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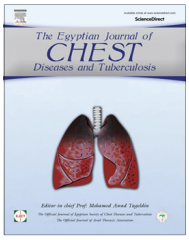

ORIGINAL ARTICLE

CT-guided biopsy versus conventional Abram's needle biopsy in malignant pleural effusion

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KEYWORDS

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Abstract *Objective:* We aimed to evaluate CT guided biopsy (CTGB) vs. standard closed pleural biopsy (CPB) in the histopathological diagnosis of the type of malignancy in patients with malignant pleural effusion.

Patients and methods: We studied 31 patients (21 male and 10 female) with malignant pleural effusion diagnosed by aspiration cytology and admitted to the medical ward of a general teaching hospital over a period of 1 year. Patients were randomized into two groups: group 1 (n = 16) underwent CTGB biopsy and group 2 (n = 15) underwent Abram's CPB. The diagnostic yield of both methods was compared.

Results: The mean age of patients was 54 ± 16 years. History of smoking was obtained in 15 (48.4%) patients. Dyspnea was reported in 22 (71%) and chest pain in 15 (48.4%). Malignant pleural effusion was left-sided in 17 (54.8%), and massive in 21 (67.7%) patients. Of note, CT imaging revealed parietal pleura as a tumor site in 20 (64.5%) patients. Pathological diagnosis of the type of malignancy was achieved in 14 (87.5%) of group 1 using CTGB and 6 (40%) of group 2 patients using Abram's CPB. The diagnostic value of CTGB was significantly higher than CPB (P = 0.009).

Conclusion: CT-guided biopsy was found to be a reliable and safe method in the histopathological diagnosis of malignant pleural effusion. Its diagnostic potential was much superior to the standard closed pleural biopsy.

Introduction

Pleural disease may present as focal pleural nodules or diffuse pleural thickening and could be due to benign or malignant etiologies. Effusion is frequently an early sign of pleural

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disease, and pleural fluid cytology is accepted as the first diagnostic test in the evaluation of unilateral pleural effusion [1].

Malignant pleural effusion (MPE) is a common complication and sometimes the initial manifestation of underlying intrathoracic, extrathoracic or far-advanced malignancies. Common cancer types causing MPEs include lymphomas, mesotheliomas, and carcinomas of the breast, lung, gastrointestinal tract, and ovaries. However, almost all tumor types have been reported to cause MPEs. The median survival after diagnosis of MPE is 4 months [2].

Standard pleural fluid cytology is a simple, safe and minimally invasive method to diagnose pleural malignancy. It could help to characterize up to 60% of malignant effusions [1]. However, in malignant mesothelioma, it is diagnostic in as low as 30% of cases [3]. Noteworthy, cytological evaluation of the pleural effusion has besides problems with sensitivity, difficulties with specificity because of limitations in differentiating between different types of cancer like adenocarcinoma, mesothelioma, lymphoma and non-malignant reactive lymphocytosis. Additional tests like assay of pleural fluid for tumor markers might improve the diagnostic yield of cytology. The diagnostic value of tumor markers for MPE, however, remains limited, with no single marker being sufficiently sensitive or specific to be introduced into routine practice [4]. Moreover, pleural fluid cytology sometimes fails to subclassify the malignant cell types, which is essential for further management of chemosensitive malignancies [5].

Pleural biopsy is still an important diagnostic tool in further characterizing the nature of pleural disease. Nonsurgical, percutaneous pleural biopsy in patients with pleural effusion was first described in the 1950s by Abrams and Cope [6,7]. This biopsy procedure can be performed at bedside, without any imaging for guidance. The use of the Abrams pleural biopsy needle has a sensitivity of up to 90% for the diagnosis of tuberculosis [8,9]. This high sensitivity rate is thought to be due to the diffuse nature of pleural involvement by tuberculosis, as opposed to the more patchy distribution demonstrated in malignant disease.

In malignant effusion, the diagnostic yield of blind pleural biopsy using Abrams or Cope needle is between 48% and 56%. The sensitivity for diagnosis of malignant mesothelioma is only 21–43%. Furthermore, the absence of pleural effusion precludes the safe deployment and use of these needles. Complications are encountered in up to 9.3% of patients and may include pneumothorax, hemothorax and vasovagal reaction [9].

