Diagnostic yield of closed pleural brushing

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ÖZET

Kapalı plevra fırçalamasının tanı değeri

Bu çalışmada kapalı plevra fırçalaması (KPF)'nın malign plevral efüzyonlu hastalarda tanı değerinin araştırılması amaçlandı. Prospektif olarak yapılan çalışmaya yaş ortalaması 62.9 ± 8.6 olan 21 erişkin hasta (20 erkek ve 1 kadın) alındı. Her hastaya torasentez, KPF, plevral fırçalamayı takiben kapalı plevra biyopsisi (KPB) uygulandı. KPF 21 olgunun 12 (%57.1)'sinde tanı sağlarken bu 12 olgunun 3'ünde plevra sıvı sitolojisi (PSS) ve KPB negatifti. PSS, KPF ve KPB'nin malign efüzyon tanısında sensitiviteleri sırasıyla %33, %57, %52 olarak hesaplandı. Üç girişim birlikte kullanıldığında sensitivite %67'ye yükseldi. KPF, KPB ve PSS'ye ek olarak uygulandığında tanı değerini %14 artırdı. Bu girişimlere bağlı bir mortalite izlenmedi. Üç (%14.2) olguda göğüs ağrısı, 2 (%9.5) olguda hipotansiyon, 1 (%4.8) olguda öksürük, 1 (%4.8) olguda pnömotoraks ve 1 (%4.8) olguda hemotoraks gelişti. Sonuç olarak, KPF güvenli, basit ve iyi tolere edilebilen bir tanısal girişim olarak malign plevral efüzyonlu hastalarda yüksek tanı oranı sağlar.

Anahtar Kelimeler: *Kapalı plevra biyopsisi, kapalı plevra fırçalaması, malign plevral efüzyonlar, torasentez.*

SUMMARY

Diagnostic yield of closed pleural brushing

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The aim of this study was to assess the diagnostic yield of closed pleural brushing (CPBR) in the diagnosis of malignant pleural effusion. Twenty-one adult patients (20 men and 1 woman); aged 62.9 ± 8.6 were participated to this prospective study. Thoracentesis, CPBR and closed pleural biopsy (CPB) following the brushing were applied to every patient. While CPBR provided diagnosis in 12 (57.1%) of 21 cases, in 3 of these 12 cases, pleural fluid cytology (PFC) and CPB were negative. The sensitivities of PFC, CPBR and CPB in the diagnosis of malignant effusions were 33%, 57% and 52%, respectively. When three procedures were used in combination, the sensitivity increased to 67%. When CPBR is performed in addition to PFC and CPB, the yield of the diagnosis increased 14% additionally. There was no mortality due to these interventions.

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Complications were chest pain in 3 (14.2%) cases, hypotension in 2 (9.5%) cases, cough in 1 (4.8%) case, pneumothorax in 1 (4.8%) case, and hemothorax in 1 (4.8%) case. In conclusion, CPBR as a safe, simple and well tolerated procedure provides high diagnostic yield in diagnosis of patients with malignant pleural effusion.

Key Words: *Closed pleural biopsy, closed pleural brushing, malignant pleural effussion, thoracentesis.*

Malignant pleural effusion is one of the most common cause of exudative pleural effusion only second to parapneumonic effusion (1). In patients older than 60 years malignant effusion is the most common cause of pleural effusions (2). Malignant effusion occurs approximately in 50% of patients with metastatic carcinoma (3). Cancer from any site or organ can metastasize to pleura; but lung cancer is the most common to metastasize to pleura and cause malignant effusion, followed by breast cancer. Although malignant mesothelioma is the primary tumor of pleura, it is a rare cause of malignant effusion (4).

Since patients with malignant effusion are frequently admitted to hospital when they are already terminally ill, it is important to obtain a fast diagnosis and formulate a treatment to improve the quality of life (3).

Pleural fluid cytologic (PFC) examination and closed pleural biopsy (CPB) are recommended diagnostic procedures for suspected malignant effusion (5). However; all patients with malignant pleural effusions can not be diagnosed with these procedures (5). Thoracoscopy and open pleural biopsy are more invasive diagnostic procedures; and performed in only selected cases. Because of the poor prognosis of diseases associated with malignant effusions, safer and better tolerated alternative diagnostic procedures are being searched. First results obtained by closed pleural brushing (CPBR) procedure published by Emad and coworkers are promising (6). In this study we evaluated diagnostic yield of CPBR procedure in patients with malignant pleural effusion.

