

Efficacy of Bronchial Wash Cytology and its Correlation with Histopathology in Diagnosis of Lung Carcinoma in a Tertiary Care Hospital

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ABSTRACT

Introduction: Cytological evaluation is an important, usually initial diagnostic modality in patients with suspected malignant lung masses. Bronchoscopic washing, bronchoalveolar lavage, bronchial brushing and fine needle aspirations may complement tissue biopsies in the diagnosis of lung cancer. This study was undertaken to compare the efficacy of bronchial wash cytology and to correlate it with histopathology in diagnosis of suspected cases of lung cancer at a tertiary care hospital.

Material and Methods: Bronchial washings and bronchial biopsy were collected from total 60 clinically suspected cases of carcinoma lung. Bronchial washing smears were stained with MGG and H&E stain and were categorized as unequivocally positive / unequivocally negative for malignancy and atypical (equivocal for diagnosis). Biopsy sections were examined for histopathological diagnosis.

Results: Cytomorphologically, 30 cases were reported as positive for malignancy, 28 cases were negative for malignancy and 02 cases were atypical. On histopathology, lung carcinoma was diagnosed in 48 patients out of them 35 cases were of squamous cell carcinoma, 7 cases were of small cell carcinoma and 6 were of large cell carcinoma.

Conclusion: Maximum diagnostic yield can be obtained by combining biopsy with cytological procedures of washing rather alone.

Keywords: Bronchial-Washing, Carcinoma, Lung, Sensitivity, Specificity

Introduction

Pulmonary lesions are mostly caused by infections such as tuberculosis/ pneumonia and lung cancer or secondaries. It usually appears as white, round shadows on x-rays or CT scan. Histopathology remains the gold standard in diagnosis of these diseases.^[1] In India, GLOBOCAN 2012 reported an incidence of lung cancer as 75,275 in all age groups and both genders.^[2] The use of cytological methods in diagnosis of malignant as well as non-malignant lesions of respiratory tract has been generally acclaimed as one of its most successful applications.^[3] Bronchoscopic washing, bronchoalveolar lavage, bronchial brushing and fine needle aspirations may complement tissue biopsies in the diagnosis of lung cancer.^[4]

Bronchial washing has proven to be an economical, safe, and cost-effective technique, particularly in cases with highly vascularized lesions or small cell carcinomas where crush artifacts are relatively common.^[5] In addition, cell samples obtained via bronchial washing can also be cultivated for micro-biological analysis.^[6] Therefore this study was undertaken to compare the efficacy of bronchial wash cytology and to correlate it with histopathology in

diagnosis of suspected cases of lung cancer at a tertiary care hospital.

Material and Methods

Total 60 clinically suspected cases of carcinoma lung were studied over a period of two years. Approval of the study was taken from Institutional Ethical Committee. Detailed relevant clinical, radiological and routine investigation findings were recorded on predesigned proforma. Past and present history of any anti-tubercular treatment taken was recorded in every patient. Complete general physical examination, examination of respiratory system and other systems was performed with special reference to metastasis and/or paraneoplastic syndromes.

CT scan was done in maximum possible cases for proper evaluation of pulmonary lesions i.e. characterizing tissue densities for providing accurate size assessment of lesion, presence and type of calcification as well as detecting mediastinal lymphadenopathy. All centrally located lesions in suspected cases of carcinoma lung were included. Exclusion criteria include peripherally situated lung lesions, cases of carcinoma metastasizing to the lung and inadequate tissue for opinion.

Bronchial washings and bronchial biopsy were collected from tracheo-bronchial lesions suspected of carcinoma lung. All samples were taken after taking signed informed consent explaining the potential hazards of bronchoscopy and topical anesthesia. The tracheobronchial tree including all the segmental and subsegmental bronchi was inspected for any visible lesion. Biopsy was taken from visible growth or lesion over the bronchus and fixed in 10% formalin. 5-10 ml normal saline was put through inner channel and washings were collected by suctioning into a trap which was connected to the bronchoscope. Biopsy as well as bronchial washings was sent to pathology department for further analysis.