Recently, image-guided biopsy of focal pleural nodules or diffuse pleural thickening has been advocated as the preferred method for diagnosis of both benign and malignant pleural diseases. It has a greater sensitivity for the diagnosis of malignant diseases compared with the Abrams biopsy and has been shown to be accurate in diagnosing malignant pleural mesothelioma [10]. Using CT or ultrasound (US) guidance, image-guided percutaneous biopsy allows a focal area of pleural abnormality to be sampled. Both CT and US can be used to localize the most suspicious area within the pleura, but the field of view for US is more limited than that of CT. Cutting needle biopsy is preferred over fine needle aspiration (FNA) because it has a higher sensitivity in the diagnosis of malignant pleural disease [10].

We aimed to assess the diagnostic yield of CT-guided pleural biopsy using a semi-automated biopsy gun versus the classic Abrams closed pleural biopsy in patients with malignant pleural effusion.

Patients and methods

We included 31 consecutive adult patients (age >18 years) with cytology-positive malignant pleural effusion. Patients were admitted to the department of Chest Medicine between May 2012 and June 2013. Patients with evidence of bleeding disorders were excluded from the study. All patients were subjected to the following: full history taking, thorough clinical examination, routine blood investigation, chest X-ray, and chest CT scan. Patients were randomized into two groups: group 1 ($n = 16$, 10 male and 6 female) underwent CT guided biopsy (CTGB) and group 2 ($n = 15$, 11 male and 4 female) underwent closed pleural biopsy (CPB). Confirmation of malignancy by pleural fluid cytology was a prerequisite prior to either closed pleural biopsy by Abrams needle or CTGB by semi-automated biopsy gun 16 French. All included patients accepted the procedure by written consent.

Cytology

Fifty milliliter sample aspirated from pleural fluid was sent for cytological exanimation. If the first sample was negative for malignant cells, a second sample was obtained which if also deemed negative a third sample in sequence was taken to confirm or rule out malignancy. The fluid was stained with Papanicolaou stain and hematoxylin eosin stain. The stained smear was then examined for the presence of malignant cell.

Closed pleural biopsy technique

Patients were given 1% lidocaine as local anesthetic. A small incision was made by a surgical blade. The reverse-beveled pleural biopsy needle (Abrams needle) was advanced into the pleural space as confirmed by free flow of fluid while aspirating and pulled back to "hook" the pleura to collect a biopsy sample. Four to six passes were usually required to obtain an adequate diagnostic specimen as described previously [8,11]. The tissue specimens were examined by an experienced pulmonary pathologist. The main contraindications for this procedure were INR >2 or low platelets' count $<50{,}000$ [12].

Technique of CT guided pleural biopsy [13]

Intravenous access, continuous pulse oximetry and vital monitoring were established prior to the procedure. Patient's position depended on the site of the lesion. Patients were asked to take small inspirations so that there would be minimal motion once the needle has passed through the pleura. This is because deeper inspirations might cause significant needle movement with greater chances of tearing the pleural surface. The grid superimposition technique was used. The skin entry site was marked using a measuring scale and laser light in correspondence to midline. After cleansing the area, a small plastic marker or hypodermic needle was placed on the skin mark and a scan was obtained at that level for confirmation. Next, a local anesthetic (1–2% lignocaine) was injected. All the needle manipulations were performed with the patient in

the designated breath hold. An oblique approach, with the biopsy needle parallel to the pleural thickening was applied. Then we introduced the automated biopsy gun to the lesion and pressed on its top to take a biopsy. We obtained small linear tissue sections suitable for histological evaluation using the automated core needle. We withdrew the biopsy gun during breathing holding maneuver. The specimen was sent for histopathological analysis in a formalin solution. Fig. 1 and Fig. 2 show the CT image of chondrosarcoma and mesothelioma in two of study patients.

