Original Research Article

Diagnostic accuracy of Lung Biopsy and Bronchoalveolar Lavage (BAL) in Lung Malignancy

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Abstract

Objective: The study was designed to correlate histopathology of lung biopsy and bronchoalveolar lavage (BAL) cytology in the diagnosis of lung malignancy and to determine the sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and diagnostic accuracy of bronchoalveolar lavage cytology using histopathology of lung biopsy as gold standard. **Study Design:** The retrospective and prospective study was conducted at Pathology Department of Tertiary care centre from October 2017 to October 2019, to investigate a total of 54 patients who were clinically/radiologically suspected of lung malignancy and who underwent both bronchial biopsy and bronchoalveolar lavage. **Results:** On histopathological examination of biopsies, 29 cases (53.7%) were malignant whereas on cytological examination of BAL 19 cases (35.18%) were correctly diagnosed as malignant and 4 cases (7.4%) as suspicious/atypical. The sensitivity, specificity, PPV, NPV and overall diagnostic accuracy of BAL was 79.3%, 100%, 100%, 86.2% and 88.9% respectively. **Conclusion:** It was observed that BAL cytology is sensitive and specific for the diagnosis of lung cancer. Cytopathological examination complements histopathology in both diagnosing and typing of lung tumours.

Keywords: Bronchoalveolar lavage (BAL), Cytology, Biopsy, Histopathology, Lung malignancy, Diagnostic accuracy.

Introduction

Lung cancer is currently the most frequently diagnosed major cancer in the world and the most common cause of cancer mortality worldwide [1].To combat the disease successfully, lung cancer should be diagnosed at earliest possible stage preferably before the lesion has reached the stage of a visible and palpable tumour. For earliest diagnosis different modalities are available which include radiology, bronchial biopsy and exfoliative cytology [1].

The sampling techniques performed at flexible bronchoscopy examination for histopathological diagnosis of lung cancer include endobronchial forceps biopsy (EBB) and transbronchial forceps biopsy (TBB) for more peripheral tumours [2]. Bronchial washing (BW), bronchoalveolar lavage (BAL) and brushing specimens can also be obtained for cytopathological examination [3-6]. The diagnostic sensitivity of bronchial biopsy in diagnosing lung malignancies ranges from 65-83% [7,8]. The sensitivity of BAL varies between 14-76% in various studies reported [3,9]. BAL can provide diagnostic information in cases of primary and metastatic lung cancer [10,11]. Though histopathological diagnosis of bronchial tissue biopsy is considered the gold standard for diagnosis of lung tumors, it has certain drawbacks. It is an invasive procedure and more expertise is required. The yield is higher in patients with endoscopically-visibletumours than in those with tumours not visible endoscopically [12]. Diagnostic ratio of bronchoscopies is lower for peripheral lesions. It is, however, in the context of more peripheral lesions that cannot be visualised that cytology has historically played a more crucial role, with bronchial brushing and washing/BAL samples being obtained from the relevant lobar segments [3,9].

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Material and Methods

The present study was conducted at Pathology Department of Tertiary care centre. The test population comprised of all the lung biopsies and bronchoalveolar lavage (BAL) fluid that were submitted between October 2017 to October 2019. The material for the study consisted of all the biopsies and bronchoalveolar lavage (BAL) fluid submitted for histopathological and cytological study from total of 54 patients clinically or radiologically suspected of lung malignancies. Only the cases in which BAL and bronchial biopsy were received simultaneously were included.For the retrospective study all the cytology slides of BAL and histopathologic slides of bronchial biopsy were taken from the departmental records and slides were reviewed in detail. In the prospective study all BAL fluid and bronchial biopsies received in the department for the specified period of time were followed.The bronchial biopsies were examined and fixed in 10% buffered formalin. The tissues were processed in the histokinette with a cycle of 16 hours, after which the processed tissues were embedded into paraffin wax blocks. Sections of 4-5 micron thickness were cut using the rotary microtome and stained by the routine H&E stain. During the HPE reporting, most of the cases were diagnosed by light microscopy. Only in certain cases where there was a diagnostic dilemma, Immunohistochemistry (IHC) markers were applied. BAL fluid was taken in clean glass test tubes

and centrifuged for 10 minutes at 3000 revolutions per minute. After discarding the supernatant fluid, three slides were prepared from the sediment. Two of the slides were fixed in methanol (wet fix) and one air dried. Two of the wet fixed slides were stained with H&E stain and PAP stain. The air dried slide was stained with Giemsa stain.

