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Research Paper

Comparison Of Bronchoalveolar Lavage (BAL) With Bronchial Biopsy In The Diagnosis Of Lung Carcinoma: A Prospective Study

Medical Science

KEYWORDS : Bronchoalveolar lavage, bronchial biopsy, lung carcinoma

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ABSTRACT

Aims and Objectives: To perform a diagnostic study and compare broncho-alveolar lavage with bronchial biopsy (the current gold standard) in the diagnosis of lung cancer. Materials and Methods: 110 patients of clinically and radiologically suspected bronchogenic carcinoma attending the Kamla Nehru Chest Hospital, Jodhpur, between 1/1/2014 and 31/8/14 were recruited for the study (after taking an informed consent). All the patients underwent a BAL followed by bronchial biopsy using flexible bronchoscope. The specimens were processed as per standard procedures of cytology and histology at Department of Pathology, Dr S.N Medical College, Jodhpur. Observations: The age of the patients varied from 35 to 90 years, and the male: female ratio was 7.46:1. Bronchial biopsy showed malignancy in 50 patients (45.45%), was non-malignant (inflammatory, tuberculous or no significant pathology) in 51.81% patients and biopsy material was found to be inadequate in 2.72%. All samples of BAL were adequate (material yield of 100%). BAL had a sensitivity of 72%, specificity of 80.70%, PPV of 76.60%, NPV of 76.66% and accuracy of 76.6%. Conclusion: It is concluded that BAL is a valuable tool and yields almost same information as biopsy. It is useful in patients with evidence of obstruction or risk of haemorrhage. It can be used in combination with bronchial biopsy to increase the material yield.

Introduction-

Bronchoscopy allows examination of bronchial tree as far as pulmonary parenchyma, and has increased the variety of diagnostic specimen obtained (bronchial biopsy, bronchoalveolar lavage, bronchial brushing, and trans-bronchial needle aspiration). The advent of bronchoscopy has shifted the emphasis from diagnosis of advanced malignancy in operable patients to the use of cytology as a first line diagnostic and management tool. The utilities of cytology are extensive and they may even help in planning the treatment without the requirement for an open biopsy.

Among various bronchoscopic techniques, bronchial biopsy has the highest sensitivity for endobronchial malignant lesions[1] and is a good tool for the exact pathological typing. However bronchial biopsy cannot be performed at certain anatomical location (peripheral tumours) or in patients at risk of haemorrhage. Hence, alternative methods for obtaining a diagnosis are required.

In view of the importance of cytological methods in diagnosis of lung tumors and paucity of such studies from our state, the current study was planned with the objective of assessing the correlation of cytology of BAL in the diagnosing lung tumors, with histopathology of bronchial biopsy taking the latter as the confirmatory diagnostic test

The aim of this study is to correlate bronchoalveolar lavage cytology with biopsy in diagnosis lung cancer.

MATERIAL & METHODS

This prospective study was conducted at Dr. S.N Medical College, Jodhpur over a period from January 2014 to August 2014. Patients having clinical and radiological suspicion of lung cancer, attending OPD at KNCH were included in this study. Informed consent was taken from all patients. Patients having any contraindication for bronchoscopy and inadequate or autolysed samples were excluded. 110 patients underwent a BAL followed by bronchial biopsy using flexible bronchoscope. 3 biopsy specimens were found to be inadequate and were excluded from the study. Thus, the analysis was done based on specimens from 107 patients meeting all the inclusion and exclusion criteria.

The BAL material was obtained from the bronchial tree by instilling 30 to 50 milliliters of isotonic saline and re-aspirating it. All the samples were preserved in 50% ethyl alcohol. The specimens were centrifuged for five minutes at 1500 revolutions per minute. Three to four slides were prepared from cell concentrate and stained with Giemsa stain.

The biopsy specimens were fixed with 10% formal saline for one day & processed in automated tissue processor and sections were prepared and stained with haematoxylin & eosin stain.

Histopathology of bronchial biopsy was taken as diagnostic reference (Gold Standard). The test performance characteristics were calculated using the Predictive Value Model of Galen and Gambino.[2]

RESULTS

Out of total 110 patients undergoing bronchoscopy, 3 biopsy samples were inadequate and were excluded from the study. Therefore a total of 107 patients were included in the study. Majority cases (88%) were males with male female ratio of 7.23:1. The mean age of the patients was 62 years with a range of 30-90 years. Out of total 107 cases studied, lung cancer was confirmed in 50 cases by histopathology of bronchial biopsy and 47 were confirmed by cytology of BAL (Table 1). Mean age for lung cancer was 61 year and majority (90%) were males.