MATERIALS and METHODS

Twenty-one patients who were suspected of malignant pleural effusion were hospitalized and enrolled in this study. Informed written consent was obtained from all patients.

If initial thoracenthesis was exudative and did not provide diagnosis, the patients underwent CPBR using Cope's needle by second thoracenthesis. CPB was also performed.

Complete blood count, routine biochemical analysis, postero-anterior (PA) and lateral chest X-ray, thorax computed tomography were obtained from all patients before the pleural interventions.

Patients were enrolled in this study only if there was clinical, radiological, routine laboratory suspicion of malignant effusion; and if one or more of the following criteria were present: Old age (> 60 years old); history of smoking; progressive dyspnea, dull chest pain and hemoptysis; lesions other than effusion on the chest X-ray; any known cancer history; exclusion of tuberculosis, pulmonary embolism, parapneumonic effusion, nonmalignant effusion or paramalignant effusion by clinical, radiological and laboratory evaluation of pleural fluid obtained at the first thoracenthesis.

Effusions were considered malignant if one of the followings were present:

1. Demonstration of malignant cells at cytologic examination or in a biopsy specimen; or

2. Histologically proven primary malignancy with exclusion of any other cause known to be associated with pleural effusions.

The localization and size of pleural fluid was assessed by PA chest X-ray. The effusion was localized as right, left or bilateral; and the size of effusion was classified as small, medium or large according to the appearance on X-ray as follows (7):

1. Small: the entire diaphragm was not covered by the fluid,

2. Medium: pleural fluid covered up to one-third of distance between the lateral chest wall and the mediastinum at the level of the hilar region,

3. Large: pleural fluid covered up more than one-third of distance between the lateral chest wall and the mediastinum at the level of the hilar region.

30 mL of pleural fluid by thoracenthesis and simultaneous blood sample were obtained from each patient. Pleural fluid and blood sample were analyzed for glucose, lactate dehydrogenase, total protein, albumin; and pleural fluid samples were analyzed for pH measurement and cytologic examination.

Brushes used for CPBR were disposable cytology brushes (Mill Rose Laboratory Inc Ohio USA) used in bronchoscopic brushing procedure. The diameters of the brushes were 2 mm diameter and their length was 11 cm. The working diameters of catheters protecting the brushes were 1.6 mm and they were 120 cm long. Brushing was performed by using Cope's needle biopsy set (Figure 1). Before starting the procedure, 5 cm distant length was marked on the brush in addition to external cannula. Pleural biopsy set cannula was introduced into pleural cavity percutaneously. The brush was inserted gradually through lumen of the cannula until the marked part; and in pleural cavity, by leaning against the parietal pleura; brush was moved back and forth without taking it outside. Samples were taken from four quadrants and fixed by 96% alcohol for at least 10 minutes after preparing a smear on slide.

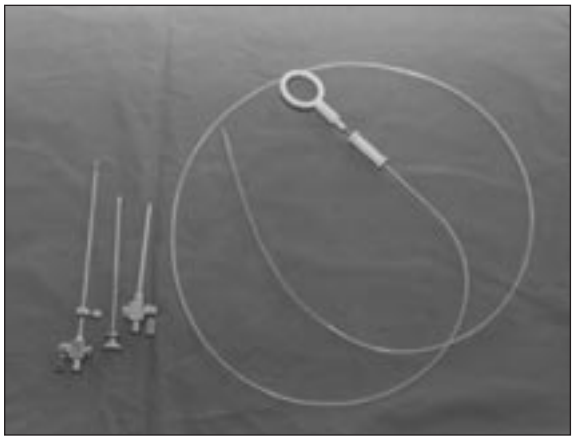

Figure 1. Cope's needle biopsy set and cytologic brush.

After CPBR; CPB was also performed by Cope's needle.

Following the biopsy chest X-ray of each patient was obtained. Pneumothorax more than 50% or increased dyspnea was accepted as an indication for chest tube placement. Patients with pneumothorax less than 50% were observed (1).

