Original Article

Efficacy of Broncho-Alveolar Lavage and Bronchial Brush Cytology in Diagnosing Lung Cancers

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Abstract

Of all the cases investigated for suspected lung cancer between June 1999 and June 2003, 196 cases were selected where flexible bronchoscopic samples of broncho-alveolar lavage (BAL) and bronchial brush (BB) cytology as well as bronchial biopsy were taken and processed as per standard procedures of cytology and histology. The aim of this study was to compare the diagnostic efficacy of BAL and BB cytology in diagnosing lung cancer, taking bronchial biopsy as the 'Gold Standard' diagnostic test. Sensitivity of BB was 87.3%; while that of BAL was 39.4%. Specificity of BB and BAL was 97.6% and 89.6%, respectively. BB was better than BAL in morphological typing of lung cancers. We conclude that bronchial brushing is a much superior technique in the diagnosis and morphological typing of lung cancers.

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Key Words : Bronchial brushing, broncho-alveolar lavage, diagnostic efficacy, lung cancer.

Introduction

The use of cytological methods in the diagnosis of malignant lesions of the respiratory tract has been generally acclaimed as one of its most successful applications.[1] Flexible fiber-optic bronchoscope revolutionized respiratory cytology, as techniques like bronchial brushings, broncho-alveolar lavage and bronchial biopsy became more easy, accessible and popular, shifting the emphasis from diagnosis of advanced malignancy in operable patients to the use of cytology as a first line diagnostic and management tool. Today respiratory tract cytology is well established throughout the world as a vital diagnostic procedure in the evaluation of any patient with suspected lung malignancy.

Broncho-alveolar lavage (BAL), which was originally developed as a therapeutic tool for pulmonary conditions like pulmonary alveolar proteinosis, cystic fibrosis and intractable asthma, also has gained acceptance and steady popularity as a tool for diagnosing lung cancer.[1] Bronchial brushing (BB) is a technique where surface of a suspected lesion, visualized through a bronchoscope, is scraped in order to collect the cytological sample.

Our aim was to study and compare the efficacy of these two very popular cytological techniques in diagnosing carcinoma of lung by correlating them with histopathological diagnosis by bronchial biopsy.

Materials and Methods

The study was conducted at the Department of Pathology at Himalayan Institute of Medical Sciences, Dehradun. Out of all the suspected cases of carcinoma lung received from June 1999 to June 2003, we selected 196 cases where boncho-alveolar lavage, bronchial brush cytology samples as well as bronchial biopsy were available. The case was not included when any of the three samples was inadequate. Histopathological diagnosis by bronchial biopsy was considered as the "Gold Standard."

The samples were obtained by flexible fiber-optic bronchoscopy done by the pulmonologist. (a)

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Broncho-alveolar lavage samples were received as 20ml aliquotes of normal saline in sterile vials. Samples were centrifuged and prepared into air-dried and wet-fixed smears. (b) Bronchial brushings were received as air-dried and wet-fixed smears of two to three brushings by disposable bronchial brush, smeared directly on to clean glass slides. The air dried smears were stained with May-Grunwald Geimsa and the wet fixed slides with Papanicolaou and Hematoxylin & Eosin stains. (c) Bronchial biopsies were received in 10% formalin.

Observations

Out of 196 cases of suspected lung cancer, 153 were males while 43 were females, with their ages ranging between 19 to 70 years. The male: female ratio was 3.6:1.

In all, 71 (36.2%) cases were diagnosed by bronchial biopsy to be suffering from lung cancer, of which 65 were males and 6 were females. The male to female ratio of these cases was 10.8: 1. Rest of the cases showed inflammatory or tuberculous lesions or no significant pathology (Table 1).

BAL cytology showed 28 True Positive cases and 112 True Negative cases, as confirmed by biopsy. Moreover, 13 cases were diagnosed as False Positive and 43 cases as False Negative by BAL. BB cytology showed 62 True Positive cases and 122 True Negative cases with only 03 cases as False Positive and 09 cases as False Negative (Table 2).

