (Pleural fluid protein/serum protein > 0.5 , pleural fluid LDH/serum LDH > 0.6 , pleural fluid LDH $>$ two-thirds the normal upper limit for serum). The patients diagnosed with exudative pleural effusion based on Light's criteria were included and those with transudative effusion were excluded from the study. From the patients with exudative pleural effusion, the following were excluded from the study: patients with positive gram stain, positive acid-fast stain, ADA > 50 U/L, definitely positive cytology for malignant cell, clinical history and image findings suggestive of pulmonary embolism, contraindication for blind biopsy (INR > 2 or platelet count $< 50,000$). All biopsies were conducted by pulmonary specialists. All these patients were given 1% lidocaine as local anesthetic. Small incision was made by surgical blade and pleural biopsy needle (Abrams needle) entered to pleural space which was confirmed by free flow of fluid while aspirating. Biopsy specimens were taken from each patient. The tissue specimens were examined by the pulmonary pathologists. The adequacy of specimens and tissue diagnosis were reported. Tuberculosis was diagnosed when typical granulomas with caseation were seen. The presence of acid-fast bacilli was not a prerequisite for

diagnosis. Malignant effusions were diagnosed when pleural biopsy was conclusively positive for malignancy. Blind Abrams pleural biopsy was not repeated in any case.

In the case of undiagnosed closed pleural biopsy, surgical biopsy was the main next procedure, but based on the practitioner's clinical decision, some of the patients underwent other investigations (bronchoscopy, CT-guide biopsy, lymph node biopsy or treatment trial with anti-TB drugs). Surgical tissue specimens were examined by the same group of pulmonary pathologists. All patients were followed up for at least 6 months. The formal ethical approval was obtained prior to the commencement of the study from Shahid Beheshti University of Medical Sciences Ethics Committee. Informed written consent was obtained from all the patients. In this study, the confirmation (Gold standard) for the negative and positive cases was assessed by follow up and surgery in addition to 11 participants who were confirmed with the other mentioned investigations. To present the demographic findings, we used mean and range. To evaluate the blind biopsy, we utilized true positive (TP), true negative (TN), false positive (FP) and false negative (FN). In addition, to evaluate the diagnosis agreement, we employed sensitivity, negative predictive value (NPV) and diagnostic accuracy with their related 95% confidence interval. All analysis were performed using SPSS version 17.0.

Results

Among the 318 patients with exudative pleural effusion, 171 patients underwent percutaneous blind pleural biopsy with Abrams needle. The age of the patients were between 15-85 years. From these, 121 patients were males (70%) and 50 cases were females (30%). Malignancy was diagnosed in 56 and TB in 52 cases with blind biopsy. From the 63 remaining patients, 15 (9%) patients had inadequate tissue specimen and 48 (28%) had inconclusive results. We had no mortality with blind biopsy but pneumothorax occurred in three (1.7%) cases and one of them needed chest tube (0.6%). Forty three of these patients underwent surgical biopsy (open or VATS). Malignancy was diagnosed in 30 and TB in 5 cases. Pathologic results in 8 of these patients were negative for TB and malignancy.

Eleven of these patients underwent other investigations (bronchoscopy, CT-guide biopsy, lymph node biopsy or anti-TB treatment trial). Nine of these patients were diagnosed

with malignancy and two patients had TB. Nine patients from the 63 undiagnosed cases following blind biopsy withdrew from the study at this stage.

Figure 1 shows the diagnostic algorithm obtained in our total patient group in the form of a flow chart. Totally, from the 162 patients with definite diagnosis by any investigations, 95 (58.6%) patients had malignancy and 59 (36.4%) cases had TB. The average age of patients with TB and malignancy was 48 and 59, respectively. Sensitivity of blind Abram's biopsy for the diagnosis of malignancy was 58.9% and for TB was 88.1%. The diagnosis of malignancy and TB was established by blind biopsy in 108 patients (sensitivity test of 70.1 %). All patients were followed up for

at least 6 months and no case of false positive was found (specificity of 100%)

Table 1 represents the sensitivity, specificity, and the positive and negative predictive values of the blind Abrams needle biopsy for all the diagnoses seen in this study. Regarding the specific histopathologic malignant diagnoses, from the 78 cases of metastatic carcinoma in the group, 50 (64%) cases were diagnosed by blind biopsy.