If the diagnosis could not be provided by PFC, CPBR or CPB, fiberoptic bronchoscopy and open pleural biopsy were performed.

20 mL of pleural fluid obtained for cytologic examination was centrifuged at 4000 rpm for 5 minutes and two smears were prepared. Specimens of pleural fluid and pleural brushing prepared for cytologic examination were stained with Papanicolou (EA-65) stain. Biopsy material was examined with light microscope after staining with hemotoxylin-eosin. Cytologic and histopathologic evaluations were performed independently by two pathologists.

To differentiate malignant mesothelioma from other malignancies, immunochemical methods such as keratine, epithelial membrane antigen (EMA), and carcinoembryonic antigen (CEA) were used.

RESULTS

Twenty-one patients including 20 men (95.2%) and 1 woman (4.8%); were enrolled to this study. The mean age was 62.9 ± 8.6 years with a range between 37 and 78.

Effusion was right sided in 11 patients and left sided in 10 patients. Size of effusion was small in 3 (14.2%), medium in 9 (42.9%) and large in 9 (42.9%) of cases.

On the PA chest X-ray of 11 (52.4%) patients only pleural effusion was observed. In other patients, atelectasis, mass, or parenchymal infiltration was observed in addition to pleural effusion. Computed tomography of all patients revealed accompanying pulmonary lesions.

All three procedures were performed to all patients. In 14 (66.7%) of 21 cases, malignancy was diagnosed by using PFC, CPBR or CPB procedures together. PFC was diagnostic in 7 (33.3%) cases; CPBR in 12 (57.1%) cases; and CPB in 11 (52.4%) cases. Six of the other 7 (33.3%) cases in whom diagnosis could not be provided by these three procedures were diagnosed by fiberoptic bronchoscopy and one case was diagnosed by open pleural biopsy. The sensitivities of PFC, CPBR and CPB in the diagnosis of malignant effusions were 33%, 57% and 52%, respectively (Figure 2). When three procedures were used in combination, the sensitivity increased to 67%. When CPBR is performed in addition to PFC and CPB, the yield of the diagnosis increased 14% additionally.

In 21 cases most frequently diagnosed malignancy was metastatic adenocarcinoma (38.1%). Metastatic small cell lung cancer was the second (23.8%). Undifferentiated type metastatic malignant epithelial tumor was the third (19%) in frequency.

PFC examination was diagnostic in 7 (33.3%) of 21 cases; in 1 case PFC plus CPB, and in 6 cases three procedures together. There was no case diagnosed only by PFC. The sensitivity of PFC on diagnosis of malignant effusions was 33%. Sixty-two point five percent of metastatic adenocarcinoma, 25% of metastatic malignant epithelial tumor, and 50% of malignant mesothelioma were diagnosed by pleural fluid cytologic examination.

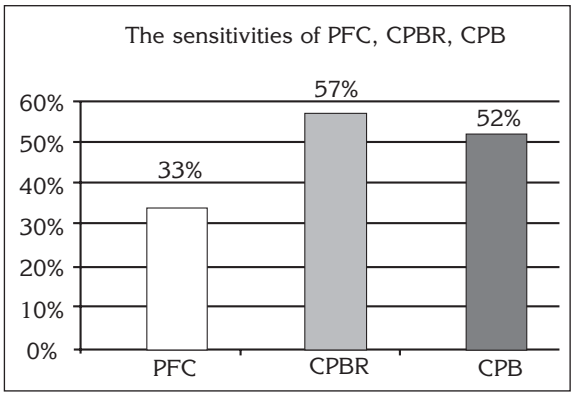

Figure 2. The sensitivities of PFC, CPBR, CPB.

CPB provided diagnosis of malignancy in 11 (52.4%) of 21 cases. In 1 case CPB alone, in 1 case CPB plus PFC, in 3 cases CPB with CPBR and in 6 cases all three procedures together provided the diagnosis. The sensitivity of CPB in diagnosis of malignant pleural effusions was 52%. CPB was diagnostic in 62.5% of metastatic adenocarcinoma, 75% of undifferentiated type metastatic malignant epithelial tumors, 40% of metastatic small cell cancers, and 50% of malignant mesothelioma.