Statistical analysis

IBM SPSS statistics version 21 (IBM® SPSS® New York, U.S.A) was used to analyze the data. Categorical variables were expressed as numbers and percentages and continuous variables as mean ± standard deviation. Fisher exact test was used to detect significant difference between categorical variables in CPB and CTGB groups. Differences in means were compared using independent samples *t*-test. A *P*-value of <0.05 was considered statistically significant.

Results

Of 31 patients with MPE, group1 included 10 male and 6 female (mean age, 48 years) while group 2 included 11 male and 4 female (mean age, 60 years). There was a significant difference in age between the two groups ($P = 0.031$). History of smoking was obtained in 15 (48.4%) patients. Dyspnea was reported in 22 (71%) and chest pain 15 (48.4%). Table 1 shows the demographic characteristics of the study patients. Malignant pleural effusion was left-sided in 17 (54.8%), and massive in 21 (67.7%) patients. Of note, CT imaging revealed parietal pleura as a tumor site in 20 (64.5%) patients. Interestingly, pathological diagnosis was significantly achieved in group 1 by the use of CTGB in 14 (87.5%) vs. 6 (40%) in group 2 using CPB ($P = 0.009$). Post-CTGB complications included bleeding 2 (12.5%) and pneumothorax 2 (12.5%). Similarly, after CPB, 2 (13.3%) patients had bleeding and 1 (6.7%) had pneumothorax. Complications were minimal and treated by conservative therapy. Table 2 displays the main radiological findings, laboratory investigation, and biopsy-related complications. Computed tomography showed single mass in 9 (29%), multiple masses 6 (19.4%), nodules 8 (25.8%) and pleural thickening 8 (25.8%) as presented in Table 3. Pathological diagnosis was not reached by CTGB in 2 (12.5%) of group 1 patients. These 2 patients later underwent thoracoscopy which uncovered the diagnosis of the tumor type. In group 2, however, 9 (60%) could not be diagnosed by CPB; they all underwent CTGB where 7 were diagnosed by CTGB and 2 subsequently diagnosed via thoracoscopy. Table 4 shows the pathological diagnosis of tumor type in patients with malignant pleural effusion.

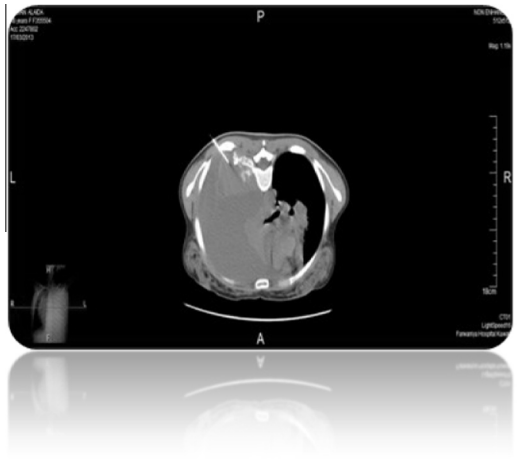

Figure 1 A 20-year old patient with chondrosarcoma.

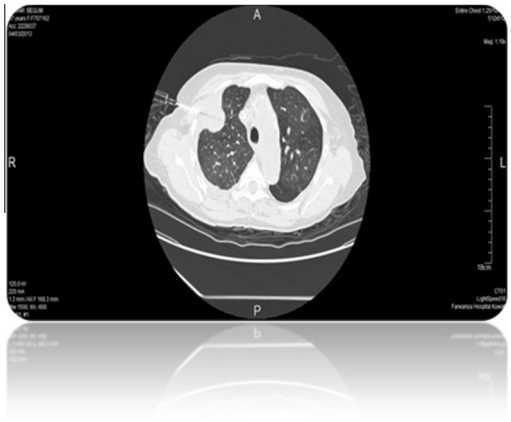

Figure 2 A 53-year old patient with mesothelioma.

Discussion

Routine investigation of pleural fluid and pleural biopsy remains the best method of diagnosis of the nature of the pleural fluid [12]. The value of blind biopsy in diagnosing malignant effusion is controversial due to low diagnostic sensitivity particularly when compared with image-guided and thoracoscopic pleural biopsies [14]. In our study the diagnostic yield of Abrams closed needle biopsy was somewhat similar to the study of Bhattacharya and coworkers [15] on 66 patients with malignant pleural effusion who underwent closed pleural biopsy and diagnosed 48% as a malignant. This relatively low yield of blind pleural biopsy was attributed to the sparse, variable and uneven distribution of the tumor invading the pleura.