Sensitivity of cytodiagnostic results of BB was 87.3%; while that of BAL was only 39.4%. Specificity of BB was 97.6% and that of BAL was 89.6%. Similarly Positive Predictive Value and Negative Predictive Value, False Negative Index and False Positive Index of BB were better than of BAL. Accuracy of brush cytology was 93.9% while that of BAL was 71.4% (Table 3).

Table 1 : Sex-wise distribution of various cases diagnosed by bronchial biopsy

Diagnosis	Males	Females	Total	%
Carcinomas	65	6	71	36.2
Inflammations/ Dysplasia	69	30	99	50.5
Tuberculosis	15	6	21	10.7
No significant pathology	4	1	5	2.6
Total	153	43	196	

Table 2 : A 2x 2 tabulation of test results

Sample	Test result				Total
	TP	TN	FP	FN	
BAL	28	112	13	43	196
Brush cytology	62	122	3	9	196

TP = True positive,TN = True negative, FP = False positive, FN = False negative

Twenty (71.4%) of the 28 cases diagnosed by BAL as lung cancer, were morphologically classified as poorly differentiated carcinoma. Similarly 33 (53.2%) of the 62 cases diagnosed by BB as lung cancer, were morphologically classified as poorly differentiated carcinoma. While only 26 (36.6%) cases out of 71 bronchial biopsies, were labeled as poorly-differentiated carcinomas. Thus biopsy specimens showed much better morphological features and helped in categorizing these cases into specific type of carcinomas in comparison to the cytological material obtained by either BAL or BB (Table 4).

Discussion

With the advent of flexible fiber-optic bronchoscope, respiratory cytology took a new turn as samples like bronchial washings, bronchial brushings, broncho-alveolar lavage and trans-bronchial needle aspirations could be collected from the respiratory tract, yielding significant amount of cytological material.[1] With this, the emphasis shifted from diagnosis of malignancy in operable patients and confirmation of metastases, to the use of cytology as a first line diagnostic procedure on which crucial management decisions could be based.[1, 3]

In our study, in comparison to BAL, bronchial brushing gave higher number of True Positive and True Negative cases, and much lesser number of False Positive and False Negative cases, showing its superiority over BAL in diagnosing lung cancers (Table 2).

Since cytological sampling by BAL technique relies mainly on cells 'exfoliated' from the malignant lesion

Table 3 : Comparison of indices of BAL and brush cytology

Indices		BAL	Brush cytology
Sensitivity	TP / (TP+FN)	39.40%	87.30%
Specificity	TN / (TN+FP)	89.60%	97.60%
Positive predictive value	TP / (TP+FP)	68.30%	95.40%
Negative predictive value	TN / (TN+FN)	72.30%	93.10%
False negative index	FN / (FN+TP)	60.60%	12.70%
False positive index	FP / (FP+TN)	10.40%	2.40%
Accuracy	(TP+TN) / (TP+TN+FP+FN)	71.40%	93.90%

TP = True positive,TN = True negative, FP = False positive, FN = False negative

Table 4 : Morphological classification of malignant cases of lung

	BAL		Brush		Biopsy	
	No	%	No	%	No	%
Squamous cell carcinoma	5	17.9	14	22.6	21	29.6
Small cell carcinoma	2	7.1	9	14.5	14	19.7
Adenocarcinoma	1	3.6	6	9.7	9	12.7
Poorly differentiated carcinoma	20	71.4	33	53.2	26	36.6
Carcinoid					1	1.4
Total	28		62		71	

in the bronchial epithelium, the adequacy of its samples depends on several vital factors, especially a) the degree of differentiation of malignant growth; b) preservation of the morphology of cytological material obtained; and c) technical skill of the pulmonologist who is retrieving the lavage fluid from the bronchus (Figs. 1 & 2). In general, less differentiated, anaplastic lesions have more loosely cohesive cells in comparison to well differentiated lesions.[3] Thus such lesions exfoliate larger number of cells into the bronchial cavity than the well-differentiated lesions. Secondly, while these exfoliated cells are lying in the bronchus, they start developing degenerative changes, thus progressively losing their morphological details which are important in differentiating them from non-malignant cells shed-off by the normal bronchial epithelial lining. Usually around 20ml. saline is instilled through the bronchoscope for BAL samples.[1] If the technique of the pulmonologist is not proper, the sample retrieved might be less in amount and thus may have lesser cytological material than expected, thus again increasing the chances of false negative results.[1, 4] All these factors, present individually or together, affect the overall yield and diagnostic value of BAL specimens.