Statement of Ethics

The study protocol was approved by the institutional ethics committee on human research.

Results

Total 54 cases were included in the study. The results of the study were as follow:

Out of 54 cases, 19 cases (35.18%) were correctly diagnosed by BAL as malignant, 4 cases (7.4%) as suspicious/atypical which later on histopathology proved to be malignant and were included in true positive category. Number of negative cases diagnosed on BAL was 31 out of which 25 were true negative and 6 were false negative. The reason for false negative cases in our study was due to non representative material. On histopathological examination of biopsy 29 cases (53.7%) were malignant whereas 25 cases (46.29%) showed no evidence of malignancy.Out of total 54 cases in this study, 35(64.81%) were Male and 19(35.18%) were female patients and the age of the study subjects was ranging from 31 to 80 years. Most of the cases were in the age group of 61 to 70 years (19 cases, 35.18%), followed by 41 to 50 years (12 cases, 22.22%) and 51 to 60 years (10 cases, 18.51 %).

According to the histopathological diagnosis, the most common malignant lesion in this study was Adenocarcinoma (11 cases, 37.93%), followed by Small cell carcinoma (7 cases, 24.13%), followed by Squamous cell carcinoma (6 cases, 20.68%) and Non small cell carcinoma (05 cases, 17.24%). Among these, 2 cases of Adenocarcinoma and 1 case of Squamous cell carcinoma required immunohistochemical confirmation. Final diagnosis of Non small cell carcinoma was given in 5 cases, because further categorization by immunohistochemistry was not possible due to scanty biopsy material.

The malignant lesions were studied according to their distribution related to the age and sex of the patient. Among 29 cases of malignancy, maximum cases were found in 61 to 70 years of age group (11 cases, 37.93%), followed by 41 to 50 years of age group (7 cases, 24.13%). Males (18 cases, 62.06%) showed more predilections for malignant lesion than females (11 cases, 37.93%). In males, there were 5 cases of adenocarcinoma (27.8%), 5 cases of squamous cell carcinoma (27.8%) and 6 cases of small cell carcinoma (33.33%). In females, adenocarcinoma was seen in 6 cases (54.54%) among the other carcinoma detected.

In our study 5 cases (21.73%) were categorized by BAL as Adenocarcinoma, 3 cases (13.04%) as Squamous cell carcinoma, 4 cases (17.39%) as Small cell carcinoma, 5 cases (21.73%) as Non small cell carcinoma, 2 cases (8.69%) as Malignant and 4 cases (17.39%) as Atypical/Suspicious.

Discussion

Early diagnosis and treatment of lung cancer has been always critical. Bronchoalveolar lavage cytology is an easy minimally invasive procedure and has been well tolerated by patients [13].

Different diagnostic modalities are available for diagnosis of bronchogenic carcinoma in early stage. It has been suggested that a combination of various techniques may give the best results [14]. A lot of variation in results is observed from center to center, as most of these techniques depend on the expertise of the specialist [15].

This study was conducted to determine the sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy of BAL cytology using histopathological diagnosis as gold standard in the diagnosis of lung malignancy at our centre.

In the present study, total 54 cases of BAL and lung biopsy were included, received in Department of Pathology from October 2017 to October 2019.