This was in contrast to mesothelioma, in which blind biopsy was diagnostic in 4 of 11 (36.3%) cases.

Table 2 represents the patients with the diagnosis of malignancy or TB following presentation with exudative pleural effusion and initial non-diagnostic thoracentesis.

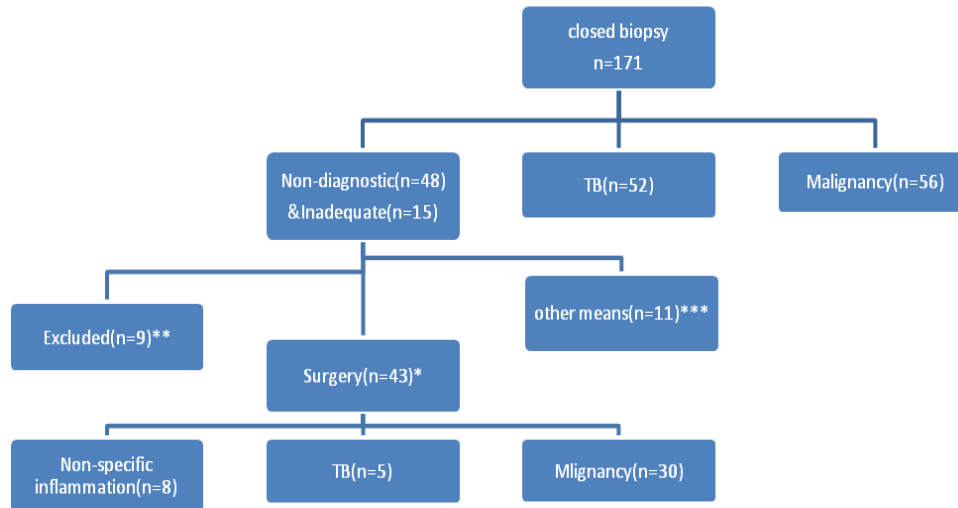


Figure 1. Diagnostic process to find the source of exudative pleural effusion

TB: Tuberculosis

*Surgery: includes open biopsy or VATS

**Excluded because of the patients' withdrawal from the study

***Other means include: bronchoscopy, CT- guide biopsy, lymph node biopsy and empiric anti-TB drug

Table 1. Sensitivity, specificity, and positive and negative predictive values of blind pleural biopsy

Variable	TP	TN	FP	FN	Sensitivity*	NPV*	Accuracy*
Malignancy	56	67	0	39	58.9 (48.9,68.3)	63.2 (53.7,71.8)	75.9 (68.8,81.9)
TB	52	103	0	7	88.1 (77.5,94.1)	93.6 (87.4,96.9)	95.7 (91.4,97.9)
M + TB	108	8	0	46	70.1 (62.5,76.8)	14.8 (7.7,26.6)	71.6 (64.2,80.0)

TP, true positive TN, true negative FP, false positive FN, false negative NPV, negative predictive value

* Value (95% Confidence Interval)

Specificity and PPV are 100 for all the Variables

Table 2. Various malignancies and TB patients diagnosed by different methods

disease	Blind Biopsy	Surgery	Other route	Total
	No	No	No	
Malignancy	56	30	9	95
Metastatic carcinoma	50	20	8	78
Mesothelioma	4	6	1	11
Lymphoma	2	3	0	5
Other	0	1	0	1
TB	52	5	2	59
Total	108	35	11	154

TB, tuberculosis

Discussion

Recently, blind Abrams needle biopsy is being superseded by newer methods like image-guided biopsies and medical thoracoscopy resulting in higher diagnostic yield in patients with malignancy (3, 4). In many developing countries like Iran, medical thoracoscopy is not readily available, so we are constrained to surgical biopsy in many cases. Surgery (including open biopsy and VATS) has higher cost, hospital stay and possible morbidity compared to blind biopsy which puts pressure on limited resources available in health system. Another point to be considered is the high prevalence of TB in these countries which might cause a difference in the overall sensitivity of blind biopsy compared to developed countries.