Bronchial brushing technique has the advantage that the surface of the suspicious lesion is scraped by the help of a brush passed in through the bronchoscope.[1] Thus this technique manages to 'dislodge' the cells from the surface of those well-differentiated malignant lesions too, which do not exfoliate cells readily. Thus, the chances of getting adequate diagnostic cytological sample by BB greatly increase in comparison to BAL samplings (Fig. 3 & 4). Moreover, since the surface of the malignant lesion is scraped by the brush, the cells retrieved show better preserved morphological details in comparison to the cells which have already exfoliated into the bronchial cavity (Figs. 2 & 4). All these factors contribute in the increased diagnostic yield of BB samplings.

In our study, the Sensitivity, Specificity and Accuracy of BAL samples were 39.4%, 89.6% and 71.4% respectively, when a single sample of BAL was collected (Table 3). Truong et al[4] reported Sensitivity of 66.0%; while Ng. & Horak[5] reported a Sensitivity as high as 74.0% for BAL. Studies have shown that increasing the number of attempts at obtaining BAL

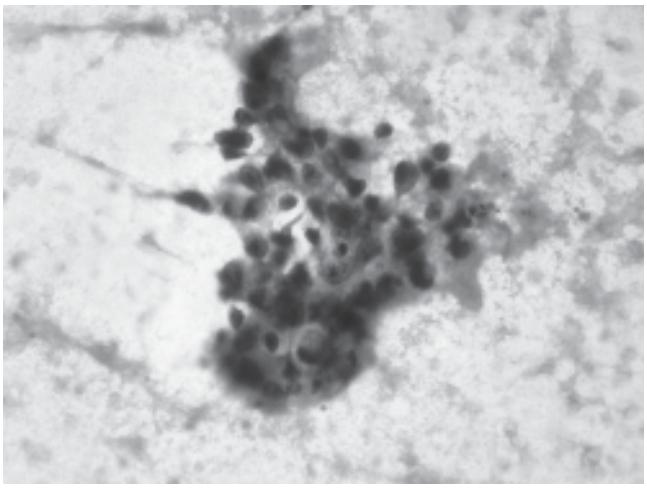

Fig. 1 : BAL smear - cluster of atypical cells with poorly preserved morphology (MGG, x 400).

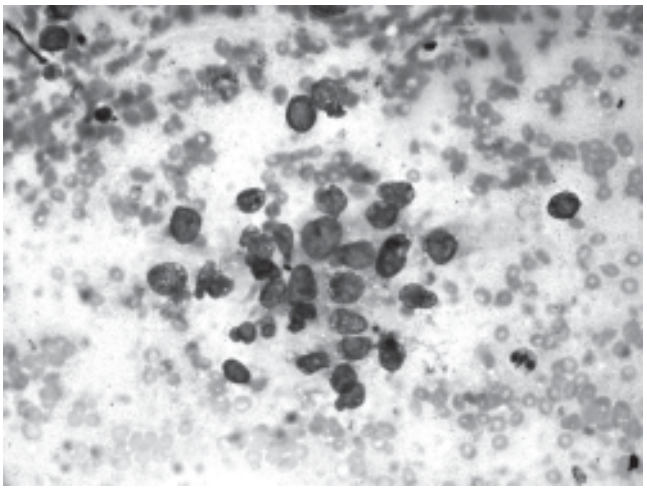

Fig. 2 : BAL smear - loose cluster of atypical cells forming vague acinar arrangement (MGG, x 400).