CPBR was diagnostic in 12 (57.1%) of 21 cases. In 3 cases CPBR provided the diagnosis despite the PFC and CPB were negative. In 3 cases both CPBR and CPB; and in 6 cases all three proce-

Table 1. The results of diagnostic procedures used for malignant effusion.

Patient no	PFC	CPBR	CPB	Diagnosis
1	+	+	+	MMET
2	_	+	_	MAC
3	_	_	_	MAC
4	_	_	+	MMET
5	+	+	+	MAC
6	+	_	+	MAC
7	_	+	+	MSCLC
8	_	+	+	MSCLC
9	+	+	+	MM
10	_	_	_	MM
11	_	+	+	MMET
12	_	_	_	MSCLC
13	_	_	_	MSCLC
14	–	+	_	MAC
15	+	+	+	MAC
16	_	–	–	MSCLC
17	_	_	_	MEC
18	_	_	_	MEC
19	+	+	+	MAC
20	+	+	+	MAC
21	–	+	–	MMET
Total	7	12	11	

(+): Diagnostic, (-): Non-diagnostic.

MMET: Metastatic malignant epithelial tumor, MAC: Metastatic adenocancer, MSCLC: Metastatic small cell lung cancer, MM: Malignant mesothelioma, MEC: Metastatic epidermoid cancer.

dures were diagnostic. In 1 case whose CPBR was negative, CPB was diagnostic, and in another case in whom CPBR was negative, both biopsy and PFC were diagnostic. The results of diagnostic procedures used for malignant effusion are shown in Table 1. The sensitivity of CPBR in malignant pleural effusions was 57%. CPBR was diagnostic in 75% of metastatic adenocarcinoma, 75% of metastatic malignant epithelial tumors, 40% of metastatic small cell cancer, and 50% of malignant mesothelioma. Histologic types of lung cancer causing malignant effusion are shown in Table 2.

The effects of size of pleural fluid on the results of the three procedures are shown in Table 3.

No mortality was observed due to procedures. The most frequent complication was mild or moderate chest pain which was observed in 3 (14.2%) cases. Hypotension was observed in 2 (9.5%) patients. Persistent cough resulted in termination of procedure in 1 (4.8%) patient. Tube thoracostomy was required in a patient who developed hemothorax. In one patient minimal pneumothorax developed and improved by nasal O_2 application without any surgical intervention.

Table 2. Results of pleural procedures with regard to cell types.

	PFC (-) n (%)	PFC (+) n (%)	CPBR (-) n (%)	CPBR (+) n (%)	CPB (-) n (%)	CPB (+) n (%)	Total* n (%)
MAC (n= 8)	3 (37.5)	5 (62.5)	2 (25.0)	6 (75.0)	3 (37.5)	5 (62.5)	7 (87.5)
MSCLC (n= 5)	5 (100)	0 (0)	3 (60)	2 (40)	3 (60)	2 (40)	2 (40)
MMET (n= 4)	3 (75)	1 (25)	1 (25)	3 (75)	1 (25)	3 (75)	4 (100)
MEC (n= 2)	2 (100)	0 (0)	2 (100)	0 (0)	2 (100)	0 (0)	0 (0)
MM (n= 2)	1 (50)	1 (50)	1 (50)	1 (50)	1 (50)	1 (50)	1 (50)
Total (n= 21)	14 (66.7)	7 (33.3)	9 (42.9)	12 (57.1)	10 (47.6)	11 (52.4)	14 (66.7)

MAC: Metastatic adenocarcinoma, MSCLC: Metastatic small cell lung cancer, MMET: Metastatic malignant epithelial tumor, MEC: Metastatic epidermoid cancer, MM: Malignant mesothelioma.
* Total number of patients diagnosed by PFC, CPBR and CPB.

Table 3. Results of pleural procedures with regard to effusion size.

	PFC (-) n (%)	PFC (+) n (%)	CPBR (-) n (%)	CPBR (+) n (%)	CPB (-) n (%)	CPB (+) n (%)
Small n= 3	2 (66.7)	1 (33.3)	1 (33.3)	2 (66.7)	2 (66.7)	1 (33.3)
Medium n= 9	7 (77.8)	2 (22.2)	4 (44.4)	5 (55.6)	6 (66.7)	3 (33.3)
Large n= 9	5 (55.6)	4 (44.4)	4 (44.4)	5 (55.6)	2 (22.2)	7 (77.8)

Eight of 21 patients died 4-141 days after procedure. Remaining 13 cases have been followed up for 116-280 days after the diagnosis. Their treatment continues. Progressive dyspnea developed in one case because of malignant effusion and chemical pleurodesis using talc was performed.

