

Prospective Study of Combined Use of Bronchial Lavages and Brushings in Diagnosis and Typing of Centrally Located Lung Tumors

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Abstract

Objective: To determine the diagnostic accuracy of examining bronchial lavage (BAL) and brushing in pulmonary cytopathology and whether BAL and brushing can complement each other in routine practice among lung specialists. **Design:** A prospective study comparing 528 BAL and brushing results, conducted during 1999-2003. Tumors were confirmed by cytopathology, imaging techniques, or clinical outcome and imaging techniques combined. **Subjects:** 528 patients (374 men; 154 women) aged 65,3 years that underwent fibreoptic bronchoscopy for various pulmonary symptoms. **Results:** Exact concordance between BAL and brushing results was obtained in 443/508 (87,2%) satisfactory specimens. In 443 cases lung cancer was diagnosed by BAL cytology (329 men, 114 women; mean age 67,8 years). Lung tumors were separated into squamous cell carcinoma, adenocarcinoma, large cell carcinoma, small cell carcinomas, undifferentiated carcinoma. BAL specimens showed non-specific findings in 329 cases (74,3%) cases. No significant differences occurred in the number of brushings taken or in the bronchoscopic presentation of these cases. Except in one case (0,2%) of a false positive cytological result, malignancy was confirmed by repeated radiography and computed tomography. In 478 cases lung cancer was diagnosed by brushing alone (346 men, 132 women; mean age 64,30 years). Non-specific cytological disorders were found in 288 cases (60,3%). Examinations had to be repeated in 46 of the 528 patients either to confirm the initial results or to resolve apparent discrepancies between results and clinical data. **Conclusions:** Examination of bronchoalveolar lavages complements bronchial brushing cytopathology in both diagnosing and typing lung tumors and could be performed more systematically in patients undergoing fibreoptic bronchoscopy.

Keywords: *BAL, bronchial brushing, cytology, lung tumor*

Introduction

Lung tumors are the most common cause of death from cancer in men and according to recent studies are now emerging as one of the most common causes of death from cancer in women [1]. Usually for appropriate management of lung tumors a tissue diagnosis and typing must be obtained and a clear distinction between small cell carcinomas and non-small cell carcinomas must be made preoperatively or before any aggressive treatment. Cytopathological investigation is very important to make the diagnosis. Recent reports based on the recommendations of the pathology committee of the International Association for the Study of Lung Cancer show, however, that an

approach that combines cytological examination and biopsy helps the search for mixed small cell and large cell carcinomas and may have important prognostic implications [2]. Moreover, bronchial brushing cannot be performed in inaccessible sites or in patients at risk of hemorrhage, and alternative methods for obtaining tissue diagnosis (bronchoalveolar lavage - BAL) are often needed.

Of the specimens that can be obtained by bronchoscopy, washings, brushing, and fine needle aspirations may complement biopsies in the diagnosis of lung cancer [3,4]. Traditionally, the bronchial secretions aspirated during fibreoptic bronchoscopy are considered to have little diagnostic value as they are

thought to contain mainly mucoid debris and are discarded [4]. Thus malignancy is often assessed by biopsies alone, whereas true carcinomatous cells can be readily recognized and typed with bronchial secretions [3,5]. The aim of our study was to determine whether the bronchoalveolar lavage (BAL) could complement bronchial brushings in the diagnosis and typing of lung tumors.

Methods

During 1999-2003 we obtained combined bronchial lavage and brushing specimens during fiberoptic bronchoscopy for various pulmonary symptoms in 528 patients (374 men; 154 women; mean age 65,3 years). A questionnaire documenting clinical data was completed by the lung specialist at the first examination and at each control stage.

BAL was obtained by installing isotonic saline into a selected zone and respirating. All samples were preserved in 70% ethyl alcohol and posted to the cytopathology laboratory with clinical, radiological, and bronchoscopic information. Specimens were centrifuged (1500 rpm, 15 min). Three to five slides were prepared from the cell concentrate and stained according to Papanicolaou procedure [6]. All slides were evaluated by two independent pathologists. Malignant cells were typed at high power field and recorded as squamous cell carcinoma-type cells, adenocarcinomatous cells, poorly differentiated carcinomatous cells, large cell carcinoma-type cells, small cell carcinoma-type cells, or undifferentiated carcinomatous cells.

Usually one to four brushing specimens were taken from abnormal areas within bronchoscopic range, two to four slides were prepared, fixed with 70% ethyl alcohol and stained according to Papanicolaou procedure. All slides were evaluated by two independent pathologists.