In one review, analysis of diagnostic yield of pleural biopsy for malignancy was 57% [16]. However, the yield varied between 40% and 75% [17–21]. In another study with Tru cut needle biopsy, it reached 85.7% [5]. In case of malignant mesotheliomas, the diagnostic yield is even lower. Attanoos and Gibbs [22] conducted a review of 45 cases postmortem in which 91% had had the same antemortem diagnosis. For definitive diagnosis closed blind pleural biopsies yielded sensitivity at as low as 16% and high specificity at 94%.

Features of contrast-enhanced CT scanning that favors the diagnosis of malignant disease rather than benign disease include nodular, mediastinal, or circumferential pleural thickening or parietal pleural thickening >1 cm [23]. In our study, chest CT scan with contrast-enhancement showed single mass, multiple masses, nodules and pleural thickening. The diagnostic yield of CTGB was significantly higher than CPB with minimal complications. In an earlier study, Maskell et al. [14] compared the sensitivity of contrast-enhanced CT-guided

Table 1 Demographic characteristics and major symptoms of patients with malignant pleural effusion.

	Group 1 CTGB ($N = 16$)	Group 2 CPB ($N = 15$)	*P* value	All patients
Age (years), mean ± SD	48 ± 17	60 ± 12	0.031	54 ± 16
Gender, male, no. (%)	10 (62.5)	11 (73.3)	0.704	21 (67.7)
Smoking, no. (%)	9 (56.3)	6 (40)	0.479	15 (48.4)
Chest pain, no. (%)	6 (37.5)	9 (60)	0.210	15 (48.4)
Dyspnea, no. (%)	12 (75)	10 (66.7)	0.704	22 (71.0)

Table 2 Main radiological findings, laboratory investigation, and biopsy-related complications in patients with malignant pleural effusion.

	Group 1 (CTGB)	Group 2 (CPB)	*P* value	All patients
CXR effusion, left, no. (%)	9 (56.3)	8 (53.3)	0.870	17 (54.8)
Massive effusion, no. (%)	12 (75)	9 (60)	0.458	21 (67.7)
Site of tumor by CT, parietal pleura, no. (%)	9 (56.3)	11 (73.3)	0.320	20 (64.5)
Platelets count, mean ± SD ($\times 10^3$)	276.9 ± 79.5	244.7 ± 59.2	0.213	261.3 ± 71.2
RBCs count, mean ± SD ($\times 10^6$)	3.77 ± 1.2	4.09 ± 1.2	0.457	3.92 ± 1.19
LDH, mean ± SD	563.8 ± 247.9	489.3 ± 232.9	0.397	527.7 ± 239.7
pH, mean ± SD	7.025 ± 0.284	7.047 ± 0.207	0.811	7.035 ± 0.246
Biopsy diagnosis of malignancy type, no. (%)	14 (87.5)	6 (40)	0.009	20 (64.5)
Post procedure bleeding, no. (%)	2 (12.5)	2 (13.3)	1	4 (12.9)
Post procedure pneumothorax, no. (%)	2 (12.5)	1 (6.7)	1	3 (9.7)

Table 3 CT findings in patients with malignant pleural effusion.

	Group 1 (CTGB) *N* (%)	Group 2 (CPB) *N* (%)	Total *N* (%)
Single mass	5 (31.3)	4 (26.6)	9 (29.0)
Multiple masses	4 (25)	2 (13.4)	6 (19.4)
Nodules	4 (25)	4 (26.6)	8 (25.8)
Pleural thickening	3 (18.7)	5 (33.4)	8 (25.8)

biopsy vs. Abrams blind biopsy among cytology-negative patients with suspected malignant pleural effusion. They found that the CT guided-biopsy had 87% sensitivity vs. 47% in Abrams' biopsy. Although both procedures had 100% specificity and positive predictive value, the negative predictive value of CT-guided biopsy was higher at 80% compared with 44% with Abram's needle.