Bronchial washing samples were centrifuged and air-dried smears were stained by May-Grunwald Giemsa (MGG). Wet fixed (95% alcohol) smears were stained by Hematoxylin & Eosin (H&E). On the basis of cytomorphology, bronchial washings results were categorized as unequivocally positive / unequivocally negative for malignancy and atypical (equivocal for diagnosis). Standard techniques for biopsy processing and preparation of tissue sections were followed. H&E-stained sections were examined for histopathological diagnosis. All the data was recorded and analyzed.

Results

In the present study, age range of the selected patients varied from 36-80 years. 79.2% cases were in the age range of 50-80 years and 20.8% cases were less than 50 years of age group. Mean age of patients was 59.08 years. 53 male and 7 female patients were included. In our study,

the major constitutional symptom was chest pain followed by anorexia and malaise. Most common respiratory symptom was chest pain, followed by shortness of breath, cough with or without expectoration and hemoptysis. The frequent physical sign was anemia and clubbing followed by cervical lymphadenopathy and superior vena cava syndrome. Bronchoscopy revealed obstruction and narrowing of bronchi in most of the cases, followed by cauliflower like irregular growth and presence of black necrotic patch.

Out of 60 bronchial washing samples, 30 cases were reported as positive for malignancy (fig 1a, b & d), 28 cases were negative for malignancy and 02 cases were atypical. On histopathology, lung carcinoma was diagnosed in 48 patients, out of which 43 (85.58%) were males and 05 (10.41%) were females with a male to female ratio of 8.6:1. In our experience, 38 cases (79.16%) of lung carcinoma were smokers and 10 cases (20.83%) were non smoker. On sub-typing, 41 cases (85.41%) were of non-small cell carcinoma while remaining 7 cases (14.58%) were of small cell carcinoma (fig 1 c & e). Out of 41 cases, 35 (85.36%) cases were of squamous cell carcinoma and 6 (14.63%) were of large cell carcinoma.

09 biopsy specimens were found to be negative for malignancy while 03 cases revealed dysplastic change but not definitive for diagnosis of malignancy. In dysplastic cases, close follow up was advised. **Three dysplastic cases on histopathology and two atypical cases on cytology were excluded from the statistical analysis of data. The sensitivity and specificity of bronchial washing samples were found to be 62.5% and 100% respectively.**

Table 1: Results of Bronchial Washings and Biopsy (n=60).

Results	Number of Cases (%)	
	Bronchial Washings	Biopsy
Positive for Malignancy	30 (50 %)	48 (80%)
Negative for Malignancy	28 (46.67 %)	9 (15%)
Atypical/ dysplastic change	02 (3.33 %)	3 (5%)
Total	60 (100%)	60 (100%)

Table 2: Histological typing of Carcinoma lung cases (n=48).

Histological diagnosis	No. of Cases	Percentage (%)
1. Squamous cell carcinoma		
Well differentiated	01	2.08
Moderately differentiated	30	62.50
Poorly differentiated	04	8.33
2. Large cell carcinoma	06	12.50
3. Adenocarcinoma	00	00
4. Small Cell Carcinoma	07	14.59
Total	48	100

Table 3: Correlation of final histopathology with cytology of bronchial washing.

Cytological diagnosis (bronchial washing)	Histopathological diagnosis		Total
	Malignant	Non-malignant	
Positive for Malignancy	30	00	30
Negative for malignancy	18	07	25
Total	48	07	55