For both BAL and brushing slides, only specimens with unequivocal malignant features were considered to be positive. No "suspicious" or "atypical" case was included in the cancer cases. The data were coded and computerized. The X2 test on paired series was used to compare categorical variables, and a probability level of 0,05 was regarded as significant.

Results

Twenty BAL samples were unsatisfactory owing to poor cellularity or the presence of too much blood. Cytological examination of brushing was impossible in 19 cases owing to poorly preserved or non-representative material.

Cytopathological comparison: *Tab.1* shows a comparison of BAL and brushing results: tumor-positive, negative and unsatisfactory. If unsatisfactory specimens are ignored, an exact concordance of BAL and brushing

was obtained in 87,2% (443/508) of cases. Negative results were obtained in 35 out of 508 BAL specimens (6,9%). All the tumors diagnosed by BAL or brushing, or both, were confirmed by histopathology (biopsy or surgery specimens, when patients could undergo an operation), computed tomography, or the combination of imaging techniques and clinical outcome, except in one case of a false positive cytological result in a patient with pneumonia.

RESULTS	BAL	BRUSHING
Positive	443 cases (87,2%)	478 cases (93,9%)
Negative	45 cases (8,9%)	12 cases (2,4%)
Unsatisfactory specimens	20 cases (3,9%)	19 cases (3,7%)
Total	508 cases	509 cases

Tab.1 The results of cytological examination of combined BAL and brushings in the patients undergoing fiberoptic bronchoscopy.

*One case was false positive cytological result in patient with pneumonia.

TUMOR TYPING	BAL	BRUSHING
Squamous cell carcinoma	294 cases (66,4%)	325 cases (68%)
Adenocarcinoma	136 cases (30,7%)	145 cases (30,3%)
Large cell carcinoma	3 cases (0,7%)	2 cases (0,4%)
Small cell carcinoma	2 cases (0,5%)	1 cases (0,2%)
Undifferentiated carcinoma	8 cases (1,7%)	5 cases (1,1%)
Non-specific findings	329 cases (74,3%)	288 cases (60,3%)
Total	443 cases	478 cases

Tab.2 Cytopathological comparison of typing in lung tumors diagnosed by both BAL and brushing.

In 443 cases lung cancer was diagnosed by BAL cytology (329 men, 114 women; mean age 67,8 years). Table II shows the agreement between BAL and brushing cytological changes and tumor typing. Lung tumors were separated into squamous cell carcinoma, adenocarcinoma, large cell carcinoma, and small cell carcinomas, undifferentiated carcinoma. BAL specimens showed non-specific findings in 329 cases (74,3%) cases. No significant differences occurred in the number of brushings taken or in the bronchoscopic presentation of these cases. Except in one case (0,2%) of a false positive cytological result, malignancy was confirmed by repeated radiography and computed tomography.

In 478 cases lung cancer was diagnosed by brushing alone (346 men, 132 women; mean age 64,30 years). Non-specific cytological disorders were found in 288 cases (60,3%).

Tab.3 shows non-specific cytological findings were divided into non-specific inflammation, suppurative-destructive changes, hyperplasia of ciliar epithelium, squamous metaplasia.

NON-SPECIFIC FINDINGS	BAL	BRUSHING
Non-specific Inflammation	11 (24,4%)	1 (8,3%)
Suppurative-destructive changes	4 (8,9)	1 (8,3%)
Hyperplasia of ciliar epithelium	16 (35,6%)	8 (66,7%)
Squamous metaplasia	14 (31,1%)	2 (16,7%)
Total	45 cases	12 cases

Tab.3 Cytopathological comparison of non-specific findings diagnosed by both BAL and brushing.

Repeated examinations: Examinations had to be repeated in 46 of the 528 patients either to confirm the initial results or to resolve apparent discrepancies between results and clinical data. Examinations had to be repeated once in 41 patients, twice in 4 patients, and three times in one patient. Overall, repeating the examinations confirmed the absence of abnormal cells in 21 cases, confirmed malignancy in 8, allowed documenting of malignancy in 14, and gave no additional information in five.

Discussion

Diagnostic value of pulmonary cytopathology: Before the introduction of the flexible bronchoscope the diagnostic value of examining bronchoalveolar lavages in detecting lung tumors was often lower than 50%: in 1964 Koss reviewed 560 patients with primary bronchial carcinomas in which examination of 288 bronchial aspirates (51.4%) yielded positive results [8]. In 1975 Atay and Brandt reported that in a study of 885 patients 79% of centrally located lung tumors could be diagnosed cytologically, whereas only 45% of peripheral tumors could be detected. In 1979 Payne et al reported that the diagnostic accuracy of examining bronchial aspirates was 46% (50 of 109 primary bronchial carcinomas).