Table No.-1
RESULTS OF FIBREOPTIC BRONCHOSCOPY GUIDED PROCEDURES (n=107)

Procedure	Malignant	Not malignant
Forceps biopsy	50	57
BAL	47	60

Performance characteristics of BAL calculated using 2x2

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table and are as follows, sensitivity- 72%, specificity- 80%, PPV- 76.6%, NPV-76.66%, Efficacy- 76.63% (Table 2&3).

Table No. -2
COMPARISON OF BAL AND BIOPSY

		BIOPSY		
		Malignant	Not malignant	Total
BAL	Malignant	36 (TP)	11 (FP)	47
	Not malignant	14 (FN)	46 (TN)	60
	Total	50	57	107

Table No. -3

Performance Characteristic	Estimated Value	95% Confidence Interval	
		Lower limit	Upper Limit
Sensitivity	72.00%	0.37	0.57
Specificity	80.70%	0.68	0.90
PPV	76.60%	0.62	0.87
NPV	76.66%	0.64	0.86
Efficacy	76.63%	-	-

PERFORMANCE CHARACTERISTICS OF BAL

Squamous cell carcinoma was the commonest subtype (60%) followed by adenocarcinoma (18%), and Small cell carcinoma (16%). Comparison of morphological differentiation by Biopsy and BAL is shown in table 4. All except 3 cases were typed by biopsy as compared to BAL by which 28 were categorised as untypable.

Table no. – 4
MORPHOLOGICAL TYPING BASED ON BIOPSY AND BAL

Type	Biopsy	BAL
Squamous Carcinoma	60%	31.91%
Adenocarcinoma	18%	2.13%
Small Cell Carcinoma	16%	6.39%
Unclassified Carcinoma	6%	59.57%

Figure 1
SMALL CELL CARCINOMA AS SEEN IN BAL SMEARS

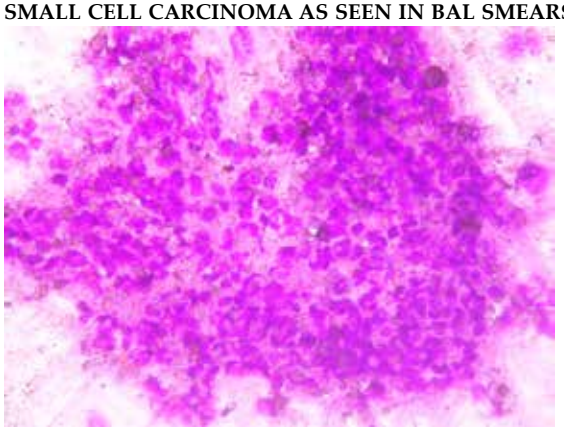


Figure 2
SQUAMOUS CELL CARCINOMA AS SEEN IN BAL SMEARS

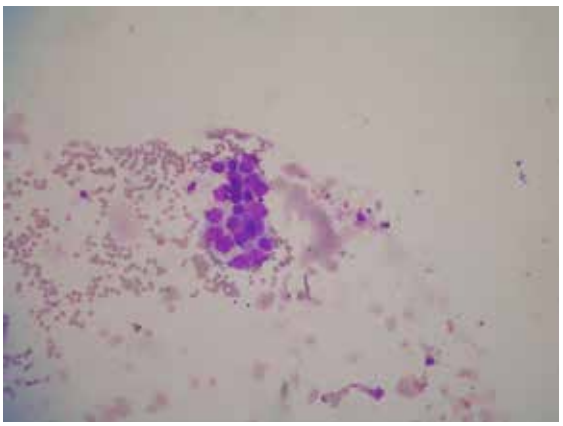


Figure 3
ADENOCARCINOMA AS SEEN IN BAL SMEARS

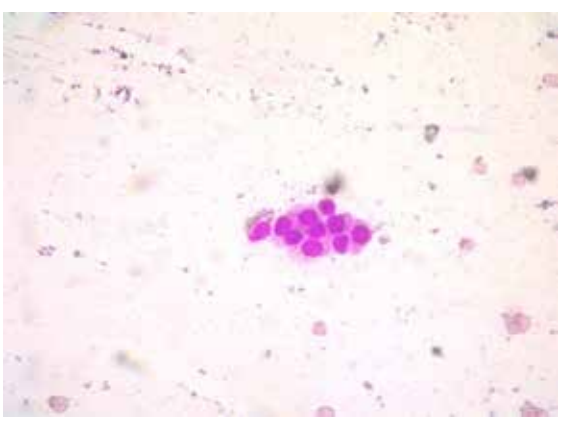
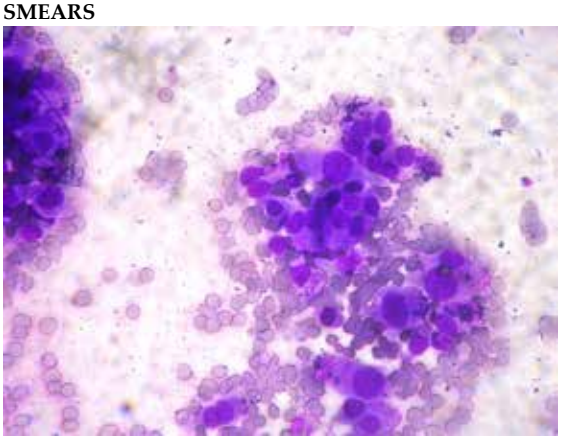