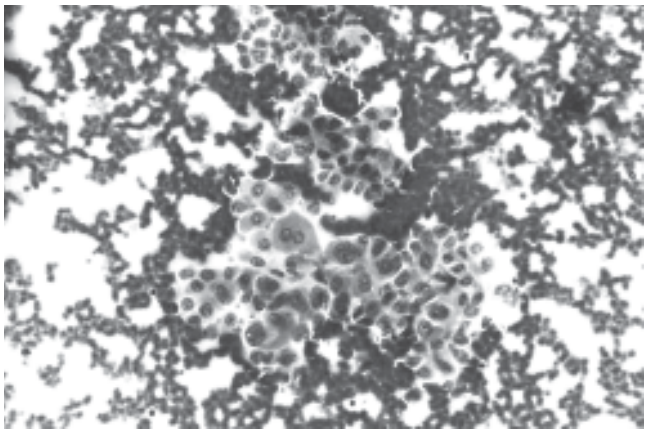

Fig. 3 : Bronchial brushing - squamous cell carcinoma with well preserved morphology (MGG, x 100).

sampling can improve its Sensitivity, Specificity and Accuracy.[4, 6, 7] However, the inconvenience caused to the patient, in spite of BAL technique being non-invasive, outweighs the benefits of multiple samplings, especially when other techniques like bronchial brushing and bronchial biopsy are available.

In our study, the values of Sensitivity, Specificity and overall Accuracy of BB were 87.3 %, 97.6 % and 93.9 % respectively, which were much superior to those of BAL (Table 3). The Sensitivity of 87.3% for BB in our study was in agreement with various other workers like Chopra et al [8] (86.3%); Zavala et al [9] (88.5%); and Solomon et al [10] (89.1%). Shroff et al[11] reported the Sensitivity of BB to be as high as 97.3% in their study. Bibbo et al[12] reported the Sensitivity for BB samples to be only 70%. However they reported the Specificity of BB to be much higher (98%) which was comparable to our study.

Various workers have tried to combine the two techniques of BB and BAL, in order to improve the yield of diagnostic cytological material. Govert et al[13] reported 85.3% Sensitivity on combining these two techniques; while Bedrossian et al[14] reported a higher Sensitivity of 92%. However, this combination has not gained much popularity due to the fact that in doing so, instead of one, the cost of two cytological procedures needs to be borne by the laboratory or the patient, for a little improvement in Sensitivity, when compared with results of BB alone.[13]

In the present study, bronchial biopsy classified 29.6% cases (n=21/ 71) as squamous cell carcinoma. While BB could diagnose 22.6% of the cases (n=14/ 62) as squamous cell carcinoma, BAL was able to diagnose only 17.9% cases (n=5/ 28) as squamous cell type. Similarly, 19.7% cases (n=14/71) were diagnosed as small cell carcinoma by biopsy. BB samples classified 14.5% cases (n=9/62) as small cell

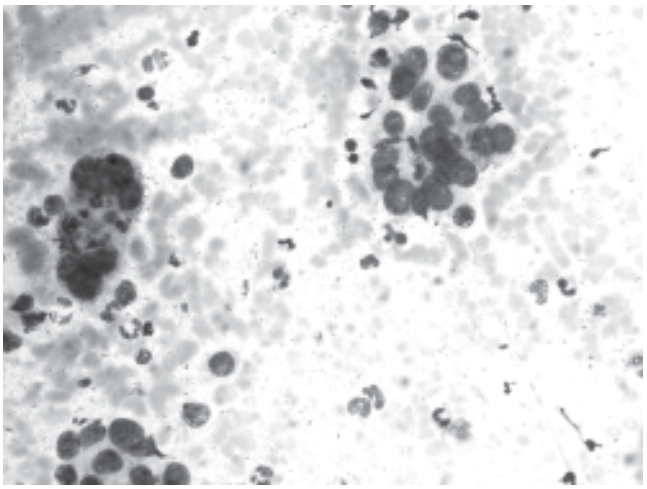

Fig. 4 : Bronchial brushing - adenocarcinoma cells forming typical acinar pattern (MGG, x 400).

carcinoma while in BAL samples only 7.1% cases (n=2/ 28) were morphologically diagnosed as small cell type. Thus it was obvious that samples obtained by BB showed better cytological details than BAL, which helped in the specific morphological classification of lung cancers.