In our study, in patients with a minimum of 6 months follow-up after biopsy, malignancy was confirmed in 95 cases, of which 56 cases were diagnosed by Abrams pleural biopsy (sensitivity 58.9%, negative predictive value of 62.5%). The use of blind biopsy in previous studies has demonstrated a disagreement between findings with a sensitivity range of 46-72% (5, 6). A study of 414 patients with pleural effusion reported an additional diagnostic yield of only 7% using blind Abrams needle biopsy over cytologic analysis of pleural fluid (5). Mungall et al. have reported the highest diagnostic rates (72% of malignant effusions and 88% of tuberculous effusions) (6). Edmonstone and McLean et al. reported slightly lower diagnostic sensitivities of 60% and 62%, respectively while Maskell et al. found the sensitivity to be 47% compared to 87% when using CT guidance (3, 7, 8). All articles reported a very high specificity. We also found the specificity to be 100%.

In present study, blind Abrams biopsy was diagnostic in 4 of 11 mesothelioma cases (sensitivity 36.3%). These results are not as good as Beauchamp et al. (sensitivity 70%), but they are comparable with the series published by Boutin et al. in which closed needle biopsy was diagnostic in 20.7% of cases, increasing to 38.7% when pleural fluid cytology was taken into account (9, 10). The diagnostic sensitivity for blind biopsy in our series was greater in metastatic carcinoma (64% of cases). This is comparable with other studies (6, 11).

In this study, TB was diagnosed in 59 patients and the sensitivity of blind biopsy for TB was 88.1%. Overall, the needle biopsy of the pleura has greater utility for the diagnosis of tuberculosis than for malignant pleurisy. In a recent study in 248 patients, closed needle biopsy alone had a yield of about 80%, and when added to AFB staining and culture, the overall yield was 91% (12). In a large number of biopsies taken at a single session or multiple, separate biopsy procedures can increase the sensitivity (13, 14). A slightly better overall sensitivity may be achieved with thoracoscopy, where in contrast to closed needle biopsy, the sampling error is reduced by visual identification of the affected pleural regions, but the advantage seems to be minimal (15,16). Also, in our study, surgical biopsy did not add significantly to the diagnostic value of closed biopsy for these group patients.

In total, adequate pleural specimens were obtained in 91% of blind biopsies performed in our study. Walshe et al. reported 71% of biopsy samples performed by non-respiratory teams contained pleural tissue (17). In contrast, Cowie et al. in a large study of 750 needle biopsies reported a 90% success rate in obtaining pleural tissue (18).

Although blind biopsy has been considered a less sensitive diagnostic technique than surgical biopsy, medical thoracoscopy and image guided pleural biopsy (4, 8, 19, 20). Blind Abrams needle biopsy established a diagnosis in approximately 70.1% of patients presenting with exudative pleural effusion secondary to malignant disease and TB in this study. The routine use of blind biopsy may mean that in about 75% of patients, the other procedures are not required. Also, complication with blind biopsy (1.7%) should be considered. This has a potential impact on health economics, as the costs of performing surgery, medical thoracoscopy or image-guided biopsy are considerable. Likewise, this will also avoid reliance on the radiology department for routine image-guided pleural biopsy as well as the hazards associated with surgery and general anesthesia. These issues become particularly relevant in those countries with limited medical resources and access to medical thoracoscopy or thoracic surgical facilities.

In conclusion, the diagnostic work up of pleural effusion that blind closed pleural biopsy provides acceptable yield in the diagnosis of TB and malignancy, the two most common causes of exudative pleural effusion. In view of low cost and easy availability, blind pleural biopsy could be worthwhile especially in the developing countries by considering the unavailability of thoracoscopy, high prevalence of TB and limited medical resources.

Acknowledgments

We thank the medical and nursing teams of Massih-Daneshvari Hospital for their collaboration in the preparation of this article and the Clinical Research Development Center personnel of Imam Hossein Medical Center for their help and support.

Funding: This study was self-funded.

Conflict of Interest: We have no conflict of interest in this study.

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