To compare the diagnostic sensitivity and complications of CT-guided biopsy with that of thoracoscopy, Metintas et al. [24] studied 124 patients with exudative pleural effusion that

Table 4 Final pathological diagnosis of tumor type in patients with malignant pleural effusion.

Tumor pathology	Group 1 CTGB ($n = 16$)		Group 2 CPB group ($n = 15$)		Total *N* (%)
	Achieved by CTGB	Required alternate procedure	Achieved by CPB	Required alternate procedure	
Adenocarcinoma of lung	5	1[*]	3	6[#]	15 (48.4)
Mesothelioma	3	–	1	1[$]	5 (16.1)
Metastatic adenocarcinoma	3	–	0	2[$]	5 (16.1)
Lymphoma	1	1[*]	2	–	4 (12.9)
Chondrosarcoma					
Large cell carcinoma	1	–	0	–	1 (3.2)
	1	–	0	–	1 (3.2)
Total	14	2	6	9	31 (100)

[*] Pathological diagnosis achieved by thoracoscopy.
[#] Pathological diagnosis achieved in two cases by thoracoscopy and in four cases by CTGB.
[$] Pathological diagnosis achieved by CTGB.

could not be diagnosed by cytological analysis. The investigators randomized the patients after a CT scan. Patients underwent either CT-guided biopsy using Abrams needle or thoracoscopy. The authors concluded that in the CT-Abram needle pleural biopsy group, the diagnostic sensitivity was 87.5% vs. 94.1% in the thoracoscopy group; the difference was not statistically significant and complication rates were relatively low.

Likewise, Adams et al. [10] found that CT-cutting needle biopsy had 86% sensitivity and 100% specificity in achieving the correct histological diagnosis of malignant mesothelioma. The complications were also minimal. In another study, Benamore et al. [25] reported pleural biopsies under CT guidance had 76% sensitivity and 100% specificity. The researchers reported no major complications. Nevertheless, pneumothorax was detected by chest radiography in 4.7% of patients, but none required a pneumothorax evacuation tube.

The limitation of this study was that only 31 cases were studied. However, this was a preliminary study and the results related to CT guided biopsy were reasonably encouraging.

In conclusion, despite the closed pleural biopsy is widely available, easy to perform, and can be performed on outpatient basis, its diagnostic yield was low. CT-guided biopsy was a reliable and safe method in the diagnosis of malignant pleural effusion. The diagnostic accuracy was much superior to the standard closed pleural biopsy. Both techniques had minimal procedure-related complications.

Conflict of interest

None exist.

References

[1] K. Ahrar, M. Wallace, S. Javadi, S. Gupta, Mediastinal, hilar, and pleural image-guided biopsy: current practice and techniques, Semin. Respir. Crit. Care Med. 29 (2008) 350–360.

[2] J.E. Heffner, J.S. Klein, Recent advances in the diagnosis and management of malignant pleural effusions, Mayo Clin. Proc. 83 (2008) 235–250.

[3] A.A. Renshaw, B.R. Dean, K.H. Antman, D.J. Sugarbaker, E.S. Cibas, The role of cytologic evaluation of pleural fluid in the diagnosis of malignant mesothelioma, Chest 111 (1997) 106–109.

[4] J.E. Heffner, Diagnosis and management of malignant pleural effusions, Respirology 13 (2008) 5–20.

[5] P. James, R. Gupta, D.J. Christopher, T. Balamugesh, Evaluation of the diagnostic yield and safety of closed pleural biopsy in the diagnosis of pleural effusion, Indian J. Tuberc. 57 (2010) 19–24.

[6] L.D. Abrams, A pleural-biopsy punch, Lancet 1 (1958) 30–31.

[7] C. Cope, New pleural biopsy needle; preliminary study, J. Am. Med. Assoc. 167 (1958) 1107–1108.

[8] C.M. Kirsch, D.M. Kroe, R.L. Azzi, W.A. Jensen, F.T. Kagawa, J.H. Wehner, The optimal number of pleural biopsy specimens for a diagnosis of tuberculous pleurisy, Chest 112 (1997) 702–706.