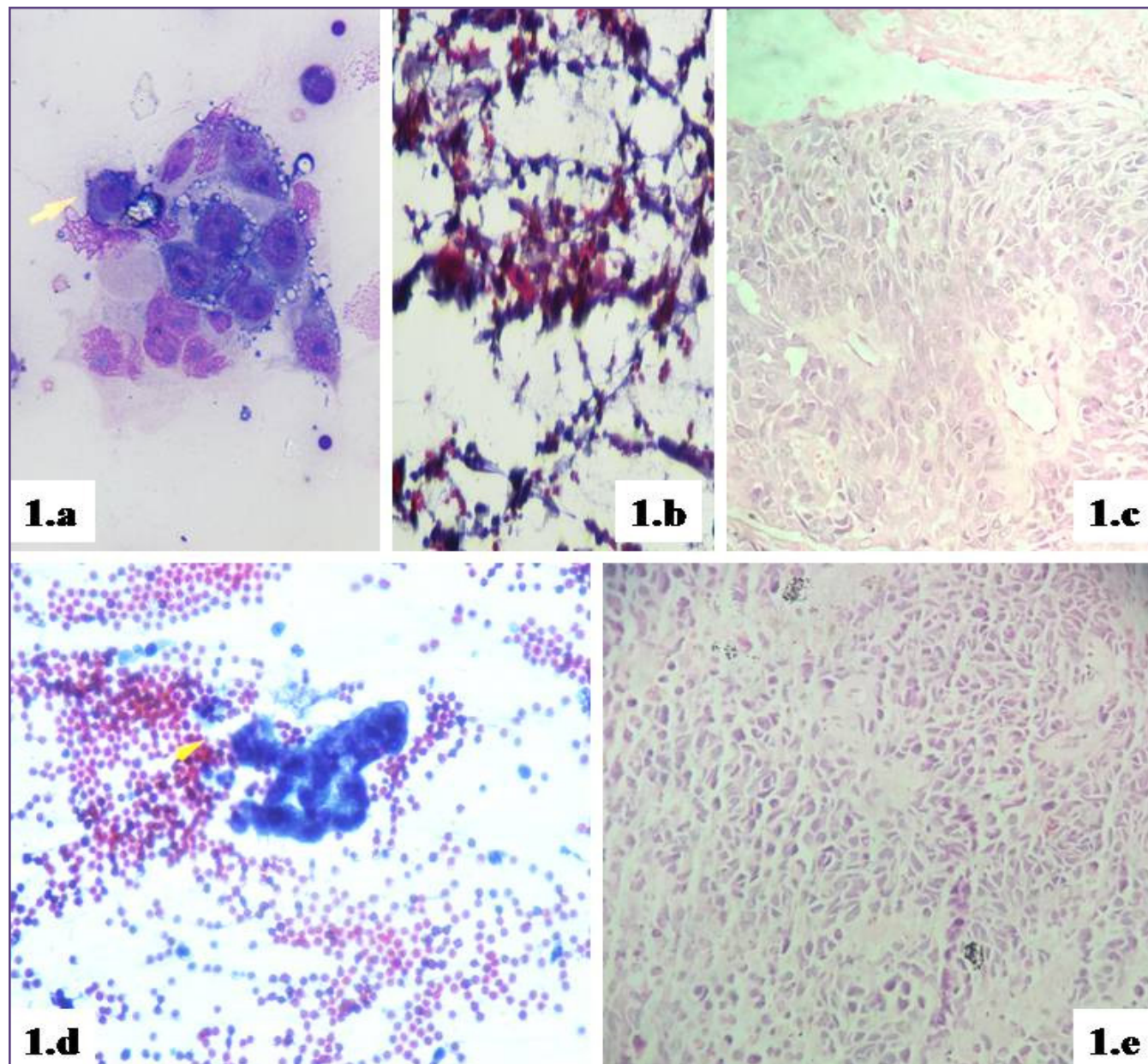


Fig. 1: a. Smear showing cluster of large atypical cells; suggestive of malignancy, bronchial washing (MGG,400X) b. Smear showing a few keratinized atypical squamous cells; suggestive of well-differentiated squamous cell carcinoma, bronchial washing(PAP,100X), c. Histomorphological features suggestive of squamous cell carcinoma, bronchial biopsy(H&E, 400X), d. Smear showing cluster of small atypical cells with high N/C ratio & dense nuclei; suggestive of small cell carcinoma, bronchial washing (MGG,400X), e. Histomorphological features suggestive of small cell carcinoma, bronchial biopsy(H&E,400X)

Discussion

Lung cancer is the most common malignant disease worldwide with 9,00,000 new cases each year in males and 3,30,000 in women.^[7] National Cancer registry program by Indian council of medical research in 3 cities (Bhopal, Delhi and Mumbai) showed lung as the commonest site for cancer among males.^[8] Male to female ratio of 8.6:1 in lung carcinoma cases was observed in our study; suggesting that the disease is more common in males which was consistent with previous studies by various authors like 4.9:1 by Wig et al⁹, 7.9:1 by Rajasekaran et al¹⁰, 6:1 by Arora et al¹¹, 8:1 by Ahmed et al¹², and 7.5:1 by Gaur et al.¹³ The incidence of lung cancer has been reported to be low before the age of 40 years in both males and females and after that it increases up to the age of 70 years.^[7] Mean age of patients was 59.08, which was in concordance with the mean age as seen by Ahmad et al¹², Gaur et al¹³, Buccheri et al¹⁴ and not correlated to the mean age (<50 years) as observed by Jha et al.^[15]