The commonest malignant tumor in our study was Adenocarcinoma. Similar finding was also observed by Binesh F et al [16]. In contrast, squamous cell carcinoma was the most common malignant tumor in studies by Krishnaveni G et al [17], Ahmed A et al [18] and Bhat N et al [1].In the present study, it was observed that Adenocarcinoma appears in cytological material as single cells and cell groups consist of three dimentional clusters or glandular configuration. The nuclei tend to have vesicular chromatin with prominent nucleoli and the cytoplasm is homogenous to vacuolated [19].Cytological diagnosis of Squamous cell carcinoma was based on the identification of malignant squamous epithelial cells with nuclear enlargement, dense hyperchromasia, angularity and dense refractile cytoplasm in background of extensive necrosis. Cells were present both singly and in cluster [19].Small cell carcinoma was diagnosed cytologically by grouping of small dissociating tumour cells with scant cytoplasm, irregular moulded nuclei, coarsely stippled chromatin and inconspicuous nucleoli. Nuclear moulding and apoptotic bodies in cytological smears were taken as a clue for small cell carcinoma [19]. Similar cytological findings of Adenocarcinoma, Squamous cell carcinoma and Small cell carcinoma were observed by Krishnaveni G et al [17].In the present study, sensitivity of BAL was 79.3% and specificity was 100%. Ahmed A et al [18] found the sensitivity of 93.4% and specificity of 100%.

Linder et al [9] found the sensitivity of BAL for the diagnosis of lung carcinoma to be similar to that of transbronchial biopsy.

In a study by Fend et al [20] BAL alone showed a sensitivity of 73.9%.

BAL provided a higher diagnostic yield (46.7%) than transbronchial biopsy (16.7%) in a study by Wongsurkait et al [21].

In a study by Tang et al [22] BAL alone revealed positive malignant cells in 18 of 37 cases (sensitivity 48.6%) and the diagnostic value significantly increased to 73.0% with BAL+TBLB.

In study by Rennard [3] BAL revealed cells diagnostic of malignancy in 68.6% of 35 patients with biopsy proven lung cancer.

The limitations of BAL cytology are the possibility of false positivity and false negativity. The present study had no false positives however false positive result can be reported due to misinterpretation of smears by cytologist due to cellular changes in chronic inflammatory disorders, squamous metaplasia and epithelial cell atypia in the background of fibrosis.False positives have very unfortunate consequences for the individual patients, therefore some advise “under reporting” instead of “over reporting” in suspicious cases [1].There were no false positives in study of Rennard [3] and Ahmed A et al [18]. Similarly Linder et al [9] found no false positive diagnosis in 386 patients.In a study by Lachman et al [4], there were no false positive cytological diagnosis. The majority (94%) of patients with a suspicious cytologic report had a final diagnosis of malignancy.False negativity in current study was 20.7%. The reason for false negative cases in our study was due to non-representative material.

The study by Fariba B et al [16] had false negativity of 33.8%. The study by Ahmed A et al [18] revealed false negativity of 6.55%.

The reasons for false negative results can be due to confounding inflammation, non representative specimen, infrequent exfoliation of malignant cells and interpretive errors. The positive predictive value of BAL in present study was 100% and negative predictive value was 86.2%.

The study by Ahmed A et al [18] showed positive predictive value of 100% and negative predictive value of 75%.

The diagnostic accuracy of BAL in present study was 88.9%, which is comparable to studies done by Fariba B et al [16] (70.5%), Prabesh et al [13] (95.03%) and Ahmed A et al [18] (94.5%).Statistical analysis in our study revealed a sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy of 79.3%, 100%, 100%, 86.2% and 88.9% respectively.

The overall results in our study certainly confirms the significant diagnostic role of BAL in the diagnosis of lung cancer.

Table 1: Correlation of BAL with biopsy

Diagnosis	BAL		Biopsy	
	Frequency	Percentage	Frequency	Percentage
Adenocarcinoma	05	21.73%	11	37.93%
Squamous cell carcinoma	03	13.04%	06	20.68%
Non small cell carcinoma	05	21.73%	05	17.24%
Small cell carcinoma	04	17.39%	07	24.13%
Malignant cells	02	8.69%	00	00%
Atypical/Suspicious	04	17.39%	00	00%
Total	23	100%	29	100%

Table 2: Comparison of BAL cytology with histopathology of biopsy

		Histopathology of lung biopsy		
		Malignancy	No malignancy	Total
BAL cytology	Malignancy	23(a)	00(b)	23(a+b)
	No malignancy	06(c)	25(d)	31(c+d)
	Total	29(a+c)	25(b+d)	54

Table 3: Test performance characteristics of BAL cytology as compared with histopathology of biopsy

