Original Article

Diagnostic role of bronchoalveolar lavage: A cytohistopathological correlation

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ABSTRACT

Keywords:

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Background: Tumors of lung are common in Nepal. The risk of malignancy has to be judged prior to surgery for which bronchoscopy is often done. Brocho-alveolar lavage and bronchial biopsy are routine procedure done for diagnosis of lung cancer during bronchoscopy. This study was done to correlate the cytology of broncho-alveolar lavage specimen with histopathology in malignant tumors of the lug in our setup.

Materials and methods: This study was conducted at department of pathology, Nobel Medical College from August 2017 to December 2018. Histopathology reports with malignancy were compared to their cytological diagnosis.

Results: A total of 141 cases were included in the study. Among the study population, Bronchogenic carcinoma was found more prevalent in female. The sensitivity, specificity, positive predictive value, negative predictive value and overall accuracy of broncho-alveolar lavage in the diagnosis of lung cancer were 88.1%, 97.98%, 94.7%, 95.1% and 95.03% respectively.

Conclusions: Brochoalveolar lavage cytology has a greater accuracy for the diagnosis of lung cancer; however, benign cases need regular follow up as there are false negative cases.

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INTRODUCTION

Diseases of the lung are very common in Nepal. Common ones include pneumonia, tuberculosis, chronic obstructive pulmonary disease (COPD), and neoplastic conditions which includes benign and malignant tumors. Malignant lung lesions have incidence rate of 4.45% in male in Nepal among all the malignant condition.[1] Common malignant tumor of lung includes squamous cell carcinoma, adenocarcinoma, small cell carcinoma and neuroendocrine carcinoma.[2]

Bronchoscopy is a minimally invasive, cost-effective, OPD

based, procedure which allows examination of bronchial tree as far as distal lung parenchyma. Moreover, it has increased the variety of specimens that can be obtained during the procedure and includes, broncho-alveolar lavage (BAL), bronchial brush, bronchial biopsy and trans-bronchial needle aspiration. Broncho-alveolar lavage is still being used as the first line of diagnostic tool for the evaluation of malignant lung lesions. Further, it has many cytological utilities and can even guide in treatment planning without having bronchial biopsy.[3] Bronchial biopsy is still considered as the most sensitive diagnostic tool and moreover, it has highest accuracy in determining the definite histological type.[4,5] Hence, BAL has emerged as important alternative tool in obtaining a diagnosis.

In view of important role of BAL and mere paucity of such study in our state, this study was planned with the primary objective of correlating the BAL cytology with bronchial biopsy, taking later as the gold standard diagnostic test for malignant lung tumor.

MATERIALS AND METHODS

This was a prospective cross sectional study conducted from August 2017 to December 2018 at Nobel Medical College and Teaching Hospital (NMCTH). Ethical clearance was taken from institutional review committee. All patients having clinical and radiological suspicion of malignancy were included in this study. Informed consent was taken in all cases. Cases having contraindication for bronchial biopsy and in cases with inadequate samples were excluded from the study.

The obtained BAL specimen was fixed in ethyl alcohol and later centrifuged at 1500 revolutions per minute. Three smears made from cell concentrate and were stained with May-Grünwald-Giemsa (MGG) and Papanicolaou (Pap) stains as per the standard guidelines. Smears having few cells or cell details, obscured by blood, and degenerative changes and artifacts were excluded from this study. Smears having inadequate number of macrophages (<10 alveolar macrophages/10 high power fields) were also not included in this study. Smears were examined by three pathologists and were categorized in to benign, suspicious for malignancy, and malignant. All inflammatory conditions and smears having benign cytological features were considered in benign category. Smears having some dysplasia not enough to consider it malignant were considered suspicious for malignancy. Smears having obvious cytological features of malignancy were considered malignant lesion. An attempt to categorize the type of malignancy was done in every case.

All bronchial biopsy specimens were fixed in 10% formalin and processed on automated tissue processor. Paraffin embedded sections were stained by hematoxylin and eosin stain. Lesions were classified into benign and malignant based upon the histological findings. Further, histological typing of tumor was also done.

All data were inserted in SPSS 17 software. Histopathological report was considered as the gold standard. For statistical analysis, suspicious of malignancy and malignant categories were considered cytologically malignant. Cytological report was correlated with histopathological diagnosis. Diagnostic accuracy of BAL was obtained by following formulas:

Sensitivity= TP/TP+FN x100   TP= True positive

Specificity=TN/TN+FP x100   TN= True negative

Positive predictive value (PPV) =TP/TP+FP x100
          FP= False positive

Negative predictive value (NPV) =TN/TN+FN x100
          FN= False negative

Accuracy= TP+TP/Total number of cases x100

RESULTS

A total of 141 cases were included in the study. Among them 88 (62.4%) were male and 53 (37.6%) with a male to female ratio of 1.6:1. Age of the patients ranged from 52 to 94 years and median age of 67 years.