Incidence of smoking history (79.16% cases) in lung carcinoma patients correlated well with Hecht et al¹⁶ and Ochsner et al¹⁷ where 82-90% cases had a history of smoking. The smoker to non smoker ratio was 3.8:1 which was slightly higher than 2.7:1 given by Jindal et al.^[18]

In this study, non-small cell carcinoma (85.41%) predominantly of squamous cell carcinoma subtype was main diagnosis on histopathology. According to literature searched also, non-small cell cancers are usually found in around 80% of the total lung cancers and small cell cancers, around 16% of carcinoma lung. No case of adenocarcinoma was noticed in this study. However, there was a selection bias because only centrally located and endoscopically visible tumors were included. Ahmed et al¹² also reported that squamous cell carcinoma is the most frequent lung cancer, being present in 68.3%, small cell carcinoma in 21.9 % and adenocarcinoma in 4.9%.

The histologic subtype pattern varies from different studies in India. According to Vishwanathan et al¹⁹, the predominant cell type was squamous cell carcinoma (50.5%), followed by adenocarcinoma (26.4%) and unclassified (21%) among 95 patients. Similarly, squamous cell carcinoma was predominant in studies by Buccheri et al¹⁴, Jindal et al,¹⁸ Arora et al.¹¹ and Bhattacharya et al²⁰. However, a changing trend in histopathological profile of lung cancer patients is being observed worldwide and adenocarcinoma has replaced squamous cell carcinoma as the predominant subtype in various studies like conducted by Kumar et al.²¹, Piplani et al,²² and Jerse et al²³.

In the present study, bronchial washings with biopsy gave 30 true positives and 07 true negatives, 18 cases

were false negative and no false positive case was detected. Exact concordance between histopathology and bronchial wash cytology was present in 30 of 48 cases (62.5%). The diagnosis by bronchial washing mainly relies on the cells that have been exfoliated in the bronchial epithelium. The adequacy of washing samples depends on several factors such as the site and size of lesion, degree of differentiation and stage of the disease, preservation of the morphology of the cytological material obtained and the skill of the pulmonologist who retrieves the samples. The poorly differentiated tumors are less cohesive than the well differentiated ones and thus exfoliate larger number of cells in the bronchial cavity. 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. The presence of inflammation, necrotic debris or crushing artifact can affect the overall yield and diagnostic efficacy of bronchial washing samples.

Variability in the sensitivity and specificity of pulmonary cytology in diagnosis of both benign and malignant lesions is seen across various studies. **In our study, sensitivity, specificity and accuracy of bronchial washing samples were 62.5% and 100% respectively.** Truong et al²⁴ reported sensitivity of 66%, while Tuladhar et al²⁵ observed sensitivity as low as 17.4%. Solomon et al²⁶ found bronchial washing to be of minimal value in the diagnosis of lung malignancy. Lam et al²⁷ reported a sensitivity of 76 % in endobronchially visible lung cancer and 52 % for non visible cancer.

A study by Mufti et al showed that combined use of bronchial wash and bronchial brush increased the sensitivity to 90.6% and specificity to 75%.^[28] Ahmed et al¹² observed values as high as 80.5 % for sensitivity, 96.6% for specificity and 87.3 % for accuracy. Gaur et al¹³ have reported sensitivity, specificity and accuracy of Bronchial Washing samples as 39.4%, 89.6% and 71.4% respectively. Rao et al found sensitivity and specificity of 52.63% and 80% which is slightly less than our study.^[29]

Conclusion

Cytological analysis of bronchial washings is of some value as it may reveal an early diagnosis in about 2/3rd of the patients and a suspicious cytology may alert the pathologist to review histopathology. However, by itself, it may not be having enough sensitivity and simultaneously taken biopsy is additive to the diagnosis. Maximum diagnostic yield can be obtained by combining biopsy with cytological procedures of washing rather alone, although bronchial washing samples become more significant when

biopsy is contraindicated. Rapid onsite evaluation for sample adequacy and wider use of ancillary techniques like immunocytochemistry may help in increasing its diagnostic accuracy.

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