[9] R.H. Poe, R.H. Israel, M.J. Utell, W.J. Hall, D.W. Greenblatt, M.C. Kallay, Sensitivity, specificity, and predictive values of closed pleural biopsy, Arch. Intern. Med. 144 (1984) 325–328.

[10] R.F. Adams, W. Gray, R.J. Davies, F.V. Gleeson, Percutaneous image-guided cutting needle biopsy of the pleura in the diagnosis of malignant mesothelioma, Chest 120 (2001) 1798–1802.

[11] D. Jimenez, E. Perez-Rodriguez, G. Diaz, L. Fogue, R.W. Light, Determining the optimal number of specimens to obtain with needle biopsy of the pleura, Respir. Med. 96 (2002) 14–17.

[12] M. Solooki, M. Miri, Approach to undiagnosed exudative pleural effusion: the diagnostic yield of blind pleural biopsy, Caspian J. Intern. Med. 4 (2013) 642–647.

[13] H. Lal, Z. Neyaz, A. Nath, S. Borah, CT-guided percutaneous biopsy of intrathoracic lesions, Korean J. Radiol. Off. J. Korean Radiol. Soc. 13 (2012) 210–226.

[14] N.A. Maskell, F.V. Gleeson, R.J. Davies, Standard pleural biopsy versus CT-guided cutting-needle biopsy for diagnosis of malignant disease in pleural effusions: a randomised controlled trial, Lancet 361 (2003) 1326–1330.

[15] S. Bhattacharya, T.D. Bairagya, A. Das, A. Mandal, S.K. Das, Closed pleural biopsy is still useful in the evaluation of malignant pleural effusion, J. Lab. Physicians 4 (2012) 35–38.

[16] J.R. Tomlinson, A.S. Sahn, Invasive procedures in the diagnosis of pleural disease, Semin. Respir. Crit. Care Med. 9 (1987) 30–36.

[17] U.B. Prakash, H.M. Reiman, Comparison of needle biopsy with cytologic analysis for the evaluation of pleural effusion: analysis of 414 cases, Mayo Clin. Proc. 60 (1985) 158–164.

[18] R.L. Starr, M.E. Sherman, The value of multiple preparations in the diagnosis of malignant pleural effusions. A cost-benefit analysis, Acta Cytol. 35 (1991).

[19] N.D. Kumar, A. Bhatia, K. Misra, J.C. Suri, Comparison of pleural fluid cytology and pleural biopsy in the evaluation of pleural effusion, J. Indian Med. Assoc. 93 (1995) 307–309.

[20] R.H. Poe, Sensitivity, specificity, and predictive values of closed pleural biopsy, Arch. Intern. Med. 144 (1984) 325.

[21] C. Escudero Bueno, M. García Clemente, B. Cuesta Castro, L. Molinos Martín, S. Rodríguez Ramos, A. González Panizo, J. Martínez Glez-Río, Cytologic and bacteriologic analysis of fluid and pleural biopsy specimens with Cope's needle. Study of 414 patients, Arch. Intern. Med. 150 (1990) 1190–1194.

[22] R.L. Attanoos, A.R. Gibbs, The comparative accuracy of different pleural biopsy techniques in the diagnosis of malignant mesothelioma, Histopathology 53 (2008) 340–344.

[23] A.L. Evans, F.V. Gleeson, Radiology in pleural disease: state of the art, Respirology 9 (2004) 300–312.

[24] M. Metintas, G. Ak, E. Dundar, H. Yildirim, R. Ozkan, E. Kurt, S. Erginel, F. Alatas, S. Metintas, Medical thoracoscopy vs. CT scan-guided Abrams pleural needle biopsy for diagnosis of patients with pleural effusions: a randomized, controlled trial, Chest 137 (2010) 1362–1368.

[25] R.E. Benamore, K. Scott, C.J. Richards, J.J. Entwisle, Image-guided pleural biopsy: diagnostic yield and complications, Clin. Radiol. 61 (2006) 700–705.