Cytological diagnosis and histopathological diagnosis is shown in table 1. In BAL cytology; Benign lesions were 102 (72.3%) followed by 36 (25.5%) malignant lesions. Histopathological diagnosis was benign 99 (70.2%) and 42 (29.7%) were malignant lesions. (Table 1) Among 42 malignant cases diagnosed in biopsy specimen; squamous cell carcinoma was the most common malignancy (n=20;

Table 1: Comparison of Cytological diagnosis with final histopathology (n=141)

Cytological Diagnosis	Number	Histopathological Diagnosis	Number	Remarks
Benign	102	Benign	97	TN
		Malignant	05	FN
Suspicious of Malignancy	03	Benign	01	FP
		Malignant	02	TP
Malignant	36	Benign	01	FP
		Malignant	35	TP

Table 2: Distribution of histopathological diagnosis of malignant tumor

Histopathological Diagnosis	Number (%)
Squamous cell carcinoma	20 (47.6%)
Adenocarcinoma	18 (42.8%)
Small cell carcinoma	02 (4.7%)
Large cell carcinoma	01 (2.4%)
Other	01(2.4%)
Total	42 (100%)

47.6%) followed by adenocarcinoma (n=18; 42.8%). (Table 2)

The BAL cytology correctly identifies 97 (95.1%) of benign, 01(33.33%) of suspicious for malignancy and 35 (94.8%) of malignant cases. The sensitivity, specificity, positive predictive value, negative predictive value and overall accuracy of BAL were 88.1%, 97.98%, 94.7%, 95.1% and 95.03% respectively. Five cases (4.9%) were considered falsely as benign lesions. Similarly, 2 benign cases were over-diagnosed as suspicious of malignancy and malignant lesion.

DISCUSSION

Early diagnosis and treatment of lung cancer has been always critical. Broncho-alveolar cytology is an easy minimally invasive procedure and has been well tolerated by patients. Various combination assays are available to improve the diagnostic precision of the BAL cytology, but this does mean that the BAL alone is invaluable. Broncho-alveolar lavage has always been an important procedure for clinicians who manage patients in whom lung cancer is suspected. This study was conducted to determine the accuracy of BAL cytology using histopathological diagnosis as gold standard in the diagnosis of lung carcinoma at our centre.

Squamous cell carcinoma was the most common malignant tumor in our study. Similar finding was also observed by Ahmed A et al.[4] In contrast, Binesh F et al found adenocarcinoma as the most common malignant tumor.[6]

Our study had a sensitivity of 88.1% which is similar to the study done by Ahmed et al.[4] In contrast, sensitivity was only 69.1% and 48.6% in a study done by Pradeep et al[7] and Tang et al.[8] These discrepancies may be explained by sampling error or the presence of benign process that mimics malignancy.

False positivity in benign conditions and false negativity in the early stage of malignant conditions are the primary limitations of BAL examination. These drawbacks could be due to poor distribution of BAL specimens, infrequent exfoliation of malignant cells and interpretive errors. Cytological sampling by BAL relies mainly on cells

exfoliated from tumors. It is well known that some lung tumors, for unknown reasons, do not exfoliate diagnostic cells regardless of number of specimens collected.

In this study 1.4% false positivity rate was encountered. Common factors responsible for false positive results include misinterpretation of the cytological findings due to reactive cellular changes in inflammatory diseases, squamous metaplasia and epithelial cell atypia in the background of fibrosis. Two out of 3 suspicious for malignancy cases turned to be malignant in biopsy report. False positivity was also negligible in studies done by Ahmed et al[4] and Pradeep et al.[7] Similarly, no false positivity was found by Lachman et al[9] and Rennard et al.[10] These results suggest that false positivity is rare and is thus a great advantage of BAL cytology.

False negativity was 3.5% in this study which is in contrast to 6.5% found by Ahmed et al.[4] Wongsurakiat et al[11] had a significant false negative result. The main factors contributing to false negative cases can be confounding inflammation, non representative specimen or hypocellular lavage.

A positive predictive value of 94.7% and negative predictive value of 95.1% was comparable to Ahmed et al and Binesh F et al.[4,6]

Statistical analysis in our study revealed a sensitivity, specificity, positive predictive value, negative predictive value and accuracy of 88.1%, 97.98%, 94.7%, 95.1% and 95.03% respectively. These results were comparable to the others where the BAL has reported sensitivity ranging from 60% to 99%, specificity 80% to 100%, positive predictive value 85% to 97%, negative predictive value 88% to 99% and accuracy 89% to 99%.[4,6,12] These varied results may be due to number of cases, subjective errors and sampling errors. The overall accuracy of 95.03% in our study certainly confirms the diagnostic role of BAL in the diagnosis of lung cancer.

CONCLUSION

Bronchioalveolar lavage has a greater accuracy and therefore we recommend routine use of BAL for the diagnosis of lung cancer.However, non-malignant cytological interpretation should be viewed with caution as there are false negative cases and thus these cases should undergo regular clinico-radiological follow up to look for any progression that will require repeat bronchoscopy.

Conflict of interest: None

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