Figure 4
UNCLASSIFIED CARCINOMA AS SEEN IN BAL SMEARS



DISCUSSION-

Lung tumours are the most common cause of death due to cancer in males and are now emerging as an important cause of neoplastic mortality in females.[3] Timely detection of the disease plays a pivotal role in the management & for the long term survival of the patients.

With the advent of Flexible Fibre-Optic Bronchoscope, the diagnosis of lung carcinoma took a new turn as samples like Bronchial Brushings, Broncho-Alveolar Lavage, Trans-Bronchial Needle Aspirations and Bronchial Biopsy could

be collected from the respiratory tract, yielding significant amount of diagnostic material.[4] With this, the emphasis shifted from diagnosis of malignancy in advanced stages and the confirmation of metastases, to the use of Fibre-Optic Bronchoscopy as a first line diagnostic procedure on which crucial management decisions could be based.[5,6]

The present study was conducted with the objectives of assessing the sensitivity and specificity of BAL cytology by comparing with the histopathology of bronchial biopsy obtained from lung tumors.

In our study the sensitivity and specificity of BAL were found to be 72% and 82 % respectively (Table No-13). Truong et al [7] reported Sensitivity of 66.0%; while Ng. & Horak [8] reported Sensitivity as high as 74.0% for BAL. Gaur et al [9] in 2007 found the sensitivity and specificity of BAL to be 39.4% and 89.6% respectively. Similarly Monisha Choudhury et al [10] in 2012 reported a sensitivity of 47.6% and specificity of 80.9% for BAL.

In our study 14 false negative cases were reported which is higher than the previous study[11].The reasons for false negative results could be superadded inflammation, non-representative material or hypocellular aspirates. Material yield of BAL depends on several vital factors –

1. Degree of differentiation of malignant growth.
2. Preservation of morphology of exfoliated cells.
3. Technique of pulmonologist

In general less differentiated tumors shed more cells as compared to more differentiated tumors leading to less cellular samples in better differentiated tumors. Similarly if the technique of pulmonologist in not proper, sample retrieved will be less. All these factors individually or in combination affect the material yield of the samples.

In our study 14 false positive cases were noted. False positivity may be due to misinterpretation by the cytopathologist due to chronic inflammatory process, epithelioid cells of tuberculosis, atypical histiocytes or squamous metaplasia. These false positive cytological results may have serious consequences for the patients in which biopsy is not possible due to risk of haemorrhage or evidence of obstruction. Therefore it is better to under report with cautious comments in suspicious/atypical cells. But this trend should not predominate at the cost of sensitivity of the cytological procedure.

It is possible that some of these false positives in the present study might be true positives as methods other than bronchial biopsy to confirm the diagnosis of lung cancer were not used in the present study. Majority of the previous studies [12, 1, 14, 15, 16] that have used other techniques such as rebronchoscopy, surgery, transthoracic needle aspiration (TTNA), tumor markers and autopsy, to prove the cases of lung cancer have shown that bronchial biopsy does not provide diagnostic yield in all cases of lung cancer. Chances of missing the diagnosis by bronchial biopsy are more in peripheral lung tumors.

One of the limitations of our study is use of only bronchial biopsy for the validation of cytological techniques and the absence of other confirmatory tests like surgical biopsy, transbronchial needle aspiration, TTNA, mediastinoscopy, biopsies of extrapulmonary lesions and autopsy. Other limitations was the inability to further typing of large cells carcinomas and sub-typing of poorly differentiated non-small cell carcinomas in the absence of tumor markers.

As shown in table 4 majority of cases were untypable on BAL cytology (60%) as compared to biopsy (6%). The reason behind this difference in percentage could be , Since cytology of BAL relies mainly on the exfoliated cells from the malignant lesion and while these exfoliated cells lying in the cavity, they start developing degenerative changes progressively losing their morphological details.

CONCLUSION:

Performance characteristics of BAL cytology suggest that it aids in the diagnosis of lung cancer with reasonable accuracy. Therefore BAL cytology may be used concurrently along with bronchial biopsy to diagnose the lung tumors.

BAL cytology may be extremely useful in -

1. Patients with obstruction
2. Patients at risk of haemorrhage
3. Tumors at peripheral location.

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