Characteristics	Calculation based upon 2x2 table	Score
Sensitivity	a/a+c x 100	79.3%
Specificity	d/b+d x 100	100%
False positive	b/b+d x 100	00%
False negative	c/a+c x 100	20.7%
Positive predictive value	a/a+b x 100	100%
Negative predictive value	d/c+d x 100	86.2%
Diagnostic accuracy	a+d/a+b+c+d x 100	88.9%

Table 4: Comparative statistical values on cyto-histological correlation

Author	No. of cases	Sensitivity (%)	Specificity (%)	Diagnostic accuracy (%)
Bhat N et al [1]	902	35.5%	78.16%	-
Prabesh et al [13]	141	88.1%	97.98%	95.0%
Binesh F et al [16]	388	46.9%	91.6%	70.5%
Wongsurakiat P et al [21]	55	46.7%	-	-
Tuladhar A et al [23]	55	66.7%	-	-
Present study	54	79.3%	100%	88.9%

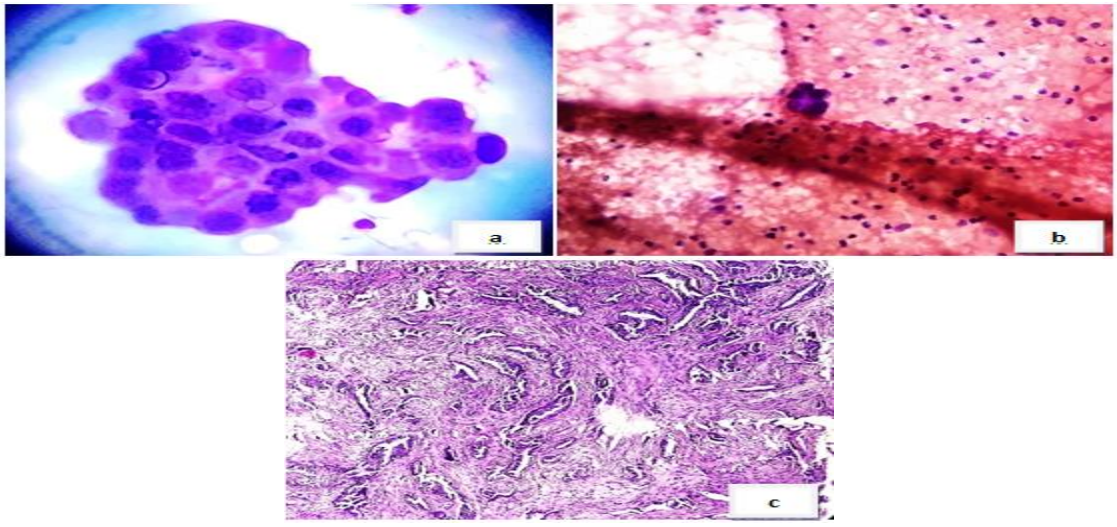

Fig.1.a: BAL smear shows malignant cells in three dimentional cluster - Adenocarcinoma (Giemsa stain, 40x)
Fig.1.b: BAL smear shows malignant cells in acinar configuration - Adenocarcinoma (H & E stain, 40x)
Fig.1.c: Corresponding Histopathological findings - Adenocarcinoma (Acinar pattern) (H & E stain, 10x)