DISCUSSION

Different rates are reported in many studies using PFC and CPB for the diagnosis of malignant pleural effusion (8,9). This is the main reason for researchers to seek less invasive new diagnostic procedures for malignant effusions. As specimens can be provided from more extended areas and there is possibility of cytological diagnosis without any additional invasive procedure to CPB; CPBR can be performed in pleural surface. In our study the sensitivity of CPBR was 57%. It was diagnostic in 6 (28.5%) cases whose PFC was negative; in 3 (14.2%) cases in whom CPB was negative; and in 3 (14.2%) cases in which both PFC and CPB were negative. CPBR was negative in one case that PFC and CPB were positive and in another case that CPB was positive. In the study of Emad and coworkers including 34 patients with malignant pleural effusion, diagnostic yield of PFC, CPB and CPBR were searched (6). While the diagnostic yield of CPBR and PFC were 58% and 67% respectively, sensitivity of CPBR was reported as 91%. They attributed this high sensitivity to take specimen from more extended areas of parietal as well as the visceral layers of the pleura. Emad's study was the first to evaluate the diagnostic yield of CPBR. Our study was the second study on this subject. In our series diagnostic yield of CPBR and PFC was lower than the results of Emad and coworkers', but there was no difference in regard to sensitivities of CPBR. This difference may be due to not preparing blocks from the materials obtained by fluid cytology and brush biopsies or due to pathologists' experience about cytology.

Diagnostic yield of CPBR varies according to cell types of tumor. In our study 75% of metastatic adenocarcinoma cases, 75% of metastatic malignant epithelial tumor cases, 40% of metastatic small cell cancer cases, and 50% of malignant mesothelioma were diagnosed by CPBR. On the other hand Emad et al diagnosed 100% of metastatic adenocarcinoma cases; 100% of metastatic epidermoid cancer cases; 100% of lymphoma cases; and 80% of metastatic malignant epithelial tumor cases by CPBR procedure (6).

In our study 1 case was diagnosed as malignant mesothelioma by use of thoracentesis, CPBR and CPB altogether. The diagnosis was confirmed by using special methods like keratin, EMA, CEA. In the literature; diagnostic yield of PFC for malignant mesothelioma is reported as 50%, and diagnostic yield of CPB was reported as 20-71% (10-12). In the study of Emad et al none of the two malignant mesothelioma cases could be diagnosed by these procedures (6). Open pleural biopsy is accepted as the best diagnostic procedure in malignant mesothelioma because it gives opportunity of direct examination and taking larger tissue samples for histological diagnosis. However, because of the tumor seeding from thoracotomy site and severe pain at incision site after the operation, it is suggested to try less invasive procedures like thoracentesis, CPB and CPBR before performing open pleural biopsy (6,11).

In our study there was no mortality due to thorasentesis, CPB or CPBR. Complications were observed in 7 cases, two of which were major. In the literature, major complication was reported as 4 to 15.5% in patients in whom thoracenthesis was performed, and 7.7-11% of cases in whom CPB were performed (13-17). In the study of Emad et al, following complications after CPBR were reported: pain (14.7%), cough (8.8%), hypotension (5.8%), and arrhythmia (5.8%). Complications after CPB were noted as pneumothorax in 5.8%, and hypotension in 2.9% of cases. Even though three procedures were performed together in our study, the ratio of complications did not exceed the rates reported in the literature. This finding may suggest that CPBR procedure does not increase the rate of complications.

In conclusion, CPBR procedure; performed via Cope's needle, provides additional diagnostic

yield in malignant pleural effusion. It is a safe, simple, and well tolerated procedure. Since the CPBR can provide diagnosis in cases in whom PFC and CPB are not diagnostic; we suggest that the combination of PFC examination, CPB and CPBR should be performed before consideration of more invasive procedures like thoracoscopy and thoracotomy with open pleural biopsy.

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