Since fiberoptic bronchoscopy was introduced as a diagnostic procedure in 1968, several methods for

obtaining satisfactory material have become available. Though examination of sputum can provide evidence of malignancy in many cases of cancer specimens collected from fiberoptic bronchoscopy yield a higher rate of positive results. In 1980 Taft et al reported that the sensitivity of bronchial aspirates in diagnosing lung cancers was 75% and could reach 88,7% when the examination was performed by two pathologists (13%). In 1991 DiBonito et al reported a sensitivity of 81% with no false positive results [5]. The present series shows a sensitivity value of 88,3% if initial brushing results are considered as the diagnostic reference, and 90,4% if both histopathology and follow up (the gold standard) are taken into account. Data about the cytopathology of bronchial secretions remain rare, and many authors have had difficulties in obtaining representative material from the bronchial tree, thus leading them to discontinue examination of bronchial secretions in favor of other cytological methods [4].

Bronchial brushings are favored by most groups for the cytological investigation of proximal lung cancers, and samples that arrive at the laboratory as prepared slides may seem much easier to handle. Standardization is very difficult to obtain, however, especially in terms of quality of fixation. Many brushings are not satisfactory.

We have shown that, provided that conditions are adequate, the diagnostic accuracy of bronchial aspirates may exceed 87%. Moreover, cases that are difficult to manage that is, contraindications for brushing, positive fiberoptic bronchoscopy findings but positive BAL and negative brushing results, mucosal abnormalities but negative BAL and brushing results are clearly resolved by repeating both examinations. Repeating examinations also led to the absence of false negative results for both diagnostic techniques together.

Conclusion

According to the WHO's classification [7] malignant epithelial tumors are separated into squamous cell carcinomas (30-60% of histopathology cases), small cell carcinomas (about 25%), adenocarcinomas (15-25%), and large cell carcinomas (10-20%). From a therapeutic point of view, lung tumors are better separated into small cell carcinomas, which require intensive chemotherapy and sometimes radiation therapy, and non-small cell carcinomas, which are better treated surgically.

As far back as 1952 Foot had shown that typing could be correctly obtained by studying sputum in 89.9%, 78.4%, and 83.5% of squamous cell carcinomas, adenocarcinomas, and small cell carcinomas respectively. 1972 Lange and Hoeg showed comparable results. In 1985 Truong et al showed that typing of squamous cell and small cell carcinomas could be correctly obtained in more than 80% of cases regardless of the cytological method used (sputum, washings, or brushings). In a recent series of 100 cases with

confirmation at necropsy, the diagnostic yield of examining bronchial aspirates reached 80% [5]. The present series shows that exact concordance can be achieved in 88,4% of cases. A correct, if not definitive, diagnosis can be obtained in almost all cases of centrally located lung tumors by examining

bronchoalveolar lavages and brushings. Moreover, when a definitive histopathological diagnosis cannot be obtained because of risk of haemorrhagia, severe respiratory failure, or inconclusive sampling diagnostic procedures such as cytological examinations of BAL become necessary.

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Проспективное исследование комбинированного применения бронхиального лаважа и браш-биопсии для диагностики и типирования центральных опухолей легких

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РЕЗЮМЕ

С целью определения диагностической точности бронхиального лаважа и браш-биопсии обследовано 528 пациентов (154 женщины, 374 мужчин, средний возраст - 65,3 лет), которым проведена бронхоскопия. Цитологическое исследование бронхиального лаважа и браш-биопсии этих пациентов показал совпаденидиагноза у 443 пациентов (87,2%). 443 пациентам диагноз опухоли был поставлен цитологическим исследованием бронхиального лаважа (114 женщин, 329 мужчин, средний возраст - 67,8 лет). Опухоли легких классифицированы как: плоскоклеточная карцинома, аденокарцинома, крупноклеточная карцинома, мелкоклеточная карцинома, недифференцированная карцинома. Неспецифические цитологические изменения выявлены в бронхиальных лаважах у 329 (74,3%) и в браш-биоптатах у 288 пациентов (60,3%). У 478 пациентов диагноз опухоли поставлен в результате цитологических исследований браш-биопсии (132 женщины, 346 мужчин, средний возраст - 64,3 лет). Повторные исследования проведены 46 пациентам. Цитологическое исследование бронхиального лаважа целесообразно для диагностики и типирования опухолей легких и следует применять при бронхоскопии более широко.

Ключевые слова: *бронхиальный лаваж, браш-биопсия, цитология, опухоль легких*