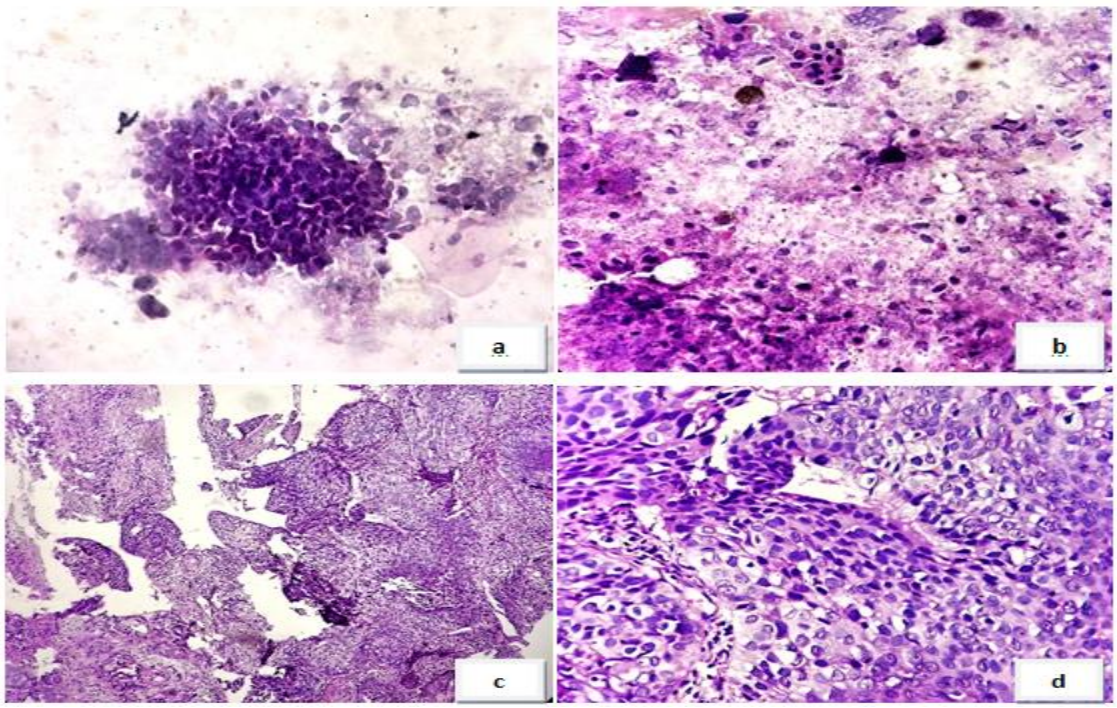

Fig.2.a: BAL smear shows cluster of malignant squamous epithelial cells - Squamous cell carcinoma (H & E stain , 40x)
Fig.2.b: BAL smear shows malignant squamous Epithelial cells in small cluster and scattered singly in background of necrosis - Squamous cell carcinoma (H & E stain , 40x)
Fig.2.c, Fig.2.d: Corresponding Histopathological section - Squamous cell carcinoma (Fig.2.a -H & E stain , 10x ; Fig.2.d -H & E stain , 40x)