A large number of samples of BB (53.2%) were classified as poorly differentiated carcinoma, indicating that BB still remained inferior to biopsy, where morphological classification was required. Biopsy samples showed only 36.6% cases to be poorly differentiated carcinomas; while rest could be specifically categorized as, squamous, small cell or other types. With BAL, due to less demonstrable cytological details, as many as 71.4% samples got classified as poorly differentiated carcinoma. Thus, BB showed superiority over BAL in morphological classification of malignant samples (Table 4).

With a good Sensitivity (87.3 %), Specificity (97.6 %) and Accuracy (93.9 %), bronchial brushing promises to be a very convenient cytological technique that can be confidently utilized for screening of doubtful cases and early diagnosis of lung cancer, as it saves the time needed for the processing of biopsy specimens. However, as BB falls short of expectations in morphological classification of lung cancers, only cases positive for malignancy may later be biopsied to confirm the morphological type of the malignant lesion.

Conclusion

Bronchial brushing is a much superior technique in the diagnosis and morphological typing of lung cancers, as it demonstrates far better Specificity, Sensitivity and Accuracy, in comparison to broncho-alveolar lavage.

References

1. Johnston WW, Elson CE. Respiratory tract. In: Bibbo M, editor. Comprehensive cytopathology. 2nd ed. Philadelphia: W.B. Saunders Company; 1997. p. 325-401.
2. Bancroft JD, Gamble M, editors. Theory and practice of histological techniques. 5th ed. New York: Churchill Living Stone; 2002.
3. Husain AN. The lung. In: Kumar V, Abbas AK, Fausto N, editors. Robbins and Cotran pathologic basis of disease. 7th ed. India: Saunders; 2004. p. 711-72.
4. Truong LD, Underwood RD, Greenberg SD, McLarty JW. Diagnosis and typing of lung carcinomas by cytopathologic methods. A review of 108 cases. *Acta Cytol* 1985; 29:379-84.
5. Ng ABP, Horak GC. Factors significant in the diagnostic accuracy of lung cytology in bronchial washing and sputum samples: II. Sputum samples. *Acta Cytol* 1983; 27: 397-402.
6. Ahmad M, Afzal S, Saeed W, et al. Efficacy of bronchial wash cytology and its correlation with biopsy in lung tumours. *J Pak Med Assoc* 2004; 54:13-6.
7. Naryshkin S, Daniels J, Young NA. Diagnostic correlation of fiberoptic bronchoscopic biopsy and bronchoscopic cytology performed simultaneously. *Diagn Cytopathol* 1992; 8:119-23.
8. Chopra SK, Genovesi MG, Simmons DH, Gothe B. Fiberoptic bronchoscopy in the diagnosis of lung cancer comparision of pre and pro bronchoscopy sputa, washings, brushings and biopsies. *Chest* 1997; 111:522-3.
9. Zavala C: Diagnostic fiberoptic bronchoscopy. Techniques and results in 600 patients. *Chest* 1975; 68:12-9.
10. Solomon DA, Solliday NH, Gracey DR. Cytology in fiberoptic bronchoscopy: comparison of bronchial brushing, washing and post-bronchoscopy sputum. *Chest* 1974; 65:616-9.
11. Shroff CP. Abrasive bronchial brushing cytology. A preliminary study of 200 specimens for the diagnosis of neoplastic and non-neoplastic broncho-pulmonary lesions. *Acta Cytol* 1985; 29:101-7.
12. Bibbo M, Fennessy JJ, Lu CT. Bronchial brushing technique for the cytologic diagnosis of peripheral lung lesions: a review of 693 cases. *Acta Cytol* 1973; 17:245-51.
13. Govert JA, Kopita JM, Matchar D, Kussin PS, SamuelsonWM. Cost effectiveness of collecting routine cytologic specimens during fiberoptic bronchoscopic for endoscopically visible lung tumours. *Pol Arch Med Wewn* 2002; 108:1193-7.
14. Bedrossian CWM, Rybka DL. Bronchial brushing during fiberoptic bronchoscopy for the cytodiagnosis of lung cancer: comparison with sputum and bronchial washings. *Acta Cytol* 1976; 20:446-53.

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