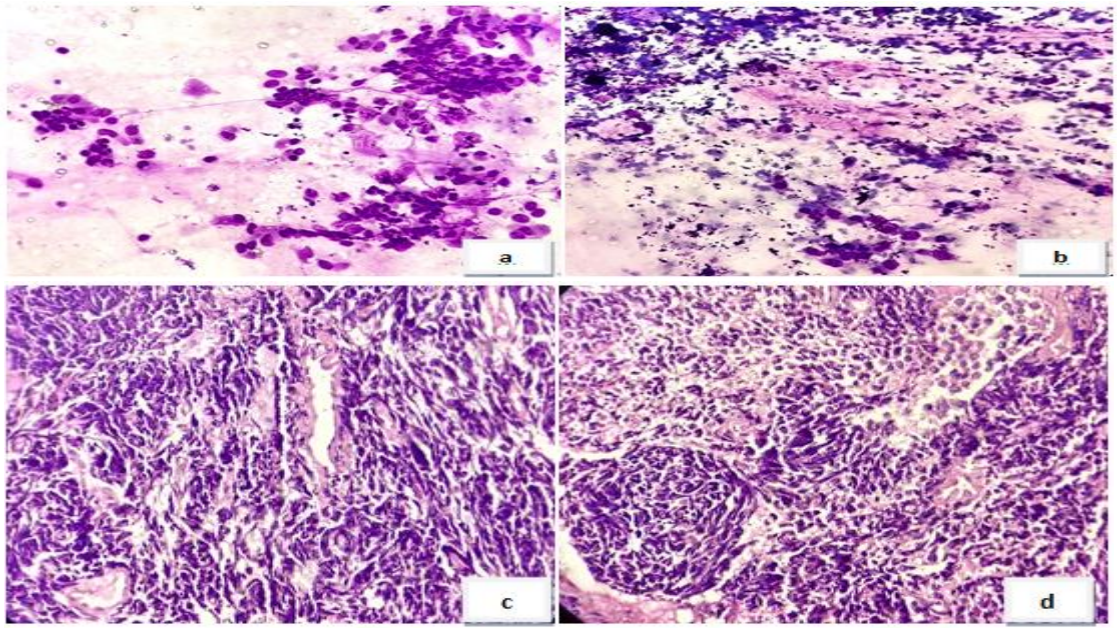

Fig.3.a: BAL smear shows malignant cells in sheets and dispersed singly having round to oval nuclei, mild cytoplasm, and nuclear moulding - Small cell carcinoma(Giemsa stain , 40x)
Fig.3.b: BAL smear shows dispersed malignant cells and dense apoptotic debris - Small cell carcinoma (Giemsastain , 40x)
Fig.3.c, Fig.3.d: Corresponding Histopathological section shows Small cell carcinoma with crush artifacts (H & E stain , 40x)

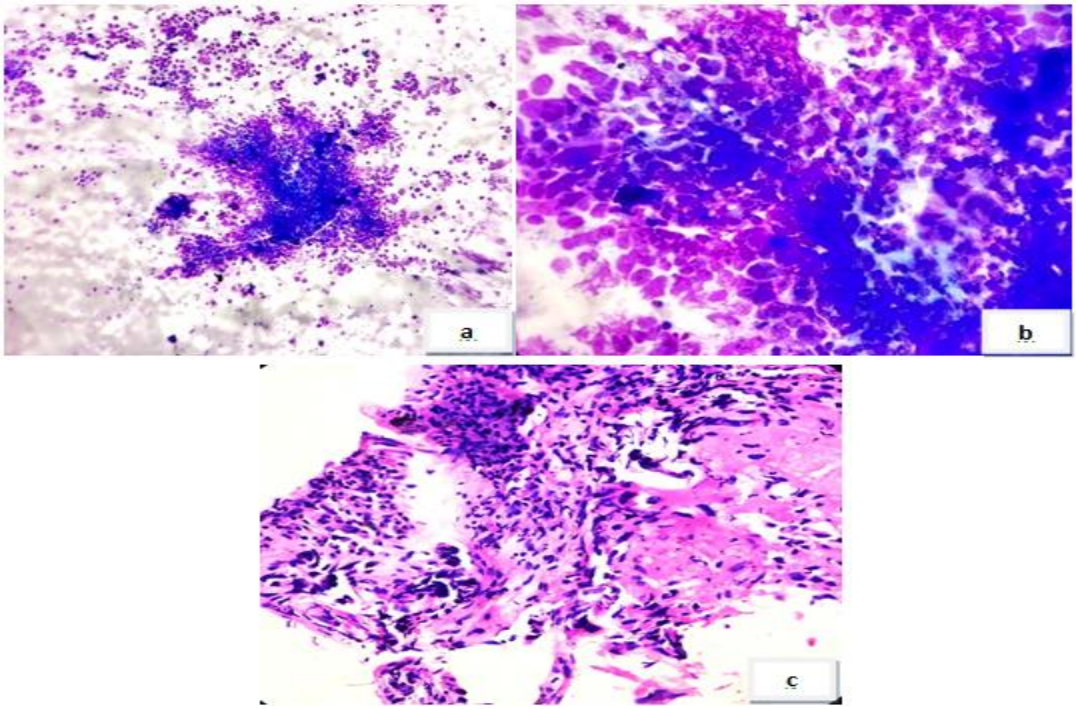

Fig.4.a, Fig.4.b: BAL smears show cluster of pleomorphic malignant cells - Non small cell carcinoma (Giemsa stain, Fig.4.a - 10x, Fig.4.b - 40x)

Fig.4.c: Corresponding Histopathological section - Non small cell carcinoma (H & E stain, 40x)

Conclusion

The sensitivity, specificity and diagnostic accuracy of BAL in present study was 79.3%, 100% and 88.9%.It was observed that BAL cytology is a sensitive and specific for the diagnosis of lung cancer.BAL is particularly useful in patients with evidence of obstruction or risk of haemorrhage and peripheral pulmonary lesion which is inaccessible to TBLB.Regarding individual typing of malignant lesions, biopsy is more effective than BAL cytology.

It is quite safe, economical and experienced cytopathologist is necessary for interpretation of smears.The combination of BAL cytology and lung biopsy can be considered as the best procedure for the diagnosis of lung cancer during bronchoscopy.

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